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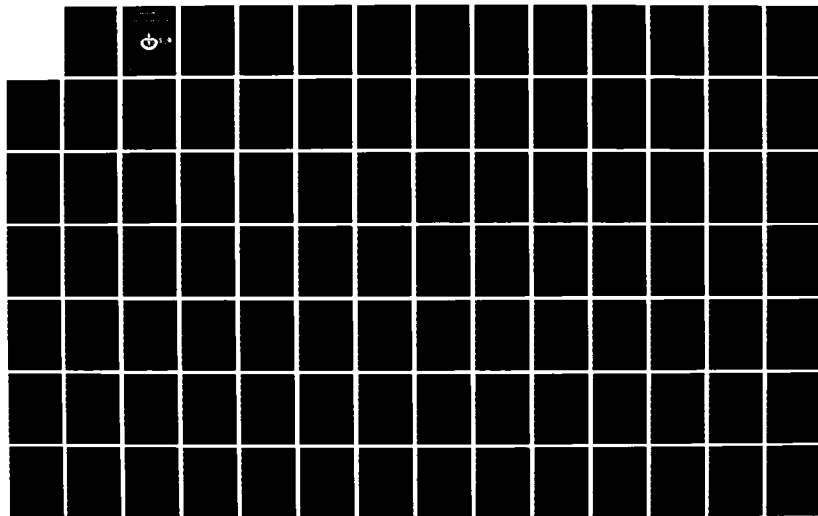
DEPARTMENT OF CLINICAL INVESTIGATION ANNUAL RESEARCH
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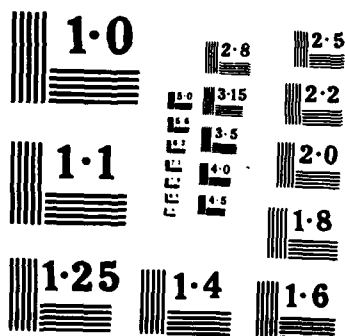
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30 September 1985

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MADIGAN ARMY MEDICAL CENTER

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19. KEY WORDS (Continue on reverse side if necessary and identify by block number) Unit summary; research protocols (objective, technical approach, progress); publications; presentations.		
20. ABSTRACT (Continue on reverse side if necessary and identify by block number) Subject report identifies those individuals who are conducting investigative protocols at Madigan Army Medical Center. An abstract of each protocol giving abbreviated technical objectives, approach, and progress is presented.		

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ANNUAL RESEARCH PROGRESS REPORT

FISCAL YEAR 1985

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

In conducting the research described in this report, the investigators adhered to the "Guide for Laboratory Animal Facilities and Care" as promulgated by the Committee on the Guide for Laboratory Animal Resources, National Academy of Sciences National Research Council, and the Guiding Principles in the Care and Use of Animals (Appendix I) approved by the Council of the American Physiological Society. The investigators follow the recommendations from the Declaration of Helsinki (Appendix II) in the performance of investigations involving human subjects.

ACKNOWLEDGEMENTS

I would like to take this opportunity to thank Nancy Whitten for the effort which is obvious in the compilation of this publication which is ever increasing in size and Genie Hough for clerical assistance.

FORWARD

During the past year, Madigan Army Medical Center personnel have demonstrated their excellence in research and investigation more than ever. They have doubled the number of publications over any previous year as well as receiving numerous honors for outstanding presentations at major medical meetings. Thus, it appears that Madigan is continuing to accomplish all of its missions with high quality. These accomplishments are, of course, due only to the hard work and the excellent quality of our medical staff and support services. The coming year looks even brighter with new goals of excellence having been established in all departments and continuing high quality staff.

The Department of Clinical Investigation would like to express our appreciation for the support derived from the hospital and its staff during the past fiscal year.

Sincerely,

A handwritten signature in dark ink, appearing to read 'Stephen R. Plymate', with a long horizontal flourish extending to the right.

STEPHEN R. PLYMATE, M.D.
Colonel, Medical Corps
Chief, Department of Clinical Investigation

fr. p. 2

The objective of this report

UNIT SUMMARY FY 85

1. Objective

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

→ to p. 4

2. Technical Approach

MANPOWER

<u>DESCRIPTION</u>	<u>RANK</u>	<u>MOS</u>
Chief PLYMATE, Stephen R., M.D., COL, MC	O6	61C9A
C, Surg & Animal Care Svc YARBROUGH, Leslie, D.V.M., MAJ, VC	O4	64C9B
C, Microbiology Svc HIGBEE, James W., Ph.D., MAJ, MSC	O5	68A9B
C, Biochemistry Svc HANNAN, Charles J., Ph.D., MAJ, MSC	O4	68C9C
C, Physiology Svc FRIEDL, Karl E., Ph.D, CPT, MSC	O3	68J9B
NCOIC SFC HAYES, James E.	E6	91T3R
Med Lab Spec SP 4 COMACHO, George	E4	92B10
OR Tech SP5 ROBBINS, John L. (Aug/Sep 85)	E5	91D2R
OR Tech SP5 WORRELL, Carleen (Oct 84/Mar 85)	E5	91D2R
Vet Animal Spec SP5 HUNTER, Robert (Oct/Dec 85)	E5	91T2R
Vet Animal Spec SP4 WESTMORELAND, Jacalyn (Jul/Sep 85)	E4	91T10
Vet Animal Spec SCHUTELLA, John R. (Sep/Oct 85)	E4	91T10
Med Tech GARRISON, Mina J.	GS9	0644

<u>DESCRIPTION</u>	<u>RANK</u>	<u>MOS</u>
Med Tech KETTLER, Thomas M.	GS9	0644
Med Tech MATEJ, Louis A.	GS9	0644
Edit Asst/Steno WHITTEN, Nancy J.	GS6	1087
Sec/Steno HOUGH, Eugenia R.	GS5	0318
Maintenance Worker KAEO, Curtis	WG7	4749

	<u>FUNDING FY 85</u>
MEDCASE Equipment	\$108,511.00
Capital Equipment	5,850.00
Civilian Salaries	143,345.00
Consumable Supplies	108,848.00
Contractual Services	12,444.00
TDY	4,361.00

TOTAL 383,359.00

3. Progress

During FY 85 there were 246 active protocols that received administrative and/or technical support during the year. Of these, 154 are presently ongoing; 68 were completed; 20 were terminated, one was transferred to another MEDCEN, and three are in a suspended status awaiting revisions.

There were 82 publications and 21 presentations at regional, national or international meetings resulting from these protocols. There were two exhibits at national meetings.

*See also Unit Summary,
Publications,
Presentations*

C O M M I T T E E M E M B E R S

Commander

Madigan Army Medical Center
BG Darryl H. Powell, M.D., MC

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Comptroller
Equal Opportunity Office
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Public Affairs Office

Non-Institutional Member: Phillip Rakestraw, Ph.D.
American Lake VA Medical Center

THE BYRON L. STEGER RESEARCH AWARD

Submissions are judged on their scientific merit, relevance, objectivity of evaluation, interpretation of results, and the potential importance of the subject of the research.

Recipient of this award for 1985:

Robert A. Arciero CPT, MC	The Effect of Arthroscopic Irrigating Solutions on the Incorporation of $^{35}\text{SO}_4$ Into Rabbit Articular Cartilage: An <i>In Vivo</i> Study

Other Nominees were:

Michael F. Lyons CPT, MC	Multiple Primary Neoplasia of the Head and Neck and Lung: The Changing Histopathology
James C. Mason CPT, MC	Vasovasostomy in the Canine Model Using Fibrin Glue
Michael J. O'Reilly CPT, MC	Sepsis from Sinusitis in Nasotracheally Intubated Patients: A Diagnostic Dilemma
Timothy J. O'Rourke MAJ, MC	CT Metrizamide Myelography in the Diagnosis of Metastatic Disease to the Axial Skeleton
Arthur H. Schipul MAJ, MC	Lactose Intolerance in Pregnancy: A Possible Etiology of IUGR? Incidence, Outcome, and Treatment (Preliminary Report)
Fredric G. Volinsky CPT, MC	Evaluation of Intravenous Fluosol in the Treatment of Experimental Decompression Syndrome: A Rat Model

PUBLICATIONS - FY 85

DEPARTMENT OF CLINICAL INVESTIGATION

Publications:

Chute CG, Baron JA, Plymate SR, Kiel DP, Pavia AT: Relationship of Risk Factors for Coronary Artery Disease and Sex Hormones in Men. Clin Res 33(2):517, 1985.

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Friedl KE, Plymate SR, Fariss BL, Garrison MJ, Matej LA: Effects of 20- α -Hydroxy-4-Pregnen-3-One Treatment of the Hypophyseal Testicular Axis in Rats. Ann NY Acad Sci 438:615-17, 1984

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Little JS, O'Reilly MJ, Higbee JW, Camp RA: Suppurative Flexor Tenosynovitis After Accidental Self-Inoculation with *Streptococcus pneumoniae*, Type I. JAMA 252:3003-04, 1984.

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Plymate SR, Moore DE, Cheng CY, Bardin CW, Southworth MB, Levinski MJ: Sex Hormone Binding Globulin Changes During the Menstrual Cycle. JCEM 61(5):993-96, 1985.

PUBLICATIONS - FY 85

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In Press:

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Plymate SR, Bremner WJ: Physiology of the Testicles in Urological Endocrinology; J. Rafer (ed), Saunders and Company, accepted September 1985.

Submitted for publication:

Jacob WL, Smith ML, Plymate SR, Fariss BL: Variations in the Composition of Human Semen. Submitted to J Androl, Feb 1985.

Lampe TH, Fariss BL, Risse SC, Plymate SR: Multiple-Day Dexamethasone Evaluation for Cushing's Disease in Psychiatric Patients with Cortisol Nonsuppression Following the Overnight Dexamethasone Suppression Test. Submitted to Amer J Psychiatry, Sep 1985.

Smith ML, Fariss BL, Jennings PB: Serum Zinc Levels in Sheep with Experimental Pancreatic Abnormalities. Submitted to Pancreas, Sep 1985.

Smith ML, Jacob WH, Plymate SR, Gregory GG: Individual Levels and Variations in the Biochemical Components of Human Semen. Submitted to J Androl, Feb 1985.

DENTAL ACTIVITY

Publication:

Klos CP, Hays GL: Prilocaine-Induced Methemoglobinemia in a Child with Shwachman Syndrome. J Oral Maxillofacial Surg 43(8):621-23, 1985.

DEPARTMENT OF EMERGENCY MEDICINE

Publications:

Checchio LM: Mast Suits. JAMA 254(8):1035, 1985.

Checchio LM, DiJulio MA: Utilization of Plain Abdominal Radiographs in Acute Gastrointestinal Hemorrhage. Med Bull USAREUR 42(9): 14-16, 1985.

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Frumkin K: Nursemaid's Elbow: A Radiographic Demonstration. Ann Emerg Med 14(7): 690-93, 1985

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Department of Emergency Medicine (Cont)

Gatrell CB: Airway Management in Potential Cervical Spine Injury - Reply.
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Gatrell CB: Asymptomatic Cervical Injuries - A Myth. Amer J Emer Med 3(3):263-64, 1985.

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Gatrell CB, Pimentel L: Abdominal Aortic-Aneurysm with Aortocaval Fistula - An Unusual Cause of Dyspnea and Edema. Ann Emerg Med 14(9), 889-96, 1985.

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Burkle FM, Rae R, Rice MM: Borderline Personality Disorder. Accepted by Ann Emerg Med, Aug 1985.

Submitted for Publication:

Parks FB, Calabro DO, Burkle, FM: Addisonian Crisis in an Adolescent Female: A Case Report. Submitted to Pedia Emerg Care Aug 1985.

Volinsky FG, Checchio LM, Friedl KE: Evaluation of Intravenous Fluosol in the Treatment of Experimental Decompression Syndrome: A Rat Model. Submitted to Undersea Biomedical Research, Jun 1985.

DEPARTMENT OF FAMILY PRACTICE

Publication:

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Nuovo J: Clinical Application of a High-Risk Scoring System on A Family Practice Obstetric Service. J Fam Prac 20(2):139-44, 1985.

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Publications:

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Jones RE, Plymate SR, Fariss BL: Activation of Palmitic Acid by Human Spermatozoa. J Andrology 6(5): 265-70, 1985.

Jones RE, Plymate SR, Fariss BL: Identification and Characterization of Long Chain Fatty Acid: CoASH Ligase (AMP) from Human Spermatozoa. J Andrology 6:125, 1985.

Knodel AR, Covelli HD, Beekman JF: Outpatient Theophylline Determinations. J West Med 140(5):741-44, 1984.

Knodel AR, Covelli HD, O'Reilly M: The Role of Mask CPAP in Preventing Post-Operative Atelectasis. Amer Rev Resp Dis 129: A110, 1984.

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Witte MC, Opal SM, Gilbert JG, Pluss JL, Thomas DA, Olsen JD, Perry ME: Incidence of Fever and Bacteremia Following Transbronchial Needle Aspiration. Accepted by Chest, Sept 1985.

Submitted for Publication:

Chamusco RF, Heppner BT, Newcomb EW, Sanders AC: Severe Iron Deficiency Anemia as the Principal Manifestation of Mitral Stenosis. Submitted Sep 1985 to Amer J Med.

Grover B, Dalessandro L, Sanders JG, Walter MH, O'Meara TF, Redmond J: Severe Viral Hepatitis A Infection, Landry-Guillain-Barre' Syndrome, and Hereditary Elliptocytosis. Submitted So Med J, Sep 1985.

Jones RE, Plymate SR, Fariss BL: Fatty Acid Oxidation by Spermatozoa Mitochondria. Submitted to J Biolog Chem, Sept 1985.

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DEPARTMENT OF NURSING

Publication:

Buckanan HK: Determining the Reliability and Validity of a Quality of Care Measuring Instrument. Thesis: Univ Washington, Master of Nursing, March 1985.

Submitted for Publication:

Reeder JM: The Lifesaver-Cell Saver TM. Submitted to AORN Journal, Nov 1984.

DEPARTMENT OF OB/GYN

Publications:

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Lee RB, Buttoni L, Dhru R, Tamimi H: Malignant Melanoma of the Vagina: A Case Report of Progression from Preexisting Melanosis. Gynecol Oncol 19:238-45, 1984.

Read JA: The Scheduling of Repeat Cesarean Section Operations: Prospective Management Protocol Experience. Amer J OB/GYN 151:557-63, 1985.

Soisson AP, Watson WJ, Benson WL, Read JA: Value of Screening Urinalysis in Pregnancy. J Reproductive Med 30(8): 588-90, 1985.

Watson WJ, Benson WL : Vaginal Delivery for the Selected Frank Breech Infant at Term. Obstet Gynecol 64:638-40, 1984.

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Benson WL, Brown RL, Schmidt PM: Comparison of Short & Long Term Courses of Ampicillin for Vaginal Hysterectomy. Accepted by J Repro Med, Jun 1985.

Dashow EE: Pancreatic Pseudocyst in Pregnancy - It's Evolution and Conservative Management. Accepted by Med Bull USAREUR, Aug 1985.

Duff P: Pathophysiology and Management of Postcesarean Endomyometritis. Accepted by Obstet Gynecol, Sep 1985.

Stovall WS, Dashow EE, Read JA: Serum Unconjugated Estriol Level as a Predictor of Pulmonary Maturity. Accepted by Amer J Obstet Gynecol Apr 1985.

PUBLICATIONS - FY 85

Department of OB/GYN (Cont)

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Dashow EE, Read JA, Coleman FH: A Randomized Comparison of Five Irrigation Solutions at Cesarean Section. Submitted to Amer J Obstet Gynecol, Nov 1984.

DEPARTMENT OF PATHOLOGY

Publication:

Turnbull JD, Meshriy R, Gere JA, Kochalka, G: Caffeine Measured in Serum From Infants Using the Theophylline Channel of the Abbott TDX. Clin Chem 30(10):1721, 1984.

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Oberhofer TR: Value of the L-Pyrrolidonyl-B-Naphthylamine (PYR) Hydrolysis Test for Identification of Select Gram-Positive Cocci. Submitted to Diag Microbiol Infect Dis, Feb 1985.

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Publications:

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Jordarski GD, Shanahan MF, Rankin JHG: Fetal Insulin and Placental 3-O-Methyl Glucose Clearance in Near-Term Sheep. J Development Physiology 7(4):251-58, 1985.

Krober MS, Bass JW, Michels GN: Diagnosis and Treatment of Streptococcal Pharyngitis - Reply. JAMA 254(7):909, 1985.

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Meidell R, Marinelli P, Pettett G: Perinatal Factors Associated with Early-Onset Intracranial Hemorrhage in Premature Infants - A Prospective Study. Amer J Dis Chil 139(2):160-63, 1985.

Meidell R, Pettett G: Echocardiographic Changes in Cardiac Function in Healthy Preterm Infants During the First Week of Life. Clin Res 33(1):113, 1985.

Moore DC: Body Image and Weight Control Behaviors in Adolescent Females. Abstracts of Society for Adolescent Medicine, p 341, July 1985.

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Moore DC: Combination Therapy in an Adolescent with Polycystic Ovaries, Hirsutism, Type-A Insulin Resistance, and Acanthosis Nigricans. Ped Res 19(6):632, 1985.

Pagon RA, Stephan MJ: Septo-Optic Dysplasia with Digital Anomalies. J Pediatrics 105(6):966-68, 1984.

In Press:

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Moore, D.C.: Prolonged Suppression of Hirsutism with Combination Therapy in an Adolescent with Insulin Resistance and Acanthosis Nigricans. Submitted NEJM, Aug 1985.

PHYSICAL AND MEDICAL REHABILITY SERVICE

Publication:

Kane MD, Karl RD, Swain JH: Effects of Gravity-Facilitated Traction on Intervertebral Dimensions of the Lumbar Spine. J Ortho Sports Phy Therapy 6(5):281-88, 1985.

PREVENTIVE MEDICINE SERVICE

Publications:

Fletcher DJ: Building a Pathway to Better Health - The Primary Care Physician's Role. Post Grad Med 77(1);297, 1985.

Fletcher DJ: Coping with Stress - How to Help Patients Deal with Life's Pressures. Postgrad Med 77(4):93, 1985.

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Fletcher DJ, Rogers DA: Diet and Coronary Heart Disease - Helping Patients Reduce Serum Cholesterol Level. Postgrad Med 77(5):319-28, 1985.

Lednar WM, Brundage JF, Diniega BM, McKenna K: Assessment of Infectious Disease Hazards Associated with Day Care Centers in Europe. Med Bull USAREUR 42:14-18, 1985.

PUBLICATIONS - FY 85

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Lednar WM, Lemon SM, Kirkpatrick JW, Redfield RR, Fields ML, Kelley PW: Frequency of Illness Associated with Epidemic Hepatitis A Virus Infections in Adults. Amer J Epidemiology 122(2): 226-33, 1985.

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Nguyen, D: Culture Shock - A Review of Vietnamese Culture and Its Concepts of Health and Disease. West J Med 142(3):409-12, 1985.

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DEPARTMENT OF PSYCHIATRY

Submitted for Publication:

Thompson JW: Research Methodologies in Organizational Development. Submitted to Army Organizational Effectiveness Journal, Nov 1984.

DEPARTMENT OF RADIOLOGY

Publication:

Sueoka BL, Johnson JF, Enzenauer R, Kolina JS: Infantile Infectious Sacroiliitis. Ped Radiology 15(6):403-05, 1985.

DEPARTMENT OF SURGERY

Publications:

Arciero RA, Shishido NS, Parr TJ: Acute Anterolateral Compartment Syndrome Secondary to Rupture of the Peroneus Longus Muscle. Amer J Sports Med 12(5):366-67, 1984.

Beirne DR, Burckhardt JG, Peters VJ: Subtalar Joint Subluxation. J Amer Podiat Assoc 74(11):529-32, 1984.

Bickerstaff L, Hollier L, VanPeenen H, Melton J, Pairolero P, Cherry K: Abdominal Aortic Aneurysm - Changing Natural History. J Vasc Surg 1:6-12, 1984.

Bickerstaff L, Hollier L, VanPeenen H, Melton J, Pairolero P, Cherry K: Abdominal Aortic Aneurysm Repair Combined with a Second Surgical Procedure: Morbid Mortal Surg 95:487-91, 1984.

Department of Surgery (Cont)

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DETAIL SHEETS
FOR
PROTOCOLS

DEPARTMENT OF CLINICAL INVESTIGATION

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 83/64 Status: On-going

Title: The Effect of 2- α -Hydroxy-4-Pregnen-3-One Treatment on Spermatogenesis and Gonadotrophins in Rats

Start Date: 20 May 83 Estimated Completion Date: Dec 83

Department: Clinical Investigation Facility: MAMC

Principal Investigator: CPT Karl E. Friedl, MSC

Associate Investigators:

COL Bruce L. Fariss, MC LTC James L. Kelley, MC

COL Stephen R. Plymate, MC Mina Garrison, DAC, B.S., M.T.

Key Words: Physiological role, direct and indirect actions

Accumulative Est Accumulative Periodic Review

MEDCASE Cost: -0- OMA Cost: \$2750.00 Results: Continue

Study Objective: To examine the possibility of a physiological role for the steroid metabolite 2- α -hydroxy-4-pregnen-3-one in the hypothalamic-pituitary testes axis.

Technical Approach: 32 young adult male rats will be anesthetized and castrated on the day prior to the start of treatments. They will then be randomly distributed into 4 treatment groups. In a second experiment, 32 intact rats from the same shipment will also be randomized into 4 treatment groups. In both experiments, the groups will be injected daily for 30 days with 1 mg progesterone, 1 mg 2- α -OHP, 5 mg 2- α -OHP, or sesame oil. After 30 days of treatment they will be guillotined and trunk blood will be collected into heparinized containers, centrifuged and plasma aliquots for the hormone assay will be made and stored at -80°C. The testes will be removed from the intact animals, decapsulated and weighed. The left testis will be divided and preserved for histology. The right testis will be frozen at -80°C until assay of intratesticular T, E₂, and androgen binding protein (ABP). For all animals, the ventral prostate and seminal vesicles will be ligated, removed and weighed. Epididymides will also be weighed from intact animals and the right epididymis will be frozen at -80°C for later assay of T, E₂, and ABP. Testes will be sectioned at 4 microns and 22 tubules representing 7th stage cellular associations will be used per animal. Spermatogonia, spermatocytes, and S7 spermatids will be counted and expressed in terms of Sertoli cell nuclei counts. Unusual features such as necrotic germ cells and high lipid content of the Sertoli cells will be noted. Means of all counts and tubule diameters will be compared between the four groups by t test. Steroids and gonadotrophins will be measured for all eight groups by RIA and then compared between intact groups and castrated groups by t test. The relationship between the quantitative assessment of spermatogenesis and hormonal changes will be compared between intact groups.

PROGRESS: Sixty-four (64) rats have been studied. Hormonal data indicate that 20- α -OHP acts on both the hypothalamic/pituitary and the testis mechanisms. The actions result in a substantial activation of the seminiferous tubule component of the testes as demonstrated by significant increases in androgen binding protein concentrations. More rats are to be studied. The results to date resulted in a presentation at the 7th International Congress of Endocrinology.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/18 Status: Completed

Title: Investigations Into the Mechanism of Medroxyprogesterone Reduction of HDLC in Men.

Start Date: 16 Nov 84 Est Completion Date: Nov 85

Department: Clinical Investigation Facility: MAMC

Principal Investigator: CPT Karl E. Friedl, MSC

Associate Investigators: COL Stephen R. Plymate, MC
Thomas Kettler, GS/09

Key Words: HDLC, medroxyprogesterone, men

Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost -0-	OMA Cost: \$1548.00	Results: N/A

Study Objective: To test the hypothesis that medroxyprogesterone decreases HDLC in men through an enhancement of T conversion to DHT.

Technical Approach: The samples represent time periods before, during, and after treatment of 30 normal young men at one of three DMPA dose levels (for a six month period of treatment).

Measurement of DHT levels will be done using DHT rabbit antiserum in a standard RIA procedure after a separation procedure. This will be achieved with ethyl acetate treated ITLC glass fiber sheet chromatography. Since a radiochromatogram scanner is not readily available, 1 cm strips will be separately counted in scintillant to determine the position of labelled DHT standards on each sheet. If sufficient serum remains after DHT and DMPA assays, a recently published quick DHT separation method requiring A ring oxidation of steroids using potassium permanganate followed by simple ether extraction of DHT will also be run to compare the validity of this method to standard methods.

To measure medroxyprogesterone levels, an attempt will be made to use existing RIA kits for progesterone measurement. Progesterone levels in male circulation are low enough that if a reasonable standard curve can be achieved with medroxyprogesterone, the method will give a reasonable approximation of the synthetic progestagen serum concentrations. If this method does not work, a request for the donation of a small quantity of specific medroxyprogesterone antibody will be made to a British lab with experience in this area. This would be used in a standard RIA procedure with the addition of any required separations.

Data will be analyzed after addition to the Ft Detrick data base containing the previous values from the same samples. The hypotheses will then be tested using the SPSS statistics package.

Progress: The assays have been performed and data analysis is almost complete.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/35 Status: On-going

Title: Physiological Changes with Weight Loss. Part 2:
Testosterone Binding Globulin and Plasma Steroids
(see page 181 for Part I and page 42 for Part III)

Start Date: 18 Jan 85 Est Completion Date: Jan 86

Department: Clinical Investigation Facility: MAMC

Principal Investigator: CPT Karl E. Friedl, MS

Associate Investigators:

COL Stephen R. Plymate,

MAJ Arthur Knodel, MC

MAJ Robert E. Jones, MC

Thomas Kettler, GS/09

MAJ T. Kaduce, MSC, USAR

Louis Matej, GS/09

Key Words: Diet, exercise, TeBG, plasma steroids

Accumulative MEDCASE

Est Accumulative

Periodic Review

Cost: -0-

OMA Cost: \$4900.00

Results: N/A

Study Objective: To examine metabolic and endocrine factors which appear to be related to the changes in plasma TeBG seen in obesity and to examine the significance of the TeBG change to steroid hormone balance.

Technical Approach: Healthy male non-smokers who have been referred for caliper measurements because they were over the Army weight standard will be randomized into three groups: Group 1 (controls - 0-5% below maximum allowable fat standard); blood samples and hydrostatic weight initially and at six months; Group 2 (diet/over fat standard); and Group 3 (diet and exercise/over fat standard). Groups 2 and 3 will be sampled once a week after an overnight fast with blood samples, caliper measurements, and hydrostatic weight. They will be asked to fill out a questionnaire at the first session, to submit a weekly food intake sheet, and to take part in weekly counselling sessions.

The mechanism of plasma TeBG suppression in obesity will be studied by measuring its restoration to normal levels during weight loss. The changes associated with TeBG alterations will be followed into a stable weight maintenance phase subsequent to the active weight loss. Testosterone, estradiol, DHEA-S, cortisol, hLH, hGH, β -lipotropin, TeBG, glucuronides, and dihydrotestosterone will be measured.

Progress: Thirty-eight subjects have been entered. Testosterone globulin has been measured in the first 50 samples in the study. No data analysis will be performed until more subjects have completed the weight loss protocol.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 85/36	Status: On-going
Title: Physiological Changes with Weight Loss. Part 3: Serum Lipids (see page 181 for Part 1 and page 41 for Part 2)		
Start Date: 18 Jan 85	Est completion Date: Jan 86	
Department: Clinical Investigation	Facility MAMC	
Principal Investigator: MAJ Charles J. Hannan, MS		
Associate Investigators:		
COL Stephen R. Plymate,	MAJ Arthur Knodel, MC	
MAJ Robert E. Jones, MC	CPT Karl E. Friedl, MS	
MAJ T. Kaduce, MS, USAR	Thomas Kettler, GS/09	
Key Words: Diet, no exercise, serum lipids, body fat		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: \$6955.00	Results: N/A

Study Objective: To determine if there is a measureable change in 12-hour fasted serum lipids during an extended period of caloric restriction (with and without exercise) and if any change is maintained after a reduced weight is established. A second objective of this study is to examine the relationship of alterations in lipid levels which are observed in this study with endocrine changes observed in the associated study with the same subjects.

Technical Approach: Healthy male non-smokers who have been referred for caliper measurements because they were over the Army weight standard will be randomized into three groups: Group 1 (controls - 0-5% below maximum allowable fat standard); blood samples and hydrostatic weight initially and at six months; Group 2 (over fat standard/diet); and Group 3 (over fat standard/diet and exercise). Groups 2 and 3 will be sampled once a week after an overnight fast with blood samples, caliper measurements, and hydrostatic weight. They will be asked to fill out a questionnaire at the first session, to submit a weekly food intake sheet, and to take part in weekly counselling sessions. Whole blood serum will be analyzed for changes in both free and total cholesterol and triglycerides.

Progress: A comparison was made between size exclusion HPLC and a monoclonal antibody RIA in the estimate of apolipoprotein A-I concentration present in the ultracentrifugally isolated HDL fraction from human serum. Although the correlation coefficient between the two assays was 0.899, there was a consistent difference between the measurements as demonstrated by a slope significantly different from unity ($p < 0.05$). Physiologically-induced changes in apolipoprotein A-I concentration in subjects who lost fat in a weight loss program were detected equally well by HPLC or RIA, but, while relative changes were consistent, absolute measurements by the four methods suggest the possibility of different subsets of A-I with a narrower range being detected by RIA.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 85/83	Status: On-going
Title: Mechanisms in Blood-Brain Barrier Function: Animal Models		
Start Date: 23 Aug 85	Est Completion Date: Dec 87	
Department: Clinical Investigation	Facility: MAMC	
Principal Investigator: MAJ Charles J. Hannan, MS		
Associate Investigators:		
COL Stephen R. Plymate, MC	CPT Mark Flanery, MC	
LTC James Temo, ANC	Alan A. Artru, M.D.	
MAJ Robert E. Jones, MC	Judy Y. Sey, Ph.D.	
MAJ Leslie Yarbrough, VC	Thomas Kettler, B.S.	
Key Words: patency, anesthesia, biochemical markers		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: \$12,848.00	Results: N/A

Study Objective: To evaluate patency of the blood-brain barrier (BBB) during anesthesia and to evaluate various cerebral spinal fluid (CSF) biochemical markers of BBB status.

Technical Approach: Three animal models with three inhalation anesthetics (halothane, isoflurane, and enflurane) will be used: (1) two strains of mice, the relatively short-lived NZB and the longer-lived C57BL mouse, will be used at different ages in biochemical studies *in vitro* with isolated cerebral capillaries; (2) Fisher 344 rats will be used in acute experiments to measure regional brain uptake of BBB permeability tracers such as ³H-water while anesthetized; and (3) macaques, anesthetized with the three agents will be prepared for CSF collection by lumbar puncture.

Progress: This protocol has not been implemented. The investigators are awaiting approval from USAMRDC before starting the protocol.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 85/59	Status: On-going
Title: Rapid Diagnosis of Leptospirosis Using Monoclonal Antibodies Against Genus Specific Leptospiral Antigen(s)		
Start Date: 19 Apr 85	Estimated Completion Date: Jun 87	
Department: Clinical Investigation	Facility: MAMC	
Principal Investigator: LTC James W. Higbee, MSC		
Associate Investigators:		
MAJ Wayne M. Lednar, MC	Mina J. Garrison, DAC	
MAJ Leslie W. Yarbrough, VC	Catherine R. Sulzer, DAC	
Key Words: Leptospirosis, monoclonal antibodies, diagnosis		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: \$3720.00	Results: N/A

Study Objectives: To isolate genus-specific antigen(s) of leptospire from selected serovars; to produce monoclonal antibodies against leptospiral antigens; to determine the specificity and sensitivity of monoclonal antibody clones against genus-specific and other reactive leptospiral antigens; and to use labeled monoclonal antibodies in leptospiral diagnosis.

Technical Approach: Genus specific antigens prepared by two methods will be compared for sensitivity and specificity. Actively growing cultures will be centrifuged and washed twice and lysed, followed by centrifugation and supernatant sucrose density gradient centrifugation. Antigenic activity of each fraction will be tested against rabbit-produced antisera. Antigens of the same serovars prepared by ethanol precipitation will be similarly tested. Antigens demonstrating broad spectrum genus-specific activity against sera for representative serovars of different serogroups will be used for testing the antibody secreting hybridoma clones. Leptospira organisms will be statically grown to approximately 10^8 organisms/ml concentration. Following harvesting, BALB/C or nude mice cells will be sensitized to leptospira using a 6-week immunization schedule. Mice will be injected intraperitoneally with 10^3 organisms in complete Freud adjuvant with additional injections with 10^8 leptospira and final intraperitoneal booster 3 days before cell fusion. Cell fusion will be conducted by combining mouse leptospira sensitized spleen cells and mouse-adapted myeloma cells in the presence of polyethylene glycol. Combined cells will be washed and suspended to approximately 25×10^6 cells per ml. When hybrids exhibit good growth, the culture supernatants will be screened for antileptospiral activity. Positive cultures will be expanded and those which continue to produce targeted antibody will be cloned. The specificity of antibody producing hybrid clones will be demonstrated against various leptospiral antigens using the MAT, ELISA FA and/or isolated antigenic fractions. Monoclonal antibodies will be labeled with horseradish peroxidase, alkaline phosphatase or fluorescein isothiocyanate and profiled against leptospiral infected animals. Assays will be conducted on samples collected at different intervals.

Progress: Two mouse adapted multiple myeloma tumor cell lines were established. Various tissue culture substrates were evaluated to identify the best serum-free medium and buffering system for routine cell maintenance and Chee's medium was selected. Actual work should begin very early in 1986.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 80/70 Status: Completed

Title: Mechanism of HCG in Spermatogenesis During Testosterone Suppression

Start Date: Aug 80 Est Completion Date: Oct 85

Department of Clinical Investigation Facility: MAMC

Principal Investigator: COL Stephen R. Plymate, MC

Associate Investigators: COL Bruce Fariss, MC

LTC George Ward, VC

Mina Garrison, MT

Key Words: Rats, sesame oil, testosterone proprionate, HCG, orchiectomy

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$840.00 Results: N/A

Study Objective: To determine if, during testosterone suppression, spermatogenesis which is reinitiated by HCG is due only to a rise in testicular testosterone or if HCG also stimulates androgen binding protein production.

Technical Approach: Three groups (20/group) of male rats >90 days will be studied. Initially, each animal will have serum drawn for LH, prolactin, FSH, and testosterone, and a unilateral orchiectomy will be done with the testicular contents assayed for androgen binding protein, testosterone, estradiol, and dihydrotestosterone plus histology. For 6 weeks, Group 1 (controls) will be injected with sesame oil alone; Groups 2 and 3 will be injected with sesame oil plus testosterone proprionate at a dose of 150 µgm/100 gm body weight. Then, for 6 more weeks both groups will continue to receive the testosterone proprionate and Group 3 will also receive the HCG at a dose of 6 U/100 gm body weight daily. Group 1 will continue to receive the sesame oil alone. At the end of this six weeks, each animal will again have serum drawn for prolactin, FSH, LH, and testosterone, and the animal will then be sacrificed with the other testicle removed and assayed for androgen binding protein, testosterone, estradiol, and dihydrotestosterone as well as histology.

Progress: The technical portion of the study has been completed, the data analyzed, and a publication is in preparation.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 82/23 Status: Completed

Title: Differentiation of Luteinizing Hormones From Different
Animal Species Utilizing the HPLC

Start Date: Jan 82 Est Completion Date: Sep 85

Department: Clinical Investigation Facility: MAMC

Principal Investigator: COL Stephen R. Plymate, MC

Associate Investigators: COL Bruce L. Fariss, MC

MAJ Willis H. Jacob, MS

Key Words: pituitary gonadotrophins, separated, quantitated

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$200.00 Results: N/A

Study Objective: To determine if high pressure liquid chromatography can be a means by which the pituitary gonadotrophins can be separated and quantitated between species.

Technical Approach: Various nanogram amounts of LH ranging from 1-50 ng/ml will be assayed by the HPLC using the protein 125 column. Human, primate, ovine, rat, and rabbit LH will be assayed. Human LH which has been labelled by chloramine-T or lactoperoxidase will also be used. The same concentrations of LH will then be added to the mouse Leydig's cell bioassay system. The results between these two techniques will be compared as well as the points at which the various LH's are detected on the HPLC. The statistical analysis will be performed by linear regression and t tests.

Progress: Adequate separation of LH subfractions was obtained, but no improvement in isolating the bioactive portion was noted.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 83/83 Status: On-going

Title: Relationship of Body Fat to Control of Synthesis by the Liver of Testosterone Estradiol Binding Globulin (TeBG) and Sex Hormones

Start Date: 16 Sep 83 Est Completion Date: Sep 86

Department: Clin Investigation Facility: MAMC

Principal Investigator: COL Stephen R. Plymate, MC

Associate Investigators:

COL Bruce L. Fariss, MC

CPT Karl E. Friedl, MSC

COL Gary L. Treece, MC

Mina J. Garrison, DAC, M.T.

MAJ Stanley P. Liebenberg, VC

Louis A. Matej, DAC, M.T.

Key Words: Beagles, estradiol valerate, tamoxifen, levothyroxine

Accumulative MEDCASE

Est Accumulative

Periodic Review

Cost: -0-

OMA Cost: \$500.00

Results: Continue

Study Objective: To determine the metabolic parameters responsible for modifying production of TeBG in weight gain.

Technical Approach: Six female beagles, not in estrus, will have 3 baseline serums drawn for T₄, T₃ uptake, T₃ RIA, TeBG, testosterone, androstenedione, and estradiol weekly for a 3-week baseline period. The animals will be weighed weekly and then allowed unlimited access to food with decreased exercise. Weekly blood samples will again be drawn until the animals have gained 30% of their starting body weight. At that point, the animal's food intake will be determined and the weight maintained at the 30% level. The animals will then be given two subcutaneous injections (two days apart) of estradiol valerate (40 mg). One and two weeks after the last injection, blood samples will again be drawn. Next, the animals will be given tamoxifen, an antiestrogen, at a dose of 10 mg t.i.d. intramuscularly and TeBG levels again drawn one week and two weeks after tamoxifen administration. The animals will then be allowed one month's rest while maintaining their weight at 30% above their ideal body weight. Baseline studies as mentioned above will then be obtained weekly for two weeks. Then the animals will be given 1 mg of levothyroxine intramuscularly weekly for two weeks, and blood studies will be repeated at the time of the second injection and for three weeks after the administration of levothyroxine. A similar group of six normal weight female beagles, age-matched and not in estrus, will be studied with similar blood drawings and administration of medications.

Progress: There was a delay in this project due to the ban on the use of dogs. Primary hepatic cultures have been established. No data nor conclusions at this time.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 83/84	Status: On-going
Title: Evaluation of Efficacy of Varicocele Repair		
Start Date: Sep 83	Est Completion Date: Oct 86	
Department: Clinical Investigation	Facility: MAMC	
Principal Investigator: COL Stephen R. Plymate, MC		
Associate Investigators MAJ Brian Miles, MC		
C. A. Paulsen, M.D.		
Richard E. Burger, M.D.		
Key Words: Infertile and fertile men, LH/RH stimulation tests, semen analysis, sperm penetration assay		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine the efficacy of varicocele repair in improving fertility in the infertile male.

Technical Approach: Four groups (75 men each) will be studied: (1) infertile men who are going to have their varicoceles repaired, (2) infertile men without varicoceles; (3) fertile men who have varicoceles, and (4) fertile men without varicoceles. Prior to entering into this study all subjects will have a complete history and physical examination done, including assessment of the presence or absence of a varicocele as well as calibrated measurement of testicular size. Each group will have 8-10 semen analyses performed, two sperm penetration assays performed at least four weeks apart, and two LH/RH stimulation tests performed using 200 mg of LH/RH. Blood samples will be drawn every 15 minutes for two hours after the injection of the LH/RH. Following repair of the varicocele, the men will have a seminal fluid analysis performed every two to four weeks, sperm penetration assay performed at 6 and 12 months after the varicocele ligation, and LH/RH again performed at six and twelve months after the varicocele ligation.

Progress: A total of 165 patients has been studied. Further testing will be done. There have been two publications and four presentations from the data analysis thus far.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 83/85 Status: Completed

Title: Role of Depression in Modulation of Hypothalamic-Pituitary-Gonadal-Axis

Start Date: 16 Sep 83 Est Completion Date: Sep 84

Department: Clinical Investigation Facility: MAMC

Principal Investigator: COL Stephen R. Plymate, MC

Associate Investigators: COL Bruce L. Fariss, MC

Thomas Lampe, M.D., Amer Lake VA Hosp

Steve R. Risse, M.D., Amer Lake VA Hosp

Key Words: Non-suppressible DST, dexamethasone, TRH

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$2000.00 Results: N/A

Study Objective: To evaluate the hypothalamic gonadal function in a biochemically defined depressive state in order to further define the role of neurotransmitters in both the depression and the control of the hypothalamic-pituitary-gonadal (HPG) axis.

Technical Approach: Subjects: Ten women and ten men admitted for depression who have nonsuppressible DST as defined by a cortisol level greater than 5 µg/dl after 1 mg dexamethasone given at 2300 hours and plasma cortisol measured at 0800, 1600, and 2300 hours the following day. Following the DST at 0800 hours, a 200 mg bolus of LH/RH will be given IV. Blood samples will be drawn at -15, 0, 15, 30, 45 and 60 minutes for LH, FSH, and prolactin. This will be followed by a 100 µg bolus of TRH with blood samples drawn at 60, 75, 90, 105 and 120 minutes for prolactin, TSH, and growth hormone. When the DST returns to normal the studies will be repeated on all patients. Any patients on phenothiazines will be excluded from the study. In addition the -15 and zero time samples will have β-lipotropin, ACTH, β-endorphin, testosterone, estradiol, and sex hormone binding globulin measured. The female patients will have a menstrual history noted. If they are cycling, the time of the blood drawing in relationship to their cycle will be calculated and confirmed by measurement of serum progesterone.

Progress: Ten subjects were studied and the data has been analyzed. A publication has been accepted by the American Journal of Psychiatry.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/31 Status: Terminated

Title: Levothyroxine Therapy in Oligospermic Men
 Start Date: Feb 84 Est Completion Date: Mar 86
 Department: Clinical Investigation Facility: MAMC
 Principal Investigator: COL Stephen R. Plymate, MC
 Associate Investigators: MAJ Wayman W. Cheatham, MC
 Louis A Matej, DAC
 Key Words: TRH stimulation test, L-thyroxine
 Accumulative MEDCASE Est Accumulative Periodic Review
 Cost: -0- OMA Cost: \$295.00 Results: N/A

Study Objective: To assess whether levothyroxine therapy in physiologic doses is associated with significant changes in sperm analysis in a group of idiopathically oligospermic men.

Technical Approach: Twenty males with a diagnosis of idiopathic oligospermia who have been evaluated for infertility be studied. Idiopathic oligospermia as a diagnosis will result when the individual has sperm density of $<20 \times 10^6$ sperm/cc or $<60 \times 10^6$ sperm/ejaculate with or without impaired motility; normal buccal smear and/or karyotype; normal testosterone; normal estradiol and prolactin; no evidence of abnormality of the hypothalamic pituitary axis; normal basal triiodothyronine (T_3 RIA), thyroxine (T_4), T_3 resin uptake (T_3U), and TSH; and no history of cryptorchidism or orchitis.

Excluded from the study will be individuals <18 or >60 years old or with evidence or history of valvular or ischemic heart disease or cardiac dysrhythmia; systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg; creatinine >1.4 mg/dl, BUN >20 mg/dl or liver enzymes outside the established range of normal; evidence of a disorder of primary sexual differentiation; a varicocele; or taking medication known to have an effect on the reproductive axis.

Individuals who qualify under these criteria will be randomly assigned to one of two groups. Baseline testosterone, LH, FSH, estradiol, prolactin, T_3U , T_4 and T_3 RIA will be drawn and a TRH stimulation test using 500 μ g TRH will be administered to both groups with blood samples taken at 0 and +30 mins. For documentative purposes a karyotype will be done. Members of both groups will also collect three separate baseline semen specimens at intervals of at least 7 days with 48 hrs abstinence prior to each collection. Data to be collected from the semen analysis will include subject, date, color, turbidity volume, pH, sperm count per cc, morphology immediate motility, and 2 hr motility. Group A will be given L-thyroxine daily, beginning after the baseline studies are completed and continuing for 120 days. Three weeks prior to the termination of the treatment period, the subject will initiate a repetition of the semen collection sequence.

Levothyroxine Therapy in Oligospermic Men - Plymate

Collection of blood for hormonal studies and a TRH stimulation test as performed prior to the beginning of the treatment period will be repeated at this time.

Members of Group B will be given a placebo. The treatment period, the semen collection, and blood test sequence will be identical to those described for Group A.

At the end of the first 120 day treatment period, members of the two groups will cross over such that those previously taking active hormone will take placebo and those formerly taking placebo will take active hormone. The individuals will then duplicate the first 120 day treatment period. At the end of the second 120 day period, the individuals will cease all medications and be released from the protocol but will continue to receive appropriate follow-up evaluation for their primary disorder.

Subjects will be evaluated in the clinic monthly during the 240 day study period or more often if they desire. Any subject who demonstrates clinical symptoms suspicious of hyperthyroidism while under study will immediately cease all medication and have blood drawn for T_3U , T_4 and $T_3(RIA)$ and a physical examination. If hyperthyroidism is confirmed, the subject will be excused from the study.

Progress: No patients were entered. The study was terminated due to a lack of clinical effects.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 84/85	Status: Completed
Title: Relationship of Endogenous Sex Hormones to Lipids and Arteriosclerotic Coronary Vascular Disease (ASCVD)		
Start Date: Sep 84	Est Completion Date: Jan 85	
Department: Clinical Investigation	Facility: MAMC	
Principal Investigator: COL Stephen R. Plymate, MC		
Associate Investigators: CPT Karl E. Friedl, MSC John Baron, M.D., Dartmouth Med Sch Louis A. Matej, GS/09		
Key Words: RIA, saturation analysis, centrifugation dialysis, cholinesterase, heparin magnanese precipitation		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: N/A

Study Objective: To define the relationships between estrogens, androgens, and certain risk factors for ASCVD in men.

Technical Approach: Serum sex hormones and lipoproteins will be measured in one diseased and two control groups (patients with: 1. severe coronary artery disease demonstrated by coronary arteriography; 2. absent or minimal coronary artery disease demonstrated by coronary arteriography within the past year; and 3. no history or symptoms of coronary artery disease, unexamined). Subjects will be white male in-patients, 35-75 years of age, who are having coronary arteriography. Patients with advanced liver disease, chronic adrenal failure, or steroid hormone therapy will be excluded. The admitting diagnosis for subjects will be unrelated to coronary artery disease or alterations in steroid hormones. Serum (15 ml) will be drawn on each subject at the time of routine pre-arteriography blood drawing. Serum hormone measurements will include total serum estradiol, total serum testosterone by RIA, serum sex hormone binding globulin by saturation analysis, serum free estradiol and free testosterone by centrifugation dialysis, serum total cholesterol by the cholinesterase method, and serum HDL cholesterol by heparin magnanese precipitation. Mean hormone levels will be compred using standard t tests in related confidence intervals. Analysis of covariants will be used if any covariants are found to be associated with the hormone levels. The relative risk odds ratio associated with various serum estrogen ranges will be computed. Adjustments for covariants will be made using logistic modelling. This technique will allow for assessment of the importance of other coronary vascular disease risk factors in influencing relationships under study.

Progress: Two hundred and twelve (212) patients were studied. Preparation of four separate publications is in progress.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/06 Status: Completed

Title: Response of Patients with Alzheimer's Disease to
Thyrotropin-Releasing Hormone (TRH)

Start Date: Oct 84 Estimated Completion Date: Apr 85

Department: Clinical Investigation Facility: MAMC

Principal Investigator: COL Stephen R. Plymate, MC

Associate Investigators:

Thomas H. Lampe, M.D., Amer Lake VA Hosp Mina Garrison, GS/09

Murray Raskind, M.D., Amer Lake VA Hosp Louis Matej, GS/09

Steven Risse, M.D., Amer Lake VA Hosp

Key Words: Advanced Alzheimer's disease, TRH, five subjects

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$1000.00 Results: N/A

Study Objective: To determine by TRH infusion if there is significant cholinergic deficiency in cholinergic cell loss in Alzheimer's disease.

Technical Approach: Five patients with advanced Alzheimer's disease off of psychotropic medications for >2 weeks will be studied. Three different doses of TRH (0.5, 1.0 and 2.0 mg, I.V.) will be administered in successively increasing dosages with at least one week separating each administration. Thirty minutes after an IV of NL saline has been established, baseline blood samples for TSH, prolactin, growth hormone, testosterone, testosterone binding globulin, LH, FSH, and cortisol will be collected. After baseline samples are collected TRH will be administered IV at a rate of 0.5 mg/min. BP and pulse will be determined every 5 min for one hr after TRH administration and then every 10 min for the duration of the test and until stable. Pre and post study orthostatic BP will be monitored in ambulatory patients. Temperature will be determined every 15 min during the test. Blood samples for TSH, prolactin, growth hormone, bioactive LH, FSH, and cortisol will be drawn at 5, 10, 20, 30, 45, 60, 90, and 120 min after TRH infusion. Results will be compared to previously determined normal patient responses done on TRH tests in age-matched controls. Data will be analyzed using SPSS and SAS.

ADDENDUM (22 Feb 85): Five additional patients with Alzheimer's disease and 10 age-matched and sex-matched control subjects with 0.5 mg given for maximal neuroendocrine stimulation and 0.1 mg for potentially submaximal stimulation. It is felt that the use of a potentially submaximal dose may help to delineate differences in response between the two groups. Two additional 15 cc blood samples at 15 minute intervals will be obtained for determination of baseline hormone values. Collection of the samples will be as described in the original protocol.

Progress: Ten patients and ten controls were studied. Data is currently being analyzed. Initial findings show a significant difference between groups.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/75 Status: Completed

Title: A Controlled Study of Malaria, Schistosomiasis and Dengue Incidence Rates as Well as Stress in Active Duty Troops

Start Date: 28 Jun 85 Estimated Completion Date: Jun 85

Department: Clinical Investigation Facility: MAMC

Principal Investigator: COL Stephen Plymate, MC

Associate Investigators: LTC James W. Higbee, MSC

MAJ Wayne M. Lednar, MC

CPT Karl E. Friedl, MSC

Key Words: detection, malaria, schistosomiasis, dengue, measurements, cortisol, testosterone, LH, prolactin, SHBG

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$3000.00 Results: N/A

Study Objective: To explore a mechanism for early detection of problems related to the morbidity and mortality from non-combat conditions as soldiers are deployed into new areas.

Technical Approach: Fifty (50) to 100 male soldiers, moving to a new environmental area over a short period of time will have blood and stool samples drawn for malaria smears, Schistosoma detection, leptospirosis antibodies, giardiasis and will have serum hormone measurements for cortisol, testosterone, LH, prolactin, and SHBG. These samples will be obtained immediately prior to departure and within two days of return to the Fort Lewis area. Samples will then be analyzed and appropriate statistical analysis performed by analysis of variance and t test as well as chi-square test.

Progress: Data collection and assays have been completed. Analysis of data is in progress.

DETAIL SHEETS
FOR
PROTOCOLS

DEPARTMENT OF EMERGENCY MEDICINE

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 82/25 Status: On-going

Title: Emergency Room Procedure Training

Start Date: Feb 82 Est Completion Date: Feb 87

Department: Emergency Medicine Facility: MAMC

Principal Investigator: COL Frederick Burkle, MC

Associate Investigators: LTC Samuel T. Coleridge, MC

MAJ Steven C. Dronen, MC

MAJ Stanley P. Liebenberg, VC

Key Words: Training techniques, invasive & life-saving procedures

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$1360.00 Results: Continue

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

Technical Approach: The procedures listed below will be performed in two separate sessions under the supervision of a staff member and the veterinarian assigned to Clinical Investigation. All animals will be anesthetized and then will be sacrificed immediately after the procedures.

PART I:

1. Femoral vein cutdown
2. Peritoneal lavage
3. Tube thoracostomy
4. Thoracotomy
5. Aortic cross-clamping
6. Control of pulmonary hemorrhage
7. Cardiac wound repair
8. Endotracheal intubation
9. Percutaneous transtracheal ventilation
10. Cricothyroidotomy

PART II:

1. Tissue pressure monitoring
2. Arterial pressure monitoring
3. Swan-Ganz catheter placement
4. Transvenous ventricular pacemaker placement
5. Transthoracic ventricular pacemaker placement
6. Pericardiocentesis
7. Segstaken-Blakemore tube placement
8. Auto transfusion from hemothorax
9. Twist drill decompression
10. Skull Trephination

Progress: Selected residents were taken to the procedures laboratory in groups of 4-6 every two to three months for a total of 16 residents. Various emergency procedures were taught and practiced, using two adult goats under general anesthesia. The residents have demonstrated improved knowledge of anatomy and more confidence and technical expertise when performing these procedures on patients in emergency situations. Two of the residents are planning to develop a videotape presentation which may be used as a teaching aid and to write for publication a descriptive paper of the teaching tools.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/22 Status: Completed

Title Comparison of Endotracheal vs Intravenous (Peripheral) vs Intraosseous Administration of Atropine

Start Date: 16 Jan 85 Estimated Completion Date: Apr 85

Department: Emergency Medicine Facility: MAMC

Principal Investigator: CPT Mark Prete, MC

Associate Investigators: COL Frederick Burkle, MC

MAJ Charles Hannan, MSC

MAJ Mel Robinson, MC

MAJ Leslie Yarbrough, VC

Key Words: Endotracheal, intravenous, intraosseous, Atropine, monkeys

Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: \$300.00	Results: N/A

Study Objective: To establish the pharmacokinetics with each route and varying blood level concentrations and the clinical response as reflected by heart rate and blood pressure.

Technical Approach: Each group will contain 6 pig-tailed macaque monkeys lightly anesthetized with IV pentobarbital and intubated with a cuffed endotracheal tube. A catheter will be placed into the aorta through the femoral artery and attached to strain gauge for recordings of aortic pressure and sampling of central drug levels. Needle electrodes will be inserted into the extremities for continuous recording of ECG. A saphenous vein catheter will be placed for peripheral access. The animals will be made bradycardic by N₂O-induced hypoxia. Each animal will be used as its own control with the injection of equivalent volumes of normal saline. The intraosseous route involves the placement of an 18 gauge pediatric catheter into the medullary compartment of the medial malleolus.

Group I: .005 mg/kg, .01 mg/kg, and .03 mg/kg of .01% atropine will be administered via peripheral IV access (saphenous vein). Central and peripheral blood samples will be taken at 30, 60, and 600 seconds. All serum samples will be saved for measured atropine levels. Group II: The same as Group I using the endotracheal route. Group III: The same as Group I using the intraosseous route. Data analysis will involve comparison of dose response curves and peak serum levels for each route.

Progress: The study was completed according to protocol. The mean time to peak atropine concentration was shortest with the I.V. route, while the intraosseous route was next, and the endotracheal route was longest. Animals exhibited considerable variability in time to peak concentration; however, the intraosseous route was quicker to reach peak plasma levels than the endotracheal. Consideration to routes of atropine administration other than the commonly employed intramuscular route which is generally slower than any of the other routes may be important in meeting the need for rapid pharmacologic response to acetylcholinesterase inhibitors. An abstract has been submitted for presentation at the 1986 Army Science Conference.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/82 Status: Completed

Title: Evaluation of Fluosol in Treatment of Decompression Syndrome (DCS)

Start Date: 21 Sep 84 Estimated Completion Date: Mar 85

Department: Emergency Medicine Facility: MAMC

Principal Investigator: CPT Fred Volinsky, MC

Associate Investigators: MAJ Lslie Yarbrough, VC
CPT Leonard M Checchio, MC

Key Words: rats, survival rate, Fluosol, decompression syndrome

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$750.00 Results: N/A

Study Objective: To evaluate the effectiveness of Fluosol DA in increasing the survival rate of rats after experimentally-induced decompression syndrome.

Technical Approach: Ten rats will be used to perfect necessary techniques for anesthesia, catheterization, and compression/decompression.

Group I (control group - 20 rats) will be anesthetized and have an external jugular vein catheterized. The rats will then be placed in a portable compression chamber (1000 PSI) and pressurized at the rate of 100 ft/min to a pressure of 7 ATM, at which pressure they will remain for one hr. They will then be rapidly decompressed at 60 ft/min (3 min) to 1 ATM. They will be removed and placed in an oxygen chamber containing 100% oxygen. At this time, they will receive an IV infusion of Dextran, 50% estimated blood volume, over 4 mins. Survival rate will be recorded until 60 min post-decompression.

Group II (experimental - 20 rats) will be anesthetized, catheterized, compressed, and decompressed in the same manner as Group I. They will be placed in 100% oxygen and receive an IV infusion of Fluosol DA-50% of estimated blood volume over a 4-minute period. Survival rates will be recorded until 60 min.

Group III (Fluosol infusion controls - 20 rats) will be anesthetized and catheterized the same as Groups I and II and then placed in a chamber which will remain open with no pressurization. At one hr, they will be placed in a 100% oxygen environment and 50% of estimated blood volume of Fluosol will be infused over 4 min. Survival rate will be recorded until 60 min. This group will provide data as to the mortality of Fluosol infusion.

Progress: The study was completed per protocol and a manuscript submitted for publication in June 1985.

The median survival time of Groups I and II were 6 and 20 minutes, respectively. All of Group III survived >60 minutes. No statistical difference in survival times of Groups I and II was found, utilizing the Mann Whitney U test. IV Fluosol was not found to be of benefit post-rapid decompression in this model.

DETAIL SHEETS
FOR
PROTOCOLS

DEPARTMENT OF FAMILY PRACTICE

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/37 Status: Terminated

Title: The Minnesota Multiphasic Inventory in Chronic Obstructive Pulmonary Disease

Start Date: 24 May 85 Estimated Completion Date: May 85

Department: Family Practice Facility: MAMC

Principal Investigator: CPT Patrick M. Carter, MC

Associate Investigator: MAJ Anthony Zold, MSC

Key Words: COPD, Minn Multiphasic Inventory, questionnaire

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: 30.00 Results: N/A

Study Objective: to examine patients hospitalized primarily for chronic obstructive pulmonary disease (COPD) to attempt to determine the personality traits that relate essentially to the COPD and not to all the other confounding variables.

Technical Approach: Patients studied will be those admitted to MAMC with a diagnosis of exacerbation of COPD. Patients with aminopterin drip, wheezing, an additional psychiatric diagnosis requiring medication or abnormal peak flow rates or PAO₂ levels will be excluded. Patients will be administered the MMPI on the second or third day of hospitalization to avoid situations of acute respiratory distress. They will also be given a short questionnaire designed to help define the patient's social situation and smoking and alcohol history, as well as severity of COPD.

A control population will be obtained by selecting the next patient admitted to the adult medicine ward at MAMC of the same sex and race and within 5 years of age of the study patient. The control patients would be limited to those without documented COPD. The exclusion criteria of the COPD subjects would also apply to the control patients. The controls would also be requested to fill out an MMPI and a questionnaire.

Analysis of the data will involve testing for bivariate, multivariate, and canonical correlation between the various items on the questionnaire and MMPI, and the presence or absence of COPD. The bivariate analysis will look for simple correlations between MMPI scale results and presence or absence of COPD. The multivariate analysis will analyse individual MMPI scales and questionnaire answers to find which test results would be significant predictors of presence of COPD. The canonical correlation procedure identifies the linear combination within each set of variables that maximizes the correlation between the sets. An example of useful information that might derive from canonical correlation would be 2 or 3 MMPI scale scores that separately do not significantly predict presence of COPD, but that taken together do provide a significant predictor.

Progress: This protocol was terminated due to the departure of the principal investigator. No report is available on number of patients entered.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/19 Status: Terminated

Title: Prevention of Adverse Reactions to Ibuprofen with
Adjunctive Therapy

Start Date: 16 Nov 84 Estimated Completion Date: Apr 85

Department: Family Practice Facility: MAMC

Principal Investigator: CPT Daniel R. Davidson, MC

Associate Investigator: CPT Bruce A. Woolman, MC

Key Words: Ibuprofen, reactions, prevention, Maalox, milk, water

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$50.00 Results: N/A

Study Objective: To determine if the gastrointestinal reactions associated with ibuprofen therapy can be prevented or palliated by taking the medication with either water, food and milk, or magnesium and aluminum hydroxide (Maalox) and to determine how soon gastrointestinal symptoms, if any, occur after ingestion of ibuprofen with the above mentioned adjuncts.

Technical Approach: Subjects (150) will fill out a pre-study questionnaire to determine smoking and coffee habits and problems taking anti-inflammatory medications. Patients will be randomly assigned to take ibuprofen, 600 mg t.i.d., plus either water, food and milk, or Maalox. After one week of treatment, patients will be followed-up by telephone to ascertain the occurrence of side effects and verify the dosage schedule and adjunct utilized. Data will be compiled for side effects and when and if the medication was discontinued in each group.

Progress: Protocol was terminated due to departure of principal investigator. No report available on number of patients entered.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 83/87 Status: Transferred

Title: A Comparison of Nystatin and 1% Hydrocortisone Cream to Nystatin Alone in the Treatment of Diaper Rashes

Start Date: 16 Sep 83 Est Completion Date: Nov 83

Dept: Family Practice Facility: MAMC

Principal Investigator: CPT Matthew Gaspar, MC

Associate Investigators: LTC James W. Higbee, MS

CPT Karl Friedl, MS

CPT Cheryl Wofford, AN

Key Words: type of rash, amount of erythema, location of rash

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: 600.00 Results: N/A

Study Objective: To test the hypothesis that the use of Nystatin cream and 1% Hydrocortisone cream significantly increases the rate of healing of simple diaper rashes when compared to Nystatin cream alone, 1% Hydrocortisone cream alone, or a placebo.

Technical Approach: Approximately 200 untreated infants of both sexes from one to 24 months of age will be evaluated as to the presence of a typical irritant type diaper dermatitis or candidiasis. Infants with seborrheic, atopic, impetiginous, or bacterial type lesions will be excluded from the study. All infants will be graded initially as to the type of rash isolated, the amount of erythema, and the location of rash. The rash will be cultured by gently scrubbing the margins of the rash with a swab moistened in transport media. The swab will be plated on Sabouraud agar for yeast and fungal growth and on McConkeys' and blood agar for gram negative and gram positive growth respectively. A questionnaire will then be completed. Mothers will then be issued in a blind, randomized fashion: water-based cream; Nystatin cream; 1% Hydrocortisone cream, or Nystatin cream with 1% Hydrocortisone cream. Mothers will be instructed to apply the cream evenly to the affected area four times daily. No other medications will be permitted during the study period. A reassessment will be made as to the effect of treatment 10 to 14 days later and the lesions or site of the lesions recultured. An instruction sheet concerning general skin care and diapering techniques will be explained and the parents will be given a follow-up appointment in 7 to 10 days. At the conclusion of the study, the patient code will be broken and statistical analysis performed using the Mann-Whitney test for non-parametric data.

Progress: Data from 40 subjects were studied and the initial results were inconclusive. MAJ Gaspar is now assigned to Womack Army Hospital where he has submitted the protocol and it has been approved. He will continue to enter patients there and CPT Karl Friedl of MAMC will continue to do the data analysis.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 84/71	Status: Completed
Title: Personnel Management Behaviors of Family Physicians		
Start Date: 17 Aug 84	Est Completion Date: Apr 85	
Dept: Family Practice	Facility: MAMC	
Principal Investigator: CPT Matthew Gaspar, MC		
Associate Investigators: None		
Key Words: Power Perception Profile, Leader Effectiveness and Adaptability Description		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: \$750.00	Results: N/A

Study Objective: To explore the personnel management behaviors of family physicians based on relationship behavior, task behavior, and power.

Technical Approach: All practicing family physicians or residents on active duty at Madigan Army Medical Center, Silas B. Hays Army Hospital, and Bremerton Naval Regional Medical Center will participate in this survey on personnel leadership skills. Because a small sample size is predicted, randomization will not occur. Proctored testing will take place during the practice board exams for Family Practice. The surveys will be administered to the staff physicians during faculty development seminars. Each physician will complete a demographic questionnaire to tabulate personal data, graduate education, business education or experience, and military experience. This will be followed by two surveys designed to assess behavioral aspects of personnel management. The first is the Power Perception Profile which quantifies power according to seven categories; coercive, connection, expert, information, legitimate, referent, and reward. This will be followed by the Leader Effectiveness and Adaptability Description which describes business management skills according to relationship behavior, task behavior, and leader effectiveness. This test measures three important aspects of personnel management that quantify a leader's perception of his interactions with his staff. The demographic data will be used to ascertain differences in management training among physicians. If marked differences exist, based on the number of courses taken by each physician, then first order statistics will determine whether training in management will bias the survey scores.

Progress: Military family physicians in the three residency training programs completed the study as described. The physicians' perception of power on the dimensions of coercion, connection, expertise, information, legitimacy, reference, and reward were similar except those with advanced military experience who had lower expert power scores and higher connection power scores, and those with background military experience who had lower information power scores. Physicians' scores were high in expert power and low in coercive and connection power. Most physicians exhibited a combination of high task and high relationship behaviors. The least frequent combination was low relationship and low task behaviors. If a physician must choose between either task or relationship behaviors, then relationship behaviors will dominate over task oriented behaviors. The exception is the intern who will choose task behaviors over relationship behaviors. A thesis has been completed as a result of this study.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/03 Status: Completed

Title: The Impact of Notification of High-Risk Status on Patient Acceptance of Influenza Immunization, on Subsequent Patient Morbidity and Mortality, and on Total Health Care Costs

Start Date: 21 Oct 83 Est Completion Date: Apr 84

Department: Family Practice Facility: MAMC

Principal Investigator: LTC David W. Roberts

Associate Investigators: LTC James W. Higbee, MSC

CPT Cheryl Wofford, ANC

CPT Stephen A. Spaulding, MC

Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: 3350.00	Results: Completed

Study Objective: To test the hypothesis that actively seeking out and notifying those patients in a given practice population that are at high risk of complications from influenza results in a significantly higher percentage of high-risk patients accepting immunization when compared to a similar high-risk population not actively notified and to test the hypotheses that such notification results in decreased morbidity and mortality due to influenza and a significant reduction in overall health care costs to the military, when compared to the non-notified group.

Technical Approach: High-risk Family Practice (FP) patients will be identified by computer and randomized to either receive no notification of their high-risk status or being notified and recommending that they take the for influenza immunization. Immunizations will follow the standard procedure and nursing staff will check to see if the individual is on the list of subject patients. All study patients suspected of having influenza will have specimens taken for viral culture. Paired acute and convalescent sera will be obtained on these patients also, with H-I titers performed. Diagnoses of influenza, pneumonia, acute URI, viral illness, or acute bronchitis will be totaled monthly and at the conclusion of the study period for all study patients. All inpatient admissions of study patients will be screened for the diagnoses of influenza or pneumonia, and/or death. Hospitalizations will be tabulated for use in the final analysis. Data to be analyzed: percentage of group receiving immunization; requiring at least one clinic visit for the diagnosis studied; and with episodes of culture-proven influenza. For comparison with prior studies, the percentage of shot-receivers with subsequent clinical visits and lab evidence of influenzal infection will be compared to the non-receivers. Total health care costs in the notified group versus the non-notified group will be analyzed.

Progress: Preliminary results show that notification is of significant benefit especially in the over 40 group.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/69 Status: On-going

Title: Preventive Cardiology Demonstration and Education
Research Grant

Start Date: 17 Aug 84 Est Completion Date: Jun 88

Department: Family Practice Facility: MAMC

Principal Investigator: LTC David W. Roberts, MC

Associate Investigators:

Daniel J. Erickson, M.D.

Craig S. Scott, Ph.D.

William Neighbor, M.D.

Steven C. Macdonald, M.P.H.

Robert L. Van Citters, M.D.

Douglas C. Schaad, M.Ed.

Marcia Hunt, B.A.

Key Words: attitudes, knowledge, clinical practice, intervention
group, residents.

Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: The primary aim of the NHLBI Education/Demonstration Preventive Cardiology Project is introducing concepts and practice relating to primary prevention of coronary disease into the basic training of Family Practice residents in the University of Washington Family Practice Residency Network. The hypothesis to be tested is that a core curriculum of preventive cardiology integrated into the existing curriculum of a Family Practice residency training program will result in measurable modification of the attitudes, knowledge, and clinical practice of an intervention group of residents as compared to internal and external controls.

Technical Approach: All residents in the Madigan Family Practice Residency will be asked to test for their attitudes and knowledge of preventive cardiology. Following testing, a curriculum in preventive cardiology will be developed. This curriculum will be developed and administered in conjunction with the staff of the Department of Family Practice at Madigan. In an attempt to personalize the process of cardiovascular risk assessment, an individual cardiovascular risk profile will be made available to the residents. Clinical practice of preventive cardiology by residents will be measured by an audit of patient charts at twice yearly intervals. The audit will be conducted by Preventive Cardiology staff auditors from the University of Washington.

Progress: During FY 85, the first year of the Preventive Cardiology curriculum was presented. Patient charts were audited using the selection techniques outlined in the protocol. A leadership conference was held in May 85 at which time changes in the exact method of delivery of the curriculum were discussed. The curriculum is scheduled to begin again in Jan 86 under a slightly different format.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/01 Status: Terminated

Title: The Early Treatment of Presumptive Streptococcal Pharyngitis with Penicillin V with Symptomatic Treatment versus Placebo with Symptomatic Treatment

Start Date: 19 Oct 84 Estimated Completion Date: Sep 85

Department: Family Practice Facility: MAMC

Principal Investigator: CPT David W. Smith, MC

Associate Investigators:

COL Marvin S. Krober, MC

LTC Thomas Oberhofer, MC

LTC James W. Higbee, MSC

LTC David T. Zumek, MSC

Key Words: rheumatic fever, prophylaxis, strep ID test

Accumulative MEDCASE

Est Accumulative

Periodic Review

Cost: -0-

OMA Cost: \$780.00

Results: N/A

Study Objective: To determine whether the early treatment of suspected streptococcal pharyngitis with Penicillin V for rheumatic fever prophylaxis, prior to throat culture results, significantly alters the natural course of pharyngitis within the first 48-72 hours of symptoms after presentation to a medical care provider.

Technical Approach: Entrance criteria include age 5-21 yr, complaint of any degree of sore throat, fever $>99.0^{\circ}\text{F}$, orally, and a positive strep ID test. Exclusion criteria include patients with immediately treatable infections, >5 -day history of sore throat, history of rheumatic fever or family member with history, parenteral antibiotics within previous 3 weeks or oral antibiotics within previous 3 days, allergies to medications being used, inability to take anything orally, or a debilitating illness such as neutropenia or immunodeficiency. After history and physical exam, symptoms of degree of sore throat, pain on swallowing, rhinorrhea, otalgia, cephalgia, malaise, nausea, vomiting, abdominal pain, cough, hoarseness, signs of cervical adenitis, erythema and exudate in the pharynx, ulcerations, palatal petechiae, and coryza will be recorded. Patients will then have a throat culture taken from the posterior pharyngeal wall and bilateral tonsillar pillars which will be plated on sheep-blood agar plates with bacitracin disc as a means of identifying Group A beta hemolytic Streptococcus in addition to the performance of a strep ID test. Every six hours prior to receiving medication over the next 72 hr, patients will fill out a questionnaire on which they will scale the degree of severity of sore throat on a scale of 0-10 (10 = most severe) and also indicate oral temperatures and times at which they took acetaminophen and 1-2-3 gargle. For four days, patients will take every 6 hours either penicillin V in doses of 250 mg q.i.d. or placebo along with acetaminophen and 1-2-3 gargle. Patients will be reexamined in 72 hours and have results of throat culture checked. If the culture is positive, the patient will be begun on an appropriate course of antibiotics.

Progress: CPT Smith was unable to complete this study before being reassigned to Germany. MAJ Richard Waldrup was to complete the study but was unable to due to time restraints. CPT Smith will pursue this study at his new duty station.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/48 Status: On-going

Title: Identification of Adolescents at Risk for Pregnancy

Start Date: 15 Mar 85 Estimated Completion Date: Apr 86

Department: Family Practice Facility: MAMC

Principal Investigator: CPT Stephen Sorsby, MC

Associate Investigators: MAJ Anthony Zold, MSC

Rita Sorenson, R.N.

Key Words: unmarried, pregnant, nonpregnant, questionnaires

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$212.00 Results: N/A

Study Objective: To identify those factors which place an adolescent girl at increased risk for pregnancy, concentrating on those items which would be easily identified by her primary care physician.

Technical Approach:

Pregnant adolescents: Every unmarried adolescent visiting the Adolescent Obstetrical Clinic in her second trimester will be asked to complete a questionnaire during the course of that clinic visit regarding family, education, social life, socioeconomic status, and other activities plus questions regarding sexual activity. This will continue for one year or until 50 girls have entered the study.

Non-pregnant adolescents: Every unmarried female adolescent enrolled in the Family Practice Clinic will be mailed a letter requesting that they fill out a modified version of the questionnaire which has additional questions regarding why the subject has not yet started sexual activity

DATA PROCESSING: After collection of the questionnaires is completed, the control and pregnant groups will be compared statistically to determine if the groups are comparable in terms of age and socioeconomic status. If so, the data obtained will be compared to determine what, if any, significant differences exist. If the two groups are not comparable, the pregnant girls will be matched with controls before evaluation of the data is carried out.

Progress: Twenty-three (23) pregnant subjects entered; findings will not be reviewed until completion of study to avoid bias. Requests for participation to control subjects were just recently distributed; no results yet.

D E T A I L S H E E T S
F O R
P R O T O C O L S

DEPARTMENT OF MEDICINE

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/57 Status: On-going

Title: Pilot Study for Treatment of Refractory Breast Cancer with Cis-Platinum and 5-Fluorouracil Infusion

Start Date: 18 May 84 Est Completion Date: May 86

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Thomas Baker, MC

Associate Investigators: MAJ Howard Davidson, MC

COL Friedrich H. Stutz, MC MAJ Timothy J. O'Rourke, MC

LTC Irwin B. Dabe, MC CPT Michael D. Stone, MC

Key Words: cis-platinum, 5FU, response rate, duration of response

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Co: -0- Results: Continue

Study Objective: To determine the anti-tumor activity of cis-platinum followed by continuous 4-day infusion of 5-FU given every 3 to 4 weeks in patients with metastatic carcinoma of the breast who have failed standard chemotherapy regimens, utilizing response rate and duration of response to measure the activity and to determine the toxicity of the combination of 5-FU by continuous infusion over 4 days and high dose cis-platinum when given with hypertonic saline, magnesium, hydration, and aggressive antiemetic therapy.

Technical Approach: Following a 24-hr urine collection and simultaneous calculated creatinine clearance >60 cc/min and adequate IV hydration with D5 and normal saline, cis-platinum, 120 mg/M², in 500 cc of 3% saline plus 500 CC solution of 20% mannitol and 3 grams of magnesium sulfate, will be given by IV infusion over 2 to 4 hours. This will be followed by continuous hydrating fluids. The day following cis-platinum chemotherapy, the patient will be started on 5-FU, 1 mg/M², by continuous IV infusion days 2 through 5. This will be followed by standard antiemetic regimens. This regimen will be repeated every three to four weeks as tolerated by the patient. Dosages will be modified as required by creatinine clearance and toxicity.

Progress: No new subjects were entered in the study in FY 85. Previously, two patients had been studied with no unexpected adverse toxicity or reactions in one patient and delayed nausea and vomiting, which subsequently subsided, in the second.

Detail Summary Sheet

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

Title: Phase II Study of Cisplatin Plus Continuous Infusion 5-Fluorouracil and Radiotherapy in Locally Advanced Esophageal Cancer (Part 1 and Part 2) - to be Done in Conjunction with the University of Indiana

Start Date: 18 Jan 85 Estimated Completion Date: Nov 86

Department/Service: Medicine/Hematology Facility: MAMC

Principal Investigator: MAJ Thomas M. Baker, MC

Associate Investigators: MAJ Andrew C. Fiore, MC

MAJ Pushpa M. Patel, MC

Key Words: Response rate, duration of remission, survival

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To evaluate: the response rate, duration of remission, and survival of patients with carcinoma of the esophagus treated concomitantly with Cisplatin plus 5-FU and radiotherapy prior to surgical resection and in non-surgical patients; the toxicity of chemotherapy given in combination with radiotherapy; the survival of patients with residual disease at surgery following additional radiotherapy post-operatively; Cisplatin plus 5-FU in locally advanced esophageal carcinoma. Also, to determine the toxicity of the proposed treatment regimen and to confirm results reported from other institutions utilizing this approach.

Technical Approach: Part 1: Patients who are thought surgically resectable will receive preoperative chemotherapy (2 courses of Cisplatin and 5-FU) and radiation therapy (3000 R over 3 weeks), concomitantly. Surgery will be done 3 weeks after completion of the second course of chemotherapy. Those patients who had a negative celiotomy with resection of the primary and are found to have residual disease in the resected esophagus or nodes will receive an additional 2000 R (daily 5 days a week for 2 weeks), to start no sooner than 3 weeks after surgery.

Part 2: Patients that are ineligible for surgery because of unresectability or inoperability or patients that refuse surgery will be treated with a combination of chemotherapy and radiation therapy (5000 R - daily 5 days a week for 5 weeks) after which response will be assessed and feasibility of subsequent surgery will be discussed with the patient.

In both parts, chemotherapy will consist of Cisplatin 20 mg/M² on days 1-4 and days 29-32; 5-FU will be given as a continuous infusion over 24 hours on days 1-4 and days 29-32.

Progress: No patients entered on this protocol.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/31 Status: On-going

Title: The Use of Serial Bone Scans, X-Rays, and CT Scans in Assessing the Response of Bone Metastasis to Systemic Treatment

Start Date: 18 Jan 85 Estimated Completion Date: Jan 87

Dept/Svc: Medicine/ Hematology Facility: MAMC

Principal Investigator: MAJ Thomas Baker, MC

Associate Investigators: COL Robert Karl, MC

COL John Redmond, MC

MAJ Howard Davidson, MC

Key Words: adenocarcinoma, multiple myeloma, lymphoma, x-rays bone scans, CT scans

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To examine the utility of bone CT scanning as compared to TC 99-M nucleotide bone scans and plain radiographs in assessing the response of bone metastasis to systemic chemotherapy treatment.

Technical Approach: Eligible patients will be those with life expectancy of at least four months with histologically proven adenocarcinoma of the breast or prostate, multiple myeloma or lymphoma who have evidence on bone scan or x-ray of bone involvement and for whom a new systemic therapy is planned. Patients will receive standard systemic treatment, either hormonal manipulation or chemotherapy. At 0, 3, and 6 months the following observations and testing will be done: area of pain and dosage of pain medication will be recorded; performance status and weight; clinical impression of response, bone scans, plain radiographs of involved lesions, and CT scan of area of concern.

Progress: Five patients had serial CT scans to follow response/progression of metastatic disease. At this time, there are no significant data to report.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/79 Status: Completed

Title: CPAP Induced Changes in Gastrointestinal Gas

Start Date: 23 Aug 85 Est Completion Date: Sep 85

Dept/Svc: Medicine/Pulmonary Facility: MAMC

Principal Investigator: COL J. Waylon Black, MC

Associate Investigators: MAJ W. Hal Cragun, MC

CPT Ronald K. Fullmer, MC

CPT Bruce S. Grover, MC

Key Words: CPAP, lung volume determination, nitrogen washout technique, body plethysmographic method, underwater weighing

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To determine if continuous positive airway pressure (CPAP) applied via a face mask causes increased gastrointestinal gas.

Technical Approach: Ten young, healthy adult volunteers will have lung volume determinations done by the nitrogen washout technique and body plethysmographic method, as well as a plethysmographic estimate of gastrointestinal gas. Subtracting the nitrogen washout determination of lung volume from the plethysmographic volume will give a measure of gastrointestinal gas. The subject will also be weighed in water. The subject will then receive 10 cm water CPAP for four hours and the above measurement will be repeated. Any change in amount of gastrointestinal gas will be recorded. A control group of 10 volunteers will be weighed underwater and then weighed a second time four hours later not having been on CPAP. Both study and control groups will be NPO from midnight until the testing is completed.

Progress: Ten subjects were studied per the protocol. Ten (10) cm H₂O of CPAP by face mask for four hours does not increase intestinal gas volume in normal subjects.

Colon catheters work as well as gastric catheters for plethysmographic measurement of intestinal gas volume.

Underwater weighing is the most sensitive method for measuring changes in intestinal gas volume.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No: 84/52 Status: Terminated

Title: Gastric Ulcer Healing by Cimetidine, Sucralfate, or Combined Therapy: Speed of Healing, Safety, and Efficacy for Ulcers Resistant to Healing by One Agent Alone

Start Date: 18 May 84 Estimated Completion Date: Jul 85

Dept/Svc: Medicine/Gastroenterology Facility: MAMC

Principal Investigator: MAJ V. Duane Bohman, MC

Associate Investigators: LTC Thomas F. O'Meara, MC
MAJ Dennis I. Greenberg, MC
MAJ Michael H. Walter, MC

Key Words: double-blind study, Tagamet, and Carafate

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$1076.00 Results: N/A

Study Objective: To determine if gastric ulcers can be healed faster and more completely with two anti-ulcer drugs than with one.

Technical Approach: Patients meeting the admission criteria will be entered no more than 72 hours after endoscopic confirmation of gastric ulceration and the absence of concomitant upper gastrointestinal disease. During the 12-week period of treatment, the patient will receive either sucralfate and cimetidine placebo, cimetidine and sucralfate placebo, or sucralfate and cimetidine on a doubleblind, randomized basis. All drugs and placebos will be swallowed with water (without chewing) one hour before the three daily meals and at bedtime. Follow-up endoscopies will be scheduled for 2, 4, and 12 weeks to allow for accelerated early healing and assessment of complete healing rates. If after 12 weeks the ulcer has not healed and the patient received only one drug, he will be given both drugs for an extra four weeks and then rechecked. Any patient showing a significant worsening of gastric ulcer disease will be dropped from the study and placed on alternative treatment and will be considered a drug failure. Smoking and coffee and alcohol consumption will be recorded as well as age, sex, occupation, family history of ulcers, and gastric pH. The critical parameter of efficacy assessment will be complete healing.

Progress: Protocol terminated due to departure of the principal investigator. Also, the number of subjects available was not sufficient to complete the protocol.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No: 85/41 Status: Terminated

Title: Healing of Esophageal Ulceration with Antacids and
Sucralfate

Start Date: 22 Feb 85 Estimated Completion Date: Jul 85

Dept/Svc: Medicine/Gastroenterology Facility: MAMC

Principal Investigator: MAJ Duane Bohman, MC

Associate Investigators: LTC Thomas O'Meara, MC
LTC Michael H. Walter, MC
MAJ Leslie Yarbrough, VC

Key Words: Drug-induced, tetracycline, dogs

Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: \$855.00	Results: N/A

Study Objective: To evaluate in a blinded, randomized fashion, the relative healing rates of drug-induced esophageal ulcers in an animal model utilizing potentially efficacious therapies.

Technical Approach: Eighteen healthy dogs will be randomized into three equal treatment groups. Baseline data will include breed, sex, weight, and oral intake average daily.

Day 1: Under general anesthesia, all dogs will be endoscopically evaluated and the length of the esophagus recorded. Any abnormality of the esophagus will exclude the dog from the study. A distance of 1/3 the length of the esophagus from the mouth to the esophagogastric junction will be localized, and the measurement recorded. An injection through a needle used to sclerose esophageal varices will be done submucosally with tetracyclin (125 mg).

Day 3: Under general anesthesia all dogs will be endoscoped in blinded fashion and the location and sizes of the ulcerations recorded. Oral intake, medications given, and additional endoscopic observations will be recorded. Following the baseline endoscopic evaluation performed on day 3, the dogs will be treated in a randomized fashion with: Group 1 - Mylanta II, 30 cc orally 1 and 3 hours after meals and at bedtime (7X/day); Group 2 - Sucralfate, 1 gram as a slurry on an empty stomach, 4X daily; Group 3 - no treatment. Food will be presented three times daily at set hours to allow proper dosing of medications.

Days 6, 10, and possibly 14 and 20: Under general anesthesia all dogs will be reendoscoped and esophageal ulcers evaluated as to the extent of healing. Size will be recorded after measuring with a standard probe with 1 mm markings to guarantee accuracy of the measurements. Oral intake, medication given, and additional endoscopic observations will be recorded with each evaluation.

PROGRESS: The project has been terminated because ulcers could not be created in several trials and an abstract was presented by investigators at another institution during this time period reporting essentially the same information.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No: 80/19 Status: Completed

Title: 5-Azacytadine in Acute Leukemia

Start Date: 15 Feb 80 Estimated Completion Date: Mar 82

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: LTC Irwin B. Dabe, MC

Associate Investigators: COL COL F. H. Stutz, MC

MAJ Lauren Colman, MC

Key Words: 5-azacytadine, every three weeks for three courses

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To examine the efficacy of 5-Azacytadine in patients with acute leukemia refractory to conventional therapy.

Technical Approach: 5-Azacytadine will be given in a dose of 300 mg/M²/day for 5 days in three or four divided doses each day. Courses will be repeated every three weeks unless there is earlier evidence of recovery from myelotoxicity. If bone marrow cellularity is less than 20% at three weeks from the last course, chemotherapy will be withheld until marrow cellularity exceeds 20%. Dosages for the next course will then be reduced by one third. If there is no improvement in the bone marrow after the initial course, the drug dosage for the second course will be increased by one third.

Progress: No patients have been entered on this protocol during the past two years. The agent was used for second or third line therapy ANLL patients. Patients in recurrent ANLL tend to be very refractory to all agents. No meaningful duration of remission was seen with this agent in patients entered in previous years.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 85/32	Status: On-going
Title: The Use of Serial Computed Tomography (C.T.) Scans to Evaluate Response to Radiation Therapy		
Start Date: 18 Jan 85	Estimated Completion Date: Jan 87	
Dept/Svc: Medicine/ Oncology	Facility: MAMC	
Principal Investigator: MAJ Howard Davidson, MC		
Associate Investigators:		
COL Robert Karl, MC	LTC Irwin B. Dabe, MC	
COL John Redmond, MC	MAJ Thomas Baker, MC	
Key Words: metastatic lesions, bone, x-rays, bone scans, CT scans		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: N/A

Study Objective: To examine the utility of bone CT scanning to assess the response of bone metastasis to radiation therapy.

Technical Approach: Patients with a life expectancy of at least six months with tissue proven metastatic lesions to bone who have not previously received radiation to the local lesion will be eligible. The lesion must be detected prior to radiation therapy by CT scanning. At 0, 3, and 6 months the following observations and testing will be done: area of pain and dosage of pain medication will be recorded; performance status and weight; clinical impression of response, bone scans, plain radiographs of involved lesions, and CT scan of area of concern.

Progress: Three patients were entered. Serial CT scans showed stable disease in one patient, progression of disease in the second, and the third patient refused follow-up CT's because of claustrophobia.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/25 Status: On-going

Title: Efficacy & Safety of Trimethoprim-Sulfamethoxazole vs Ampicillin in the Treatment of Upper Urinary Tract Infections

Start Date: 18 Jan 85 Estimated Completion Date: Jun 85

Dept/Svc: Medicine/Infectious Disease Facility: MAMC

Principal Investigator: COL Peter J. Gomatos, MC

Associate Investigators: MAJ John W. Gnann, MC

CPT Michael Lyons, MC

Key Words: Pyelonephritis, intravenous antibiotics

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To compare the safety, clinical efficacy, and bacteriological efficacy of trimethoprim-sulfamethoxazole and ampicillin in the treatment of hospitalized patients with infections of the upper urinary tract.

Technical Approach: Patients with suspected pyelonephritis requiring IV antibiotics will be randomized to receive trimethoprim-sulfamethoxazole 10 ml (160 mg trimethoprim plus 800 mg sulfamethoxazole) I.V. every 12 hr plus gentamicin 1 mg/kg every 8 hr (adjusted for creatinine) or ampicillin 500 mg I.V. every 6 hr plus gentamicin 1 mg/kg every 8 hours (adjusted for creatinine). Medications will be given for at least 72 hr or until the patient has been afebrile for 24 hours. If urine culture does not reveal *Pseudomonas aeruginosa* or other resistant pathogens, the gentamicin will be discontinued after 24 hours. After the antibiotics are stopped, the patient will receive the corresponding oral preparation to complete a 14 day course. Urine culture and analysis, blood culture, CBC, SGOT, and creatinine will be obtained at predetermined intervals. Symptoms and physical findings will be recorded daily. Studies on urine bacteria isolates will include quantitation, antibiotic disc susceptibility testing, and MIC determination. Specimens will be sent to the University of Washington for ACB determination, *E. coli* serotyping, and piliation studies.

Progress: MAJ John Gnann was the original principal investigator on this protocol. Upon his departure 26 June, COL Gomatos became the principal investigator. Nine of 34 subjects had organisms resistant to ampicillin and none resistant to trimethoprim-sulfamethoxazole. Two patients required a change in treatment due to antimicrobial resistance. Complications included one patient with ampicillin-induced drug eruption and a recurrent urinary tract infection in one patient treated with ampicillin and one treated with trimethoprim-sulfamethoxazole. Preliminary results indicate that patients can be safely treated with I.V. followed by oral trimethoprim-sulfamethoxazole for pyelonephritis. Due to antimicrobial resistance to ampicillin, it is also recommended that trimethoprim-Sulfamethoxazole should be treatment of choice.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 83/81	Status: On-going
Title: Studies on Fatty Acid Activation in Spermatozoa: Kinetics and Localization		
Start Date: 16 Sep 83	Est Completion Date: Sep 84	
Dept/Svc: Medicine/Endocrine	Facility: MAMC	
Principal Investigator: MAJ Robert E. Jones, MC		
Associate Investigators: COL Bruce L. Fariss, MC COL Stephen R. Plymate, MC		
Key Words: Palmitic acid, ATP, Mg++, CoASH, time and protein dependency curves, enzyme location/latency		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: \$785.00	Results: Continue

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 use 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 microcuries 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 200 million per ml. The assay mixture will contain palmitic acid, ATP, Mg++ and CoASH and will be initiated by the addition of the washed sperm preparation. Time and protein dependency curves will be run to determine the length of incubation needed to achieve first order kinetics in the measurement of initial velocities. Both Lineweaver-Burk plots and hyperbolic best-fit will be used to calculate approximate Km values for each substrate. Temperature, pH curves, and rates with alternate substrates will also be run. Enzyme location/ latency will be determined by assaying separate cell fractions prepared by sonication and differential centrifugation of the isolated sperm. The effects of sufhydrl reagents, albumin, and detergents will be studied to assist in estimation of latency.

Progress: The saturated free fatty acid substrate specificity for ligase was determined using even chain fatty acids with chain lengths ranging from 12 to 22 carbons. Activity was only seen with myristic (14:0), palmitic (16:0), and stearic (18:0) acids. The maximum activity was seen with 16:0 followed by 18:0 and 14:0 showing 41.5% and 22.5% of the activity observed with 16.0. The Km's for these fatty acids were identical ranging from 4-5 μ M. This study resulted in a publication in the Journal of Andrology and a presentation at the 3rd International Congress of Andrology.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/83 Status: Completed

Title: *In Vitro* Characterization of a LH-TSH Secreting Pituitary Macroadenoma

Start Date: 21 Sep 84 Est Completion Date: Dec 84

Dept/Svc: Medicine/Endocrine Facility: MAMC

Principal Investigator: MAJ Robert E. Jones, MC

Associate Investigators: COL Bruce L. Fariss, MC

COL Stephen R. Plymate, MC

LTC James W. Higbee, MSC

Mina G. Garrison, M.T., DAC

Key Words: LH, TSH, FSH, growth hormone, calcium

Accumulative MEDCASE

Est Accumulative

Periodic Review

Cost: -0-

OMA Cost: \$1200.00

Results: N/A

Study Objective: To establish a human TSH secreting pituitary adenoma in tissue culture in order to study the TSH secretory response to a variety of secretagogues.

Technical Approach: Adequate tissue was obtained at surgery for histologic studies. The additional tumor will be placed in sterile media, consisting of 2.5% collagenase, 5% trypsin and 0.2 µg/ml DNase (in Hanks balanced salt solution) for 80 minutes to achieve cell disposal. Fetal calf serum will be added as a non-specific enzyme inhibitor, and the cells will be gently resuspended by manual pipetting, washed in media 199 and plated in 10 ml wells (≈0.5-1 million cells/well). The cells will be cultured in media 199 fortified with 10% fetal calf sera, Hanks salts and streptomycin/penicillin to retard bacterial growth. The tissue will be incubated at 37°C using a humidified atmosphere consisting of 5% CO₂ and 95% air. Media will be changed every two days and will be saved for baseline hormone determinations. Twenty-four hours prior to testing with LHRH, TRH, and somatostatin, the fortified media will be replaced with serumless 199. The hypothalamic hormones will be introduced in nanomolar quantities and the culture will be returned to the incubator. After 24 hours, the media will be removed for assay (LH, TSH, FSH, growth hormone, and two subunits) and exchanged for the fortified 199. The effects of calcium will be studied by performing similar experiments in calcium free Hanks or by co-incubating the cells with verapamil.

Progress: The analysis of the spent tissue culture media has been completed. The assays performed on the media included TSH, free alpha subunit, beta immunoreactive LH, and bioactive LH. Initially, the tumor secreted 100 µU/well/day of TSH, 3000 ng/well/day of immunoreactive LH, and 300 ng/well/day of alpha subunit. Biologically, Sephadex G75 demonstrated that the LH was actually uncombined free alpha and beta subunits. This study resulted in a presentation to the 2nd Annual Army American College of Physicians Regional Meeting, September 1985.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 85/17	Status: Ongoing
Title: Establishment of a Long Term Mammalian Hepatocyte Tissue Culture		
Start Date: 19 Nov 84	Estimated Completion Date: Nov 85	
Dept/Svc: Medicine/	Facility: MAMC	
Principal Investigator: MAJ Robert E. Jones, MC		
Associate Investigators: COL Stephen R. Plymate, MC		
LTC James W. Higbee, MSC		
CPT Karl E. Friedl, MSC		
Key Words: Biomatrix, rabbit, rat, liver		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: \$1075.00	Results: Continue

Study Objective: To examine the feasibility of establishing a hepatocyte monolayer culture using a homologously derived bio-matrix.

Technical Approach: Both rat and rabbit livers will be used. The animals will be anesthetized and the liver will be perfused *in situ* with Hank's BSS with 0.5 mM EGTA and 0.05 M HEPES, followed by a RPMI 1640-based collagenase solution. Upon completion of the dispersal step, the liver will be excised, trimmed, and gently disrupted. The hepatocytes will be harvested by centrifugation and counted to insure a proper plating density. Liver biomatrix will be prepared, isolated, and sterilized by exposure to gamma rays. The biomatrix will be layered in tissue culture wells, utilizing RPMI 1640 supplemented with insulin, glucagon, ECG, prolactin, growth hormone, linoleic acid, and trace elements as the nutrient medium. Penicillin, streptomycin, and fungizone will be added to retard bacterial/fungal growth. The cells will be grown in a humidified incubator at 37°C in a 95% air/5% CO₂ atmosphere. The media will be changed in the laminar flow hood every 48-72 hr and the viability of cells will be intermittantly assessed by measuring trypan blue exclusion.

Progress: Four animals have been sacrificed according to protocol in an attempt to perfect the tissue culture technique. To date, progress is satisfactory.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/74 Status: Ongoing

Title: Influence of Acute Verapamil Infusion on Pituitary
Responsiveness to Exogenous GnRH

Start Date: 28 Jun 85 Est Completion Date: Jan 86

Dept/Svc: Medicine/ Endocrine Facility: MAMC

Principal Investigator: MAJ Robert E. Jones, MC

Associate Investigators: COL Stephen R. Plymate, MC

CPT Karl E. Friedl, MSC

Louis A. Matej, B.S., DAC

Key Words: verapamil, GnRH, LH

Accumulative MEDCASE

Est Accumulative

Periodic Review

Cost: -0-

OMA Cost: \$1673.20

Results: N/A

Study Objective: To ascertain what role the calcium/calmodulin system plays in modulating the GnRH-stimulated secretion of biologically active lutenizing hormone (LH).

Technical Approach: Six normal male volunteers will be solicited. The subjects will be randomized into two groups; Group I will receive GnRH alone followed in one week by GnRH plus verapamil; Group II will undertake the testing scheme in reverse order. The testing will be performed after an overnight fast and at the same time of the day. The GnRH tests will be conducted over three hours with blood being obtained at 15 minute intervals. Verapamil will be started at time 0 and will be administered IV at a rate of 5 mg/hr. GnRH will be given as a 200 µg bolus at time + 60 minutes. Blood will be analyzed for LH by RIA and by bioassay. LER 907 (NIAMDD) will be used as the standard in both assays. LH will be iodinated using the Iodogen method and the RIA will be conducted according to published methods. The LH bioassay will be performed with the Swiss-Webster mouse Leydig cell model. Parameters to be scrutinized will be LH deltas, per cent change in LH, and total area under the LH curve. A Student's paired t test will be used to test for significant differences between the control GnRH challenge and the test performed during the verapamil infusion.

Progress: Subjects have been recruited and testing will start in the next few weeks.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 85/84	Status: On-going
Title: Purification of Long Chain Fatty Acid: CoASH Ligase From Human Spermatozoa		
Start Date: 23 Aug 85	Est Completion Date: Sep 86	
Dept/Svc: Medicine/ Endocrine	Facility: MAMC	
Principal Investigator: MAJ Robert E. Jones, MC		
Associate Investigators: COL Stephen R. Plymate, MC MAJ Charles J. Hannan, MSC		
Key Words: cellular location, molecular size, functional relationship, hepatic/mitochondrial forms		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: 708.00	Results: N/A

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: The requisite reagents have been acquired and the initial Triton extraction of ligase from sperm has been started. Nearly 5 mg of the crude Triton mixture has been obtained.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 85/85	Status: On-going
Title: Kinetics of Polyunsaturated Fatty Acid (PUFA) Activation in Human Sperm		
Start Date: 23 Aug 85	Est Completion Date: Sep 86	
Dept/Svc: Medicine/Endocrinology	Facility: MAMC	
Principal Investigator: MAJ Robert E. Jones, MC		
Associate Investigators: COL Stephen R. Plymate, MC MAJ Charles J. Hannan, MSC		
Key Words: PUFA, ligase activity, human sperm, acyl CoA		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: 700.00	Results: N/A

Study Objective: To determine the kinetics and substrate specificities of PUFA as related to acyl CoA synthesis in human sperm.

Technical Approach: Semen samples will be obtained from the semen analysis laboratory. Only those ejaculates deemed normal by standard criteria will be utilized in this study. The samples will be frozen at -70°C until use.

Two different techniques for determining ligase activity will be used. The first is a radioligand-millipore filter assay which measures acyl CoA formation via the incorporation of 3H-CoASH. The second measures the rate of 3H-palmitic acid conversion to palmitoyl CoA. The former assay is nonspecific in detecting activation of virtually all saturated or unsaturated medium to long chain (12 carbons or greater) fatty acid while the latter is specific for palmitic acid. The incubation mixture, which has been previously optimized, will be identical for both techniques. Protein will be measured colorimetrically with a BioRad kit, and kinetic constants (K_m , V_{max} , K_i) will be calculated using standard formulae and plots.

The following two questions will be addressed: what is the PUFA specificity for sperm ligase and are PUFA and saturated fatty acids activated by the same enzyme. The experimental approach is summarized as follows:

Experiment	Assay	Variables	Data Collected
PUFA specificity	3H-CoASH	16:1, 18:1, 18:2, 18:3 20:4, 22:1, 22:6	K_m , V_{max}
Double Bond specificity	3H-CoASH	16:1 (cis, trans)	K_m , V_{max}
Competition curve	3H-PA	Coincubation of 16:0 (0-10 μM) with 0, 5, 10 μM PUFA	K_m/K_i , V_{max}

Progress: The following polyunsaturated fatty acids have been studied: 18:1, 18:2, 20:4, 22:1, and 22:6. Of these fatty acids, 20:4 (arachidonic acid) was not activated and 22:1 (erucic acid) was slowly, if at all, activated. The K_m 's for the remaining fatty acids (18:1, 18:2, 22:6) were similar in the 3-5 μM range but the maximal velocities appeared to be inversely related to the degree of unsaturation. Competition curves (Dixon plots) have not been completed.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/80 Status: On-going

Title: A Comparison of Thallium Stress Testing and Cardiac Pacing Stress Testing in the Preoperative Evaluation of Patients Undergoing Abdominal Aortic Aneurysmectomy and/or Aorto-femoral Revascularization

Start Date: 21 Sep 84 Est Completion Date: Oct 85

Dept/Svc: Medicine/Cardiology Facility: MAMC

Principal Investigator: LTC John W. Kirk, MC

Associate Investigators: COL Charles Andersen, MC
COL Stanton Brown, MC

Key Words: treadmill stress testing, thallium perfusion imaging

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: Continue

Study Objective: To determine the utility of treadmill stress testing with thallium perfusion imaging and cardiac pacing stress testing in the preoperative evaluation of patients with evidence of heart disease who are scheduled to undergo major vascular surgery involving the abdominal aorta, the iliac arteries, and/or the femoral arteries.

Technical Approach: Each subject will undergo treadmill stress testing followed by thallium perfusion imaging. A week later, each patient will undergo a right atrial pacing stress test followed by selective left and right coronary angiography and contrast left ventriculography from a brachial artery. If contrast left ventriculography is not performed or is of suboptimal technical quality, a blood pool radionuclide angiogram will be obtained within 48 hours. Patients will be followed through induction of anesthesia and the post-operative period for cardiac complications, and the vital status will be determined at one and six months. Coronary arteriography will be employed as the gold standard to determine the sensitivities, predictive values, specificities, and accuracies of these two diagnostic tests in identifying coronary artery disease, particularly left main and severe three vessel coronary disease. In order to determine the ultimate value of any of these tests in increasing operative survival and reducing perioperative complications, surgical results in these patients will be compared with those of a similar group of patients who underwent the same type of surgery without such extensive preoperative evaluation.

Progress: Of 15 patients studied, 13 had coronary disease by angiography. Abnormalities diagnostic of ischemia were detected in 10 of the 13 by right atrial pacing and in 5 of 12 by the thallium stress testing. Of the 6 patients with left main or 3-vessel disease, right atrial pacing was positive in 4, thallium stress in 2. As a result of these findings, 3 patients have been referred for coronary bypass surgery. Results to date indicate that right atrial pacing stress testing may be more sensitive than thallium stress testing in detecting significant coronary artery disease in these patients. More testing is planned. This study resulted in a presentation to the 14th Annual Session of the Association of Army Cardiologists.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/28 Status: Terminated

Title: The Utility of the Echocardiographic Left Atrial Emptying Index in Patients with Clinical Congestive Heart Failure and Normal Left Ventricular Systolic Function

Start Date: 18 Jan 85 Estimated Completion Date: May 86

Dept/Svc: Medicine/ Cardiology Facility: MAMC

Principal Investigator: LTC John W. Kirk, MC

Associate Investigators: None

Key Words: Echocardiograph, right heart catheterization, normal systolic left ventricular function

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objectives: To determine the prevalence of left heart failure due solely to diastolic dysfunction in patients with clinical evidence of congestive heart failure who are referred for radionuclide angiography and to determine the sensitivity and specificity of the left atrial emptying index (measured echocardiographically) in detecting left ventricular diastolic dysfunction.

Technical Approach: Patients <75 years of age with suspected or definite clinical CHF who are found to have normal systolic left ventricular function by MUGA scan and who meet other criteria as detailed in the protocol will have breakfast and their usual drug regimen. Subjects will be premedicated with Valium. Three hours after breakfast, an echocardiogram will be done and within an hour after this the patient will undergo right heart catheterization.

Progress: The study was terminated because of an inadequate number of patients. The two patients who were entered and underwent right heart catheterization experienced no complications. The echocardiograms were of less than optimal technical quality for the precise type of measurement required by the study.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 79/77 Status: Completed

Title: Evaluation of Radiation Therapy in the Management of Endoscopically Visible Tumors of the Lung

Start Date: 18 May 79 Est Completion Date: Sep 85

Dept/Svc: Medicine/Pulmonary Facility: MAMC

Principal Investigator: MAJ Arthur Knodel, MC

Associate Investigators: COL Donald Kull, MC

LTC Jerome Beekman, MC

LTC Henry D. Covelli, MC

MAJ Barry Weled, MC

CPT James Wallingford, MC

Key Words: Lung, tumors, endoscopically visible, radiotherapy

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To evaluate in a prospective manner the utility of using radiation therapy to decrease tumor size in obstructing carcinomas of the lung.

Technical Approach: A minimum of 15 patients with carcinoma of the lung will be evaluated in the usual manner. If the patient is a non-operable candidate with endoscopically visible lesions, he will receive radiation therapy and/or chemotherapy in the usual manner with reassessment of pulmonary functions, arterial blood gases, and fiberoptic bronchoscopy approximately one month after radiation and again approximately six months after radiation. The parameters used to evaluate progression or regression of disease will be changing roentgenographic effect (collapse, atelectasis) in the area of involvement, alteration of pulmonary function and arterial blood gases, and changing luminal size of obstructing lesions as noted by fiberoptic bronchoscopy. Repeat biopsy results from prior areas of involvement will also be used to assess therapeutic results.

Progress: This protocol has been completed and the investigators are preparing a paper to submit for publication.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/38 Status: Completed

Title: Face Mask CPAP in the Treatment of Post-Operative
Atelectasis

Start Date: 22 Feb 85 Estimated Completion Date: Jan 86

Dept/Svc: Medicine/Pulmonary Facility: MAMC

Principal Investigator: MAJ Arthur R. Knodel, MC

Associate Investigators: COL J. Waylon Black, MC

MAJ Hal Cragun, MC John Sinclair, M.D.

CPT Ron Fullmer, MC Dan Mould, Pulmonary Tech

Key Words: Continued incentive spirometry, continuous positive
airway pressure, chest x-ray, arterial gases, WBC

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To evaluate the usefulness of continuous positive airway pressure (CPAP) delivered by a face mask as a measure to treat post-operative pulmonary atelectasis.

Technical Approach: All patients undergoing upper abdominal and thoracic surgery will be evaluated postoperatively for atelectasis. Those patients who develop fever, leukocytosis, cough, abnormal chest auscultation, and abnormal chest x-ray will be entered into the study and randomized to receive continued incentive spirometry or mask CPAP. Each form of therapy will be given for 15 minutes every two hours during the waking hours. The effectiveness of therapy will be determined by serial histories, examinations, temperatures, WBC's, chest x-rays, pulmonary function tests, and arterial blood gases. Patients with pneumonia, ARDS, congestive heart failure, acute MI, and bronchospasm will be excluded. Measurements/Data Collection: spirometry FEV₁ and FVC, chest x-ray, arterial blood gases, white blood cell count, all on a daily basis.

Progress: Seventy-five patients were studied. Data analysis is almost complete and a paper is in progress.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/57 Status: Completed

Title: Multiple Primary Neoplasia of the Head and Neck and Lung:
The Changing Histopathology

Start Date: 19 Apr 85 Estimated Completion Date: May 85

Dept./Svc: Medicine/Internal Medicine Facility: MAMC

Principal Investigator: CPT Michael F. Lyons, MC

Associate Investigator: COL John Redmond, MC

Key Words: chart review, Field Squamous Cancerization

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To review the association between multiple primary neoplasia of the head and neck and lung at Madigan in order to compare the Madigan experience with the "Field Squamous Cancerization Theory" of Slaughter and Gluckman.

Technical Approach: Patient records from the tumor registry at Madigan for the years 1967 to 1984 will be reviewed. Cases of oral head and neck cancer and lung cancer will be identified. Malignancies of the face, lip, and esophagus will be excluded. The criteria of Warren and Gates as modified by Gluckman will be used to diagnose multiple primary neoplasia: (1) the neoplasm must be clearly malignant as determined by histologic evaluation; (2) each neoplasm must be geographically separate and distinct, and lesions should be separated by normal-appearing mucosa. If a second neoplasm is contiguous to the initial primary tumor or is separated by mucosa with intraepithelial neoplastic change, the two should be considered as confluent growths rather than multiple primary carcinomas; (3) the possibility that the second neoplasm represents a metastasis should be excluded. The observation that an invasive carcinoma arises from an overlying epithelium that demonstrates a transition of carcinoma *in situ* to invasive carcinoma is helpful; and when the separate foci have significant differences in histology, the diagnosis of the separate primary neoplasms is appropriate." The histologic diagnosis will have been made in each case by the Department of Pathology at Madigan, with the histology reviewed by the Armed Forces Institute of Pathology. The staging system of the American Joint Committee for Cancer will be used. Synchronous lesions will be defined as occurring within six months of the primary lesion. Lung cancer will be judged as primary based on endobronchial tumor invasion only.

Of 1313 records reviewed, 25 subjects with either synchronous or metachronous MPN were identified. Twenty-three of these patients were and were heavy abusers of cigarettes and alcohol. Twenty-one had squamous carcinoma of the head and neck; however, two had squamous carcinoma of the lung. This study supports the concept of "field squamous cancerization" of the head and neck and lung, rather than patients at high risk having a high incidence of non-squamous bronchogenic carcinoma similar to that seen in patients with primary bronchogenic carcinoma. An abstract was published in Proc ASCO 4: 1985. The study has been accepted for publication in Cancer.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/54 Status: On-going

Title: Determination of a Possible Association Between Migraine Headaches and Attention Deficit Disorders in Children

Start Date: 18 May 84 Est Completion Date: Jun 86

Dept/Svc: Medicine/Neurology Facility: MAMC

Principal Investigator: MAJ Joseph P. McCarty, MC

Associate Investigators: None

Key Words: Migraine headaches, ADD, questionnaire

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$35.00 Results: Continue

Study Objective: To determine if there is an unusually high incidence of migraine headaches in children with attention deficit disorders.

Technical Approach: For purposes of this study, migraine will constitute any headache with three or more of the following characteristics: throbbing, presence of an aura before the headache, unilateral pain, history of sleep walking or motion sickness, nausea or vomiting with the headache, or positive family history of migraine headaches. Attention deficit disorder syndrome is defined as a syndrome of developmentally inappropriate inattention and impulsivity. Hyperactivity may be an associated feature but is not required for diagnosis.

A questionnaire will be given to all new patients referred to the Pediatric Clinic for evaluation of attention deficit disorder. This questionnaire will be reviewed by the examining physician, and he will complete an additional questionnaire. The same questionnaire will be utilized with patients who come to the Pediatric Clinic for routine school physicals. This group will serve as a control group. From these questionnaires, the number of patients with attention deficit disorder and migraine can be compared to the number of controls with migraine. As attention deficit disorder is seen primarily in males, the controls will be adjusted by sex and age to match the study group. It is estimated that approximately 100 patients in the study group and 200 patients in the control group will provide more than sufficient numbers for statistical significance.

Progress: Six new subjects were entered during FY 85. There was some delay in entering more subjects due to the departure of MAJ McCarty. COL Charles Onufer is scheduled to assume the responsibility for this protocol in November 1985.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 85/80	Status: On-going
Title: The Utility of Including Iron Assay on an Automated Chemistry Panel		
Start Date: 23 Aug 85	Est Completion Date: Aug 86	
Dept/Svc: Medicine/Gastroenterology	Facility: MAMC	
Principal Investigator: LTC Thomas F. O'Meara, MC		
Associate Investigators:		
CPT Bradley T. Heppner, MC		
COL John Redmond, MC	CPT Margaret Richardson, MC	
COL Carl Stones, MC	CPT Donald Zedalis, MC	
Key Words: physician response, high and low serum iron values		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: \$1620.00	Results: N/A

Study Objective: to assess how physicians respond to an unsolicited chemical abnormality found in their patients, and to correlate high and low values of serum irons performed as part of an automated chemistry screen with more standard assays.

Technical Approach: For several months, an iron assay was added to the SMAC profile. For an arbitrary three week period, over 300 values which were high or low were identified. To assess how physicians responded to the abnormal values, each outpatient record will be pulled at least three months after the labs were drawn and a systemic review of the physician's action or inaction recorded. Clinical impression based on the laboratory abnormality and further evaluation via other lab work will be looked for. To assess the accuracy of the SMAC iron, serum iron, and total iron binding capacity, ferritin values will be run on stored serum. If patient contact is deemed necessary, it will go through the primary physician. If no physician action was initiated by the abnormal iron values, the primary physician will be notified to do so when the high serum iron is confirmed as high and low irons are confirmed in patients who are anemic or in patients >45 years of age. When assessing pediatric serum iron values, the physicians will use a standard chart for pediatric values. Charts of children less than one year of age will be excluded. Chi² test and frequency distribution will be used for data analysis. If the numbers of pediatric and pregnant patients are too low, these will not be used for data analysis.

Programs: All of the low serum iron charts that were refutable have been reviewed. It is anticipated that in January 1986 the high iron charts will be reviewed and the data tabulated on all charts and run by the laboratory.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 83/62 Status: Completed

Title: High Dose Intravenous Gammaglobulin for Chronic Idiopathic Thrombocytopenic Purpura

Start Date: 20 May 1983 Est Completion Date: Mar 85

Dept/Svc: Medicine/Hematology Facility: MAMC

Principal Investigator: MAJ Timothy J. O'Rourke, MC

Associate Investigators:

COL Friedrich H. Stutz, MC MAJ Thomas M. Baker, MC

LTC James Congdon, MC MAJ Alfred H. Chan, MC

LTC Irwin B. Dabe, MC MAJ Howard Davidson, MC

Key Words: IV gammaglobulin, ITP, failed conventional therapy

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: Completed

Study Objective: To evaluate the efficacy of human immunoglobulin in treatment of chronic idiopathic thrombocytopenic purpura (ITP) that has not responded to conventional therapy and to observe changes in the serum proteins pertinent to the immune system during therapy.

Technical Approach: This is to be a multicenter study among the Army MEDDACS. It is anticipated that 5-6 patients will be needed to begin a valid study. At MAMC, 1-2 patients per year are expected. All patients with ITP documented by a compatible bone marrow picture and absence of secondary etiologies will be eligible. This will be restricted to patients who have failed conventional therapy, have severe thrombocytopenia and/or have spontaneous hemorrhage. Patients who are otherwise being treated but have life-threatening hemorrhage or who must undergo surgery may be included at the discretion of the study coordinator.

Patients will be treated with 0.4 mg/kg/day I.V. gammaglobulin as an infusion on each of five successive days. Should a response occur, weekly or biweekly maintenance will be continued. If the response is prolonged, the frequency will be lengthened and ultimately stopped.

Progress: Two patients were entered in previous years. This treatment is now considered as standard for refractory ITP.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/02 Status: Completed

Title: CT Scanning and Myelography in the Diagnosis of Metastasis to the Axial Skeleton

Start Date: 21 Oct 83 Est Completion Date: Mar 85

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Timothy J. O'Rourke, MC

Associate Investigators: COL John Redmond, MC

LTC Howard Davidson, MC

MAJ William Fill, MC

Key Words: algorithm, CT scan, myelography, NMR

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$3250.00 Results: N/A

Study Objective: To examine the utility of CT scanning compared to plain radiographs in the diagnosis of metastatic disease of the spine; to investigate the role of CT Metrizamide myelography in detection of subclinical compromise of the spinal canal; and to observe the course of patients with subclinical compromise of the spinal canal evaluated in this way.

Technical Approach: Patients enrolled in this study must have: (a) normal neurologic exam, or at least absence of neurologic findings attributable to spinal cord or nerve root compression and (b) either abnormal bone scan with new findings in a patient with known metastatic or high risk primary malignancy or multiple myeloma or other neoplasms with high frequency of false negative bone scan who have back pain. Patients will be evaluated as follows: Carcinoma patients with a positive bone scan and a positive x-ray will go on to a CT/metrizamide myelogram and treatment; those with a negative x-ray will go on to a CT and then (if the CT is positive) to the CT/metrizamide myelogram and treatment (if the CT is negative no further testing); those with a positive bone scan and a negative x-ray and CT will have no further testing. Patients with multiple Myeloma and back pain will follow the same schedule through x-ray, CT, and CT/metrizamide myelogram. Treatment will be at the discretion of the treating physician and radiotherapist. Follow-up will be as appropriate for the individual patients. Bone scan will be repeated as needed for new symptoms or every three to four months in the absence of new symptoms. CT scans and CT metrizamide myelograms will be repeated as needed.

Amendment, Nov 84: Five selected patients would have NMR scanning of the spine. The investigators will compare NMR and CT - Metrizamide scanning in patients with subclinic cord compromise.

Progress: Sixty patients were entered. This approach allowed the early and accurate diagnosis of spinal metastasis and epidural tumor as well as the diagnosis of benign disease and was useful in planning optimal local therapy. The study has been replaced by an expanded study under the direction of COL John Redmond, MC. A paper has been accepted for publication.

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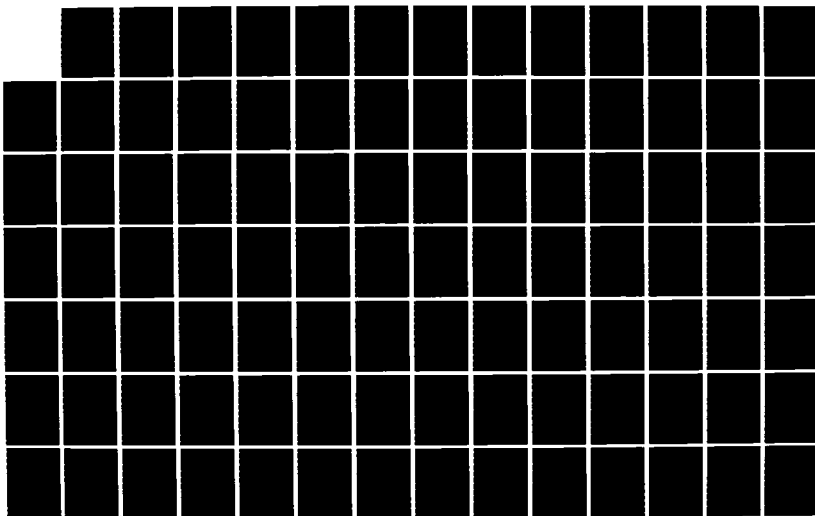
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2.5



2.2



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1.8

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/81 Status: On-going

Title: CT Scanning, CT Myelography, and Magnetic Resonance Imaging in the Diagnosis of the Metastasis to the Axial Spine

Start Date: 23 Aug 85 Est Completion Date: 1 Jun 87

Department: Medicine Facility: MAMC

Principal Investigator: COL John P. Redmond, III, MC

Associate Investigators:

COL Robert Karl, MC

MAJ Loren Colman, MC

LTC Irwin Dabe, MC

MAJ David Dunning, MC

MAJ Thomas Baker, MC

Lawrence D. Cromwell, M.D.

MAJ Howard Davidson, MC

Theodore Roberts, M.D., DAC

Key Words: Axial spine, metastasis, CT scanning, CT myelography, magnetic resonance imaging

Accumulative MEDCASE

Est Accumulative

Periodic Review

Cost: -0-

OMA Cost: -0-

Results: N/A

Study Objective: To investigate the role of spinal CT scanning, CT metrizamide myelography, and spinal magnetic resonance imaging in the detection of subclinical compromise of the spinal canal using an algorithm.

Technical Approach: Patients will be studied using the following algorithm: Patients who have an abnormal bone scan or have back pain in a tumor that tends to show up on a bone scan will receive plain x-rays and then undergo spinal CT's. If the spinal CT shows only evidence of benign disease, patients will receive no further evaluation. If the spinal CT demonstrates evidence of spinal metastasis, the films will be carefully reviewed by radiologists to see if there is evidence of tumor eroding into the neural canal. If there is no evidence of tumor eroding into the neural canal but the patient has symptoms of metastatic disease to the bone, he will be referred for radiation therapy. If there is no evidence of erosion into the spinal canal and the patient has no symptoms of metastatic disease, the patient will not receive radiation therapy but will have a repeat spinal CT in one month. If there is evidence of the tumor eroding into the neural canal, then the patient will undergo a CT metrizamide myelogram to see if there is evidence of damage to the spinal cord and will be referred for radiation therapy. All patients will be asked to undergo the nuclear magnetic resonance scan within two weeks after the spinal CT scan.

Follow-up: Bone scans will be repeated as needed for new symptoms or every three to four months in the absence of symptoms. CT scans and CT metrizamide myelograms will be repeated as clinically indicated and as indicated by the study algorithm.

PROGRESS: This is a new study. The investigators are in the process of recruiting subjects.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/53 Status: Terminated

Title: Assessment of the Effect of Theophylline on Exercise Performance in Patients with Irreversible Chronic Obstructive Lung Disease

Start Date: 19 Apr 85 Estimated Completion Date: Apr 86

Dept/Svc: Medicine/Pulmonary Facility: MAMC

Principal Investigator: MAJ Richard J. Robinson, MC

Associate Investigators:

COL J. Waylon Black, MC MAJ Arthur R. Knodel, MC

MAJ W. Hal Cragun, MC Daniel F. Mould, C.R.P.T.

Key Words: theophylline, exercise, COPD, double-blind, crossover

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: 650.00 Results: N/A

Study Objective: To determine if the use of theophylline in patients with moderate irreversible obstructive lung disease will improve exercise performance.

Technical Approach: The study will be a double blind, crossover study. Patients seen for routine pulmonary functions with a moderate obstruction, <70 years old, without reversibility, and an FEV₁ of 1.0 - 1.5 liters will be studied. Twenty patients (two groups of 10) will have full pulmonary function tests to include pre and post bronchodilator spirometry, TLC and FRC determination by body plethysmography, resting ABG's and DLCO. After one week off bronchodilators, each patient will have a formal exercise study using the Medical Graphics 2001 System with concurrent ear oximetry and postexercise spirometry to rule out exercise induced bronchospasm. The day following the initial exercise study, the patients will be asked to perform at a constant work load for six minutes, corresponding to 60% of the max work load achieved the day before. This will serve as the baseline for the tests to follow. After all baseline studies are completed, the patients will be placed on either aminophylline in normal saline or normal saline without aminophylline by continuous IV infusion. Each patient will be bolused at a rate calculated to give a peak theophylline level of 15 µg/ml. Approximately 45 minutes after the bolus is infused, a theophylline level will be obtained. If the level is therapeutic, the IV will be discontinued and exercise performance will be assessed at the 60% maximum work load for six minutes. If the level is not therapeutic, the patient will be rebolused and the level will be reassessed. It will be the responsibility of the physician adjusting the dosages to treat placebo patients in the same fashion as those receiving aminophylline. After the exercise study is completed, the patient will be crossed over to the remaining group and after seven days the procedure will be repeated.

Progress: Shortly after the approval process was completed on this study, three articles were noted in the literature that had obtained the information to be studied. Therefore, it was decided that not enough further information could be obtained to warrant continuation of the study.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/12 Status: On-going

Title: Western Washington Randomized Trial of Intravenous Streptokinase in Acute Myocardial Infarction

Start Date: 18 Nov 83 Est Completion Date: Nov 86

Dept/Svc: Medicine, Cardiology Facility: MAMC

Principal Investigator: COL Theodore Steudel, MC

Associate Investigators: COL John Hill, MC

LTC Roger F. Chamusco, MC

LTC John W. Kirk, MC

MAJ Michael Newcomb, MC

MAJ Stanley E. Pearson, MC

Key Words: I.V., streptokinase, acute myocardial infarction

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: see*

Study Objective: To determine if high dose infusion of streptokinase administered early in the course of a myocardial infarction will reduce hospital mortality when compared to conventional CCU care.

Technical Approach: Patients with a clinical and electrocardiographic diagnosis of acute, transmural myocardial infarction of <6 hours duration will be randomized to control or streptokinase treatment group and stratified according to the time of onset of symptoms and location of myocardial infarction. Controls will receive conventional therapy and IV heparin. The treatment group will receive streptokinase, 1,500,000 units in 250 ml of D₅W, as a 1-hr infusion, followed by full dose IV heparin anticoagulation. CPK or CPKMB isoenzymes will be drawn every 4 hours during the first 24 hours. These CPK curves will be used to define the occurrence of acute myocardial infarction and to give evidence of reperfusion. A gated blood pool radionuclide angiogram will be obtained at 0-48 hours after randomization to assess early left ventricular function. A coronary angiogram and contrast left ventriculogram will be performed prior to discharge at 7-14 days. If contrast ventriculography is declined by the patient, a second isotope radionuclide ventriculogram will be obtained. At 30-45 days, subjects will have a tomographic 201-Thallium quantitative myocardial perfusion study. performed. At the same visit, each patient will have a standard radionuclide blood pool study for global EF, as well as a tomographic blood pool study for analysis of regional EF. Each patient's vital status will be determined at 6 months and one year. After 100 subjects have been studied, an independent monitor will analyze the data for significant findings before entering more patients.

Progress: COL Steudel became the principal investigator on this protocol upon the retirement of COL Hill. Patients are still being entered. One adverse reaction (cerebral hemorrhage) has been reported. *Consent form was revised upon continuing review.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 84/14	Status: On-going
Title: Danazol Therapy for Idiopathic Thrombocytopenia (ITP)		
Start Date: 18 Nov 83	Est Completion Date: Nov 86	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: CPT Michael D. Stone, MC		
Associate Investigators:		
COL F.H. Stutz, MC	MAJ Alfred H. Chan, MC	
LTC Irwin B. Dabe, MC	MAJ Howard Davidson, MC	
MAJ Thomas M. Baker, MC	MAJ Timothy J. O'Rourke, MC	
Key Words: Danazol, ITP, radioactive antiglobulin test, radio-labelled staphylococcal protein A		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: \$4870.00	Results: Continue

Study Objective: To determine the response of ITP patients to therapy with Danazol.

Technical Approach: Patient Eligibility: (1) All patients must meet the clinical definition of ITP to include a platelet count $<100,000/\text{mm}^3$, with normal or increased megakaryocytes on bone marrow aspirate and no drug use or other disease excepting SLE present known to cause thrombocytopenia. (2) Patients must be refractory to Prednisone or require unacceptably high doses to remain in clinical remission. (3) Patients may or may not have received prior splenectomy or other drug therapy. (4) All pregnant patients will be excluded.

Antiplatelet antibodies will be measured pretreatment. Danazol will be started at a dose of 200 mg QID and continued at this level for a period of 12 weeks. Antiplatelet antibodies will then be remeasured. A radioactive antiglobulin test and a radiolabelled staphylococcal protein A will be performed on each sample. All concurrent medications will be continued at the outset of the study. If during the first 12 weeks an excellent response is obtained, concurrent medications for ITP may be decreased or at the end of the 12 weeks, the drug will be discontinued in those patients with transient or poor response. In patients with excellent, good, or fair response, the dose may be modified in an attempt to continue response at a lower drug level. Danazol may be continued indefinitely in those patients who respond with acceptable toxicity.

Progress: One patient has been entered in this study.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/56 Status: On-going

Title: Weekly Low Dose CCNU for Extensive Adenocarcinoma of the Colon and Rectum

Start Date: 18 May 84 Est Completion Date: May 86

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: CPT Michael D. Stone, MC

Associate Investigators: COL F.H. Stutz, MC

MAJ Thomas M. Baker, MC

Key Words: Adenocarcinoma, colon, rectum, CCNU, weekly

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: Continue

Study Objective: To determine the response rate of refractory adenocarcinoma of the colon or rectum to weekly low dose CCNU therapy and to determine the toxicity of weekly low dose CCNU therapy.

Technical Approach: CCNU will be administered by mouth at an initial dose of 40 mg/wk. The dose will be escalated by 10 mg after each 6 week period. Maximum dose will be 80 mg/wk. Therapy will continue until there is unequivocal evidence of tumor progression or until unacceptable toxicity occurs.

Study monitoring: CBC weekly, SMAC every three weeks, physical exam and toxicity notation every three weeks, and tumor measurement by appropriate studies every 12 weeks or more frequently at the discretion of the investigator.

Progress: This protocol has been slowly accruing patients. Because of the absence of any hematologic toxicity at the original starting dose of 40 mg Q wk, the starting dose was increased to 60 mg Q wk after continuing review and approval of the increase by the IRB. Thus far, there have been no adverse sequelae of this change. Because many of these patients are end stage, 25-30 more patients will be needed in order to meet the goal of 15-20 evaluable patients. Thus far, there have been 0/12 responses noted.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 81/56	Status: On-going
Title: The Effect of Nephrosis on Treated Hypothyroidism		
Start Date: 20 Mar 81	Est Completion Date: Sep 86	
Dept/Svc: Medicine/Endocrinology	Facility: MAMC	
Principal Investigator: COL Gary L. Treece, MC		
Associate Investigators:		
COL Bruce L. Fariss, MC	MAJ Lawrence Agodoa, MC	
COL Stanton Brown, MC	MAJ Edward Lelonek, MC	
COL Stephen R. Plymate, MC	MAJ James W. Little, MSC	
COL Poong S. Shim, MC	MAJ Louis N. Pangaro, MC	
	MAJ David Turnbull, MSC	
Key Words: Hypothyroidism, treated, L-thyroxine		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: \$2425.00	Results: Continue

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; subjects with hyperthyroidism; with hypothyroidism, primary untreated; with hypothyroidism treated for one month with L-thyroxine; with the nephrotic syndrome; subjects with the nephrotic syndrome 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: One patient was entered on the protocol in FY 85 for a total of 6 subjects. Progress on the protocol has been slow due to slow acquisition of study patients and recent changes in the staff of the Nephrology Service. No further effort has been expended to establish the urinary thyroxine/triiodothyronine assay.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 82/05 Status: On-going

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

Start Date: 20 Nov 81 Est Completion Date: Sep 86

Dept/Svc: Medicine/Endocrinology Facility: MAMC

Principal Investigator: COL Gary L. Treece, MC

Associate Investigators: COL Bruce Fariss, MC
MAJ Robert Jackson, MC

Key Words: adrenal insufficiency, urinary free cortisol, monitor, hydrocortisone, cortisone

Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: \$700.00	Results: Continue

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: A total of four patients has been entered on this protocol. Progress on the protocol has been slow due to the infrequent presentation of study patients. Recently, several patients have been located and have tentatively agreed to participate in the study. A total of 10 patients is desirable before the data would be analyzed.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 83/37	Status: On-going
Title: The Effect of Rapid, Short Term Blood Glucose Control on Leukocyte Function in Diabetic Patients		
Start Date: 21 Jan 83	Est Completion Date: Sep 86	
Dept/Svc: Medicine/Endocrinology	Facility: MAMC	
Principal Investigator: COL Gary L. Treece, MC		
Associate Investigators:		
COL Bruce L. Fariss, MC	MAJ Michael Fincher, MC	
COL Stephen Plymate, MC	MAJ Robert E. Jones, MC	
LTC James Higbee, MS	CPT Leroy Southmayd, MC	
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: \$3000.00	Results: Continue

Study Objective: To study the effect on leukocyte function testing *in vitro* of rapid and sustained normalization of blood glucose levels in poorly controlled diabetic patients. Blood glucose control is to be accomplished using the Biostator - GCIIS (Glucose Controlled Insulin Infusion System).

Technical Approach: Six Type I and six Type II adult non-pregnant, non-infected, poorly controlled diabetic patients will be the subjects for this study. They will not be taking antibiotics, glucocorticoids or other drugs known to affect hormonal or cellular immunity or leukocyte or bacterial activity. Diabetic drug therapy will be discontinued during the period of Biostator Control. After admission to the hospital, each patient will be connected to the Biostator, initially in Monitor Only mode, and blood for baseline fasting blood glucose, insulin, SMA-20, CBC, blood culture, triglycerides, Hg A₁C, and leukocyte function will be drawn. The Biostator will then be programmed to lower the blood glucose to 100 mg % and maintain the blood glucose at 100 mg % for 24-72 hrs with the patient ingesting a weight maintaining diet divided into sevenths (2/7, 2/7, 2/7, 1/7). Blood for leukocyte function will be drawn at 2, 4, and 6 hours after normalization of blood sugar and every 6 hours thereafter. Should it be determined that leukocytic function can be altered with less than 6 hours of blood glucose normalization, the Biostator will be programmed to raise the blood glucose to 200 mg % 12 hours prior to termination of the study period. After 6 hours of a sustained blood glucose of 200 mg %, blood for leukocytic function will again be drawn. Then the blood glucose will be raised to 300 mg % for an additional 6 hours followed by repeat leukocytic function testing. Biostator control of the patient's blood glucose will then be terminated and the patient placed back on prior treatment regimen.

Progress: Progress on this protocol has been slow due to difficulty in establishing a reproducible leukocyte function assay, using techniques reported in the literature. CPT Southmayd, who has been added to the protocol as associate investigator, has made progress in establishing a fluorescent microscopic technique using the differential staining of live versus dead organisms within leukocytes to determine phagocytic and microbiocidal function of isolated leukocytes. With establishment of the leukocyte function assay, further progress on the protocol should be hastened.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/40 Status: On-going

Title: Treatment of Graves' Ophthalmopathy with Cyclosporin
Start Date: 16 Mar 84 Est Completion Date: Sep 86
Dept/Svc: Medicine/Endocrinology Facility: MAMC
Principal Investigator: COL Gary L. Treece, MC
Associate Investigators: COL Leonard Wartofsky, MC
COL Stanley Allison, MC MAJ Robert E. Jones, MC
COL Francis G. LaPianan, MC CPT Andrew Ahmann, MC
Key Words: Graves' ophthalmopathy, cyclosporin, group study
Accumulative MEDCASE Est Accumulative Periodic Review
Cost: -0- OMA Cost: \$200.00 Results: Continue

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: A total of four patients Army-wide has been entered into this protocol. The one patient entered at MAMC was randomized to take cyclosporin first. Nausea and vomiting necessitated discontinuation of the drug. The patient had a past history of peptic ulcer disease. UGI was subsequently normal and symptoms resolved quickly with no sequelae.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 85/24	Status: On-going
Title: Physiological and Biochemical Changes During Thyroid Extract Withdrawal		
Start Date: 18 Jan 85	Estimated Completion Date: May 85	
Dept/Svc: Medicine/Endocrinology	Facility: MAMC	
Principal Investigator: COL Gary L. Treece, MC		
Associate Investigators: COL Stephen R. Plymate, MC		
LTC Anthony P. Zavadil, MC		
MAJ Robert E. Jones, MC		
Key Words: Thyrolar, L-thyroxine, metabolism		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: \$1810.00	Results: N/A

Study Objective: To evaluate the physiological and biochemical changes that take place during thyroid extract withdrawal in order to better understand the origin of these patients' symptoms.

Technical Approach: Nonpregnant patients >21 years of age will fill out a symptom questionnaire and have a complete history and physical exam. A blood sample and a resting metabolic rate will be taken after an overnight fast. Patients will then receive an injection of TRH and have blood samples drawn at 30 and 60 min. Each patient will have systolic time intervals measured in a fasting or late postprandial state. Blood samples will be obtained four hours after ingestion of the daily thyroid hormone preparation on a day other than the day the TRH test is done. Patients will then be switched to L-thyroxine for 6 weeks with appropriate dosage modifications. At the end of the 6 weeks, the patients will have all the above tests performed. Patients will then be treated with the thyroid hormone preparation as determined by patient preference in consultation with the primary physician. Baseline data will be compared with the treatment data using Student's t test. The baseline and treatment data will also be compared with established normals or with age, sex, and weight matched control values.

Progress: Five females and one male have been entered into the protocol. Four to six additional patients are to be studied prior to complete blood profiling and analysis of data. Age, sex, and weight matched controls are being sought.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 85/42	Status: On-going
Title: The Treatment of Refractory Paget's Disease of Bone with Synthetic Human Calcitonin		
Start Date: 22 Feb 85	Estimated Completion Date: Indefinite	
Dept/Svc: Medicine/Endocrinology	Facility: MAMC	
Principal Investigator: COL Gary L. Treece, MC		
Associate Investigator: MAJ Robert E. Jones, MC		
Key Words: Cibacalcin, clinical and biochemical evaluation		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: N/A

Study Objective: To evaluate the clinical and biochemical response to synthetic human calcitonin in a patient refractory to diphosphonates and salmon calcitonin as an alternative to mithramycin treatment.

Technical Approach: A 67 year-old white female with incomplete control of Paget's disease of bone despite treatment with diphosphates and salmon calcitonin, but responsive to mithramycin, is deemed to be a candidate for treatment with human synthetic calcitonin as an alternative to mithramycin treatment (deemed to be a more toxic drug than human calcitonin). Human synthetic calcitonin will be administered S.C. or I.M. initially q.d., decreasing to q.o.d. as feasible. Baseline symptom history, physical examination, SMA-20, 24-hr urine for hydroxyproline, bone scan, and appropriate radiographs will be obtained prior to institution of the treatment. The response to the drug will be monitored by clinical and biochemical evaluation of one or more of the above parameters at least every three months or more often as feasible. The drug will be discontinued if an effect is not observed or if any significant adverse reactions occur.

Progress: The patient being treated was refractory to salmon calcitonin and diphosphonates. Her response to human calcitonin has been salutary with relief of right hip and leg pain and near normalization of serum alkaline phosphatase. It is anticipated that Cibacalcium will be FDA approved in the near future which will obviate the need for this protocol.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/38 Status: Terminated

Title: Efficacy of Weekly Pulse Methotrexate in the Treatment of Rheumatoid Arthritis: A Double Blind Crossover Study

Start Date: 16 Mar 84 Est Completion Date: Sep 85

Dept/Svc: Medicine/Rheumatology Facility: MAMC

Principal Investigator: MAJ James Yovanoff, MC

Associate Investigator: MAJ Robert C. Hays, MC

Key Words: rheumatoid arthritis, methotrexate, group study

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$787.00 Results: Terminate

Study Objective: Part I: To evaluate the effectiveness of weekly pulse methotrexate therapy to control the activity of rheumatoid arthritis who have failed therapy with gold salt and D-penicillamine. Part II: To evaluate the potential of long-term weekly pulse methotrexate therapy to halt or decrease the progression of destructive changes of the articular cartilage and periarticular bone. Part III: To evaluate the potential for hepatic toxicity of weekly pulse methotrexate. In addition, careful evaluation of longitudinal evaluations of hepatic morphology will allow for close monitoring of potential changes to prevent progression of methotrexate-induced fibrosis to cirrhosis.

Technical Approach: This will be a multicenter study. Part I will be a double blind crossover study of weekly pulse methotrexate therapy compared to a placebo. Patients will be randomized to the methotrexate or the placebo and treated at increasing dose levels until a response is obtained for a 13-week period. Patients then will be crossed over to the opposite agent and treated in a similar manner for the second 13-week period. Patients will be clinically followed for the duration of the study by a single physician blinded as to the medication being received. Activity of disease, response to therapy, and drug toxicity will be evaluated. PART II: Patients will have x-ray evaluation of affected joints at the initiation of therapy with methotrexate and at six month intervals for the duration of therapy. Patients treated with methotrexate but not included in Part I of the study will be included in Part II if the route of administration and dosage range are the same and they meet inclusion criteria. X-ray films will be blinded, graded, and evaluated for potential progression of disease. Part III: Biochemical liver function studies will be monitored monthly. Liver biopsy will be performed at initiation of therapy and at appropriate intervals as indicated. When not contraindicated, laparoscopic directed liver biopsy will be performed to aid in the sensitivity of detection of potential liver injury. Percutaneous liver biopsy will be performed if standard contraindications to laparoscopy exist. Data on hepatic toxicity if noted will be compared to the patient's clinical status, concurrent medications, other evidence of toxicity, and methotrexate dosages.

Progress: This was a multicenter study that had its double-blind crossover component terminated in 1984. Thus no patients were entered during FY 85.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/04 Status: Completed

Title: The Influence of Thyroid Hormone Status on the Release of Melatonin by the Rat Pineal

Start Date: 19 Oct 84 Estimated Completion Date: Mar 85

Dept/Svc: Medicine/Endocrinology Facility: MAMC

Principal Investigator: LTC Anthony P. Zavadil, MC

Associate Investigators: None

Key Words: Thyroid hormone, release, melatonin, rat pineal

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$1940.00 Results: Completed

Study Objective: To determine the effect of thyroid hormone status on the secretion of melatonin by the pineal gland in the rat.

Technical Approach: This study will utilize a longitudinal design that allows comparison of each individual with itself. Hypothyroid rats will be observed, then rendered euthyroid by the administration of L-thyroxine, and observed again. The rats will be allowed to become hypothyroid again and reobserved. Likewise, normal rats will be observed, rendered thyrotoxic by the administration of thyroid hormone, and reobserved. The rats will be allowed to return to the euthyroid state and be observed for a third time. Body weight, 24-hr urinary excretion of 6-OH melatonin and creatinine, thyroid hormone concentration, and plasma concentrations of epinephrine and norepinephrine will be measured.

Progress: The technical portion of this protocol has been completed. The principal investigator has been transferred to WRAIR, and collected specimens have been transferred to WRAIR where the principal investigator will complete the data analysis.

DETAIL SHEETS
FOR
PROTOCOLS

DEPARTMENT OF NURSING

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/08 Status: Completed

Title: MAMC Department of Nursing Process Audit

Start Date: 21 Oct 83

Est Completion Date: Oct 84

Department: Nursing

Facility: MAMC

Principal Investigator: CPT Holly Buchanan, ANC

Associate Investigators: CPT Susan Alderson, ANC

LTC Mary A. Feske, ANC

CPT Karl Friedl, MSC

LTC Margaret Kulm, ANC

Rita Sorenson, DAC

MAJ Linda Guttman, ANC

Sandy Inazu, Amer Red Cross Volunteer

Key Words: quality, nursing practice, MAMC, audit

Accumulative MEDCASE

Est Accumulative

Periodic Review

Cost: -0-

OMA Cost: -0-

Results: Completed

Study Objective: To assess the quality of nursing practice, identify areas that need improvement, and evaluate improvements for implementation at MAMC.

Technical Approach: A process audit study was performed by the Division of Nursing, Rush-Presbyterian St. Luke's Medical Center, and the Medicus Corporation. This process was utilized at WRAMC with computer development and support from TRIMIS Army and Fort Detrick. The original protocol included 357 criteria and is published in 3 volumes available from NFIS. For this study, 69 questions have been selected requiring four types of review: chart audit; observation; patient interview; and nurse interview. A pilot test, involving three nursing units at MAMC, will be done to establish the validity of the items selected for use. The investigators will evaluate collected data and adjust audit forms as necessary. Individuals from the Department of Nursing selected by the QA Committee will be trained in the proper conduct of the audit process and will then audit all nursing units at MAMC on a quarterly basis. Random sampling (random number table) will be used (10 patients minimum per unit). The nursing staff will be blinded to the audit. Responses to the survey will be analyzed by questions and divided by wards. The questions will be summarized into six principal categories of nursing care: plan of nursing care formulated; physical needs of patient; non-physical needs of patient; achievement of nursing care objectives evaluated; unit procedures followed for protection of patients; delivery of nursing care facilitated by administrative management. The summarized data will be evaluated by the Patient Care Evaluation Committee and used for staff development and continuing education. Subsequent audits will evaluate the effectiveness of program improvement undertaken by the unit. This study will be used by the nursing staff as part of the QA program.

Progress: A pilot study was conducted which resulted in a revised process audit. After implementation of this audit and data analysis, the investigators concluded that none of the instruments, as a whole or as used in this study, met the minimum standards for internal consistency. A thesis submitted as partial fulfillment for an M.N. by MAJ Buchanan was approved.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/45 Status: Completed

Title: Determination of Adequate Discard Volume of Blood to Obtain Accurate Partial Thromboplastin and Thrombin Time Specimens from Arterial Lines

Start Date: 20 Apr 84 Est Completion Date: Jan 85

Department: Nursing Facility: MAMC

Principal Investigator: MAJ Pamela K. Burns, ANC

Associate Investigator: MAJ Patricia M. McCormack, ANC

Key Words: partial thromboplastin and thrombin time, measurement

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$396.00 Results: Completed

Study Objective: To determine an adequate discard volume required to obtain accurate measurement of the partial thromboplastin and thrombin times on specimens drawn from arterial lines in critically ill patients.

Technical Approach: Thirty patients in the Intensive Care Unit with in-dwelling arterial catheters will have discard specimens of 1.1, 4.5, 5.6, and 8.3 ml drawn with 2.7 ml test specimens and flush periods in between each drawing. A stop-watch will be started before the first arterial drawing and will be stopped after the flush period after the last discard specimen is drawn. A 2.7 ml venous specimen will be obtained as a control specimen immediately before the arterial specimens are drawn.

Progress: Twenty-five subjects were studied. One-tailed paired t-tests and correlation coefficient, Pearson r, performed on the PTT and TT results demonstrated accuracy for all arterial specimens when compared to controls. Accurate PTT's and TT's can be obtained from this RAC after discarding the dwell volume plus 4.5 ml (5.6 ml total), using either the interrupted or uninterrupted withdrawal technique. The study resulted in a publication and a presentation.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/82 Status: On-going

Title: An Evaluation of the Impact of the ANA's Standards of Nursing Practice at MAMC

Start Date: 23 Aug 85 Est Completion Date: Oct 85

Dept/Svc: Nursing/ANC Anesthesiology Course Facility: MAMC

Principal Investigator: CPT Lisa D. Chinlund, ANC

Associate Investigators:

LTC Joseph Kanusky, ANC

IRA P. Gunn, MSN, CRNA, State Univ of New York, Buffalo

Key Words: retrospective audit, implementation, audit tool

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To evaluate the impact of the nursing Quality Assurance Program and the use of the ANA's Standards of Nursing Practice Guidelines on clinical nursing practice.

Technical Approach: A retrospective audit of thirty charts taken from the period immediately upon initiation of the implementation of the ANA's Standards of Practice as Quality Assurance criteria (to enable the investigator to use DA Form 3888 and DA Form 3888-1 in the analysis of both time periods as these forms were initiated at the same time as the Standards of Practice) and thrity charts taken at one year after the implementation of these nursing QA standards will be performed. Fifteen charts from both time periods for medical (acute MI) and surgical (cholecystectomy) will be evaluated. An audit tool developed at TAMC consisting of 33 items based on the ANA's Standards of Practice will be used. MAMC uses an abbreviated version of this tool which evaluates primarily administrative actions rather than nursing care. The basis for the selected time periods is to provide an opportunity to evaluate nursing care before the ANA Standards of Practice were used as the QA audit criteria and to allow nurses sufficient time to become familiar with the new QA evaluation standards after implementation. Charts will have dates covered prior to analysis to avoid investigator bias.

Progress: This protocol is new and has not been started.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/23 Status: Completed

Title: Mothers, Toddlers, Compliance, and an Oral Liquid Medication - A Descriptive Study

Start Date: 18 Jan 85 Estimated Completion Date: Mar 85

Department: Nursing Facility: MAMC

Principal Investigator: MAJ Jeannine W. Granberg, ANC

Associate Investigator: MAJ Kathleen Mauro, ANC

Key Words: Amoxicillin, home visits, interview, strategies,

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To describe the strategies used by mothers in achieving the task of giving an oral liquid medication to their toddlers (12-24 months); to determine commonalities among these strategies; and to see if there is a correlation between the degree of difficulty in getting a toddler to take an oral medication and the rate of noncompliance.

Technical Approach: The study sample will consist of a convenience sample of 30 mothers who bring their children to the Pediatric Clinic for medical care. Criteria for inclusion in this study will be: a) mother with a child between the ages of 12 and 24 months with the diagnosis of otitis media, currently being treated with oral liquid Amoxicillin, b) mother's native language is English, and c) mother consents to a home visit. A home visit will be made within the next 6-9 days at the convenience of the subject and a tape recorded interview will pursue. The investigator will observe the subject giving a dose of Amoxicillin to the toddler and the investigator will measure the remaining medication. The entire interview will last approximately thirty minutes. Spearman's Rho will be used to analyze the data.

Progress: Thirty subjects were studied per protocol. Mothers were very much at ease giving an oral liquid medication. Children usually would open their mouths immediately. Mothers who were instructed to give the Amoxicillin TID rather than every eight hours had less difficulty in compliance - usually associated medicine with an activity such as meal or before sleep. Mothers who were instructed to give the medicine every eight hours found it upsetting to wake child or set alarm for themselves to wake up for the 2 A.M. dose. Medications were usually given later than originally intended. Most mothers saw the health care provider for the first time and were very pleased with the attention and instructions given to them. Not all mothers received a syringe to given the medicine and thus dosages varied slightly, but mothers knew to give all the medicine. The results of this study were presented at the Parent-Child Nursing Department at the University of Washington in August 1985.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/69 Status: Completed

Title: The Impact of Additional Graduate Core Curriculum Content on Army Student Nurse Anesthetists' Clinical Practice, A Pilot Study

Start Date: 28 Jun 85 Estimated Completion Date: Nov 85

Department: Nursing/Nurse Anesthetist Course Facility: MAMC

Principal Investigator: CPT Maureen Jewitt, ANC

Associate Investigators: CPT George E. Maule, ANC

LTC James M. Temo, ANC CPT Duane A. Ornes, ANC

MAJ Robert Holzman, MC CPT Mark K. Zygmund, ANC

Key Words: audit, medical/anesthesia records, educational preparation, clinical practice

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$200.00 Results: N/A

Study Objective: To determine if there is a relationship between the addition of graduate core curriculum content to a nurse anesthesia program and professionalism in the student nurse anesthetist as indicated by clinical practice.

Technical Approach: A retrospective audit of medical and anesthesia records will be carried out in an attempt to establish a relationship between educational preparation and professionalism. A review of current educational literature has established that audit can be utilized to evaluate clinical practice as an indicator of professionalism. A convenience sample will be selected consisting of all senior student nurse anesthetists educated at the Academy of Health Sciences and at Madigan Army Medical Center and who graduated from the program in the years 1981-1984. The basis for this selection is to examine the students' clinical practice for two years prior to the change in the curriculum and students' practice two years after the change. Medical records for a specific type of surgical procedure for which the senior student nurse anesthetists administered a general anesthetic will be reviewed. The anesthetic record and the progress notes will be audited utilizing a tool developed by the investigators. Data will be examined to determine if there is a relationship between educational preparation and clinical practice.

Progress: The documentation of clinical practice of two groups of students, one educated within a nongraduate school curriculum (Group I) and the other educated within a graduate school curriculum (Group II), within the same institution was examined. Statistically significant differences were demonstrated between Group I and Group II using documentation as an indicator of proficiency in clinical practice. Group II scored higher in the preoperative phase, intraoperative phase, and in total score. The design of this project as a pilot study did not lend itself to formulation of concrete conclusions based on the results. Results did demonstrate the possible existence and direction of a relationship between the addition of a graduate core curriculum to a nurse anesthesia program and documentation of clinical practice. A thesis based on this study is being prepared.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/13 Status: Completed

TITLE: Behavior and Attitude Changes in the Postpartum Period
Start Date: 16 Nov 84 Estimated Completion Date: May 85
Department: Nursing Facility: MAMC
Principal Investigator: MAJ Kathleen Mauro, ANC
Associate Investigator: MAJ Elizabeth La Du, ANC
Key Words: changes, behavior, attitude, postpartum, questionnaire
Accumulative MEDCASE Est Accumulative Periodic Review
Cost: -0- OMA Cost: \$38.00 Results: Completed

Study Objective: To examine some behavior and attitudes of postpartum women. These behaviors and attitudes will be compared and contrasted with Reva Rubin's classic nursing theory of puerperal change. According to her theory, during labor women's egos become constricted and in the puerperium women's psyches reexpand. The first period "taking-in" lasts the first three days postpartum and the second period "taking-hold" begins on the fourth postpartum day.

Technical Approach: Approximately 500 women with uncomplicated vaginal or uncomplicated C-section deliveries and whose infant is considered low risk will be asked to participate. The sample will be one of convenience and no attempt will be made to screen subjects on the basis of gravity, parity, socioeconomic status, ethnicity, age, or marital status. On the morning following delivery and on subsequent mornings while the patient is hospitalized, she will be asked to complete a questionnaire. Data will be collected for three consecutive days from women having had a vaginal delivery and for five days from women having had a C-section. Each questionnaire will be scored for "taking-in" and "taking hold" activities. The sample mean for each item and each day postpartum for both vaginal and C-sections will be determined. T-tests will be used to compare group means. Additional analysis will be conducted as indicated or recommended.

Progress: One hundred eighteen subjects were entered. Subject entry is completed and the data are now being analyzed.

DETAIL SHEETS
FOR
PROTOCOLS

DEPARTMENT OF OB/GYN

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 83/59 Status: Completed

Title: Mezlocillin Therapy for Empiric Treatment of Serious Gynecological Infections

Start Date: 15 Apr 83 Est Completion Date: Apr 85

Department: OB/GYN Facility: MAMC

Principal Investigator: COL William Benson, MC

Associate Investigators: LTC James Higbee, MSC
MAJ Shannon Harrison, MC

Key Words: gynecological infections, mezlocillin, therapy

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: Completed

Study Objective: To compare the outcome of single drug therapy with Mezlocillin to a multiple drug regimen of ampicillin, gentamicin, and clindamycin in serious gynecological infections.

Technical Approach: Two hundred women with serious genital tract infections will be studied. Patients in which an anaerobic organism is suspected or in which patients are ill enough to indicate initial treatment with a drug directed at anaerobes will be included in the study unless they are allergic to penicillin. Patients who have been treated with an antibiotic within the past 7 days will not be entered in this study. All subjects will have urine analysis and culture, CBC, SMA-20, chest x-ray, and aerobic and anaerobic cultures of blood and presumed site of infection done as appropriate. Patients will be randomly assigned to one of the two treatment groups: Group I: Mezlocillin, 300 mg/kg/day, IV, divided into 6 doses or Group II: ampicillin, 2 gms Q 4 hrs, clindamycin, 600 mgs Q 8 hrs, gentamicin, 2 mg/kg loading dose, then 1.5 mg/kg Q 8 hrs IV. Subjects will have temperatures taken at 4 hour intervals. All patients will have a CBC and ESR daily and a serum creatinine biweekly. Patients in Group II will have gentamicin levels determined at 24-36 hrs and biweekly with gentamicin dose adjusted to produce peak levels at 5-8 mcg/ml and trough levels less than 2 mcg/ml. Treatment will be continued for 5 days unless terminated earlier because of drug reaction or toxicity; pathogens resistant to the antibiotic are documented; or worsening in condition requires change in antibiotic, addition of heparin, or surgery. The treatment will be considered successful if, by completion of 5 days of therapy, the patient has been afebrile for 48 hours and has a normal examination. Following successful treatment, the patient will be followed at weekly intervals for three weeks.

Progress: Data analysis is in progress. Preliminary analysis indicates no statistically significant difference in mean fever index, mean maximum fever, mean days treatment, or failure rates between a group given triple antibiotics and a group given mezlocillin alone.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 85/03	Status: On-going
Title: Antithrombin III, Uric Acid, and Platelet Levels as Predictors of Preeclampsia		
Start Date: 19 Oct 84	Estimated Completion Date: Oct 85	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: CPT Mary N. Brumfiel, MC		
Associate Investigators: MAJ Gary Price, MS		
COL John A. Read, MC	MAJ Arthur Schipul, MC	
LTC Carl Stones, MC	Ruth A. Meshriy, B.S	
Key Words: Antithrombin III, uric acid, platelets, preeclampsia		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine whether the development of preeclampsia can be predicted by early changes in maternal levels of antithrombin III, uric acid, and platelets.

Technical Approach: Serial measurements of platelets, uric acid, and antithrombin III will be made throughout pregnancy to determine mean levels and trends, both in normal and preeclamptic pregnancies.

Subjects: 100 nulliparous pregnant women of any age, seen by 20 weeks gestation and followed in the Madigan OB Clinic for the duration of their pregnancy.

Exclusions: Any patient with a history of chronic hypertension, renal disease (other than UTI), multiple gestation, diabetes mellitus, or collagen vascular disease, and any patient who refuses to participate in the study.

Patients will receive routine OB check-ups and care, with laboratory and antepartum testing as indicated. In addition, CBC with platelets, uric acid, and antithrombin III will be measured at 20, 24, 28, 32, and 36 weeks and on admission for delivery.

A card for each patient will be completed at delivery, indicating delivery date, week gestation, and whether the patient was preeclamptic, including criteria used for making the diagnosis.

Progress: Approximately 75 women have been entered in the study. The investigators plan to enter subjects until 100 subjects are entered.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/26 Status: On-going

Title: The Pharmacokinetics of Clindamycin and Gentamicin in Patients with Postcesarean Endometritis

Start Date: 18 Jan 85 Estimated Completion Date: May 85

Department: OB/GYN Facility: MAMC

Principal Investigator: COL Patrick Duff, MC

Associate Investigators: MAJ Jerome Kopelman, MC

MAJ Charles Hannan, MS

Key Words: postcesarean endometritis, pharmacokinetics, clindamycin, gentamicin, revised schedule

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$5500.00 Results: N/A

Study Objective: To measure serum antibiotic concentrations in patients receiving a revised dosage schedule of clindamycin-gentamicin for treatment of postcesarean endometritis.

Technical Approach: Fifteen patients being treated with clindamycin/gentamicin for postcesarean endometritis will form the study group. On the second day of therapy, peripheral venous samples will be collected 30 min, 2 hr, 4 hr, and 7 hrs after infusion of a scheduled dose of the drugs. Serum will be separated from the samples and then assayed for clindamycin and gentamicin concentrations. The former will be determined by bioassay or HPLC; the latter will be determined by polarized immunofluorescence.

Results will be expressed as mean concentration at each sampling interval. Serum concentrations of the two drugs then will be compared to reported MIC values for the major pathogens responsible for postcesarean endometritis: aerobic streptococci, anaerobic streptococci, coliform organisms, and *Bacteroides* species.

Progress: Two subjects have been entered to date. Serum specimens for assay of clindamycin concentrations have been obtained and frozen. Gentamicin concentrations were measured. Peak and trough concentrations have been in the approximate range, using the revised dosing criteria.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/27 Status: On-going

Title: An Investigation of Neutrophil Phagocytic Function in Obstetric Patients

Start Date: 18 Jan 85 Estimated Completion Date: Sep 85

Department: OB/GYN Facility: MAMC

Principal Investigator: COL Patrick Duff, MC

Associate Investigators: LTC James W. Higbee, MSC

MAJ Jerome Kopelman, MC

Key Words: vaginal delivery, cesarean delivery, antibiotic therapy

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To determine whether changes in host neutrophil phagocytic function occur during labor and the immediate puerperium; to determine whether neutrophil phagocytic function is different in women delivering by cesarean section and women delivering vaginally; and to evaluate neutrophil phagocytic function in women who develop puerperal endometritis; specifically, to determine whether antibiotic therapy influences efficiency of phagocytosis.

Technical Approach: Four groups (20 pts/group) will be studied:

- Group 1: healthy non-pregnant women who are not utilizing oral contraceptives or glucocorticoids as controls
- Group 2: term patients who have uncomplicated pregnancies and who undergo vaginal delivery
- Group 3: term patients who undergo elective repeat c-section
- Group 4: term patients who undergo unscheduled cesarean delivery

Controls will have blood samples taken during a routine appointment at the OB/GYN Clinic. Patients undergoing vaginal delivery or unscheduled cesarean delivery will have venous blood collected early in labor (<4 cm dilation), late in labor (4-9 cm dilation), and 12-24 hours postpartum. In women undergoing scheduled cesarean delivery, peripheral venous blood will be collected immediately preoperatively and then 18 to 24 hours postoperatively. Patients who develop puerperal endometritis will have blood samples collected at the time of diagnosis of infection and then 12 to 24 hours after institution of antibiotic therapy. If abnormalities are found after 10 patients have been entered in each group and these abnormalities are found spread throughout the groups, a fifth group will be added consisting of non-pregnant women who are undergoing comparable surgery with a similar anesthetic.

Progress: Because of a shortage of time and laboratory resources, the investigator has been unable to begin this project. These resources should be available within the next few months in order to start the project.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/70 Status: On-going

Title: A Comparison of Two Single-Dose Antibiotic Regimens for Treatment of Uncomplicated Lower Urinary Tract Infections in Obstetric Patients

Start Date: 28 Jun 85 Est Completion Date: Jun 86

Department: OB/GYN Facility: MAMC

Principal Investigator: COL Patirck Duff, MC

Associate Investigators: MAJ Andrew Robertson, MC

MAJ Jerome Kopelman, MC

Key Words: amoxicillin, sulfisoxazole, bacteriuria, acute cystitis

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: 100.00 Results: N/A

Study Objective: To compare two single-dose oral antibiotic regimens for the treatment of uncomplicated lower urinary tract infections in obstetric patients: Regimen A: Amoxicillin 2 gms and Regimen B Sulfisoxazole 2 gms

Technical Approach: Obstetric patients (100) experiencing their initial episode of asymptomatic bacteriuria or acute cystitis will be randomized to receive either a single 2 gram oral dose of amoxicillin or a single 2 gram oral dose of sulfisoxazole. The investigators will be blinded as to the drug received by the patient.

Asymptomatic bacteriuria will be defined as $>10^5$ colonies/ml of a recognized uropathogen in urine obtained by clean-catch, midstream technique. For evaluation of acute cystitis urine will be obtained by catheterization. A presumptive diagnosis of cystitis will be made if there are >5 wbcs/hpf and/or any bacteria in a high power field. Symptomatic patients will be treated on the basis of the urinalysis results. The diagnosis will be considered confirmed only if the urine culture subsequently shows $>10^2$ col/ml of a recognized uropathogen. Urine cultures will be obtained within 3-4 days after therapy. Patients with persistence of the original infecting organism will be considered treatment failures. They will be retreated with a conventional course of antibiotics. The chi-square test will be used to evaluate differences in treatment effect between the two groups.

Patients with a history of recurrent UTI, patients with organisms resistant to the study drugs, individuals who have acute pyelonephritis, women allergic to either of the study drugs, and patients >36 weeks gestation will be excluded from the study. The investigators will insure that there is no evidence of premature labor before entry into the protocol.

Progress: Forty-two subjects have been entered. After 50 patients have completed therapy, the data will be reviewed to assure that an inferior treatment modality is not being used unnecessarily. To date, 80% of patients have been cured. This is comparable to cure rates with more extended courses of therapy.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/71 Status: On-going

Title: A Comparison of Clindamycin plus Cefazolin versus Mezlocillin for Treatment of Postcesarean Endometritis and Posthysterectomy Pelvic Cellulitis

Start Date: 28 Jun 85 Est Completion Date: Jun 86

Department: OB/GYN Facility: MAMC

Principal Investigator: COL Patrick Duff, MC

Associate Investigators: MAJ I. Keith Stone, MC

COL William L. Benson, MC

Key Words: cefazolin, alternative to aminoglycoside, single agent vs combination

Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: 100.00	Results: N/A

Study Objective: To compare two antibiotic regimens for treatment of postoperative infections in obstetric and gynecologic patients.

Technical Approach: The study group will be composed of patients who have either postcesarean endometritis or posthysterectomy pelvic cellulitis. Patients allergic to any of the study medications will be excluded. Patients will be randomly assigned to receive either clindamycin, 900 mg Q8h plus Cefazolin 2 gm Q8h or Mezlocillin, 4 gm Q6h. Blood, urine, and operative-site cultures will be obtained prior to the start of therapy. The following variables will be used to evaluate treatment effect: incidence of cure with antibiotics alone, fever index, need for additional surgery, need for change in antibiotic therapy, duration of hospitalization, incidence of side effect failures. Patients will be treated with parenteral antibiotics for 48 hours beyond the time that they become afebrile and asymptomatic. Treatment failures will be defined as individuals who fail to experience improvement in the physical and laboratory manifestations of infection within 72 hours of the start of therapy. In patients in either group who fail to experience a response to therapy but who have no evidence of wound infection or abscess, therapy will be changed to clindamycin (900 mg Q8h), penicillin (5 mil units Q6h), and gentamicin (60-80 mg Q8h).

Progress: This protocol has not yet been activated because the investigators were completing a previous protocol comparing two antibiotic regimens for the treatment of postoperative pelvic infections.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/72 Status: On-going

Title: A Comparison of Cefazolin versus Cefonicid as Single-Dose Prophylaxis for Prevention of Postcesarean Endometritis

Start Date: 28 Jun 85 Est Completion Date: Jun 85

Department: OB/GYN Facility: MAMC

Principal Investigator: COL Patrick Duff, MC

Associate Investigators: COL John A. Read, MC

MAJ Jerome Kopelman, MC

MAJ Andrew Robertson, MC

Key Words: single dose, prophylaxis, cefazolin, cefonicid

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: 100.00 Results: N/A

Study Objective: To evaluate the efficacy of two single-dose antibiotic regimens as prophylaxis for prevention of postcesarean endomyometritis.

Technical Approach: The study will be restricted to patients who are having unscheduled cesarean delivery. Patients who already are infected at the time of surgery or who are allergic to either of the study drugs will be excluded. Upon entry into the study, patients will be randomized to receive either cefonicid (1 gm) or cefazolin (1 gm). The drugs will be administered intravenously after delivery of the fetus. Both the patient and physician will be blinded as to the actual drug administered.

Postoperatively, patients will be evaluated for evidence of infection-related morbidity. Measures of morbidity will include: standard febrile morbidity, fever index, endometritis, UTI, wound infection, need for therapeutic antibiotics, development of serious sequelae of primary infection (bacteremia, septic shock, pelvic abscess, septic pelvic thrombophlebitis), and duration of hospitalization. Patients will be evaluated in the outpatient clinic six weeks after surgery to determine if late sequelae of infection have developed. Differences in treatment effect will be evaluated by means of the chi-square test (discrete data) and independent-sample t-test (continuous data).

Progress: Investigators are awaiting HSC approval before implementing the protocol.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 85/16	Status: On-going
Title: A Randomized Comparison of Oral Terbutaline vs Oral Ritodrine for Prevention of Recurrent Premature Labor		
Start Date: 16 Nov 84	Estimated Completion Date: May 86	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: MAJ Jerome N. Kopelman, MC		
Associate Investigators: COL John A. Read, MC		
LTC Patrick Duff, MC		
MAJ Arthur Schipul, MC		
Key Words: recurrent, premature labor, oral terbutaline, oral ritodrine, safety, efficacy, cost		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: See below*

Study Objective: To determine if either terbutaline or ritodrine, two widely accepted and widely used oral tocolytic agents, is more effective in the prevention of recurrent premature labor.

Technical Approach: Premature labor patients will be managed according to the SOP at MAMC. Subjects will be randomized to receive either terbutaline or ritodrine (50 in each arm). Oral medications will be continued until the 37th week of gestation. Patients will be followed weekly with records kept on maternal heart rate, cervical exam, contractions, side effects, and dosage. If PML recurs, patients once again will be placed on parenteral ritodrine and then continue on the same oral drug to which they were initially randomized.

Progress: This protocol was subjected to continuing review in June 1985 because of questions regarding obtaining informed consent from patients in labor. The investigators reworded the plan to state that informed consent would not be obtained and the patient entered on the protocol until she has been stabilized for 12 hours. The consent form was rewritten to state that there are no known risks to the baby and to add a signature line for the father to sign if he is available.

Patients are continuing to be entered with no adverse effects reported.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/40 Status: Completed

Title Evaluation of Betamimetic Induced Cardiac Ischemia During Tocolysis

Start Date: 22 Feb 85 Estimated Completion Date: Aug 86

Department: OB/GYN Facility: MAMC

Principal Investigator: MAJ Jerome Kopelman, MC

Associate Investigators: COL John A. Read, MC

LTC Patrick Duft, MC

MAJ Arthur H. Schipul, MC

Key Words: ritodrine, myocardial ischemia, ECG changes, CEP

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$645.00 Results: N/A

Study Objective: To evaluate obstetric patients being treated with tocolytics for evidence of myocardial ischemia, as reflected by ECG changes and serial cardiac enzyme profiles (CEP). Specifically, to determine whether utilization of beta mimetics at MAMC is associated with myocardial ischemia or myocardial necrosis and if patients at risk for these complications can be identified.

Technical Approach: Fifty patients undergoing tocolytic treatment will be asked to participate in this study. Prior to initiation of therapy an ECG with 2-minute rhythm strip will be done, and a blood sample will be drawn for enzyme studies and serum potassium. No extra venipuncture will be needed as bloods are drawn routinely for CBC and SMAC; ECG is SOP as well. Twenty-four hours after initiation of IV ritodrine another blood specimen and ECG will be obtained. Forty-eight hours (+ 4 hr) after initiation of therapy, a third set will be obtained. Lab studies will be SGOT, LDH, CPK, and CPK-MB.

In the event of any abnormality in enzymes or ECG, a cardiology consult will be obtained. In the event of an excess of 5% adverse effects, the SOP for ritodrine will be suspended and the management procedures reevaluated.

Progress: Fifty subjects were studied with no adverse effects. Data are now being analyzed.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 83/17	Status: On-going
Title: External Cephalic Version with Tocolysis Using Ritodrine		
Start Date: 19 Nov 82	Est Completion Date: Dec 85	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: MAJ David J. Magelssen, MC		
Associate Investigators: COL Edward E. Dashow, MC		
COL Patrick Duff, MC		
COL John A. Read, MC		
MAJ Jerome Kopelman, MC		
MAJ Andrew Robertson, MC		
MAJ Arthur H. Schipul, MC		
Key Words: breech birth, external cephalic version, Ritodrine		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine if the incidence of breech birth can be decreased by external cephalic version using Ritodrine to relax the uterus.

Technical Approach: One hundred gravidas with breech presentation >36 weeks gestation will be studied. Ultrasonography will be performed to confirm the breech presentation; measure biparietal fetal diameter to assess gestational age; quantify amount of amniotic fluid; rule out fetal cephalic anomalies and/or hyperextension; and localize placenta. If the mother is Rh negative, a Kleihauer-Betke test will be done pre and post procedure. Rhogam will be administered if indicated. Pre and post procedure fetal activity determination tests will be done by external fetal monitoring. The subjects will then be randomized to a treatment group and a control group. The treatment group will be administered Ritodrine by IV infusion at 200 µg/min for 20 min. External cephalic version will then be attempted and a successful procedure will be confirmed by ultrasonography. The treatment group will go straight to the external cephalic version. Any patients with evidence of a compromised fetus with a nonreactive fetal activity determination test, congenital anomalies by ultrasonography, oligohydramnios, or placenta previa will be excluded.

Progress: Approximately 60 subjects have been entered. More patients will be entered before the data are analyzed.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 85/11	Status: On-going
Title: The Effect of Estrogens on the Renal Actions of Calcium-Regulating Hormones in Postmenopausal Women		
Start Date: 16 Nov 84	Estimated Completion Date: Jan 86	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: CPT William J. Polzin, MC		
Associate Investigators: LTC Gary L. Treece, MC		
MAJ I. Keith Stone, MC		
Key Words: Estrogen, renal, calcium, parathyroid, postmenopausal		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: \$3700.00	Results: N/A

Study Objective: This study proposes to clarify the mechanism whereby estrogens favorably affect calcium metabolism in postmenopausal women by evaluating the estrogen effect on the renal actions of calcium-regulating hormones (PTH, calcitonin, and $1,25(\text{OH})_2\text{D}_3$).

Technical Approach: Subjects will be 20 chronically estrogen deficient postmenopausal women for whom estrogen therapy has been advised. They will be placed on an approximate 400 mg/day calcium diet (no dairy products or calcium-containing medication) for one week prior to testing, before and after 6 weeks of Premarin therapy. Serum PTH, cAMP, SMA 20, and calcitonin will be done. Urine (2 hr collection) protein, creatinine, calcium, phosphorous, and cAMP, will be collected after 12-hr fast.

One set of assays would be collected before and at six weeks after instituting therapy with Premarin at a dose of 0.625 mg, qd, in 10 patients and 1.25 mg, qd, in ten patients. After the six weeks of Premarin therapy alone, subjects will be treated conventionally with Premarin with or without Provera as determined in consultation with the subject's primary physician. Pre and post treatment values of serum calcium, PO_4 , creatinine, cAMP, $1,25(\text{OH})_2\text{D}_3$, urine creatinine clearance, fraction calcium excretion, total and nephrogenous cAMP, TRP, and TMP/GFR will be compared using paired and independent t tests as appropriate.

Progress: Fifteen patients have been entered. Two withdrew because of side effects (rash, nausea) and three withdrew because of the inconvenience. Investigators will continue to enroll patients until a minimum of 20 is attained.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 83/01	Status: Completed
Title: Comparison Study of Intrauterine Irrigation versus Intravenous Use of Mandol or Claforan During Cesarean Sections		
Start Date: 15 Oct 82	Est Completion Date: Oct 85	
Department: OB/GYN	Facility: MAMC	
Principal Investigator:	COL John Read, MC	
Associate Investigators:	COL Edward E. Dashow, MC	
COL Patrick Duff, MC	LTC Fred H. Coleman, MC	
COL Carl Stones, MC	MAJ Arthur Schipul, MC	
Key Words: irrigation, I.V., Mandol, Claforan, cesarean sections		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Completed

Study Objective: To compare the effects of Mandol and Claforan in reducing febrile morbidity and the incidence of endomyometritis following cesarean section.

Technical Approach: Mandol (cefomandole natate), in the original protocol, was compared to moxalactam disodium, cephapirin sodium, and ampicillin. In view of the overwhelming success in decreasing the post-cesarean section endomyometritis rate of Mandol used as an intrauterine irrigation agent (22% vs 3%, $p=.01$), the investigators revised the protocol to study intrauterine irrigation vs intravenous use of Mandol and Claforan (cefotaxime sodium). Patients undergoing cesarean section without a history of allergic reaction to cephalosporins and penicillin and without evidence of clinical infection and no antibiotic therapy will be studied. Endometrial cultures will be obtained prior to irrigation and also post-partum if infection is suspected. Solu-B-forte will be added to the irrigant for disguise. Four groups of 70 patients will be treated as follows: Group 1: 2 gm Mandol in 800 cc saline irrigation; 100 cc saline IV; Group 2: 2 gm Claforan in 800 cc saline irrigation; 100 cc saline IV; Group 3: 800 cc saline irrigation; 2 gm Mandol in 100 cc saline IV; Group 4: 800 cc saline irrigation; 2 gm Claforan in 100 cc saline IV.

No additional antibiotics will be given unless indicated for complications. All patients will receive aerobic and anerobic endometrial cultures at the time of cesarean section prior to irrigation. Two days following cesarean they will again receive aerobic and anerobic cultures of the endometrial cavity. Patients will be followed at two and six weeks post-op.

Progress: Two hundred and forty-two (242) patients were studied. There were no statistically significant differences between groups with respect to incidence of standard febrile morbidity and endomyometritis in all patients or in the subset of unscheduled deliveries. The cost of antibiotic preparation and administration was approximately the same in the four groups. The investigators conclude that all of the regimens are satisfactory means of providing prophylaxis against postcesarean infection. A paper has been submitted for publication.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 83/02	Status: On-going
Title: Randomized Trial of Ambulation vs Oxytocin for Labor Enhancement		
Start Date: 15 Oct 82	Est Completion Date: Oct 86	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL John A. Read, MC		
Associate Investigators: COL Edward E. Dashow, MC LTC Frederick H. Coleman, MC		
Key Words: ambulation, oxytocin, labor enhancement		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To compare the efficacy of ambulation vs oxytocin in cases of dysfunctional labor or so called dystocia.

Technical Approach: Patients who have failed to progress in labor for one hour, >4 cm dilated, and requiring augmentation of labor will be studied. Membranes shall have been ruptured and direct internal fetal monitoring in use, showing no evidence of fetal distress. Patients should not have received analgesia or sedations for at least one hour and should not be drowsy or exhausted. Patients will be placed on the fetal monitor in the right or left lateral decubitus position. There will be a 30 minute observation period during which time uterine activity will be quantified: uterine activity units on line, Montevideo units; contraction frequency; intensity and baseline tonus; fetal heart rate pattern and variability; and progress in effacement, dilation, and station.

Group I: Using either a cable or 2-channel telemetry the patient will assume the vertical position. Exams will be conducted at one and two hours, noting the parameters stated above. If after 2 hours no progress has occurred, the patient will be returned to bed and oxytocin utilized. If good progress is being accomplished, the patient may continue ambulation if she chooses.

Group II: Continuous IV infusion of oxytocin will begin at 0.5 mu/min and increased every 15 min until contractions are every 2 1/2-3 min and >50 mmHg in intensity. Patient will be in the right or left lateral decubitus position and the parameters noted above will be measured. If at the end of two hours there is no progress and other conditions are met, the patient will be given the option to ambulate.

Length of labor, time from study entry to delivery, type delivery, 1 and 5 min Apgar scores, cord blood gasses, maternal pain perception, newborn weight and neonatal problems will also be noted.

Progress: No patients have been entered due to time constraints. The investigators have requested that this protocol be left open in order to activate it during the coming year.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 83/12 Status: On-going

Title: The Detection of Fetal Maternal Hemorrhage in External Version and OCT via Alpha-feto-protein

Start Date: 15 Oct 82 Est Completion Date: Sep 86

Department: OB/GYN Facility: MAMC

Principal Investigator: COL John A. Read, MC

Associate Investigators: LTC Fred H. Coleman, MC

LTC Edward E. Dashow, MC

MAJ Arthur Schipul, MC

Key Words: fetal-maternal bleeding, external cephalic version, oxytocin challenge testing, serum alpha-feto-protein, Kleihauer-Betke testing

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: Continue

Study Objective: To test for possible fetal-maternal bleeding during external cephalic version and oxytocin challenge testing using serum alpha-feto-protein and Kleihauer-Betke tests.

Technical Approach: Patients will be selected for oxytocin challenge testing or version by current management criteria used in the OB/GYN Department. Fifty patients reporting for versions and 100 patients reporting for oxytocin challenge testing will have pre and post blood samples drawn. The AFP levels will be determined via AFP radioimmunoassay kit and the Kleihauer-Betke via standard kit. The results will be correlated with each other and the procedures performed to determine the rate of fetal maternal bleeding.

Progress: Approximately 30 patients were entered in the study. The assays have not been completed to date.

Upon the departure of MAJ Schipul in July 1985, COL John A. Read became the principal investigator.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/05 Status: On-going

Title: Effects of Position on the Second Stage of Labor and Delivery

Start Date: 21 Oct 83 Est Completion Date: Oct 86

Department: OB/GYN Facility: MAMC

Principal Investigator: COL John A. Read, MC

Associate Investigators:

COL Edward E. Dashow, MC MAJ Arthur H. Schipul, MC

LTC Fred H. Coleman, MC CPT Virginia Hallinan, MC

Key Words: position, labor, delivery, supine, lateral Sims group, upright group

Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To examine and correlate the effects of various positions on the length of the second stage of labor, the strength and frequency of contractions, the patient's comfort, and the fetal heartbeat.

Technical Approach: A group of 75 patients, pregnant for the first time, will be randomly assigned to one of three groups (supine, lateral Sims, or upright. Patients will be uncomplicated, at term (between 37 and 42 weeks), and have had a normal first stage. Internal monitoring of uterine activity and fetal heart condition will be done on a continuous basis throughout the second stage. All tracings will be examined for frequency, duration, and amplitude of contractions, uterine activity and Montevideo units, fetal distress, length of second stage, patient comfort, and the development of complications of delivery. No anesthesia other than local will be used. The results will be compared using Student's t test, chi square, or Mann-Whitney U test as required by the various types of data collected.

Progress: No patients have been entered due to limitations of manpower. The investigators have requested that this protocol be left open in the hope of commencing the protocol in the near future.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/68 Status: Terminated

Title: Clinical Evaluation of a Continuous Tissue pH Monitor for Intrapartum Fetal Monitoring

Start Date: 15 Jun 84 Est Completion Date: Jul 86

Department: OB/GYN Facility: MAMC

Principal Investigator: COL John A. Read, MC

Associate Investigators: MAJ Jerone N. Kopelman, MC
MAJ Arthur H. Schipul, MC

Key Words: continuous, tissue pH monitor, intrapartum, complications, fetal scalp and umbilical arterial samples

Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Terminate

Study Objective: To ascertain the clinical accuracy during labor of continuous tissue pH with simultaneous measurement of fetal scalp and umbilical arterial pH samples; in particular to document pH and its changes in postdates patients with thick meconium; document factors which might cause discrepancies between methods; ascertain practicality and reliability of fetal tpH monitoring system and skill level required for use; determine *in vivo* drift of system in clinical use; determine incidence and type of maternal and fetal complications due to tpH probe.

Technical Approach: The probe will be used in conjunction with standard fetal monitoring. Probe will be applied only to patients where pH measurements are clinically indicated in term or post-date tetuses with vertex presentations and cervical dilation of at least 6 cm and descent to station 0 or below. The cervix should not be posterior. The clinical appearance and the palpated turgor of the fetal scalp will be recorded and the probe prepared and attached per instructions in the manual. Difficulties in application, bleeding, or obtaining data will be noted, along with problems of mother or fetus caused by application. Intrapartum fetal scalp capillary pH measures will be obtained while monitoring the tpH and compared to the tpH value. Fetal scalp capillary pH will be obtained during Stage II of labor for comparison with the simultaneous intrapartum tpH values. Umbilical arterial blood pH will be obtained at delivery for comparison with last intrapartum tpH or simultaneous tpH post-partum. Maternal venous pH will be measured during monitoring as a check on both the tpH and the capillary pH and as an indication of the cause of fetal pH changes. Corometrics pH system will be used in addition to laboratory determinations.

Progress: Due to the small number of patients that were enrolled at MAMC, the company that provided the monitor chose to remove it for use at an institution that would have more subjects to study.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 81/73 Status: Completed

Title: Diamine Oxidase Levels and Asthma in Pregnancy

Start Date: 17 Apr 81 Est Completion Date: Oct 85

Department: OB/GYN Facility: MAMC

Principal Investigator: CPT Gloria A. Richard-Davis, MC

Associate Investigators:

MAJ James S. Little, MSC CPT Julie Ducey, MC

MAJ Rebecca Sullivan, MC CPT Diane J. Madlon-Kay, MC

Key Words: serum diamine oxidase, disease activity

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$600.00 Results: N/A

Study Objective: To determine if a correlation exists between serum diamine oxidase levels and disease activity in pregnant asthmatic women.

Technical Approach: Approximately 25 new obstetric patients who have had an asthma attack within the previous three years and a control group of 12 newly pregnant non-asthmatic women will have a detailed history taken. In particular, any history of allergy, hayfever, or smoking will be noted, and in asthmatics the frequency and severity of attacks and their treatment. In addition to the routine initial laboratory tests, the patients will have determinations of their diamine oxidase levels and spirometry measurements of FVC AND FEV. At every clinic visit, the asthmatic patients will be examined for wheezing and questioned in particular about their respiratory symptoms and medications. Every four weeks and at six weeks postpartum both the control and asthmatic patients will have spirometry and diamine oxidase determinations. Asthmatic patients' clinical conditions during pregnancy will be classified as worse, unchanged, or improved by evaluating the change in respiratory symptoms, severity of wheezing on physical exam, medication changes required, and spirometry. A chi-square analysis will be done to determine if any correlation exists between the diamine oxidase levels and the asthmatic patients' clinical conditions.

Progress: All data has been collected and is now being analyzed.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 80/48	Status: On-going
Title: Impact on Fetal Monitoring on the Premature Infant		
Start Date: 20 Jun 80	Est Completion Date: Sep 85	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL David Sa'Adah, MC		
Associate Investigators:		
COL Joseph Sakakini, MC	E. B. Larson, M.D.	
MAJ Alexander Smythe, MC	K. K. Shy, M.D.	
D. A. Luthy, M.D.	G. VanBelle, M.D.	
Key Words: impact, electronic fetal monitor, premature infants		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To analyze the effects of electronic fetal monitoring versus traditional auscultation in infants of very low birth weight with respect to the following endpoints: (1) perinatal mortality; (2) perinatal morbidity including Apgar scores, acid-base status at birth, and frequency of intracranial hemorrhage; (3) maternal morbidity including rates of cesarean section; (4) infant neurological and psychomotor development to one year of age; (5) provider satisfaction; (6) consumer satisfaction; (7) medical decision making; and (8) cost effectiveness analysis.

Technical Approach: Follow-up will be performed on infants who have had fetal monitoring. Those fetuses who have had electronic fetal monitoring and fetal scalp blood sampling done will be followed and compared to randomized traditional auscultation fetal heart rate. Comparisons of fetal outcome and well-being will be made. A comparison will be made of infants <1100 gm and >1100 gm. Infants will be followed and evaluated for evidence of retardation, cerebral palsy, and hearing loss at 6 months, 1 year, 1 1/2 years, and 2 years.

Progress: Subjects are still in follow-up (two year period). Accrual of patients took longer than expected, and therefore the protocol has taken longer than expected to complete. Data analysis should begin in early 1986.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/10 Status: Completed

Title: Lactose Intolerance in Pregnancy: Its Identification and Treatment

Start Date: 21 Oct 83 Est Completion Date: Apr 85

Department: OB/GYN Facility: MAMC

Principal Investigator: MAJ Arthru Schipul, MC

Associate Investigators:

COL Edward Dashow, MC COL Carl Stones, MC

COL Charles Mitchell, MC CPT Virginia Hallinan, MC

COL John Read, MC GS/09 Rita Thompson, R.N.

Key Words: lactose, intolerance, pregnancy

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$1600.00 Results: Completed

Study Objective: Part A: to identify lactose intolerance in grvida patients with a history of milk intolerance and/or current clinical suspicion of intrauterine growth retardation (IUGR). Part B: to treat identified lactose intolerant grvida patients with supplemental calcium and a lactose enzyme in milk for ingestion.

Technical Approach: PART A: Dietary and obstetrical histories will be obtained from patients undergoing clinical IUGR workup, and subjects will be questioned regarding possible milk intolerance. Patients with a positive history of milk intolerance but with normal grvida status will form the study group and controls will consist volunteers with a negative history of milk intolerance and normal grvida states. Milk-drinking habits are not to be altered. Lab assays to include CBC, SMAC-20, and Mg will be performed on fasting blood specimens of all subjects. These same assays will be performed on the cord blood and the mother at the time of delivery. A 3^o glucose tolerance test and a calcium meal load test will be done for those patients with abnormal lactose tolerance test. Blood lactose tolerance tests and hydrogen breath assays will be done on all patients and controls in this study. Routine IUGR screening will be performed ante-partum on all subjects. Evaluation of infants will consist of routine newborn parameters, and Ponderal indexes, Brazelton scores, and hydrogen breath analysis will be recorded. Lactose intolerance will be determined by blood assay lactose tolerance test and hydrogen breath analysis assay. Prior to the morning lactose challenge, the patient will have had an overnight fast. After identification and evaluation of a statistically significant number of patients and controls, Part A will be completed.

PART B: Part B will consist of the identification of additional grvida lactose intolerant patients. Lactose intolerant patients will be randomly assigned to either a treatment group or a non-treatment control group. Therapy will consist of calcium supplementation and the use of a lactase enzyme in refrigerated milk 24 hours prior to ingestion. All prenatal clinic patients routinely have prenatal vitamins prescribed for daily use. Compliance will be stressed. All assays given in the data base above will be performed on these patients also.

Progress: Patients (n=257) have been evaluated and data analyzed. A paper for publication is now being prepared.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/20 Status: On-going

Title: Microsurgical Technique

Start Date: 16 Jan 85 Estimated Completion Date: Indefinite

Department: OB/GYN

Facility: MAMC

Principal Investigator: MAJ I. Keith Stone, MC

Associate Investigator: MAJ Leslie W. Yarbrough, VC

Key Words: Residents, proficiency, reproductive tracts, rabbits

Accumulative MEDCASE

Est Accumulative

Periodic Review

Cost: -0-

OMA Cost: \$400.00

Results: N/A

Study Objective: To develop proficiency with instrument and suture handling when using the operating microscope.

Technical Approach: Residents in the Department of Obstetrics and Gynecology who are rotating through the Infertility Service will be obligated to demonstrate proficiency with microsurgical dissection and reanastomosis of rabbit reproductive tracts. Rabbits will be anesthetized with ketamine and midline laparotomies will be performed. Using the organic operating microscope, dissection and proper realignment of reproductive structures will be accomplished under staff supervision. Sutures and instruments will duplicate those used in the reanastomosis of human oviducts. The rabbits will be recovered from surgery and will at approximately four weeks postoperatively undergo laparotomy excision of the oviducts for histologic examination and methylene blue instillation to determine patency. The animal model will then be terminated.

Progress: Ten training sessions have been conducted. Resident acceptance has been extremely positive. Those residents who have performed the laboratory procedures have noted a positive impact on their operating room technical abilities.

Detail Summary Sheet

Date: 30 Sep 86 Protocol No.: 84/75 Status: Completed

Title: Serum Haptoglobin in Ovarian Cancers

Start Date: 17 Aug 84 Est Completion Date: Aug 85

Department: OB/GYN Facility: MAMC

Principal Investigator: CPT Patsy J. Webber, MC

Associate Investigators: COL William L. Benson, MC

COL Roger B. Lee, MC

COL Carl Stones, MC

Key Words: cancer, ovarian, serum haptoglobin

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To determine if serum haptoglobin levels are elevated with ovarian cancer and if they decrease with tumor response to therapy in those patients found to have ovarian cancer.

Technical Approach: Sixty consecutive patients admitted for exploratory laparotomy for pelvic mass will be enrolled in the study. A pre-op serum sample will be drawn for haptoglobin analysis. Those patients found to have ovarian cancer will be followed every three weeks with serum levels for as long as they are receiving treatment for the cancer and then every three months for two years while the cancer is in remission. The serum haptoglobin concentrations will be correlated with the course of the disease and the results of the second laparotomy.

Progress: Forty-one patients were entered on the study. The data are now being analyzed.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/02 Status: Completed

Title: Hormone Measurements in Response to Clomiphene Therapy
Start Date: 19 Oct 84 Estimated Completion Date: Aug 87
Department: Dept OB/GYN Facility: MAMC
Principal Investigator: CPT Patsy Webber, MC
Associate Investigators: COL Stephen R. Plymate, MC
CPT Karl E. Friedl, MSC
CPT Gloria Richard-Davis, MC
Key Words: Hormones, Clomiphene, anovulatory women
Accumulative MEDCASE Est Accumulative Periodic Review
Cost: -0- OMA Cost: \$500.00 Results: N/A

Study Objective: To determine changes in sex hormone binding globulin levels in response to clomiphene therapy given to induce ovulation.

Technical Approach: Ten oligo or anovulatory women who are attempting pregnancy will be enrolled in the study. The initial evaluation will include history, physical exam, semen analysis, and serum prolactin as would be performed in the routine infertility work-up. Patients will then be placed on clomiphene citrate in a dose decided upon by the investigator, based upon their clinical judgment as to which dose is appropriate for that individual. Subjects will have blood samples drawn every other day for 30 days, beginning five days before clomiphene administration with the onset of menses. Six to seven ml of blood will be drawn each day for a total of 100 ml of blood drawn over the 30 day period. Serum ferritin will be measured on days 1, 15, and 30. If a change in serum ferritin is noted, iron replacement will be initiated. Blood samples will have SHBG, estradiol, progesterone, and HDL measured. A basal body temperature chart will be kept during the clomiphene cycle and serum luteinizing hormone will be measured to determine the time of ovulation. Data analysis will be performed using SPSS and SAS statistical analysis with one-way analysis of variance and Duncan's test.

Progress: Four women who had been taking clomiphene citrate and had been shown to be ovulatory were studied. In these four women there was a failure of the normal rise in SHBG during the luteal phase of the cycle, and, in fact, a decline in SHBG was seen. This suggests that although clomiphene citrate may stimulate good follicular development and ovulation occurs, the peripheral anti-estrogenic effects may be a factor in inhibiting pregnancy and account for the discrepancy between ovulatory events and pregnancies in patients treated with clomiphene citrate.

A paper has been submitted for presentation at the OB-GYN Armed Forces Seminar in October 1985.

DETAIL SHEETS
FOR
PROTOCOLS

DEPARTMENT OF PEDIATRICS

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/93 Status: On-going

Title: Duration of Positive Pressure (DPP) as a Measure of Lung Compliance

Start Date: 20 Sep 85 Est Completion Date: Jun 86

Department: Pediatrics Facility: MAMC

Principal Investigator: CPT Ralf Brueckner, MC

Associate Investigator: CPT Glenn D. Jordan, MC

Key Words: peak inspiratory pressure, positive end expiratory pressure, inspiratory and expiratory times, flow, compliance, and resistance.

Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: N/A

Study Objective: To determine which variables (compliance, resistance, pressure, time, flow) affect DPP; to test the hypothesis that compliance is the major variable affecting DPP; and to test the hypothesis that DPP correlates with changes in ventilatory requirements during the course of idiopathic respiratory distress syndrome (IRDS) in neonates.

Technical Approach: Phase I: A Bourns model LS 130 infant lung simulator, a Sechrist model IV-100B infant ventilator, and a model 400 airway pressure monitor will be used. A Novamatrix model 1230A Pneumoguard will be used for recording of pressure waveforms. DPP will be measured from these waveforms. Independent variables include: peak inspiratory pressure (PIP), positive end expiratory pressure (PEEP), inspiratory and expiratory times (IT, ET), flow, compliance and resistance. These will be varied over ranges typically required in the ventilation of infants. The dependent variable DPP would be expected to be directly proportional to compliance. Data will be analyzed using multiple linear regression.

Phase II: DPP will be recorded on 20 infants with IRDS undergoing conventional ventilator management, along with PIP, PEEP, IT, ET, and flow. The diagnosis of IRDS will be made by the infants primary physician with the supervision of the attending neonatologist. Initially, measurements will be recorded every 6 hours, beginning at the onset of mechanical ventilation. It is expected that changes in ventilator requirements would be preceded by changes in compliance, and, hence, changes in DPP. Correlation studies will be used to analyze results.

Progress: This is a new study and no subjects have been entered.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 84/44	Status: Terminated
Title: Beta-Thromboglobulin (BTG) Levels in the Newborn		
Start Date: 16 Mar 84	Est Completion Date: Jul 84	
Department: Pediatrics	Facility: MAMC	
Principal Investigator: CPT Virginia Hallinan, MC		
Associate Investigators: COL Gary Pettett, MC		
MAJ Philip V. Marinelli, MC		
Key Words: baseline, change, duration of labor, BTG, newborns		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: \$538.00	Results: N/A

Study Objective: To establish baseline levels of BTG in healthy, term infants at delivery; to ascertain if BTG levels remain stable or change in the immediate post-natal period; and to investigate the relationship between duration of labor and BTG levels in the newborn.

Technical Approach: Fifty healthy, appropriate for gestational age, term infants will be studied. Polycythemic infants will be excluded. Two cc's of whole blood will be obtained from the umbilical cord at the time of delivery and by venipuncture at four hours of life. BTG determinations will be made utilizing beta thromboglobulin RIA kits. Whole blood (0.3 cc's) obtained from initial cord samples and the four-hour venipuncture samples will be placed in CBC tubes. Spun hct's and platelet counts will be obtained on these samples. Two cc's of blood will be obtained from 10 healthy adults and BTG levels will be measured to insure reliability of the assay. Data will be analyzed to establish:: (1) average level of BTG in 25 term male infants; (2) average level of BTG in 25 term female infants; (3) intersex difference between the above groups; (4) effect of duration of labor on BTG levels; (5) effect of platelet count on BTG levels; (6) any change in BTG level over the first four hours of life.

Progress: In FY 84, 24 infants were studied. Initial BTG levels in newborns delivered after active labor appear to be much higher than normal adult levels. Interestingly, the few samples obtained from patients with elective C-section have normal adult levels.

The investigator was unable to obtain enough BTG kits to complete the protocol before she was transferred to Europe.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/77 Status: On-going

Title: Eating Attitude Questionnaire

Start Date: 21 Sep 84 Est Completion Date: Jun 85

Department: Pediatrics Facility: MAMC

Principal Investigator: LTC Dan C. Moore, MC

Associate Investigators: None

Key Words: body weight and appearance, dissatisfaction, efforts to alter, methods

Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine the prevalence among an unselected population of military adolescents of dissatisfaction with body weight or appearance, of efforts to alter weight, and of methods used.

Technical Approach: Questionnaires will be given to 1,000 consecutive adolescent patients (male and female). Those self-identified as having a problem with eating who request help will be appropriately evaluated and counselled. Questionnaires will be analyzed to develop a statistical profile of eating behaviors in the population studied. If warranted by the data, an ongoing program may be developed to identify and treat patients with eating problems. Data will be organized descriptively and subsequently analyzed using analysis of variance.

Progress: Male subjects are still being entered in the study.

Eight hundred females were entered and classified as normal, thin, heavy, underweight, or overweight, based on weight for height and age. Dissatisfaction with body weight was present in 67% of patients, including 53% of normal. Of the normal patients who were dissatisfied, 96% wanted to lose weight and 33% wanted to lose an inappropriate amount. Of the thin group, 42% were dissatisfied with body weight and 62% of these wanted, inappropriately, to lose weight. Patients who had indulged in binge eating or weight control behaviors were more likely to be dissatisfied with body weight than those who had not, and more extreme behaviors such as purging and stimulant use were associated with more dissatisfaction (90-94%) than were fasting (83%) or dieting (72%). Patients who had engaged in purging or stimulant use behavior were also more likely to have engaged in binge eating, fasting, or dieting. This trend was present in the normal group as well as the heavy and overweight groups. A significant number of adolescent females have a distorted idea of normal body weight for height and tend to engage in increasingly desperate weight control behaviors as their dissatisfaction with body weight increases.

The information gained from this study was presented at the Annual Meeting of the Society for Adolescent Medicine.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 74/19 Status: Terminated

Title: A Teaching Model for Pediatric Intubation Utilizing
Ketamine-Sedated Kittens

Start Date: May 74 Est Completion Date: Indefinite

Department: Pediatrics Facility: MAMC

Principal Investigator: COL Gary Pettett, MC

Associate Investigators: COL Errol R. Alden, MC
COL Paul B. Jennings, VC
LTC Ronald W. Brenz, MC

Key Words: teaching model, intubation, pediatric, kittens

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$550.00 Results: Terminate

Study Objective: To teach infant resuscitation procedures to nurses, nurse clinicians, OB-GYN residents, and other nonpediatric physicians who may be called upon to treat pediatric emergencies.

Technical Approach: Weaned kittens, weighing 0.5 to 1.0 kg will be used in these teaching sessions. Ketamine hydrochloride (22 mg/kg) plus atropine sulfate (0.04 mg/kg) will be administered intramuscularly to each kitten. Intubation will be performed with the kittens on their backs, using a pediatric laryngoscope, and sizes 8-14 French endotracheal tubes. Kittens may be used for several consecutive weekly sessions until they grow too large to be utilized.

Progress: After the suspension of the use of cats for research this protocol was suspended for most of FY 85. No procedures were performed. The protocol was terminated due to the PCS of COL Pettett and the lack of interest of physician personnel to take over the protocol.

There was a publication that was well received from this protocol and an exhibit was presented at four scientific meetings. It won the Gold Award for Outstanding Exhibit for Teaching Value at the Annual Meeting of the American Academy of Pediatrics, 1976.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 83/35 Status: Terminated

Title: Techniques of Advanced Life Support

Start Date: 21 Jan 83 Est Completion Date: Indefinite

Department: Pediatrics Facility: MAMC

Principal Investigator: COL Gary Pettett, MC

Associate Investigators:

COL Stan Harris, MC

MAJ Steve Dronen, MC

COL William A. Madden, MC

MAJ Philip V. Marinelli, MC

COL Barry Wolcott, MC

MAJ Stanley P. Liebenberg, VC

Key Words: training protocol, thoracotomy, percutaneous/venous puncture, arterial venous cutdown, vascular line insertion, tracheostomy placement

Accumulative MEDCASE

Est Accumulative

Periodic Review

Cost: -0-

OMA Cost: -0-

Results: Terminate

Study Objective: To provide experience for physicians/nurse personnel in the techniques of advanced life support.

Technical Approach: The animal models will be mongrel dogs. Each animal will be properly prepared for standard surgical techniques by shaving and scrubbing. Surgical procedures will be performed in a sterile manner with the animal fully anesthetized and supported by proper ventilatory technique. Each animal will then undergo the following surgical procedures using techniques currently in hospital practice for humans:

- (1) thoracotomy with pleural tube insertion
- (2) percutaneous arterial and venous cannulation with IV lines
- (3) arterial and venous cutdown with IV line insertion
- (4) tracheostomy insertion

At the conclusion of the experiment, surgical sites will be properly closed and the animal given a lethal dose of barbiturate without being allowed to regain consciousness.

Progress: After the suspension of the use of dogs for research this protocol was suspended for most of FY 85. No procedures were performed. The protocol was terminated due to the PCS of COL Pettett and the lack of interest of physician personnel to take over the protocol.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 84/81	Status: Terminated
Title: Changes in Reading Performance of Children with Reading Delays and Optometric Binocular Dysfunction When Treated with Vision Therapy, Prospective Investigation		
Start Date: 21 Sep 84	Est Completion Date: Apr 85	
Department: Pediatrics	Facility: MAMC	
Principal Investigator: COL Carl A. Plonsky, MC		
Associate Investigators: CPT Quentin A. Humberd, MC CPT John B. Van Ginhoven, MSC		
Key Words: changes, reading performance, vision therapy		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Terminate

Study Objective: To test the hypothesis that vision training in children with reading delays and optometric binocular dysfunction can improve reading performance more than standard treatment over a five-month study period, using a standardized educational test to measure change in reading performance.

Technical Approach: Subjects will be selected from eligible military dependent children with known delays in reading who are enrolled in special remedial reading classes. A standardized educational test of reading performance will be administered by a qualified educational psychometrician to determine the child's baseline reading performance and severity of reading delay. All educators and evaluators will be blinded to any subsequent treatment group assignment during the study period. The children will then be evaluated for binocular dysfunction, and those children found to have optometric binocular dysfunction will be entered in the study. No child will be accepted if he has ever received optometric or vision therapy in the past. The general learning abilities will be in the normal or average range with a fairly specific problem in the area of reading. No student will be accepted who has more extensive neurodevelopmental delays or behavior problems requiring medication. Participants will be stratified by severity of reading delay, age, and severity of diagnosed binocular dysfunction. In addition, each stratum will be blocked in groups of 6 so that the investigator will randomly assign treatment groups from equal numbers of participants in each stratum. Group A will receive individualized vision therapy for a 5-month period. Group B will be receive individualized remedial instruction at the Pediatric Clinic and with the parents for 5 days each week. This group's activities will be designed to parallel Group A in terms of the time used for intervention. Group C will continue to receive only the same educationally based remedial reading for a 5-month period. At the completion of the 5-month study period, all subjects will be retested to determine change in reading delay.

Progress: CPT Van Ginhoven was reassigned shortly after approval of this protocol. A request to the DCCS for another optometrist to assist in the project was denied.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 85/52	Status: On-going
Title: Child Abusive Attitudes and Social Support - A Descriptive Study of A Military Environment		
Start Date: 19 Apr 85	Estimated Completion Date: Jun 85	
Department: Pediatrics	Facility: MAMC	
Principal Investigator: Carl Stracener, M.D., COL, USA (Ret), DAC		
Associate Investigator: Sandra A. Roybal, R.N., USNR		
Key Words: Child abuse, military environment, social support		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: N/A

Study Objective: To describe the relationship between child abuse as measured by the Child Abuse Potential Inventory (CAP) and social support as measured by the Personal Resource Questionnaire (PRQ) and to explore the findings for indications of what factors are influencing child abuse in the military. A long range goal would be to use these tools as part of an early identification/education program for individuals at high risk for abusing their child.

Technical Approach: This study will be a descriptive analysis of child abuse in two US military communities in Washington state. An abusive group (30) and a control group (convenience sample of 30) will be studied, using data derived from the Child Abuse Potential Inventory and the Personnel Resources Questionnaire. Variables that have been found to be significant in previous research on child abuse in military communities will be considered. Both groups must have a child below the age of 12, speak English, and must have been in their present domicile for at least six months. The two groups will be matched for gender, age, military rank, and educational level. In the abusive group, both parents will be asked to fill out the questionnaire. All forms will be color coded for controls, abusive parent, and non-abusive parent. Only the questionnaires from the abusive parent will be used. An analysis of data will be done when 15 subjects and 15 controls have been entered to determine the reliability of the sampling process.

Progress: The control group is completed, with all information being analyzed. Enrollment in the abusive group continues to lag, as fewer numbers of this category are available.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 84/11	Status: On-going
Title: The Coping Process of Families of Children with Birth Defects		
Start Date: 18 Nov 83	Est Completion Date: Feb 86	
Department: Pediatrics	Facility: MAMC	
Principal Investigator: MAJ Glenn Tripp, MC		
Associate Investigators: William N. Friedrich, Ph.D., Univ Wash Lorna T. Willturner, Ph.D. (Candidate) Joyce Shaffer, Ph.D., Western St Hosp		
Key Words: questionnaire, family organization and functioning		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To explicate the relationship of stress and various moderator variables to familial functioning and adaptation in families of children with birth defects.

Technical Approach: This will be a multimodal study of parents of 1,000 children with birth defects, done in conjunction with five other institutions. Each of the parents will complete a survey assessing their coping resources and perceived outcome. In addition to the basic survey, the following procedures will be utilized with subsamples of the total population: 150 subjects will be compared with families of children who manifest no noticeable disability; a group of 100 subjects will be compared to a control group of 100 subjects having a new baby with no handicap, matched as to father's rank, number of children in the family and parental education; selected index and control families will be compared at the beginning and end of the study period to evaluate the effects of longitudinal changes in family composition and function; additional ratings on 150 subjects will be completed by primary care personnel at the treatment institution and thus provide multimodal assessment of these families; a 12-month follow-up questionnaire will be administered to 150 selected families; problem solving interviews with 60 mothers will be conducted; 100 families who received the questionnaire prior to the formal diagnosis of birth defect will receive a 9-month, 12-month, and 18-month post diagnosis follow-up questionnaire, the assessment of change in these families being especially significant in understanding both the coping process during the time period immediately following the crisis and the effect of differential professional involvement on the family's coping during this crucial phase; and additional commonly utilized self-report instruments will be administered to 150 parents. The disabilities of the index cases will be rated by the severity of impairment on a scale of mild, moderate, or severe in nature.

Progress: Only ten subjects have been entered in the protocol at MAMC due to logistical problems and the departure of MAJ Tripp. The protocol will resume entering patients at MAMC when a new principal investigator has been approved for the protocol.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 84/73	Status: On-going
Title: Prophylactic Intravenous Immunoglobulin in High Risk Neonates		
Start Date: 17 Aug 84	Est Completion Date: Sep 87	
Department: Pediatrics	Facility: MAMC	
Principal Investigator: MAJ Bruce Willham, MC		
Associate Investigators: COL Gary Pettett, MC		
MAJ Robert V. Jarrett, MC		
CPT Virginia Hallinan, MC		
Key Words: immunoglobulin, neonates, high risk, prophylactic		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To evaluate the effectiveness of intravenous immunoglobulin (IVIG) with high titer to known disease producing types of Group B streptococci (GBS) in preventing GBS disease in the high risk neonate.

Technical Approach: This will be a double-blind group study with prescreened IVIG and control drug (5% albumin) supplied to each institution in a prerandomized fashion. Subjects will be neonates >2000 grams or 34 weeks at birth and >12 hours of age. Infants of mothers with immune deficiency syndrome will be excluded. The drugs will be used as a single infusion, 500 mg/kg. All infants will have constant temperature, heart rate, respiratory rate, and blood pressure (if on umbilical arterial catheter) monitoring. If umbilical arterial catheter is not present, BP will be obtained before, midway through, and at the completion of the infusion. Fifteen minutes post-infusion a whole blood sample for serum total of IgG and GBS antibodies will be obtained. At 1, 2, and 8 weeks, another blood sample will be taken for antibody studies, a history will be recorded, and routine development assessment will be done.

Progress: No patients were entered on this protocol due first to logistical problems and then to the departure of the principal investigator. The protocol will be started as soon as IRB approval is received for a new principal investigator, MAJ Jose Garcia, MC.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/58 Status: Terminated

Title: Normal Blood Chemistry Values for Term Infants During the First Week of Life

Start Date: 19 Apr 85 Estimated Completion Date: Nov 85

Department: Pediatrics Facility: MAMC

Principal Investigator: MAJ Bruce E. Willham, MC

Associate Investigators: MAJ Robert V. Jarrett, MC

COL P. Gary Pettett, MC MAJ Barbara Williams, ANC

COL Carl Stones, MC CPT Karl Friedl, MSC

Key Words: Blood chemistry, term infants, first week

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: 288.00 Results: N/A

Study Objective: To determine the normal variations in serum electrolytes (Na^+ , K^+ , Cl^- , CO_2^-), blood urea nitrogen (BUN), and glucose in term infants during the first week of life. An attempt will be made to compare state of hydration with the serial values.

Technical Approach: Serial measurements of serum electrolytes, BUN, and glucose will be obtained from several groups of healthy, term, appropriate for gestational age infants. Groups will include babies delivered vaginally vs C-section, because mode of delivery can affect a baby's initial blood volume. Those who are strictly breast-fed will be compared to formula-feeders, because of potentially different total fluid intake. Each group will contain approximately 20 babies. The first sample will be cord blood and the remainder will be capillary samples starting at approximately 12 hours, then 24 hours, 48 hours, and so on daily through the seventh day. Thus there would be a total of 9 samples. The blood drawing will consist of capillary heelstick obtained after warming the heel then cleaning with 70% isopropyl alcohol and allowing it to air dry. Other information to be obtained will include: daily weights; a daily random urine specific gravity while in hospital; and an estimate of daily total fluid intake for formula feeders. The data will be assimilated with mean values and standard deviations calculated for each group and time interval. Trends will be assessed and the groups compared. Statistical relationships between serum electrolytes, weight loss and urine specific gravity will be evaluated.

Progress: This protocol was terminated in September 1985 in accordance with a directive from the Clinical Investigation Program, HSC.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 83/80 Status: Completed

Title: Descriptive Study of Characteristics of Adolescent Women Who Have Had Unplanned Pregnancies with a Comparison Study of Those Who Have Not

Start Date: 16 Sep 83 Est Completion Date: Dec 83

Department: Pediatrics Facility: MAMC

Principal Investigator: LTC Gentry Yeatman, MC

Associate Investigator: Juvann M. Wolff, R.N.

Key Words: questionnaire; categories: demographic, attitude and knowledge of contraception, reproductive knowledge, perceived severity, perceived susceptibility, perceived benefits of action, and self-esteem

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: Completed

Study Objective: To identify the high risk and the low risk parameters for teenage pregnancies in order to better educate teenage girls in the area of avoiding unplanned pregnancies.

Technical Approach: A minimum of 100 adolescent women ages 14-19 will be provided with a cover letter and a questionnaire. A quiet private location will be provided in which to complete the questionnaire. After completion, the questionnaire will be placed in a sealed envelope by the participant and returned to the researcher or receptionist. The questionnaire consists of 32 items, divided into 8 categories: demographic, attitude toward contraception, knowledge of contraception, reproductive knowledge, perceived severity, perceived susceptibility, perceived benefits of action, and a self-esteem scale.

Progress: This protocol was completed with the acceptance of a thesis for a M.N. at the University of Washington by Ms Wolff. The findings suggest there are differences between sexually active and non-sexually active women, as well as among those sexually active women who have experienced a pregnancy during adolescence. The findings demonstrate that:

1. Sexually active adolescent women worry more about becoming pregnant than non-sexually active women.
2. Those who had experienced an adolescent pregnancy saw themselves as more susceptible/vulnerable to pregnancy compared to those who had not experienced pregnancy.
3. Higher self esteem is found in those women who have had at least one pregnancy.
4. The higher the self esteem, the more likely the woman is to see herself as susceptible/vulnerable to pregnancy.

D E T A I L S H E E T S
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DEPARTMENT OF PSYCHIATRY

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/32 Status: Completed

Title: Psychological, Parental, and Environmental Factors Related to the Developmental Level of the Child

Start Date: 17 Feb 84 Est Completion Date: Sep 84

Department: Psychiatry Facility: MAMC

Principal Investigator: CPT Vladimir Nacev, MS

Associate Investigators: MAJ Glenn Tripp, MC

MAJ Anthony Zold, MSC

Christian Rubio, B.S.

Key Words: child abuse, parenting skills, stress levels

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: Completed

Study Objective: To study the relationship between child abuse potential as measured by the Child Abuse Potential Inventory; preventive factors such as stress, parenting skills, parent-child interactions, and support system variables; and the developmental level of the child.

Technical Approach: The research data will be collected from research volunteers who, at the present, have a 2 year old child. Approximately 50 subjects will be needed.

A brief questionnaire covering demographic and selected psychosocial variables, the CAP-Inventory, the Vineland Adaptive Behavioral Scale, and the Bayley Infant Development Scale will be administered.

Statistical analysis will include descriptive statistics and correlations (Pearson-r), ANOVA, and contingency table analysis (chi-square) on the demographic variables, the preventive factors, the child abuse potential, and the developmental variables.

Progress: The results suggest that the child's temperament, sharing in the care of the child by the spouses, parental agreement on how to discipline the child, experiencing financial problems, and the degree of comfort in the living environment have a strong and significant relationship with the "child abuse potential". However, no significant relationship was found between the CAP inventory and the ZAB's scores.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/39 Status: Completed

Title: Neuropsychological Status of Insulin-Dependent Diabetic Children and Adolescents

Start Date: 22 Feb 85 Estimated Completion Date: Jun 85

Department: Psychiatry Facility: MAMC

Principal Investigator: CPT Steven C. Parkison, MS

Associate Investigator: CPT Barry S. Anton, MS, USAR

Key Words: Neuropsychological test battery, questionnaire, chronic illness, metabolic control, cognitive functioning

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To investigate the history and effects on the neuropsychological functioning of children afflicted with insulin-dependent diabetes mellitus and to determine if there is a relationship between test scores, chronicity of illness, recent metabolic control, and level of cognitive functioning.

Technical Approach: Subjects will be 15 insulin-dependent diabetic children 9-16 years old with an established diagnosis of diabetes for at least one year. There will also be a control group of chronically ill children matched for age and sex and another control group of children who are free of chronic disease and considered normal, also age and sex matched. All subjects will be administered the neuropsychological test battery and parents will be asked to complete a problem check list and a detailed medical history questionnaire. Blood samples will be drawn after the questionnaire is completed to determine glycosolated hemoglobin values, which have been found to be a reliable indicator measure of metabolic control.

Progress: The neuropsychological battery consisted of tests that assessed intelligence, visuospatial processes, learning, memory, attention, mental and motor speed, and school achievement. Additional information including demographic, medical, and data from the Child Behavior Checklist (CBC) [Achenbach, 1981] was also collected. Univariate analysis indicated that while performance IQ of Wechsler Intelligence Scale for Children (WISC-R) narrowly missed significance, the Block Design subtest of the WISC-R yielded significant deficits in performance for the diabetic and chronic cardiac groups when compared to their normal siblings. On dominant hand/finger agnosia, the diabetic and chronic cardiac groups performed significantly better than the control group. This result is puzzling in light of known diabetic and cardiac dysfunction sequelae which suggest frequent peripheral sensory impairment. Other measures, including behavioral characteristics measured by the CBC failed to indicate group differences. Several variables on the CBC showed trends consistent with other reports of behavior problems in diabetic and cardiac diseased children. The significance of the neuropsychological findings suggests that insulin-dependent diabetic children and chronic cardiac disease children may develop specific cognitive deficits rather than global deficits. Thus, careful neuropsychological screening in children with these disorders appears to be warranted in order to provide appropriate educational placement and remediation.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 81/59 Status: Completed

Title: Psychological Variables Related to Childbirth and Early Infant Development

Start Date: 20 Mar 81 Est Completion Date: Sep 83

Department: Psychiatry Facility: MAMC

Principal Investigator: MAJ Anthony C. Zold, MS

Associate Investigators: CPT Richard H. Rubes, MS
CPT Maren Stavig, ANC, USNR

Key Words: first pregnancies, interview, depression scale data, demographic data, 2-month post-partum follow-up

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: Completed

Study Objective: To study selected psychological and behavioral variables during pregnancy which may affect ease of delivery, medical complications, and early growth and development of the infant. Specifically, the independent variables to be investigated are: maternal expectations of delivery and of the infant; mother's perception of the husband's emotional support; orgasmic history of the mother; participation in various childbirth preparation programs; and significant depression during pregnancy.

Technical Approach: Obtain interview and depression scale data from volunteers at 30-36 weeks gestation. After the birth, re-contact mother for a brief follow-up interview to obtain mother's subjective rating of the delivery and the infant. Conduct record search for selected variables: length of labor, presence of complications, status of newborn, and the bonding rating between mother and child. At the 2-month well-baby follow-up visit, request mother to repeat the Zung Self-Rating Depression Scale and do a record search on the development of the infant. Data analysis will include descriptive statistics, correlation, and contingency table analysis.

Progress: All data has been collected and analyzed. No report is available at this time to give results.

D E T A I L S H E E T S
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DEPARTMENT OF SURGERY

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 83/33 Status: Completed

Title: Treatment of Recurrent Otitis Media: Chemoprophylaxis
Versus Tympanostomy Tubes

Start Date: Dec 82 Est Completion Date: Jul 83

Dept/Svc: Surgery/Otolaryngology Facility: MAMC

Principal Investigator: MAJ James E. Arnold, MC

Associate Investigators: CPT James B. Erhart, MC

CPT Alan G. Getts, MC

CPT Stephen R. Pratt, MC

Key Words: Gantrisin, tympanostomy tubes, recurrent otitis media

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$100.00 Results: Completed

Study Objective: To compare the effectiveness of treatment with PE tubes or antibiotic prophylaxis in children with recurrent otitis media.

Technical Approach: Children with recurrent otitis media will be randomly assigned to:

Group A: Bilateral myringotomies with placement of PE tubes.

Group B: Prophylactic antibiotic regimen consisting of Gantrisin, 500 mg for six months.

Group C: A placebo will be given for six months.

They will be followed for six months to determine the most effective treatment modality.

During an episode of acute otitis media, patients will be treated with appropriate antibiotics, and the study medicine will be discontinued until the episode is resolved. A failure will be defined as two or more episodes of recurrent otitis media within a three month period after entering the study. Those patients who fail will be treated in the following manner: Patients in Group A will be treated with the Gantrisin regimen. Patients in Groups B & C will then undergo myringotomy and PE tube placement.

Progress: The children studied at MAMC were combined with children studied under an identical protocol at FAMC, resulting in a total of 66 children. Children who received Gantrisin as a prophylactic drug or PE tubes to prevent recurrent otitis media did significantly better than children who received a placebo. At MAMC, both the children treated with Gantrisin and those treated with PE tubes had an equal success rate in the prevention of otitis media. At FAMC, the children who received PE tubes had a slightly lower rate of otitis media than children given Gantrisin; however, both of these groups did much better than children receiving the placebo. A manuscript has been accepted for publication in Laryngoscope and a paper will be presented at the eastern section of the Triologic Meeting.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 79/57	Status: On-going
Title: The Effect of Dimethyl Sulfoxide on the Uptake of Cisplatin From the Urinary Bladder of the Dog		
Start Date: 24 Jan 79	Est Completion Date: Indefinite	
Dept/Svc: Surgery/Urology	Facility: MAMC	
Principal Investigator: COL William Belville, MC		
Associate Investigators:		
LTC Samuel J. Insalaco, MC	MAJ Eduardo S. Blum, MC	
LTC Willis Jacob, MS	MAJ Roger Schoenfeld, MC	
LTC George S. Ward, VC	CPT Carl Cricco, MC	
Key Words: cisplatin, dimethyl sulfoxide, urinary bladder, dog		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: \$1050.00	Results: Continue

Study Objective: To determine if intravesicular cisplatin can be more effectively transported through the urinary bladder wall using DMSO as a carrier.

Technical Approach: Thio-TEPA was the original drug to be used in this study. The investigators were unable to develop a successful thio-TEPA assay so cisplatin was used in the study due to the ease of measurement by atomic absorption spectrometry and because its medium-sized molecular weight avoids excessive absorption. The test solution will be instilled into the urinary bladder of each animal and maintained there for one hour. The test solutions are: Group I (4 dogs) cisplatin in 50% DMSO; Group II (4 dogs) cisplatin in an isotonic salt solution; and Group III (2 dogs) 50% DMSO in an isotonic salt solution. Group III animals are to verify that DMSO does not interfere with cisplatin identification. Blood samples will be obtained from the caudal vena cava and the external jugular vein immediately before instillation of the test solution and at 5, 10, 20, 40, and 60 min after instillation. One blood sample will be taken from a small vein on the bladder surface at 15 min and the test solution will be withdrawn from the bladder at 60 min. Two dogs from Groups I and II will be studied for toxicity following a complete treatment regime, consisting of 4 weekly treatments as described above. These animals will have bone marrow, liver, kidney, and spleen biopsies before the first treatment. One week following the last treatment, the dogs will be sacrificed and tissue sections of the same organs plus the urinary bladder and lens will be taken. These tissues will be examined histopathologically for evidence of toxic changes. CBC's will also be performed at weekly intervals. The remaining two dogs in Groups I and II will have a section of urinary bladder removed following the test solution instillation. This tissue section will be divided and one part homogenized and extracted for cisplatin analysis and the other section evaluated histopathologically. The withdrawn test solution, blood samples, and bladder tissue extracts will be analyzed by spectrophotometry to determine levels of cisplatin.

Progress: No work was done on this protocol due to the suspension of the use of dogs in research. The investigators are in the process of amending the protocol to use another animal model.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/51 Status: On-going

Title: Orchiectomy and Observation in the Treatment of Clinical Stage I Nonseminomatous Germ Cell Tumor of the Testis (NSGCTT)

Start Date: 18 May 84 Est Completion Date: May 89

Dept/Svc: Surgery, Urology Facility: MAMC

Principal Investigator: COL William Belville, MC

Associate Investigators: COL Alfred S. Buck, MC

COL Victor J. Kiesling, MC

COL Freidrich H. Stutz, MC

Key Words: NSGCTT, treatment, orchiectomy, observation

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: Continue

Study Objective: To determine the efficacy of orchiectomy alone in the treatment of clinical Stage I NSGCTT. The factors that predispose to relapse with Stage I disease will be analyzed.

Technical Approach: At present, clinical Stage I NSGCTT is treated by radical orchiectomy and radical retroperitoneal lymph node dissection. To avoid the ejaculatory impotence associated with the radical retroperitoneal lymph node dissection, the investigators propose to follow orchiectomy patients monthly for two years and then quarterly for two years with no further treatment unless relapse occurs. Subjects must have histologically confirmed carcinoma (not pure seminoma nor pure choriocarcinoma) at the testis. Postorchiectomy evaluation must have been completed within four weeks of the diagnosis of the primary tumor. Patients with involvement of the spermatic cord or evidence of epididymal invasion; evidence of tumor outside the testis by any other diagnostic means; or a second malignancy (except a squamous or basal cell skin cancer) will be excluded. Patients who after careful counselling elect to undergo a radical retroperitoneal lymph node dissection will be followed as per protocol. Pre-orchiectomy evaluation will include complete history, physical, WBC and platelet count, HGB, bilirubin, alkaline phosphatase, SGOT, SGPT, serum calcium, BUN, creatinine, uric acid, chest x-ray, and serum tumor markers to include α -fetoprotein, β -Hcg, and LDH. Post-orchiectomy evaluation will include bipedal lymphangiogram, abdominal and chest CT, excretory urography, and normal serum tumor markers which have returned to normal at a rate predicted by the known serum half-life of the respective marker. Patient follow-up will include history, physical exam, SMAC 20, CBC with platelet count, chest x-ray or CT, and serum tumor markers. During the first two years of follow-up, the patient will undergo abdominal CT every three months, and then annually for two additional years.

Progress: Two patients have been entered. At review on follow-up one was found to have no evidence of disease (Stage I). The other patient was found to be Stage II at first follow-up.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/10 Status: Completed

TITLE: Percutaneous Pinning of Symptomatic Scaphoid Nonunions
Start Date: 16 Nov 84 Estimated Completion Date: June 1985
Dept/Svc: Surgery/Orthopedics Facility: MAMC
Principal Investigator: COL Ricahrd Camp, MC
Associate Investigator: CPT Michael Q. Cosio, MC
Key Words: scaphoid nonunions, pinning, percutaneous
Accumulative MEDCASE Est Accumulative Periodic Review
Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To determine whether percutaneous pinning of symptomatic scaphoid nonunions can result in the same high rate of bony union as open bone grafting, but with minimal morbidity.

Technical Approach: Subjects with a nonunion of the scaphoid of 4 months or more with no progresion toward union and symptoms of sufficient severity as to interfere with activities of daily living and/or performance of military duties will be studied. Contraindications will be periscaphoid arthrosis, previous bone grafting, pseudoarthrosis, intercarpal instability, or displacement >1 mm.

Under regional or general anesthesia, multiple C-wires measuring .045" in diameter will be inserted under fluoroscopic guidance into the scaphoid tuberosity, across the nonunion into the proximal fragment, but not across the wrist. A standard scaphoid cast will be applied. Patients will be followed at regular intervals until the fracture heals as demonstrated by bridging trabeculae. The cast will then be replaced by a brace while the patient rehabilitates the wrist.

Progress: This protocol was originally submitted by CPT Cosio. Upon his departure from MAMC, COL Camp became the principal investigator.

Although the series was small with a follow-up of only 10.3 months, it is interesting that a high success rate of union without bone grafting was achieved (77%). Mean length of time to union was 18.5 weeks. The patients had some loss of motion primarily in extension and radial deviation, but this was troublesome to only a minority of the patients. The one major complication was a septic wrist. The long-term effects of this treatment are, as yet, undetermined pending longer follow-up. The use of historical controls has limitations in that one is using a different population, different techniques, and different investigators for comparison.

A manuscript has been accepted for publication by the Journal of Hand Surgery.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/35 Status: On-going

Title: Scrotal Blood Flow Following Shouldice Herniorrhaphy
Start Date: 17 Feb 84 Est Completion Date: Feb 85
Dept/Svc: Surgery/Urology Facility: MAMC
Principal Investigator: CPT Rodney Davis, MC
Associate Investigators:
COL Stanton Brown, MC MAJ Eddie Reddick, MC
COL Alfred S. Buck, MC CPT Mark Ludvigson, MC
Key Words: shouldice herniorrhaphy, scrotal, blood flow
Accumulative MEDCASE Est Accumulative Periodic Review
Cost: -0- OMA Cost: -0- Results: Continue

Study Objective: To determine the normal scrotal blood flow following inguinal herniorrhaphy in the adult male.

Technical Approach: Patients undergoing routine inguinal herniorrhaphy will be asked to participate in the study. Scrotal scans will be done within 3 days of surgery. One day postoperatively the patient will be re-scanned. If the scan is found to be abnormal, an additional scan will be done at the two week follow-up visit.

Nuclear Medicine Service personnel will interpret the scans without a clinical history in order to blind the interpreter.

Each member of the General Surgery Team will be given postoperative criteria to evaluate the patients. The criteria will include presence or absence of scrotal swelling, hematoma, and ecchymosis. The swelling will be graded 1+ (minimal), 2+ (moderate = 2 x NL), or 3+ (severe with tense testicle and tenderness). The pain will be graded 1+ (minimal requiring no medications for pain), 2+ (moderate p.o. pain medication) or 3+ (severe requiring IV or IM pain medications).

Clinical and nuclear scan data will be compared using χ^2 analysis.

After 25 patients have been studied, the data will be evaluated to determine if more patients need to be studied for statistical purposes.

Progress: This study is on-going. Two patients were entered in FY 85 for a total of ten patients entered.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 84/42	Status: On-going
Title: The Effects of the Shaw Scalpel on Wound Healing		
Start Date: 16 Mar 84	Est Completion Date: Apr 84	
Dept/Svc: Surgery/Otolaryngology	Facility: MAMC	
Principal Investigator: CPT Milton B. Ellis, MC		
Associate Investigators: COL William H. Gernon, MC		
MAJ Stanley P. Liebenberg, VC	Alvin Novack, M.D.	
CPT Steve Koopmeiners, MC	James Wells, M.D.	
Key Words: temperature, Shaw scalpel, skin incisions		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: \$838.00	Results: Continue

Study Objective: To document how different temperatures of the heated (Shaw) scalpel affect canine and porcine skin incisions and to examine and compare wound breaking strength and histology.

Technical Approach: Six adult mongrel dogs and six weanling piglets will be used. The six dogs will be studied first to perfect techniques. The information obtained from the piglet work will be most representative of the effects of the Shaw scalpel on human skin because porcine and human skin have been shown to correlate closely histologically.

The backs of the animals will be shaved, surgically prepped, and two sets of 5 cm paramedian incisions will be made through the back skin using a #10 Bard-Parker scalpel blade, the Shaw scalpel at 88°C, and the Shaw scalpel at 119°C for a total of six incisions on each animal. The incisions will be closed with standard surgical staples to provide carefully controlled closures. The animals will be cared for in a routine and uniform manner. The animals' condition and the characteristics of their incisions will be monitored daily. The incisions will be photographed at regular intervals. Two animals of each species will have excisions of all skin incisions at 7, 14, and 21 days post-operatively. These new skin incisions will receive primary closure with a nonabsorbable suture material placed in an interrupted pattern. One set of incisions will be examined histologically and the other functionally. Those to be examined for function will have the wound breaking strength determined by a calibrated tensionmeter.

Progress: The technical portion of the protocol was completed as planned. Analysis of the samples is in progress in anticipation of writing an article for publication.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 84/23	Status: On-going
Title: Sinusitis Secondary to Foreign Bodies in the Nasal Cavity and Its Relationship to Sepsis in the Severely Ill Patient		
Start Date: 20 Jan 84	Est Completion Date: Jan 85	
Dept/Svc: Surgery/Otolaryngology	Facility: MAMC	
Principal Investigator: CPT James B. Erhardt, MC		
Associate Investigators:		
COL Waylon Black, MC	MAJ DelRay Maughan, MC	
COL (Ret) Leonard Hays, MC	MAJ Eddie Reddick, MC	
MAJ William Fill, MC	CPT Robert Holzman, MC	
Key Words: sinusitis, sepsis, foreign bodies, nasal cavity		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: \$500.00	Results: Continue

Study Objective: To determine the incidence of sinusitis in severely ill patients who have nasotracheal tubes in place; to define which sinuses are commonly involved in these cases; to determine which organisms, may be involved; to determine whether CT examination provides more accurate and/or earlier diagnosis than conventional x-ray films in these cases; and to determine the correlation between roentgenographic evidence of sinusitis and clinical evidence of sepsis in these patients.

Technical Approach: A minimum of 50 patients with nasotracheal intubation tubes in place for >72 hrs will be evaluated as follows: physical exam of the head and neck; and plain x-ray films and CT exam of the paranasal sinuses. If the plain films or the CT scan demonstrates no sinus pathology, repeat films (plain films and CT films) will be obtained every 10-14 days while the nasotracheal tube remains in place. If the plain films or CT scan demonstrate opacification of the maxillary sinuses, antral punctures will be performed for aerobic and anaerobic cultures. If the plain film or CT scan demonstrates opacification of the ethmoid or sphenoid sinuses, attempts will be made to obtain bedside sinus cultures. When the patient's prognosis is such that an extended intubation is anticipated, consideration will be given to placement of a tracheostomy at which time the ethmoid and sphenoid sinuses will be concurrently cultured. If, at any time, a patient with a nasotracheal tube develops a picture of sepsis and no obvious source other than opacification of the sinuses is identified, the patient will undergo surgical decompression of the involved sinuses in the main operating room with cultures obtained at that time.

Progress: Patients are still being entered. Accumulation of patients is much slower than expected.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/49 Status: On-going

Title: Synovial Fluid Changes Following Arthroscopy in Patients with Effusions

Start Date: 19 Apr 85 Estimated Completion Date: May 86

Dept/Svc: Surgery/Orthopedics Facility: MAMC

Principal Investigator: CPT Joseph M. Erpelding, MC

Associate COL Richard A. Camp, MC MAJ Charles Hannan, MSC

Investigators: LTC Thomas J. Parr, MC MAJ Gary Price, MAJ, MSC

Key Words: synovial fluid, changes, arthroscopy

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$1300.00 Results: N/A

Study Objective: To monitor changes in characteristics and composition of the synovial fluid of patients undergoing arthroscopic surgery of the knee in various disease states and to assess the level/amount of pain, range of motion, strength and swelling.

Technical Approach: Patients (50) scheduled for arthroscopy will have an initial evaluation using a preoperative questionnaire completed by the subject and the arthroscopist, to include injury, duration, preoperative NSAID's, age of patient, activity level, allergies, history of previous injury or operation, level of pain, swelling/effusion, range of motion, strength, symptoms, and existing disease. An intraoperative synovial fluid sample will be obtained to evaluate WBC and differential, glucose, protein, lactic acid, pH, and fibrin split products. Findings with respect to cartilage, menisci, ligaments (including EUA), synovium, and loose bodies will be noted. Subjects will be treated in the usual post-arthroscopic manner. Five to seven days after arthroscopy, a second synovial fluid sample will be obtained and evaluated in the same manner as the intraoperative sample, if a significant synovial effusion is present. Pain level, swelling/effusion, range of motion, and strength will be evaluated in all subjects. At 6 weeks, the pain level, swelling/effusion, range of motion, strength and any measurable atrophy would be assessed and a notation of when the patient returned to his/her normal activity level will be recorded. Data analysis will include pre- and post-operative fluid data and paired values analysis, history variables correlation, and intraoperative procedures and findings comparison.

Progress: A reliable method for analyzing and recording synovial fluid samples has been established. Patient entry has been delayed due to a TDY assignment of the investigator.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/50 Status: On-going

Title: The Effect of Nonsteroidal Anti-inflammatory Agents on
Synovial Fluid Following Arthroscopy

Start Date: 19 Apr 85 Estimated Completion Date: May 86

Dept/Svc: Surgery/Orthopedics Facility: MAMC

Principal Investigator: CPT Joseph M. Erpelding, MC

Associate Investigators: COL Richard A. Camp, MC

LTC Thomas J. Parr, MC

Key Words: synovial fluid, arthroscopy, nonsteroidal agents

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$400.00 Results: N/A

Study Objective: To determine the effect of non-steroidal anti-inflammatory agents on the synovial fluid composition and properties.

Technical Approach: Patients (50) scheduled for arthroscopy will have an initial evaluation using a preoperative questionnaire completed by the subject and the arthroscopist, to include injury, duration, preoperative NSAID's, age of patient, activity level, allergies, history of previous injury or operation, level of pain, swelling/effusion, range of motion, strength, symptoms, and existing disease. An intraoperative synovial fluid sample will be obtained to evaluate WBC and differential, glucose, lactic acid, pH, hyaluronic acid level, FSP, viscosity, and boundary lubrication. Findings with respect to cartilage, menisci, ligaments (including EUA), synovium, and loose bodies will be noted. Subjects will be treated in the usual post-operative manner. The group will also be randomly treated with either a pure analgesic (Tylenol 10 gr) or an analgesic and anti-inflammatory agent (Ibuprofen 600 mg) 4 times a day for 4 weeks. At day 7-10, a second synovial fluid sample will be obtained (if a significant effusion is present) and evaluated in the same manner as the intraoperative sample. Pain levels, swelling/effusion, range of motion and strength will be evaluated, and the patient will fill out a questionnaire. At 6 weeks, the pain level, swelling/effusion, range of motion, strength and any measurable atrophy will be assessed and when the patient returned to his/her normal activity level will be recorded. Assessment of changes will be accomplished by comparison of fluid aspirated at the time of arthroscopy and fluid aspirated (if a significant effusion exists) at a fixed time postoperatively. The results will be analyzed for any statistically significant clustering of variables and/or correlations with respect to both subjective and objective assessments, synovial fluid findings, disease state, rate and degree of recovery, and preoperative variables (with matching).

Progress: This protocol has not been started due to a delay in obtaining the medications and TDY for the principal investigator. A drug company had originally agreed to supply the drugs, but later withdrew their support.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 82/55 Status: Terminated

Title: Canine Training Model for Endoscopic Laryngeal Surgery
Using the CO₂ Laser

Start Date: Jun 82 Est Completion Date: Indefinite

Dept/Svc: Surgery/Otolaryngology Facility: MAMC

Principal Investigator: MAJ Gregory Garth, MC

Associate COL Leonard Hays, MC MAJ Del R Maughan, MC

Investigators: MAJ Stanley Liebenberg, VC CPT Wallace Taylor, MC

Key Words: training model, laryngeal surgery, CO₂ laser

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$100.00 Results: Terminate

Study Objective: To train ENT residents in the use of the CO₂ laser in a non-human subject in a controlled setting simulating a human situation prior to performing in an actual clinical setting.

Technical Approach: Twelve large mongrel dogs will be anesthetized with ultra-short acting barbiturate and placed in dorsal recumbency. Suspension laryngoscopy will then be employed to visualize the larynx. ENT residents will use the CO₂ laser to perform a partial laryngectomy. Supplemental oxygen will be administered to the animal using the Saunders jet ventilating device to displace CO₂ from the lower airways and to facilitate viewing of the operative site during actual tissue removal with the laser. The opposite hemilarynx will be left unoperated to serve as a control. Each dog will be placed on a liquid diet for 24 hours post-op and will then be fed a semi-soft diet for the next 5 days. Each dog will be endoscoped at weekly intervals until healing is completed.

Progress: No further sessions were done on this protocol in FY 85 due to the difficulty of obtaining animals, and the investigators requested that it be terminated. The staff who trained on this protocol showed an increased confidence when working with humans.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/21 Status: On-going

Title: Advanced Trauma Life Support Course
Start Date: 16 Jan 85 Estimated Completion Date: Indefinite
Dept/Svc: Surgery/General Facility: MAMC
Principal Investigator: COL Stanley C. Harris, MC
Associate Investigator: MAJ Leslie W. Yarbrough, VC
Key Words: residents, venous cutdown, cricothyroidotomy, tube
thoracostomy, peritoneal lavage, pericardiocentesis,
goat model
Accumulative MEDCASE Est Accumulative Periodic Review
Cost: -0- OMA Cost: \$1600.00 Results: N/A

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 after major trauma.

Technical Approach: During a laboratory session involving goat surgery, each student in the group will be directly involved in a hands-on performance of a venous cutdown, a cricothyroidotomy, a tube thoracostomy, peritoneal lavage, and pericardiocentesis. This course will be conducted 3-4 times/year at MAMC.

Progress: Three ATLS health provider courses and one instructor course were held during FY 85.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 79/64 Status: On-going

Title: Implantation of Intraocular Lenses
 Start Date: 16 Mar 79 Est Completion Date: Indefinite
 Dept/Svc: Surgery/Ophthalmology Facility: MAMC
 Principal Investigator: LTC Thomas H. Mader, MC
 Associate Investigators:
 COL Stanley C. Allison, MC MAJ Kevin J. Chismire, MC
 COL Stanley C. Sollie, MC MAJ Leslie P. Fox, MC
 LTC John C. Goodin, MC MAJ Paul H. Ryan, MC
 LTC Christopher G. Knight, MC MAJ Lawrence J. White, MC
 MAJ Bruce D. Bellin, MC CPT Lawrence E. Hannon, MC
 Key Words: intraocular lenses, implantation
 Accumulative MEDCASE Est Accumulative Periodic Review
 Cost: -0- OMA Cost: \$200.00 Results: Continue

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: Approximately 200 IOL's were implanted in FY 85 with no adverse reactions. IOL's have withstood the test of time and cost are now considered safe for most patients. Most IOL's are no longer considered investigational. However, the protocol will remain open in order to use updated lenses that are still investigational.

Upon the departure of COL Allison in the fall of FY 84, LTC Mader, Chief, Ophthalmology, became the principal investigator on the protocol.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/51 Status: On-going

Title: The Transconjunctival Oxygen Monitoring System as a Predictor of Carotid Stenosis

Start Date: 19 Apr 85 Estimated Completion Date: Jun 85

Dept/Svc: Surgery/Ophthalmology Facility: MAMC

Principal Investigator: LTC Thomas H. Mader, MC

Associate Investigators: CPT Karl Friedl, MS

Linda Bickerstaff, M.D., DAC

Key Words: carotid arteriograms, carotid stenosis, normals

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$650.00 Results: N/A

Study Objective: To determine if the transconjunctival oxygen measuring device can predict carotid patency.

Technical Approach: Ten (10) conjunctival eyelid oxygen sensors will be purchased from the Orange Medical Instruments Company. The Eyelid Oxygen Monitor will then be leased for the price of the sensors. This equipment constitutes a functional oxygen measuring system.

Twenty patients (selected by MS Bickerstaff) will have had carotid arteriograms as a part of standard patient care. Approximately half will have various degrees of documented carotid stenosis and half will be normals. Without prior knowledge of carotid artery patency, the transconjunctival oxygen monitoring system will be placed bilaterally in the conjunctival sacs. The conjunctival oxygen tension will then be measured and recorded. The data obtained will be compared to the known carotid arteriogram information and conclusions drawn. Drs. Mader and Friedl will do the monitoring and will be blinded as to the results of the arteriogram.

Progress: Patients are being entered in the protocol. More subjects will be entered upon the receipt of additional eye sensors.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 85/86	Status: On-going
Title: Intraocular Lenses in Pilots. A Review of the U.S. Army Experience		
Start Date: 23 Aug 85	Est Completion Date: Jun 86	
Dept/Svc: Surgery/Ophthalmology	Facility: MAMC	
Principal Investigator: LTC Thomas H. Mader, MC		
Associate Investigators: MAJ William G. Carey, MC MAJ William Wilson, MC CPT Karl Friedl, MS		
Key words: intraocular lenses, pilots, questionnaire, examination		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: N/A

Study Objective: To note any eye abnormalities in personnel now on flight status who have had cataract extractions with intraocular lens implants; to obtain responses to a detailed questionnaire regarding the pilots' experiences with the lens implants; to summarize and examine the above data, looking for any consistent findings.

Technical Approach: Doctors Carey and Wilson at Ft Rucker will review the aeromedical files and identify the aviators who have had intraocular lens implants. The aviators' duty stations will be noted. Each pilot's flight surgeon will be notified and informed of the study intentions who will arrange an appointment for the aviators to be examined by an Army ophthalmologist.

The study will consist of two parts and will be done in the office of the ophthalmologist. Part I will consist of a detailed questionnaire to be filled out by the pilot. Part II will be the eye exam given by the ophthalmologist.

Progress: Five subjects have been entered in this study.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/70 Status: Completed

Title: Reanastomosis of the Vas Deferens in the Canine Model Using Fibrin Glue

Start Date: 17 Aug 84 Est Completion Date: Mar 85

Dept/Svc: Surgery/Urology Facility: MAMC

Principal Investigator: CPT James C. Mason, MC

Associate Investigators: LTC Victor J. Kiesling, MC
CPT Rodney Davis, MC

Key Words: reanastomosis, vas deferens, fibrin glue, canine

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$2305.00 Results: Completed

Study Objective: To determine if the use of an inhibitor of fibrinolysis increases the tensile strength or alters the time of lysis of fibrin glue and to determine if the use of fibrin glue with reanastomosis of the vas deferens can improve the patency results of vasovasostomy compared to simple suture reanastomosis.

Technical Approach: Tensile strength of fibrin glue will be determined using the Ingstrom tensometer and clots will be tested for tensile strength. Clot lysis will be determined by observing the time interval from clot formation until clot liquefaction is apparent. Bilateral vasectomy will be performed on 8 male dogs using the glue with the greatest tensile strength and longest dissolution time. Eight right anastomoses will be made; four with fibrin glue and four without. Two serosal sutures of 7-0 prolene will be placed 1 cm on either side of the anastomosis for later measurement of possible dehiscence. Approximately one month after vasovasostomy a semen analysis will be done. The right anastomoses will then be surgically removed with a large segment of vas deferens and evaluated for patency and histopathological changes. Concurrent vasovasostomy will be performed on the left vas deferens, using glue on the dogs in the reverse order as before. The anastomoses will be removed and evaluated as before. Semen analysis in each animal will be performed a minimum of 4 times - pre-vasectomy, post-vasectomy, and post-unilateral vasovasostomy with and without fibrin glue (unilateral anastomosis will be performed twice in each dog).

Progress: At the concentration used, amicar did not seem to improve the tensile strength nor prolong the lysis time of fibrin glue. Perhaps these results can be attributed to the mixing technique. Fibrin glue demonstrated effective tissue adhesive properties when applied to dermal skin surfaces and increased the breaking strength of the vasal anastomosis when compared to sutures alone. The degree of inflammation and granuloma formation was negligible. A 100% patency rate was attained using the fibrin glue and reinforcing sutures in the canine model. Vasovasostomy utilizing the fibrin gluing technique seems to be a highly accurate means of re-establishing patency of the vas deferens.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 82/68 Status: Terminated

Title: Immunologically Mediated Persistent Infertility in Patients Following Vasovasotomy

Start Date: 20 Aug 82 Est Completion Date: Sep 84

Dept/Svc: Surgery/ Urology Facility: MAMC

Principal Investigator: LTC Michael R. Moon, MC

Associate Investigators: COL William D. Belville, MC

COL Stephen R. Plymate, MC

LTC James W. Higbee, MSC

Key Words: infertility, vasovasotomy, immunological

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$1200.00 Results: N/A

Study Objective: To investigate the relationship between immunologically mediated infertility in patients after vasovasotomy and its treatment by corticosteroids.

Technical Approach: Thirty males who are going to have vasovasotomies performed will, prior to surgery, have serum samples analyzed for antisperm antibodies using the Isojima and Kibrick techniques as described by Linnet. They will have two serum samples measured at least one week apart. Following vasovasotomy, monthly semen analyses will be performed, and upon the first appearance of sperm in the ejaculate, serum and semen will be analyzed by the above method antisperm antibodies. Monthly semen analyses will be followed, and, when sperm samples for two consecutive months are >20 million/ml with >20% motility, a sperm penetration assay (SPA) will be performed as well as a repeat antibody study. If the SPA is negative, patients will be treated with 1 mg dexamethasone three times a day for one month. One month following the dexamethasone treatment, a repeat SPA will be performed as well as serum drawn for antibodies. If the patient's spouse becomes pregnant during the study, serum and semen antibodies will be drawn and a SPA performed as soon as the pregnancy is recognized.

Progress: Terminated due to small number of patients available for the study and also due to Dr. Moon's transfer from Urology to Anesthesia.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 84/43	Status: Terminated
Title: Cystoscopy Associated Bacteriuria and Its Prevention by Trimethoprim/Sulfamethoxazole (TMP/SMX)		
Start Date: 18 May 84	Est Completion Date: Mar 85	
Dept/Svc: Surgery/ Urology	Facility: MAMC	
Principal Investigator: LTC Michael R. Moon, MC		
Associate Investigators: COL William D. Belville, MC		
COL Victor J. Kiesling, MC	CPT James C. Mason, MC	
MAJ Brian J. Miles, MC	CPT Thomas A. Rozanski, MC	
LCDR Joseph A. Fernandez, MC	Ray Hackett, M.D.	
CPT Rodney Davis, MC	Herbert C. Kennedy, M.D.	
Key Words: bacteriuria, cystoscopy, prevention, TMP/SMX		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: \$3455.00	Results: Terminated

Study Objective: To determine the incidence of cystoscopically induced bacteriuria following elective cystoscopy at MAMC and the VA Hospital, Seattle; to determine the risk factors for cystoscopy-induced bacteriuria; and to determine the effectiveness of prophylactic precystoscopy trimethoprim and (TMP/SMX).

Technical Approach: Dr. Ray Hackett, Urology Svc, University of Washington, Hackett will provide a randomization list, placebos, and medication. Study patients (1000) will be adult patients undergoing elective cystoscopy. Patients excluded from the study: who have a history of allergy to TMP/SMX or its components; who have taken an antibiotic within 2 weeks of the study; who have additional procedures performed at cystoscopy; <18 years of age; pregnant patients; with a history of folate deficiency; and with severe glucose-6-phosphate dehydrogenase deficiency. The patients will be randomly assigned to either the TMP/SMX or a placebo group. A cystoscopy will then be performed and data recorded. Urine will be collected for each patient pre-cystoscopy and one day and one week post- cystoscopy. The incidence (percentage) of infection will be determined for both the control and treatment groups for their subcategories (age and pre-existing conditions) using chi square analysis.

Progress: Protocol was terminated due to reassignment of principal investigator and the inability to recruit enough patients.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 85/66	Status: On-going
Title: A Hemodynamic Comparison of Protamine Reversal of Bovine Lung vs Porcine Intestinal Mucosal Heparin in Vascular Surgical Patients		
Start Date: 24 May 85	Estimated Completion Date: Aug 85	
Department/Service: Surgery/General Surgery	Facility: MAMC	
Principal Investigator: CPT Mark Nyreen, MC		
Associate Investigators:		
COL Charles Andersen, MC	CPT Robert Martindale, MC	
CPT Mark F. Flanery, MC	Linda Bickerstaff, M.D., DAC	
Key Words: porcine and bovine heparin, protamine reversal, vascular surgery		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: \$3748.00	Results: N/A

Study Objective: To determine whether bovine lung or porcine intestinal mucosal heparin causes the least hemodynamic changes in the clinical setting.

Technical Approach: In an attempt to eliminate changes in hemodynamics secondary to fluid shifts and to eliminate unclamping a major vessel at approximately the same time as heparin administration, patients having carotid endarterectomies alone will be studied. An intraoperative pulmonary artery catheter will be placed as well as the arterial catheter routinely used for these procedures. Patients needing emergency vascular procedures will be excluded. Pre-op evaluation of patients will be no different than that used clinically. Subjects will be assigned to heparinization with bovine lung heparin or porcine intestinal mucosal heparin (10 in each group). A protamine only control will not be included due to the ethical considerations of giving patients a drug that is not indicated other than for the study. Pre-drug parameters measured will be arterial BP, PTT, PAP, HR, CO by thermodilution, CVP, PCN, age, sex, weight, height, and BSA. Filling pressures will be maintained constant insofar as possible. Measurements will be recorded: prior to heparin injection; 10 minutes after heparin bolus; 1, 2.5, 5 and 15 minutes after protamine reversal. Heparin doses will be calculated, drawn up, then diluted to 20 ml with normal saline and injected at a rate of 1 ml/second so each patient will have the same volume infused. Blood loss will be recorded to assure no significant differences. Protamine will be diluted in the same manner and given at a rate of 0.1 mg/kg/minute. Data will be analyzed by Student's t test.

Progress: Two patients have been entered in the study.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 85/65	Status: On-going
Title: Biologic Ingrowth Total Hip Replacement		
Start Date: 24 May 85	Estimated Completion Date: Jul 89	
Dept/Svc: Surgery/Orthopedics	Facility: MAMC	
Principal Investigator: LTC Thomas J. Parr, MC		
Associate Investigators: MAJ Jonathan P. Bacon, MC		
Key Words: hip replacement, biologic ingrowth, non-cemented		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: N/A

Study Objective: To evaluate the use of a new total hip prosthesis undergoing FDA evaluation for approval as an uncemented device.

Technical Approach: Patients (50-60) > 21 years of age will be entered into the study at each of approximately 15 clinical centers. The patient's age, weight, general medical condition and history, extent of injury, expected activity level, and mental alertness will be given full consideration before surgical intervention. Contraindications to use of the device are overt infection, inadequate neuromuscular status, poor prognosis for good wound healing, marked bone loss or osteoporosis, and revision procedures for which an adequate press fit of the prosthesis cannot be achieved. The surgeon must evaluate each patient and document these evaluations preoperatively, at surgery, and at 1, 3, 6, 12, 18, and 24 months. Pre-operative patient assessment includes routine blood work and radiography. The surgery will be carried out per standard SOP for hip replacement surgery. In order to assess bone-prosthesis contact, AP and lateral radiographs will be made to profile the undersurface of the femoral collar. These same radiographs will be made at the 1, 3, 6, 12, 18, and 24 month evaluations. Evaluation of the device will be based on the incidence and severity of complications. The results will be presented according to a number of baseline and operative factors (e.g., primary diagnosis, age, sex, bone quality, operative complications) to determine if there are particular subgroups of the target population at high risk for certain complications. The incidence of complications will be compared to published results on follow-up of patients with cemented and non-cemented prostheses to determine if the risk of complications is equivalent to the published results. The Harris Hip Score and the Charnley Modified D'Aubigne Scale will be used to evaluate the effectiveness of the device.

Progress: Six patients have had hip replacement using this device. All patients have done extremely well with less morbidity than expected for a conventional total hip system.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 83/75 Status: On-going

Title: Ultrasonic Localization of Internal Fixation Devices
Within Connective Tissues

Start Date: 16 Sep 83 Est Completion Date: Sep 84

Dept/Svc: Surgery/Orthopedics Facility: MAMC

Principal Investigator: CPT Davis C. Peterson, MC

Associate Investigators: LTC Thomas J. Parr, MC
MAJ William Fill, MC
MAJ Stanley P. Liebenberg, VC

Key Words: internal fixation devices, connective tissues,
ultrasonic

Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: \$400.00	Results: Continue

Study Objective: To determine the feasibility of A-mode ultrasonography in determining the extent of hardware penetration during internal fixation procedures.

Technical Approach: PHASE I: A 3.5 MHz ultrasonic transducer with a rapid sweep oscilloscope monitor will be coupled through a glycerin contact with a machined 5/32" diameter stainless steel Steinman pin with 90°+ 2 min faces via a machined brass jig incorporating an air chamber to minimize noise as well as shear wave interference in the near field and a 90° centered contact with respect to the transducer face. The exact length will allow calculation of the sound conduction velocity by measuring the time delay from initial to the reflected wave from the distal face. The reflected wave form characteristics will also be determined. The initial phase will be conducted in air and fluid media. A stainless steel reflector plate will then be positioned at 1 mm increments from the pin tip in a saline bath to determine the effect of acoustic impedance and beam attenuation on the reflected waveform. An attenuation coefficient will be determined as a reference for tissue comparison. Connective tissue samples will then be interposed to again determine the wave patterns and attenuation coefficients. If the bone/metal acoustic impedance interface difference is too great to allow resolution of reflected waves from bone media through stainless steel, metals such as vitallium and titanium with density and elastic moduli nearer that bone will be used. PHASE II: Phase I will be repeated using machined pins with 45° tetrahedral tips and 90° faces with precise length measurements with the intent of maximizing the amplitude of the reflected wave and minimizing base width in a cutting tip. PHASE III: Clinical feasibility will be determined by using previously designed and tested hardware in an articular tissue block stratified with perpendicular planes of cancellous bone, subchondral bone, and articular cartilage. Correlation of the strata level by direct mapping of a cross section will be compared with depth measurement determined directly from a machined nylon core guide. Patterns of reflection will be recorded in the previous manner with progressive advancement of the pin to correlate wave form with level of penetration.

Progress: Phases I and II of the protocol have been completed.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/47 Status: Ongoing

Title: The Effect of Staged Hormonal Manipulation (Orchiectomy) on Survival of Nude Mice Inoculated with Human Prostate Carcinoma

Start Date: 15 Mar 85 Estimated Completion Date: Jun 85

Dept/Svc: Surgery/Urology Facility: MAMC

Principal Investigator: CPT Thomas Rozinski, MC

Associate Investigators:

COL William D. Reiballe, MC COL Stephen R. Plymate, MC

COL Victor J. Klesling, Jr, MC Stephen Loop, M.S.

Key Words: orchiectomy, human carcinoma, mice, survival time

Accumulative MED AB Periodic Review

Cost: -0- Results: N/A

Study Objective: To determine if staged hormonal manipulation at various periods after cancer cell inoculation will alter the life span of nude mice inoculated with human prostatic carcinoma.

Technical Approach: Seventy mice will be randomized into seven study groups:

- Ten mice will undergo orchiectomy. Blood will be taken from the tail vein and placed in a heparinized tube for determination of serum testosterone, LH, and FSH levels. These levels will be assayed prior to orchiectomy and on days #5 and #15 postorchiectomy.
- Ten mice will be inoculated with 5 million cancer cells.
- Ten mice will be inoculated with 5 million cancer cells and undergo orchiectomy on day #5 postinoculation.
- Ten mice will be inoculated with 5 million cancer cells and undergo orchiectomy on day #10 postinoculation.
- Ten mice will be inoculated with 15 million cancer cells.
- Ten mice will be inoculated with 15 million cancer cells and undergo orchiectomy on day #5 postinoculation.
- Ten mice will be inoculated with 15 million cancer cells and undergo orchiectomy on day #10 postinoculation.

In order to account for individual and other variations that occur in mice, they will be done 2:1 from each group at the same time rather than doing a group at a time. Serum testosterone, FSH, and LH levels will be compared pre- and post-orchiectomy in Group A. End point of experiment in Groups B through F will be death, to evaluate any effect of orchiectomy on survival. If the animal responds to orchiectomy, an addendum will be submitted to include more in-depth studies. Life table analysis will be used in order to follow the data over a period of time to mortality.

Progress: Forty-five mice have been studied. Injection of ALVA-31 cells (primary human prostate adenocarcinoma cell culture) has resulted in 100% tumor nodule induction. Orchiectomies have been performed on a number of mice with a monthly rate of 15-20%. To date, there appears to be no difference in tumor induction or nodule growth and size between normal and orchidectomized animals. Experiments are ongoing, including the effect of orchiectomy and the dosage of tumor inoculation.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/67 Status: Completed

Title: Training Protocol for Bowel Surgery

Start Date: 24 May 85 Est Completion Date: Jun 85

Department: Surgery Facility: MAMC

Principal Investigator: MAJ Jess A Strand, MC

Associate Investigators: MAJ Leslie Yarbrough, VC
CPT Jon Bowersox, MC

Key Words: ileo-anal anastomosis, dogs, training protocol

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$150.00 Results: N/A

Study Objective: To familiarize the surgeons with an infrequently performed procedure which is soon to be utilized in the clinical setting.

Technical Approach: The ileal pouch will be performed per SOP on an anesthetized dog to reacquaint the surgeons with the procedure in anticipation of its clinical application. At the end of the procedure, the dogs will be euthanized with an overdose of barbiturate.

Progress: Training bowel surgery was performed on two dogs. Training and practice, which were the purposes of the protocol, were accomplished.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/92 Status: On-going

Title: Voice Quality, Acceptability and Intelligibility of
Partially Laryngectomized Persons

Start Date: 20 Sep 85 Est Completion Date: Nov 85

Dept/Svc: Surgery, Otolaryngology Facility: MAMC

Principal Investigator: Kenton Yockey, M.S.

Associate Investigator: Ernest Lancaster, B.A.

Key Words: laryngectomy, voice quality, acceptability and
intelligibility, anatomic areas, tape recordings

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To analyze the post-surgery voice quality, acceptability, and intelligibility characteristics of persons who have had sub-total laryngectomy and to correlate with the type(s) of operative procedure or surgical intervention that was conducted on the respective clients.

Technical Approach: Six to twelve months post-surgery for partial laryngectomy, three groups of subjects will be selected for the study: supraglottic, hemilaryngectomy, and subtotal. After surgery, but before each subject is entered, one of the investigators will interview the subject in order to get a description of the pre-op voice plus any unusual characters of the voice or impediments of speech. Each subject will be recorded in a sound treated room. Subjects will be required to perform three verbal tasks (sustained vowel production, read a paragraph, and spontaneous speech). Tape recordings of the speech samples will be analyzed in regard to vocal quality, acceptability, and intelligibility. Data for vocal quality (air flow, spectral noise, jitter and shimmer), fundamental frequency, rate and average vocal intensity will be derived from sound spectrographic analysis. Acceptability and intelligibility scores will be determined from listener response forms completed by 25 speech pathology/audiology undergraduate students.

Progress: This is a new protocol. The investigators are in the process of setting up the protocol.

DETAIL SHEETS
FOR
PROTOCOLS

CHIEF OF STAFF

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/61 Status: Completed

Title: A Study to Determine If There Is a Significant Difference
In Patients' Level of Satisfaction for Those Patients
Utilizing a Centralized Versus a Decentralized System for
Scheduling Outpatient Appointments

Start Date: 24 May 85 Estimated Completion Date: Aug 85

Unit: Chief of Staff Facility: MAMC

Principal Investigator: CPT Glenn N. Raiha, MSC

Associate Investigators: Jay Dalton, ARC Volunteer

Key Words: outpatient scheduling systems, satisfaction, survey

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To determine randomly selected patients' level of satisfaction with the scheduling method for outpatient appointments (either centralized or decentralized) at MAMC.

Technical Approach: A review of the appointment system currently utilized at MAMC to thoroughly familiarize the investigators with the system will be conducted. A pre-tested and approved questionnaire will be used as the survey instrument. To insure a response rate of 400 people, a sample size of 500 will be surveyed in all clinics using an appointment system. The number surveyed in each clinic will be determined by percentage of clinic appointments to total hospital appointments for that day. The survey instrument will be mailed out to 1000 subjects with a response rate of 20% anticipated. Analysis of data will be accomplished by compiling the responses to individual questions. A numerical value from one to five will be assigned to each response on the satisfaction scales. In addition, an overall satisfaction score will be computed for each respondent by averaging responses for all six questions. An analysis of variance will be performed to determine if there is a significant difference in the level of satisfaction between patients using a centralized versus a decentralized appointment system. Analysis of each individual question relating to the appointment system will be conducted to determine the practical significance of each specific issue such as waiting time for an appointment, lag time from making the appointment to actual appointment date, the way the patient was treated by the appointment clerk, information given by the appointment clerk, and the overall opinion of the appointment system. The completed findings of the research will be presented to the Commander, MAMC, to provide him with information on the patient population's satisfaction with the current appointment systems being utilized at MAMC.

Progress: This graduate research project was completed in July 1985 and has been submitted to Baylor University for approval. Findings were that patients are overall more satisfied with a decentralized appointment system; however, the difference in levels of satisfaction was significant in only four of the six areas studied.

DETAIL SHEETS
FOR
PROTOCOLS

NUTRITION CARE DIVISION

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/30 Status: Completed

Title: Assessment of the Impact of the Weight Program at Fort Lewis and MAMC

Start Date: 17 Feb 84 Est Completion Date: Jan 85

Division: Nutrition Care Facility: MAMC

Principal Investigator: CPT Cecilia M. Dewinne, AMSC

Associate Investigators:

COL Stephen R. Plymate, MC CPT Karl E. Friedl, MSC

MAJ Diana M. Barefoot, AMSC 1LT Rogan L. Taylor, AMSC

Key Words: Army weight program, three different type units, body fat determinations, number who achieve goals

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To determine if there is a need for additional weight loss assistance for troops in the weight loss program for Ft Lewis and MAMC. Three hypotheses will be tested: overweight troops are being accurately detected by the current methods of weight and fat evaluation; overweight troops are successfully losing weight; and overweight troops who achieve their weight standard and are deleted from the program are successfully maintaining the standard.

Technical Approach: Three study groups will be followed for 12 months: an infantry unit, a support unit, and MAMC, an estimated 300-400 overweight troops. The three different types of units have been selected for comparison in order to determine if the consistency of the application of the regulation and the distribution of individuals with weight disorders are related to unit mission. Following a regular weigh-in, each unit will be asked to submit weigh-in lists with weight, height, age, sex, rank, and overweight program status for every individual obtainable. This will provide information on current percent of troops overweight. Body fat assessments on these individuals will be submitted to the Nutrition Clinic. Individuals who are overweight at the first weigh-in will be followed by weigh-ins at subsequent intervals of 6 and 12 months. If possible, information on individual methods of weight loss will be obtained. Initial body weights and subsequent 6 and 12 month weights will be used to determine the proportions who: are on schedule with their weight goals but which have not yet achieved the standard at six months; achieve their weight goals and are deleted from the program; achieve their weight goals, are deleted from the program, and are again overweight; have been lost from observation due to transfer or other administrative action; and were not picked up on the weight program even though they are overweight.

Progress: Data were collected and analyzed in four principal areas of the Army Weight Control Program (AWCP): distribution of fatness in soldiers exceeding Army body composition standards; proportion of the active duty population over the weight standards and proportion over the fat standards; sources of error in the skinfold measurements; and outcome of soldiers entered into the AWCP. A manuscript has been submitted to Military Medicine for publication.

DETAIL SHEETS
FOR
PROTOCOLS

PHYSICAL AND MEDICAL REHABILITATION SERVICE

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/34 Status: On-going

Title: Physiological Changes with Weight Loss. Part I:
 Reliability of Various Methods of Body Fat Determination
 Start Date: 18 Jan 85 Estimated Completion Date: Jan 86
 Service: Physical & Medical Rehabilitation Facility: MAMC
 Principal Investigator: 1LT Rogan L. Taylor, AMSC
 Associate Investigators: COL Stephen R. Plymate, MC
 MAJ Diana Barefoot, AMSC CPT Karl Friedl, MSC
 MAJ Robert E. Jones, MC CPT W. Shine, Inf
 MAJ Arthur Knodel, MC 1LT Cecilia DeWinne, AMSC
 CPT P. Fitzgerald, MSC, USARIEM Mr. Richard Hassan
 Key Words: Calipers, hydrostatic weight, diet, exercise
 Accumulative MEDCASE Est Accumulative Periodic Review
 Cost: -0- OMA Cost: \$825.00 Results: N/A

Study Objective: To evaluate the method of body fat determination which is currently used by the Army (caliper measurements) in terms of the rates of change in body fat with dietary weight loss and with the combination of dietary weight loss and exercise.

Technical Approach: Healthy male non-smokers who have been referred for caliper measurements because they were over the Army weight standard will be randomized into three groups: Group 1 (controls - 0-5% below maximum allowable fat standard): blood samples, caliper measurements, and hydrostatic weight initially and at six months; Group 2 (diet); and Group 3 (diet and exercise). Groups 2 and 3 will be sampled once a week after an overnight fast with blood samples, caliper measurements, and hydrostatic weight. They will be asked to fill out a questionnaire at the first session, to submit a weekly food intake sheet, and to take part in weekly counselling sessions. Data will be expressed in terms of time, weight loss, and fat loss from hydrostatic weight. As a further comparison, a panel of officers will perform a visual appraisal of how well individuals meet the Army standard from photographs taken before, midway, and at the end of the study.

Progress: Thirty subjects have been studied. Data analysis will be performed when the final five subjects complete the study.

D E T A I L S H E E T S
F O R
P R O T O C O L S

P R E V E N T I V E M E D I C I N E S E R V I C E

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/94 Status: On-going

Title: A Clinical Trial of a Training-Associated Injury Prevention Program in Active Duty Soldiers

Start Date: 20 Sep 85 Estimated Completion Date: July 1986

Service: Preventive Medicine Facility: MAMC

Principal Investigator: MAJ Eric T. Evenson, MC

Associate Investigators:

COL Elmer M. Casey, MC MAJ Wayne M. Lednar, MC

COL Frederick J. Erdtmann, MC Frederick Connell, M.D., M.P.H

Key Words: lower extremity, training exposure, prevention program

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$270.00 Results: N/A

Study Objective: To determine the incidence rates of lower extremity injuries in typical Army units; to document those physical training exposures which contribute to the development of lower extremity injuries in Army personnel, and to analyze the costs versus the benefits of an alternative physical training regimen.

Technical Approach: A typical Army battalion (500-600 soldiers) will be identified as the population at risk. The differences in injury incidence between units using standard fitness programs and units using a modified fitness program will be examined in a single blind study, with the soldiers uninformed about their participation in the study. The presenting complaint of all members of the study battalion will be evaluated according to specific criteria and case ascertainment will occur through the review of medical records. A questionnaire will be completed by the injured soldier outlining the circumstances of the injury. Training exposure is defined as any planned, structured, and repetitive bodily movement done to improve or maintain one or more components of physical fitness. Training will be classified according to its frequency, intensity, duration, and type, and a daily log of all training activities will be maintained. An individual report of usual off-duty training will be completed by all personnel. A person-time approach (such as soldier months) will be used to quantify training exposure. The standard fitness program to be used consists of 45 minutes of calisthenics and running 3 day/wk. The modified program will consist of five minutes each of warm-up and cool-down stretching, bracketing a 2-3 mile run, selected calisthenics, and upper body strengthening exercises. Training will take place by ability groups on smooth training surfaces and rapid increases in the frequency, duration, and intensity of training will be avoided. APRTs will be performed at the beginning and the end of the study period as these are associated with aerobic fitness capacity.

Progress: This protocol is a new protocol and has not been started.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/12 Status: Completed

Title: The Epidemiology of Acute Pharyngitis in Active Duty Personnel at Fort Lewis, Washington

Start Date: 16 Nov 84 Estimated Completion Date: Aug 85

Service: Preventive Medicine Facility: MAMC

Principal Investigator: MAJ Clement J. Hanson, MC

Associate Investigators: LTC James W. Higbee, MSC
MAJ William H. Weaver, MC
CPT David L. Paton, MC

Key Words: pharyngitis, active duty personnel, lost duty time

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$1400.00 Results: N/A

Study Objective: To determine the frequency of acute pharyngitis in Ft Lewis active duty personnel; to establish a weekly surveillance system at sampled medical treatment facilities for respiratory sick call rate; to document the impact of respiratory morbidity on troops in terms of needs for medical care and lost duty time; to determine if agents causing endemic pharyngitis are the same as those causing epidemic pharyngitis; to identify agents causing respiratory morbidity with particular emphasis on treatable and preventable causes.

Technical Approach: Subjects will be given a questionnaire to complete; it will be self-administered and reviewed by the physician investigator at the time of the clinic visit. The patient will then be briefly examined by the investigator. Cultures and serologies will be taken from the patient and sera for convalescent serologies will be drawn 3-4 weeks later. Each MTF selected for study will be sampled one week per month, preferably to include all duty days of the selected weeks. On the return visit for convalescent serologies, the total number of days of restricted or lost duty will be recorded. Individual patient medical records will be reviewed on the return visit to validate the patient's report of lost or restricted duty time. Agents to be investigated in the study: influenza A, B, parainfluenza, adenovirus, RSV, EBV, *M. pneumoniae*, Grp A BH strep, *B. pertussis*, *B. parapertussis*, and *Chlamydia*. Should the weekly sick call rate for respiratory complaints become greater than 10% of unit strength, epidemic sampling will be initiated. Epidemic sampling will involve the same technique, procedures, and questionnaires as for endemic sampling.

Progress: One hundred acute pharyngitis cases and 100 controls were studied. Agents were identified in 16 of 100 pharyngitis cases. Surveillance of the respiratory sick call rate at the two treatment facilities failed to demonstrate an epidemic. Comparison of cases with controls suggested exposure to sick children two weeks prior to clinic visit as a potential risk factor for pharyngitis. Comparison of the 16 cases with the 84 remaining cases demonstrated that fever and pharyngeal exudate were potential identifying physical findings due to an identifiable agent. Cases with an identifiable agent were more likely than other cases to have been hospitalized or placed on quarters.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/33 Status: On-going

Title: Cancer Incidence and Magnetic Field Exposure

Start Date: 18 Jan 85 Estimated Completion Date: Jan 86

Service: Preventive Medicine Facility: MAMC

Principal Investigator: MAJ Wayne M. Lednar, MC

Associate Investigators:

David B. Thomas, M.D., Dr. P.H. Sidney Marks, M.D., Ph.D.

Richard K. Severson, Ph.D. William Kaune, Ph.D.

Key Words: Nonlymphocytic leukemia, interview, magnetic field measurements

Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: 0.00	OMA Cost: 0.00	Results: N/A

Study Objective: To test the hypothesis that an association exists between the occurrence of acute nonlymphocytic leukemia and residential wiring configurations or magnetic field exposure.

Technical Approach: This study will include an in-person interview with nonlymphocytic leukemia patients or the next of kin, review of hospital charts, and direct magnetic field measurements of subjects' houses. Healthy control subjects will be studied similarly. These direct magnetic field measurements will be correlated with disease status and with surrogate magnetic field measurements based on wiring configurations. Appropriate statistical analyses will be utilized to test for associations between measures of exposure and acute nonlymphocytic leukemia.

Progress: Most of the questionnaires have been distributed. Distribution should be complete within four months.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/68 Status: On-going

Title: Genital Herpes During Pregnancy: Historical Cohort
Study of Newborn and Maternal Outcomes

Start Date: 24 May 85 Est Completion Date: May 87

Service: Preventive Medicine Facility: MAMC

Principal Investigator: MAJ Wayne Lednar, MC

Associate Investigator: Marsha E. Wolf, MS., Ph.C.

Key Words: genital herpes, vaginal vs cesarean, controls

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To assess the effect of maternal genital herpes exposure during pregnancy on the infant outcomes of congenital malformation, low birth weight, low Apgar score, infant morbidity, and infant mortality and to describe current obstetric practices in pregnant women with genital herpes by evaluating herpes status at time of delivery and describing the rate different types of delivery and apparent of indication for each and the postpartum complication rate of endometritis.

Technical Approach: A population based historical cohort study will be used to investigate live-births (1100) whose mothers had herpes during pregnancy as identified from the 1980-83 birth certificates in King, Pierce, and Snohomish Counties. Two comparison groups, matched and unmatched for method of delivery, as well as matched for hospital of delivery and year of birth, will be randomly selected from non-herpes-exposed pregnancies. All hospitals in the designated study area with identified herpes exposed pregnancies will be invited to participate. Data will be abstracted from hospital charts with approximately 200 studied at MAMC. Type of data to be collected from hospital records will include parental sociodemographics, neonatal data, pregnancy and health history, current pregnancy, postpartum recovery, and labor and delivery. Data collection and handling procedures will be designed to maximize strictest confidentiality by using specially coded numbers, a single master list of personal identifiers and codes, locked files, and a limited number of personnel with access to data.

Progress: A pilot study has been conducted utilizing >200 charts from the University of Washington and Group Health of Tacoma. The investigators are now making arrangements to abstract the charts at MAMC.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 85/95	Status: On-going
Title: Day Care Diarrhea: A Concurrent Prospective Study		
Start Date: 20 Sep 85	Estimated Completion Date: June 1986	
Service: Preventive Medicine	Facility: MAMC	
Principal Investigator: MAJ Douglas F. Phillip, MC		
Associate Investigators:		
COL Frederick J. Erdtmann, MC	Frederick Connell, M.D., M.P.H.	
MAJ Wayne M. Lednar, MC	Hjordis Foy, M.D., Ph.D.	
Key Words: Ft Lewis Day Care Center, day care with <6 children, diarrhea, ages 6 weeks to 5 years		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: \$2700.00	Results: N/A

Study Objective: To determine if a full-time day care group of children experience a significantly increased rate of diarrhea as compared to a non-day care center group and to determine if there are external factors to the day care center which may augment or predispose the day care and/or non-day care child to contracting diarrhea.

Technical Approach: The study group will be 160 full-time enrollees in the Fort Lewis Child Care Facility, age 6 weeks to <5 5 years old. Age-matched children with the same number of siblings from the Child Care Facility's fulltime waiting list who presently receive day care with six or fewer children will serve as controls. Children > 2 who no longer are in diapers but receive daily child care with children wearing diapers from other families will be excluded from the comparison group. Initial questionnaire will be given to both groups and a medical chart review will be conducted on study children to aid in data collection, diarrhea case identification, and to limit misclassification. Monitoring of both groups will involve biweekly telephone contact with parents to determine incidence of diarrhea for each child for the previous two weeks. Diarrhea will be defined as three or more watery stools in a 24-hour period plus a constitutional or gastrointestinal symptom. Major dietary concerns that may influence stool quantity and consistency will be assessed in the questionnaires. Changes in certain child care activities during the six month study interval will be reassessed every two months via telephone monitoring. In order to possibly increase the ability to generalize the results of the investigation, a concurrent recording using two-week time periods of 6 month to 5 year old children who present to the MAMC Family Practice Clinic as diarrhea cases will be done and compared to the number of cases in the other two groups.

Progress: This is a new protocol with the investigators awaiting approval of revisions.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/14 Status: Completed

Title: Risk of Injury in Active Duty Personnel and Design of an Injury Control Program at Fort Lewis, Washington

Start Date: 16 Nov 84 Estimated Completion Date: Apr 85

Service: Preventive Medicine Facility: MAMC

Principal Investigator: LTC J. Pitt Tomlinson, MC

Associate Investigator: MAJ Cloyd B. Gatrell, MC

Key Words: injury, military, sports, occupational

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To determine the incidence and associated risk factors of injuries in active duty personnel. Having identified risk factors associated with preventable injuries, an injury control program is to be designed.

Technical Approach: Approximately 1500 active duty soldiers receiving care at the Troop Medical Clinics will be sampled during a six month period. The distribution of sampling weeks will consider season, day of the week and month, training schedules, and other factors for balanced data collection. Injured soldiers will be asked to fill out a questionnaire eliciting demographic data as well as information about the injury. A medical officer will fill out a questionnaire regarding the type of injury and loss of duty time. Controls similar to the injured subjects will be asked the same questions except for information about the injury.

Progress: The study has been completed and a manuscript has been submitted for publication. Four hundred and seventy-eight (478) subjects were entered. Each TMC was monitored for two one-week periods, sequentially. All new injuries were documented during normal operating hours and the MAMC emergency room was monitored 24 hours a day. Hospital admission and discharge sheets and post safety office reports were reviewed to ensure complete enumeration of injuries. The overall incidence rate was 81 injuries/100 soldiers/year. Most injuries (66.4%) occur on duty and 55.8% occur while participating in exercise and sports. Sixty (60%) of all injured soldiers are unable to return immediately to full duty. Musculoskeletal injuries account for the greatest number of disabled soldiers. Risk factors for injury include age, sex, location of housing, amount of weekly exercise and unit of assignment.

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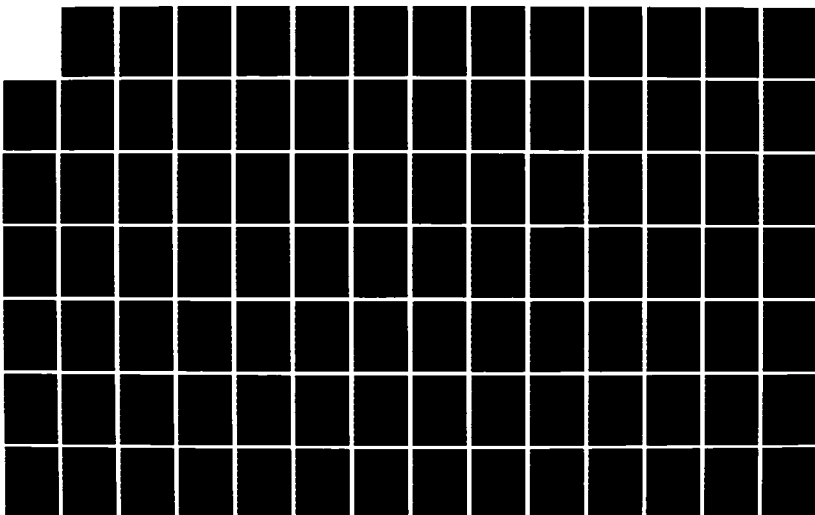
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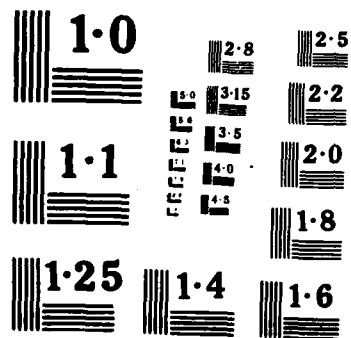
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DETAIL SHEETS
FOR
PROTOCOLS
SOCIAL WORK SERVICE

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/60 Status: On-going

Title: Family Violence: Prevention and Treatment

Start Date: 24 May 85 Estimated Completion Date: May 87

Service: Social Work Facility: MAMC

Principal Investigator: LTC Donald L. Greenhalgh, A.C.S.W., MSC

Associate Investigators: Robert L. Bradley, M.A., COL, Ret

Thomas R.. Egnew, M.A. Jerry L. McKain, Ph.D., COL, Ret

Dennis C. McBride, Ph.D. David D. McKee, M.S.W., MAJ, USAR

Key Words: conduct, evaluate, family violence therapeutic model

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$200.00 Results: N/A

Study Objective: To conduct and evaluate a family violence therapeutic intervention model which was developed as part of a Department of Army, FORCCOM, Family Advocacy research project.

Technical Approach: Patients will be assigned to either a conventional treatment program (controls) or to the protocol treatment program on an alternating basis as they enter for treatment. Only those patients who agree to be randomized will be utilized. Controls will be matched for pay grade, age, years married, and number of children. Several instruments designed to tap either the incidence of violent behavior or the learned and culturally reinforced "belief systems" of the subjects and interaction patterns which can culminate in violent behavior will be administered to the treatment group at in-take and at a two-month follow-up session. These include a modified version of a questionnaire concerning wife battering developed by Giles-Sims (1983); The Index of Spouse Abuse (ISA) developed by Hudson (1982); The Child Abuse Potential Inventory (CAP) developed by Milner (1977); and the Family Adaptability and Cohesion Evaluation Scales (FACES II) developed by Olesen, Portner, and Bell (1978). Ten treatment couples involved with spouse abuse and ten treatment couples involved with child abuse will meet as a group for four sessions of 4 hours. There will be an individual two-month follow-up when the questionnaires are readministered. A follow-up will be performed from medical records at one year on all subjects still assigned to the Ft Lewis area. The control group will receive conventional therapy and will completed the study instruments at in-take and again at two months. The major goal of this evaluation is to determine whether or not the training program has affected either the incidence of violent behavior or those belief systems and interactions patterns which can potentially culminate in violent behavior. The scores from the indicators will be used to help make this determination. The "gain" scores between pre and post treatment scores will be computed using a t-ratio (Elifson, et al, 1983 p 318) between treatment and control groups for these gain scores. This will help ensure that any observed differences in scores is due to the offender class and not some extraneous cause.

Progress: This project has not been started due to the imminent departure of LTC Greenhalgh. The protocol will commence in approximately three months under the direction of the new Chief, Social Work Service.

DETAIL SHEETS
FOR
PROTOCOLS

9TH INFANTRY DIVISION

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/63 Status: Completed

Title: High Dose Acetazolamide and Acute Mountain Sickness -
Clinical Efficacy and Effect on Military Performance

Start Date: 18 May 84 Est Completion Date: Sep 84

Division: 9th Infantry Facility: MAMC

Principal Investigator: MAJ Lawrence C. Mohr, MC

Associate Investigators: COL William N. Bernhard, MC (USAR)
CPT Jerome Pierson, MSC

Key Words: mountain sickness, acetazolamide, high dose

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$600.00 Results: Continue

Study Objective: To determine the efficacy of high dose acetazolamide in preventing acute mountain sickness in soldiers making a rapid ascent of Mount Rainier and to determine the effect of high dose acetazolamide on the performance of soldiers during a rapid ascent of Mount Rainier.

Technical Approach: Approximately 30 soldiers who are making a rapid ascent of Mount Rainier as part of their training will be recruited for this study. Subjects will have a complete medical history, review of systems and physical examination performed prior to the ascent. Soldiers will be excluded from the study if they have evidence of heart or pulmonary disease, or renal, hepatic, or adrenal dysfunction. Venous blood samples will be drawn prior to ascent and after ascent and at the summit to determine serum electrolyte, bicarbonate, glucose, osmolality, cortisol, endorphin, testosterone and lactate. Saliva samples for cortisol and testosterone will be collected. Soldiers will eat a standard diet of C-Rations or MRE-Rations three times/day during the ascent and water intake and urine output will be recorded. Subjects will be assigned to receive acetazolamide (Diamox) or a placebo, every 12 hours beginning 24 hours prior to ascent. A standard Environmental Symptoms Questionnaire will be completed at the summit and immediately before and after the climb. Performance will be assessed by having each subject connect the dots of a standard Bender pattern and copy a standard Bender solid-line figure before and after the climb and at the summit. The following measurements will be made in each subject at each altitude at which the subjects complete the questionnaire: pulse rate; blood pressure; tissue pO₂; vital capacity; minute ventilation; and peak expiratory flow. Data from the acetazolamide and placebo groups will be evaluated with paired and unpaired Student's t test, chi square test with Yate's continuity correction, or Fisher's exact test.

Progress: Bad weather delayed the climbs until the summer of 1985 when three climbs to the summits of Mount Ranier and Mount Adams were completed with 14 individuals completing the protocol. The data has been analyzed and a manuscript is being written. Data collected from a pilot study in the summer of 1984 resulted in a presentation of endocrine findings to the Andrology Society in April 1985.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/76 Status: Completed

Title: Efficacy of Diphenylhydantoin in the Prevention of Acute Mountain Sickness

Start Date: 17 Aug 84 Est Completion Date: Aug 85

Division: 9th Infantry Facility: MAMC

Principal Investigator: MAJ Lawrence C. Mohr, MC

Associate Investigators: COL William N. Bernhard, MC (USAR)

COL Stephen R. Plymate, MC CPT Jerome Pierson, MSC

CPT Karl E. Friedl, MSC Allan Cymerman, Ph.D., USARIEM

Key Words: mountain sickness, diphenylhydantoin, prevention

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$760.00 Results: Completed

Study Objective: To determine the efficacy of diphenylhydantoin (Dilantin) in a dosage of 200 mg 2 times daily after a 600 mg loading dose in preventing acute mountain sickness in soldiers making a rapid ascent of Mount Rainier and to determine the effect of Dilantin on the performance of soldiers during the rapid ascent.

Technical Approach: Subjects will be selected on the basis of fitness, motivation and mountaineering aptitude and will be divided into two groups, matched closely for age, weight, fitness, and previous altitude experience. Subjects will be given either Dilantin or a placebo every 12 hours from 24 hours before ascent until descent. A loading dose will be given orally in 2 doses 6 hrs apart. Blood will be drawn before and after the climb for analysis. The subjects will drive to the starting point (about 5400 feet), climb to between 10,000 and 11,500 feet, remain eight hours for repeat testing, and then proceed to 14,000 feet where they will remain for 1-2 hours of tests before descending. In a subsequent climb, the order of treatment groups will be reversed. The ARIEM Environmental Symptoms Questionnaire (ESQ) will be administered before going to 5400 feet, at each stage of the ascent and after descent. Subjects will be tested by ESQ and performance tests over a similar duration of time without ascent to altitude with the same Dilantin regimen to distinguish interactions between Dilantin and altitude effects. Performance will be assessed with the finger tapping speed test and the paced serial addition test at the various stages of the experiment. Physiological measurements will be made for each subject at the same stages as the ESQ test to include corticosteroids, catecholamines, osmolarity, electrolytes, vital capacity, minute ventilation, peak expiratory flow rates, pulse, blood pressure, and degree of hypoxia.

Progress: A loading dose to achieve therapeutic levels of Dilantin in men under the stress of a mountaineering expedition was established. This experiment will be continued in a future study in a hypobaric chamber where variables can be better controlled.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/05 Status: Terminated

Title: Effects of Motrin on Tendon Healing

Start Date: 19 Oct 84 Est Completion Date: Dec 85

Division: 9th Infantry Facility: MAMC

Principal Investigator: CPT Cris P. Myers, MC

Associate Investigator: MAJ Leslie Yarbrough, VC

Key Words: tendon healing, Motrin, rats

Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: \$300.00	Results: N/A

Study Objective: To determine if Motrin, an anti-inflammatory agent, reduces the speed of tendon healing.

Technical Approach: Eighteen (18) rats will be randomly divided into two groups. The right Achilles tendon of each rat will be severed completely 3 mm above the calcaneal-Achilles tendon junction. The approach (surgical) will be through a 1.0 cm lateral incision adjacent to the Achilles tendon. After the connective tissue is bluntly dissected through down to the tendon, the tendon will be lacerated with a perpendicular incision, using a No. 11 surgical blade. The tendon will then be reapproximated using a 5-0 surgical steel suture. The skin will then be closed with 4-0 nylon simple sutures. Group 1 (9 rats) will be controls and Group 2 (9 rats) will be treated with Motrin. Each rat in Group 2 will receive a dose of 500 mg/kg/day divided into 3 doses. The two groups will then be evaluated as follows: after one week, three controls and three treated rats will be sacrificed. The right and the left leg of each rat will then be dissected and the Achilles tendon isolated. All structures supporting the leg will then be ligated at the level of the Achilles tendon. The proximal aspect of the leg will then be clamped into position on the table. A hole will be drilled through the calcaneal bone and a large wire will be passed through the hole. The wire will then be attached to scale and straight line tension will be applied to the scale (1/2 lb added per 10 second interval) until the tendon ruptures. This will be done on both the right and the left legs of each rat. At the end of the second and the third weeks, this same procedure will be repeated.

Progress: This protocol was terminated due to the reassignment of the principal investigator before he could implement the protocol.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 83/34 Status: Suspended

Title: Ranger Medic Procedures Training

Start Date: 21 Jan 83 Est Completion Date: Indefinite

Division: 9th Infantry Facility: MAMC

Principal Investigator: CPT William Tynum, MC

Associate Investigators: MAJ Stanley P. Liebenberg, VC

CPT Robert E. Kane, MC

Key Words: training, Ranger medics, life-saving measures

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: \$1830.00 Results: Suspend

Study Objective: To provide training to acquire the necessary manipulative skills in performing emergency life-saving measures in support of wartime field operations.

Technical Approach: The Medical Platoon of the 2/75th Infantry (Ranger) consists of two MC officers and approximately 20 additional enlisted personnel (MOS 91B). Each of these 20 personnel will be trained on a quarterly basis. Classes will be conducted monthly utilizing the two MC officers as preceptors, training 6-7 Ranger medics at each session. Two mongrel dogs will be used for each training class with the exception of debridement exercises which will each use four sheep as animal models. All animals will initially be anesthetized with sodium pentobarbital with anesthesia maintained by halothane throughout the duration of each class. Wounds for debridement will be caused by a Captive Bolt pistol. Upon completion of the exercise, all animals will be euthanized by lethal injection of sodium pentobarbital without allowing the animal to regain consciousness. The carcasses will be disposed of by incineration. Procedures to be performed on dogs consist of:

Peripheral venous cutdown (femoral/jugular)	Pericardiocentesis
Tube thoracotomy (chest tube insertion)	Peritoneal lavage
Resuscitative techniques	Suturing techniques
Reversal of hypovolemic shock	Cricothyroidotomy

Progress: Due to the ban on the use of dogs in research, this protocol was suspended until the investigators consult with MAJ Yarbrough, the present veterinarian assigned to Department of Clinical Investigation, on the animal models that are to be used.

DETAIL SHEETS
FOR
PROTOCOLS

ACTIVE DUTY FULL TIME STUDENTS

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/53 Status: Completed

Title: An Explanatory Study of the Exceptional Family Member Program

Start Date: 18 May 84 Est Completion Date: Sep 84

Activity: Student Program, HSC Facility: MAMC

Principal Investigator: MAJ Robert H. Gemmill, MS

Associate Investigators: LTC Virginia Randall, MC

Key Words: Exceptional Family Member Program, soldiers, perception

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: Completed

Study Objective: To describe characteristics of the exceptional family member population and to study how Army active duty personnel with exceptional family members perceive the Exceptional Family Member Program.

Technical Approach: This protocol will be conducted at MAMC, BAMC, and WBAMC. A questionnaire will be distributed to all adult soldiers who voluntarily come to the Pediatric Clinic to initiate processing for The Exceptional Family Member Program. The questionnaire will also be distributed to those soldiers who are eligible to participate in the program, but who have not yet enrolled. The questions to be explored are: what are the characteristics of the exceptional family member population; how much accurate knowledge is there about the program? how well is the program being accepted; how can the program be improved or made more productive; what are the strengths and weaknesses of the program; and how accurately are the goals of the program being perceived by the recipients of the program.

Progress: The sample of 65 active duty soldiers that entered the study had 161 children and 76 of these children (47%) were exceptional children. The majority (91%) of these exceptional family members are <11 years of age, with about 25% being adopted or under legal guardianship. They experience both chronic medical and educational problems, tend to be multihandicapped, and obtain the majority of their medical care and health-related services from the federal government. The soldiers' responses to questions that pertained to specific aspects of the EFM Program were always more positive than negative. This suggests that soldiers are optimistic or receptive toward the EFM Program even though some soldiers, specifically officers, have reservations about particular aspects of the program. A majority of the soldiers believed that the EFM Program was a good program and that it would meet the needs of their family.

A thesis has been accepted in partial fulfillment of a Ph.D. in Social Work for MAJ Gemmill.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 84/62	Status: On-going
Title: Screening of Infants for Movement Deficits		
Start Date: 18 May 84	Est Completion Date: May 85	
Activity: Student Program, HSC	Facility: MAMC	
Principal Investigator: LTC Jane K. Sweeney, AMSC		
Associate Investigators: COL Carl Plonsky, MC		
MAJ Gleen Tripp, MC	Lynette S. Chandler, Ph.D.	
Catherine Yokan, M.D.	Margon B. Holm, Ph.D.	
Key Words: movement deficits, infants, Chandler Movement Assessment of Infants - Screening Test		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To establish norms for the Chandler Movement Assessment of Infants Screening Test (CMAI-ST); to establish inter-rater reliability, test-retest reliability, and predictive validity for the CMAI-ST.

Technical Approach: Fifty infants will be examined in age groups of 2, 4, 6, and 8 months, plus or minus one week. The infants will be examined in only one of those time frames in order to establish norms. Thirty infants from the 200 will be observed by two examiners simultaneously to determine inter-rater reliabilities. An additional 30 infants will be examined during two time frames to establish test-retest reliability. The outcome of the CMAI-ST will be correlated with physician assessment at the regularly scheduled 12-month exam to establish predictive validity. Half of the children from each group will be male and half will be female and distinct races will be represented to match the population of infants of military personnel. A Denver Prescreening Development Questionnaire will be completed by the parents. The high risk profiles of the 30 infants tested twice for test/retest reliability will be compared with those infants tested once. Only those twice-tested infants who maintain a high risk profile or increase their apparent degree of involvement will be considered at risk. All once-tested infants will be evaluated on their original profile. Pearson-product-movement correlations will be calculated to determine the predictive validity of twice-tested and once-tested infants. Percent of false positives and false negatives from each group will also be calculated.

Progress: The number of subjects tested to date is 169. Because of the marked variation of movement patterns in normal subjects, it would appear that an ideal age for screening infants for movement dysfunction is 4 1/2 to 5 1/2 months. It is at this time that primitive reflexes have diminished their influence on movement and automatic postural reactions are consistent. The collection of follow-up data on infants screened by the CMAI-ST has begun. All data collection and data analysis should be completed by the end of summer 1986.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/15 Status: On-going

Title: Physiologic Correlates of Neurobehavioral Assessment
Start Date: 16 Nov 84 Estimated Completion Date: Oct 85
Activity: Student Program, HSC Facility: MAMC
Principal Investigator: LTC Jane K. Sweeney, AMSC
Associate Investigators: LTC Philip G. Pettett, MC
CPT Alice Stone, ANC

Key Words: neonates, muscle tone, reflexes, visual and auditory responses

Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: N/A

Study Objective: To analyze the physiologic responses of neonates to neurobehavioral assessment procedures. Heart rate, respiratory rate, and oxygenation level in newborns will be measured during the administration of the Neurological Examination of the Preterm and Full Term Infant (Dubowitz & Dubowitz 1981).

Technical Approach: Thirty medically stable newborns from the NICU and the Newborn Nursery will be studied in two groups of 15 each: (a) full-term group (39-41 weeks gestation) (random selection) and (b) preterm group (32-34 weeks gestation) selection of total population of age-eligible infants admitted during Jan-Apr 1985. Exclusions: Infants with birth defects or chromosomal abnormalities and infants on ventilatory or infusion equipment will be excluded from the study. A cardiorespirograph and a transcutaneous oxygen monitor will be used to gather data on heart rate, respiratory rate, and oxygenation. Adhesive skin electrodes will be utilized for non-invasive physiologic data collection. Orientation Responses and Tone/Reflexes, subtests of The Neurological Examination of the Preterm and Full Term Newborn Infant (Dubowitz & Dubowitz 1981), comprise the neurobehavioral assessment protocol. The physiologic parameters of heart rate, respiratory rate, and oxygenation will be measured on all subjects 15 minutes before, 15 minutes during and 15 minutes after administration of the neurobehavioral assessment. Each infant will serve as his own control. The neurobehavioral assessment consists of an examination of muscle tone and developmental reflexes and an evaluation of visual and auditory orientation responses. The following statistical methods will be used: ANOVA, paired t-test, and Mann-Whitney U Test (distribution free test).

Progress: Thirty-two subjects have been studied and will be used as a pilot study for a larger sample. The investigator has requested a revision to the protocol to add the parameter of blood pressure.

D E T A I L S H E E T S
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CHILDRENS CANCER STUDY GROUP PROTOCOLS

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 79/46 Status: Completed

Title: CCG #861: Surgery, Radiation Therapy, and Chemotherapy with Bleomycin, Vinblastine, Cis-Platinum Diamine Dichloride, Actinomycin-D, Cyclophosphamide, and Adriamycin in the Treatment of Local and Metastatic Malignant Germ Cell Ovarian Tumors of Childhood (Phase II Study)

Start Date: 17 Nov 78 Est Completion Date: Indefinite

Department: Pediatrics Facility: MAMC

Principal Investigator: LTC Allan R. Potter, MC

Associate Investigators: LTC Charlene Holt, MC
LTC Alan Mease, MC

Key Words: ovarian tumors, childhood, surgery, radiotherapy, chemotherapy

Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Completed

Study Objective: To determine, in patients with germ cell ovarian malignancy which has been completely excised by surgery, treated with 6-drug chemotherapy, and perhaps with radiation therapy, the length of disease free interval and the percentage of patients having long term survival; to determine, in patients with residual or metastatic disease treated with surgery, 6-drug chemotherapy, and radiation therapy, the effectiveness of the treatment program as indicated by percent of patients experiencing CR or PR and the length of the remission periods; to examine the relationship between age, tumor type, staging, and pathology with prognosis; and to determine if a single arm study of an infrequent childhood tumor is practical and produces significant conclusions.

Technical Approach: Patients will be treated with chemotherapy for 18 weeks. At week 18, a second look laparotomy is performed. If there is residual or persistent tumor present, radiation therapy will be given. If there is no residual or persistent tumor, radiation therapy will not be administered. If at 24 weeks the patient has progressive disease, the patient will be taken off the study. Patients on the study will continue chemotherapy until week 102. The patient will be taken off the study if there is progressive disease after 24 weeks of therapy or if recurrent or metastatic disease appears after six months of therapy.

PROGRESS: No patients have been entered in this study at MAMC.

D E T A I L S H E E T S
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FRED HUTCHINSON CANCER RESEARCH CENTER GROUP PROTOCOLS

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 83/30	Status: On-going
Title: FHCRC #11 - Protocol for Treatment of Adult Acute Nonlymphocytic Leukemia, Study V.		
Start Date: 21 Jan 83	Est Completion Date: Jan 85	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: LTC Irwin B. Dabe, MC		
Associate Investigators:		
COL Friedrich H. Stutz, MC	MAJ Thomas M. Baker, MC	
LTC James E. Congdon, MC	MAJ Alfred H. Chan, MC	
LTC Howard Davidson, MC	MAJ Timothy J. O'Rourke, MC	
Key Words: nonlymphocytic leukemia, acute, chemotherapy		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine the complete remission rate with intensive induction in patients with ANL; to determine if therapy with high-dose Ara-C, Asparaginase, AMSA, and VP-16 will decrease the rate of leukemic relapse; to determine whether the wider application of marrow transplantation using allogeneic, partially-matched, unrelated, and autologous marrow will increase the cure rate of ANL in patients less than 30 years of age; and to determine if marrow transplantation should be carried out in first remission or at first sign of relapse in patients age 30-50.

Technical Approach: All Patients <75 years with adult nonlymphocytic leukemia, previously untreated except for the administration of hydroxyurea are eligible. Diagnoses to be included: acute myelocytic, promyelocytic, monocytic, myelomonocytic, acute undifferentiated, and erythroleukemic. Daunomycin, Ara-C, 6-thioguanine, vincristine, and prednisone will be used in Cycle I as the induction regimen; Cycle 2 will be high-dose Ara-C and asparaginase; Cycle III - same as Cycle I; Cycle IV will be high dose AMSA and VP-16; cycle V - same as Cycle I, Cycle VI will be vincristine, prednisone, 6-mercaptopurine, and methotrexate. Regardless of remission status, patients <30 will be offered bone marrow transplantation after Cycle 2. Patients 30-50 years of age who have not achieved complete remission after two courses or who relapse after remission will be offered transplantation. Patients >50 will receive chemotherapy only. All patients will continue on chemotherapy, regardless of transplantation status.

Progress: No patients were entered in FY 85. One patient entered in FY 84. The patient had fairly severe side effects to the chemotherapy with multiple admissions for infection and leukopenia.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 83/48	Status: Completed
Title: FHCRC #143: Treatment of Relapsed Acute Nonlymphocytic Leukemia with AMSA, and Use of in Vitro Studies (Stem Cell Assay) to Predict a Response in Vivo.		
Start Date: 18 Feb 83	Est Completion Date: Jan 85	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: LTC Irwin B. Dabe, MC		
Associate Investigators:		
COL Friedrich H. Stutz, MC	MAJ Thomas M. Baker, MC	
LTC James E. Congdon, MC	MAJ Alfred H. Chan, MC	
LTC Howard Davidson, MC	MAJ Timothy J. O'Rourke, MC	
Key Words: nonlymphocytic leukemia, AMSA, stem cell assay		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Completed

Study Objective: To determine the ability of AMSA to induce remission for patients with acute nonlymphoblastic leukemia in relapse.

Technical Approach: Patients who have relapsed after successful induction of remission with daunomycin and cytosine arabinoside, as well as patients who have failed two cycles of remission induction therapy, are eligible for this study. The factors that will be analyzed include duration of first remission, nature and amount of previous chemotherapy received, age and number of cycles of therapy to first complete remission. Patients will receive AMSA 120 mg/M² for five days. A bone marrow exam will be done on day 14. If the marrow has more than 30% blasts when the marrow is hypocellular or more than 10% when the marrow is normocellular, a second incution course will be given. A minimum of two courses is needed to evaluate response. If after two courses a complete remission is not reached and the patient has not had undue toxicity, a third course may be given.

Progress: No patients entered at MAMC in FY 85. One patient was entered at MAMC in FY 84 with a partial response only. AMSA remains one of the few agents with acitivity in AML relapsed patients after prior treatment, but overall groupwide response rate is low with severe cytopenia and short duration of response.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 83/47	Status: On-going
Title: FHCRC #152: Combined Modality Treatment for Non-Hodgkin's Lymphomas of Intermediate and High-Grade Malignancy		
Start Date: 18 Feb 83	Est Completion Date: Jan 85	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: LTC Howard Davidson, MC		
Associate Investigators:		
COL Friedrich H. Stutz, MC	MAJ Thomas M. Baker, MC	
LTC James E. Congdon, MC	MAJ Alfred H. Chan, MC	
LTC Irwin B. Dabe, MC	MAJ Timothy J. O'Rourke, MC	
Key Words: non-Hodgkin's lymphoma, intermediate, high-grade		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To compare in patients with extensive (stage III and IV), aggressive (intermediate and high-grade malignancy) non-Hodgkin's lymphoma (NHL) the response rate, duration, and survival after treatment with: (1) combined cyclophosphamide, adriamycin, vincristine, and prednisone (CHOP) chemotherapy combined with total body irradiation (TBI), or (2) CHOP chemotherapy combined with upper and lower hemibody irradiation (HBI); and to determine the response rate, duration and survival of patients with limited (stage I, II, and certain stage III and IV), aggressive NHL treated with CHOP chemotherapy with local radiotherapy.

Technical Approach: After appropriate tests to determine the extent of the lymphomas, patients will receive 4 cycles of multi-agent chemotherapy to include cytoxan, adriamycin, oncovin and prednisone. At the end of 4 cycles of chemotherapy, given 4 wks apart, patients will be restaged to determine the extent of remaining disease. If there is at least a 50% reduction in the observed disease, the patients will proceed to Phase II consisting of radiation therapy. All patients will receive prednisone every other day by mouth and vincristine IV every other week. Those patients with disease involving <50% of the body will receive limited radiation therapy to sites of known lymphoma involvement. Those patients with extensive disease will be randomized to receive either low dose total body radiation or low dose sequential hemibody radiation therapy. At the completion of Phase II, all patients will receive 4 more cycles of CHOP with the intervals lengthened to 8 weeks. At the end of Phase III, if there is no evidence of remaining disease, patients will be taken off therapy and observed.

Progress: One patient was entered in FY 85. Second cycle CHOP post-radiotherapy caused neutropenic fever. Patient recovered and subsequent doses were reduced.

D E T A I L S H E E T S

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GYNECOLOGY ONCOLOGY GROUP PROTOCOLS

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 82/07	Status: On-going
Title: GOG #26C: A Phase II Trial of Cis-Platinum Diamminedichloride		
Start Date: 20 Nov 81	Est Completion Date: Indefinite	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: advanced malignancy, refractory to prior therapy		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

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: A total of three patients has been entered in this protocol. One died from progression of cancer. Two patients are alive but have failed to cis-platinum.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 83/18	Status: On-going
Title: GOG #26D: A Phase II Trial of VP-16 in Patients with Advanced Pelvic Malignancies		
Start Date: 19 Nov 82	Est Completion Date: Indefinite	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: pelvic malignancies, advanced, resistant		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine the efficacy of VP-16 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 VP 16 as a Phase II drug to determine its efficacy. The drug will be given as 100 mg/M² intravenously on days 1, 3, and 5, every four weeks. Patients who respond or demonstrate disease will continue to receive the agent until progression has occurred.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 83/19	Status: On-going
Title: GOG #26E: A Phase II Trial of Glactitol 1,2:5,6-Dianhydro in Patients with Advanced Pelvic Malignancies		
Start Date: 19 Nov 82	Est Completion Date: Indefinite	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: pelvic malignancies, advanced, resistant		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine the efficacy of glactitol 1,2:5,6-dianhydro 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 glactitol 1,2:5,6-dianhydro as a Phase II drug to determine its efficacy. The drug will be given as 60 mg/M² slow I.V. push weekly. If no toxicity has occurred after 4 doses, the dosage will be increased to 75 mg/M² weekly. Patients will continue to receive the agent until progression occurs.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 83/20	Status: On-going
Title: GOG #26G: A Phase II Trial of ICRF-159 in Patients with Advanced Pelvic Malignancies		
Start Date: 19 Nov 82	Est Completion Date: Indefinite	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: pelvic malignancy, advanced, resistant, ICRF-159		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine the efficacy of ICRF-159 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 ICRF-159 as a Phase II drug to determine its efficacy. The drug will be given by mouth as 1.5 gm/M², in three divided doses, one every 6 hours, on day 1, repeated weekly as marrow recovery permits. Patients will continue to receive the agent until progression occurs.

Progress: No patients entered in FY 85. One patient was entered in FY 83, exhibited no response to ICRF, and died from disease in FY 84.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 83/21	Status: On-going
Title: GOG #26I: A Phase II Trial of AMSA in Patients with Advanced Pelvic Malignancies		
Start Date: 19 Nov 82	Est Completion Date: Indefinite	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: pelvic malignancy, advanced, resistant		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine the efficacy of AMSA 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 AMSA as a Phase II drug to determine its efficacy. The drug will be given as 60 mg/M² I.V. once every 28 days. Patients will continue to receive the agent until progression occurs.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 83/22	Status: On-going
Title: GOG #26J: A Phase II Trial of Yoshi 864 in Patients with Advanced Pelvic Malignancies		
Start Date: 19 Nov 82	Est Completion Date: Indefinite	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: pelvic malignancy, advanced, resistant		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine the efficacy of Yoshi 864 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 Yoshi 864 as a Phase II drug to determine its efficacy. The drug will be given as 1.5 mg/kg/d x 5 I.V. every six weeks. Patients will continue to receive the agent until progression occurs.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 83/52 Status: On-going

Title: GOG #26L: A Phase II Trial of Tamoxifen (NSC 180793) in
Patients with Advanced Epithelial Ovarian Carcinoma,
Part II

Start Date: 18 Mar 83 Est Completion Date: Jul 88
Department: OB/GYN Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC
Associate Investigator: COL William Benson, MC
Key Words: epithelial ovarian carcinoma, advanced, resistant
Accumulative MEDCASE Est Accumulative Periodic Review
Cost: -0- OMA Cost: -0- Results: Continue

Study Objective: To determine the efficacy of tamoxifen 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 tamoxifen as a Phase II drug to determine its efficacy. The drug will be given as 20 mg PO b.i.d. until adverse effects prohibit further therapy. A minimum trial will be defined as receiving a minimum of eight weeks of therapy.

Progress: One patient was entered in FY 85 and is alive with disease.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 83/23	Status: On-going
Title: GOG #26M: A Phase II Trial of PALA in Patients with Advanced Pelvic Malignancies		
Start Date: 19 Nov 82	Est Completion Date: Indefinite	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: pelvic malignancies, advanced, PALA		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine the efficacy of PALA 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 PALA as a Phase II drug to determine its efficacy. The drug will be given as 5.0 mg/M² I.V. every three weeks. Patients will continue to receive the agent until progression or adverse effects prohibit further therapy.

Progress: No patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 83/24	Status: On-going
Title: GOG #26N: A Phase II Trial of Dihydroxyanthracenedione (DHAD) in Patients with Advanced Pelvic Malignancies		
Start Date: 19 Nov 82	Est Completion Date: Indefinite	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: pelvic malignancies, advanced, DHAD		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

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.

Progress: One patient was entered in FY 85 and is alive with progression of disease. One patient was entered in FY 83 with progression of disease and death from carcinoma of the cervix.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 82/30	Status: On-going
Title: GOG #26-O: A Phase II Trial of Aziridinybenzoquinone (AZQ) in Patients with Advanced Malignancies		
Start Date: 19 Feb 82	Est Completion Date: Indefinite	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: malignancies, advanced, AZQ		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine the efficacy of AZQ 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 AZQ as a Phase II drug to determine its efficacy. The drug will be given as 30 mg/M² given every three weeks. Patients will continue to receive the agent until progression or adverse effects prohibit further therapy.

Progress: No patient entered in FY 85. One patient entered at MAMC during FY 84 with no response to AZQ; death by cancer of cervix.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 83/25	Status: On-going
Title: GOG #26P: A Phase II Trial of AT-125 in Patients with Advanced Pelvic Malignancies		
Start Date: 19 Nov 82	Est Completion Date: Indefinite	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: pelvic malignancies, advanced, AT-125		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine the efficacy of AT-125 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 AT-125 as a Phase II drug to determine its efficacy. The drug will be given as 12-15 mg/M² I.V. daily for five days every three weeks. Patients will continue to receive the agent until progression or adverse effects prohibit further therapy.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 83/26	Status: On-going
Title: GOG #26Q: A Phase II Trial of Aminothiadiazole in Patients with Advanced Pelvic Malignancies		
Start Date: 19 Nov 82	Est Completion Date: Indefinite	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: pelvic malignancies, advanced, aminothiadiazole		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

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: One patient was entered in FY 85 and died from squamous cell carcinoma of the cervix.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/25 Status: On-going

Title: GOG #26R: A Phase II Trial of Progesterone in the Treatment of Advanced or Recurrent Epithelial Ovarian Cancers that Have Failed Combination Chemotherapy

Start Date: 20 Jan 84 Est Completion Date: Nov 88
Department: OB/GYN Facility: MAMC

Principal Investigator: COL Roger B. Lee, MC

Associate Investigator: COL William Benson, MC

Key Words: epithelial ovarian, advanced, recurrent, progesterone

Accumulative MEDCASE Est Accumulative Periodic Review
Cost: -0- OMA Cost: -0- Results: Continue

Study Objective: To determine the efficacy of progesterone 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 C.T. Provera as a Phase II drug to determine its efficacy. The drug is given at 50 mg (1 tablet) t.i.d until progression of disease.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 84/64	Status: On-going
Title: GOG 26-S: A Phase II Trial of Teniposide in Patients with Advanced Pelvic Malignancies		
Start Date: 15 Jun 84	Est Completion Date: Jun 89	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: pelvic malignancies, advanced, Teniposide		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

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: Two patients were entered at MAMC in FY 85. One is alive with disease and the second died of disease.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 84/65	Status: On-going
Title: GOG 26-T: A Phase II Trial of 4'-Deoxydoxorubicin in Patients with Advanced Pelvic Malignancies		
Start Date: 15 Jun 84	Est Completion Date: Jun 89	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: pelvic malignancies, advanced, 4'-Deoxydoxorubicin		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine the efficacy of 4'-deoxydoxorubicin 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 4'-deoxydoxorubicin as a Phase II drug to determine its efficacy. The drug will be given at a dosage of 30 mg/M² every three 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 85	Protocol No.: 85/87	Status: On-going
Title: GOG 26 U: A Phase II Trial of Ifosfamide (NSC #109724) and the Uroprotector, Mesna (NSC #25232), in Patients With Advanced Pelvic Malignancies		
Start Date: 20 Sep 85	Est Completion Date: Indefinite	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William L. Benson, MC		
Key words: ifosfamide, mesna, advanced pelvic malignancies		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: N/A

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 85 Protocol No.: 85/88 Status: On-going

Title: GOG 26V: A Phase II Trial of N-Methylformamide in Patients with Advanced Pelvic Malignancies

Start Date: 20 Sep 85 Est Completion Date: Indefinite

Department: OB/GYN Facility: MAMC

Principal Investigator: COL Roger B. Lee, MC

Associate Investigator: COL William Benson, MC

Key Words: pelvic malignancies, advanced, N-Methylformamide

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To determine the efficacy of N-Methylformamide 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 N-Methylformamide as a Phase II drug to determine its efficacy. N-Methylformamide will be given at a dosage of 800 mg/M² daily X 5 for five days 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 85	Protocol No.: 81/24	Status: On-going
Title: GOG #34: A Randomized Study of Adriamycin as an Adjuvant After Surgery and Radiation Therapy in Patients with High Risk Endometrial Carcinoma Stage I and Occult Stage II		
Start Date: 6 Jan 81	Est Completion Date: Jan 84	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee MC		
Associate Investigator: COL William Benson, MC		
Key Words: carcinoma, endometrial, adriamycin, adjuvant		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To study differences in morbidity and patient survival as functions of various tumor growth patterns as well as treatment in the high risk Stage I and, optionally, high risk Stage II occult endometrial carcinoma.

Technical Approach: Patients with primary, previously untreated, histologically confirmed invasive carcinoma of the endometrium, Stage I or II occult, all grades, with one or more of the following high risk criteria are eligible: (1) all lesions with equal to or greater than 1/2 myometrial involvement; (2) positive pelvic and/or para-aortic nodes; (3) microscopic evidence of cervical involvement but no gross clinical involvement of the cervix; (4) adnexal metastasis. Surgery will be followed in 2-6 weeks by "tailored" radiation therapy, pelvic and/or para-aortic, depending on node positivity. Prior to the initiation of radiation, therapy patients will be randomized to no further therapy or to adriamycin beginning 2-4 weeks after radiation therapy.

Progress: No new entries in FY 85. A total of eight subjects has been entered. All eight are alive without recurrence.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 81/68 Status: Completed

GOG 37: A Randomized Study of Radiation Therapy Versus Pelvic Node Resection for Patients with Invasive Squamous Cell Carcinoma of the Vulva Having Positive Groin Nodes

Start Date: 20 Mar 81 Est Completion Date: Indefinite

Department: OB/GYN Facility: MAMC

Principal Investigator: COL Roger B. Lee, MC

Associate Investigator: COL William Benson, MC

Key Words: vulva, squamous cell carcinoma, radiation therapy, node resection, positive groin nodes

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: Completed

Study Objective: To determine the benefit and morbidity of adding adjunctive radiation therapy to pelvis and groin for patients found to have positive groin nodes at the time of radical vulvectomy and bilateral groin dissection.

Technical Approach: Eligible patients are those with primary previously untreated histologically confirmed invasive squamous cell carcinoma of the vulva, such that radical vulvectomy suffices to remove all of the local lesion, and whose surgery revealed that there were nodes in the groin on one or both sides containing metastatic carcinoma. Patients will be randomized to receive pelvic node dissection (the dissection will be carried out only on the side containing positive groin nodes or a bilateral if both sides are positive) or to receive bilateral groin and pelvic node irradiation. Major parameters to be studied are survival and time to recurrence. Patients will be followed quarterly for three years and every six months thereafter.

Progress: No entries at MAMC. Group-wide, 112 patients were accrued and 90 patients were evaluable. The radiation therapy arm had superior progression-free interval and survival.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 81/79	Status: On-going
Title: GOG #40: A Clinical-Pathologic Study of Stages I and II Uterine Sarcomas		
Start Date: 15 May 81	Est Completion Date: Indefinite	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key words: sarcoma, uterine, pathologic study		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

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: One patient was entered in FY 85 for a total of six patients. Four patients have died with disease, one is alive with disease, and one is alive with no evidence of disease.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 81/25	Status: On-going
Title: GOG #44: Evaluation of Adjuvant Vincristine, Dactinomycin, and Cyclophosphamide Therapy in Malignant Germ Cell Tumors of the Ovary After Resection of all Gross Tumor, Phase III		
Start Date: 17 Dec 80	Est Completion Date: Jun 83	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: germ cell, ovary, adjuvant, chemotherapy		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To evaluate the effect of combined prophylactic vincristine, dactinomycin, and cyclophosphamide (VAC) chemotherapy in patients with endodermal sinus tumor, embryonal carcinoma, immature teratoma (Grades 2 and 3), choriocarcinoma, and malignant mixed germ cell tumors of the ovary, Stages I and II, after total removal of all gross tumor; to evaluate the role of serum markers, especially alpha-feto-protein and human chorionic gonadotropin (betaHCG), when these are present in predicting response and relapse; to determine the role of restaging laparotomy in determining response, predicting relapse, and planning further therapy.

Technical Approach: Patients with histologically confirmed malignant germ cell tumors of the ovary, Stage I or II, if previously untreated and completely resected, (excluding patients with pure dysgerminoma) will be eligible. Patients with Grade 2 or 3 immature teratoma are eligible. After adequate recovery from required surgery, patients will receive 6 courses of VAC chemotherapy. If progression is noted during chemotherapy, patients will be transferred to the appropriate protocol. Patients with no evidence of disease after 6 courses will then undergo a restaging laparotomy. Those showing evidence of progression will be transferred. If laparotomy reveals no evidence of disease, patients will receive an additional 3 courses of VAC and then be followed on no further therapy.

Progress: No new entries in FY 85. Two patients entered at MAMC during FY 84. Both patients completed the VAC chemotherapy and are alive with no evidence of disease.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 84/46	Status: On-going
Title: GOG 45: Evaluation of Vinblastine, Bleomycin, and Cis-Platinum in Stages III and IV and Recurrent Malignant Germ Cell Tumors of the Ovary		
Start Date: 20 Apr 84	Est Completion Date: Mar 89	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: germ cell, ovary, VBP, VAC		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To evaluate the effect of four cycles of combined vinblastine, bleomycin and cis-platinum (VBP) chemotherapy in the management of patients with endodermal sinus tumor, embryonal carcinoma, immature teratoma (all grades), choriocarcinoma, and malignant mixed germ cell tumors of the ovary with advanced or recurrent disease, incompletely resected; to evaluate the role of serum markers, especially alphafetoprotein and human chorionic gonadotropin when these are present in predicting response and relapse; to determine the role of restaging laparotomy in patients in clinical remission in assessing completeness of response and in planning further therapy; to evaluate and compare the effect of vincristine, dactinomycin, and cyclophosphamide (VAC) in patients found to have persistent disease at the time of restaging laparotomy.

Technical Approach: Patients with advanced or recurrent germ cell tumors of the ovary are eligible for this protocol using VBP. Those patients who respond to chemotherapy will have re-exploratory laparotomy. All patients determined to have a surgically complete response will be followed without any further therapy. Those patients who still have cancer or who progressed under VBP will be treated with VAC.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 81/43	Status: Completed
Title: GOG #48: A Study of Progestin Therapy and a Randomized Comparison of Adriamycin vs Adriamycin Plus Cyclophosphamide in Patients with Advanced Endometrial Carcinoma After Hormonal Failure (Phase III Study)		
Start Date: 20 Feb 81	Est Completion Date: Feb 86	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: carcinoma, endometrial, progestin, chemotherapy		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Completed

Study Objective: To evaluate the response of advanced or recurrent endometrial carcinoma to oral progestins in patients who have received no prior hormonal therapy for cancer; and to compare a combination of adriamycin and cyclophosphamide to adriamycin alone as therapy for advanced or recurrent endometrial carcinoma which no longer responds to or has failed to respond to progestins in patients who have received no prior cytotoxic drugs.

Technical Approach: Patients with documented primary stages III or IV, recurrent or residual endometrial adenocarcinoma, adenocanthoma, or adenosquamous carcinoma, whose potential for cure by radiation therapy or surgery alone or in combination is very poor, are eligible for this study. Patients who have received previous chemotherapy are ineligible. Patients will be randomized.

Regimen 1: adriamycin 60 mg/M² IV q 3 wks x 8 courses. Responders will have follow-up only. Those with progression will be transferred to Protocol #26.

Regimen 2: adriamycin 60 mg/M² IV q 3 wks x 8 courses plus cyclophosphamide 500 mg/M² IV q 3 weeks x 8 courses. Responders will receive follow-up only. Those with progression will be transferred to Protocol #26. Those patients with no prior hormonal therapy will be placed on C.T. Provera for a minimum of 12 weeks. Those with progression of disease at any time after 12 weeks will be randomized as above.

Progress: One patient entered in FY 85 for a total of five subjects. Four patients died from disease and one is alive with disease.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 81/71	Status: On-going
Title: GOG #50: A Study of Adriamycin as Postoperative Therapy for Ovarian Sarcoma, Primary or Recurrent, With no Prior Chemotherapy		
Start Date: 20 Mar 81	Est Completion Date: Indefinite	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: sarcoma, ovarian, adriamycin, postoperative therapy		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To evaluate the efficacy of adriamycin in the treatment of primary ovarian sarcomas, primary or recurrent, through historic controls; and to accumulate additional surgical-pathological data relative to ovarian sarcomas.

Technical Approach: Patients must have histologically confirmed primary Stage I-IV or recurrent ovarian sarcoma. Cases without histologic confirmation of recurrence must be documented by submission of original slides. Optimal reductive surgery is required for cases with advanced disease, whether primary or recurrent. Patients may have measurable disease, nonmeasurable disease, or no residual disease postoperatively. The endometrium must be examined to exclude an endometrial origin of the tumor. Patients with prior chemotherapy are ineligible. All patients will receive chemotherapy as soon as the acute effects of surgery have resolved. After completion of a total cumulative dose of 550 mg/M², patients with clinically complete responses or detectable disease which is thought to be resectable will undergo second look surgery. Those patients with progression will be entered on Protocol #26. At second look those with NED will have no further therapy and follow-up for five years; those with stable disease or progression will be entered on Protocol #26.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 81/105 Status: Completed

Title: GOG #52: A Phase III Randomized Study of Cyclophosphamide Plus Adriamycin Plus Platinol Versus Cyclophosphamide Plus Platinol in Patients with Optimal Stage III Ovarian Adenocarcinoma

Start Date: 21 Aug 81 Est Completion Date: Aug 86

Department: OB/GYN Facility: MAMC

Principal Investigator: COL Roger B. Lee, MC

Associate Investigator: COL William Benson, MC

Key Words: adenocarcinoma, ovarian, chemotherapy

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: Completed

Study Objective: To determine, in optimal Stage III ovarian adenocarcinoma, if the addition of adriamycin to cyclophosphamide plus cis-platinum improves progression-free interval, frequency of negative second-look laparotomy and survival. This protocol replaces GOG #25.

Technical Approach: Eligible patients are those more than six weeks post-operative with proven primary Stage III ovarian adenocarcinoma confined to the abdominal cavity and its peritoneal surfaces with residual tumor masses after surgery no larger than 1 cm in diameter. Patients with prior chemo- or radiotherapy are ineligible. Patients will be randomized to cyclophosphamide plus Plantinol every three weeks for eight courses or to cyclophosphamide and Plantinol plus adriamycin every three weeks for eight courses. After eight courses those with less than clinically complete response will go off study and be followed for survival; those with clinically complete response will have second-look surgery to validate the complete response or to remove residual tumor masses. Patients will then be followed for approximately five years for survival rates.

Progress: No new entries in FY 85. Six patients were studied. Three died from disease, two are alive with disease, and one is alive without disease.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 81/116 Status: On-going

Title: GOG 54: The Treatment of Women with Malignant Tumors of the Ovarian Stroma with Combination Vincristine, Dactinomycin, and Cyclophosphamide--Phase III; and a Phase II Evaluation of Adriamycin in Malignant Tumors of the Ovarian Stroma Refractory to Primary Chemotherapy

Start Date: 18 Sep 81 Est Completion Date: Sep 88

Department: OB/GYN Facility: MAMC

Principal Investigator: COL Roger B. Lee, MC

Associate Investigator: COL William Benson, MC

Key Words: ovarian stroma, malignant tumors, primary, refractory

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: Continue

Study Objective: To evaluate the effectiveness of combined vincristine, dactinomycin, and cyclophosphamide (VAC) in treatment of malignant tumors of the ovarian stroma in patients with residual, recurrent or advanced disease; to confirm completeness of response to VAC treatment with restaging laparotomy; to evaluate response to adriamycin in patients who fail primary treatment with VAC; to evaluate the endometrium histologically to learn more about the relationship between stromal tumors and endometrial cancer.

Technical Approach: Eligible patients must have histologically confirmed malignant tumors of the ovarian stroma (granulosa cell tumor, granulosa theca cell tumor, Sertoli-Leydig cell tumor, androblastoma, gynandroblastoma, unclassified sex cord-stromal tumor, sex cord tumor with annular tubules) not amenable to cure by further surgery or radiation therapy. Patients who have received chemotherapy at any time or those who have received radiotherapy <4 weeks prior to entry are ineligible for study. Patients admitted to this study will have undergone an exploratory laparotomy with removal of as much tumor as is prudent. Chemotherapy will be followed within four weeks and not later than six weeks following surgery. Patients must have recovered from surgery. All patients will receive VAC for a minimum of three cycles or a maximum of ten cycles. Patients who exhibit a complete response or a partial response after ten cycles which makes remaining disease resectable will undergo a restaging laparotomy. If all residual disease is resected at restaging laparotomy, patients will receive adriamycin. If there is no evidence of disease at restaging laparotomy, patients will receive intermittent cyclophosphamide. If progression is observed during cyclophosphamide therapy, patient will be removed from study. Patients who exhibit progression of disease after three cycles of VAC will receive adriamycin. If further progression is observed on adriamycin therapy, the patient will be removed from the study. All patients will be followed for five years or until death.

Progress: No patients entered during FY 85. One patient entered during FY 84; alive without evidence of disease.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 81/44	Status: On-going
Title: GOG #55: Hormonal Contraception and Trophoblastic Sequelae After Hydatidiform Mole, Phase III		
Start Date: 20 Feb 81	Est Completion Date: Jun 83	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: hydatidiform mole, contraception, hormonal		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine whether the administration of estrogen progesterone oral contraceptives following the evacuation of a hydatidiform mole and prior to the HCG titer reaching undetectable levels affects the incidence of trophoblastic sequelae requiring chemotherapy.

Technical Approach: Patients with a histologically verified diagnosis of hydatidiform mole evacuated by suction evacuation of the uterus with uterine conservation are eligible. All patients must have a pelvic ultrasound and arterial blood gases performed within 2 weeks of evacuation. Patients will be randomly assigned to Regimen 1: hormonal contraception - oral contraception to be commenced as soon as the patient has been randomized and will continue for at least 12 weeks; or Regimen 2: mechanical contraception - a. sheath and foam preparation; b. IUD inserted once the uterus has become involuted, again used with foam; c. diaphragm used with contraceptive cream or foam. The principal investigator will choose the method of mechanical contraception and it will be commenced as soon as the patient has been randomized and will continue for at least 12 weeks. At the end of 12 weeks, all patients will be evaluated for development or nondevelopment of trophoblastic sequelae. Further birth control will be at the discretion of the patient and the investigator. All patients will remain on the study for a minimum of six months after primary evacuation of the molar pregnancy.

Progress: Two entries in FY 85 at MAMC for a total of five subjects. Three patients are alive with no evidence of disease. Two patients on oral contraception needed methotrexate chemotherapy.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 82/08	Status: On-going
Title: GOG #56: A Randomized Comparison of Hydroxyurea Versus Misonidazole as an Adjunct to Radiation Therapy in Patients with Stage II _B , III, and IV _A Carcinoma of the Cervix and Negative Para-Aortic Nodes (Phase III)		
Start Date: 20 Nov 81	Est Completion Date: Jul 86	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: cervix, negative para-aortic nodes, chemotherapy		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine whether hydroxyurea or misonidazole is superior as a potentiation of radiation therapy in advanced cervical cancer; and to compare the toxicity of hydroxyurea versus misonidazole when given concurrently with radiotherapy.

Technical Approach: All patients with invasive squamous cell carcinoma of the cervix, Stages II_B through IV_A will undergo preoperative clinical staging. This will include traditional staging as permitted by FIGO rules. Extended clinical staging utilizing lymphangiography, computerized transaxial tomography, and/or sonography is required. Subsequently, patients will undergo a para-aortic lymphadenectomy and peritoneal exploration. Selected patients may be excluded from this procedure if percutaneous needle biopsy provides histologic proof of metastasis to the aortic nodes. All patients with cancer confined to the pelvis are eligible for treatment. They will receive pelvic irradiation and will be randomly assigned to receive concomitant hydroxyurea or misonidazole. Patients with metastasis outside the pelvis are not eligible for treatment.

Progress: Two entries at MAMC during FY 85 for a total of five subjects. One patient died from squamous cell carcinoma of the cervix and four are alive with no evidence of disease.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 82/31	Status: On-going
Title: GOG #57: A Randomized Comparison of Multiple Agent Chemotherapy with Methotrexate, Dactinomycin, and Chlorambucil versus the Modified Bagshawe Protocol in the Treatment of "Poor Prognosis" Metastatic Gestational Trophoblastic Disease (Phase II)		
Start Date: 19 Feb 82	Est Completion Date: Feb 87	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key words: gestational trophoblastic disease, multiple agent chemotherapy, modified Bagshawe protocol		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To evaluate the effectiveness and toxicity of the Modified Bagshawe Protocol (MBP) in patients with "poor prognosis" metastatic gestational trophoblastic disease (MGTD); and to compare the effectiveness and toxicity of the MBP with standard triple agent chemotherapy with methotrexate, dactinomycin, and chlorambucil (MAC).

Technical Approach: Patients who have a histologic diagnosis of gestational trophoblastic disease and an elevated HCT titer, who are considered "poor prognosis" on the basis of the criteria set forth in the protocol, will be randomized to either a drug combination of MAC or to a modified Bagshawe Protocol.

Progress: No entries at MAMC during FY 85. One patient entered (FY 83) with a complete response to the Bagshawe regimen.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 81/117	Status: On-going
Title: GOG #59: A Randomized Comparison of Extended Field Radiation Therapy and Hydroxyurea Followed by Cisplatin or no Further Therapy in Patients with Cervical Squamous Cell Carcinoma Metastatic to High Common Iliac and/or Para-aortic Lymph Nodes--III		
Start Date: 18 Sep 81	Est Completion Date: Jul 86	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigators: COL William Benson, MC COL Donald Kull, MC		
Key Words: cervical squamous cell carcinoma, iliac, para-aortic lymph nodes, chemotherapy, radiation therapy		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine if cis-diamminedichloroplatinum, cis-platin, given in an adjuvant setting will decrease the risk of geographic failure or improve the survival rate or progression-free interval in patients who have squamous carcinoma of the cervix with metastases to high common iliac and/or para-aortic lymph nodes, proven by either histologic or cytologic means; to evaluate the role of scalene fat pad biopsy in this group of patients before initiation of extended field irradiation therapy; to accumulate clinical/ surgical pathologic data on this high risk group of patients to expedite development of further protocols.

Technical Approach: Eligibility: patients with primary, previously untreated, histologically confirmed, invasive squamous cell carcinoma of the uterine cervix, all clinical stages, with metastasis to high common iliac or para-aortic lymph nodes proven by cytologic or histologic means. Patients will undergo preoperative clinical staging utilizing lymphangiography, computerized axial tomography, and/or sonography as well as traditional methods. Subsequently, the patients will undergo a para-aortic lymphadenectomy and peritoneal exploration. Selected patients may be excluded from this procedure if percutaneous needle biopsy provides cytologic proof of metastasis to extrapelvic nodes. All patients with para-aortic metastasis and negative scalene node biopsies are eligible for treatment. They will receive pelvic and para-aortic irradiation and hydroxyurea and will be randomly assigned to receive cisplatin or no further therapy. An adequate trial will be defined as completion of the prescribed radiation therapy, completion of one course of cisplatin and survival of four weeks, or survival of eight weeks after radiation therapy for the no-further-treatment regimen. Patients will be followed quarterly for two years and every six months for three additional years.

Progress: One entry at MAMC (FY 84) on the cis-platin arm with no evidence of disease.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 81/118	Status: On-going
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, Stages III & IV		
Start Date: 18 Sep 81	Est Completion Date: Sep 84	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: adenocarcinoma, ovarian, chemotherapy		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine if the addition of BCG to doxorubicin plus cyclophosphamide plus cisplatin improves remission rate, remission duration, or survival in suboptimal Stages III and IV ovarian adenocarcinoma; to determine the frequency and duration of true complete remission using these regimens as judged at second-look laparotomy.

Technical Approach: Eligibility: Patients with established suboptimal Stage III or Stage IV ovarian epithelial cancer. Patients must have optimal surgery for ovarian cancer, with at least an exploratory laparotomy and appropriate tissue for histologic evaluation. Patients with measurable or nonmeasurable disease will be evaluated. Patients with histologically confirmed serous adenocarcinoma, mucinous adenocarcinoma, clear-cell adenocarcinoma, endometrioid adenocarcinoma, undifferentiated carcinoma, or mixed epithelial carcinoma will be eligible. Patients who have received previous chemotherapy or radiotherapy will be ineligible. Patients will be randomized to receive either doxorubicin, cyclophosphamide, and cisplatin every 3 weeks for 8 courses; or the above regimen plus BCG (Days 3 & 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: One patient was entered in FY 85 for a total of five subjects. Four patients have died from disease and one patient was lost to follow-up.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 82/09 Status: Completed

Title: GOG #61: Phase III Randomized Study of Cis-Platinum Plus Cyclophosphamide versus Hexamethylmelamine After Second-Look Surgery in Nonmeasurable Stage III Ovarian Adenocarcinoma Partially Responsive to Previous Regimens Containing Cis-Platinum and Cyclophosphamide.

Start Date: 20 Nov 81 Est Completion Date: Nov 86

Department: OB/GYN Facility: MAMC

Principal Investigator: COL Roger B. Lee, MC

Associate Investigator: COL William Benson, MC

Key Words: adenocarcinoma, ovarian, chemotherapy

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: Completed

Study Objective: To determine in nonmeasurable but residual Stage III ovarian adenocarcinoma, partially responsive after treatment with regimens containing cis-platinum and cyclophosphamide, if the progression-free interval and survival are improved by continuing cyclophosphamide plus cis-platinum or by changing treatment to hexamethylmelamine.

Technical Approach: With the increasing use of second-look laparotomy after combination chemotherapy for ovarian cancer, more Stage III patients are being identified who show a partial response or stable disease when compared with the original findings. The GOG has two studies involving cyclophosphamide and cis-platinum, but not hexamethylmelamine (Protocols #47 and #52), in which partial responders (as judged at second look) currently go off study. We propose to randomize such patients to more cyclophosphamide plus cis-platinum or to hexamethylmelamine. This additional treatment will be given for a finite period of 12 months since we do not propose a third look that might provide an endpoint for treatment but probably would not benefit most patients as there is no promising third line treatment if residual disease were found and it is unlikely that debulking surgery would be of consistent benefit at this point and it may be difficult to do adequate biopsies after two prior laparotomies. Also, some of these patients may progress slowly even though they do not respond to the additional treatments.

Progress: No new entries in FY 85. Four patients were entered at MAMC. Three patients died from ovarian cancer and one patient is alive without disease.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 82/36	Status: On-going
Title: GOG #63: A Clinical-Pathologic Study of Stages II _B , III, and IV _A Carcinoma of the Cervix		
Start Date: 19 Mar 82	Est Completion Date: Mar 88	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: carcinoma, cervix, stages II _B , III, IV _A , pathologic		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To evaluate the sensitivity and specificity of non-invasive procedures such as sonography, computerized transaxial tomography and lymphangiography in detection of metastases; to better understand the significance of various surgical and pathologic factors involved in staging and therapy for advanced cervical cancer. The accumulated clinical/surgical/pathological data may then play a role in modification or design of future protocols; to determine by observations of five-year survival and disease-free interval, the validity of current FIGO staging in comparison to histopathologic prognostic factors such as size of lesion, location of lesion, histology, grade, pelvic lymph node metastases, and aortic lymph node metastases, in patients with Stages II_B, III, and IV_A carcinoma of the cervix.

Technical Approach: All eligible patients with invasive carcinoma of the cervix, Stages II_B through IV_A, will undergo preoperative clinical staging, including traditional staging as permitted by FIGO rules. Extended clinical staging utilizing sonography, lymphangiography, and computerized transaxial tomography are mandatory. When these tests reveal an aortic nodal metastasis, the patient will have a fine needle biopsy; however, if the tests are negative, the patient will have an aortic lymphadenectomy. Patients who have a positive fine needle biopsy or positive aortic lymphadenectomy will undergo scalene node biopsy before consideration for a GOG treatment protocol. It is anticipated that all patients will be considered for entry into a GOG protocol for which they are suitable when such protocols are available.

Progress: One new entry at MAMC in FY 85 for a total of three subjects. All subjects are alive without disease.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 82/37	Status: Completed
Title: GOG #84: A Randomized Comparison of Rapid vs Prolonged (24-Hour) Infusion of Cisplatin in Therapy of Squamous Cell Carcinoma of the Cervix.		
Start Date: 19 Mar 82	Est Completion Date: Mar 85	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: cervix, squamous cell carcinoma, infusion, rapid, prolonged, cisplatin		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Completed

Study Objective: To determine whether the frequency and duration of objective response of squamous cell carcinoma of the cervix is altered significantly by prolonging to 24 hours the duration of the infusion of a dose of cisplatin as compared to administration at a rate of 1 mg/min; and to determine whether the administration of a dose of cisplatin as a continuous 24-hour infusion alters the frequency and/or severity of drug-related nausea and vomiting as compared to the administration of the same dose at a rate of 1 mg/min.

Technical Approach: Eligible patients are those with histologically confirmed, locally advanced, recurrent, persistent, or metastatic squamous cell carcinoma of the cervix which is resistant to curative treatment with surgery or radiotherapy. Cis-platinum (50 mg/m²) will be given as a 24-hour infusion or at a rate of 1 mg/min IV once every three weeks. Treatment will be repeated every three weeks for eight courses unless disease progression or adverse effects dictate cessation.

Progress: No patients entered during FY 85. One patient was entered in FY 83. There was no response to cis-platinum and the patient died from the cancer.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 83/40	Status: On-going
Title: GOG #66: Ultrastructural, Staging, and Therapeutic Considerations in Small Cell Carcinoma of the Cervix, Phase II		
Start Date: 18 Feb 83	Est Completion Date: Jun 86	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: cervix, small cell carcinoma, ultrastructural, staging, therapeutic		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine the incidence of neuroendocrine carcinoma of the cervix in cases which are histologically classified as small cell carcinomas, and to determine the response rate to combination chemotherapy in patients with Stage IV_B small cell carcinoma of the cervix or progressive local disease after radiation therapy.

Technical Approach: Eligible patients: Those with histologic diagnosis of small cell carcinoma of the cervix. Patients who have small cell carcinoma mixed with large cell keratinizing carcinoma or large cell nonkeratinizing carcinoma or adenocarcinoma are eligible, providing that the small cell elements comprise 50% of the tumor. Only patients with primary Stage IV_B disease or recurrent disease after local therapy are eligible for chemotherapy. Chemotherapy patients must have measurable disease by palpation or by an appropriate x-ray or ultrasound procedure. Patients with disease localized to the pelvis and regional lymph nodes will receive standard therapy according to the discretion of the investigator. Patients with disease beyond the pelvis or abdominal nodes with no previous irradiation will receive vincristine, 2 mg, doxorubicin, 50 mg/M², and cyclophosphamide, 750 mg/M², IV every 21 days. Patients with previous irradiation will receive vincristine, 2 mg, doxorubicin, 40 mg/M², and cyclophosphamide, 600 mg/M², IV, every 21 days. These regimens will be repeated every three weeks if toxicity permits. Doxorubicin will be discontinued at a cumulative dose of 400 mg/M². Patients in whom tumor progression occurs on this regimen will be treated with VP-16, 100 mg/M² (no previous irradiation) or 80 mg/M² (previous irradiation) IV on days 1, 3, and 5, every four weeks to time of progression. Patients will be followed until expiration or for five years. In the unusual instance of Stage IV_B on the basis of brain metastasis alone, patients will be given whole brain irradiation to a dose of 3000 rads in 10 fractions.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 83/63	Status: On-going
Title: GOG #70: A Randomized Comparison of Single Agent Chemotherapy (Methotrexate and Methotrexate with Folinic Acid Rescue) in "Good Prognosis" Metastatic Gestational Trophoblastic Disease		
Start Date: 20 May 83	Est Completion Date: Indefinite	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: trophoblastic, gestational, single agent chemotherapy		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To judge the relative efficacy of scheduling variation in the chemotherapeutic management of good prognosis metastatic gestational trophoblastic disease and to ascertain the relative toxicities of the two regimens.

Technical Approach: Eligible patients: those with metastatic gestational trophoblastic disease who are good prognosis with duration of disease <4 months from antecedent pregnancy, antecedent molar pregnancy, ectopic pregnancy, or abortion, serum beta-hcg titer <42,000 mIU/ml, no liver or brain metastasis, and no prior chemotherapy.

Regimen I: methotrexate 0.4 mg/kg IM, up to 25 mg daily x 5; repeat every 12 days (7 day window).

Regimen II: methotrexate, 1 mg/kg IM, days 1, 3, 5, and 7. Folinic acid, 0.1 mg/kg, IM, days 2, 4, 6, and 8. Repeat every 14 days (6 day window).

An adequate trial is defined as receiving one course. After the first normal titer (three consecutive weekly normals), each patient will receive one more full course. If she attains remission, therapy will be discontinued. If the titer should re-elevate prior to three consecutive weekly normals, then chemotherapy will continue until the above criteria are fulfilled. All patients will receive chemotherapy as outlined until there is documented remission, severity of toxicity requires a change, or non-response.

Progress: One patient was entered in FY 85 and one patient was entered in FY 83. The former is responding to methotrexate and the latter is free of disease.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 83/41 Status: On-going

Title: GOG #71: Treatment of Patients with Suboptimal Stage IB Carcinoma of the Cervix: A Randomized Comparison of Radiation Therapy and Post-Treatment Para-Aortic and Common Iliac Lymphadenectomy, Versus Radiation Therapy, Para-Aortic and Common Iliac Lymphadenectomy and Adjunctive Extrafascial Hysterectomy, Phase III

Start Date: 18 Feb 83 Est Completion Date: Jun 86

Department: OB/GYN Facility: MAMC

Principal Investigator: COL Roger B. Lee, MC

Associate Investigator: COL William Benson, MC

Key Words: cervix, carcinoma, radiation, lymphadenectomy, hysterectomy

Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To evaluate the role of adjunctive extrafascial hysterectomy in the treatment of suboptimal Stage IB carcinoma of the cervix, the survival and patterns of failure in bulky IB cervix cancer, and the prognostic value of pretreatment endometrial sampling in suboptimal Stage IB carcinoma of the cervix; and to study the toxicity of a combined radiation and surgical therapeutic program.

Technical Approach: Eligible patients: patients with primary, untreated, histologically confirmed invasive carcinoma of the uterine cervix, FIGO Stage IB, as confirmed by cervical biopsy and endometrial sampling.

Regimen I: Following recovery from radiation therapy, patients will undergo para-aortic and common iliac nodal sampling, abdominal washings, and intra-abdominal exploration.

Regimen II: Following recovery from radiation therapy, patients will undergo para-aortic and common iliac nodal sampling, abdominal washings, and intra-abdominal exploration plus total extrafascial hysterectomy.

All patients will be followed for five years. Patients found to have more extensive disease (i.e., positive para-aortic nodes, intra-abdominal metastasis) will be treated at the discretion of the physician and will be followed for five years.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 84/33	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: 17 Feb 84	Est Completion Date: Dec 88	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: tumor, ovarian, natural history, melphalan, cisplatin		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To evaluate the biologic behavior of ovarian tumors of low malignant potential; to evaluate the effectiveness of chemotherapy against this disease (initially, a Phase II study of melphalan); and to evaluate the response rate to cisplatin in melphalan failures.

Technical Approach: Patients without prior chemotherapy or radiotherapy who have had adequate surgical staging will be eligible. Patients with no grossly visible residual disease will receive no treatment and be followed for 5 years if there is no subsequent disease. If there is no grossly visible clinically apparent residual for 12 months, the patients will have second look surgery and then proceed to melphalan treatment (5 days every four weeks) or follow-up (complete response). With progression after melphalan, patients will proceed to third look and cis-platin treatment (once every three weeks for eight weeks) or follow-up. If there is no evidence or response after three courses of cis-platin, 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: One patient entered in FY 84; free of disease.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/26 Status: On-going

Title: GOG #73: A Clinicopathologic Study of Primary Malignant Melanoma of the Vulva Treated by Modified Radical Hemivulvectomy

Start Date: 20 Jan 84 Est Completion Date: Nov 88

Department: OB/GYN Facility: MAMC

Principal Investigator: COL Roger B. Lee, MC

Associate Investigator: COL William Benson, MC

Key Words: melanoma, vulva, hemivulvectomy, clinicopathologic

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: Continue

Study Objective: To determine the relationship of histopathologic parameters (including microstaging of primary malignant melanoma of the vulva) to FIGO staging, nodal status, and ultimate prognosis and to ultimately recommend appropriate therapy for malignant melanomas of the vulva based on histopathologic and microstaging data.

Technical Approach: Patients receiving primary surgical therapy for primary malignant melanoma of the vulva with at least a modified radical hemivulvectomy will be studied. Patients with a history of primary cutaneous melanoma other than of genital tract origin or patients who have received previous chemotherapy or radiotherapy are ineligible. The primary parameters to be studied are maximum diameter of primary lesion, depth of invasion, initial surgical management (including lymph node dissection), nodal status, FIGO staging, microstaging, progression-free interval, and survival probability. Collected data will be used in an attempt to identify possible prognostic factors. Specific statistical goals will be defined as experience is gained.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 84/27	Status: On-going
Title: GOG #74: Early Stage I Vulvar Carcinoma Treated With Ipsilateral Superficial Inguinal Lymphadenectomy and Modified Radical Hemivulvectomy		
Start Date: 20 Jan 84	Est Completion Date: Nov 88	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: carcinoma, vulvar, lymphadenectomy, hemivulvectomy		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To document the rates and patterns of recurrence of patients with early Stage I vulvar carcinoma treated with ipsilateral superficial inguinal lymphadenectomy and modified radical hemivulvectomy and to document the survival and recurrence-free interval in the same group of patients.

Technical Approach: Patients who present with primary, untreated, squamous cell carcinoma of the vulva, with no capillary space involvement, and with a lesion measured *in vivo* ≤ 2 cm, and with histologic evidence of invasion below the basement membrane ≤ 5 mm, will be eligible for further evaluation and entry into this protocol. If the frozen section on the superficial inguinal lymph nodes reveals no evidence of cancer, the patient will go on to have a modified radical hemivulvectomy. If the patient has positive lymph nodes on frozen section, she can be treated with radical vulvectomy and bilateral groin dissection per GOG Protocols 36 and 37. If the final pathology section shows metastatic carcinoma to nodes, the patient can be treated with radical vulvectomy and bilateral groin dissection, per protocols 36 and 37, the surgery to be carried out within six weeks of the time of the initial groin dissection. The patient will be followed every three months for two years and every six months for three additional years. The principal parameters employed to examine the therapeutic effect of hemivulvectomy will be progression-free interval, survival time, and observed adverse effects.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 84/28	Status: On-going
Title: GOG #75: Postoperative Pelvic Radiation in Stages I and II Mixed Mesodermal Sarcomas of the Uterus		
Start Date: 20 Jan 84	Est Completion Date: Nov 88	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: sarcomas, uterus, radiation, postoperative		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine if pelvic postoperative radiation therapy will decrease local and regional recurrence rates and improve median progression free interval in patients with Stages I and II mixed mesodermal sarcomas of the uterus.

Technical Approach: Patients with clinical Stage I or II mixed mesodermal sarcomas of the uterus undergoing a simple extrafascial abdominal hysterectomy, bilateral salpingo-oophorectomy, or selective pelvic or para-aortic lymphadenectomy will be randomized to receive postoperative radiation therapy or no further treatment. The principal parameters employed to examine the therapeutic effect of postoperative pelvic radiation are local and regional recurrence rates, the duration of progression-free interval, observed survival time and the incidence and severity of observed adverse effects. The patients will be followed until death or for at least ten years.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/74 Status: On-going

Title: GOG 78: Evaluation of Adjuvant Vinblastine, Bleomycin, and Cisplatin Therapy in Totally Resected Choriocarcinoma, Endodermal Sinus Tumor, or Embryonal Carcinoma of the Ovary, Pure and Mixed with Other Elements

Start Date: 17 Aug 84 Est Completion Date: Jul 89

Department: OB/GYN Facility: MAMC

Principal Investigator: COL Roger B. Lee, MC

Associate Investigator: COL William Benson, MC

Key Words: ovary, embryonal carcinoma, choriocarcinoma, endodermal sinus tumor, vinblastine, bleomycin, cisplatin

Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

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 alphafetoprotein 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.

Technical Approach: Patients with totally resected Stage I choriocarcinoma, endodermal sinus tumor, or embryonal carcinoma of the ovary with negative peritoneal washings, normal (or falling at a rate that does not suggest residual disease) serum AFP and beta-HCG levels, and adequate bone marrow, renal, and hepatic function will be studied. Stages II and III will also be eligible if all gross tumor is resected. After recovery from surgery, patients will receive 3 cycles of VBP therapy. Patients who show evidence of progression while on VBP therapy will be candidates for GOG Protocol 26. Patients completing three cycles of treatment clinically free of disease will undergo reassessment laparotomy. Patients with recurrent disease at reassessment laparotomy will be candidates for GOG Protocol 26. To be evaluable a patient will receive at least one week of chemotherapy and live another two weeks. Each patient will remain on study until adverse effects prohibit further therapy or until evidence of progression is noted.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 85/89	Status: On-going
Title: GOG 79: Single Agent Weekly Methotrexate (NSC #740) Therapy in the Treatment of Nonmetastatic Gestational Trophoblastic Disease		
Start Date: 20 Sep 85	Est Completion Date:	Indefinite
Department: OB/GYN		Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William L. Benson, MC		
Key Words: trophoblastic, gestational, methotrexate, weekly		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: N/A

Study Objective: To determine the efficacy of weekly methotrexate therapy for nonmetastatic gestational trophoblastic disease; to ascertain the toxicity of this regimen; and to demonstrate the cost effectiveness of this regimen.

Technical Approach: Patients with nonmetastatic gestational trophoblastic disease with antecedent molar pregnancy or postabortal status and no prior chemotherapy who meet the criteria listed in the protocol will receive initial treatment with methotrexate, 30 mg/M², IM, based on ideal or actual weight, once a week. All patients will receive chemotherapy until remission, severity of toxicity requires a change in therapy, or nonresponse. Nonresponders will go off study and be treated with Dactinomycin. Dosage will be modified according to toxicity encountered. An adequate trial is defined as three one week courses

Progress: New protocol - no entries.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 85/90	Status: On-going
Title: GOG 83: A Clinico-Pathologic Study of Simultaneous Endometrial and Ovarian Carcinomas		
Start Date: 20 Sep 85	Est Completion Date: Indefinite	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William L. Benson, MC		
Key Words: carcinoma, ovarian, endometrial, simultaneous		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: N/A

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: New protocol - no entries.

D E T A I L S H E E T S
F O R
P R O T O C O L S

NATIONAL CANCER INSTITUTE PROTOCOLS

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 81/19	Status: Completed
Title: NCI #I78-10: Guidelines for the Clinical Use of Hexamethylmelamine (Group C Guidelines)		
Start Date: 17 Dec 80	Est Completion Date: Nov 82	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: COL Friedrich H. Stutz, MC		
Associate Investigators: COL Roger B. Lee, MC LTC Archie W. Brown, MC LTC Irwin B. Dabe, MC		
Key Words: hexamethylmelamine, clinical use, guidelines		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Completed

Study Objective: To provide an investigational drug of proven efficacy, not previously released for general use, to MAMC patients under Group C NCI Guidelines. Also to determine the extent and variety of side effects with hexamethylmelamine that have not been previously described.

Technical Approach: Hexamethylmelamine will be used in patients whose cancer of the ovary has become refractory to therapy with alkylating agents or in patients where therapy with alkylating agents is contraindicated. Hexamethylmelamine will be given daily by mouth, either continuously or intermittently depending on response, toxicity, and other drugs which the patient may be taking concomitantly. The treatment will continue for as long as the disease is stable or the tumor shrinks.

Progress: No new patients were entered on this protocol in FY 85. Eight entries in previous years. Nausea and neutropenia were reported as adverse reactions.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 81/102	Status: On-going
Title: NCI #180-12: Group C Guidelines for the Use of Delta-9-Tetrahydrocannabinol		
Start Date: 24 Jul 81	Est Completion Date: Jul 83	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: COL Friedrich H. Stutz, MC		
Associate Investigators: LTC Irwin B. Dabe, MC LTC Alan D. Mease, MC MAJ Lauren K. Colman, MC		
Key Words: delta-9-tetrahydrocannabinol, guidelines		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine untoward side effects not previously described with THC and to make available this antinausea drug to patients on chemotherapy.

Technical Approach: Delta-9-THC will be used as an antiemetic therapy in cancer chemotherapy patients refractory to standard antiemetic agents. A starting dose of 5 mg/m² p.o., will be administered 6-8 hours prior to the administration of chemotherapy and for 12 hours thereafter. Should the 5 mg/m² dose prove to be ineffective, and in the absence of significant side effects, the dose may be escalated to 7.5 mg/m². Any untoward side effects will be reported to the NCI.

Progress: Two new patients were entered in FY 85. Of the total of 13 entries, drowsiness was the only reported side effect.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 81/45	Status: Completed
Title: NCI #7601 - Selected Stage I _{Ai} - I _{Bi} Ovarian Cancer (Well and Moderately Differentiated)		
Start Date: 20 Feb 81	Est Completion Date: Jun 85	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: cancer, ovarian, selected stage I _A - I _B		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Completed

Study Objective: To define the natural history of patients treated by surgery; to determine whether prophylactic, adjuvant chemotherapy with melphalan alters the natural history; to study the effect of various potential prognostic factors on the natural history of patients treated by each form of therapy; to establish the value of various staging parameters on the stage of disease and its natural history.

Technical Approach: To be eligible, patients must have a histopathologic diagnosis of common epithelial ovarian cancer, either serous, mucinous, or other (endometrioid, transitional, mesonephroid, adenocanthoma, mixtures and intermediate types, and unclassifiable). Patients will be stratified by histology, histologic grade, and stage. After staging laparotomy and total abdominal hysterectomy or bilateral salpingo-oophorectomy, patients will be randomized to observation with no chemotherapy or to a chemotherapy regimen of melphalen (0.2 mg/kg/day PO for 5 days). The chemotherapy will be repeated every four weeks for 18 months or after 12 cycles of therapy, whichever comes first. Chemotherapy will be discontinued for unacceptable toxicity or at 18 months if the patient is free of disease at that time. If patient relapses, she will be taken off study at that time. Second-look will occur at 18 months after randomization using peritoneoscopy or laparotomy.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 81/33	Status: On-going
Title: NCI #7602: All Stage IC and II (A, B, C) and Selected Stage IAii and IBii Ovarian Cancer		
Start Date: 16 Jan 81	Est Completion Date: Jun 85	
Department: OB/GYN	Facility: MAMC	
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: cancer, ovarian, natural history		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To define the natural history of patients treated surgery plus either chemotherapy or radioisotope; to study the effect of various potential prognostic factors on the natural history of patients treated by each form of therapy; to determine the patterns of relapse for each form of therapy; to establish the value of various staging parameters on the stage of disease and its natural history.

Technical Approach: All patients with common epithelial ovarian cancer are eligible, if after definitive staging procedures the patient is zoned to be in Stages 2A, 2B, 2C, IAii, IBii, or IAI or IBI with poorly differentiated tumors. Patients with prior therapy are ineligible. Patients will be stratified by histology, histological grade, and stage group for Regimen I. Regimen I will have staging laparotomy, total abdominal hysterectomy and bilateral salpingo-oophorectomy with no macroscopic residual disease found. Patients will then be randomized to receive melphalan or radioisotopes. Regimen II will be stratified by histology, histological grade, and extent of disease after surgery. Patients will have staging laparotomy, total abdominal hysterectomy, and bilateral salpingo-oophorectomy. If IIB, IIC, residual disease is found, will be randomized to pelvic radiotherapy plus melphalan alone. If after 18 months of therapy, the patient remains free of disease, chemotherapy will be discontinued. Second look will be done if the patient is free of disease after 18 months of chemotherapy.

Progress: One patient was entered during FY 85 and one during FY 84. Both patients are alive without disease.

D E T A I L S H E E T S

F O R

P R O T O C O L S

SOUTHWEST ONCOLOGY GROUP PROTOCOLS

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 78/42	Status: On-going
Title: SWOG 7804: Adjuvant Chemotherapy with 5-Fluorouracil, Adriamycin, and Mitomycin-C (FAM) vs Surgery Alone for Patients with Locally Advanced Gastric Adenocarcinoma		
Start Date: 16 Jun 78	Est Completion Date: Jun 80	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: COL Friedrich H. Stutz, MC		
Associate Investigators: LTC H. Irving Pierce, MC Suresh B. Katakhar, M.D., DAC		
Key Words: adenocarcinoma, gastric, adjuvant FAM vs surgery		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine the efficacy of adjuvant chemotherapy with FAM on the disease-free interval and survival of patients with TNM stage-groups I_B, I_C, II and III gastric adenocarcinoma compared to potentially curative surgery alone.

Technical Approach: Patient Eligibility: patients must have TNM stage-group I_B, I_C, II, or III gastric adenocarcinoma and no microscopic or gross residual postoperatively; no prior chemotherapy or radiotherapy; no medical contraindications to chemotherapy with FAM; serum bilirubin <2.0 mg/100 ml; SGOT and SGPT <3 times the upper limit of normal values; creatinine clearance >75 cc/min; BUN <25 mg%; serum creatinine <1.5 mg%; WBC >4,000; platelets >100,000.

Treatment: After surgery, patients will be randomized to either:

Treatment 1 (no further therapy) or

Treatment 2: FAM - 5-FU, 600 mg/M² IV days 1 & 8, 29 & 36
adriamycin, 30 mg/M² IV days 1 & 29
mitomycin-C, 10 mg/M² IV day 1

A total of 6 courses, one every 8 weeks, will be administered. After 12 months, the active therapy phase is completed. The patient will be followed at six month intervals for five years if remission continues.

Progress: No entries in FY 85. One entry in FY 84 at MAMC on the observation arm. No recurrence from August 84 to October 85.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 78/47	Status: On-going
Title: SWOG 7808, Combination Modality Treatment for Stages III and IV Hodgkin's Disease, MOPP #6		
Start Date: 11 Aug 78	Est Completion Date: Jul 80	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: COL Friedrich H. Stutz, MC		
Associate Investigators: LTC H. Irving Pierce, MC LTC James E. Congdon, MC Suresh B. Katakhar, M.D., DAC		
Key Words: Hodgkin's disease, stages III and IV, MOPP #6		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

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.

Treatment 1: Normal marrow patients will receive six cycles of MOP-BAP.

Treatment 2: 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 ten total cycles of MOP-BAP, patient will continue study on MOPBAP therapy at the discretion of the investigator.

Progress: No patients entered at MAMC in FY 85. Six patients were entered in previous years.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 79/96 Status: Ongoing

Title: SWOG 7827: Combined Modality Therapy for Breast Carcinoma, Phase III

Start Date: 21 Sep 79 Est Completion Date: Sep 81

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: COL Friedrich H. Stutz, MC

Associate Investigators: LTC James E. Congdon, MC

LTC Irwin B. Dabe, MD

Key Words: carcinoma, breast, combined modality therapy

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: Continue

Study Objective: To compare the disease-free interval and recurrence rates in: (1) estrogen receptor positive (ER+) premenopausal patients with Stage II disease using combination chemotherapy alone vs combination chemotherapy and oophorectomy; (2) ER+ postmenopausal patients with Stage II disease using combination chemotherapy plus tamoxifen vs tamoxifen alone vs combination chemotherapy alone; (3) estrogen receptor negative (ER-) patients with Stage II disease using one vs two years of combination chemotherapy; to compare the effect of adjuvant therapy in Stage II breast cancer using partial mastectomy and radiation vs modified radical or radical mastectomy; to compare the effect of the various adjunctive therapy programs upon survival patterns; and to correlate the estrogen receptor status with disease-free interval and survival.

Technical Approach: Patients with a histologically proven diagnosis of breast cancer (Stage II or Stage III) with one or more pathologically involved axillary nodes will receive one of the following treatments: (CMFVP = cyclophosphamide, methotrexate, 5-FU, vincristine, and prednisone):

- (1) CMFVP for 1 yr - pre or postmenopausal ER- patients.
- (2) CMFVP for 2 yr - pre or postmenopausal ER- patients.
- (3) CMFVP for 1 yr - premenopausal ER+ patients.
- (4) Oophorectomy + CMFVP - premenopausal ER+ patients.
- (5) Tamoxifen alone for 1 yr - postmenopausal ER+ patients.
- (6) CMFVP for 1 yr - postmenopausal ER+ patients.
- (7) Tamoxifen + CMFVP for 1 yr - postmenopausal ER+ patients.

Patients undergoing segmental mastectomy (lumpectomy) will receive 6 wks of radiation therapy in addition to the treatment they are randomized to receive.

Progress: One new patient was entered at MAMC in FY 85 for a total of 25 entries.

Group-wide the ER- arm has been closed to entry, but data analysis will not begin until patients complete treatment. The ER+ premenopausal arm continues to accrue patients very slowly and the ER+ postmenopausal arm continues to accrue rapidly with approximately 3 1/2 years needed to reach the required 350 patients/arm.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 81/80	Status: On-going
Title: SWOG 7984: The Treatment of Chronic Stage CML with Pulse, Intermittent Busulfan Therapy With or Without Oral Vitamin-A, Phase III		
Start Date: 15 May 81	Est Completion Date: Mar 83	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: LTC Irwin B. Dabe, MD		
Associate Investigators: COL Friedrich H. Stutz, MC MAJ Lauren K. Colman, MC		
Key Words: CML, intermittent busulfan, with or without Vitaman A		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine the efficacy of standard pulse, intermittent busulfan therapy plus oral vitamin A in prolonging the chronic phase of CML, and hence in prolonging survival.

Technical Approach: Patients with a diagnosis of chronic stage CML for one year or less with no prior therapy are eligible, except patients who had prior hydroxyurea and/or leukopheresis for <7 days will not be excluded. Patients will be stratified into those who had a splenectomy and those who did not. Randomization will be to busulfan alone or busulfan plus oral vitamin A. Stratification is also by age, <20 or >20 years. Treatment will continue for as long as the patient responds to the treatment and does not have unacceptable toxicity.

Progress: No entries at MAMC. Group-wide the accrual rate is presently slightly over three patients per month. If this rate is sustained, the accrual goal of 75 evaluable patients/arm will be met after September 1986.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 80/33	Status: Completed
Title: SWOG 7990: Intergroup Testicular Study		
Start Date: 22 Feb 80	Est Completion Date: Nov 81	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: COL Friedrich H. Stutz, MC		
Associate Investigators: LTC Irwin B. Dabe, MC		
Suresh B. Katakhar, M.D., DAC		
Key Words: testicular, surgery, surgery plus chemotherapy		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Completed

Study Objective: To compare the disease-free survival and overall survival for surgery alone (with chemotherapy for relapsers) vs surgery plus early adjuvant chemotherapy in patients with resectable Stage II testicular cancer; to register and follow patients with nonseminoma, nonchoriocarcinoma Stage I testicular cancer to define prognostic variables which may predict recurrence in this stage group; to define the difference in disease-free rates and patterns of recurrence, based upon histologic subtypes and extent of disease on initial presentation; to evaluate the role of marker substances such as HCG, alpha-fetoprotein, and lactic dehydrogenase in the early detection and management of recurrence in patients with Stage I and Stage II testicular carcinoma; to evaluate the accuracy of lymphangiograms, CAT scans, and ultrasound studies for staging of retroperitoneal nodal involvement.

Technical Approach: Patients with histologically confirmed carcinoma (not pure seminoma or choriocarcinoma) of the testis Stage I or Stage II who have had an orchiectomy will be eligible. Patients will undergo bipedal lymphangiogram with the intent of retroperitoneal node dissection. Serum markers may be obtained prior to orchiectomy and must be obtained prior to lymphadenectomy and 1-2 weeks after. If at two weeks any marker is positive but falling, markers will be repeated at 3-4 weeks and the 4-week value must be normal or serial determinations must be declining with time at a rate predicted by the known serum halflife of the marker. Entry will be at 2-4 weeks postoperatively. Stage I patients will be followed routinely and tumor markers should be negative 4 weeks postop. Stage II unresectable patients are not eligible. Stage II resectable patients will be treated in two treatment groups. Group I: no adjuvant chemotherapy with monthly follow-up until recurrence. Group II: adjuvant chemotherapy with vinblastine, bleomycin, and cis-platinum. Stages I and II who were originally randomized to the follow-up group and Stage II relapsing after chemotherapy will be further treated with vinblastine, bleomycin, and cis-platinum. Patients in complete or partial remission or showing improvement after relapse induction will receive maintenance treatment with vinblastine, repeated every 4 weeks until complete remissions have received 104 weeks of therapy and partial remissions and improvements may continue indefinitely. All other patients will go off study.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 82/13	Status: On-going
Title: SWOG 8049: Treatment of Resected, Poor Prognosis Malignant Melanoma: Stage I: Surgical Excision vs Surgical Excision + Vitamin A		
Start Date: 20 Nov 81	Est Completion Date: Oct 83	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: LTC Howard Davidson, MC		
Associate Investigators:		
COL Friedrich Stutz, MC	MAJ Thomas M. Baker, MC	
LTC James E. Congdon, MC	MAJ Alfred H. Chan, MC	
LTC Irwin B. Dabe, MD	MAJ Lauren K. Colman, MC	
Key Words: melanoma, surgical excision, vitamin A		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine the efficacy of surgical excision or surgical excision plus vitamin A in preventing the recurrence of high risk, Stage I malignant melanoma by determination of remission or disease-free interval; to determine the immunocompetence of patients with malignant melanoma and to determine the influence of vitamin A upon that immunocompetence.

Technical Approach: Patients will be equally randomized between the two treatment arms: vitamin A versus no further treatment. Patients will be stratified by depth of invasion, sex, and type of surgery. Those patients randomized to receive vitamin A will receive a dose of 100,000 I.U. daily. Treatment will continue for 18 months. Patients who receive no treatment will be followed until relapse and removal from the study.

Progress: One entry at MAMC in 1982 who was taken off study due to light-headedness and a metallic taste in the mouth. Headache and fatigue have been the most common toxicities of vitamin A, although the only severe toxicities noted have been nausea in two patients. Approximately 18 more months will be needed to accrue a sufficient number of patients if the present accrual rate continues.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 83/05	Status: On-going
Title: SWOG 8107: Management of Disseminated Melanoma, Master Protocol, Phase II-III.		
Start Date: 15 Oct 82	Est Completion Date: Sep 84	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: LTC Howard Davidson, MC		
Associate Investigators:		
COL Friedrich H. Stutz, MC	MAJ Thomas M. Baker, MC	
LTC James E. Congdon, MC	MAJ Alfred H. Chan, MC	
LTC Irwin B. Dabe, MD	MAJ Timothy J. O'Rourke, MC	
Key Words: melanoma, disseminated, combination chemotherapy		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine the effectiveness of cranial irradiation given electively in disseminated melanoma patients with lung and/or liver metastasis to prevent or delay the clinical appearance of brain metastasis and to determine the efficacy of high intermittent doses of cis-platinum with the use of IV hydration and mannitol diuresis in patients with advanced malignant melanoma refractory to higher priority protocols.

Technical Approach: This protocol employs some of the newer kinetic concepts of chemotherapy and radiation therapy. All patients with advanced disease are eligible. Patients with brain or lymph and/or node metastases only will go directly to chemotherapy randomization. Patients with lung and/or liver metastases only can go directly to chemotherapy radiation at their request and/or the doctor's discretion. Other patients with lung and/or liver metastases only will be randomized to receive 3000 rads of prophylactic whole brain radiation therapy versus close observation for the development of brain metastasis. Second randomization will be to one of the three chemotherapy arms:

- ARM 1 - DTIC and Actinomycin D.
- ARM 2 - Cis-platinum, Velban and Bleomycin
- ARM 3 - Cis-platinum

All chemotherapy agents will be given intravenously once every three weeks. Should there be objective evidence of disease progression during the course of the study, the patient will be crossed over to a treatment arm composed of drugs not used in the first treatment arm.

Progress: No new patients in FY 85. Two patients were entered in FY 84. Both died of disease with no untoward reactions to the treatment. Groupwide toxicity has been more severe on the DDP, velban, bleomycin arm with approximately 60% of patients experiencing severe or worse toxicity as compared to 40% on the DTIC + ACT-D arm. Approximately one and a half more years will be needed to accrue the required number of patients.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 82/51	Status: Completed
Title: SWOG 8119: Evaluation of Bisantrene Hydrochloride in Hepatoma, Phase II		
Start Date: 21 May 82	Est Completion Date: May 84	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: LTC Howard Davidson, MC		
Associate Investigators:		
COL Friedrich H. Stutz, MC	MAJ Thomas M. Baker, MC	
LTC James E. Congdon, MC	MAJ Alfred H. Chan, MC	
LTC Irwin B. Dabe, MD	MAJ Lauren K. Colman, MC	
Key Words: hepatoma, bisantrene hydrochloride		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Completed

Study Objective: To determine the response rate and response duration of hepatomas treated with bisantrene hydrochloride used in a single dose, every-three-week schedule; to define the qualitative and quantitative toxicities of bisantrene administered in a Phase II study.

Technical Approach: This is a Phase II clinical trial evaluating a new chemotherapy agent, bisantrene hydrochloride, in the treatment of malignant primary carcinoma of the liver. The patients will have failed on prior standard treatments including surgery, radiation therapy, and chemotherapy. This drug has demonstrated some effectiveness in controlling primary liver cancer in a variety of laboratory animals. The drug has been tested in Phase I clinical trials in human beings and its toxicities, including temporary nausea, emesis, alopecia, transient mild hypotension, transient mild myelosuppression, and localized pain at the injection site, have been recognized. All patients entered into the study will have met a number of performance and laboratory eligibility criteria as outlined in the protocol. Bisantrene hydrochloride will be administered through the side tubing of a freely flowing IV line in an amount determined by the patient's body surface area. Unless unusual toxicities are encountered, the treatments will be repeated at three week intervals, for a minimum of two cycles or until objective evidence of disease progression is ascertained.

Progress: No patients registered on the protocol at MAMC.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/29 Status: Completed

Title: SWOG 8122: Combined Modality Treatment of Extensive Small Cell Lung Cancer, Phase III.

Start Date: 18 Jan 85 Estimated Completion Date: Nov 86

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Thomas M. Baker, MC

Associate Investigators:

COL F.H. Stutz, MC MAJ Timothy O'Rourke, MC

LTC Irwin B. Dabe, MC CPT David Bryson, MC

MAJ Howard Davidson, MC CPT Michael Stone, MC

Key Words: lung cancer, small cell, adriamycin, BCNU, cis-platinum, cyclophosphamide, thiotepa, vincristine, BP-16

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To compare the response rate and duration of a new induction program (multiple alkylating agents + vincristine), with emphasis on complete response, to the combination of vincristine, adriamycin, and cyclophosphamide in the treatment of extensive small cell lung cancer; to examine the effect of radiation consolidation on relapse in the chest and liver in patients without widespread skeletal disease; to assess qualitative and quantitative toxicity of this combined modality approach and to perform a prospective analysis, by electron microscopy, of the available material for clinicopathologic correlation; to evaluate the effectiveness of a more aggressive radiation therapy approach to clinically evident brain metastases; to evaluate the impact of chest radiation therapy following relapse as to the duration of response and survival and to improve survival and the quality of life in patients with extensive small cell lung cancer.

Technical Approach: Patients whose bone marrow is free of disease and who have no evidence of metastatic bone disease outside of the area specified for radiation therapy will be entered in Group A. Patients who have bone marrow involvement and/or bone metastasis to areas outside of the planned radiation therapy fields will be entered in Group B.

Group A - CAV induction chemotherapy, radiation therapy, reinduction chemotherapy with VP-16 and Cis-platinum, and CAV and late intensification chemotherapy with VP-16 plus Cis-platinum.

Group B - Either CAV or BTOC induction chemotherapy, plus radiation therapy for patients with chest relapse, reinduction chemotherapy with VP-16 plus Cis-Platinum and CAV or BTOC, and late intensification chemotherapy with VP-16 plus Cisplatin.

Investigators at MAMC will be entering only in Group A as Group B was closed on 16 Mar 84 because sufficient accrual of patients.

Progress: One patient was entered at MAMC. Preliminary results of the group-wide study show no significant differences between the groups.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 85/07	Status: On-going
Title SWOG 8213: Evaluation of Aclacinomycin A in Refractory Multiple Myeloma, Phase II		
Start Date: 16 Nov 84	Estimated Completion Date: Oct 86	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: LTC Irwin B. Dabe, MC		
Associate Investigators:		
COL F.H. Stutz, MC	MAJ Timothy O'Rourke, MC	
LTC Howard Davidson, MC	CPT David Bryson, MC	
MAJ Thomas Baker, MC	CPT Michael Stone, MC	
Key Words: multiple myeloma, aclacinomycin A		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: N/A

Study Objective: To determine the response rate and duration of remission of aclacinomycin A used in a weekly schedule (followed by two weeks rest) for patients with refractory multiple myeloma.

Technical Approach: Patients with histologically confirmed multiple myeloma, refractory to initial therapy and who meet other criteria, will receive an initial dose of aclacinomycin A of 65 mg/M₂ to be given as an IV infusion, weekly for four weeks, followed by a two week rest period. An adequate trial will is defined as two or more six week courses in which myelosuppression is observed. After two courses of therapy, the patient will be removed from the study if there is progression of disease or a rise in protein.

Progress: One patient has been entered at MAMC (FY 85) who subsequently expired from hypercalcemia, renal failure, and congestive heart failure associated with his multiple myeloma.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 83/67 Status: Completed

Title: SWOG 8215: Comparison of Combination Chemotherapy with VP-16 and Cis-Platinum vs BCNU, Thiotepe, Vincristine, and Cyclophosphamide in Patients with Small Cell Carcinoma of the Lung Who Have Failed or Relapsed Primary Chemotherapy, Phase III

Start Date: 15 Jul 83 Est Completion Date: Jun 85

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Thomas M. Baker, MC

Associate Investigators: LTC Howard Davidson, MC

COL Friedrich H. Stutz, MC MAJ Alfred H. Chan, MC

LTC James E. Congdon, MC MAJ Manuel J. Martinez, MC

LTC Irwin B. Dabe, MD MAJ Timothy J. O'Rourke, MC

Key Words:

Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Completed

Study Objective: To confirm the efficacy of combination VP-16-213 (VP-16) Cis-platinum in the treatment of patients with small cell carcinoma of the lung who have failed or relapsed on firstline treatment protocols; and through a randomized trial to compare the remission rate, duration of remission and toxicity between the combination of VP-16 plus Cis-platinum and the combination of BCUN, thiotepe, vincristine, and cyclophosphamide in the same group of patients.

Technical Approach: Patients will be randomized to either one of two treatments:

Arm I: BCNU, thiotepe, vincristine, and cyclophosphamide (BTOC) every three weeks until progression of disease occurs. Poor risk patients will receive reduced doses of the same regimen.

Arm II: VP-16 and Cis-Platinum every four weeks until progression occurs. Poor risk patients will receive reduced doses of the same regimen.

Progress: No entries at MAMC in FY 85. One patient was entered in FY 83 and expired after several weeks of therapy. There were no unexpected adverse reactions.

The study was closed to all patients after the last SWOG meeting. The results were discouraging. An apparent advantage for the VP-16/CCDP high dose groups was based on small numbers and incomplete follow-up.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 84/18	Status: On-going
Title: SWOG 8216/38 : Comparison of BCG Immunotherapy and Adriamycin for Superficial Bladder Cancer, Phase III		
Start Date: 18 Nov 83	Est Completion Date: Sep 85	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: LTC Howard Davidson, MC		
Associate Investigators:	MAJ Thomas M. Baker, MC	
COL Friedrich H. Stutz, MC	MAJ Alfred H. Chan, MC	
LTC William D. Belville, MC	MAJ Timothy J. O'Rourke, MC	
LTC Irwin B. Dabe, MC	CPT Michael D. Stone, MC	
Key Words: cancer, bladder, BCG immunotherapy, adriamycin		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

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: No patients entered in FY 85. Three patients were entered at MAMC during FY 84. One patient developed flu-like reactions to BCG injections, ulcerative lesions, and possible systemic BCG infection. Groupwide data suggest a significantly better response to the BCG than the Adriamycin.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 83/44 Status: Completed

Title: SWOG 8217: Evaluation of Spirogermanium (NSC-192965) in Adenocarcinoma of the Prostate, Phase II

Start Date: 18 Feb 83 Est Completion Date: Jan 85

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

COL Friedrich H. Stutz, MC MAJ Thomas M. Laker, MC

LTC James E. Congdon, MC MAJ Alfred H. Chan, MC

LTC Irwin B. Dabe, MD MAJ Timothy J. O'Rourke, MC

Key Words:

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: Completed

Study Objective: To determine the response rate and remission duration of adenocarcinoma of the prostate when treated with spirogermanium used as a 60 minute infusion in a 3 X weekly schedule, and to define the qualitative and quantitative toxicities of spirogermanium administered in a Phase II study.

Technical Approach: Patients will receive a dose of spirogermanium based upon their body height and weight, given IV on an outpatient basis, three times a week. This treatment regimen will continue for a period of one year, until unusual side effects develop, or until evidence of objective disease progression is noted.

Progress: One entry at MAMC during FY 85. One patient was entered in FY 83 and experienced lethargy and confusion; more likely due to underlying OBS than to the drug. The patient had progressive disease and was taken off study.

Groupwise, there were no life-threatening or fatal toxicities, but 5 of 41 patients had severe toxicities. One of 40 patients evaluated for response had a partial response lasting 4 months. There have not been any complete responses. Eight patients were classified as having stable disease with durations of 9, 12, 13, 14, 19, 20, 22, and 29 weeks. The response rate including stable disease is estimated to be 22%. The estimate of the median survival for eligible patients is 4.5 months.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 83/60	Status: On-going
Title: SWOG 8219: Evaluation of Combined or Sequential Chemo-Endocrine Therapy in the Treatment of Advanced Adenocarcinoma of the Prostate, Phase III		
Start Date: 15 Apr 83	Est Completion Date: Mar 85	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: LTC Howard Davidson, MC		
Associate Investigators:		
COL Friedrich H. Stutz, MC	MAJ Thomas M. Baker, MC	
LTC James E. Congdon, MC	MAJ Alfred H. Chan, MC	
LTC Irwin B. Dabe, MD	MAJ Timothy J. O'Rourke, MC	
Key Words: prostate, adenocarcinoma, chemo-endocrine therapy		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To compare the efficacy of the sequential use of endocrine therapy followed at the time of progression by cytotoxic chemotherapy (Adriamycin and cyclophosphamide) versus the combination of endocrine therapy and chemotherapy in the treatment of advanced adenocarcinoma of the prostate by determination of the response rate, response duration, and duration of survival.

Technical Approach: Patients will be stratified as to the type of endocrine therapy (orchiectomy or diethylstilbestrol [DES]), performance status, and good risk or poor risk. Patients will be randomized to either Arm I (endocrine therapy followed at the time of progression by chemotherapy with cyclophosphamide and Adriamycin) or Arm II (endocrine therapy combined with cyclophosphamide and Adriamycin beginning two weeks after the orchiectomy or the initiation of DES). Endocrine therapy for both arms will consist of a bilateral orchiectomy or, if the patient refuses surgery, DES. Courses will be repeated every 21 days. A minimum of two cycles will be considered an adequate trial. When a total of 300 mg/M² adriamycin in good risk or 200 mg/M² in poor risk patients has been given, it will be discontinued and cyclophosphamide will be given alone at a dose of 1000 mg/M² (good risk) or 750 mg/M² (poor risk) every three weeks. Cyclophosphamide will be discontinued in patients who are in complete or partial remission or who have stable disease after one year of chemotherapy. Patients with progressive disease after the sequential or combined chemo-endocrine therapy will be treated on another protocol.

Progress: One patient has been entered at MAMC (FY 84) on the sequential arm. Groupwide, 117 patients have been entered with no unexpected toxicity.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 84/19	Status: On-going
Title: SWOG 8221: Treatment of Advanced Bladder Cancer with Preoperative Irradiation and Radical Cystectomy Versus Radical Cystectomy Alone, Phase III		
Start Date: 18 Nov 83	Est Completion Date: Oct 85	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: LTC Howard Davidson, MC		
Associate Investigators:		
COL William Belville, MC	MAJ Thomas M. Baker, MC	
COL Donald Kull, MC	MAJ Alfred H. Chan, MC	
COL Friedrich H. Stutz, MC	MAJ Timothy J. O'Rourke, MC	
LTC Irwin B. Dabe, MC	CPT Michael Stone, MC	
Key Words: cancer, bladder, irradiation, cystectomy		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To compare survival and pelvic recurrence rates in patients with transitional cell bladder cancer treated with radical surgery alone versus patients treated with preoperative irradiation with 2,000 rads followed by cystectomy.

Technical Approach: Patients eligible to be entered, must have histologically proven transitional cell carcinoma of the urinary bladder, and must have one of the following characteristics:

1. Evidence of muscle invasion.
2. Rapidly recurring superficial high-grade tumors and/or diffuse carcinoma *in situ* not amenable to trans-urethral 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: No entries in FY 85. One patient was entered during FY 84 and was randomized to cystectomy alone. To this point she has tolerated the procedure well. At the present accrual rate, it will take approximately three more years to complete the study.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 83/55 Status: On-going

Title: SWOG 8228 - Correlation Between Progesterone Receptor and Response to Tamoxifen in Patients with Newly Diagnosed Breast Disease, Phase II

Start Date: 18 Mar 83 Est Completion Date: Mar 85

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

COL Friedrich H. Stutz, MC

MAJ Thomas M. Baker, MC

LTC James E. Congdon, MC

MAJ Alfred H. Chan, MC

LTC Irwin B. Dabe, MD

MAJ Timothy J. O'Rourke, MC

Key Words:

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: Continue

Study Objective: To determine the prognostic role of progesterone receptor in patients with newly diagnosed metastatic breast disease by correlating progesterone receptor levels with objective response rates in women treated with tamoxifen.

Technical Approach: ER+, non-pregnant female patients with new metastatic breast carcinoma are eligible. Patients who have received prior hormonal adjuvant therapy are eligible provided that they have not failed during therapy and the therapy has been stopped for at least three months. Patients with adjuvant chemotherapy alone are eligible. Patients with massive liver involvement are not eligible.

Tamoxifen, 10 mg/M² po, b.i.d, will be given alone until there is documented progression of the disease. Clear cut response may not be observed until 6-12 weeks of tamoxifen therapy. Therefore, therapy will not be discontinued unless there is evidence of disease progression at four weeks or unsatisfactory stable disease after eight weeks of therapy.

Progress: No entries at MAMC. Tamoxifen has been well tolerated in group-wide studies.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 83/61	Status: On-going
Title: SWOG 8229/30: Combined Modality Therapy for Multiple Myeloma, VMCP-VBAP for Remission Induction Therapy: VMCP + Levamisole vs Sequential Half-Body Radiotherapy + Vincristine-Prednisone for Patients Who Fail to Achieve Remission Status with Chemotherapy Alone, Phase III		
Start Date: 15 Apr 83	Est Completion Date: Mar 85	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: LTC Howard Davidson, MC		
Associate Investigators:		
COL Friedrich H. Stutz, MC	MAJ Thomas M. Baker, MC	
LTC James E. Congdon, MC	MAJ Alfred H. Chan, MC	
LTC Irwin B. Dabe, MD	MAJ Timothy J. O'Rourke, MC	
Key Words: multiple, myeloma, chemotherapy, radiotherapy		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To compare the effectiveness of two intermittent pulse schedules of combination of vincristine, melphalan, cyclophosphamide and prednisone (VMCP), and vincristine, BCNU, ardiamycin and prednisone (VBAP) for induction of remission in previously untreated patients with multiple myeloma. Results will also be compared with other combination chemotherapy regimens in previous SWOG studies. In patients proven to acheive remission, to compare the value of 12 months of chemo-immunotherapy maintenance, VMCP + levamisole, vs a consolidation program consisting of sequential half-body radiotherapy along with vincristine and prednisone followed by unmaintained remission. In patients who only achieve improvement, to determine whether sequential halfbody radiotherapy along with vincristine and prednisone will increase the remission rate. To determine whether sequential half-body radiotherapy along with vincristine and prednisone can serve as an effective form of induction therapy for patients who fail to respond to chemotherapy or suffer early relapse.

Technical Approach: Patients with previously untreated multiple myeloma will be stratified as to tumor mass status and then randomized to induction therapy on VMCP alternated every three wks weeks with VBAP for a minimum of 6 months to a maximum of one yr or to VMCP for 3 cycles followed by 3 cycles of VBAP. Each course will be repeated every 3 weeks. Courses will be repeated for a minimum of 6 months to a maximum of one year. Upon completion of induction, patients with documented 75% regression with chemotherapy alone will be randomized to receive VMCP + levamisole, repeated every three wks or to sequential half-body radiotherapy and concomitant vincristine and prednisone. Partial responders or nonresponders following induction therapy will receive sequential half-body radiotherapy and vincristine and prednisone for six weeks.

Progress: Two patients were entered at MAMC during FY 84. Group-wide 67 patients have achieved a complete response and have entered the maintenance phase.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 83/68	Status: On-going
Title: SWOG 8231: Chemotherapy of Extragonadal Germinal Cell Neoplasms, Phase III		
Start Date: 15 Jul 83	Est Completion Date: Jun 85	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: LTC Howard Davidson, MC		
Associate Investigators:	MAJ Thomas M. Baker, MC	
COL William Belville, MC	MAJ Alfred H. Chan, MC	
COL Friedrich H. Stutz, MC	MAJ Timothy J. O'Rourke, MC	
LTC Irwin B. Dabe, MC	CPT Michael Stone, MC	
Key Words: neoplasms, germinal cell, extragonadal, chemotherapy		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine the effectiveness of alternating combination chemotherapy consisting of VBP (vinblastine, bleomycin and cis-platinum) and EBAP (bleomycin, adriamycin, cis-platinum and VP-16) in patients with metastatic germinal cell neoplasms arising in extragonadal sites; to determine the overall toxicity of the alternating combination of VBP and EBAP; to determine the role of surgical removal of residual disease following this drug combination in partially responding patients; to compare the response rates observed in this study with those reported by other investigators.

Technical Approach: This study will utilize alternating combination chemotherapy, with first and third cycles consisting of VBP and the second and fourth cycles consisting of EBAP. There are reduced "poor risk" doses for patients who are over 65 or have neutropenia, thrombocytopenia, markedly abnormal liver function, or prior radiation therapy.

Following completion of the four cycles, patients with a complete response will be observed; those with stable disease, minimal response, or partial response will have surgical resection of residual disease, if possible, followed by 2 more cycles of chemotherapy if malignant tumor is found at surgery.

Progress: No entries at MAMC. Group-wide, there have been 11 complete responses in 13 patients evaluated in the high dose group. Toxicity appears to be high for this drug combination with one fatal toxicity and nine life threatening toxicity episodes.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 83/45	Status: Completed
Title: SWOG 8232: Treatment of Limited Small Cell Lung Cancer with VP-16/Cis-Platinum Alternating with Vincristine/Adriamycin/Cyclophosphamide and Radiation Therapy versus Concurrent VP-16/Vincristine/Adriamycin/Cyclophosphamide and Radiation Therapy, Phase III		
Start Date: 18 Feb 83	Est Completion Date: Jan 85	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: LTC Howard Davidson, MC		
Associate Investigators:		
COL Friedrich H. Stutz, MC	MAJ Thomas M. Baker, MC	
LTC James E. Congdon, MC	MAJ Alfred H. Chan, MC	
LTC Irwin B. Dabe, MD	MAJ Timothy J. O'Rourke, MC	
Key Words: cancer, small cell lung, chemotherapy, radiotherapy		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Completed

Study Objective: To compare the efficacy of alternating non-cross-resistant, multidrug regimens with concurrent combination chemotherapy as remission induction in patients with limited small cell lung carcinoma and to determine the toxicity of these treatment programs.

Technical Approach: After appropriate laboratory tests to determine that the patient has limited disease, the patient will be randomized to one of two treatment arms: ARM 1 - includes 4 agents, VP-16, vincristine, adriamycin and cyclophosphamide. These agents will be given IV every 3 weeks for a total of 6 courses. ARM 2 - consists of VP-16 and cis-platinum alternating every 3 weeks with vincristine, adriamycin, and cyclophosphamide. These regimens will be repeated for a total of 6 treatments or 3 treatments of each group of drugs. At the end of 6 cycles of therapy, the patients will be restaged. Patients with no evidence of disease remaining or those who have had a large decrease in the size of their tumor with only residual tumor remaining in the chest will receive radiation therapy to mediastinal and hilar regions and prophylactic whole brain radiation therapy. At the completion of this phase of treatment, the patients will receive 6 more cycles of the same chemotherapy regimen that they received prior to radiation therapy.

Progress: One patient was entered at MAMC in FY 85 for a total of four entered at MAMC. The EVAC regimen had 50% CR and 31% PR. The alternating regimens had 55% CR and 28% PR. Both regimens had six instances of fatal toxicity among 182 patients.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 83/72	Status: Completed
Title: SWOG 8237: Evaluation of Continuous Infusion Vinblastine Sulfate in Pancreatic Adenocarcinoma, Phase II		
Start Date: 19 Aug 83	Est Completion Date: Jun 83	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: MAJ Thomas M. Baker, MC		
Associate Investigators:		
COL Friedrich H. Stutz, MC	MAJ Alfred H. Chan, MC	
LTC Irwin B. Dabe, MC	MAJ Timothy J. O'Rourke, MC	
LTC Howard Davidson, MC	CPT Michael D. Stone, MC	
Key Words: adenocarcinoma, pancreatic, vinblastine sulfate		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Completed

Study Objective: To determine the clinical response rate of a 5 day continuous infusion of vinblastine sulfate in pancreatic adenocarcinoma.

Technical Approach: Patients will be treated with vinblastine sulfate at a starting dose of 1.4 mg/M²/day by continuous infusion for five days. Vinblastine sulfate will be repeated every three weeks provided granulocyte and platelet counts are satisfactory. If the counts do not recover until four weeks, the chemotherapy will be given on a four week cycle at the same dose. If the counts have not recovered within four weeks, vinblastine sulfate will be given at a one dose level of reduction when the counts have recovered. Therapy will be continued as long as there is stable disease, partial response, or complete response and acceptable clinical toxicity. An adequate trial will be defined as two cycles of continuous infusion vinblastine therapy.

Progress: No entries at MAMC. Groupwide, 34 patients were registered. No summary is available at this time.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 85/76	Status: On-going
Title: SWOG 8269: Concurrent Chemo-Radiotherapy for Limited Small Cell Carcinoma of the Lung, Phase II		
Start Date: 27 Aug 85	Est Completion Date: Jun 87	
Dept/Svc: Medicine/Hematology	Facility: MAMC	
Principal Investigator: MAJ Thomas M. Baker, MC		
Associate Investigators:		
LTC Irwin B. Dabe, MC	MAJ Michael D. Stone, MC	
MAJ Howard Davidson, MC	CPT David R. Bryson, MC	
Key Words: carcinoma, lung, small cell, chemo-radiotherapy		
Accumulative MEDCARE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: N/A

Study Objective: To explore the response rate with the concurrent use of radiation therapy plus chemotherapy utilizing cis-platinum, VP-16, and vincristine in limited small cell carcinoma of the lung and to observe the toxicities of this combined modality program.

Technical Approach: Patients will be started on chemotherapy consisting of cis-platinum, VP-16, and vincristine and concurrent radiation therapy to the primary site. After completion of radiation therapy to the chest, prophylactic cranial radiation therapy will be given. After a brief rest period, the patients will be treated with 12 more weeks of conventional chemotherapy consisting of adriamycin, cytoxan, VP-16, vincristine, and methotrexate. Patients who show a complete response will be followed. Patients with less than a complete response will be taken off study and offered alternative therapy.

Progress: One patient has been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 84/36	Status: Completed
Title: SWOG 8273: FUVAC with Intensive Consolidation for ER-Metastatic Breast Cancer, Phase II-Pilot		
Start Date: 16 Mar 84	Est Completion Date: Mar 86	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: COL Friedrich H. Stutz, MC		
Associate Investigators: COL Donald H. Kull, MC		
LTC Howard Davidson, MC		
MAJ Thomas Baker, MC		
Key Words: cancer, breast, metastatic, ER-, FUVAC		
Accumulative MEDCARE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Completed

Study Objective: To determine the feasibility and toxicity of combination chemotherapy induction, followed by consolidation therapy with sequential half-body irradiation or high-dose cyclophosphamide with total body irradiation and autologous bone marrow infusion, in patients with disseminated, estrogen receptor negative breast cancer; to determine complete and partial response rates; and to describe response duration and survival of patients treated with such a regimen.

Technical Approach: Patients will receive induction therapy of six courses of FUVAC chemotherapy. Following this, patients who are good risk and whose marrow is negative for tumor cells will receive consolidation therapy with cyclophosphamide and total body irradiation. Poor risk patients or those patients with the presence of tumor cells in the marrow will receive sequential hemi-body irradiation only, beginning on week 13 of the study. Following this, no further therapy will be administered. Patients with progressive disease after one course of induction therapy or failure to achieve at least an objective or subjective improvement by the end of four induction courses will be removed from the study. The study has been amended to allow ER unknown patients with life-threatening liver involvement of lymphangitic lung metastasis to be entered. These patients will be entered into that group of patients who will receive sequential half-body consolidation.

Progress: No entries in FY 85. One patient was entered at MAMC in FY 84. She had progression on treatment and expired from disease.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/47 Status: On-going

Title: SWOG 8293: Intergroup Phase III Protocol for the Management of Locally or Regionally Recurrent but Surgically Resectable Breast Cancer

Start Date: 20 Apr 84 Est Completion Date: Mar 86

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

COL Friedrich H. Stutz, MC

MAJ Alfred H. Chan, MC

LTC James E. Congdon, MC

MAJ Timothy J. O'Rourke, MC

MAJ Thomas M. Baker, MC

CPT Michael Stone, MC

Key Words: cancer, breast,

Accumulative MEDCASE

Est Accumulative

Periodic Review

Cost: -0-

OMA Cost: -0-

Results: Continue

Study Objective: To better define the relative roles of systemic and local treatments in the care of resectable locally or regionally recurrent cancer of the breast in patients who have no evidence of disease after resection; to assess the effects of chemotherapy and radiation therapy (singly or in combination) administered immediately after surgical resection on local control, disease-free interval, and pattern of re-recurrence; to determine the effect of the administration of systemic chemotherapy or radiation therapy, which has been delayed until local, regional, re-recurrence, on local and regional control, disease-free survival, patterns of relapse, and survival; and to determine the influence of disease-free interval, size, and extent of local or regional recurrence on the effectiveness of treatment with chemotherapy and radiation therapy (singly or in combination).

Technical Approach: After patients with technically resectable loco-regional recurrent breast cancer have been rendered clinically free of disease (NED) by surgical resection and appropriate staging, they will be allocated to Schema A, B, or C. Schema A will receive 9 cycles of chemotherapy. If found to be NED after therapy, these patients will proceed to observation or to consolidation radiation therapy. Schema B will be randomized to radiation therapy followed by observation or to 9 cycles of chemotherapy followed by consolidation radiation therapy. Schema C will receive either radiation therapy or chemotherapy. Those who receive radiation therapy will be observed without further treatment. Those who receive chemotherapy and who are found NED after 9 cycles of treatment will receive consolidation radiation therapy or observation without further treatment. All patients will be followed for local and/or distant re-recurrence. Patients who experience local re-recurrence during active induction chemotherapy will come off study. Patients who experience local re-recurrence during primary radiation therapy will stop radiation therapy, excision if feasible, and 9 cycles of chemotherapy. Patients who develop local re-recurrence during consolidation radiation therapy will come off study and followed. Patients who develop local re-recurrence during the observation phase of Treatment Arms II and III will remain on study and will be treated per schema. Patients who develop distant recurrence will come off study and will be followed for survival.

PROGRESS No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 83/56	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: 18 May 83	Est Completion Date: Feb 85	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: LTC Howard Davidson, MC		
Associate Investigators:		
COL Friedrich H. Stutz, MC	MAJ Thomas M. Baker, MC	
LTC James E. Congdon, MC	MAJ Alfred H. Chan, MC	
LTC Irwin B. Dabe, MD	MAJ Timothy J. O'Rourke, MC	
Key words: cancer, breast, operable, node negative, chemotherapy		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To assess the impact of short-term intensive chemotherapy with CMF 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 cms in diameter who are estrogen receptor positive will be followed by close observation only to determine the natural history of their tumor. All other patients who have a somewhat greater likelihood of relapse will be randomized to receive either close observation only or 6 cycles of systemic chemotherapy. The chemotherapy will consist of 4 agents: cyclophosphamide, methotrexate, 5-fluorouracil, and prednisone given for six 28 day cycles. The dosage of the individual agents will be determined by body height and weight.

Progress: Four patients were entered in FY 85 for a total of eight entries. Only mild side effects have been noted.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/08 Status: On-going

Title: SWOG 8300: Treatment of Limited Non-Small Cell Lung Cancer: Radiation versus Radiation Plus Chemotherapy (FOMi/CAP), Phase III

Start Date: 16 Nov 84 Estimated Completion Date: Oct 86

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Thomas Baker, MC

Associate Investigators:

COL F.H. Stutz, MC MAJ Timothy O'Rourke, MC

LTC Irwin B. Dabe, MC CPT David Bryson, MC

LTC Howard Davidson, MC CPT Michael Stone, MC

Key Words: lung, limited non-small cell, radiation, chemotherapy

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To compare combination chemotherapy (FOMi/CAP: 5-FU, vincristine, and mitomycin-C alternating with cyclophosphamide, Adriamycin, and cis-platinum) plus radiotherapy to radiotherapy alone for patients with limited, non-small cell lung cancer (NSCLC) in a randomized study with stratification for known important prognostic factors with regard to response rate, response duration, and survival duration; to determine the toxicity of radiotherapy plus FOMi-CAP relative to radiotherapy alone for patients with limited NSCLC; to evaluate the responsiveness of smaller tumor burdens (less than metastatic disease) to FOMi-CAP; to determine the pattern of relapsing disease in each treatment arm and in subgroups of patients determined by histology and response to FOMi/CAP; and to determine if prophylactic brain irradiation will decrease the chances for brain metastasis and influence toxicity or survival.

Technical Approach: Patients will be randomized to four treatment arms: (1) radiation alone to the chest; (2) radiation therapy to the chest and prophylactic radiation to the brain; (3) chemotherapy with FOMi/CAP followed by radiation therapy to the chest (those patients showing some response will receive two additional cycles of chemotherapy after completion of radiation therapy); (4) same treatment as in #3 with the addition of concomitant prophylactic brain irradiation to 3750 rads.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 84/49	Status: Completed
Title: SWOG 8303: Evaluation of 2'Deoxycoformycin in Refractory Multiple Myeloma, Phase II		
Start Date: 20 Apr 84	Est Completion Date: Apr 86	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: LTC Irwin Dabe, MC		
Associate Investigators:		
COL Friedrich H. Stutz, MC	MAJ Alfred H. Chan, MC	
LTC Howard Davidson, MC	MAJ Timothy J. O'Rourke, MC	
MAJ Thomas M. Baker, MC	CPT Michael Stone, MC	
Key Words: myeloma, multiple, refractory, 2'deoxycoformycin		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Completed

Study Objective: To determine the response rate and response duration of refractory multiple myeloma treated with low dose 2'deoxycoformycin used in a single dose, every two week schedule, and to define the qualitative and quantitative toxicities of 2'deoxycoformycin administered in a Phase II Study.

Technical Approach: After vigorous hydration, an initial dose of 2'deoxycoformycin (4 mg/M²) will be given on day 1 and repeated every 14 days. PO fluids will be given days 1-5 of the cycle of therapy. Each patient will receive three courses of therapy to be considered evaluable for response. If no response is observed after three courses or there has been <25% tumor reduction after four courses of treatment, patient will be removed from the study.

Progress: No entries in FY 85. One patient was entered at MAMC in FY 84. This drug had very minimal activity.

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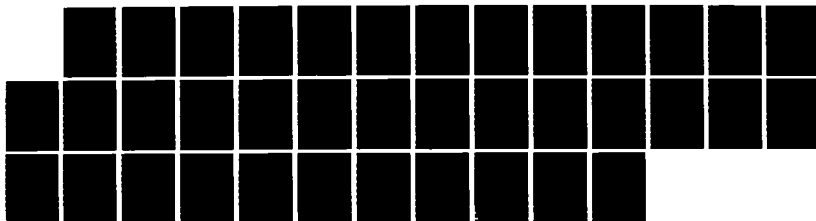
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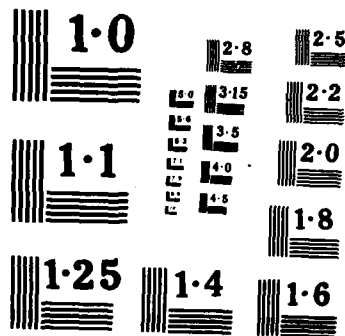
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Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/78 Status: On-going

Title: SWOG 8308: Combination Cis-Platinum and Dichloromethotrexate in Patients with Advanced Bladder Cancer, Phase II

Start Date: 21 Sep 84 Est Completion Date: Jun 86

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators: MAJ Thomas M. Baker, MC

COL Friedrich H. Stutz, MC MAJ Timothy J. O'Rourke, MC

LTC Irwin B. Dabe, MD CPT Michael Stone, MC

Key words: cancer, bladder, cis-platinum, dichloromethotrexate

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: Continue

Study Objective: To obtain data regarding the activity and toxicity of combination cis-platinum and dichloromethotrexate in patients with objectively measurable metastatic transitional cell carcinoma of the bladder who have good renal function and who have not previously received chemotherapy and to investigate the single agent activity and toxicity of dichloromethotrexate in previously untreated patients with impaired renal function.

Technical Approach: Patients with measurable metastatic disease, adequate hepatic and cardiac function, adequate bone marrow reserve, and no prior systemic chemotherapy will be eligible. Patients who have impaired renal function will receive dichloromethotrexate alone; patients with good renal function will receive dichloromethotrexate and cisplatin. Cis-platinum will be given 70 mg/M², the first and the fifth week with normal saline hydration, pre and post. Dichloromethotrexate will be given once weekly on an escalating dose schedule, starting at 400 mg/M² in good risk patients and 300 mg/M² in poor risk patients. After eight weeks of treatment, there will be a three week rest period; non-responding patients will be taken off study and responding patients will go to a less intensive maintenance phase.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 85/62	Status: On-going
Title: SWOG 8310: Evaluation of Aziridinybenzoquinone (AZQ) (NSC-182986) in Refractory Relapsing Myeloma, Phase II		
Start Date: 24 May 85	Estimated Completion Date: Apr 87	
Dept/Svc: Medicine/Hematology	Facility: MAMC	
Principal Investigator: MAJ Thomas Baker, MC		
Associate Investigators:		
COL F.H. Stutz, MC	MAJ Timothy O'Rourke, MC	
LTC Irwin B. Dabe, MC	CPT David Bryson, MC	
MAJ Howard Davidson, MC	CPT Michael Stone, MC	
Key Words: AZQ, refractory relapsing myeloma		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: N/A

Study Objective: To determine the antitumor activity of AZQ in patients with refractory and relapsing multiple myeloma by determination of the response rate and the remission duration.

Technical Approach: AZQ will be given at 10 mg/M² weekly for four consecutive weeks, followed by a rest period of at least two weeks. Patients will be treated in this manner, until there is evidence of progression of disease.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/72 Status: On-going

Title: SWOG 8312, Megestrol Acetate and Aminoglutethimide/Hydrocortisone in Sequence or in Combination as Second-Line Endocrine Therapy of Estrogen Receptor Positive Metastatic Breast Cancer, Phase III

Start Date: 17 Aug 84 Est Completion Date: Jun 86

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Thomas M. Baker, MC

Associate Investigators: LTC Howard Davidson, MC

COL Friedrich H. Stutz, MC MAJ Timothy J. O'Rourke, MC

LTC Irwin B. Dabe, MC CPT Michael D. Stone, MC

Key Words: cancer, breast, ER+, metastatic, chemotherapy

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: Continue

Study Objective: To determine whether combination hormonal therapy with aminoglutethimide and hydrocortisone plus megestrol acetate, agents thought to have different mechanisms of action, offers an improved response rate with prolonged response duration and increased patient survival over the sequential use of each agent in ER+ patients who have progressed after responding to primary hormonal treatment with tamoxifen; to assess the relative toxicities of megestrol acetate and medical adrenalectomy; and to assess the value of progesterone receptors in predicting subsequent responses to a variety of hormonal therapies.

Technical Approach: Patients who have had an adequate trial of tamoxifen and have achieved at least a partial response or maintained stable disease for a minimum of six months with documented disease progression and clear-cut bone scan evidence of cortical bone metastases will be randomized to: Arm I - megestrol acetate, 40 mg p.o., 4 times daily given alone until there is documented evidence of disease progression; Arm II - aminoglutethimide, 250 mg p.o., twice daily for two weeks, then 250 mg p.o. four times daily plus hydrocortisone, 20 mg p.o. upon rising, 20 mg p.o. at 1700 hrs, and 60 mg p.o. at bedtime, daily for two weeks, then 10 mg p.o. upon rising, 10 mg p.o. at 1700 hrs, and 20 mg p.o. at bedtime; or Arm III megestrol acetate as in Arm I plus aminoglutethimide as in Arm II plus hydrocortisone as in Arm II. An adequate trial of each arm will consist of at least eight weeks of daily therapy in the absence of documented evidence of disease progression. Patients in Arms I and II with documented progressive disease after an adequate trial will be crossed over to the other treatment arm. The only exception to crossover will be patients who develop life threatening brain, liver, or pulmonary metastases who require systemic chemotherapy. Patients randomized to Arm III will go off study at the time of disease progression.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 84/59	Status: On-going
Title: SWOG 8313: Multiple Drug Adjuvant Chemotherapy for Patients with ER Negative Stage II Carcinoma of Breast, Phase III		
Start Date: 18 May 84	Est Completion Date: May 86	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: LTC Howard Davidson, MC		
Associate Investigators: MAJ Thomas Baker, MC		
COL Friedrich H. Stutz, MC	MAJ Timothy J. O'Rourke, MC	
LTC Irwin B. Dabe, MD	CPT Michael D. Stone, MC	
Key Words: carcinoma, breast, ER-, adjuvant, multiple drug		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To compare through a randomized prospective study the recurrence rates and disease-free intervals for postoperative axillary node positive estrogen receptor negative breast cancer patients given adjuvant therapy with either short term intense chemotherapy (FAC-M) or one year standard chemotherapy (CMFVP); to compare the effect of these two adjuvant therapies on survival; to compare the relative toxicity of the two therapies; to compare the quality of life of patients with operable breast cancer randomized to receive one year of CMFVP or a short intensive regimen of FAC-M x 4 courses; and to compare a multiple item questionnaire for assessing quality of life.

Technical Approach: Women who have histologically proven breast cancer with axillary lymph node metastasis and negative estrogen receptors will be entered 14-21 days post-lumpectomy or within 14-42 days postmastectomy. They will be randomly allocated to receive either:

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.

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.

Questionnaires to compare quality of life will be completed at 72 hours prior to chemotherapy.

Progress: One patient has been entered at MAMC (FY 85). This patient had more than usual leukopenia requiring substantial dose reduction. Groupwide no fatal toxicities have been recorded. Perforated ulcer and shock lung have been reported.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/60 Status: Completed

TITLE: SWOG 8316: Evaluation of Fludarabine Phosphate (NSC-312887) in Renal Cell Carcinoma, Phase II

Start Date: 18 May 84 Est Completion Date: May 86

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Thomas Baker, MC

Associate Investigators: LTC Howard Davidson, MC

COL Friedrich H. Stutz, MC MAJ Timothy J. O'Rourke, MC

LTC Irwin B. Dabe, MD CPT Michael D. Stone, MC

Key Words: carcinoma, renal cell, fludarabine phosphate

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To determine the response rate and remission duration of renal cell carcinoma when treated with fludarabine phosphate and to define the qualitative and quantitative toxicities of fludarabine phosphate administered in a Phase II study.

Technical Approach: Fludarabine phosphate, 25 mg/M², will be given IV daily for five consecutive days and repeated every 28 days. Patients showing a complete or partial response will continue to receive therapy until disease relapse or until they have received therapy for one year after achieving a complete remission. Patients with progressive disease or relapse after two courses of therapy will have therapy with fludarabine phosphate discontinued.

Progress: One patient entered at MAMC in FY 84 with no adverse effects. Group wide, there were no fatal toxicities but half of the 36 patients evaluated for toxicity had one or more life-threatening toxicities. All 36 patients had either granulocytopenia or lymphocytopenia of some degree. There have been no partial or complete responses in the 31 patients evaluated for response. The median survival was 7.4 months.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 84/61	Status: On-going
Title: SWOG 8367: Combined Modality Treatment of Regional Non-Small Cell Lung Cancer, Phase I-II Pilot		
Start Date: 18 May 84	Est Completion Date: May 86	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: LTC Howard Davidson, MC		
Associate Investigators:		
COL Friedrich H. Stutz, MC	MAJ Alfred H. Chan, MC	
LTC Irwin B. Dabe, MC	MAJ Timothy J. O'Rourke, MC	
MAJ Thomas M. Baker, MD	CPT Michael D. Stone, MC	
Key Words: cancer, lung, non-small cell, combined modality		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine the feasibility and acute toxicity of a sequential approach with combination chemotherapy and neutron based radiation therapy in the treatment of regional (limited, unresectable) non-small cell lung carcinoma; to determine complete and partial response rates and response duration with such a program, and to assess survival and long-term side effects in this treated population.

Technical Approach: Patients will receive outpatient vinblastine and mitomycin-C followed three weeks later by inpatient vinblastine and cis-platinum. Following three weeks rest, neutron radiation therapy to the chest and photon therapy to the brain (prophylaxis) will be given. Upon completion of radiation therapy (wk 14), two additional cycles of VeMi/VeP will be given. Upon completion of chemotherapy, no further therapy will be administered and the patient will be followed.

Progress: One patient was entered at MAMC with decreased hearing secondary to cis-platinum and possible herpes zoster after radiation.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 85/91	Status: On-going
Title: SWOG 8369: Combination Chemotherapy with Mitoxantrone, Cis-Platinum, and MGBG for Refractory Lymphoma, Phase II		
Start Date: 20 Sep 85	Est Completion Date: Aug 87	
Dept/Svc: Medicine/Hematology	Facility: MAMC	
Principal Investigator: MAJ Howard Davidson, MC		
Associate Investigators:		
LTC Irwin B. Dabe, MC	MAJ Michael D. Stone, MC	
MAJ Thomas Baker, MC	CPT David R. Bryson, MC	
Key Words: mitoxantrone, cis-platinum, MBGB, refractory lymphoma		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: N/A

Study Objective: To determine if the 3-drug combination of mitoxantrone, cis-platinum, and methylglyoxal bis-guanylhydrazone (MGBG) has reasonable activity (response rate >30%) in patients with refractory unfavorable histology non-Hodgkin's lymphoma; to assess response duration, and to determine the toxicities of this combination of drugs.

Technical Approach: DHAD, MGBG, and cis-platin will be given IV on day 1 and repeated every 21 days provided granulocyte and platelet counts are adequate. Drugs will be given in the order shown so those with severe GI toxicities will be given last. Poor risk patients will receive reduced doses of the same treatment plan. An adequate trial will consist of two courses of therapy embracing a six week observation period. If tumor response or stable disease is noted, therapy will be continued until progression. If tumor progression is noted on a non-myelosuppressive dose of drugs, therapy will be continued at a one dose level increase. If progression of disease with myelosuppressive doses occurs, the patient will be removed from the study.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 84/07	Status: On-going
Title: SWOG 8370: Vinblastine and Cis-Platinum in the Treatment of Refractory Sarcomas, Phase II - Pilot		
Start Date: 21 Oct 83	Est Completion Date: Sep 85	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: LTC Howard Davidson, MC		
Associate Investigators:		
COL Friedrich H. Stutz, MC	MAJ Alfred H. Chan, MC	
LTC Irwin B. Dabe, MC	MAJ Timothy J. O'Rourke, MC	
MAJ Thomas M. Baker, MD	CPT Michael D. Stone, MC	
Key Words: sarcoma, refractory, vinblastine, cis-platinum		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To evaluate the response rate of refractory soft tissue sarcoma to the drug combination of vinblastine and cis-platinum.

Technical Approach: This is a prospective, one arm pilot study for the treatment of measurable, refractory (to standard therapy) sarcomas. CisPlatinum is given on day 1 after appropriate hydration, followed by a 5 day continuous infusion of vinblastine. The treatment will continue for as long as it can be tolerated and controls the disease (stable disease or response).

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 84/37	Status: On-going
Title: SWOG 8378: Evaluation of Fludarabine Phosphate in Chronic Lymphocytic Leukemia		
Start Date: 16 Mar 84	Est Completion Date: Feb 86	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: MAJ Thomas M. Baker, MC		
Associate Investigators:		
COL Friedrich H. Stutz, MC	MAJ Alfred H. Chan, MC	
LTC Irwin B. Dabe, MC	MAJ Timothy J. O'Rourke, MC	
LTC Howard Davidson, MD	CPT Michael D. Stone, MC	
Key Words: leukemia, lymphocytic, chronic, fludarabine phosphate		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: Continue

Study Objective: To determine the response rate and remission duration of relapsing or refractory chronic lymphocytic leukemia treated with fludarabine phosphate used in a daily times five, every four week schedule and to define qualitative and quantitative toxicities of fludarabine phosphate in a Phase II study in this population.

Technical Approach: To achieve maximum tolerated lymphotoxicity, the initial dose will be escalated in increments not to exceed 25% as a maximum of five patients are accrued to the initial dose and the toxicity of fludarabine phosphate is evaluated. The initial dose will be 20 mg/M² daily for five days to be administered as a rapid IV infusion and repeated every 28 days. Patients will receive an initial three courses of fludarabine phosphate. If there is evidence of progression of disease, treatment will be discontinued and the patient will be taken off the study. If there is evidence of response, the patient will receive three more courses for a total of six courses of therapy. Patients will then be re-evaluated and categorized as either responders or non-responders. Patients achieving a complete response will be followed without further therapy to disease relapse. Patients achieving a partial response after six courses of fludarabine phosphate will receive six additional courses at which time they will be reclassified as complete response or partial response. Patients remaining in partial response will be taken off study and patients in complete remission will be followed to disease relapse.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/54 Status: On-going

Title: SWOG 8384: Evaluation of Fludarabine Phosphate (NSC-312887)
in Small Cell Lung Carcinoma, Phase II

Start Date: 19 Apr 85 Estimated Completion Date: Mar 87

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Thomas M. Baker, MC

Associate Investigators:

COL F.H. Stutz, MC

MAJ Timothy O'Rourke, MC

LTC Irwin B. Dabe, MC

CPT Michael Stone, MC

LTC Howard Davidson, MC

CPT David Bryson, MC

Key Words: carcinoma, lung, small cell, fludarabine phosphate

Accumulative MEDCASE

Est Accumulative

Periodic Review

Cost: -0-

OMA Cost: -0-

Results: N/A

Study Objective: To determine the response rate and response duration of fludarabine phosphate used in a daily times five, every four week schedule as salvage therapy for patients with small cell carcinoma of the lung and to define the qualitative and quantitative toxicities of fludarabine phosphate administered in a Phase II study.

Technical Approach: All patients will receive fludarabine phosphate 18 mg/M² daily times five days to be given as a rapid IV infusion over 30 minutes. Courses of fludarabine phosphate will be given for five days every 28 days. Patients showing a complete response or partial response will continue to receive therapy until disease relapse or until they have received therapy for one year after achieving a complete remission. Patients with progressive disease after two course of therapy or relapse will have therapy with fludarabine phosphate discontinued. An adequate trial will consist of 8 weeks of therapy (2 courses).

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/55 Status: Suspended

Title: SWOG 8403: Evaluation of Fludarabine Phosphate in Squamous Cell Carcinoma of the Head and Neck Region, Phase II

Start Date: 19 Apr 85 Estimated Completion Date: Mar 87

Dept/Svc: Medicine/Hematology Facility: MAMC

Principal Investigator: MAJ Thomas J. Baker, MC

Associate Investigators:

COL F.H. Stutz, MC MAJ Timothy O'Rourke, MC

LTC Irwin B. Dabe, MC CPT David Bryson, MC

MAJ Howard Davidson, MC CPT Michael Stone, MC

Key Words: fludarabine phosphate, response rate, remission duration, squamous cell carcinoma, head and neck

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To determine the response rate and remission duration in patients with advanced squamous cell carcinoma of the head and neck treated with fludarabine phosphate and to define further the qualitative and quantitative toxicities of fludarabine phosphate.

Technical Approach: Patients who have squamous cell carcinoma of the head and neck region who have not received prior chemotherapy (up front "adjuvant" chemotherapy is allowed) will be treated with one of two dosage schedules. Patients who are good risk (no prior chemotherapy or radiation therapy) will receive fludarabine phosphate 25 mg/M² daily times 5 days, repeated every 28 days. Poor risk patients (prior chemo or radiation therapy) will receive fludarabine phosphate 13 mg/M² daily times 5 days every 28 days, continued for as long as it controls the tumor. An adequate trial will be defined as four weeks (one course) of therapy with fludarabine phosphate.

Progress: No patients entered at MAMC. This protocol has been suspended, pending further study of neurotoxicity.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/43 Status: Suspended

Title: SWOG 8409: Evaluation of Fludarabine Phosphate in
Refractory Multiple Myeloma, Phase II

Start Date: 15 Mar 85 Estimated Completion Date: Feb 87

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Thomas M. Baker, MC

Associate Investigators:

COL F.H. Stutz, MC

MAJ Timothy O'Rourke, MC

LTC Irwin B. Dabe, MC

CPT David Bryson, MC

LTC Howard Davidson, MC

CPT Michael Stone, MC

Key Words: fludarabine phosphate, refractory, multiple myeloma

Accumulative MEDCASE

Est Accumulative

Periodic Review

Cost: -0-

OMA Cost: -0-

Results: N/A

Study Objective: To determine the response rate and response duration to fludarabine phosphate in patients with refractory multiple myeloma when treated on a daily times five, every three week schedule and to define the qualitative and quantitative toxicities of fludarabine phosphate administered in a Phase II setting.

Technical Approach: Patients with multiple myeloma who are no longer responsive to standard chemotherapy will be treated with fludarabine phosphate, 15 mg/M², IV daily times five, repeated every 3 weeks. Poor risk patients will receive 12 mg/M². Patients with progression of disease after two courses of therapy will be taken off study. Patients with a complete remission will receive three additional courses beyond the point of achieving a complete remission and followed with no further treatment. Patients who obtain a partial remission will be treated until disease progression or until a total of 12 courses has been given. Patients with stable disease after two courses can receive an additional three courses at the discretion of the treating physician.

Progress: No entries at MAMC.

This study has been suspended, pending evaluation of neurotoxicity.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/09 Status: Completed

Title: SWOG 8410: Combination Chemotherapy of Intermediate and High-Grade Non-Hodgkin's Lymphoma with m-BACOD, Phase II

Start Date: 16 Nov 84 Estimated Completion Date: Oct 86

Dept/Svc: Medicine/Oncology Service Facility: MAMC

Principal Investigator: MAJ Thomas M. Baker, MC

Associate Investigators:

COL F.H. Stutz, MC

MAJ Timothy O'Rourke, MC

LTC Irwin B. Dabe, MC

CPT David Bryson, MC

LTC Howard Davidson, MC

CPT Michael Stone, MC

Key Words: lymphoma, non-Hodgkin's, chemotherapy, combination

Accumulative MEDCASE

Est Accumulative

Periodic Review

Cost: -0-

OMA Cost: -0-

Results: N/A

Study Objective: To determine an approximate complete remission rate and remission duration for the treatment program of cyclophosphamide, doxorubicin, vincristine, dexamethasone, and bleomycin with intervening moderate dose of methotrexate and leucovorin rescue (m-BACOD) in patients with intermediate and high grade non-Hodgkin's lymphoma and to assess the feasibility of using this regimen in the SWOG with the intent of using m-BACOD in a future Phase III trial.

Technical Approach: Patients will be stratified according to marrow reserve status and creatinine clearance. Treatment will consist of ten 3-week courses. Cytosan, adriamycin, vincristine, and bleomycin will be given IV on day 1. Dexamethasone will be given by mouth daily for 5 days, and methotrexate will be given on days 8 and 15 at 200 mg/M². Leucovorin will be given 10 mg/M² by mouth after each methotrexate injection every 6 hours for eight doses. An adequate trial will be defined as the completion of two complete cycles of m-BACOD. Patients with documented progressive disease or less than complete response after an adequate trial will be taken off study. Those with complete response will continue on study with no further chemotherapy.

Progress: Two patients were entered at MAMC with no adverse reactions.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 85/44	Status: On-going
Title: SWOG 8411: Evaluation of DTIC in Metastatic Carcinoid, Phase II		
Start Date: 15 Mar 85	Estimated Completion Date: Feb 87	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: MAJ Thomas Baker, MC		
Associate Investigators:		
COL F.H. Stutz, MC	MAJ Timothy O'Rourke, MC	
LTC Irwin B. Dabe, MC	CPT David Bryson, MC	
LTC Howard Davidson, MC	CPT Michael Stone, MC	
Key Words: carcinoid, metastatic, non-amenable to surgery, DTIC		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: N/A

Study Objective: To determine the effectiveness of dimethyl triazeno imidazole carboxamide (DTIC) in the treatment of metastatic carcinoid and to determine the survival of patients with metastatic carcinoid receiving DTIC.

Technical Approach: Patients with metastatic carcinoid not amenable to surgery who have had no prior chemotherapy or have had no radiotherapy with six weeks will be eligible. Patients will receive DTIC, 850 mg/M² IV, every 28 days. Poor risk will receive 650 mg/M². An adequate trial will be defined as two cycles of therapy with evidence of increasing disease. Patients with stable disease or in PR of CR will continue on therapy until increasing disease or relapse occurs.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 85	Protocol No.: 85/45	Status: On-going
Title: SWOG 8418: Evaluation of Cis-Diamminedichloroplatinum in Unresectable Diffuse Malignant Mesothelioma, Phase II		
Start Date: 15 Mar 85	Estimated Completion Date: Feb 87	
Dept/Svc: Medicine/Oncology	Facility: MAMC	
Principal Investigator: MAJ Thomas Baker, MC		
Associate Investigators:		
COL F.H. Stutz, MC	MAJ Timothy O'Rourke, MC	
LTC Irwin B. Dabe, MC	CPT David Bryson, MC	
LTC Howard Davidson, MC	CPT Michael Stone, MC	
Key Words: mesothelioma, diffuse, unresectable, cis-platinum		
Accumulative MEDCASE	Est Accumulative	Periodic Review
Cost: -0-	OMA Cost: -0-	Results: N/A

Study Objective: To test the response rate of cis-platinum in previously untreated patients with unresectable diffuse malignant mesothelioma and to test the response rate of cis-platinum in patients with unresectable diffuse malignant mesothelioma previously treated with, at most, one prior chemotherapy program.

Technical Approach: All patients will receive cisplatinum, 100 mg/M², rapid IV infusion every 21 days as tolerated. Adequate hydration will be closely monitored. Treatment will be repeated every three weeks as tolerated by the patient until tumor progression is documented in the presence of drug toxicity. An adequate trial will be defined as one course of therapy followed by a 21 day observation period. For statistical purposes, patients will be stratified as no prior chemotherapy or one prior chemotherapy program.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/63 Status: Completed

Title: SWOG 8421: Cyclophosphamide, Methotrexate, and 5-Fluorouracil in the Treatment of Stage D₂ Adenocarcinoma of the Prostate, Phase II

Start Date: 24 May 85 Estimated Completion Date: Apr 87

Dept/Svc: Medicine/Hematology Facility: MAMC

Principal Investigator: MAJ Thomas Baker, MC

Associate Investigators: MAJ Howard Davidson, MC

COL William Belville, MC MAJ Timothy O'Rourke, MC

COL F.H. Stutz, MC CPT David Bryson, MC

LTC Irwin B. Dabe, MC CPT Michael Stone, MC

Key words: cyclophosphamide, methotrexate, 5-FU, stage D₂ adenocarcinoma, prostate

Accumulative MEDCAGE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To test the effectiveness and toxicity of CMF (Cyclophosphamide, methotrexate, and 5-FU) in the treatment of Stage D₂ adenocarcinoma of the prostate.

Technical Approach: Patients must have a histologically metastatic adenocarcinoma of the prostate, have failed endocrine manipulation, have had no prior chemotherapy, and have not had any prior radiotherapy to areas used for following disease or hormonal therapy. Patients will be stratified into three groups: (1) patients with measurable disease other than prostate by exam, chest x-ray, and/or CT scan of the pelvis, with or without bone metastases or elevated markers; (2) patients with bone or other nonmeasurable but evaluable disease plus elevated serum markers and/or symptoms; and (3) patients with disease by bone scan only, asymptomatic. All patients will receive cyclophosphamide, 100 mg/M² PO, every day, methotrexate, 15 mg/M² IV, day 1 of every week, and 5-FU, 300 mg/M² IV, day 1 of every week. CMF will be given continuously unless toxicity dictates delays. An adequate trial will be defined as eight weeks of treatment.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/46 Status: On-going

Title: SWOG 8460: Combination Chemotherapy (COPE) and Radiation Therapy for Extensive Small Cell Lung Cancer, Phase II, Pilot

Start Date: 15 Mar 85 Estimated Completion Date: Feb 87

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

COL F.H. Stutz, MC MAJ Timothy O'Rourke, MC

LTC Irwin B. Dabe, MC CPT David Bryson, MC

MAJ Thomas Baker, MC CPT Michael Stone, MC

Key Words: cancer, lung, small cell, chemotherapy, radiation

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To determine the overall and complete response rates to the combination of cyclophosphamide, VP-16 (etoposide) and cis-platinum followed by vincristine plus porphyllactic or therapeutic whole brain and chest irradiation in responders in extensive small cell carcinoma of the lung, to assess qualitative and quantitative toxicities of this treatment program, and to measure time to progression and survival of the patients treated.

Technical Approach: Patients will be stratified according to basis of diagnosis and performance status. All patients will receive COPE induction chemotherapy for a total of four cycles. Therapy will be given every three weeks for four cycles, delivered over approximately 12 weeks. Radiotherapy will be given to responding patients (CR and PR) beginning on or about week 12, to include chest and whole brain. Patients presenting with initial brain involvement will begin therapeutic brain irradiation on Day 1 with induction chemotherapy with chest irradiation to begin at approximately Day 84. Late intensification will consist of two additional courses of COPE given on weeks 24 and 48. An adequate trial will be defined as one course of induction therapy (three weeks on study).

Progress: Four patients have been entered at MAMC with no unexpected toxicities.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 84/79 Status: Terminated

Title: SWOG 8490: Phase II Study of PAC (Cis-Platinum, Adriamycin, and Cyclophosphamide) in Treatment of Invasive Thymoma, Intergroup Study

Start Date: 21 Sep 85 Estimated Completion Date: Aug 86

Dept/Svc: Medicine/Hematology Facility: MAMC

Principal Investigator: MAJ Thomas Baker, MC

Associate Investigators:

COL F.H. Stutz, MC

MAJ Timothy O'Rourke, MC

LTC Irwin B. Dabe, MC

CPT David Bryson, MC

LTC Howard Davidson, MC

CPT Michael Stone, MC

Key Words: thymoma, invasive, chemotherapy, PAC

Accumulative MEDCASE

Est Accumulative

Periodic Review

Cost: -0-

OMA Cost: -0-

Results: N/A

Study Objective: To determine the objective response rate in extensive and limited invasive thymoma treated with PAC and to determine the duration of remission of patients with limited invasive thymoma treated with split course radiotherapy plus PAC and patients with extensive disease treated with PAC alone.

Technical Approach: Patients will receive PAC on day 1 every three weeks. After two courses of PAC, patients will be evaluated. Non-responders will go off study. Responders with limited disease will receive split course radiotherapy to be given in weeks 7, 8, and 12, followed four weeks later by six additional courses of PAC. Responders with extensive disease or limited disease with prior chest radiotherapy will receive six additional courses of PAC at three week intervals.

Progress: No entries at MAMC. Study was terminated due to low accrual rate.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/56 Status: On-going

Title: SWOG 8493: Simultaneous Cis-Platinum and Radiation Therapy Compared with Standard Radiation Therapy in the Treatment of Unresectable Squamous or Undifferentiated Carcinoma of the Head and Neck

Start Date: 19 Apr 85 Estimated Completion Date: Feb 87

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

COL F.H. Stutz, MC MAJ Timothy O'Rourke, MC

LTC Irwin B. Dabe, MC MAJ Michael D. Stone, MC

MAJ Thomas M. Baker, MC CPT David R. Bryson, MC

Key Words: carcinoma, head and neck, cis-platinum, radiotherapy

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To compare the effectiveness of simultaneous cis-platinum radiation therapy with that of radiotherapy alone in improving patient survival and the disease-free interval in patients with unresectable Stage III-IV squamous cell or undifferentiated carcinoma of the head and neck; to compare the toxicity of cis-platinum radiotherapy with that of radiotherapy alone in patients with locally advanced head and neck cancer, and to compare patterns of relapse or treatment failure between the two regimens.

Technical Approach: Patients will be stratified by performance status, primary tumor, and nodal status. Patients will be randomized to receive radiotherapy alone or radiotherapy plus concomitant cis-platinum, 20 mg/M² every seven days, for the duration of radiotherapy. At the completion of therapy on either treatment, all patients will be observed until progression, at which time they will be taken off study and offered alternative therapy.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/77 Status: On-going

Title: SWOG 8494: A Comparison of Leuprolide with Flutamide and Leuprolide in Previously Untreated Patients with Clinical Stage D₂ Cancer of the Prostate, Phase III, Intergroup (INT-0036)

Start Date: 19 Apr 85 Est Completion Date: Feb 87

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Thomas Baker, MC

Associate Investigators: LTC Howard Davidson, MC

COL William D. Belville, MC CPT David Bryson, MC

LTC Irwin B. Dabe, MC CPT Michael Stone, MC

Key Words: cancer, prostate, untreated, leuprolide, flutamide

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To evaluate and compare the efficacy of the combination of leuprolide and flutamide versus leuprolide alone followed at time of progression by addition of flutamide in the treatment of newly diagnosed, previously untreated patients with metastatic (D₂) adenocarcinoma of the prostate and to compare time to progression, survival, response rate, and toxicity of patients treated with either treatment program.

Technical Approach: Patients with histologically confirmed Stage D₂, previously untreated prostate cancer will be randomized to leuprolide plus flutamide or leuprolide plus placebo. Those given leuprolide plus flutamide will go off study at progression. Those on leuprolide plus placebo will have flutamide added to the therapy, which will continue until progression at which time they will taken off study and followed.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/78 Status: On-going

Title: SWOG 8503: Combination Chemotherapy of Intermediate and High Grade Non-Hodgkin's Lymphoma with ProMACE-Cytabom, Phase II

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Howard Davidson, MC

Associate Investigators:

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Key Words: lymphoma, non-Hodgkin's, chemotherapy, ProMACE-Cytabom

Accumulative MEDCASE

Est Accumulative

Periodic Review

Cost: -0-

OMA Cost: -0-

Results: N/A

Study Objective: To determine the complete remission rate, remission duration, and survival duration for patients with intermediate and high grade non-Hodgkin's lymphomas treated with cyclophosphamide, doxorubicin, etoposide, and prednisone, followed by cytarabine, bleomycin, vincristine, and methotrexate with leukovorin (ProMACE-CytaBOM) and to assess the feasibility of using this regimen in the Southwest Oncology Group with the intent of using ProMACE-CytaBOM in a future Phase III trial.

Technical Approach: Patients with no prior chemotherapy or radiotherapy will receive cyclophosphamide, adriamycin, and etoposide IV on day 1, prednisone PO days 1-14, cytarabine, bleomycin, vincristine, and methotrexate IV on day 8, and leukovorin PO every six hr times four, beginning 24 hours after methotrexate. All patients will be treated until a complete clinical remission is obtained and two additional cycles of chemotherapy have been given or until progressive disease develops. A minimum of six cycles must be given to each CR before therapy is discontinued. All patients will receive initial treatment with full doses of drugs regardless of age or other risk factors.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/73 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 Study, EST 2382)

Start Date: 28 Jun 85 Est Completion Date: May 87

Dept/Svc: Medicine/Oncology Facility: MAMC

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Key Words: carcinoma, head and neck, squamous, chemotherapy, radiotherapy, surgery

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

Study Objective: To test whether the addition of chemotherapy to surgery and radiotherapy prolongs disease-free survival and survival between the two study groups; to test whether the addition of chemotherapy to surgery and radiotherapy increases local control rates at the primary site and/or the cervical neck nodes; and to determine if the patterns of failure have been changed with the addition of chemotherapy.

Technical Approach: After surgery, patients will be randomized to either chemotherapy plus radiation therapy or radiation therapy alone. In the chemotherapy plus radiation therapy group, the chemotherapy will start 2-4 weeks after surgery and the radiotherapy will start approximately two weeks after completing chemotherapy. In the radiation therapy alone group, the radiation therapy will begin 2-4 weeks after surgery. Chemotherapy will be cis-platinum give day 1 and 5 FU given days 1-5 and repeated every 21 days for three courses. Patients who develop local or distant recurrence following therapy will be treated at the physician's discretion.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 85 Protocol No.: 85/64 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: 24 May 85 Estimated Completion Date: Apr 87

Dept/Svc: Medicine/Oncology Facility: MAMC

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Key Words: adenocarcinoma, colon, surgical, levamisole, 5-FU

Accumulative MEDCASE Est Accumulative Periodic Review

Cost: -0- OMA Cost: -0- Results: N/A

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 followup 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 followup without adjuvant therapy, adjuvant therapy with levamisole alone, or adjuvant therapy with levamisole plus 5-FU.

Progress: One patient has been entered at MAMC with no unexpected side effects.

APPENDIX I

GUIDING PRINCIPLES OF THE CARE AND USE OF ANIMALS

Approved by the
Council of the American Physiological Society

Only animals that are lawfully acquired shall be used in this laboratory, and their retention and use shall be in every case in strict compliance with state and local laws and regulations.

Animals in the laboratory must receive every consideration for their bodily comfort; they must be kindly treated, properly fed, and their surroundings kept in a sanitary condition.

Appropriate anesthetics must be used to eliminate sensibility to pain during operative procedures. Where recovery from anesthesia is necessary during the study, acceptable technic to minimize pain must be followed. Curarizing agents are not anesthetics. Where the study does not require recovery from anesthesia, the animal must be killed in a humane manner at the conclusion of the observations.

The postoperative care of animals shall be such as to minimize discomfort and pain and in any case shall be equivalent to accepted practices in schools of veterinary medicine.

When animals are used by students for their education or the advancement of science, such work shall be under the direct supervision of an experienced teacher or investigator. The rules for the care of such animals must be the same as for animals used for research.

APPENDIX II

Recommendations from the Declaration of Helsinki

I. Basic Principles

1. Clinical research must conform to the moral and scientific principles that justify medical research and should be based on laboratory and animal experiments or other scientifically established facts.

2. Clinical research should be conducted only by scientifically qualified persons and under the supervision of a qualified medical man.

3. Clinical research cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject.

4. Every clinical research project should be preceded by careful assessment of inherent risks in comparison to foreseeable benefits to the subject or to others.

5. Special caution should be exercised by the doctor in performing clinical research in which the personality of the subject is liable to be altered by drugs or experimental procedure.

II. Clinical Research Combined with Professional Care

1. In the treatment of the sick person, the doctor must be free to use a new therapeutic measure, if in his judgment it offers hope of saving life, reestablishing health, or alleviating suffering.

If at all possible, consistent with patient psychology, the doctor should obtain the patient's freely given consent after the patient has been given a full explanation. In case of legal incapacity, consent should also be procured from the legal guardian; in case of physical incapacity, the permission of the legal guardian replaces that of the patient.

2. The nature, the purpose, and the risk of clinical research must be explained to the subject by the doctor.

3. a. Clinical research on a human being cannot be undertaken without his free consent after he has been informed; if he is legally incompetent, the consent of the legal guardian should be procured.

b. The subject of clinical research should be in such a mental, physical, and legal state as to be able to exercise fully his power of choice.

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