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DEPARTMENT OF CLINICAL INVESTIGATION

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The findings in this report are not to be construed as an official Department of the Army position unless so designated by other authorized documents.

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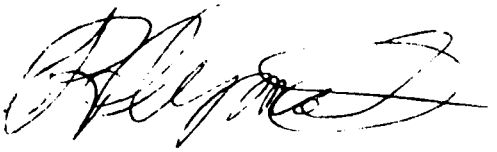
In conducting the research described in this report, the investigators adhered to the "Guide for the Care and Use of Laboratory Animals" as prepared by the Committee on the Care and Use of Laboratory Animals of the Institute of Laboratory Animal Resources, National Institutes of Health, and Title 9,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

ACKNOWLEDGEMENTS

I would like to take this opportunity to thank Nancy Whitten for the effort which is obvious in the compilation of this publication.

FORWARD

During the past fiscal year, research at Madigan Army Medical Center has proceeded well as is evidenced by the publications and presentations from the various departments. The research endeavors have been supported vigorously by our headquarters at Madigan to include BG Darryl Powell, Colonel Leslie Burger, and Colonel Thurman Pittman. Without the support of these individuals productivity would have been much less. In addition, the Clinical Investigation Activity at Health Services Command has increasingly shown responsiveness to problems that have occurred, and we would like to thank them for their support in the last year. Finally, the staff at the Department of Clinical Investigation, to include LTC Higbee, MAJ Hannan, MAJ Hayre, CPT Friedl, Mrs. Nancy Whitten, and Mrs. Eugenia Hough, as well as the animal and laboratory support staff, have performed in an exemplary manner during the past fiscal year. Their work reflects not only upon this department but upon the entire hospital. This report is a summary of the activities which have taken place in the research arena at Madigan Army Medical Center during fiscal year 1987.



STEPHEN R. PLYMATE, M.D.
COL, MC
Chief, Department of
Clinical Investigation

UNIT SUMMARY FY 87

1. Objective

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

2. Technical Approach

DESCRIPTION	MANPOWER RANK	MOS
Chief PLYMATE, Stephen R., M.D., COL, MC	O6	61C9A
C, Clinical Studies Service JONES, Robert E., M.D., LTC, MC	O5	61C9B
C, Surg & Animal Care Svc (Oct-Dec 86) YARBROUGH, Leslie, D.V.M., MAJ, VC	O4	64C9B
C, Surg & Animal Care Svc (Jan-Sep 87) HAYRE, Michael D., D.V.M., MAJ, VC	O4	64C9B
C, Microbiology Svc HIGBEE, James W., Ph.D., LTC, 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. (Sep-Jun 86)	E6	91T3R
NCOIC SGT CAMPBELL, Naomi (Jul-Sep 87)	E5	91T2R
Med Lab Spec SP4 THOMAS, Gregory (Sep 86-Aug 87)	E4	92B10
Med Lab Spec SP4 GONZALEZ/RESTO, Alexander (Sep 87)	E4	92B10
OR Tech SGT ROBBINS, John L.	E5	91D2R
Vet Animal Spec SGT SCHILLER, Bradley J.H. (Jan-Sep 87)	E5	91T2R
Vet Animal Spec SP4 WESTMORELAND, Jacalyn	E4	91T10

DESCRIPTION	RANK	MOS
Med Tech GARRISON, Mina J. (Oct 86-May 87)	GS9	0644
Med Tech KETTLER, Thomas M.	GS9	0644
Med Tech MATEJ, Louis A.	GS9	0644
Med Tech WRIGHT, JAMES (Aug-Sep 87)	GS9	0644
Edit Asst/Steno WHITTEN, Nancy J.	GS6	1087
Sec/Steno HOUGH, Eugenia R.	GS5	0318
Maintenance Worker KAEO, Curtis	WG7	4749
Computer Programmer Analyst PATIENCE, Troy (temporary) (Aug-Sep 87)	GS7	0334

FUNDING FY 86

MEDCASE Equipment	$158,000.00
Capital Equipment	21,917.00
Civilian Salaries	153,403.00
Consumable Supplies	106,997.00
Contractual Services	26,489.00
TDY	1,750.00
Transportation	0.00
Rent	600.00
TOTAL	$469,156.00

3. Progress

During FY 87 there were 315 active protocols that received administrative and/or technical support during the year. Of these, 213 are presently ongoing; 69 were completed; 23 were terminated, and 10 are in a suspended status awaiting revisions.

There were 59 publications, 24 articles are in press, and an additional 25 papers have been submitted for consideration for publication. There were 69 presentations at regional, national or international meetings.

COMMITTEE MEMBERS

Commander

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

INSTITUTIONAL REVIEW BOARD

Comprised of the Clinical Investigation Committee,
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†*Chief, Professional Services
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American Lake VA Medical Center

*Member, Human Use Committee
†Member, Animal Use Committee

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 1987:

Polzin, William J. CPT, MC	The Effect of Estrogen on the Renal Actions of Calcium Regulating Hormones in Postmenopausal Women

Other Nominees were:

Broder, Jeffrey N. CPT, MC	Efficacy of the Abusa Stick and Physician Clinical Assessment for the Rapid Estimation of the Blood Alcohol Level in the Emergency Department
David, David R. CPT, MC	Descriptive Analysis of the Latex Fixation Test for Rapid Detection of Group B Streptococci in Suspected Chorioamnionitis
Pearce, William A. CPT, MC	Ultrasonography in the Initial Evaluation of Acute Pyelonephritis
Robertson, Andrew W. MAJ, MC	A Comparison of Treatment of Lower Tract Infections in Obstetric Patients Utilizing Three Different Dosage Regimens of Amoxicillin-Clavulanic Acid
Robertson, Andrew W. MAJ, MC	External Cephalic Version at Term: Tocolytic Necessary?
Rozanski, Thomas A. CPT, MC	Effects of Androgen Depletion on the Growth of Human Prostate Tumor in Athymic Mice

PUBLICATIONS - FY 87

DEPARTMENT OF CLINICAL INVESTIGATION

Publications:

Chute CG, Baron JA, Plymate SR, Kiel DP, Lozner EC: Endogenous Sex Steroids and Heart Disease in Men. Amer J Epidem, Sept 87

Friedl KE, DeWinne CM, Taylor RL.: The Use of the Durnin-Womersley Generalized Equations for Body Fat Estimation and Their Impact on the Army Weight Control Program. Mil Med 152(3):150-55, 1987

Friedl KE, Holmes WN: The Effect of Relative Humidity on Osmoregulation in the Squirrel Monkey *(Saimiri sciureus)*. Primates 27 (4): 465-70, 1986

Garden GA, Hannan CJ, Spencer CA, Plymate SR: The Role of Non-sex Hormone Binding Globulin Bound Testosterone (nSHBG-T) on Luteinizing Hormone (LH) in Hyperthyroid Men. Clinical Research 35 (1): 119, 1987

Garden GA, Hannan CJ, Spencer CA, Plymate SR: The Role of Non-sex Hormone Binding Globulin Bound Testosterone (nSHBG-T) on Luteinizing Hormone (LH) in Hyperthyroid Men. Clin Research 35(3): 395, 1987

Jacob WH, Friedl KE, Douglas JF, Hodge JW, Dick KE: Product Evaluation of the Dual Barrel Autoinjector, MARK II. Proceedings of the 6th Medical Chemical Defense Bioscience Review, US Army Med Res Inst of Chem Defense, Aug 87.

Kettler T (ed): Inky Captions. Newsletter of the Tacoma Mushroom Society. October 86 - September 87 editions

Nagao RR, Plymate SR, Berger RE, Perrin EB, Paulsen CA: Comparison of Gonadal Function Between Fertile and Infertile Men with Varicoceles. Fertil Steril 46(5): 930-33, 1986

Plymate SR, Nagao RR, Muller CH, Paulsen CA: The Use of Sperm Penetration Assay in Evaluation of Men with Varicocele. Fertil Steril 47(4): 680-83, 1987

Plymate SR, Vaughan GM, Mason AD, Pruitt BA: Central Hypogonadism in Burned Men. Hormone Res 27(3):152-58, 1987

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Friedl KE, Plymate SR, Bernhard WN, Mohr LC: Elevation of Plasma Estradiol in Healthy Men During a Mountaineering Expedition. Hormone and Metabolic Res

Lampe TH, Fariss BL, Risse SC, Plymate SR: Laboratory Evaluation for Cushing's Disease in Psychiatric Patients with Cortisol Nonsuppression Following the Overnight Dexamethasone Suppression Test. Biol Psychiatry

Lampe TH, Plymate SR, Risse SC, Cubberley L, Kopeikin H, Raskind MA: TSH Responses to Two TRH Doses in Males with Alzheimer's Disease. Psychoneuroendocrinology

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

Plymate SR, Paulsen CA: Klinefelter's Syndrome. IN: The Genetic Basis of Common Diseases, Arno Motulsky (ed), Oxford Univ Press

Plymate SR, Paulsen CA: Male Hypogonadism: IN: Principals and Practices of Endocrinology and Metabolism, K Becker (ed), Lippincott, 1987

Plymate SR, Ward GS, Friedl KE, Matej LA: Maintenance of Spermatogenesis with Normal Germ Cell Relationships in Testosterone Treated Rhesus Monkeys. Ann NY Acad Sci

Submitted for consideration for publication:

Friedl KE, Plymate SR: Parallel Changes of HDL-cholesterol (HDLC) and Testosterone Binding Globulin (TeBG) in Body Builders During Self Administration of Anabolic Steroids. JAMA

Hannan CJ: β-phenylethylamine Induced Changes in Brain Monoamine Metabolites of Retired Breeder Gerbils. Neuroscience Letters

Hannan CJ, Kettler TM, Artru AA, Aronstam R: Blood-Brain Barrier (BBB) Permeability During Hypocapnia in Halothane Anesthetized Monkeys. Ann NY Acad Sci

Hannan CJ, Kettler TM, Friedl KE, Plymate SR.: Analysis of Apolipoprotein A-I by High Performance Liquid Chromatography and Radioimmunoassay. Clinical Chemistry

Plymate SR, Matej LA, Jones RE, Friedl KE: Regulation of Sex Hormone Binding Globulin (SHBG) Production in the Human Hepatoma (Hep G2) Cell Line by Peptide Hormones and Sex Steroids. JCEM

Tenover JS, Matsumoto AM, Plymate SR, Bermner WJ: The Effects of Aging in Norman Men on Bioavailable Testosterone and Brain Control of Luteinizing Hormone Secretion: Response to Clomiphene Citrate. JCEM

DENTAL ACTIVITY

Publication:

Hand Held X-Ray (Appraisal Report). ADEA Report #A170, 30 Sep 87.

DEPARTMENT OF EMERGENCY MEDICINE

Publications:

Dronen SC: Lack of Efficacy of Naloxone in a Fixed-Volume Hemorrhage Model. Ann Emer Med 15:1145-50, 1986

Gibson DE: Treating Meningitis. Ann Emerg Med 16(5):601-02, 1987

Gibson DE, Verono AA: Dentistry in the Emergency Department. J Emerg Med 5(1):35-44, 1987.

Prete MR, Hannan CJ, Burkle FM: Plasma Atropine Concentrations via the Intravenous, Endotracheal, and Intraosseous Routes of Administration. Amer J Emerg Med 5(2):100-04, 1987

Robinson M, Seward PN: Environmental Hypothermia in Children. Pediatr Emerg Care 2(4):254-57, 1986

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Broder JN: Efficacy of the Abusa Stick and Physician Clinical Assessment for Rapid Estimation of the Blood Alcohol Level in the Emergency Department. Ann Emer Med

DEPARTMENT OF FAMILY PRACTICE

In Press:

Saglio SD, Henley CE: Rapid Assay Kits for Common Microbiologic Agents. Am Fam Physician 35(5):169-78, 1987

DEPARTMENT OF MEDICINE

Publications:

Addison JF: Calcium Carbonate as a Phosphate Binder. New England Journal of Medicine 38(2):110, 1987.

Carpenter PD, Heppner BT, Gnann JW: DF-2 Bactermia Following Cat Bites. Report of Two Cases. Am J Med 83(3):621-23, 1987

Charney DI, Mercado DL: Secretory Diarrhea and Thyrotoxicosis (letter to the editor). Ann Int Med 106(2):332, 1987.

Cox RA, Britt LA, Michael RA: Isolation of *Coccidioides immitis* F Antigen by Immunoaffinity Chromatography with Monospecific Antiserum. Infection and Immunity, 55:227, 1987.

Horan MP, Redmond J, Gehle D, Dabe IB, Fort SL: Post Polycythemic Agnogenic Myeloid Metaplasia, Sweet's Syndrome, and Acute Myeloid Leukemia. J Amer Acad Dermatol 16(2):458-62, 1987

Jade KB, Lyons MF, Gnann JW: *Paecilomyces lilacinus* Cellulitis in an Immunocompromised Patient. Arch Dermatol 122(10):1169-70, 1986

Jones RE, Plymate SR: Interactions Between Selected Fatty-Acids and the Activation of Palmitic Acid in Spermatozoa. J Andrology 8(1):40, 1987.

Kollef MH: Chronic Ammonium Hydroxide Exposure. Ann Int Med 107 (1):118, 1987

Kollef MH: Elevated Lactate Levels Without Metabolic Acidosis in Medical Treatment of Obstructive Lung Disease. Amer Rev Respir Dis 135(4), 1987.

Stone MD, Richardson MG: Pulmonary Toxicity of Lomustine. Cancer Treatment Reports 71(7-8):786-87, 1987

In Press:

Black JW, Grover BS: A Hazard or Pressure Support Ventilation. Chest

Cushner HM, Lindberg JS, Copley JB, Foulks CJ: Calcium Citrate, A NonaluminumContaining Phosphate-Binding Agent for Treatment of Patients with Chronic Renal Failure. Kidney International

Jones RE, Plymate SR: Thioesterification of Polyunsaturated Fatty Acids in Human Sperm. Ann NY Acad Sci

Knodel DH, Kirk JW: Ovarian Cancer Presenting with Exertional Hypotension Secondary to Inferior Vena Cava Obstruction. So Med J

Kollef MH: Hyperlactatemia Without Acidosis in Medical Treatment of Obstructive Lung Disease. Chest

Redmond J, Friedl KE, Cornett P, Stone M, O'Rourke T, George CB: Clinical Usefulness of an Algorithm for the Early Diagnosis of Spinal Metastatic Disease. J Clin Oncol

Submitted for consideration for publication:

Campbell DL, Kessler JB: Pulmonary Function Evaluation in Army Aviators. J Occupational Med

Chamusco RF, Heppner BT, Newcomb EW, Sanders AC: Mitral Stenosis: An Unusual Association. Mil Med

Colman LK, Porter BA, Redmond J, III, Olson DO, Stimac GK, Dunning DM, Friedl KE: Comparison of Magnetic Resonance Imaging to Computer Tomography in the Early Diagnosis of Metastases to the Axial Skeleton. Cancer

Elam M, Laird JR, Johnson S, Stratton, JR: Swallow Syncope Associated with Complete Artrioventricular Block - A Case Report. West J Med

Jones RE, Plymate SR: Evidence for the Regulation of Fatty Acid Utilization in Human Sperm by Docosahexaenoic Acid. Biol Reproduc

Jones RE, Plymate SR: Synthesis of Docosahexaenoic Coenzyme in Human Spermatozoa: Evidence to Suggest a Single Fatty and Activating Enzyme in Sperm. Biochim Biophys Acta.

DEPARTMENT OF OB/GYN

Publications:

Duff P, Brady WK, Robertson AW: An Important Medical Use for the Baggie. NEJM (UK) 315(26):1681, 1986

Duff WP, Kopelman JN: Subclinical Intra-amniotic Infection in Asymptomatic Patients with Refractory Preterm Labor. Obstet Gynecol 68(5):756-59, 1987

Harlass F, Magelssen DJ, Soisson AP: Supernumerary Ovary. A Case Report J Repro Med 32(6):459-61, 1987

Ilika KL, Duff P: Use of the Urinary Director Appliance for Management of Voiding Problems after Radical Vulvectomy. Am J Obstet Gynecol 156(1): 1987

Kopelman JN, Duff P, Karl RD, Schipul AH, Read JA: Computed Tomographic Pelvimetry in the Evaluation of Breech Presentation. Obstet Gynecol 68(4):455-58, 1986.

Lee RB, Stone IK, Magelssen D, Belts RP, Benson WL: Presacral neurectomy for Chronic Pelvic Pain. Obstet Gynecol 68(4):517-21, 1986

In Press:

Duff WP: Prophylactic Antibiotics for Cesarean Delivery: A Simple Cost-Effective Strategy for Prevention of Postoperative Morbidity. Amer J OB GYN

Duff WP, Robertson AW, Read JA: Single-Dose Cefazolin Versus Cefonicid for Antibiotic Prophylaxis in Caesarean Delivery. Obstet Gyencol

Robertson AW, Kopelman J, Read JA, Duff WP, Magelssen D, Dashow E: External Cephalic Version at Term: Is a Tocolytic Necessary? Obstet Gynecol

Submitted for consideration for publication:

Duff WP, Southmayd K, Read JA: Outcome of Trial of Labor in Patients with a Single Prior Low Transverse Cesarean Section for Cystocia. Obstet Gynecol

Harlass FE, Magelssen DJ: Benefits of Posturethropexy Bladder Conditioning - Fact or Fiction? Obstet Gynecol

Robertson AW, Duff WP: A Comparison of Two Single Dose Antibiotic Regimens for Treatment of Uncomplicated Lower Urinary Tract Infections in Obstetric Patients. Obstet Gynecol

DEPARTMENT OF PATHOLOGY

Publications:

Price G, Paquet RJ, Rose HN: Adaptation of Technicon RA Systems Theophylline Reagents to the Coulter Dacos. Clin Chem 33(6): 1023, 1987

DEPARTMENT OF PEDIATRICS

Publications:

Brueckner RP, Guller B: QRS Areas Improve the Electrocardiographic Interpretation of Right Ventricular Hypertrophy. Comp Biomed Res 20(1):99-103, 1987.

Brunader REA, Moore DC: Evaluation of the Child with Growth Retardation. Am Fam Phys 35(2):165-76, 1987.

Jarrett RV, Jordan GD, Shankaran S, et al: Additional Statistical Analysis of Antenatal Phenobarbital for Prevention of Neonatal Intracerebral Hemorrahge. Am J Obstet Gynecol 156(2):1987

Jordan GD, Themelis NJ, Messerly SO, Jarrett RV, Garcia J, Frank CG: Doxapram and Potential Benzyl Alcohol Toxicity: A Moratorium on Clinical Investigation? Pediatrics 78(3): 540-41, 1986

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Moore DC: Prolonged Suppression of Hirsutism with Combination Therapy in an Adolescent with Insulin Resistance and Acanthosis Nigricans. J Adol Hlth Care 8(5):445-48, 1987

Onufer CN, Stephan MJ, Thuline HC, Char F: Chromosome 13 Long Arm Interstitial Deletion Associated with Features of Noonan Phenotype. Annales de Genetique 30(4): 236-39, 1987

Reynolds JF, Daniel A, Kelly TE, Gollin SM, Stephan MJ, Carey J, Adkins WN, Webb MJ, Char F, Jimenez JF, Opitz JM: Isochromosome 12p Mosaicism (Pallister Mosaic Aneuploidy or Pallister-Killian Syndrome): Report of 11 Cases. Amer J Med Genetics 27(2):257-74, 1987

Sweeney JK: Physiologic Adaptation of Neonates to Neurological Assessment. Phy Therapy 67(5): 768, 1987

Sweeney JK: The High-Risk Neonate. Developmental Therapy Perspectives. The Haworth Press, Inc., New York, 1987.

In Press:

Madden WA, Reeder J, Cragun W, Krug EF, Brown S: Evolution of Military Ethics Committees. Mil Med

Moore, D.C.: Precocious Sexual Development. Practice of Pediatrics

Olson TA, Fischer GW, Lupo MC,Garcia VF, Maybee DA, Hartman KR: Broviac Catheter Infections in Pediatric Hematology Oncology Patients. J Ped Surg

Submitted for consideration for publication:

Glassheim JW: Persistent Truncus Arteriosus: A Review of Diagnosis and Current Management. Amer J Dis Children

Hartman KR, Triche TT, Kinsella TJ, Miser JA: Histopathology: A Significant Prognostic Factor in Ewing's Sarcoma. A Review of 56 Cases of Distal Extremity Primary Tumors. Cancer

Nickels DA, Moore DC: Cortisol Response in Febrile Children. J Pediatrics

Rawlings JS, Garcia J: Predictive Value of Data on Length of Hospitalization of Premature Infants. Pediatrics

Weir MR: *Adolescents Blood Pressure Increases with Sexual Maturity.* J Adolescent Health Care

Weir MR: Atypical Idiopathic Hypercalciuria in an Adolescent. J Adolescent Health Care

Weir MR: Intravascular Injuries from Intramuscular Penicillin. Clinical Peds

PHARMACY SERVICE

Publications:

Abbasi I, Sorsby S: Prolonged Toxicity From Atenolol Overdose in an Adolescent. Clin Phar 5(10):836-37, 1986.

PREVENTIVE MEDICINE SERVICE

Publications:

Byrne J, Mulvihill JJ, Myers MH, Connelly RR, Naughton MD, Krauss MR, Steinhorn SC, Hassinger DD, Austin DF, Bragg K, Holmes GF, Holmes FF, Latourette HB, Weyer PJ, Meigs W, Teta MJ, Cook JW, Strong LC: Effects of Treatment on Fertility in Long-Term Survivors of Childhood or Adolescent Cancer. NEJM 317(21):1315-21, 1987.

Tomlinson JP, Lednar WM, Jackson JD: Risk of Injury in Soldiers. Mil Med 152(2):60, 1987

DEPARTMENT OF PSYCHIATRY

In Press:

Garland FN, Robichaud MR: Knowledge of Battle Fatigue Among Division Combat Medics and the Effectiveness of Training. Mil Med

DEPARTMENT OF RADIOLOGY

Publications:

Karl RD: Radiology for Todays Physical Therapist. 1. Physical Therapy 67(5): 762, 1987.

Karl RD: Radiology for Todays Physical Therapist. 2. Physical Therapy 67(5): 787, 1987.

DEPARTMENT OF SURGERY

Publications:

Arciero RA, Little JS, Liebenberg SP, Parr TJ: Irrigating Solutions Used in Arthroscopy and their Effect on Articular Cartilage, An *In Vivo* Study. Orthopedics 9(11): 1511-1515, 1986

Holzman RS, Worthen HM, Johnson KL: Anaesthesia for Children with Junctional Epidermolysis Bullosa (Letalis). Can J Anaesth 34 (4):395-99, 1987

Letterie GS, Venbrux A, Vaccaro JA: Coexistent Renal, Mullerian and Alimentary Tract Development Defects: A Case Report. J Reproduc Med 32(2):153-56, 1987

Mader TH, Carey WG, Friedl KE, Wilson WR: Intraoculr Lenses in Aviators: A Review of the U.S. Army Experience. Avia Space Environ Med 690-94, 1987

PUBLICATIONS - FY 87

Mader TH, Friedl KE, Mohr LC, Bernhard WN: Conjunctival Oxygen Tension at High Altitude. Avia Space Environ Med 58:76-79, 1987

Morris MR, Clark SK, Porter BA, Delbeco RJ: Chondrosarcoma of the Temporomandibular Joint - Case Report. Head Neck Surg 10(2):113-117, 1987

Morris MR, Moore DW, Shearer GL: Bilateral Multiple Benign Lymphoepithelial Cysts of the Parotid Gland. Otolaryngol Head Neck Surg 97(1):87-90, 1987

Morris MR, Woody EA: A Closer Look at the Thyroglossal Cyst. Ear Nose Throat J 66(9):42-45, 1987

Wells JR, Gernon WH: Bony Ossicular Fixation Using 2-Cyano-butylacrylate Adhesive. Arch Otolaryngology Head Neck Surg 113(6): 1987

Wells JR, Jaindl MA, Gernon WH: A Technique for the Placement of a Long-Term Hyperalimentation Catheter in the Head and Neck Oncology Patient Otolaryngol Head Neck Surg 95(5):598-601, 1986

In Press:

Fox CW, Vaccaro JA, Kiesling VJ, Belville WD: Seminal Vesicle Abscess: The Use of Computerized Coaxial Tomography for Diagnosis and Therapy. J Urology

Wheeler BR: Ankle Fractures in Slow-pitch Softball: The Army Experience. Mil Med

Submitted for consideration for publication:

Evans C, Vaccaro J, Storrs B, Christ P: Suprarenal Occurrence of an Adenomatoid Tumor. J Urology

Martindale RG, Witte M, Hodges G, Kelley J, Harris S, Andersen C: Necrotizing Fasciitis as a Complication of Percutaneous Endoscopic Gastrostomy. J Parenteral & Enteral Nutrition

VETERINARY ACTIVITY

Publication:

Romatowski J: What is Your Diagnosis - Radiologic Diagnosis - Osteochondrosis of the Right and Left Cubiti and Secondary Degenerative Hypertrophic Osteoarthritis. J Am Vet Med Assoc 190(2):211-212, 1987.

PRESENTATIONS - FY 1987

DEPARTMENT OF CLINICAL INVESTIGATION

Chute CG, Baron JA, Plymate SR, Kiel DP, Lozner EC: Endogenous Sex Steroids and Heart Disease in Men. SER Annual Meeting, Worcester, MA, Jun 87

Friedl KE, Plymate SR, Bernhard WN, Mohr LC: Elevation of Plasma Estradiol (E2) in Healthy Men During a Mountaineering Expedition. 5th International Hypoxia Symposium, University of Calgary, Alberta, Canada, Feb 87. Abstract #48

Garden GA, Hannan CJ, Spencer CA, Plymate SR: The Role of Non-sex Hormone Binding Globulin Bound Testosterone (nSHBG-T) on Luteinizing Hormone (LH) in Hyperthyroid Men. American Federation of Clinical Research (Western Region), Carmel, CA, Feb 87

Garden GA, Hannan CJ, Spencer CA, Plymate SR: The Role of Non-sex Hormone Binding Globulin Bound Testosterone (nSHBG-T) on Luteinizing Hormone (LH) in Hyperthyroid Men. American Federation of Clinical Research (National Meeting), San Diego, CA, May 87

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Hannan CJ, Kettler TM, Artru A, Aronstam R: Blood-Brain Barrier (BBB) Permeability During Hypocapnia in Halothane Anesthetized Monkeys. New York Academy of Sciences, 4th Colloquim in Biological Sciences, New York, NY, Nov 86.

Jacob WH, Friedl KE, Douglas JF, Hodge JW, Dick KE: Product Evaluation of the Dual Barrel Autoinjector, MARK II. Proceedings of the 6th Medical Chemical Defense Bioscience Review, US Army Medical Research Institute of Chemical Defense, Aug 87

Lampe TH, Veith RC, Plymate SR, Risse SC, Kopeikin H, Raskind MA: Norepi and BP Following ARH in Alzheimer's Disease. 140th Annual Meeting of the American Psychiatric Assoc, Chicago, IL, May 87.

Mohr LC, Friedl KE, Bernhard WN, Mader TH: Effectiveness of Acetazolamide Administered in the First 24 Hours of Mountain Ascent. 5th International Hypoxia Symposium, University of Calgary, Alberta, Canada, Feb 87, Abstract #32

Plymate SR, Jones RE, Matej LA, Friedl KE: Regulation of Sex Hormone Binding Globulin Production in Hep G2 Cells by Insulin. International Congress of Steroid Protein Interactions. Torino, Italy, Sep 87

Plymate SR, Muller CH, Paulsen CA: Relationship of Pregnancy to Gonadal Function Following Varicocele Repair. 43rd Annual Meeting of the American Fertility Society, Reno, NV, Sep 87.

Plymate SR, Myers JS, Matej LA, Bremner WJ: Diurnal and Age Related Changes in Testosterone, Sex-Hormone-Binding Globulin, and Calculated Free Testosterone. 3rd Annual Army Regional Meeting of the American College of Physicans, San Francisco, Oct 86.

Plymate SR, Paulsen CA, Muller CH: Studies on Testicular Function Following Varicocele Ligation. The American Fertility Society, Reno, NV, Sep 87.

Plymate SR, Ward GS, Friedl KE, Matej LA: Maintenance of Spermatogenesis with Normal Germ Cell Relationships in Testosterone Treated Rhesus Monkeys. 1986 Testis Workshop, Vanderbilt University, Nashville, TN, Oct 86.

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Tenover JS, Plymate SR, Matsumoto AM, Bremner WJ: The Effect of Aging in Normal Men on Bioavailable Testosterone. 69th Annual Meeting of the Endocrine Society, Indianapolis, IN, Jun 87, Abstract #869.

DEPARTMENT OF EMERGENCY MEDICINE

Broder JN: Efficacy of the Abusa Stick and Physician Clinical Assessment for Rapid Estimation of the Blood Alcohol Level in the Emergency Department. Emergency Medicine Tri-Services Symposium, San Antonio, TX, Apr 87

DEPARTMENT OF MEDICINE

Baker TM, Davidson H, Redmond J, Karl R: CT vs Bone Scan to Evaluate Response to Therapy of Bone Metastasis. American Society of Clin Oncology, Atlanta, GA, May 87.

Bryson D: Combined Pre Op Chemotherapy/RT for Locally Advanced Adenocarcinoma of the Rectum. Present Concepts in Internal Medicine, American College of Physicians Meeting, San Francisco, CA, Oct 86

Colman LK: CT, CT Myelography and MRI in the Diagnosis of Metastases to the Axial Skeleton. Present Concepts in Internal Medicine, American College of Physicians Meeting, San Francisco, CA, Oct 86

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Dabe IB: Management of ATP at Delivery. Present Concepts in Internal Medicine, American College of Physicians Meeting, San Francisco, CA, Oct 86.

Dunning D: Non-secretory Myeloma. Present Concepts in Internal Medicine, American College of Physicians Meeting, San Francisco, CA, Oct 86.

Jones RE, Plymate SR: Interactions Between Selected Fatty Acids and the Activation of Palmitic Acid in Spermatozoa. American Society of Andrology, Denver, CO, May 87.

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Kollef MH: Elevated Lactate Levels Without Metabolic Acidosis in Medical Treatment of Obstructive Lung Disease. Joint Annual Meeting of the American Lung Association and the American Thoracic Society, New Orleans, LA, May 87

Kollef MH, Cragun WH: Hyperlactatemia Without Metabolic Acidosis in Medical Treatment of Obstructive Lung Disease. Present Concepts in Internal Medicine, American College of Physicians Meeting, San Francisco, Oct 86.

Michael RA: Multitest Anergy in HIV Positive Patients. 15th Annual Meeting of the Association of Military Allergists, Feb 87.

Pearce WA, Gorman PD, Karl RD, Lyons MF: Ultrasonography in the Initial Evaluation of Acute Pyelonephritis. Present Concepts in Internal Medicine, American College of Physicians Meeting, San Francisco, CA, Oct 86. First place as best paper.

Pinholt EM, Kroenke KK: Reducing Polypharmacy in the Elderly: A Controlled Study. American Geriatrics Society 44th Annual Meeting, New Orleans, May 87.

Treece GL, Polzin WJ, Stone IK, Price GH: The Effect of Estrogen on the Renal Actions of Calcium Regulating Hormones in Postmenopausal Women. 69th Annual Meeting of the Endocrine Society, Indianapolis, IN, Jun 87, Abstract #61.

Witte MC: Airway Hyperresponsiveness and Macroscopic Bronchial Sarcoid. American College of Physicians Meeting, San Francisco, Oct 86.

DEPARTMENT OF OB/GYN

Duff WP, Kopelman JN: Incidence of Subclinical Infection in Asymptomatic Patients with Refractory Preterm Labor. AFD-ACOG, San Diego, CA, Oct 86.

Ilika KL, Duff WP: Use of A Funnel Device for Voiding Problems After Radical Vulvectomy. AFD-ACOG, San Diego, CA, Oct 86.

Ilika KL, Kopelman JN, Duff WP: Course of Labor at Term in Multiparas with Long Intervals Between Deliveries. AFD-ACOG, San Diego, CA, Oct 86.

Johansen RK, Duff WP: Glycosylated Hemoglobin Concentrations in Mothers of Macrosomic Infants. AFD-ACOG, San Diego, CA, Oct 86.

Kopelman JN, Duff WP: Ritodrine Associated Angina: A Case Report. AFD-ACOG, San Diego, CA, Oct 86.

Kopelman JN, Duff P, Karl PT, Schipul AH, Read JA: Computed Tomographic Pelvimetry in the Evaluation of Breech Presentation. AFD-ACOG, San Diego, CA, Oct 86.

Kopelman JN, Duff WP, Read JA: A Randomized Trial of Oral Ritodrine vs Oral Terbutaline for the Prevention of Recurrent Preterm Labor. AFD-ACOG, San Diego, CA, Oct 86.

Kopelman JN, Duff WP, Read JA: Enzymatic Evidence of Myocardial Damage in Asymptomatic Patients Receiving Betamimetic Tocolysis. AFD-ACOG, San Diego, CA, Oct 86.

Lee RB, Elg SA, Stones C, Webber PJ, Benson WL: Serum Haptoglobin Level in Patients with Ovarian Cancer. AFD-ACOG, San Diego, CA, Oct 86.

Mukai M, Stone K: Ovarian Abscess After Vaginal Hysterectomy. AFD-ACOG, San Diego, CA, Oct 86.

Parks KD: Ectopic Pregnancy and the Availability of Serum HCG. AFD-ACOG, San Diego, CA, Oct 86.

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Rawlins NW, Duff WP: Hemoglobin and Hematocrit Changes in the Uncomplicated Vaginal Delivery. AFD-ACOG, San Diego, CA, Oct 86.

Read JA, Brumfiel MN, Sorenson RZ: Routine Ultrasound Use in an Adolescent Pregnancy Clinic. AFD-ACOG, San Diego, CA, Oct 86.

Robertson AW, Duff WP: A Comparison of Two Single Dose Antibiotic Regimens for Treatment of Uncomplicated Lower Urinary Tract Infections in Obstetric Patients. AFD-ACOG, San Diego, CA, Oct 86.

Soisson AP, Eldridge E, Kopelman JN, Duff WP: Acute Pyelonephritis Complicated by Respiratory Insufficiency. AFD-ACOG, San Diego, CA, Oct 86.

DEPARTMENT OF PATHOLOGY

Price G, Paquet RJ, Rose HN: Adaptation of Technicon RA Systems Theophylline Reagents to the Coulter Dacos. 39th National Meeting of the American Association for Clinical Chemistry, San Francisco, CA, Jul 87

DEPARTMENT OF PEDIATRICS

Hartman KR, Mallet, Wright DG: Antibodies to Actin in Autoimmune Peutropenia. American Society of Hematology

PREVENTIVE MEDICINE SERVICE

Aduddell MD, Lednar W, Erdtman F: Fort Lewis Behavioral Risk Factor Prevalence Survey: Tobacco Use. American College of Military Osteopathic Physicians & Surgeons, Mar 87.

Aduddell MD, Lednar W, Erdtman F: Fort Lewis Behavioral Risk Factor Prevalence Survey: Tobacco Use. Prevention 87, Atlanta GA, Apr 87.

Aduddell MD, Lednar W, Erdtman F: Fort Lewis Behavioral Risk Factor Prevalence Survey: Tobacco Use. Annual Preventive Medicine Symposium, WRAIR, Wash, DC, Summer 87.

Carroll DA: Correlates of Smoking Status Among Male Soldiers. Annual Preventive Medicine Symposium, WRAIR, Wash, DC, Summer 87.

Sanchez RJ: Assessing Potential Predictor Variables of Overweight in A Military Population. Preventive Medicine Symposium, Walter Reed Army Institute of Research, Washington, DC, May 87.

DEPARTMENT OF RADIOLOGY

Karl RD: Radiographic Assessment of the Pelvis and Lower Extremities. Southeast Minnesota Orthopedic Study Group, Rochester, MN, Nov 86.

DEPARTMENT OF SURGERY

Belville WD: LHRH Receptor on Human Prostate Carcinoma: Preliminary Evidence. 34th Kimbrough Urological Seminar, San Antonio, TX, Oct 86.

Erpelding JM: Synovial Fluid Changes Following Arthroscopy in Patients with Effusions. Society of Military Orthopaedic Surgeons Annual Meeting, Nov 86.

Hall RL, Jones JC, Andersen CA: Diagnosis of Myocardial Contusion. Gary Wratten Symposium. El Paso, TX, Apr 87.

Hall RL, Jones JC, Andersen CA: Diagnosis of Myocardial Contusion. Washington State Chapter, American College of Surgeons, Jun 87

Rozanski TA: *In Vitro* Culture of Primary Human Prostate Carcinoma. NW Urologic Society, Tacoma, WA, Dec 86, Best Resident Research Paper

Rozanski TA, Loop S.: Effects of Androgen Depletion on Human Prostate Tumor Cell Growth in the Athymic Balb/C Mouse. 34th Kimbrough Urological Seminar, San Antonio, TX, Oct 86.

Smith DB: Intraoperative Monitoring of Recurrent Laryngeal Nerve Function in Swine. Tacoma Surgical Society, May 87.

Smith DB: Intraoperative Monitoring of Recurrent Laryngeal Nerve Function in Swine. Annual Meeting of Otolaryngology, Head and Neck Surgergy Society, Sep 87.

Strand J, Yarbrough L: Total Colectomy with Ileo-Anal Anastomosis and Longitudinal Myectomy in the Porcine Model. Pierce County Surgical Society, Jun 87.

Tylka BL, Harris S, Carter P: Segmentectomy versus Modified Radcal Mastectomy. Gary Wratten Surgical Symposium, El Paso, TX, Apr 87.

Vaccaro JA: Transrectal Resection of Adenocarcinoma of the Rectum. Kimbrough Urological Seminar, San Antonio, TX, Oct 86.

Vaccaro JA: Transrectal Resection of Adenocarcinoma of the Rectum. NW Urological Society, Tacoma, WA, Dec 86.

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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 CLINICAL INVESTIGATION

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 83/64	Status: On-going

Title: The Effect of 20α-Hydroxy-4-Pregnen-3-One Treatment on Spermatogenesis and Gonadotrophins in Rats

Start Date: 20 May 83	Estimated Completion Date: Dec 87
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 MEDCASE Cost: -0-	Est Accumulative OMA Cost: $2750.00	Periodic Review: Jul 87

Study Objective: To examine the possibility of a physiological role for the steroid metabolite 20α-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 treatment. They will 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 thirty days with 1 mg progesterone, 1 mg 20α-OHP, 5 mg 20α-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, E_2, and androgen binding protein (ABP). For all animals, the ventral prostate and seminal vesicles will be ligated, removed and weighed. Epididymides will be weighed from intact animals and the right epididymis will be frozen at -80°C for later assay of T, E_2, 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 counts and tubule diameters will be compared between the 4 groups by t test. Steroids and gonadotrophins will be measured for all 8 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: No further work was done on this protocol during FY 87 due to commitments to other studies. Preliminary data collected in FY 86 indicated 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.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/101	Status: On-going

Title: Atropine Absorption After Administration with 2-Pralidoximine Chloride by Automatic Injector. A Comparison Between Injection of the Drugs Into the Same Intramuscular Site and Separate Intramuscular Sites

Start Date: Jan 87	Est Completion Date: Jun 87
Department: Clinical Investigation	Facility: MAMC
Principal Investigator: CPT Karl E. Friedl, MS	
AssociateInvestigators:	LTC Thomas Mader, MC
COL Stephen R. Plymate, MC	LTC Robert Smallridge, MC
LTC Robert Jones, MC	MAJ Charles Hannan, MS
Key Words: atropine, single vs separate injections, autoinjector	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $30,000.00* Periodic Review: May 87

Study Objective: To determine if the absorption of atropine by autoinjector is equally effective when administered at a single intramuscular injection site compared to two separate intramuscular injection sites.

Technical Approach: In alternate experiments, one week apart, 20 healthy males (ages 19-30) will be injected with the MARK-I delivery system and with the multichambered autoinjector delivery system. After an overnight fast, the subjects will be connected to an ECG machine and an indwelling catheter with heparin lock will be inserted into the antecubital vein. Subjects will sit quietly on a bed at an approximate 45° angle. After a minimum 30 minute quiescent period a baseline ECG will be recorded and a 4 ml blood sample will be taken for pre-test CPK. Then the drug will be administered and the subjects will be asked to rate the degree of pain. Blood samples will be be drawn at 3, 6, 10, 15, 20, 30, 40, and 50 minutes and at 1, 1.5, 2, 2.5, 3, 4, 5, 6, 9, and 12 hours. An ECG will be recorded and pupillary diameters will also be estimated at these time intervals. Subjects will be asked to remain supine during the testing. An additional 4 ml blood sample will be drawn for post-injection CPK. Atropine and pralidoxime assays will be performed. Two way ANOVA analysis and t-test will be used for statistical analysis when comparing the different groups.

Progress: The technical aspects of the study have been completed. Data analysis is complete and a report for USAMRDC and several manuscripts are in preparation.

*Funding provided by USAMRDC

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/102	Status: Completed

Title: Effects of Oral and Injectable Testosterone Preparations on Serum Lipoproteins in Healthy Men. A Comparison of the Lipoprotein Effect and the Effect on Related Factors: Hepatic Triglyceride Lipase Activity, TeBG Concentration, and Androgen Metabolism

Start Date: Oct 86	Est Completion Date: Sep 88	
Department: Clinical Investigation		Facility: MAMC
Principal Investigator:	CPT Karl E. Friedl, MS	
Associate Investigators:	COL Stephen Plymate, MC LTC Robert Jones, MC MAJ Charles Hannan, MS SP4 Gregory Thomas	
Key Words:	testosterone, oral, injectable, serum lipoproteins	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $4137.00	Periodic Review: N/A

Study Objective: To examine qualitative differences in the effects of oral (methyl testosterone) and injectable testosterone preparations (testosterone enanthate) which may be related to their different routes of entry (portal-hepatic vs peripheral). In a second comparison, the experiment will evaluate the role of estradiol in HDLC suppression by the addition of testolactone, an aromatase inhibitor, to the injected group.

Technical Approach: Eighteen male subjects (ages 20-25 years) preferably non-smokers, >15% body fat, after a PE, will be tested once in a control period and will be randomized to the following groups: Group 1: Methyl testosterone pills, 20 mg 2 BID, daily for 12 weeks. Group 2: Testosterone enanthate, IM injection, 280 mg once a week for 12 weeks, and Group 3: Testosterone enanthate, IM injection, 280 mg, once a week for 12 weeks plus testolactone pills, 250 mg 4 times a day, daily for 12 weeks. Subjects will be checked weekly for side effects and variations in eating or exercise habits and have a fasting blood sample drawn. Salivary samples will be obtained after 3-5 minutes of chewing parafilm. At 0, 1, 2, 4, 8, and 16 weeks subjects will be injected with heparin and 10 mls of blood will be drawn 10 minutes later. At 0, 4, 8, and 12 weeks, body densities will be obtained by hydrostatic weight. Semen sampling will be done at 12 weeks. The same sample schedule will be followed during the 12 post-treatment weeks. Comparisons will be made between the TE and MeT and between the TE and TE+testolactone groups over time of treatment and recovery. Determinants of HDLC change and HTGLA will be examined in a multivariate analysis with the samples from all groups, once generalizable relationships are indicated.

Progress: The results indicate that E_2 may be an important modulator of bioavailable testosterone through its regulation of SHBG and that E_2 has no additional effect on the testosterone feedback inhibition of LH during high dose testosterone administration. An abstract has been accepted for the Amer Fed Clin Res meeting, Feb 87.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 85/36	Status: On-going

Title: Physiological Changes with Weight Loss. Part 3: Serum Lipids (Part 2 completed FY 86)

Start Date: 18 Jan 85	Est completion Date: Jan 87
Department: Clinical Investigation	Facility MAMC

Principal Investigator: MAJ Charles J. Hannan, MS

Associate Investigators:

COL Stephen R. Plymate, MAJ Arthur Knodel, MC
LTC 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 Cost: -0-	Est Accumulative OMA Cost: $8155.00	Periodic Review: Oct 87

Study Objective: To determine if there is a measureable change in 12-hr 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. Subjects will fill out a questionnaire at the first session, submit a weekly food intake sheet, and take part in weekly counselling sessions. Serum will be analyzed for changes in both free and total cholesterol and triglycerides.

** This protocol was reviewed by the IRB in April 1986. At that time additional funding was approved because the costs of the ultracentrifugation and HPLC had not been adequately reflected in the original protocol. There had also been some criticism of the project because further identification of apolipoproteins separated by HPLC was not proposed. For this reason, isoelectric focusing will be done to further specifically identify proteins in HPLC eluents.

Progress: Sample analysis was completed in FY 87 and integration and evaluation of the results with data from parts 1 and 2 are now in progress.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 85/33	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 Robert E. Jones, MC	Alan A. Artru, M.D.
LTC James Temo, ANC	Judy Y. Sey, Ph.D.
MAJ Leslie Yarbrough, VC	Thomas Kettler, B.S.

Key Words: patency, anesthesia, biochemical markers

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $12,848.00	Periodic Review: Oct 87

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 ^{3}H-water while anesthetized; and (3) macaques, anesthetized with the three agents will be prepared for CSF collection by lumbar puncture.

Progress: Preliminary studies indicate that, although evidence for BBB disruption by halothane has been reported, only extreme hypocapnia with 0.5% halothane and N_2O produced increased permeability. With the arrival of a new blood gas analyzer, the investigators continued the study with more closely monitored blood gas measurements. A paper has been accepted by the Annals of the New York Academy of Sciences.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/41	Status: On-going

Title: Age Related Effects in Blood-Brain Transport of Hormones: I. Testosterone

Start Date: Jan 87	Est Completion Date: May 87
Department: Clinical Investigation	Facility: MAMC
Principal Investigator:	MAJ Charles Hannan, MS
Associate Investigators:	COL Stephen R. Plymate, MC SGT Naomi Campbell William Bremner, M.D. Lisa Meyers, M.D.
Key Words:	blood-brain transport, hormones, testosterone

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $945.00	Periodic Review: N/A

Study Objective: This study will measure the transport across the blood-brain barrier (BBB) of testosterone in plasma from young and old males.

Technical Approach: Serum will be obtained from five to eight healthy men in each of two groups: young (age 20-35) and old (age 50 and over). The right carotid artery of a 200-400 gram rat will be isolated and a total volume of 200 µl consisting of 0.5 µCi ^{14}C-butanol and 0.1 µCi ^{3}H-testosterone along with the serum from either young or old subjects will be injected as a bolus. Fifteen seconds after injection, the animal will be decapitated and the brain removed. The right hemisphere will be isolated and dissolved and liquid scintillation cocktail will be added before radioactivity is measured. The percent of steroid available to the brain will be calculated as follows:

$$\text{Brain uptake index (BUI)} = \frac{^{3}H \text{ dpm}/^{14}C \text{ dpm (brain)}}{^{3}H \text{ dpm}/^{14}C \text{ dpm (injected)}}$$

Testosterone and SHBG will be measured by established methods which are routinely used in our laboratory.

The brain uptake index will be calculated for each group and compared by Student's t test.

Progress: Approximately 20 rats were used to evaluate the transport of testosterone from blood to brain when in serum from young or old men. There is some indication of age-related effects. However, statistical significance has not been found.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/86	Status: On-going

Title: Role of γ-Endorphin Processing in the Age-specific Development of Phenylethylamine-Induced Stereotypy

Start Date: 19 Jun 87	Est Completion Date: Sep 90	
Department: Clinical Investigation		Facility: MAMC
Principal Investigator:	MAJ Charles Hannan, MS	
Associate Investigators:	Charles W. Wilkinson, M.D. American Lake VA Medical Center	
Key Words: stereotypy, γ-endorphin,	phenylethylamine-induced, rats	age specific,
Accumulative MEDCASE Cost: -0-**	Est Accumulative OMA Cost: -0-**	Periodic Review: N/A

Study Objective: To determine if γ-E and related peptides play a role in the expression of PEA induced stereotypy.

Technical Approach: Male Fischer 344 rats will be used in this study. (1) Acute endorphin-PEA relationship: Regional cerebral γE-type peptides will be measured after a one hour analysis of PEA-induced behavior in young and aged rats. A single IP injection of PEA (50 mg/kg) or saline control will be used. Comparisons will be made between young and aged animals in the measures of γE-type peptide concentrations and in behavioral measures. Also, correlations between behavior and γE-type peptide concentrations will be examined. (2) Dose response of microinfused PEA: A dose response relationship will be determined for PEA bilaterally microinfused into the caudate nuclei of young and aged rats. PEA or saline control will be microinfused for two weeks while behavioral measures of stereotypy are continuously monitored. (3) Effect of PEA infusions into the caudate nucleus on regional γE-type peptides: The time course for the development of sensitivity to PEA during microinfusions into the caudate nucleus will be determined based upon the dose response to PEA. Based on these results, four appropriate time periods during development of the maximum stereotypy response will be selected to terminate animals in order to measure regional γE-type peptides in both young and aged aged rats. (4) Effect of mesolimbic infusions of γE peptides on response to PEA infused into caudate: γE-type peptides will be infused bilaterally into nucleus accumbens (mesolimbic area will actually be receiving the infusion product) Simultaneously, a dose of PEA as determined from the dose response studies will be infused into the caudate nuclei. Two weeks of behavioral evaluation will be used to determine the effect of the γE-type peptides upon the PEA-induced stereotypy.

Progress: This protocol has not been started. The investigators are awaiting approval of a joint VA-DoD grant.

**Proposed funding to be provided by a joint VA/DoD grant.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/97	Status: On-going

Title: Efficacy of Liposome-Encapsulated Bovine Hemoglobin as a Red Cell Substitute

Start Date: 21 Aug 87	Est Completion Date: Dec 87	
Department: Clinical Investigation		Facility: MAMC
Principal Investigator: MAJ Michael D. Hayre, VC		
Associate Investigators: MAJ Kip Hartman, MC		
Key Words: red cell substitute, liposome-encapsulated bovine hemoglobine, rats		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-**	Periodic Review: N/A

Study Objective: To determine the efficacy of liposome-encapsulated bovine hemoglobin (LEBH) as a red cell replacement by demonstrating that respiration and cardiac function are maintained in the absence of sufficient red cells. The effects of transfusion with LEBH on major organ histology and function will be studied, as well as the antigenic potential of the solution. Questions regarding *in vivo* cardiovascular responses and stability, RES, renal and hematologic toxicity, and antigenicity will also be addressed.

Technical Approach: An isovolemic exchange transfusion will be performed in rats replacing 95% of each animal's normal blood with LEBH, saline/albumin, or saline/albumin filled liposome. Arterial and venous catheters will be placed via a cutdown exposing the right carotid artery and jugular vein. During the exchange procedure, hematocrit, ECG, mean arterial pressure, and venous pressure will be continuously monitored. Arterial and mixed venous blood gases will be measured and hemoglobin concentration and O_2 contents assayed. At the end of the exchange transfusions, 15 of the rats receiving LEBH will be given euthanasia and necropsied. The remaining animals will be returned to the holding area for a period of 14 days. At the end of the 14 days these animals will also be given euthanasia and necropsied with section of major organ systems prepared for histopathology. At the beginning of the study and prior to euthanasia, 0.3 ml blood samples will be obtained from each animal for evaluation of antibovine hemoglobin antibodies in the serum.

Progress: No work has been done on the study while the investigators are awaiting funding. The protocol is scheduled to begin in mid-October, 1987.

** Funding provided by Department of the Navy, Naval Research Lab, Washington, DC

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 85/59	Status: Terminated

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
MAJ Leslie W. Yarbrough, VC
Mina J. Garrison, B.S.
Catherine R. Sulzer, B.S.

Key Words: Leptospirosis, monocolonal antiboides, diagnosis

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $3720.00	Periodic Review: N/A

Study Objectives: To isolate genus-specific antigen(s) of leptospires 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 2 methods will be compared for sensitivity and specifity. 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 statistically grown to $\approx 10^8$ organisms/ml concentration. After harvesting, BALB/C mice cells will be sensitized to leptospira using a 6-week immunization schedule, then injected intraperitoneally with 10^3 organisms in complete Freund 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 $\approx 25 \times 10^6$ cells/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 taken at different intervals.

Progress: Balb/c mice were immunized with whole cell leptospira grown in PLM-5 using 6 different serrovars. Spleenocytes were harvested and cloned with mouse-adapted multiple myeloma cells. After 10 day incubation, microwells were observed for hybrids and reincubated or split following media supplement. Selected supernates were aspirated and tested for immunoglobuins. Although most of the screening was inconclusive because of protein concentrations, it appeared that IgM was present in 3 of the 6 strains tested (Landamana, bataviae, and pomona). The project was terminated due to the departure of LTC Higbee.

Detail Summary Sheet

Date: 30 Sep 87	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: Clinical 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, B.S., M.T.	
MAJ Stanley P. Liebenberg, VC	Louis A. Matej, B.S., M.T.	
Key Words: Beagles, estradiol valerate, tamoxifen, levothyroxine		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $500.00	Periodic Review: Nov 86

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

Technical Approach: The investigators originally planned to use female beagles for this protocol. When restrictions were placed on the use of dogs in research, the investigators conducted this study *in vitro* using a human hepatoma cell line, Hep G2, grown to confluence in Dulbecco's Minimum Essential Median (DMEM) with 10% FCS. Additions of T_4, insulin, estradiol, and testosterone were then begun daily for three days with DMEM without FCS, and media were collected at the end of each three day period and assayed for SHBG using a radioimmunometric assay specific for human SHBG. At the end of each experiment, the cells were harvested and counted in each flask. SHBG production was normalized for cell number. Each hormone addition was performed in triplicate per experiment.

Progress: The investigators continued to study additional cultures during FY 87. Results of studies done thus far were presented at the 2nd International Congress on Steroid Binding Protein and a paper has been accepted for publication in Steroids. The data thus far demonstrate that insulin as well as thyroxine and sex steroids can affect SHBG production. Typically, as in the case of obese women with polycystic ovary disease (PCOD), SHBG production has appeared to be under the control of sex steroids. In PCOD non-SHBG bound testosterone is elevated but the steroids do not further contribute to their own elevation by lowering SHBG; instead it is the characteristic elevation of insulin production which is inversely correlated with SHBG. These data suggest a role for insulin in this pathogenesis. It has been noted that the insulin levels in women with PCOD are not related to obesity but insulin is strongly associated with levels of testosterone. In addition, as relative weight increases in PCOD subjects, SHBG deonstrates further decreases and this relationship also holds for normal obese women with upper body fat localization. Although the liver may be resistant to the effects of insulin in obesity, it continues to respond in terms of protein production and lipid metabolism. The fact that insulin can continue to exert its effects in the face of estrogen and thyroid hormone may also explain why SHBG levels are consistently low in women with PCOD in spite of evidence chat some of these women will have elevated levels of estrogen.

Detail Summary Sheet

Date: 30 Sep 87	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. Berger, M.D.

Key Words: Infertile and fertile men, LH/RH stimulation tests, semen analysis, sperm penetration assay

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 86

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: An additional 15 subjects were studied during FY 87. A paper has been accepted for publication by Fertility and Sterility and a paper was presented at the American Fertility Society in September 1987.

Sperm counts in the proven fertile men receiving a ligation increased from a geometric mean of 12.3 mil/ml to 28.5 mil/ml after ligation, while in those with unproven fertility, mean sperm counts were 18.4 mil/ml and 20.1 mil/ml. LH response to LHRH was not significantly different after ligatin in either group. There was a trend to normal FSH responses after ligation. Sperm penetration assays were not predictive of fertillity before or after ligation in either group. Even though sperm production tended to increase in the proven fertility group, the preliminary data suggest that present methods of assessing testicular function do not permit clear evidence of changes in fertility status in men whose varicocele was ligated.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/61	Status: Completed

Title: Effect of Danazol on Serum & Salivary Testosterone Levels

Start Date: Apr 86	Est Completion Date: Jun 87
Department: Clinical Investigation	Facility: MAMC
Principal Investigator: COL Stephen R. Plymate, MC	
Associate Investigators:	
MAJ Charles J. Hannan, MS	C. Alvin Paulsen, M.D.
CPT Karl Friedl, MS	Rae Nagao, M.D.
Key Words: testosterone, serum, salivary, levels, effect	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $306.00	Periodic Review: Jul 87

Study Objective: To confirm our previous observation that there is a disproportion and alteration in the protein bound testosterone versus free testosterone following administration of danazol to normal men.

Technical Approach: Four normal men age 20 to 45 years will have a complete history and physical examination. There will be a one-week control period and a two-week drug exposure period followed by a four-week postdrug recovery period. During drug exposure, the men will receive 400 mg of danazol orally a day. Serum and saliva samples will be collected on days 2 and 7 of the baseline period; days 3, 7, 10 and 14 of the drug exposure period; and at weeks 6 and 7 of the study. At each collection period, approximately 30 mls of blood will be taken and 20 mls of saliva collected by chewing paraffin for approximately 30 minutes. Saliva and blood samples will be measured for dihydrotestosterone, HDL cholesterol, and SHBG. Testosterone measurements will be made both before and after HPLC separation and SHBG will be measured by both dextran coated charcoal saturation analysis and radioimmunoassay.

Progress: All subjects have completed the study with no adverse effects. All assays have been run. The data is now being analyzed and a paper is in preparation.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/62	Status: Completed

Title: Physiologic Consequences of Impaired Blood Brain Barrier Transport of Steroid Hormones

Start Date: Jun 86	Est Completion Date: Jun 87
Department: Clinical Investigation	Facility: MAMC
Principal Investigator: COL Stephen R. Plymate, MC	
Associate Investigators:	
MAJ Charles J. Hannan, MC	Louis Matej, DAC
SGT John Robbins	Wendy Garden, B.S.
Key Words: hormones, steroid, blood brain barrier	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $950.00	Periodic Review: Jul 87

Study Objective: To determine if the elevated LH level in hyperthyroid men is the consequence of increased sex hormone binding globulin (SHBG) and subsequent retarded availability of testosteronc and estradiol to the pituitary and hypothalamus.

Technical Approach: Serum will be obtained from 5 to 10 hyperthyroid and 10 euthyroid men. The amount of testosterone or estradiol available for transport across the blood brain barrier will be determined by a single pass carotid injection technique. In this procedure the right carotid artery of a 200-400 gm rat is isolated and the test solution is then injected as a bolus. Fifteen seconds after injection, the animal is decapitated and the brain removed. The right hemisphere is isolated, placed in solvent and counted. The injection solution is a total volume of 200 µl consisting of 0.5 µCi C^{14} H_2O and 0.1 µCi H^3 testosterone or estradiol along with test serum. Following counting, the percent of steroid available to transverse the blood brain barrier will be calculated by the following formula:

$$\text{Brain Uptake Index (BUI)} = \frac{\text{test dpm/ref DPM (T)}}{\text{test dpm/ref DPM (injection)}}$$

LH and FSH will be measured using materials obtained from the National Pituitary Agency by established methods. Testosterone and estradiol will be measured by procedures established in the laboratory at the Department of Clinical Investigation, MAMC. SHBG will be measured by materials obtained as a gift from Dr. C.Y. Cheng of the Population Council, Cornell University. Data will be analyzed using the STATGRAPHICS program.

Progress: Serum was obtained and the brain uptake index for testosterone (BUI-T) was determined as specified. The data suggest that SHBG is a significant determinant of the BUI-T. LH levels inversely correlated well with both BUI-T and calculated nSHBG-T. These data demonstrate that the rise in SHBG with hyperthyroidism decreases significantly both BUI-T and nSHBG-T and is associated with the increased LH. These results also indicate a physiologic role for SHBG on testosterone-dependent cellular feedback on LH. Data from this study were used in presentations at the Second International Steroid Hormone Binding Protein Symposium and the Meeting of the American Federation for Clinical Research.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/24	Status: On-going

Title: Chemical Characterization of Sex Hormone Binding Globulin (SHBG)

Start Date: Nov 86	Est Completion Date: Jun 87	
Department: Clinical Investigation		Facility: MAMC
Principal Investigator:	COL Stephen R. Plymate, MC	
Associate Investigators:	COL Carl Stones, MC MAJ Charles J. Hannan, MSC MAJ Robert E. Jones, MC Philip H. Petra, Ph.D., Univ Washington Louis A. Matej, B.S., DAC	
Key Words: sex hormone binding globulin, production, structure		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $814.00	Periodic Review: N/A

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

Technical Approach: Blood from second trimester pregnancy plasma will be purified and amino acid sequencing will be performed. Once sequencing has been completed, the appropriate cDNA probe will be obtained from a cDNA library obtained from HEP G-2 cells. The cDNA probe will be tritiated and the studies using insulin, growth hormone, prolactin, estradiol, and testosterone will be performed on the HEP G-2 cell cultures with subsequent cDNA hybridization. When these experiments are complete, media will be assayed by RIA or DCC binding assay for SHBG, and RNA will be extracted from the cells. Basically, the cells will be placed in freshly constituted homogenization buffer and disrupted using a polytron homogenizer. The extracts will be left overnight at 4°C and then centrifuged at 2000g for 30 mins. The precipitate pellet will be washed and dissolved in 50 m/mole tris buffer pH 5 containing 10% SDS and extracted twice with phenylmethylchloride. RNAs will then be precipitated with ethanol dissolved in 10% SDS. Following this, northern blot analysis using 10 mg of RNA will be performed by electrophoresis on 1% agarose formaldehyde gels. Following northern blot analysis, the RNA will be hybridized using either H^3 or P32 labelled cDNA probe. After hybridization has occurred, audioradiography will be performed using Kodax XR5 film and quantitation of mRNA synthesis will be determined using scanning densitometer.

Progress: Isoelectric focusing has been started.

Detail Summary Sheet

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

Title: Direct Effects of Sex Hormone Binding Globulin of Plasma on the Metabolic Clearance Rate and Hypothalamic/Pituitary Feedback of Testosterone and Estradiol in the Pigtail Macaque *(Macaca Nemistrina)*

Start Date: Mar 87	Est Completion Date: Jul 88	
Department: Clinical Investigation		Facility: MAMC
Principal Investigator: COL Stephen R. Plymate, MC		
Associate Investigators: MAJ Charles Hannan, MS Phillip H. Petra, Ph.D.		
Key Words: testosterone, estradiol, SHBG, metabolic clearance rate, hypothalamic/pituitary feedback, pigtail macaque		
Accumulative MEDCASE Cost: -0-	Est accumulative OMA Cost: $2100.00	Periodic Review: N/A

Study Objective: To aid in the understanding of which determinants allow sex steroids to be effective.

Technical Approach: Six male pigtail macaque monkeys will be preconditioned in a primate restraining chair before the study begins. At least 48 hours before the study, the animals will be implanted with in-dwelling catheters under ketamine HCl anesthesia. Polyethylene tubing will be inserted aseptically into the left femoral vein and polyvinyl tubing into the right femoral artery and vein. The animals will then be fitted with a special vest to protect the catheters, placed in a primate restraining chair, and allowed to recover for 24-48 hours. Blood pressure will be continuously monitored during the study. After recovery from the placement of the catheters, tritiated labelled testosterone and estradiol will be infused following a bolus to give a constant rate of tritiated labelled testosterone or estradiol per 2 ml of infusate per hour. Infusions will be continued for six hours. Blood samples will be collected every 10 minutes and every hour the plasma will be separated and the red cells resuspended in physiologic buffer and infused back into the animal. Following the initial determination of the metabolic clearance rate (MCR) and LH pulse frequency, the animals will be removed from the chair and allowed at least four weeks of rest. Then they will be infused with SHBG for a three hour period of time. After the initial three hour infusion of SHBG, an antibody to SHBG will be infused and LH pulse frequency and the MCR of testosterone and estradiol will be determined. In addition, plasma SHBG, testosterone, dihydrotestosterone, and LH pulse frequency will be measured at the beginning and end of each experiment and albumin concentration will be estimated.

Progress: Several animals have been studied. Preliminary results indicate that an increase in SHBG binds E_2, decreases the E_2 MCR and testosterone available for feedback on LH and a sudden decrease in SHBG causes a decrease in E_2 MCR.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/63	Status: Terminated

Title: Maintenance of Spermatogenesis in Testosterone Treated Rhesus Monkeys *(Macaca Mulatta)*

Start Date:	Est Completion Date:	
Department: Clinical Investigation		Facility: MAMC
Principal Investigator:	COL Stephne R. Plymate, MC	
Associate Investigators:	COL Geroge Ward, VC MAJ Michael Hayre, VC CPT Karl E. Friedl Louis Matej, DAC, B.S.	
Key Words:	spermatogenesis, maintenance, testosterone, monkeys	
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost:	Periodic Review: N/A:

Study Objective: To determine the relationship between intratesticular testosterone concentrations and Sertoli cell function in maintenance of spermatogenesis in intact rhesus monkeys administered exogenous testosterone.

Technical Approach: Sixteen adult male rhesus monkeys (4 animals/group) will be treated for 12 weeks with one of three doses of testosterone enanthate (10, 50, and 125 mg I.M. per week), and a sesame oil control group will be used. The animals will be weighed weekly and blood samples drawn immediately prior to each injection for baseline evaluation. One week following the last injection, blood samples will again be drawn and the animals hemicastrated. Blood samples will be spun and the serum frozen, and the epididymis and testis will be weighed and a portion of the testis fixed in Bouin's solution for histology while the remaining testis and epididymis will be frozen in dry ice at -70°C until assays are performed. Semen analyses will be obtained by electro-ejaculation on an every other week basis. Samples will be measured for testosterone, estradiol, LH and FSH by bioassay as well as RIA and sex hormone binding protein. Testes and epididymides will have androgen binding protein measured by RIA. Intratesticular testosterone and estradiol as well as epididymal levels of these hormones will be measured and germ cell relationships will be made in approximately 20 round tubules from each testis in each animal. Results will be analyzed by Kruskal-Wallace analysis of variance on an IBM STAT Graphics program.

Progress: This was protocol was terminated because COL Ward had other unexpected commitments which did not allow him the time to do the surgeries.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/82	Status: On-going

Title: Differences in the Hypothalamic-Pituitary-Gonadal Axis Between Young and Elderly Men Before and After Testosterone Replacement

Start Date: Apr 88	Est Completion Date: Apr 91	
Deparatment: Clinical Investigation		Facility: MAMC
Principal Investigator:	COL Stephen R. Plymate, MC	
Associate Investigators:	William Bremner, M.C, Ph.D. Joyce S. Tenover, M.D. MAJ Charles J. Hannan, MS CPT Karl E. Friedl, MS	
Key Words:	hypothalamic-pituitary-gondal axis, testosterone	
Accumulative MEDCASE Cost: -0- **	Est Accumulative OMA Cost: -0- **	Periodic Review: N/A

Study Objective: To further elucidate the mechanism of the differences in the hypothalamic pituitary testicular axis, bioavialable testosterone, and totol testosterone in young and elderly men, and to determine the significance of these changes in the aging process as well as explore whether treatment can safely alleviate some of the changes which occur with age and physical stress.

Technical Approach: Four groups will be studied: 15 men 21-30 years of age, 15 men 30-50 years of age, and 30 men 60 years of age or older (divided into two groups; those with T levels <3.5 ng/ml and those with T levels >3.5 ng/ml.) Screening laboratory studies will include CBC, platelet counts, LFT, glucose electrolytes, and prostatic specific androgen. This will be a double blind cross-over trial for 3 months each of placebo or 50 mg testosterone enanthate, I.M., twice weekly. During the study, CBC's, platelet counts, LFT's, general blood chemistries, tesicular size and grip strength will be performed monthly. Dihydrotestosterone, SHBG, nSHBG-T, E_2, FSH, LH bioassay and LH pulses (over an 8-hour period), lean body mass measurement, total cholesterol, triglycerides, HDL cholesterol, fractions 2 and 3, apo A-1 protein, fasting insulin glucose and SHBG (by RIA and a dextran coated charcoal binding assay), glycosylated hemoglobin, and changes in cardiac risk factors will be measured at 0, 3, and 6 months. Prostate size will be estimated by ultrasound in patients >55 years of age. Factors which affect SHBG production and are found to be different between young and elderly men will be examined *in vitro* for their effects on SHBG production by Hep G-2 cells. Testosterone and estradiol clearance studies will be done in rats before and after the infusion of purified SHBG, both native and deglycoslated. SHBG from young and elderly individuals both before and after testosterone treatment will be examined by isoelectric focusing to determine if changes in isoelectric forms explain the effects of SHBG levels with aging or androgen treatment. Serum from treated subjects will be put through the Pardridge/Oldendorf brain uptake assay to determine the effect of SHBG in each group on rate of uptake of testosterone and estradiol into the brain and prostate.

Progress: The study has not started. The investigators are awaiting approval of a joint VA-DoD grant.

** All funding to be provided by a proposed VA/DoD grant.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/20	Status: Completed

Title: Total Colectomy with Ileo-Anal Anastomosis and Longitudinal Myectomy in the Porcine Model - A Pilot Study

Start Date: 15 Nov 85	Est Completion Date: Jun 86
Department: Clinical Investigation	Facility: MAMC

Principal Investigator: MAJ Leslie Yarbrough, VC

Associate Investigators:

COL Stephen Plymate, MC	CPT Robert Hall, MC
MAJ Jans A. Strand, MC	Gordon Klatt, M.D., USAR

Key Words: colectomy, ileo-anal anastomosis, longitudinal myectomy, porcine model

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $1450.00	Periodic Review: N/A

Study Objective: To assess the ability of longitudinal myectomy to safely create an ileal reservoir above an ileo-anal anastomosis and to determine the time required for the reservoir to develop in the porcine model.

Technical Approach: To assess the passive creation of an ileo-anal reservoir and the time required for same, total colectomy will be performed on six swine. Straight ileo-anal anastomosis without myectomy will be performed on one swine and five swine will have two 15 cm strip myectomies removed from the terminal ileum before performing the ileo-anal anastomosis. The swine will be kept on a clear liquid diet for 24-hours prior to surgery and for four days postoperatively. In the postoperative period, the following observations will be made to assess if a reservoir is developing and how soon it is developing: general health, weight, and hygiene (assessment of stool frequency and continence); stool consistency and frequency, normal defactory posturing; barium contrast x-ray of terminal ileal reservoir at 3, 6, and 9 weeks; and pull through manometry to demonstrate low pressure reservoir and intact sphincture at 3, 6, and 9 weeks. Blood sampling to include CBC will be used as deemed necessary. The swine will be euthanatized and necropsied at the end of the study for direct observation of the terminal ileal reservoir. Reservoirs will be harvested for evaluation after euthanasia for histopathologic exam.

*ADDENDUM (September 1986): Change of principal investigator to MAJ Leslie Yarbrough, VC. Nine additional pigs will be studied. Four pigs will have a total colectomy with ileo-anal anastomosis without myectomy to act as controls. Five pigs will have a surgically created J-pouch anastomosis, which is the current standard of treatment, to compare with five pigs that have had a myectomy in the pilot study.

Progress: Four additional pigs were studied. These studies indicate that dual longitudinal myectomy may provide a simpler and safer method of creating a pelvic reservoir for use in patients needing an ioeoanal anastomosis. The results of this study were presented at two separate regional meetings.

D E T A I L S H E E T S

F O R

P R O T O C O L S

DENTAL ACTIVITY

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/18	Status: Completed

Title: Clinical and Field Testing of the National Bureau of Standards (NBS) Hand-Held Dental X-Ray System

Start Date: Jan 87	Est Completion Date: Feb 87	
Unit: Dental Activity		Facility: MAMC
Principal Investigator:	MAJ Edward A. Koditek, DC	
Associate Investigator:	MAJ Patrick Harrison, DC	
Key Words:	x-ray system, dental, hand-held, field testing	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-**	Periodic Review: N/A

Study Objective: To test the National Bureau of Standards hand-held dental x-ray system for ease of use and quality of radiographs and portability and to gain ideas of how to make the system more useful for field dental radiography.

Technical Approach: The hand-held dental x-ray system is a digital system developed solely for dental use and it can be used to expose self-developing dental films. The Radiation Protection Officer will first evaluate the system to measure skin dose rates in the fluoroscopic and pulsed modes for both patients and operators. Fifty adult subjects presenting to dental clinics at Ft Lewis, WA, for normal dental treatment and sick call who require x-rays will be studied. In the first phase, the system will be used in routine and emergency patients in the clinic. Hard copy records of the digital radiographs will be made with a Polorid camera. A conventional dental x-ray may also be taken if the dentist feels it is necessary. The second phase of the test will consist of field tests. No conventioanl x-ray capability will be available. Primarily emergency patients will be treated. If the dentist feels that conventional dental radiographs are needed, he will use the hand-held system with self-developing "D speed" dental film. The followind data will be kept for each patient: number of hand-held x-ray exposures and conventional exposures, Polaroid photogrphs from hend-held system, standrad radiographs, operator notes on device operation, chief complaint, and final diagnosis. The efficacy of the digital system to aid in the diagnosis will be determined by whether the dentist felt that the digital radiograph contained enough information or whether he required a retake of the radiograaph with conventional means.

Progress: The study has been completed and a report has been published for the US Army Development and Employment Agency (ADEA Control #A170). Results of this informal appraisal indicate that the Field Dental X-Ray developed by NBS and USAIDR appears to be a significant breakthrough in field dental technology. The appraisal verified its ability to produce diagnostic-quality x-ray images quickly. Its light weight, easily transportable design, ability to operate from a variety of power sources (including batteries), and ease of operation make it particularly suitable for use at division clearing stations.

**Funding provided by ADEA

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/35	Status: On-going

Title: A Comparison of Blood Glucose Levels Obtained From Blood Incidental to Dental Procedures versus Antecubital Vein Blood

Start Date: Jan 87	Est Completion Date: Apr 87	
Department: Dentistry		Facility: MAMC
Principal Investigator: LTC Stanley S. Levsky, DC		
Associate Investigator: COL Gary L. Treece, MC		
Key Words: blood glucose, antecubital vein, samples obtained from dental procedures, hyperglycemia, Chemstrip BG		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $150.00	Periodic Review: N/A

Study Objective: To determine the relevance of Chemstrip BG determinations of blood glucose levels in blood obtained incidental to dental cleaning or treatment and to test the feasibility of screening for hyperglycemia in the dental clinic.

Technical Approach: One hundred consecutive patients >18 years of age who undergo teeth cleaning or other dental procedures will be studied. Patients who exhibit intraoral bleeding during the dental procedure will have that blood tested with the Chemstrip BG. Blood will be taken from the dental instrument for use on the Chemstrip BG. These samples will be obtained before any irrigation solutions are used in order to avoid contamination by the solution. Immediately after the Chemstrip BG is obtained, peripheral blood will be obtained by venipuncture. A portion of this blood will be used for a Chemstrip BG test in order to compare the two sources on the Chemstrip BG. The remainder of the venous sample will be submitted to the Pathology Lab for determination of whole blood glucose and plasma glucose. The Chemstrips will be visually read as well as read with the assistance of an Accu-Chek II Reflectance Meter. The difference between the blood glucose levels by the different methodologies will be recorded for each patient and submitted to statistical analysis using the Student's t test. The effect of salivary contamination of intraoral samples will be studied by intentional contamination of multiple samples.

Progress: Patient entry has been slow because it is more difficult to fit the protocol into the clinic schedule than expected. However, seven patients have been sampled and the investigators will continue to enter patients as time permits.

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 EMERGENCY MEDICINE

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/75	Status: On-going

Title: Patient Classification in the Emergency Department

Start Date: 15 May 87	Est Completion Date: Jul 87	
Department: Emergency Medicine		Facility: MAMC

Principal Investigator: 1LT Patrick J. Bennett, ANC

Associate Investigators: None

Key Words: tool, analysis, staffing requirements, validity

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

Study Objective: To assess the cross institutional validity of an emergency department patient classification tool in differentiating between groups of patients by quantity of nursing care consumed.

Technical Approach: Categorization of the amount of nursing care required will be done using a four category scheme that differentiates between groups of patients based on assessment of admission, status of care provider, complexity of care, amount of nursing contact with patient and significant others, patient's physical and psychological status, and priority for care. Consistency of ratings will be assured by having only the principal investigator performing categorizations. For actual data collection, the investigator will station himself in or around the nursing station. Direct nursing care will be defined as nursing functions that involve immediate contact by nurse or medic with patients or significant others. This ranges from data collection and counseling to interventions to simple observation within five feet of patient. The times for direct nursing care will be recorded on a flow sheet that also provides for specification of status of the nursing care provider, medical diagnosis, and total length of stay of patient. Other factors to be evaluated include correlation of estimation of nursing care consumption by primary RN coordinating care to category classification (this will assess the validity of patient classification by nursing estimation as compared with observed direct times). Also evaluated will be the relationship between primary nurses' backgrounds and quantity of total direct care time as well as proportion of RN care times to paraprofessional care times. Medical diagnosis, length of stay, category of care, and nursing backgrounds will also be examined to determine their respective effects on intensity of direct nursing care services.

Progress: The principal investigator is doing this study as part of a Master's program at the University of Washington. He has not implemented the project to date because he is awaiting approval of the Human Use Committee at the University of Washington.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/15	Status: Completed

Title: Efficacy of the Abusa Stick for Rapid Estimation of Blood Alcohol Level in the Emergency Department

Start Date: Nov 86	Est Completion Date: Jun 87	
Department: Emergency Medicine		Facility: MAMC
Principal Investigator: CPT Jeffrey N. Broder, MC		
Associate Investigators: MAJ Mel D. Robinson, MC		
Key Words: blood alcohol level, Abusa Stick, saliva		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A

Study Objective: To determine the efficacy of the Abusa Stick®, using saliva, for rapid estimation of the blood alcohol level in the Emergency Department.

Technical Approach: The study group will include all patients entering the Medical-Surgical Casualty area at MAMC who have a blood alcohol level taken. Patients will be checked with the Abusa Stick for saliva estimate of the blood alcohol level and a comparison will be made between levels by routine determination and results obtained by the Abusa Stick. Any residues from alcohol and certain reducing substances may affect the Abusa Stick for up to 5-8 minutes after ingestion. Therefore, samples will be taken not sooner than 10 minutes after the patient has arrived in the medical casualty area. The physician will estimate the patient's blood alcohol, based on clinical knowledge, using a scale of 1-6 (0.01 - 0.45+) before the saliva test is done. The physician estimate will be compared with both methods of alcohol level determinations to compare efficacy against physician judgement. Statistical analysis, including chi square tables, correlation graph, and sensitivity/specificity, will be used to examine the efficacy of the Abusa Stick. Results obtained from the Abusa stick will be recorded in the data using a number coding system.

Progress: This study has been completed. Forty-two (42) patients, ranging from mildly intoxicated to unconscious, were tested. Significant but poor correlation was found between the Abusa Stick and serum blood alcohol concentration. When the serum blood alcohol concentration was low the Abusa Stick measured low, but with a serum blood alcohol concentration of 0.01% the Abusa Stick value ranged from 0.02-0.30%, encompassing all possible measured Abusa Stick levels. The correlation between physician clinical assessment and serum blood alcohol levels was found to be slightly better thatn the Abusa Stick correlation. The concept of a dipstick for the rapid determination of blood alcohol concentration is an important one and it is important that more work be done to improve the accuracy of this product.

A paper based on this study was presented at the Emergency Medicine TriServices Sumposium in April 1987 and a manuscript has been submitted to the Annals of Emergency Medicine.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/36	Status: Completed

Title: Aortic Balloon Occlusion During Asystole: Its Effects on Vital Organ Blood Flow in the Swine

Start Date: Jan 87	Est Completion Date: May 87	
Department: Emergency Medicine		Facility: MAMC
Principal Investigator:	S. Joanna Dames, M.D., M.Ph.	
Associate Investigators:	MAJ Charles Hannan, MS CPT Mark Nyreen, MC CPT Frank Parks, MC	
Key Words: asystole, blood flow, aortic balloon occlusion, swine		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $1898.00	Periodic Review: N/A

Study Objective: To determine whether aortic ballon occlusion significantly increases vital organ blood flow during asystole in the swine model.

Technical Approach: Ten swine will be anesthetized, intubated, and placed on a ventilator. The Percluder (aortic ballon occluder) will be inserted in 1/2 of the animals (Group A). A left ventricular catheter for injection of microspheres, a right brachial artery catheter for monitoring systemic arterial gases, a left brachial artery catheter for withdrawal of blood samples, and a peripheral vein catheter for administration of drugs will then be inserted. CPR will be performed using a ventilator and a mechancal chest compressor. The chest will be compressed 60 times/min with a 50% compression phase. After every 5 chest compressions, a ventilation will be interposed with a pressure of 20 cm H20. CPR will be started within 30 sec of placing the animal into ventricular fibbrillation and the first sample of radionuclide microspheres will be injected and a reference blood sample drawn. At 3 min of fibrillation, 1 mg epinephrine hydrochloride and 1 mg of atropine sulfate will be given peripherally. After allowing 4 min for full circulation of the drugs, a second injection of the radionuclide microsphere suspension will be injected and a reference blood sample drawn. At 10 min of ventricular fibrillation, the Percluder will be inflated in Group A and at 13 min the third injection of radionuclide microspheres will occur and a blood sample drawn. After this, the animals will be euthanized and whole organ samples will be removed from the brain, heart, lung, and kidneys, and radioactivity measured in CPM. Blood pressures will be monitored continuously and arterial blood gases will be drawn before each microsphere injection. Regional blood flow will be evaluated by t-tests, and blood flow during CPR will be determined by analysis of variance for repeated measures. Significant findings will be examined by Scheffe's test.

Progress: Eight animals were studied. There was no flow to the kidneys, both with and without inflating the Percluder. Though not statistically significant, cardiac output decreased with inflation of the Percluder.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/56	Status: On-going

Title: Assessment of a Rapid Theophylline Assay in the Outpatient Setting

Start Date: Mar 87	Est Completion Date: Aug 87	
Department: Emergency Medicine		Facility: MAMC
Principal Investigator:	CPT William Hurley, MC	
Associate Investigators:	MAJ Cloyd Gatrell, MC MAJ Charles Henley, MC CPT Stephan Saglio, MC	
Key Words: theophylline, assay (Accu-Level), rapid, assessment		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $1440.00	Periodic Review: N/A

Study Objective: To study the accuracy, time saving, cost effectivness, and reliability of a rapid, blood theophylline assay (Accu-Level, Syntex Medical Diagnostics, Palo Alto, CA) in the Emergency Room and Family Practice Clinic.

Technical Approach: Thirty subjects from whom STAT theophylline levels are obtained as part of their normal care will be studied and the data will be examined to determine if a range (low, intermediate, and high) of theophylline levels has been included in order to determine the efficacy of the assay at all levels. If this range is seen, the data will be analyzed for statistical significance and more patients will be studied if necessary. If the range of theophylline levels is not seen, then the investigators will redetermine the method of subject selection and revise the protocol. The treating physician will identify patients for whom he wishes a STAT theophylline level and determine if patient had coffee or cola in the past 8 hours. Blood will be drawn in the usual fashion and an aliquot will be taken by pre-measured pipet for analysis by the rapid theophylline assay. The identify of the patient, other medications, diagnosis, time blood drawn, the values and reporting times of the rapid assay and laboratory results will be recorded. The report form for the assay will be initialed in order to to control for any difference in the method of performing the assay. The levels obtained by laboratory analysis and rapid assay will be compared by chi-square analysis using the laboratory findings as the standard. Linear regression and the determination of correlation coefficients will also be used. Cost comparisons will be done between the rapid assay, the MAMC laboratory, other hospital laboratories, and private laboratories. Additional, limited studies are planned consisting of concentration curves to correlate the assay system with known concentrations of theophylline in whole blood, serum, and plasma in order to see if a predictable relationship exists betwen the sample type and the resulting value.

Progress: Sixty patients have been studied. The investigators are awaiting delivery of additional assay kits to complete the assays.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/91	Status: Completed

Title: Clinical Effect of Succinylcholine Intraosseously in Sheep

Start Date: Nov 86	Est Completion Date: Feb 87
Department: Emergency Medicine	Facility: MAMC
Principal Investigator: Stephen A. Pace, M.D., DAC	
Associate Investigator: MAJ Mel D. Robinson, MC CPT Gregory P. Moore, MC	
Key Words: succinylcholine, intraosseously, effect, sheep	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $1225.00	Periodic Review: Aug 87

Study Objective: To determine if succinylcholine will work by the intraosseous route and to compare the response to the intravenous and intramuscular routes.

Technical Approach: Sheep will be put in four point restraints and vital signs will be taken. Halothane anethesia will be given and the animal will be intubated. The animal will have the intraosseous site of the tibia and the overlying skin anesthetized and 200 cc of normal saline will be bolused to ensure that it is functioning. The animal will be allowed to lighten up so that it is breathing spontaneously and then ketamine will be used. The animal will be observed for 10 minutes with repeat vital signs done. Succinylcholine will be administered in a dose of 1 mg/kg. If no effect is observed, a second dose of 1 mg/kg will be given. The animal will be observed for fasciculations and respiratory arrest. Paralysis will be noted by absence of response to nerve stimulator; train of four will be placed over femoral nerve (this will cause leg to kick). This will be tested every 15 seconds. The animal's respirations will be supported until the effect of succinylcholine has worn off (5-10 minutes). Repeat vitals will be done 10 minutes later and as required. The intraosseous line will be removed, topical bacitracin applied, and the site bandaged. No post trial of anesthesia will be given. The animal will be observed for three days for signs of local infection. After 6 animals have been done using the intraosseous technique, the same 6 animals will be put through the protocol with the succinylcholine given intramuscularly and then given intravenously. At least two days will separate trials.

Progress: The principal investigator was changed in August 1987 to Dr. Pace upon the departure of CPT Moore.

Seven animals were studied. The intraosseous route was determined to be a little slower than but comparable to intravenouus administration. It was much faster than intramuscular. A paper is now being prepared to submit for publication.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/77	Status: Completed

Title: Usefulness of Chlamydiazyme Test in the Emergency Department

Start Date: Jul 86	Est Completion Date: Nov 86	
Department: Emergency Medicine		Facility: MAMC
Principal Investigator: CPT James A. Pfaff, MC		
Associate Investigators: MAJ Mel D. Robinson, MC CPT Laura Pimental, MC		
Key Words: chlamydiazyme test, *Chlamydia* ER, management		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jul 87

Study Objective: To define the usefulness of the Chlamydiazyme Assay in the population of women who are seen in the ER/AIC with complaints in which a sexually transmitted disease is suspected, and, more specifically, to determine the extent to which patient care is altered by the tests.

Technical Approach: Chlamydiazyme kits will be included in the pelvic setup of every patient undergoing a pelvic exam in which a gonorrhea culture or wet mount/KOH slides are made. A data sheet will be completed on each patient to standardize follow-up and it characteristics. The data sheets will be filled out by individual physicians at the time of the exam. Positive Chlamydiazyme cultures will be followed by the the ER chief resident or the investigator as is presently done. Charts of all patients in the study will be reviewed to determine the extent to which management is altered with respect to the following major points: (a) those cases in which antibiotic therapy is instituted or changed as a result of the test result; (b) those cases in which referral is made to the Sexually Transmitted Diseases Clinic for follow-up; and (c) the incidence of *Chlamydia* in the ER population of patients suspected of having sexually transmitted diseases. Chlamydiazyme tests are routinely run on these patients. This will be a data collection protocol only.

Progress: The project has been completed. Over a four-month period 326 exams were performed. Of 36 patients (11%) with positive tests, only 16 (44%) were treated clinically for pelvic inflammatory disease. These results confirm the importance of Chlamydial antigen testing on female patients presenting to the Emergency Department with complaints possibly consistent with pelvic pathology.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/06	Status: Completed

Title: Determining the Optimal Gastric Lavage Solution for Iron Poisoning

Start Date: Oct 86	Est Completion Date: Oct 87	
Department: Emergency Medicine		Facility: MAMC
Principal Investigator: CPT James A. Pfaff, MC		
Associate Investigators: MAJ Raymond P. TenEyck, USAF MAJ Charles Hannan, MS		
Key Words: poisoning, iron, gastric lavage		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $2250.00	Periodic Review: N/A

Study Objective: To study the relative efficacy of various lavage solutions in decreasing the absorption of iron ingested in excessive doses.

Technical Approach: While under anesthesia, five rabbits per group will be intubated and catheters will be placed in the left femoral artery and in a peripheral ear vein. After a baseline blood sample has been taken, an orogastric lavage tube will be placed and a moderately toxic dose of elemental iron (120 mg/kg) in the form of $FeSO_4$ tablets will be given via the lavage tube and the tube then removed. After 30 min of having received the $FeSO_4$, the lavage tube will again be placed and gastric lavage performed for another 30 min with one of five blinded solutions. Each solution will provide 250 cc of fluid per exchange for a total of three liters of fluid per procedure. The five solutions to be used are saline, bicarbonate, deferoxamine, urate, and deferoxamine plus bicarbonate. The animals will be allowed to recover and blood samples for electrolytes, arterial blood gases, BUN/creatinine, calcium, LFT's, U/A, serum iron, TIBC, and phosphate will be taken at 1, 2, 4, 6, 12, 24, and 48 hours. All surviving animals will be maintained for 6 weeks and then evaluated for evidence of gastric damage by necropsy. The serum iron levels will be evaluated, as an indicator of the extent of iron absorption. The remaining values will be evaluated to determine if there is any significant variance among treatment groups due to the possible adverse effects of the iron on the treatment itself. The KUB will be evaluated for radio-opaque fragments in each group. Correlation will be sought regarding the number of fragments vissible on the film and the lavage solution. The stomach of each animal will be removed and examined for ulceration or pyloric stricture.

Progress: The animals were tested according the the protocol and the data are being analyzed.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 82/25	Status: Suspended**

Title: Emergency Room Procedure Training

Start Date: Feb 82	Est Completion Date: Feb 87
Department: Emergency Medicine	Facility: MAMC
Principal Investigator:	MAJ Mel D. Robinson, MC
Associate Investigators:	COL Frederick Burkle, MC 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 Cost: -0-	Est Accumulative OMA Cost: $1360.00
	Periodic Review: Feb 87**

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: No procedures have been performed on this protocol during FY 87.

**The IRB recommended continuation of this protocol with the provision that the actual written protocol be revised to meet current guidelines and to state that the model being utilized is a goat. LTC Cloyd Gatrell, Chief, Emergency Medicine, is in the process of revising this protocol.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/98	Status: Completed

Title: Adult Vascular Headaches

Start Date: Oct 86	Est Completion Date: Mar 87	
Department: Emergency Medicine		Facility: MAMC
Principal Investigator:	MAJ Stephen W. Smith, MC	
Associate Investigator	1LT Patrick J. Bennett, ANC	
Key Words: vascular headaches, secobarbital, meperidine, placebo		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A

Study Objective: To compare the efficacy of two standard therapies for adult vascular headache; parenteral narcotic (Meperidine) versus oral sedative-hypnotic Secobarbital.

Technical Approach: Fifty (50) adult patients with a throbbing, disabling headache with nausea will be randomized to either Secobarbital, 200 mg p.o. plus an IM saline placebo or to Meperidine, 75 mg IM, plus an oral placebo. Patients will be contacted by telephone one week after the therapy (by a physician blinded to therapy) and asked to rate the headache on a ten point scale and to specify the time of onset of relief, duration of relief, whether symptoms have recurred within one week, any side effects of therapy and whether the patient has consulted his primary care provider for follow-up.

Progress: The principal investigator was reassigned before he was able to study the 50 patients stated in the technical approach. He plans to continue this study at his new duty station (FAMC).

Between Nov 86 and Apr 87, 47 patients were initially asked to participate in the study. Of these 22 refused to enter after reading the consent form, 2 had focal neurologic deficits, 2 had emesis, and 1 had a first (nonrecurrent) headache. Of the 20 remaining patients who were entered in this study, two had classic migraine, two had tension headache, and the remaining 16 had common migraine. For all types of headaches, secobarbital provided moderate to complete relief in 75% of patients while meperidien relieved symptoms in only 33.3%. In the category of common migraine, secobarbital provided relief in 66.6% while meperidine relieved 33.3%. For classic migraine, secobarbital relieved 1 of 1 for which it was used while meperidine relieved also 1 of 1 patients. For the two tension heacaches seconal was used for both and relieved both. Secobarbital given for later use in the patient's home seems at least equal in effectiveness to parenteral meperidine given in the emergency room. Statistical analysis of the results are in progress. It is obvious that the small sample size does not yet allow the results to achieve high significance.

D E T A I L S H E E T S

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DEPARTMENT OF FAMILY PRACTICE

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/64	Status: On-going

Title: Analysis of EDTA Chelation of Amniotic Fluid to Improve the Efficacy of the Latex Fixation Test for Rapid Detection of Group B Streptococci

Start Date: 17 Apr 87	Est Completion Date: 30 Nov 87
Department: Family Practice	Facility: MAMC
Principal Investigator: CPT David R. David, MC	
Associate Investigators: MAJ Charles E. Henley, MC CPT Mark S. Raney, MC CPT John C. Schilhab, MC	
Key Words: Group B streptococci, latex fixation test	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $352.00	Periodic Review: N/A

Study Objective: To attempt to significantly reduce the unacceptably high incidence of inconclusive results on the latex fixation test for Group B streptococci (GBS) in amniotic fluid.

Technical Approach: When amniotic fluid specimens are submitted for both culture and the latex fixation test for Group B streptococci, they will be tested by two different methods. One method will use chelation with EDTA prior to testing with the Wellcogen Strep B kit. The other method will forego the chelating step and simply test the specimen in accordance with laboratory protocol. For the EDTA chelation method, 50 µl of amniotic fluid will be placed in 1.5 ml microcentrifuge tube and added to 150 µl of a 0.1 M solution of EDTA and then the tubes will be vortexed. The specimen will then be heated for five minutes in a boiling water bath and then cooled to room temperature and clarified by centrifugation. Then 20 µl of the test latex will be placed in one circle on a test card and 20 µl of controlled latex will be placed in a separate circle. Forty microliters of the supernatant will then be placed next to each drop of latex. Without delay and using separate mixing sticks, the latex reagents will be mixed with the body fluid samples and the mixture spread over as much of the circle as possible. The card will then be slowly rocked to and fro and observed for agglutination for three minutes. The data will be compiled and statistically analyzed to determine if the hypothesis that the incidence of inconclusive results obtained by the Wellcogen Strep B test procedure can be reduced from 37% from a previous study to below 10% in this study. A comparison will be made of the efficacy of the test based on its sensitivity and specificity compared to the cultue results to simultaneously determine if the high level of efficacy is maintained.

Progress: Approximately 30 of the desired 50 or more tests have been done.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/77	Status: On-going

Title: Evaluation of Trainee Clinical Performance in Geriatrics

Start Date: 15 May 87 Est Completion Date: Nov 89

Department: Family Practice Facility: MAMC

Principal Investigator: MAJ Charles Herley, MC

Associate Investigators: Phillip Rakestraw, Ph.D.
Carol Milner, Ph.D.
Barbara Simpson, M.S.W.
CPT Ellen Pinholt, MC

Key Words: geriatrics, trainees, evaluation

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

Study Objectives: To evaluate the clinical accuracy of elderly simulated patients, to establish the reliability and validity of elderly simulated patients in clinical performance evaluation, and to compare clinical simulations with existing methods of clinical evaluation for residents.

Technical Approach: Phases 1 and 2 of this study will consist of the development and testing of case simulations from 4 actual cases: 1 depression, 1 dementia, and 2 multiple diagnostic problems including 1 with depression and 1 with dementia. The simulations will be performed for Team 1 (six professionals) who will do a workup and calculate weighted aggregate scores for the Comprehensive Older Persons' Evaluation (COPE). Team 2 will do a medical workup of the simulations using their usual workup format. These workups will be videotaped and reviewed for elements present or absent from the COPE instrument. Team 2 will then use the simulation for the purpose of developing weighted aggregate scores to compare to the weighted scores of Team 1. If differences between the teams are detected, reevaluation and revisions will be conducted. Phase 3 will then begin with the residents doing a workup of either a depression or a dementia case (randomly assigned) by their usual format, and the patient interactions will be evaluated by a preceptor. The simulated patient will be asked to rate the resident's performance on measures of interpersonal skills, communication, and professional manners and the resident will be asked to complete a self-evaluation using the same parameters. The resident will then do a workup using the COPE instrument which will include the same primary diagnosis but will include other medical problems and complications. Data will be analyzed using aggregate scores on the COPE and the evaluations completed by the preceptors, patients, and residents. Comparisons will be made between the original aggregate scores on the COPE established by the preceptor teams to the student scores on the COPE, the performance using the "usual" workup between the professionals and residents, and the first simulation performance scores will be compared to the second simulation performance scores to look for evidence of improvement of any identified shortcomings.

Progress: This study has not been implemented. The investigators are awaiting approval of a VA/DoD grant.**

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/114	Status: On-going

Title: An Analysis of Perinatal Outcome and Its Various Determinants Among Blacks and Whites in Pierce County, Washington

Start Date: 18 Sep 87	Est Completion Date: 30 May 88
Department: Family Practice	Facility: MAMC
Principal Investigator:	MAJ John P. Kugler, MC
Associate Investigators:	MAJ Charles E. Henley, MC, MAMC Frederick A. Connell, M.D.,USPHS Durlen Hickok, M.D., Swedish Hospital
Key Words:	perinatal outcome, determinants, blacks, whites

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

Study Objective: To analyze perinatal outcome data in Tacoma-Pierce County among the black and white population groups and to evaluate systems of health care delivery, level of pre-natal care, income, age, parity, and smoking status differences and to determine potential associations with more adverse perinatal outcomes. Specifically, the major objective of the study will be an attempt to more clearly delineate the factors contributing to the frequently noted differences in perinatal outcome between white and black communities.

Technical Approach: Birth certificate data linked with death certificate data will be obtained from public access tapes for Pierce County births from 1982-85. Analysis will include all balck and white infants born in Pierce County to mothers residing in Pierce County and delivered at a medical facility in Pierce County. The principal investigator will perform a stratification analysis of this data considering income, parity, system of care, maternal age, smoking, marital status, and race and the impact of these variables on several outcomes: level of prenatal care, birthweight, neonatal mortality rate, infant mortality rate, and postneonatal mortality rate. Prenatal care and birth weight will be separately analyzed as dependent variables to determine their impact on mortality rates. The Mantel-Haentszel test will be the primary statistical tool, but if time permits a mathematical model utilizing logistic regression will be attempted.

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

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/53	Status: Completed

Title: Faculty Development and Organizational Systems Behavior in Military Teaching Medical Centers

Start Date: 27 Feb 87	Est Completion Date: May 87	
Department: Family Practice		Facility: MAMC
Principal Investigator: LTC David J. Magelssen, MC		
Associate Investigator: MAJ Charles Henley, MC		
Key Words: behavioral influence, military organizational systems, professional development, faculty		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $150.00	Periodic Review: N/A

Study Objective: To assess the military organizational systems behavioral influence upon the professional development of medical corps faculty assigned to military medical teaching centers.

Technical Approach: Elements of organizational behavior to be studied are systems structure, group norms, resource allocations, statement of mission, task definition and objectives, reward systems, power and authority, information processing, group performance and intra-group conflicts. Organizational behavior and faculty development will be studied using two methods. First, qualitative data will be gathered by participant-observer methods within Madigan Army Medical Center. This data will be gathered by literature review, interviews of organizational staff members and participant observations by the author. Second, a questionnaire will be sent to all professional staff members assigned to the military's teaching medical centers. The questionnaire is constructed to measure the respondant's perception of his personal esteem, professional career growth, intrinsic motivation, identity with task performance, group identity, realization of personal objectives, career satisfaction, and productivity, as well as the organizational elements previously stated. Each question will be coded to measure one of the organizational elements or faculty development factors. Demographic data will be gathered for each respondent by institution, department, rank, career longevity, and professional responsibility. A composite score will be tabulated from the total values of the survey qeustions that relate to organizational behavior. A similar composite score will be derived from the total scores of test items that are coded for faculty development. Chisquare tests of significance will be applied to the composite scores representing individual faculty development factors cross-tabulated against the composite score of the organizational elements in a bivariate analysis. Qualitative anbalysis will be made of the same elements from the participant-observer data. Organizational behavior will be defined that facilitates faculty development.

Progress: 1,220 physicians were surveyed at 15 military medical centers. The findings indicate that the perceived impersonal complexity of the medical department's structure, the systems sluggish responsiveness in procuring adequate resources and providing support personnel, and a military reward system that is ineffectually applied and viewed with little regard are the greatest deficiences perceived by the respondants. The overall composite scores for organizational behavior and faculty development were highest among Army physicians although similar concerns were indicated by all groups. This study is to be presented at the Military Teaching Chiefs Meeting in Nov 87.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/37	Status: Completed

Title: Satisfaction Among Army Family Practice Faculty: A Descriptive Study

Start Date: 16 Jan 87	Est Completion Date: Apr 87	
Department: Family Practice		Facility: MAMC
Principal Investigator: MAJ John M. Powers, MC		
Associate Investigators: MAJ Charles Henley, MC		
Key Words: Family Practice faculty, satisfaction, questionnaire		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A

Study Objective: To provide a descriptive portrayal of the Family Practice Faculty at the six residency training programs by means of demographic and educational background data, to determine the level of satisfaction of individual faculty members, and to identify any significant differences between the satisfied and dissatisfied subgouprs in facet specific areas of satisfaction or demographic profile.

Technical Approach: Each faculty member at each of the six Army Family Practice Programs (63) will be mailed an anonymous questionnaire assessing demographic, educational, professional and satisfaction data. Responses will be collated with computation of means and standard deviations where appropriate. The group will be dichotomized into satisfied and dissatisfied subgroups based on responses to global satisfaction questions. Significant differences between the two subgroups in facet specific areas of satisfaction and demographic profile will be determined by means of two sample t-test using an alpha level of .05. Conclusions will be generalized only to faculty in Army Family Practice programs.

Progress: Fifty-nine faculty members returned completed questionnaires with 67.8% being classified as satisfied and 32.2% being classified as dissatisfied. Compared to faculty members from seven years ago, today's faculty members are slightly oler, have more practice experience, more opportunities for fellowhip training, and are less likely to have remaining mandatory millitary obligation. The satisfied subgroup had significantly higher mean satisfaction scores in the areas of intern quality, input into and ability to influence departmental decisions, job description, status both within the hospital and department, opportunity for advancement, control over professional life, administrative responsbilibty, and departmental goals and objectives. Significantly larger percentages of the dissatisfied subgroup planned to leave the Army and had yet to achieve board recertification. Definite changes could be implemented to enhance satisfaction among present faculty.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 84/69	Status: Suspended

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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Feb 87

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 availabe 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: Due to the departure of LTC Roberts, the protocol has been suspended since Feb 87. At the request of the present Director of the Faculty Development Program in the Department of Family Practice (Dr. Henley), the protocol has been left in this status until he can get the study reorganized and take over the project as principal investigator at which time it will take only a few months to complete.

D E T A I L S H E E T S

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DEPARTMENT OF MEDICINE

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/74	Status: Completed

Title: Methotrexate in the Treatment of Steroid Dependent Asthma

Start Date: Jun 86	Est Completion Date: May 87	
Dept/Svc: Medicine/Allergy/Immunology		Facility: MAMC
Principal Investigator:	LTC William P. Andrade, MC	
Associate Investigators:	LTC Gary B. Carpenter, MC MAJ Michael Witte, MC Michael F. Mullarkey, M.D.	
Key Words: asthma, steroid dependent, treatment, methotrexate		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $435.00	Periodic Review: Jul 87

Study Objective: To demonstrate a statistically significant reduction in the cortisone requirements of asthmatic patients who used a minimum of 10 mg/day of prednisone or its equivalent during the preceding year and who are clearly Cushingoid. Patients with adverse reactions from corticosteroids will be sought for this study.

Technical Approach: Diagnosed asthmatics, 18-70 years of age, who have required an average of 10 mg/day of prednisone or its equivalent during the preceding year will be entered in a double blind crossover study of 24 weeks duration. Patients will be randomly assigned to receive methotrexate (2.5 mg) or placebo for 12 weeks. At 12 weeks the crossover will occur and patients will receive the alternate treatment. Patients will receive a complete medical history and physical examination prior to entry and will be given a diary in which to record the date, daily cortisone usage, and subjective rating of asthma symptoms. Patients will be seen at least every three weeks during the study period for collection of diary data, directed examination, pulmonary function tests, monitoring of compliance of medication, and a review of any adverse reactions. Data analysis will be performed using the two tailed t-test to determine the effect on cortisone usage. Analysis will be done to compare the effect of methotrexate versus placebo on symptom scores, pulmonary function to include DL_{CO}, WBC, SGOT, theophylline levels, presence or absence of positive allergy skin tests, prior dosage of steroid as determinant of response, and adverse occurrences.

Progress: Fourteen patients with corticosteroid-dependent bronchial asthma completed this study. On the average the patients used 36.5% less prednisone when taking methotrexate. Forced vital capactiy and forced expiratory volume in one second showed no deterioration in patients who reduced corticosteroids. The patients' subjective assessment of breathing showed improvement. Adverse effects in these patients from methotrexate were limited to transient nausea in three patients and an evanescent rash in one patient. Nine patients have continued to use methotrexate from 3 to 10 months after the study's conclusion. Each of these patients has experienced further reduction in steroid requirements and f patients have discontinued prednisone. The authors conclude that methotrexate exerts a significant steroid-sparing effect in corticosteroid-dependent asthma with little short-term toxicity. A paper has been accepted for publication in the New England Journal of Medicine.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 85/31	Status: Completed

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 LTC Howard Davidson, MC	
Key Words: adenocarcinoma, multiple myeloma, lymphoma, x-rays bone scans, CT scans	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Feb 87

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: Nineteen sites of bone metastasis were evaluated in 10 patients. CT demonstrated healing during the first three months of treatment which appeared as progression on bone scans. CT often demonstrated progression when bone scan remained unchanged. The authors conclude that bone scans are an insensitive method of monitoring response to therapy of bone metastasis. An abstract of this work was presented at the Meeting of the American Society of Clinical Oncology, May 1987.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 84/80	Status: Completed

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:	MAJ Phillip W. Berger, MC
Associate Investigators:	LTC John W. Kirk, MC COL Charles Andersen, MC COL Stanton Brown, MC
Key Words:	treadmill stress testing, thallium perfusion imaging
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-
	Periodic Review: Jan 87

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: The principal investigator was changed to MAJ Berger in January 1987. Due to time constraints and an unexpected reassignment, Dr. Berger was unable to enter additional patients. Originally, 32 patients were studied. Preliminary results indicated that right atrial pacing stress testing may be more sensitive than thallium stress testing in detecting significant coronary artery disease in these patients.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/118	Status: On-going

Title: Reversion of Oropharyngeal Colonization in Patients Discharged From A Critical Care Unit

Start Date: 14 Sep 87	Est Completion Date: Dec 87	
Dept/Svc: Medicine/Internal Medicine		Facility: MAMC
Principal Investigator: CPT Kenneth A. Bertram, MC		
Associate Investigator: LTC Rodney A. Michael, MC		
Key Words: oropharyngeal, colonization, reversion, CCU		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $4080.00	Periodic Review: N/A

Study Objective: To determine the time to reversion to normal oropharyngeal microflora after discharge from a critical care unit in a group of patients hospitalized for greater than 72 hours in a critical care setting.

Technical Approach: Sixty adult patients admitted to the ICU will have nasal and oropharyngeal swabs for culture upon admission to the ICU and thereafter at 24, 48, 72, and 120 hours. After discharge from the ICU, swab cultures will also be done at 1, 2, and 4 weeks after discharge and evaluated for the presence of gram-negative bacilli and *Staphylococcus aureus* The data will be evaluated for total number of gram-negative isolates and *S. aureus* isolates, incidence of colonization by category of patient, incidence of colonization correlated with time in the ICU environment, and time to reversion to normal flora. Chi-square and trend analysis will be used to statistically analyze data.

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

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/52	Status: Completed

Title: Pulmonary Function in Army Rotary Wing Aviators and Crewmembers

Start Date: 27 Feb 87	Est Completion Date: Mar 87	
Dept/Svc: Medicine/Pulmonary		Facility: MAMC
Principal Investigator:	David L. Campbell, A.S., (CPT, USA, Ret)	
Associate Investigators:	LTC Hal Cragun, MC MAJ Thaddeus Dunn, MC CPT Douglas Crawford, MC CPT Robert M. Henderson, MC SGT Tanya R. Jones	
Key Words:	function, pulmonary, aviators, crewmembers	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $98.00	Periodic Review: N/A

Study Objective: To determine the prevalence of impairment in lung function among Army rotary wing aviators and crewmembers.

Technical Approach: Two hundred Army aviators between 18 and 45 years old will be tested during their annual flight physical. Active duty personnel will be used as the test group and a control group will be established consisting of aviation applicants and active duty personnel performing non-aviation duties. Each aviator or control will perform at least three flow-volume loops. The best loop will be selected based upon established criteria by the American Thoracic Society. The results of the control group will be compared to results from the aviators. Results will be paired by age ranges, height groupings, sex, smoking histories, and race. Each subject will be asked to estimate their approximate accumulative flight hours. The data will be cross tabulated and tested for significance using the chi-square test.

Progress: The data collection has been completed and is presently being analyzed. One hundred ninety (190) subjects were tested. Preliminary evaluation of the data suggests that pulmonary impairment in aviators and air crews of rotrary wing aircraft increases with increasing flight hours of exposure. A manuscript is being prepared.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/83	Status: On-going

Title: Investigation of Effects of Calcium Channel Blockers on Production of Testosterone

Start Date: 15 Aug 86	Est Completion Date: Aug 87	
Dept/Svc: Medicine/Endocrinology		Facility: MAMC
Principal Investigator:	CPT Kevin J. Carlin, MC	
Associate Investigators:	COL Stephen R. Plymate, MC COL Gary L. Treece, MC LTC Robert E. Jones, MC MAJ Daniel H. Knodel, MC	
Key Words: testosterone, production, calcium channel blockers		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $3891.00	Periodic Review: Jun 87

Study Objective: To determine the effects of calcium channel blockers on testicular function, using testosterone levels in 10 healthy males before and after administration of medication for one week and to observe subjects for altered testicular function after stimulation with HCG (both on and off med medication).

Technical Approach: Ten helathy males (18-40) will have a history and physical exam plus CXR, EKG, SMA-20, CBC, and UA. Stage I: Off all medication, subjects in AM will have baseline levels of LH by RIA, LH bioactive, testosterone, estradicl, and SHBG drawn. HCG (3000 units IM) will be given and the repeat levels of testosterone, estradiol, and SHBG will be drawn at 1,2,3, and 72 hours. Subjects will then be started on verapamil, 80 mg po QID. On day 8 the baseline levels will be repeated and subjects will be injected with HCG as previously done. At 1, 2, 3, and 72 hours after administration the blood levels will again be drawn and then medication will be stopped. Stage II: After a two week rest period without medication, the procedures in Stage I will be repeated using diltiazem, 60 mg po QID. Stage III: Again, after a two week rest period with no medication, the procedures will be repeated utilizing nifedipine, 10 mg (2) po qid. There will be a postmedication pill account to monitor compliance with medication. Patients will have post-investigation physical, SMA-20, CBC, and EKG to make sure no ill side effects have occurred.

Addendum June 1987: In order to better delineate the etiology of the lowering of testosterone, the investigators will perform two HCG stimulation tests 10 days apart and draw testosterone levels at baseline, 1, 2, 3, and 72 hours, similar to the original plan but on no medications and using the same subjects.

Progress: Eight subjects were studied. Several interesting findings have developed from this study. Baseline testosterone levels significantly decreased on all three medications. These findings led to the addendum of June 1987. The technical portion of this addendum has been completed and the data are being analyzed. A paper has been accepted for presentation at the American College of Physicians Meeting in October 1987.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 84/56	Status: Completed

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:	LTC Lauren Colman, MC
Associate Investigators:	COL F.H. Stutz, MC MAJ Thomas M. Baker, MC CPT Michael Stone, MC
Key Words:	Adenocarcinoma, colon, rectum, CCnu, weekly

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jul 87

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.

Amendment (Feb 85): 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.

Progress: All patients (16) completed therapy. No responses were noted.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86796	Status: Completed

Title: Bone Scan Versus Spinal Magnetic Resonance Imaging in the Evaluation of New Back Pain in Women with Cancer

Start Date: Sep 86	Est Completion Date: Dec 87
Dept/Svc: Medicine/Oncology	Facility: MAMC
Principal Investigator: LTC Lauren K. Colman, MC	
Associate Investigators:	MAJ Thomas Baker, MC
COL Irwin B. Dabe, MC	MAJ David Dunning, MC
COL Robert Karl, MC	Dana Olson, M.D.
COL John Redmond, MC	Bruce Porter, M.D.
LTC Howard Davidson, MC	Gary Stimac, M.D., Ph.D.
Key Words: bone scan, spinal magnetic resonance imaging, cancer	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $10,000.00 Periodic Review: Feb 87

Study Objective: To determine the relative sensitivity and specificity of spinal magnetic resonance imaging (MRI) using the STIR (short inversion time recovery) sequencing technique versus radionuclide bone scanning in the detection of spinal metastases in women with breast cancer.

Technical Approach: Prior to entry, 10 female patients >20 years with a history of breast cancer plus new or progressive back pain lasting >2 weeks, not attributable to known benign disorder, and with normal neurologic exam or neurologic deficits not attributable to cord or nerve root compression will have history and PE, plain radiographs of spine, bone scan, and spinal MRI using STIR sequence with or without additional MRI using T1 spin-echo sequence at the discretion of the radiologist. If both bone scan and MRI are interpreted as benign, both studies will be repeated in 3 months. If bone scan is indeterminate or if either bone scan or spinal MRI is interpreted as showing metastatic disease, a spinal CT will be performed. Five millimeter CT transverse sections will be obtained from the top of the vertebral body above to the bottom of the vertebral body below the area of abnormality on either bone scan or MRI. If destruction of the bony cortex adjacent to the spinal canal is noted on spinal CT, a metrizamide myelogram with 5 mm CT transverse sections will be ordered.

TREATMENT: All patients with destruction of pedicles or posterior cortex or vertebral body will be referred for radiation therapy after metrizamide myelography to delineate the extent of cord impingement. Other patients will receive radiation therapy, hormonal therapy, chemotherapy at the discretion of the primary oncologist. Follow-Up: Bone scans and MRI scans will be obtained as outlined above. Additional scans will be obtained at the discretion of the primary oncologist.

Addendum - 2-27-87: The inclusion criteria were changed to include other forms of solid tumor. Therefore, the title was changed to leave out the word "breast".

Progress: Fourteen patients were studied. MRI appears to be more sensitive than bone scan in detecting involved vertebral bodies, based on follow-up with spinal CT. MRI identified all spinal metastases identified by spinal CT. A manuscript is being prepared.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/70	Status: On-going

Title: High Dose Cisplatin, VP-16 with or Without Radiation Therapy in Advanced Non-small Cell Lung Cancer

Start Date: 17 Apr 87	Est Completion Date: Dec 90
Dept/Svc: Medicine/Hematology	Facility: MAMC

Principal Investigator: LTC Lauren K. Colman, MC

Associate Investigators:

COL Irwin B. Dabe, MC	MAJ David Dunning, MC
COL Donald H. Kull, MC	MAJ Ruben Sierra, MC
LTC Howard Davidson, MC	CPT Margaret Barnes, MC
MAJ Thomas M. Baker, MC	CPT David R. Bryson, MC

Key Words: nonsmall cell lung cancer, high dose cisplatin, VP-16 radiation vs no radiation

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

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

Technical Approach: Approximately 20 patients will be treated in three groups. Treatment will be determined by extent and location of cancer and by previous therapy.

Group I: Limited non-small cell lung cancer (NSCLC) with prior radiotherapy will be treated with cis-platinum, 100 mg/M^2, days 1, 8, 29, 36, 57, and 64 plus VP-16, 100 mg/M^2, on day 1-3, 29-31, and 57-59. There will be no radiotherapy.

Group II: Limited NSCLC, no prior radiotherapy, will be treated with cis-platinum, 100 mg/M^2, days 1, 8, 29, 36, 57, and 64 plus VP-16, 100 mg/M^2, days 1-3. They will also receive radiotherapy to the chest for 5-6 weeks starting day 29. Prophylactic whole brain radiotherapy will be given for three weeks starting 3-4 weeks after chest radiotherpy is completed for patients achieveing clinical partial or complete remission.

Group III: Extensive NSCLC will be treated with cis-platinum, 100 mg/M^2, days 1, 8, 29, 36, 57, 64 plus VP-16, 100 mg/M^2, days 1-3, 29-31, and 57-59.

Response rate will be defined as number of patients who have achieved a complete or partial response divided by the total number of patients evaluable for response (those who completed at least four weeks of the treatment program). Patients will be considered to be evaluable for toxicity if they received at least one dose of chemotherapy.

Progress: Eleven patients have been entered. It is too early to assess response rate. Ten patients had moderate ototoxicity and two had moderate myelosuppression, but no severe toxicity has been noted.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/113	Status: On-going

Title: Assessment of Calcium Acetate as a Phosphate Binder and Calcium Supplement in Patients with Chronic Renal Failure

Start Date: 18 Sep 87	Est Completion Date: Apr 88
Dept/Svc: Medicine/Nephrology	Facility: MAMC
Principal Investigator:	MAJ Howard Cushner, MC
Associate Investigators:	COL John B. Copley, MC, BAMC MAJ Jeff Addison, MC, MAMC MAJ Charles Nolan, MC, Wilford Hall
Key Words:	renal failure, chronic, calcium acetate, binder

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $500.00	Periodic Review: N/A

Study Objective: To assess the usefulness of calcium acetate as a phosphate binder and calcium supplement in patients with end-stage renal disease.

Technical Approach: Patients 18 to 80 years will have phosphate binding agents discontinued for one week. A serum phosphorus will be drawn pre-dialysis one week after discontinuance of the phosphate binding agent(s). Only those patients who have a serum phosphorus >5.5 mg/dl off phosphate binders will be entered. The patients will be treated with either an aluminum-containing phosphate-binding agent, calcium acetate, or calcium carbonate in a double blinded fashion. Pre-study PA20, C terminal parathyroid hormone level, serum aluminum level, and CBC will be drawn. Every two weeks during the study, a PA 20 will be drawn mid-week pre-dialysis. At 4 and 8 weeks after beginning the study drug, serum aluminum and C terminal PTH levels will be drawn. At the completion of two months on the study drug, the patients will be switched to one of the other phosphate binding agents and evaluated in an identical fashion. Then the third drug will then be evaluated in an identical fashion. In patients with chronic renal failure, not on dalysis, similar labs will be drawn at similar time periods. Dosage adjustments of stddy medications will be made in order to achieve a serum calcium of 10-10.5 mg/dl and serum phosphorus 4.5-5.5 mg/dl. A three day dietary history will be obtained at the beginning of each treatment period in order to determine the average phosphorus and calcium intake. A questionnaire will be administered to all patients which includes the following information: was constipation present; complaints about any of the drugs and, if so, what were they; which drug was prefered with respect to the taste and easiness to swallow. Mean and standard deviation for serum calcium, phosphorus, calcium phosphate products, C-PTH, alkaline phosphatase, and serum aluminum levels will be determined and compared between the treatment periods using repeated measures ANOVA to analyze the data.

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

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/57	Status: On-going

Title: The Effect of Nonsteroidal Anti-inflammatory Agents (NSAIAs) on the Template Bleeding Time

Start Date: 18 Apr 86	Est Completion Date: Apr 88	
Dept/Svc: Medicine/Hematology		Facility: MAMC
Principal Investigator: COL Irwin B. Dabe, MC		
Associate Investigator: CPT Michael D. Stone, MC		
Key Words: anti-inflammatory agents, nonsteroidal, template bleeding time, degree, duration		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jul 87

Study Objective: To determine the degree and duration of effect of various NSAIAs on the bleeding time when given at clinically used doses for a duration long enough to achieve steady state levels.

Technical Approach: Sixty patients with normal platelet count, renal function, hepatic function, alkaline phosphatase, and total bilirubin will be studied. Persons not receiving NSAIAs will undergo a baseline bleeding time and receive one of the study drugs at the dose and for the duration listed below. A repeat bleeding time will be done two hours after the last dose. The bleeding time will be repeated every 24 hours until normalization. Patients already receiving a NSAIA will have a bleeding time done done two hours after their last dose. They will discontinue the drug and repeat bleeding times will be done every 24 hours until it normalizes. At that point, drug therapy will be restarted at the previous dose.

Drug doses: Ibuprofen - 800 mg p.o. T.I.D. x 12 doses
Indomethacin - 25 mg p.o. T.I.D. x 12 doses
Sulindac - 200 mg p.o., B.I.D. x 8 doses
Prioxacam - 20 mg p.o., QD x 14 doses

Patients will be assigned to a drug in the order they are entered in the protocol until there are 15 patients in each group.

Progress: Two additional patients were entered on this study in FY 87 for a total of 12 patients entered.

COL Dabe was named as the principal investigator in July 1987 due to the departure of CPT Stone.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 85/32	Status: Completed

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: LTC Howard Davidson, MC	
Associate Investigators:	
COL Robert Karl, MC	COL 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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: May 87

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: No new patients were entered on this study during FY 87. A paper was presentation at the 1987 meeting of the American Society of Clinical Oncologists.

Serial CT scans of treated bone lesions show that lesions which have more radionuclide uptake on the three month bone scan were actually healing in response to radiation therapy and they often show progression or response of the lesions which occurred after treatment in patients whose bone scans were interpreted as unchanged. Overall, it appears that CT scans give a more accurate assessment of results to therapy.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/28	Status: On-going

Title: Phase II Study of Ifosfamide and Mesna Alone or as Part of Combination Chemotherapy in Refractory Testicular Cancer

Start Date: 17 Jan 86	Est Completion Date: Jan 88	
Dept/Svc: Medicine/Oncology		Facility: MAMC
Principal Investigator: LTC Howard Davidson, MC		
Associate Investigators: COL John Redmond, MC MAJ David Dunning, MC		
Key Words: testicular, cancer, ifosfamide, mesna, combination		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: May 87

Study Objective: To determine the objective response rate and duration of remission of ifosfamide in patients with testicular cancer refractory to cis-diamminedichloroplatiunm (CDDP) combination chemotherapy; the objective response rate and duration of remission of Ifosfamide combination chemotherapy for remission reinduction in patients not cured with initial therapy, the toxicity of Ifosfamide in refractory testicular cancer; the toxicity of ifosfamide in combination with cisplatin ± VP-16, VP-16 alone, or vinblastin ± bloemycin in refractory testicular cancer.

Technical Approach: After one 5-day course of either treatments A, B, C, D, E, or F (see below) response to therapy will be evaluated. If disease has decreased and/or some symptom relief is noted with no increase in disease, therapy will continue on the same schedule for as long as response is noted for a maximum of 6 courses of therapy. If there is no response after 6 courses, the treatment will be stopped. Patients will receive Ifosfamide alone or in combination based on prior experience with chemotherapy. Treatment will be repeated every 3 weeks for patients who do not demonstrate progression for a maximum of 6 courses. In patients with subsequent resection of residual carcinoma, 2 additional post surgical courses will be done. Treatment A: Ifosfamide - single agent; Treatment B: Ifosfamide + platinum; Treatment C: Ifosfamide + Platinum + VP-16; Treatment D: Ifosfamide + Platinum plus Velban; Treatment E: Ifosfamide + VP-16 + Bleomycin; Treatment F: Ifosfamide + Velban ± Bleomycin. This study is being done in conjunction with the University of Indiana.

Progress: No new patients were entered at MAMC in FY 87. One patient was entered in FY 86 and severe neutropenia and neutropenic fever with staph epidermitis sepsis were reported, which required reduction of ifosfamide and velban doses in cycles 2, 3, and 4.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/87	Status: Ongoing

Title: Radiation Survival of Human Prostate Carcinoma Cells

Start Date: 15 Aug 86	Est Completion Date: Nov 87	
Dept/Svc: Medicine/Oncology		Facility: MAMC
Principal Investigator:	MAJ David Dunning, MC	
Associate Investigators:	COL Donald Kull, MC CPT Joseph Hellman, MS Richard Ostenson, M.D. Stephen Loop, M.S.	
Key Words:	cells, carcinoma, prostate, survival, radiation	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $1943.00	Periodic Review: Dec 86

Study Objective: To determine *in vitro* survival following incremental exposure to radiation of several prostate cancer cell lines that have been established and maintained in tissue culture medium.

Technical Approach: Confluent tissue culture flasks or cell suspension will be exposed to incremental doses (100-1400 rads) of radiation (approximately 100 rads/min) using a Co 60 source. Throughout the procedures, all cells will be kept on ice to maintain viability. Following radiation treatment, the adherent tumor cells will be trypsinized for 5-10 minutes at 37°C. The cells will be washed several fold in PBS containing 1% FCS to inhibit further enzyme action. Cell numbers will be determined by direct counting in a hemacytometer. Cell viability will be ascertained by trypan blue exclusion. Irradiated suspension cultures and control cultures will be treated in an analogous fashion. Control cultures will consist of TC flasks or suspension cultures harvested at the time of the initiation of the experiment and maintained on ice throughout the radiation period.

Progress: A paper has been accepted for presentation at the 4th Annual Hematology/Oncology Scientific Meeting (a part of the ACP Meeting) in October 1987.

Data thus far indicate that there no significant differences in the radiation sensitivity parameters for either the cell suspension or the cell monolayer cultures. By this methodology, measurements of radiation survival could be accurately made to levels as low as 0.01% of the control values. Survival curves determined by direct counting of tumor cells demonstrated a decrement in surviving cell number at all radiation doses tested. These results suggest that prostate tumor cells are less sensitive to radiation than that reported for most human adenocarcinomas. An average SF2 of 0.54 suggests that prostate tumor cells are similar to melanoma in radiosensitivity. These data demonstrate that the tritiated thymidine incorporation assay is a rapid, easy method for determining radiation sensitivity of human tumor cells *in vitro*.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/54	Status: Suspended

Title: The Natural History of HTLV-III Infection and Disease in a United States Military Population

Start Date: has not started	Est Completion Date: Not known	
Dept/Svc: Medicine/Infectious Disease		Facility: MAMC
Principal Investigator: COL Peter Gomatos, MC		
Associate Investigators: None		
Key Words: HTLV-III, natural history, progression, military		
Accumulative MEDCASE Cost: $5,920.00**	Est Accumulative OMA Cost: $1,940,064.00**	Periodic Review: Feb and Sep 87

Study Objective: To assess the impact of HTLV-III infection on fitness for duty by systematically defining the natural disease progression in individuals with documented HTLV-III infections in the general military population; to determine the impact of cofactors, i.e., drug abuse, physical activity, on disease progression; and to form an information base and a study cohort upon which numerous other studies can be built, i.e., drug treatment of HTLV-III.

Technical Approach: Currently, all military health care beneficiaries with serological evidence of HTLV-III infection are referred to an Army medical center for evaluation by an Infectious Disease specialist. These patients will be evaluated by the complete standard battery of testing done for HTLV-III patients, plus patient education and counselling. Each HTLV-III infected individual will be staged according to the Walter Reed Staging Classification. The only additional requirement of individuals enrolled in this study is that information gathered from each individual as a consequence of this study will be centralized in a common data base located at WRAIR. These subjects will have repeat evaluation every 6 months for up to five years with communication continued via letters at three month intervals to maintain contact and provide any new information to the subjects. At a minimum, the occurrence/staging of disease progression will be determined with time interval, age, sex, risk factor, ethnic group, coinfection with EBV, CMV, and HBV representing individual variables.

Progress: This protocol has not received final approval for funding. However, Walter Reed AMC has agreed to provide the laboratory support. Dr. Gomatos requested that the protocol be left in a suspended status since it appears that the funding will be forthcoming.

**All funds to be provided by Medical R & D Command.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/65	Status: Suspended

Title: A Comparison of 7 vs 14 Days Therapy with Trimethoprim-Sulfamethoxazole in the Treatment of Acute Pyelonephritis

Start Date: 17 Apr 87	Est Completion Date: May 89
Dept/Svc: Medicine/Infectious Disease	Facility: MAMC
Principal Investigator: CPT Patrick D. Gorman, MC	
Associate Investigators: LTC Rodney A. Michael, MC CPT William A. Pearce, MC	
Key Words: pyelonephritis, trimethoprim-sulfamethoxazole, days	

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

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

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

Progress: This protocol has been suspended until the investigator completes the revisions required by the Institutional Review Board.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/55	Status: Completed

Title: Comparison of Bronchial Washings versus Formal Bronchoalveolar Lavage in the Cytologic Diagnosis of Peripheral Pulmonary Neoplasms

Start Date: Apr 86	Est Completion Date: Mar 87
Dept/Svc: Medicine/Pulmonary	Facility: MAMC
Principal Investigator: CPT Bruce S. Grover, MC	
Associate Investigators:	COL J. Waylon Black, MC
MAJ W. Hal Cragun, MC	MAJ Michael Witte, MC
MAJ Thaddeus L. Dunn, MC	CPT Ronald Fullmer, MC
Key Words: neoplasms, pulmonary, diagnosis, washings, lavage	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-
	Periodic Review: Oct 86

Study Objective: To determine if formal 240 cc bronchoalveolar lavage (BAL) increases the diagnostic yield of bronchoscopy in the evaluation of patients with peripheral pulmonary neoplasms. In addition, the yield of BAL is to be compared with that of the traditional small volume washes.

Technical Approach: Forty subjects, >18 years of age, with lung nodules suspicious for malignancy, will have standard fiberoptic bronchoscopy performed. The lesion will be localized as well as possible by fluoroscopy. A radiopaque catheter will be used to identify the relevant subsegmental bronchus, and the bronchoscope will be wedged into the subsegmental orifice, and small volume washes will be done in the orifice. After the small volume wash (7 cc return), a large volume wash will be done by adding sterile room temperature saline in 30 cc aliquots according to the method of Watters et al (ARRD 133:105), with harvest of the fluid by hand suction. The effluent will be placed into Saccomanno's solution. Then, if clinically indicated, brushings and transbronchial biopsies will be performed, followed by a repeat small volume wash. Supplemental oxygen will be provided during the procedure; both electrocardiographic and oximeter monitoring will be employed. The procedure will be terminated if >100 cc of lavage fluid remains "unharvested" at any point to preclude undue hypoxemia.

The large volume (BAL) and small volume washes will be compared on the basis of yield of diagnosis, with the endpoint being whether or not malignancy can be diagnosed by cytologic examination of the fluid. The small volume washes, pre and post transbronchial biopsy, will also be compared on the basis of yield of diagnosis of malignancy. The chi^2 test will be used in the statistical analysis.

Progress: There was positive cytologic diagnosis in only one patient (positive in both the BAL and the small volume wash). A paper was presented at the ACCP (Oct 86) which showed there was minimal yield with BAL on the cytologic diagnosis of peripheral tumors and no additive yield above a small volume wash.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/73	Status: Completed

Title: Pleuroscopy in the Sheep with a Flexible Fiberoptic Bronchoscope

Start Date: 20 Jun 86	Est Completion Date: Jan 87
Dept/Svc: *Medicine/Pulmonary*	Facility: MAMC
Principal Investigator:	CPT Bruce S. Grover, MC
Associate Investigators:	COL J. Waylon Black, MC MAJ Hal W. Craqun, MC MAJ Thaddeus L. Dunn, MC MAJ Michael C. Witte, MC
Key Words:	pleuroscopy, fiberoptic bronchoscope, flexible, sheep

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review Oct 87

Study Objective: To determine the best technique for the use of the fiberoptic bronchoscope in pleuroscopy.

Technical Approach: The animals will be given a general anesthetic for pain control and an area will be shaved in the lateral thorax 5 to 6th intercostal space along the posterior axillary line. The site will be infiltrated with a local anesthetic. A 1-2 cm incision will be made in the skin and a purse string suture of #0 silk placed around it. With sharp dissection, the incision will be extended through the intercostal muscles. By blunt dissection the pleural space will be entered. The sterilized fiberoptic bronchoscope will be inserted into the pleural space with a purse string ligature to maintain an airtight seal. Pleural fluid will be removed through the suction channel of the bronchoscope to clear the pleural space. Air will be introduced as needed through the suction channel to produce a small controlled pneumothorax for better visualization. Pleural space will then be systematically explored visually with the bronchoscope. Biopsy forceps will be inserted through the suction channel and biopsies will be taken. The air will be sucked out from the thorax as the bronchoscope is being removed. The area will then be closed with the #0 silk suture. The same procedure will then be performed again. The only difference in technique will be that an endotracheal tube will be inserted through the hole in the chest cavity and the fiberoptic bronchoscope will then be inserted directly through the endotracheal tube. The two methods will be compared for ease of maneuverability of the scope to see which gives better visual access and which is the most efficient in obtaining biopsies. A third method will be performed using a thicker scope, the flexible sigmoidoscope.

Progress: Five sheep were studied. Several scopes (flexible and rigid) were evaluated. It was determined that flexible scopes provide inadequate visualization. The rigid laparoscope/thoracoscope was preferred and ordered for human use.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/78	Status: On-going

Title: Evaluation of Prednisone as an Anti-tussive During Bronchoscopy

Start Date: 18 Jul 86	Est Completion Date: Nov 86
Dept/Svc: Medicine/Pulmonary	Facility: MAMC
Principal Investigator: CPT Bruce S. Grover, MC	
Associate Investigators:	MAJ Thaddeus L. Dunn, MC
COL J. Waylon Black, MC	MAJ Michael C. Witte, MC
MAJ Hal W. Cragun, MC	CPT Marin Kollef, MC
Key Words: bronchoscopy, anti-tussive, prednisone, placebo	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $50.00	Periodic Review: Sep 87

Study Objective: To determine if prednisone given prior to bronchoscopy will help reduce the incidence and severity of coughing during bronchoscopy.

Technical Approach: Thirty adult patients scheduled for bronchoscopy will be randomized. Arm I will receive prednisone the night prior to and at 6 hr prior to the procedure. Arm II will receive a placebo on the same schedule. Spirometry will be done 72 hr prior to, immediately prior to, and immediately after the bronchoscopy. Patients will receive atropine and codeine 20-30 minutes prior to the procedure. Nebulized lidocaine and lidocaine jelly will be administered in one nostril and bronchoscopy will then be initiated in the usual manner. Once the bronchoscope is through the nasal passage, all coughs during the procedure will be recorded with the amount of topical lidocaine used as a cough suppressant noted. At the end of the procedure, the patient will be asked to complete a questionnaire, stating tolerance of the procedure, what he disliked most about the procedure, and whether or not he would undergo the procedure again. Statistical analysis will be done using analysis of variance. The amount of coughing and the degree of patient tolerance will be compared between the prednisone and placebo groups. The bronchoscopy will be divided into 15 min periods and the coughs will be counted as coughs per 15 min period and also as coughs per minute. If there is a significant difference in coughing or patient tolerance, an analysis will be done to determine whether there is a difference in response between the groups with and without bronchodilator response during pulmonary function testing. The data will be analyzed after 30 subjects have been studied to determine if more subjects need to be studied in order to achieve statistical significance.

Progress: Twenty additional patients were studied in FY 87 for a total of 30 patients studied. In the overall group, there was no significant difference in the number of coughs during bronchoscopy in the prednisone versus the placebo group. In the small number of patients with reversible obstructive airways disease (OAD), there seemed to be less coughing in the prednisone group. The investigators plan to study at least 10 more patients with reversible OAD to determine if the trend is confirmed.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/02	Status: On-going

Title: Effect of Testosterone on Bone Density in Males on Chronic Prednisone Treatment for Obstructive Airways

Start Date: Sep 86	Est Completion Date: Mar 88	
Dept/Svc: Medicine/Pulmonary		Facility: MAMC
Principal Investigator: CPT Bruce Grover, MC		
Associate Investigators:	COL Gary L. Treece, MC	
COL Stanton Brown, MC	MAJ Thaddeus Dunn, MC	
COL Robert Karl, MC	MAJ Michael Witte, MC	
COL Stephen Plymate, MC	CPT Kevin Carlin, MC	
Key Words: bone density, OAD, prednisone, testosterone		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: 200.00	Periodic Review: N/A

Study Objective: To determine if testosterone therapy can inhibit or reverse the bone loss incurred during long term glucocorticoid therapy in males with obstructive lung disease.

Technical Approach: Subjects: 20-40 males, >21 years

Patients with asthma or COPD currently on glucocorticoids will be evaluated basally with T_4, T_3U, TSH, CBC, SMA 20, PTH, 25 hydroxy vitamin D, testosterone, SSBG, LH, FSH, prealbumin, arterial blood gas, 24-hour urine for Ca Cr, spirometry, maximal inspiratory pressure (MIP), metabolic bone survey, and a bone density measurement of L2-L4 and the femoral head by dual photon bone densitometer. Utilizing a double-blind study, each patient will receive 1500 mg calcium/day and 50,000 U of vitamin D/week. All patients will be maintained on theophylline compounds and inhaled beta agonists. The prednisone dosage will be maintained as low as the respiratory status will allow. Patients will be randomized into two groups. Group 1 will receive depotestosterone, 200 mg IM, every two weeks. Group 2 will receive a placebo injection. Bone density will be measured, utilizing the dual photon bone densitometer, when the patient enters the protocol, and at 3,6,9, and 12 months. A repeat metabolic bone survey will be taken at 12 months. Spirometry and MIP will be repeated at 3, 6,9, and 12 months.

Statistical analysis: Bone density measurements before and after treatment in the treated and placebo groups will be compared using the two-tailed T test. Regression analysis will be used to determine the influence of baseline total and free testosterone on the response to treatment. Semi-quantative evaluation of clinical factors such as patient well being, prednisone requirements, libido, bone pain, and development of new or progression of compression fractures will also be made.

Progress: No patients have been entered. The study will begin as soon as all the equipment is obtained. The dual photon densitometer is to be purchased from Department of Radiology MEDCASE funds and has been deleted from Clinical Investigation MEDCASE funds to avoid duplication.

Detail Summary Sheet

Date: 30 Sep 87	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:	LTC 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 Cost: -0-	Est Accumulative OMA Cost: $785.00	Periodic Review: Nov 86

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

Technical Approach: Normal human semen samples will be used to establish a ligase assay. Ligase activity will be measured using a sensitive radioligand/millipore filter procedure that utilizes (3H)-coenzyme A as the radioactive trace. Approximately 0.2 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: Pilot studies with whole sperm indicate that ligase can be inactivated by trypsin in a time dependent fashion. This would suggest that ligase is associated with the sperm plasma membrane. Completion of this protocol hinges upon the purification of ligase (see MAMC protocol #85/84 by Jones).

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 85/17	Status: Terminated

Title: Establishment of a Long Term Mammalian Hepatocyte Tissue Culture

Start Date: 19 Nov 84	Estimated Completion Date: Nov 85
Dept/Svc: Medicine/Endocrinology	Facility: MAMC
Principal Investigator:	LTC 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 Cost: -0-	Est Accumulative OMA Cost: $1075.00	Periodic Review: Nov 86

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

Technical Approach: Both rat and rabbit livers will be used. The animals will be anesthetized and the liver 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% CO_2 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: No further work was done on this protocol in FY 87 due to the acquisition of the human hormone responsive hepatoma cell line, Hep G2, from the Wistar Institute.

Detail Summary Sheet

Date: 30 Sep 87	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: LTC Robert E. Jones, MC	
Associate Investigators: COL Stephen R. Plymate, MC MAJ Charles J. Hannan, MSC	
Key Words: cellular location, mulecular size, functional relationship, hepatic/mitochondrial forms	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: 708.00	Periodic Review: Nov 86

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 investigators have continued to have technical difficulties with this protocol. Several column elutions have been tried; unfortunately, protease activity has not been inhibited and ligase activity has been lost. It is planned at this time to add para-aminobenzamidine to the elution buffer.

Detail Summary Sheet

Date: 30 Sep 87	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: LTC 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 Cost: -0-	Est Accumulative OMA Cost: 700.00	Periodic Review Nov 86

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

Technical Approach: Only ejaculates deemed normal by standard criteria will be utilized in this study. 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 (Km, Vmax, Ki) will be calculated using standard formulae and plots. 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 experimentall 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	Km, Vmax
Double Bond specificity	3H-CoASH	16:1 (cis, trans)	Km, Vmax
Competition curve	3H-PA	Coincubation of 16:0 (0-10 μM) with 0, 5, 10 μM PUFA	Km/Ki, Vmax

Progress: In prior studies, the investigators have shown that 22:6 was a noncompetitive inhibitor of 16:0 activation. Using a similar assay procedure but with ^{14}C-22:6 and unlabelled 16.0, it was shown that 16:0 is a competitive inhibitor of 22:6 CoA synthesis. In addition, 22:6 CoA synthesis demonstrated an identical pH optimum to 16:0 activation (8.4) suggesting that both fatty acids are acted upon by the same enzyme. When 22:6 was the acyl substrate and CoASH was varied, a pattern of negative cooperativity was encounted, explaining the mechanism of the regulation of ligase by 22:6.

A paper was presented at the American Society of Andrology in March 1987 and a paper has been accepted by the New York Academy of Sciences. Two manuscripts have been submitted for publication.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/70	Status: On-going

Title: Hormonal Regulation of Rabbit *(Oryctolagus cuniculus)* Liver Long Chain Fatty Acid:CoASH Ligase (AMP). Effects of Insulin, Glucagon, Glucocorticoids and Thyroid Hormones

Start Date: 20 Jun 86	Est Completion Date: Jul 87	
Dept/Svc: Medicine/Endocrine		Facility: MAMC
Principal Investigator: LTC Robert E. Jones, MC		
Associate Investigator: COL Stephen R. Plymate, MC		
Key Words: long chain fatty acid: CoASH ligase, rabbit liver, hormonal regulation, effects		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $2388.00	Periodic Review: Jul 87

Study Objective: To determine if rabbit liver ligase is modulated by hormonal influences by testing the effects of various hormones on the kinetics of fatty acid activation in cultured hepatocytes.

Technical Approach: Hepatocytes will be obtained and cultured using modifications of a previously approved MAMC protocol. The biomatrix (collagen-coating) will be synthetically generated using commercially available collagen. The wells will be allowed to air dry and will be recoated within 24 hours. After the biomatrix has set, the plates will be covered in paraffin film and stored at 4°C. To guarantee culture plate sterility, the wells will be exposed to 10,000 rads from a cobalt source prior to cell plating. Hormonal testing, in triplicate, will then be done (T_4, dexamethasone, insulin [without SGF-7 and in CEM 2000 minus insulin], and glucagon) using varying concentrations, including zero concentration. All hormones will be tested at a 50 nM concentration with CEM 2000 and SGF-7. The effects of time exposure will be assessed. After the incubations have been completed, the cells will be harvested by collagenase digestion, identical conditions will be pooled, and the cells counted. Per cent cellular viability will be determined, cells will be centrifuged, washed in sucrose 5mM Tris, and homogenized. The homogenate will be centrifuged to remove cellular debris/plasma membranes and the resulting supernatant will be centrifuged at 10,000 g. The pellet containing mitochondria will be saved and the supernatant with the microsomal fragments will be centrifuged at 105,000 g. Both pellets will be washed and recentrifuged as outlined above. Plasma membranes will be isolated and purity determined by enzymatic analysis. Ligase activity will be measured using a minor modification of the method of Polokoff and Bell (J Lipid Res 1975). One way ANOVA will be used to determine differences within a given hormone treatment group. If a difference is found ($P<0.05$), a t test or multiple range comparison will be used to identify the specific deviations. A similar approach will be used to study differences between different hormone incubations.

Progress: Hepatocytes from three rabbits were studied in FY 86 to optimize the conditions for culture. If contamination was avoided, the hepatocytes survived for two weeks, but normal biochemical function could not be readily documented. No further progress was made on the study in FY 87.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/23	Status: On-going

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

Start Date: 21 Nov 86	Est Completion Date: Dec 87	
Department: Clinical Investigation		Facility: MAMC
Principal Investigator:	LTC Robert E. Jones, MC	
Associate Investigators:	COL Stephen R. Plymate, MC MAJ Charles J. Hannan, MC CPT Kevin J. Carlin, MC	
Key Words:	spermatozoa, phospholipids, palmitic acid, docosahexaenoic acid, acyl transferase, Land's pathway	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $1600.00	Periodic Review: N/A

Study Objectives: To determine if sperm can replenish phospholipids after they have been partially hydrolyzed to the lyso-forms by the action of phospholipases A_2 or A_1 and to attempt to identify and characterize sperm acyl transferase.

Technical Approach: Acyl CoA:1-acyl-sn-glycero-3-phosphocholine O-acyl transferase will be screened by conincubating human sperm with labelled fatty acids, CoASH, ATP, Mg^{2+}, and Tris. The reaction will be terminated by delipidating the sperm with $CHCl_3$:MeOH, and the organic phase will be chromatographed on silica gel TLC plates. These plates will be developed and spots will be scraped and counted. If the labelled fatty acid is found to be contained within a phospholipid region, cofunctioning of ligase and acyl transferase will be assumed to occur. Studies to characterize acyl transferase activity will be performed using an assay based on the liberation of CoASH which reacts with DTNB, resulting in a change in absorption at 414 nm. Either palmitoyl or docosahexaenoyl CoA will be used as the acyl donor to lyso-phosphytidyl choline. The conversion of lyso-phosphatidyl choline to phosphatidyl choline will be chromatographed. This assay will be optimized for pH, ionic strength, substrate levels and amount of enzyme before kinetic constants are determined. For carnitine-dependent transacylation, D,L-palmitoyl carnitine and lyso-phosphatidyl choline will be coincubated with washed sperm, delipidated and the products chromatographed as above. If the amount of lyso-phosphatidyl choline declines while phosphatidyl choline increases, a carnitine dependent mechanism will be presumed to exist. Alternatively, carnitine dependency could be screened by using ^{3}H-palmitoyl carnitine and looking for labelled phosphatidyl choline formation. The effect of 22:6 on 16:0 incorporation into phospholipids will be assessed by incubating unlabelled 22:6 with ^{3}H-16:0 and following the appearance of 16:0 in phosphatidyl choline. Conversely, the effect of 16:0 on ^{14}C-22:6 will be studied.

Progress: Acyl transferase activity in whole sperm has been evaluated by measuring ^{3}H-palmitic acid and ^{14}C-docosahexaenoic acid incorporation into phosphatidyl choline and separating the phospholipids by TLC. The synthesis of phosphatidyl choline from lyso-phosphatidyl choline was dependent upon the presence of coenzyme A in the incubation, thereby implying cofunctioning of long chain fatty acid:CoASH ligase (AMP) and acyl transferase.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/19	Status: Suspended

Title: Transhepatic Lipoprotein Gradients and Their Relationship to Sex Steroid Concentrations

Start Date: 15 Nov 85	Est Completion Date: Sep 86	
Dept/Svc: Medicine/Endocrine		Facility: MAMC
Principal Investigator: MAJ Daniel H. Knodel, MC		
Associate Investigators:		
COL Stephen R. Plymate, MC	MAJ Charles J. Hannan, MS	
LTC John W. Kirk, MC	Thomas M. Kettler, B.S., GS/09	
Key Words: sex steroids, HDL2, HDL3, apolipoprotein A1 and A2		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: 200.00	Periodic Review: Feb 87

Study Objective: To examine the changes in high density lipoprotein cholesterol fractions HDL2 and HDL3, apolipoprotein A1 and apolipoprotein A11 (Apo A1 and Apo A11) concentrations that occur as blood passes through the liver in male patients presenting for heart catheterization. Further, to investigate the relationship between sex steroid levels and different transhepatic lipoprotein gradients.

Technical Approach: Subjects: Ten male subjects already scheduled for routine right and left heart catheterization will be recruited for this pilot study. Patients with unstable angina and acute or subacute myocardial infarctions will be excluded from the study. Procedure: During right heart catheterization, as the catheter is passed up the femoral vein and through the inferior vena cava, the hepatic vein will be catherterized and a 5 cc sample of blood will be drawn. During the left sided catheterization procedure, a 5 cc sample of arterial blood will be drawn. Testing of Samples: Testosterone, estradiol, SHBG and calculated non-SHBG bound T will be determined by methods previously described (Plymate et al., J Clin Endocrinol and Metab 52:1246, 1981). Total cholesterol and triglycerides will be measured by the methods of Friedl, et al (Friedl, Plymate and Paulsen, Contraception 31:409-420, 1985). HDL fractions II and III and apolipoprotein A1 and A11 will be measured by the methods of Hannan, et al (Analysis of apolipoprotein A1 by high-performance liquid chromatography and radioimmunoassay, to be submitted to Clinical Chemistry). Statistics will be performed as appropriate, using the SPSS and STAT graphics programs.

Progress: No additional patients were entered in this study in FY 87. The principal investigator was reassigned in July 1987. The protocol has been suspended until a decision is made as to who will be selected as the new principal investigator.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/22	Status: Terminated
Title: Potentiation of Tricyclic Antidepressants by Triiodothyronine		
Start Date: 15 Nov 85	Est Completion Date: Jun 87	
Dept/Svc: Medicine/Endocrine		Facility: MAMC
Principal Investigator: MAJ Daniel H. Knodel, MC		
Associate Investigators: COL Stephen Plymate, MC; COL Gary Treece, MC; LTC John Wamble, MC; Bill Finch, GS/0; Doug Oberding, GS/07, DAC		
Key Words: tricyclic antidepressants, triiodothyronine		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $3000.00	Periodic Review: Apr 87

Study Objective: To determine whether or not low dose triiodothyronine potentiates the action of desipramine, a tricyclic antidepressant, in the treatment of unipolar depression and to determine if thyrotropin releasing hormone stimulation tests (TRH stimulation tests) can predict responders.

Technical Approach: Fifty patients will be recruited for the study. After 20 patients have completed the protocol, statistical data will be analyzed and a decision made on whether to continue further patient investigation. For inclusion in the study the patients will meet the RDC and DSM III criteria for major depression and have an initial Hamilton Depression Scale Rating of at least 18. Excluded from the study will be patients who are pregnant and patients with a history of heart disease, <21 or >60 years of age, having physical findings consistent with hyperthyroidism or laboratory evidence of hyperthyroidism or hypothyroidism. Both a psychiatric and a medical evaluation will be completed. The psychiatric evaluation will include two evaluators completing the Hamilton Depression Scale as well as the patient completing the Beck Depression Inventory. Medical evaluation will include an abbreviated physical exam, blood determinations of T3 RU, T4, FTI, T3 by RIA, TSH, TRH stimulation test, ACE level, testosterone binding globulin level, and dexamethasone suppression test. During the six week study period the Hamilton Depression Scale will be repeated at one, two, three, four, and six weeks. At four weeks the baseline medical test will be repeated. The study will be double blinded. All patients will receive the baseline studies mentioned above. Half of the patients will receive desipramine 50 mg t.i.d. plus a placebo. The other half will receive desipramine 50 mg t.i.d and triiodothyronine 25 μg daily. After four weeks of therapy the placebo and the triiodothyronine will be discontinued.

Progress: Four patients entered the study before the associate investigator from Psychiatry who was to perform the psychiatric evaluations was reassigned. Dr. Knodel and an investigator (psychiatrist) from the American Lake VA Medical Center submitted this study to the Human Use Committee there and it did not pass. Since psychiatric assistance was not available, the protocol was terminated.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/08	Status: Terminated

Title: Atrial Natriuretic Factor (ANF) Levels in the Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH)

Start Date: 17 Oct 86	Est Completion Date: Jun 87
Dept/Svc: Medicine/Endocrinology	Facility: MAMC
Principal Investigator:	MAJ Daniel Knodel, MC
Associate Investigators:	COL Stephen Plymate, MC COL Gary Treece, MC LTC Robert Jones, MC LTC Dan Moore, MC Louis Matej, B.S., Med Tech
Key Words:	SIADH, ANF, sodium chloride, salt wasting

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

Study Objective: To demonstrate whether or not atrial natriuretic factor (ANF) is elevated in the syndrome of inappropriate antidiuretic hormone secretion (SIADH). If elevated, the action of ANF could be responsible for the salt wasting seen in SIADH, when sodium chloride is given to patients with SIADH.

Technical Approach:

Subjects: 20 patients, $\geq$ 18 yrs, male or female

Evaluations before entry: Physical examination showing patient to be euvolemic; serum osmolality, lytes, BUN, Cr, Glu; urine lytes and osmolality; U/A; and no evidence of adrenal or thyroid insufficiency.

Twenty patients will be enrolled in the study at the time they are diagnosed as having SIADH. Baseline lab data will have been obtained. A 7 ml blood sample will be obtained for measurement of ANF levels. The patients will be treated in an appropriate fashion for SIADH. After sodium returns to normal, repeat baseline studies and repeat blood samples for ANF levels will be drawn.

Method of data analysis: A t test will be used to determine if high levels of ANF are associated with untreated SIADH and to determine if these levels return to normal with treatment of SIADH.

Progress: No patients were entered in this study. It was terminated in July 1987 due to the departure of the principal investigator.

Detail Summary Sheet

Date: 30 Sep 86	Protocol No.: 87,19	Status: Terminated
Title: Atrial Natriuretic Factor Levels Associated with Hyporeninemic Hypoaldosteronism (HHA)		
Start Date: 21 Nov 86	Est Completion Date: Sep 86	
Dept/Svc: Medicine/Endocrinology		Facility: MAMC
Principal Investigator: MAJ Daniel Knodel, MC		
Associate Investigators: COL Gary Treece, MC LTC Robert Jones, MC Louis Matej, B.S., Med Tech		
Key Words: ANF, HHA, HDL_2, HDL_3, Apo A_1, Apo$_{II}$, sex steroids		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $200.00	Periodic Review: N/A

Study Objective: To demonstrate the relationship of hyporeninemic hypoaldosteronism (HHA) and atrial natriuretic factor (ANF) levels.

Technical Approach:

Subjects: 16 subjects, $\geq$ 18, male or female

Evaluations before entry: Patients with suspected HHA will be referred to Endocrinology. This would presume that other potential causes of hyperkalemia have been considered and ruled out prior to entry.

Sixteen patients being evaluated for HHA will be enrolled in the study. Those who do not meet the criteria for HHA will be used as controls. Baseline renin and aldosterone levels will be drawn. Renin and aldosterone will be drawn again after 40 mg of p.o. Lasix and a 4 hour period of standing. ANF levels will be drawn as a baseline and after renin and aldosterone stimulation. Plasma ANF samples will be collected and frozen at -70°C and measured at monthly intervals using RIA kits. Baseline and stimulated ANF levels in patients who demonstrate findings consistent with HHA will be compared with patients whose renin and aldosterone levels are inconsistent with HHA. The t-test will be used to determine if significant differences in ANF levels exist between patients with HHA and matched controls.

Progress: One patient was entered in this study. The study was terminated in July 1987 due to the departure of the principal investigator.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/20	Status: Terminated

Title: Atrial Natriuretic Factor Stimulation Testing in Patients with Idiopathic Edema

Start Date: 21 Nov 86	Est Completion Date: Jun 87	
Dept/Svc: Medicine/Endocrinology		Facility: MAMC
Principal Investigator: MAJ Daniel Knodel, MC		
Associate Investigators: COL Gary Treece, MC LTC Robert Jones, MC Louis Matej, B.S., Med Tech		
Key Words: ANF, saline fluid loading, idiopathic edema		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $300.00	Periodic Review: N/A

Study Objective: To demonstrate that patients with idiopathic edema do/do not have an abnormal ANF response to normal saline fluid loading.

Technical Approach:

Subjects: 10 subjects and 10 age and sex-matched controls, $\geq$ 18 years of age, male or female

Evaluations prior to study: abbreviated history and physical, albumin, creatinine, liver function tests, UA

A water excretion test will be performed on all subjects and controls as follows:

a. patients will be fasting and will avoid tobacco products
b. blood sample drawn for baseline ANF determination
c. a 20 ml/kg body weight water load will be ingested
d. 30 min later the subjects will void and discard the specimen
e. urine volumes will be measured hourly for four hours while the participants maintain an upright posture
f. in addition to the baseline ANF level, stimulated levels will be drawn at 90 and 150 min after water loading

Baseline ANF levels, stimulated levels, and change in ANF levels will be tabulated. A t-test will be used to determine if there are statistical differences between patients with idiopathic edema and controls in baseline ANF levels or in their reponse to normal saline.

Progress: No patients were entered in this study. The study was terminated in July 1987 due to the departure of the principal investigator.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/29	Status: Completed

Title: Atrial Natriuretic Factor (ANF) and Postoperative Diuresis

Start Date: 16 Jan 87	Est Completion Date: Jun 87
Dept/Svc: Medicine/Endocrine	Facility: MAMC
Principal Investigator:	MAJ Daniel Knodel, MC
Associate Investigators:	COL Gary Treece, MC CPT Jon Boxwersox, MC CPT Peter H. Greenman, MC Louis Matej, B.S., DAC
Key Words:	ANF, postoperative diuresis

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $1400.00	Periodic Review: N/A

Study Objective: To follow ANF levels during the perioperative period and investigate the possibility that ANF plays an important role in postoperative diuresis.

Technical Approach: Subjects: 10 (male or female); Age 18-60.

Evaluation before entry: history and physical exam to rule out renal or cardiac disease.

Patients scheduled for cholecystectomy will be enrolled in the study. Immediately before preoperative medications and immediately post-induction of anesthesia, laboratory specimens will be obtained for ANF, ADH, serum osmolality, urine electrolytes, osmolality, serum electrolytes, BUN, and creatinine. Beginning at 8 hr after surgery, these samples will be repeated every 4 hours until 48 hr post surgery.

Method of data analysis: Multiple analysis of variance techniques (Scheffe Test) will be used to determine the presence of significant changes in the dependent variables of minute urine volume and ADH and ANF levels over time. These variables will then be compared by regression analysis.

Progress: Eight subjects were studied. The results of this study show that in postoperative patients, atrial natriuretic peptides (ANP) levels vary inversely with urine output. This probably reflects the atrial response to positive fluid balance during the first 12 hr after induction of anesthesia. In older patients, the greater changes in ANP levels and the higher maximum ANP values during the postoperative low urine output phase suggest that these patients have decreased vascular compliance and are more sensitive to the fluid loading that occurs during surgery. Older patients may be more dependent upon the properties of ANP to maintain appropriate vascular volume in the postoperative period.

A paper has been accepted for presentation at the Current Concepts in Medicine Meeting in October 1987.

Detail Summary Sheet

Date: 30 Sep 86	Protocol No.: 86/81	Status: Terminated

Title: Investigation of the Use of Parenteral Solumedrol (Methylprednisolone Sodium Succinate) versus Inhaled Beclomethasone Dipropionate in Patients with a Mild or Moderate Exacerbation of Chronic Obstructive Lung Disease (COLD)

Start Date: 15 Aug 86	Est Completion Date: Aug 87	
Dept/Svc: Medicine/Pulmonary		Facility: MAMC
Principal Investigator: CPT Marin H. Kollef, MC		
Associate Investigators: MAJ William Craqun, MC		
Key Words: COLD, parenteral methylprednisolone sodium succinate inhaled beclomethasone dipropionate, route		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A

Study Objective: To determine if the route of corticosteroid administration has any effect on patient outcome in patients with exacerbation of COLD requiring hospitalization for mild to moderate exacerbations when equivalent clinical doses of corticosteroids are used in parenteral and inhaled forms.

Technical Approach: Patients with suspected exacerbation of COLD will have FEV_1, FVC, pH, pO_2, PCO_2, O_2 used, BP, HR, RR, theophylline levels done on admission. FEV_1 and FVC will be measured daily. Steroids, theophylline, beta agonist, and other medications used will be recorded. Patients will be treated with the following standardized regimen: metaproterenol sulfate via mechanical nebulizer initially 2-3 times in ER followed by treatments every 4 hours followed by usage of metered inhaler 2 puffs every 4 hrs; oxygen therapy as needed to maintain PaO_2 >55 mm Hg; aminophylline IV dosage based on prior usage and admission level to achieve desired therapeutic level of 10-20 mg/l as determined by admitting physician for 12-36 hours and then switched to an equivalent oral dosage; atropine via nebulization will not be used; antibiotics for treatment of bronchitis or pneumonia at the discretion of the admitting physician (these patients will be studied separately). Patients will be randomly assigned to either methylprednisolone, 60 mg IVPB every 12 hours, or beclomethasone dipropionate (42 mcg metered dose per inhalation), 5 puffs every 4 hours. The above doses will be used for the first 48 hours of hospitalization after which, if clinically indicated, the admitting physician may taper the dose of the inhaled beclomethasone or switch to oral prednisone in the parenteral group. The main parameters to be measured will be length of hospitalization, length of time on the initial form of corticosteroid before tapering is begun, FEV_1 and FVC measured daily from admission, and clinical parameters as stated above. Upon discharge patients will be maintained on respective tapering schedule of corticosteroid as determined by the admitting physician.

Progress: This protocol was terminated after four months of attempts to solicit patients from the medical wards. Only three patients were entered in the study during that period.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/17	Status: Terminated

Title: The Mechanically Ventilated Patient: Optimization of Work of Breathing

Start Date: Nov 86	Est Completion Date: Feb 87
Dept/Svc: Medicine/Pulmonary	Facility: MAMC
Principal Investigator: CPT Marin H. Kollef, MC	
Associate Investigator: MAJ Thaddeus Dunn, MC	
Key Words: ventilation, mechanical, cardiac output, oxygen consumption, pressure support mode	

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

Study Objective: To determine the optimal mode of mechanical ventilation in adult patients requiring mechanical ventilation in the Intensive Care Unit.

Technical Approach: Ten stable patients requiring mechanical ventilation and who have pulmonary artery and radial arterial catheters in place will be studied. All patients will be receiving mechanical ventilatory support in the synchronized intermittent mandatory ventilation (SIMV) mode. During baseline mechanical ventilation, the following measurements will be made: mandatory and spontaneous ventilatory rates; tidal volume; mean, peak, expiratory airway pressures, arterial hemoglobin saturation, arterial blood pressure and pulse; determination of static respiratory compliance; cardiac output; oxygen consumption; and during a 2 min period of removal from the ventilatory support mode, spontaneous ventilatory rate and tidal volume will be performed and determined. Inspiratory pressure assist with PSV will be added to the spontaneous ventilation of the patient and the initial level of pressure support will be designed to result in a tidal volume that approximates the SIMV delivered mandatory tidal volume. Patients will be observed for 10-15 min for regularity of the spontaneous respiratory rate, changes in SaO_2, and subjective comfort. All baseline measurements will be repeated. Based on the measured variables the optimal mode of ventilation for the patient will be chosen and continued. The optimal mode will be the one meeting the needs of ventilation (pCO_2 arterial <50) with maximum cardiac output and minimum oxygen consumption. The patient will be maintained on the optimal mode of ventilation based on the hemodynamic and work-characteristics data. Once measurements have been completed and the patient is placed on the optimal mode of ventilation as determined by the protocol, any physiologic changes that require ventilatory mode or characteristics changes will be accommodated.

Progress: On the two patients placed on the protocol, determination of possible hypoventilation on the pressure support mode could not be adequately monitored and the cardiac output readings using the thermodilution technique were not consistent; therefore the investigators decided that they would be unable to complete the study.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/98	Status: On-going

Title: The Effects of Ibuprofen on Airflow in Patients with Chronic Obstructive Lung Disease (COLD)

Start Date: 21 Aug 87	Est Completion Date: Feb 88	
Dept/Svc: Medicine/Pulmonary		Facility: MAMC
Principal Investigator: CPT Marin H. Kollef, MC		
Associate Investigator: LTC William Cragun, MC		
Key Words: COLD, airflow, Ibuprofen, placebo		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $350.00	Periodic Review: N/A

Study Objective: To assess the effect of Ibuprofen on airflow in patients with COLD.

Technical Approach: Patients (>35 years) with clinical signs and spirometric evidence of moderate to severe chronic obstructive lung disease will be entered in the study. Baseline physical examination, spirometric data (FEV_1, FVC) and history will be obtained. Patients will undergo a randomized, blinded crossover study with placebo or ibuprofen over four weeks according to the following schema: Week 1: washout of prior ASA/NSAID use; Week 2: start placebo or ibuprofen; Week 3: washout period; Week 4: start crossover placebo or ibuprofen. Spirometry, history, and physical examination will be obtained at the end of each treatment period. Outcome variables will include changes in the FEV_1, FVC, and dyspnea score at the end of weeks 2 and 4.

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

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/99	Status: On-going

Title: Investigations into Immune Phenomena Associated with Thyroid Autoimmune Disease

Start Date: Oct 86	Est Completion Date: Jun 88	
Dept/Svc: Medicine/Endocrinology		Facility: MAMC
Principal Investigator: MAJ Jennifer A. Nuovo, MC		
Associate Investigators:	COL Gary Treece, MC	
COL Kenneth Burman, MC	LTC Robert Jones, MC	
COL Stephen Plymate, MC	MAJ Daniel Knodel, MC	
Key Words: thyroid autoimmune disease, insulin, goiter, cancer		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $3260.00	Periodic Review: Oct 86

Study Objective: To continue work in the area of thyroid immunology screening for evidence of concomitant autoimmunity to insulin and insulin receptors in patients with autoimmune thyroid disease and to observe changes in antibody production during the course of the disease; to look for evidence of thyroid and insulin autoimmunity in these patients and patients with thyroid disease not usually felt to be autoimmune; to further characterize the IgG to insulin found previously in sera of patients with Graves' disease.

Technical Approach: Study A: Measurement of insulin antibodies in the serum of 50 normal subjects (sex- and age-matched to diseased patients); 50 patients with Graves' disease at diagnosis, during therapy, and following definitive therapy; 50 patients with Hashmoto's thyroiditis; 10 patients with thyroiditis; 10 patients with lupus or rheumatoid arthritis; 20 patients with simple goiter and 20 with multinodular goiter; and 50 patients with diabetes mellitus, using an ELISA test that has been modified for detecting insulin antibodies. If blood glucose levels are abnormal, insulin and C-peptide levels will be obtained. Study B: Insulin receptor binding studies will be performed on the subjects and controls listed in Study A. Study C: Immunoglobulin detected by ELISA will be purified by means of insulin affinity columns to determine if the immunoglobulin is a specific anti-insulin antibody. The immunoglobulin adhering to the column will be eluted, dialyzed, and concentrated, and then retested using the ELISA assay to test the ability of the antigen/antibody complex to inhibit insulin binding in previously positive sera.

Progress: Insulin antibody ELISA technique has been applied to the serum of 182 patients with autoimmune thyroid disease or rheumatoid disease and results compared to insulin antibody by RBA. Twenty-one samples were positive by ELISA and 2 were positive by RBA. There was poor correlation of insulin antibody results by these 2 methods. Data is being gathered on samples from patients with acute Grave's disease to study for the presence of insulin antibody during several time points of their course. The investigators are also working to modify the assay to improve specificity.

A paper has been accepted for presentation at the American Diabetes Association International Research Symposium in October 1987.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/74	Status: On-going

Title: Association of Risk Factors for Osteoporosis with Suspected Stress Fractures in Active Duty Women

Start Date: 17 Apr 87	Est Completion Date: Dec 87
Dept/Svc: Medicine/Endocrine	Facility: MAMC
Principal Investigator: MAJ Jennifer Nuovo, MC	
Associate Investigator: CPT Karl Friedl, MS	
Key Words: osteoporosis, stress fractures, risk factors	

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

Study Objective: To estimate the size of the subset of active duty women who may have experienced lower extremity stress fractures during exercise and to determine whether or not this group is characterized by any potential risk factor(s) for osteoporosis.

Technical Approach: A questionnaire will be mailed to the work address of all active duty women stationed at Ft Lewis, WA. An identifying postcard will be enclosed for return under separate cover in order to locate initial non-respondents. A second mailing, two weeks after the first, will be made only to soldiers not returning the postcards. The questionnaire will elicit information on age, race, menstruation, children, method of birth control, smoking, weight control, exercise, pain in shins and feet, bone fractures, and family history of fractures or bone malformations. The returned data will be analyzed by frequency and cross tabulation procedures. Women answering yes to questions regarding fractures or pain will be compared to the remaining respondents for differences in the prevalence of amenorrhea, late menarche, parity, gynecologic age, smoking history, above or below normal weight, and exercise habits. Age and ethnic background will be handled as known covariates.

Progress: 2,460 active duty women have been surveyed for risk factors for osteopenia and incidence of stress fracture. There were 1500 responses. The data is being collated and will be summarized within the next month.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/83	Status: On-going

Title: Clinical Trial of Pergolide Mesylate in the Treatment of Amenorrhea-Galactorrhea or Sexual Dysfunction Due to Prolactin Secreting Pituitary Tumors

Start Date: 15 May 87	Est Completion Date: May 1988
Dept/Service: Medicine/Endocrine	Facility: MAMC
Principal Investigator: MAJ Jennifer A. Nuovo, MC	
Associate Investigators: COL Stephen R. Plymate, MC COL Gary L. Treece, MC	
Key Words: tumor,pituitary, prolactin, pergolide	

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

Study Objective: To determine the usefulness of pergolide mesylate in the treatment of prolactin-secreting pituitary tumors and in the restoration of normal sexual function.

Technical Approach: This study is open to patients of either sex who have responded poorly to bromocriptine or whose tumor, because of surgery or irradiation, is not measureable. Patients must have been diagnosed as having a pituitary tumor 5 mm or greater in size that may or may not have been treated with radiotherapy or surgery. Patients must have elevation of prolactin levels on both baseline measurements taken two to seven days prior to taking pergolide. Growth hormone levels may also be elevated. Women of child bearing potential must use a mechanical means of contraception. Patients will be started on 25 µg of pergolide taken orally with the evening meal the first three days. If the patient has no adverse experiences, the dose will be raised to 50 µg given with the evening meal on the fourth day. The doses will not be increased to 50 µg until the patient is able to tolerate the 25 µg dose without adverse experiences. The daily dose may be increased by 25 to 50 µg increments until a satisfactory suppression of prolactin levels is achieved, up to a maximum of 1000 µg. If adverse experiences are encountered at doses of 50 µg or more, the dose may be reduced to as little as 25 µg or the therapy discontinued. Patients will be treated with pergolide until either there is a loss of efficacy of pergolide, the patient can not tolerate the drug at an effective dose, the patient becomes pregnant, or no further therapy is needed. If there is no evidence of response after three months, the patient will be taken off the study. To be evaluable, a patient must receive a minimum of two months of daily pergolide therapy. However, if there is no suppression of prolactin levels after one month at the maximum dose per day, the case will be considered evaluable and included in the analysis of results as a therapeutic failure.

Progress: Two patients have agreed to enter the study. The investigators will start these patients as soon as the medication is received from the manufacturer.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 85/80	Status: Completed

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 Cost: -0-	Est Accumulative OMA Cost: $1620.00	Periodic Review: Feb 87

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 specimens were drawn and a systemic review of the action or inaction of the physician will be 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 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. Chi^2 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.

Progress: The chart review was completed and the blood reanalyzed. However, ferritin levels were not determined and the blood has been discarded. The investigators considered comparing the SMAC iron level with the determined ferritin, TIBC levels and the response of the physicians to the SMAC iron. However, due to staff shortages this part of the study could not be undertaken and the protocol was terminated.

The chart review showed without question that physicians did not remark on abnormal iron levels.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 85/25	Status: Completed

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: CPT William A. Pearce MC	
Associate Investigators: COL Peter Gomatos, MC MAJ John W. Gnann, MC CPT Michael Lyons, MC	
Key Words: Pyelonephritis, intravenous antibiotics	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Mar 87

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: Five additional patients were enrolled in FY 87. No unexpected adverse reactions were seen. Of 60 patients enrolled at MAMC and approximately 30 enrolled at Harborview in Seattle, it was found that treatment failures due to microbial resistance are five times more common in patients randomized to ampicillin. No isolates were resistant to TMP/SMX. Statistical compilations of the study are now being finished at Harborview in preparation of submission for publication.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/59	Status: Suspended

Title: Symptomatic versus Conventional Treatment of Duodenal Ulcer Disease Using Ranitidine

Start Date: 20 Mar 87	Est Completion Date: Sep 88	
Dept/Svc: Medicine/Internal Medicine		Facility: MAMC
Principal Investigator:	CPT Gregory E. Schlepp, MC	
Associate Investigators:	LTC Thomas F. O'Meara, MC LTC Michael H. Walter, MC MAJ Marshall E. McCabe, MC Gari Sisk, R.N.	
Key Words: ulcer, duodenal, healing, recurrence, Ranitidine		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A

Study Objective: To compare healing and recurrence of duodenal ulcers treated with Ranitidine only when symptomatic to those treated with a conventional ulcer treatment regimen of fixed duration.

Technical Approach: Approximately 100 patients, either sex, >18 years with endoscopically confirmed, symptomatic duodenal ulcers will be prospectively entered into the study and randomly assigned to receive either Ranitidine 300 mg once daily for four weeks (control group) or 300 mg once daily for a minimum of one week and thereafter only when needed for pain relief (study group). Initial evaluation on entry will include a history profile. Patients will receive a symptom log on which they will record symptoms, adverse reactions, medication consumption, and tobacco, alcohol, and coffee consumption daily. Patients will be contacted by telephone at one and three weeks to assess symptoms and progress. Patients will return to the clinic at two weeks following entry for a pill count to assess compliance. The subjects will be endoscopically evaluated at the end of the four-week period to assess ulcer healing by a physician blinded to the treatment status.

Patients whose ulcers are healed will undergo repeat endoscopy at eight weeks from entry to assess for ulcer recurrence. Patients with unhealed ulcers at four weeks will undergo an additional four weeks of treatment with Ranitidine, 300 mg orally once daily. They will continue to complete daily symptom logs and have a pill count performed at eight weeks. These patients will undergo repeat endoscopy at eight weeks to evaluate ulcer healing.

Ulcer healing will be the primary parameter of comparison between the two groups and will be analyzed using a chi square analysis. Duration of treatment, demographics, symptoms, and adverse reactions will be analyzed and compared using covariant analysis.

Progress: No patients were entered in this study due to the reassignment of the principal investigator. At the request of Dr. O'Meara, the protocol has been placed in a suspended status until a new principal investigator is assigned.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/01	Status: On-going

Title: Sequential Therapy with Methotrexate and 5-FU in Advanced Colorectal Carcinoma

Start Date: 17 Oct 86	Est Completion Date: Oct 88
Dept/Svc: Medicine/Hematology-Oncology	Facility: MAMC

Principal Investigator: MAJ Ruben Sierra, MC

Associate Investigators:

COL Irwin B. Dabe, MC	MAJ David Dunning, MC
LTC Lauren K. Colman, MC	CPT Denis Bouvier, MC
LTC Howard Davidson, MC	CPT Donna Mercado, MC
MAJ Thomas Baker, MC	D. White, M.D.

Key Words: carcinoma, colorectal, methotrexate, 5-FU, sequential

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

Study Objective: To evaluate a treatment schedule in terms of therapeutic effectiveness: response rate, survival, and toxicities in patients with colorectal carcinoma.

Technical Approach: Patients with histologic evidence of colorectal carcinoma will receive methotrexate, 100 mgs/M^2 IV, followed by 5-FU, 1250 mgs/M^2 in an 18 hour IV infusion. Leucovorin will be given orally at a dose of 10 mgs every 6 hours for 6 doses, beginning 24 hours after the methotrexate is given. Beginning with the second course the 5-FU dose will be increased to 1500 mg/M^2 and will be adjusted thereafter as necessary in response to side effects. This regimen will be given every two weeks (or as soon as there is evidence of hematologic recovery from the prior course) until progression or unacceptable toxicity is encountered. Pre-study evaluation will include history and physical examination, CBC, LFT, BUN, creatinine, CEA, liver CT scan, endoscopy to evaluate intraluminal lesion (if any), bone scan, and CXR. Further evaluation will include CBC, LFT, BUN, and creatinine every 15 days; CEA every four weeks; and evaluation of endoluminal lesions every two months.

Progress: Of the 15 patients entered, 7 had received prior chemotherapy and 8 had received no prior chemotherapy. Thirteen patients were evaluable for response. Of the 7 who had received no prior chemotherapy, 3 had stable disease for more than 2 months. Of the 6 evaluable patients who had received prior chemotherapy, there was one partial response and one with stable disease. There were no complete responses. Overall, there was an objective response rate of 8%. Thirty-one percent maintained stable disease for over 2 months and none have progressed to date. The median duration of response has not yet been reached. The median survival for non-responders is 24 weeks. For those with partial response or stable disease, it has not been reached at 36 and 28 weeks, respectively. The preliminary data shows that although this protocol is very well tolerated, the response rate of 8% is lower than that expected for single agent 5-FU.

A paper has been accepted for presentation at the ACP/4th Annual Army Regional Meeting in October 1987.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/42	Status: On-going

Title: Western Washington Tissue Plasminogen Activator - Emergency Room Trial

Start Date: 16 Jan 87	Est Completion Date: Jan 88
Dept/Svc: Medicine/Cardiology	Facility: MAMC
Principal Investigator: COL W. Theodore Steudel, MC	
Associate Investigators:	MAJ Everett W. Newcomb, MC
LTC Roger F. Chamusco, MC	MAJ Matthew M. Rice, MC
MAJ Philip W. Berger, MC	CPT Mary D. Boyer, MC
MAJ Cloyd D. Gatrell, MC	Steven Pace, M.D, DAC
MAJ Blake P. Gendron, MC	J. Ward Kennedy, M.D.
Key Words: tissue plasminogen activator, acute myocardial infarction, efficacy, safety, practicality	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-
	Periodic Review: N/A

Study Objective: To evaluate the efficacy, safety, and practicality of administering intravenous recombinant tissue plasminogen activator (rt-PA) emergently to patients with acute myocardial infarction (AMI) in hospital emergency rooms.

Technical Approach: Patients <75 years of age with symptoms of AMI with onset within six hours or presentation lasting more than 20 minutes (unrelieved with nitroglycerin), an electrocardiogram compatible with AMI, and in whom no more than 60 minutes have elapsed since initial evaluation will be infused with rt-PA with an initial bolus of 6 mg IV push. The infusion will be continued using an IV infusion pump to deliver 60 mg rt-PA in the first hour, 20 mg over the second hour, and 5 mg for the next four hours. When the rt-PA infusion is completed, IV heparin will be started at 1000 IU per hour. PTT will be drawn at two hours after start of heparin and infusion rate adjusted to maintain PTT in the 6-80 second range. PTT's will be drawn every 6 hours and adjusted to maintain systemic anticoagulation for at least 96 hours following rt-PA infusion. The patient will be started on aspirin 325 mg/day one day prior to discontinuation of the heparin infusion. Routine CCU care will be followed per the cardiologist's orders. Cardiac angiography will be done at 7-10 days after initial rt-PA treatment and, six weeks following hospitalization, the patient will be offered a nuclear medicine determination of ejection fraction and infarct size, and a repeat two dimensional echocardiogram.

Progress: This protocol originally called for 150 mg total dose of rt-PA and was amended in April 1987 to a lower total dose of 100 mg after two episodes of intracerebral bleed were reported at other institutions. Since then there have been no further bleeding problems. At MAMC, the experience with rt-PA in 15 patients has been very positive. Most patients have lysed their thrombus. No hemorrhagic complications or other side effects have been encountered. All patients subsequently had cardiac catheterization and most were found to have a patent vessel to the infarct region, albeit with severe underlying fixed disease.

Detail Summary Sheet

Date: 30 Sep 87	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 Edward Lelonek, MC
COL Stanton Brown, MC	MAJ James S. Little, MSC
COL Stephen R. Plymate, MC	MAJ Louis N. Pangaro, MC
COL Poong S. Shim, MC	MAJ David Turnbull, MSC
MAJ Lawrence Agodoa, MC	CPT Jeffrey Addison, MC

Key Words: Hypothyroidism, treated, L-thyroxine

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $2425.00	Periodic Review: Oct 86

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

Technical Approach: SUBJECTS: normals; normals treated with L-Thyroxine for one month; patients with hyperthyroidism; patients with hypothyroidism, primary untreated or treated for one month with L-thyroxine; and patients with the nephrotic syndrome untreated or treated for one month with L-thyroxine. All subjects will have a 24-hr urine for volume, creatinine, total protein, urine protein, electrophoresis, T_4, and T_3. Fasting samples will be drawn for SMAC-20, T_4, T_3 resin, T_3 by RIA, TSH, THAT (an extra tube will be drawn for free T_4, reverse T_3, and TBG). A fasting TRH test will be done and blood for TSH will be drawn at 0, 30, and 60 mins post injection. The above procedures will be repeated after at least 30 days on one or more doses of T_4 for the treated groups. Urine protein electrophoresis will not be performed on urine with a total protein of <150 mg for 24 hrs; patients with known cardiovascular disease or >50 years will be excluded from the treated groups; and 24-hr urines will be obtained prior to or at least 72 hours after the TRH test.

Progress: No additional patients were entered in FY 87.

Eight patients have previously been studied and additional patients are being sought. The thyroid function tests will be rerun utilizing the highly sensitive TSH assays. T_3 and T_4 levels have not yet been determined pending the application of a suitable technique.

Detail Summary Sheet

Date: 30 Sep 87	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: LTC Robert Jones, MC MAJ Daniel Knodel, MC		
Key Words: adrenal insufficiency, urinary free cortisol, monitor, hydrocortisone, cortisone		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $700.00	Periodic Review: Feb 87

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

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

Progress: Two additional patients were added in FY 87 for a total of four entries. Patient recruitment is proceeding. The available blood/urine remains frozen for batch analysis when patient recruitment is complete.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 83/37	Status: Terminated

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	LTC Robert E. Jones, MC	
COL Stephen Plymate, MC	MAJ Michael Fincher, MC	
LTC James Higbee, MS	CPT Leroy Southmayd, MC	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $3000.00	Periodic Review: Feb 87

Study Objective: To study the effect on *in vitro* leukocyte function testing 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 A_1C, 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 blood glucose will then be terminated and the patient placed back on prior treatment regimen.

Progress: This protocol was terminated due to the technical difficulties encountered in establishing a clinically useful leukocyte function assay and due to the excessive logistical requirements imposed by the protocol. In addition, the results of a similar study were published in J Clin Path 37:1029-30, 1984. No patients were entered on the study.

Detail Summary Sheet

Date: 30 Sep 87	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	LTC Robert E. Jones, MC
COL Francis G. LaPianan, MC	CPT Andrew Ahmann, MC

Key Words: Graves' ophthalmopathy, cyclosporin, group study

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $200.00	Periodic Review: Apr 87

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

Technical Approach: This will be a collaborative study with the Endocrine Services at the other MEDCEN's. The study will be composed of a random cross-over design comparing cyclosporin treatment to the most commonly employed current therapy, high dose oral prednisone. Since responses tend to be seen rapidly the drugs will each be administered for three weeks. Each patient's response to one drug will be compared to his own response to the other drug. A total of 20 patients will be evaluated initially with random alternating allocation to either Group A or Group B:

Group A: (1) prednisone, 40 mg, T.I.D. x three weeks
(2) full evaluation of response
(3) cyclosporin 5-10 mg/kg/day x three weeks

Group B: Reverse order of Group A.

Clinical assessment will be weekly with ophthalmopathy index and T_4, T_3, etc, at 0, 4, 6, 9, and 12 weeks. TRH will be done at 0, 4, and 9 weeks, and cyclosporin or prednisone levels will be done at 2, 3, 4, 7, 8, and 9 weeks.

Progress: No patients were entered in this study at MAMC in FY 87. One patient was entered prior to FY 87.

Detail Summary Sheet

Date: 30 Sep 87	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 LTC Robert E. Jones, MC
Key Words: Thyrolar, L-thyroxine, metabolism	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $1810.00	Periodic Review: Feb 87

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

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: Two additional subjects were entered in FY 87 for a total of 12 subjects. The technical portion of this study has been completed. Currently, the data are being analyzed for the purpose of submitting an abstract to the 1988 American Thyroid Association Annual Meeting.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 85/42	Status: Completed

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 Investigatos: LTC Robert E. Jones, MC		
Key Words: Cibacalcin, clinical and biochemical evaluation		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Feb 87

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: This protocol is considered completed because the drug has been approved by the FDA for marketing.

The patient being treated remains on Cibacalcin and has experienced no adverse effects while maintaining a clinical remission of the Paget's disease. The patient's serum alkaline phosphatase remains normal.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/46	Status: Completed

Title: Assessment of the Incidence of Bronchial Hyperreactivity to Methacholine in Patients with Sarcoidosis

Start Date: March 1986	Est Completion Date: March 1987
Dept/Svc: Medicine/Pulmonary	Facility: MAMC
Principal Investigator: MAJ Michael C. Witte, MC	
Associate Investigators: LTC Pierre Andrade, MC	
Key Words: bronchial hyperreactivity, methacholine, sarcoidosis	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Apr 87

Study Objective: To determine the frequency with which nonspecific bronchial hyperreactivity to methacholine occurs in consecutive patients with sarcoidosis.

Technical Approach: Fifty (50) patients with a tissue-proven diagnosis of sarcoidosis will be studied. A form will be initiated for each patient to provide data on total incidence of sarcoidosis and to indicate whether those who decline methacholine challenge differ in any significant way from those who agree to participate. The patient will then be referred for an allergy screen. The physician in the Allergy Clinic will complete those questions on the form which refer to personal and family history of atopic disease. Volunteers of the same age range, with negative personal and family history for asthma or allergic rhinitis will serve as normal controls. A complete methacholine challenge with determination of a provocative dose FEV_1 20% will be performed only in those patients whose baseline FEV_1 is 70% or greater of predicted. In those patients whose baseline FEV_1 is 60-70% of predicted, a methacholine challenge may be initiated but will be terminated upon the occurrence of a 20% fall in FEV_1 from baseline. An attempt will be made to reevaluate all patients who have been placed on corticosteroids for their sarcoidosis at 3-4 months and in other patients after approximately 6 months.

Progress: Macroscopic plaques and nodules were found in 6 of 28 patients. Twenty four of 28 patients had symptoms that would not allow distinction of sarcoid from asthma. The responsiveness to inhaled methacholine using pC_{20} was assessed in each patient with the concentration causing a 20% fall in forced expiratory volume in one second. Nine of the patients had airway hyperresponsiveness. Of these 9, five had a history of reactive airways. Of the remaining 4 patients, all had macroscopic evidence of endobronchial sarcoid. Of the 19 patients having a negative bronchoprovocation challenge, only 2 had bronchial involvement macroscopically. Thus 4 of 6 patients with macroscopic endobronchial sarcoidosis had positive methacholine challenges, whereas none of 19 patients without endobronchial disease had a positive challenge. The investigators conclude that in the absence of a previous history of asthma, patients with obvious airway granulomas have a strong likelihood of having airway hyper-responsiveness. A paper was presented at the ACP Meeting in October 1986.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/47	Status: Terminated

Title: The Effect of Abnormal Thyroid States on the Metabolism of Theophylline and Methylprednisolone

Start Date: 21 Mar 86	Est Completion Date: March 87	
Dept/Svc: Medicine/Pulmonary		Facility: MAMC
Principal Investigator: MAJ Michael C. Witte, MC		
Associate Investigator: LTC Robert Jones, MC		
Key Words: abnormal, thyroid, theophylline, methylprednisolone		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $250.00	Periodic Review: May 87

Study Objective: To investigate the effect of hypothyroidism and hyperthyroidism on the metabolism of theophylline and methylprednisolone.

Technical Approach: Patients (18-60 years) with idiopathic or Hashimoto's hypothyroidism, iatrogenically hypothyroid subjects who have been thus prepared for the purpose of follow-up scans for assessment of thyroid carcinoma, patients with Graves' hyperthyroidism, and patients with iatrogenic hyperthyroidism for suppression of thyroid nodules will be studied. Hypothyroid patients must have a TSH >50 to be included. Hyperthyroid patients must have a FT_4I of >6, $T_4 \geq 14$, and $T_3 \geq 250$ to be included.

Medications: *Loading dose: aminophylline, 6 mg/kg IV over 30 min* and methylprednisolone, 40 mg/1.75M^2 IV over 2-3 min.

METHOD: Serum will be obtained for baseline T3, T4, TSH, theophylline, and methylprednisolone levels. A loading dose of aminophylline and methylprednisolone will be given. Serial levels of T3, T4, and theophylline or methylprednisolone will be obtained at 30, 60, and 90 minutes and at 2, 3, 4, 5, 6, 8, 10, and 12 hours. Patients will be monitored with a cardiac monitor for the first four hours and for any adverse drug reactions. Some subjects may be reluctant to participate for a full 12 hours. A minimum of 8 hours will be required and every attempt will be made to achieve a full 12 hours of study. Subjects will eat meals at their accustomed times. Serum specimens will be separated and frozen for use at a later date. Methylprednisolone and a-theophylline kinetics will be studied concurrently. Subjects with spontaneous hypo- or hyperthyroidism will be studied before therapeutic intervention has occurred and then after they have achieved a euthyroid state. Iatrogenically hypothyroid subjects will be studied at that time. Generally, such patients are later returned to a state of low-grade hyperthyroidism for suppression of thyroid nodules or thyroid cancer. They will then be restudied while in the low-grade hyperthyroid state.

Progress: This protocol was terminated due to the departure of the principal investigator. No patients were entered at MAMC due to time constraints on the investigators.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/17	Status: Suspended

Title: Colon Inflammation in Reiter's Syndrome: Response to Sulfasalazine. Results of a Controlled Study.

Start Date: 15 Nov 85	Est Completion Date: Jul 89	
Dept/Svc: Medicine/Rheumatology		Facility: MAMC
Principal Investigator: MAJ James Yovanoff, MC		
Associate Investigator: LTC Thomas O'Meara, MC MAJ Robert C. Hays, MC		
Key Words: colon inflammation, Reiter's syndrome, sulfasalazine		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $300.00	Periodic Review: Jan 87

Study Objective: Part I: To evaluate the incidence of occult inflammatory lesions of the bowel in patients with Reiter's syndrome, regardless of the presence or absence of gastrointestinal symptoms. Part II: To treat Reiter's patients who are refractory to conventional therapy with sufasalazine and document subjective and objective changes in the patient's arthropathy. (Double blind study)

Technical Approach: Part I: Patients who are 18 years, either sex, and fulfill the Amer Rheumatism Assoc criteria for Reiter's syndrome will receive colonoscopy with colonic mucosal biopsies as well as baseline data to include stool culture for Yersinia, Shigella, Campylobacter, and stool collection for ova cysts and parasites. Serial stool hematest determinations will be obtained and serum will be drawn for ANA, rheumatoid factor, HLA B27, Westergren sedimentation rate, CRP, serum protein electrophoresis, and quantitative immunoglobulins. A thorough drug history will be obtained and patients cannot have taken laxatives, cathartics, or had enemas for the 2 weeks prior to colonoscopy. Colon biopsies will be graded by both a severity of disease index and a chronicity of disease index using established criteria. Part II: Patients who have not responded to standard therapy consisting of one or more nonsteroidal anti-inflammatory drugs for a 6 month period prior to the study will be treated with sulfasalazine over a 12 week period. Multiple subjective and objective parameters will be measured to assess the clinical activity of the patient's arthritis. Upon completion of 12 weeks of therapy the patients with initially abnormal biopsies will receive repeat colonoscopy with biopsy to assess macroscopic and microscopic evidence of improvement in the inflammatory process. All colonic biopsies will be graded as in Part I. After 3 months of treatment (or five months if the dose is increased to 4.0 grams), the medication will be discontinued and the patient will be reevaluated at monthly intervals for 2 additional months. Data will be analyzed from all patients who meet ARA criteria for Reiter's syndrome and from the group of patients who had a syndrome consistent with Reiter's syndrome without urethritis. These two groups will be analyzed together and separately.

Progress: Due to time constraints and the departure of the principal investigator, no patients have been entered. Dr. O'Meara has requested that the protocol be put in a suspended status until a new principal investigator can be appointed.

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 NURSING

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 85/82	Status: Completed

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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review Nov 86

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 thirty 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: All the data has been collected and a paper is in final preparation to meet the requirements of the State University of New York/Buffalo for a Masters of Science Degree and the Anesthesia for Officers Course, U.S. Army.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/78	Status: On-going

Title: The Glasgow Coma Scale: Observer Variability and Correctness of Scores Obtained with Its Use

Start Date: 15 May 87	Est Completion Date: Jul 87
Department: Nursing	Facility: MAMC
Principal Investigator:	CPT Luisa M. Janosik, AN
Associate Investigators:	Sharon Fought, R.M., M.S.M., Ph.D. University of Washington
Key Words:	Glasgow Coma Scale, scores, variability

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

Study Objective: To determine interrater reliability of the Glasgow Coma Scale when used by various levels of health care professionals to score a patient examination on videotape.

Technical Approach: Approximately 40 staff members, both nursing and medical, from areas of the hospital which provide care for head-injured patients and use the Glasgow Coma Scale as a standard method of assessing level of consciousness will be studied. Data collection will take place on wards and medical departments on a rotating schedule. Data collection will coincide with two of three shift changes in a 24-hour period on two consecutive days. Each subject will be asked to complete a demographic questionnaire. A videotape of examination of Patient A according to Glasgow Coma Scale criteria will then be shown. Concurrently, subjects will complete Glasgow Coma Scale A. The instructional videotape will then be shown. This tape is approximately 5-8 minutes in length and will demonstrate the correct method of using the Glasgow Coma Scale. Subjects will then view the examination tape of Patient B while completing the corresponding Glasgow Coma Scale form. After data collection has been completed, feedback will be provided to interested units. Data will be analyzed descriptively and statistically. Statistical measurements anticipated for assessment of interrater reliability will include percentage agreement, percentage disagreement, Cohen's kappa, phi, and T-tests.

Progress: Data collection has been completed. Data analysis is in progress. Preliminary analysis indicates definite variability in Glasgow Coma Scale scores when used by health care providers with varying professional backgrounds.

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 OB/GYN

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/49	Status: On-going

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

Start Date: 27 Feb 87	Est Completion Date: Apr 88	
Dept/Svc: OB/GYN		Facility: MAMC
Principal Investigator:	CPT Timothy J. Boley, MC	
Associate Investigators:	COL Patrick Duff, MC LTC Keith Stone, MC	
Key Words:	hysterectomy, Cefazolin, cefotetan, prophylaxis	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $600.00	Periodic Review: N/A

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

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

Progress: Fifty-one patients were considered for the study. Five were not included because two of them had surgery cancelled, two underwent abdominal hysterectomy secondary to difficulty at surgery, and one was given multiple prophylactic doses secondary to extended operative time. Twenty-eight patients received Drug A and 18 received Drug B. Preliminary data indicate relatively equal results between the two antibiotics in regard to febrile morbidity, fever index, postoperative hospital stay, and infectious complications.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/03	Status: On-going

Title: Prophylactic Tocolysis of Twins

Start Date: 17 Oct 86	Est Completion Date: Dec 88
Department: OB/GYN	Facility: MAMC
Principal Investigator: MAJ William K. Brady, MC	
Associate Investigator: COL John A. Read, MC	
Key Words: twins, tocolysis, prophylactic, terbutaline, bed rest	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $952.00	Periodic Review: N/A

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

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

Progress: Fourteen (14) patients have been entered in the study.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/04	Status: On-going

Title: Evaluation of the Latex Fixation Test in Detection of the Group B Streptococcus in the Lower Genital Tract of Women in Labor

Start Date: 17 Oct 86	Est Completion Date: May 87	
Department: OB/GYN		Facility: MAMC
Principal Investigator: MAJ William K. Brady, MC		
Associate Investigators: COL Patrick Duff, MC		
Key Words: Latex Fixation Test, Group B Strepococcus, women, labor, lower genital tract		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $900.00	Periodic Review: N/A

Study Objective: To determine if the Group B streptococci latex fixation test is sufficiently sensitive to identify streptococcal colonization of the lower genital tract in obstetric patients.

Technical Approach: Three hundred women at term who present in labor with intact membranes will undergo sterile speculum examination with duplicate sterile swabs taken from the endocervix and vagina during the admission assessment. One swab will be inoculated immediately onto a blood agar plate for culture. The duplicate swab will be run with the Wellcogen Strep B Latex Fixation Test. Neonates will be evaluated for the first month of life.

Results of the Group B Streptococcus Latex Fixation Test will be compared to the subsequent culture results to determine the reliability of the Group B Streptococcus Latex Fixation Test.

Results of the latex fixation test will be evaluated with respect to sensitivity, specificity, predictive value, and efficiency.

Progress: Approximately 100 patients have been studied.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/05	Status: On-going

Title: Plasma Fibronectin Concentrations in Obstetric Patients

Start Date: 17 Oct 86	Est Completion Date: May 87	
Department: OB/GYN		Facility: MAMC

Principal Investigator: MAJ William K. Brady, MC

Associate Investigator: COL Patrick Duff, MC

Key Words: plasma fibronectin, term, uncomplicated, chorioamnionitis, unscheduled cesarean delivery

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $520.00	Periodic Review: N/A

Study Objective: To measure the plasma fibronectin concentration in uncomplicated term patients, term patients with chorioamnionitis, and term patients undergoing unscheduled cesarean delivery.

Technical Approach: In the first phase of the investigation, 25 normal patients will have a blood sample drawn early in labor and again just prior to delivery to determine if the fibronectin concentration changes during labor.

In the second phase, 25 term women with chorioamnionitis will have blood samples obtained at the time the diagnosis is established to determine what happens to the serum fibronectin concentration in response to intrauterine infection. Fibronectin concentrations in infected patients will be compared to those in uninfected parturients.

In phase 3, plasma samples will be obtained from 100 women prior to cesarean delivery. Fibronectin concentrations in women who remain uninfected will be compared to those who develop postcesarean endomyometritis.

Plasma fibronectin concentrations will be determined by a turbidimetric immunoassay. Differences in mean plasma fibronectin concentrations will be evaluated by means of the paired and unpaired t test.

Progress: Dr. Duff was the original principal investigator on this study. Dr. Brady was assigned as the principal investigator in April 1987 because he was seeing most of the patients due to time constraints on Dr. Duff.

Thirty patients were entered in the study in FY 87.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/69	Status: On-going

Title: Low-Dose Aspirin in the Prevention of Pregnancy-Induced Hypertension and Pre-eclampsia in Primigravida Women.

Start Date: 17 Apr 87	Est Completion Date: Apr 89
Department: OB/GYN	Facility: MAMC
Principal Investigator:	MAJ William Kim Brady, MC
Associate Investigators:	COL William L. Benson, MC COL Patrick Duff, MC COL John A. Read, MC MAJ Jose Garcia, MC MAJ Charles J. Hannan, MS MAJ Frederick E. Harlass, MC

Key Words: pre-eclampsia, hypertension, prevention, low-dose aspirin, primigravida women

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $5952.00	Periodic Review: N/A

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

Technical Approach: Healthy primigravida women will be enrolled in the study at 22 weeks gestation. Pre-entry evaluations will include CBC, platelet count, PT/PTT, and ultrasound to confirm dates. Patients will be randomized to either 81 mg of aspirin per day or a placebo in a double blind fashion to be taken until delivery. There will be approximately 300 women in each group. Patients will receive standard antenatal care with visits every 2 weeks until 36 weeks and weekly visits thereafter. Index of aspirin ingestion will be determined by measuring malondialdehyde levels at 28 weeks and again when the patient presents for delivery. Levels of thromboxane B_2 and 6-keto-prostaglandin F1 alpha will be measured via 24 hour urine collections performed at 28 and 36 weeks gestation. The thromboxane B_2 and 6-keto-prostaglandin F1 alpha urine specimens will be collected and 50 samples from each group of patients will be randomly selected and respective radioimmunoassays will be performed. The thromboxane A_2/prostacyclin balance between the two groups will be compared. Malondialdehyde assays will be run on all samples. Mode of delivery, neonate apgar scores, and routine neonatal laboratory tests will also be compared.

Progress: The placebo and the study tablets have been purchased. The study tablets have been assayed by a reference lab to confirm that the study tablets do, in fact, contain 81 mg of aspirin. No patients have been entered.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/66	Status: Completed

Title: A Comparison of Cefazolin Versus Cefotetan as Single-Dose Prophylaxis for Prevention of Postcesarean Endometritis

Start Date: Sep 86	Est Completion Date: Indefinite
Department: OB/GYN	Facility: MAMC
Principal Investigator: COL Patrick Duff, MC	
Associate Investigators: COL John A. Read, MC MAJ Andrew Robertson, MC	
Key Words: endometritis, postcesarean, prophylaxis, cefazolin cefotetan, single-dose	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $1000.00
	Periodic Review: Aug 87

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

Technical Approach: Utilizing a double blind format, 200 patients having cesarean delivery will be studied. Patients who already are infected at the time of surgery or who are allergic to either of the study drugs will be excluded from the investigation. Upon entry into the study, patients will be randomized to receive either cefotetan (2 gm) or cefazolin (2 gm). The drugs will be administered intravenously after delivery of the fetus.

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, development of serious sequelae of primary infection (bacteremia, septic shock, pelvic abscess, septic pelvic thrombophlebitis), and duration of hospitalization.

Patients also 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 the chi-square test (discrete data) and independent sample t-test (continuous data).

Progress: Approximately 170 more patients were entered in the protocol in FY 87. The overall infection rate is consistent with other investigators from this department using other antibiotic regimens. The investigators are in the process of analyzing data on the individual drugs.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/115	Status: Ongoing

Title: Treatment of Bacterial Vaginosis in Pregnancy

Start Date: 18 Sep 87	Est Completion Date: Oct 88	
Department: OB/GYN		Facility: MAMC
Principal Investigator: COL Patrick Duff, MC		
Associate Investigators: David A. Eschenbach, Univ Washington		
Key Words: vaginosis, bacterial, pregnancy, treatment		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A

Study Objective: To determine if treatment of bacterial vaginosis during pregnancy will decrease the incidence of preterm delivery and/or the incidence of postpartum infection.

Technical Approach: Women with bacterial vaginosis will be identified by screening Gram stains of vaginal discharge. Subjects will be entered between the 15th and 25th weeks. Once the woman consents, a second Gram stain will be done and a vaginal swab taken for isolation of group B streptococci, *Ureaplasma urealyticum*, *Mycoplasma hominis*, *Lactobacillus sp*, and *Gardnerella vaginalis*. Subjects will then be randomized to either amoxicillin or placebo in a double-blind fashion. Subjects will take the drug or placebo orally three times per day for 14 days. Subjects will complete a questionnaire on demographic, lifestyle, and pregnancy history questions. At one month from the beginning of treatment, subjects will have a repeat Gram stain and will be asked to obtain a self-administered Gram stain if they develop signs and symptoms of bacterial vaginosis before presentation for delivery. At the time of delivery, the subjects will have a repeat Gram stain and a summary of labor and delivery will be abstracted from their charts to a standardized data form. At one month postpartum, the subjects will complete a questionnaire concerning medication compliance and side effects, and at six weeks postpartum they will be telephoned to obtain information on symptoms of postpartum endometritis and the recurrence of bacterial vaginosis. The major comparisons of interest will be the rates of prematurity, premature rupture of membranes, and postpartum endometritis among women treated with amoxicillin compared to women who received placebo. Analysis will be done by multivariate logistic regression to allow for adjustments for multiple potential confounding factors.

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

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/40	Status: On-going

Title: Infection Prevention in Patients Undergoing Radical Hysterectomy

Start Date: Feb 86	Est Completion Date: Feb 88
Department: OB/GYN	Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC	
Associate Investigator: COL William Benson, MC	
Key Words: hysterectomy, infection, cefamandole	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Feb 87

Study Objective: To determine the effectiveness of antibiotics (cefamandole) in preventing infectious morbidity of radical abdominal hysterectomy.

Technical Approach: Approximately 120 patients with gynecologic cancer undergoing radical hysterectomy with bilateral pelvic lymphadenectomy, without active infection or allergy to the study antibiotic will be eligible. Patients will be randomly assigned to receive 2 g cefamandole in 100 cc D5W IV or I.V. placebo (D5W) in the induction room and at two hours from time of skin incision.

Preoperative evaluation will include chest radiograph, CBC, serum electrolytes, serum hepatorenal profile, and urinalysis. CBC, urinalysis, serum electrolytes, and hepatorenal profile will be obtained on postoperative days 2 and 4 and at any other times indicated.

Infection rate, surgical site infections, and febrile morbidity by the fever index among the two groups will be compared.

Progress: Two additional patients were entered in the study in FY 87 for a total of four entries.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/61	Status: On-going

Title: A Phase III Trial of Intraperitoneal Interferon vs Intraperitoneal Cis-platinum for Minimal Residual Ovarian Carcinoma Following Systemic Chemotherapy (Schering C86-504)

Start Date: 20 Mar 87	Est Completion Date: Indefinite
Department: OB/GYN	Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC	
Associate Investigators: COL William L. Benson, MC	
Key Words: ovarian carcinoma, prior chemotherapy, interferon, cis-platinum, intraperitoneal, efficacy, toxicity	

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

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

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

Progress: No patients have been entered in this study.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 83/17	Status: Completed

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:	LTC 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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 86

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, oligohydramnious, or placenta previa will be excluded.

Progress: The study has been completed and the data analyzed. A manuscript has been accepted for publication in Obstetrics and Gynecology.

Lack of tocolytic did not increase the incidence of maternal or fetal complications. Fetal heart rate changes did not occur more frequently in the no-tocolytic group. There were no instances of feto-maternal hemorrhage in either group and delivery outcomes were similar in both groups.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/90	Status: Terminated

Title: A Comparison of Cefotetan and Doxycycline with Gentamicin, Clindamycin, and Vibramycin in the Treatment of Pelvic Inflammatory Disease

Start Date: 19 Jun 87	Est Completion Date: May 88	
Department: OB/GYN		Facility: MAMC
Principal Investigator: CPT Mary C. Nace, MC		
Associate Investigator: LTC I. Keith Stone, MC		
Key Words: pelvic inflammatory disease, cefotetan, doxycycline, gentamicin, clindamyin, Vibramycin		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A

Study Objective: To determine whether cefotetan and doxycycline is an effective alternative for the treatment of pelvic inflammatory disease (PID).

Technical Approach: Fifty patients admitted with a diagnosis of PID will have a physical exam, blood cultures, CBC, and cervical cultures for gonorrhea and chlamydia. They will then be randomized to cefotetan, 2 gm IV twice a day for four days plus doxycycline, 100 mg by mouth for 10 days; or doxycycline, 100 mg by mouth for 10 days, plus gentamicin, 70-140 mg IV three times a day for four days, plus clindamycin, 900 mg three times a day for four days. Patients who fail to improve in four days will be treated according to standard of care with possible change in treatment from cefotetan to gentamicin and clindamycin with doxycycline. Cervical cultures for gonorrhea and chlamydia and WBC will be obtained on the fourth hospital day and vital signs will be taken every four hours. Vital signs will be taken every four hours and daily evaluation for subjective improvement in pain will be done. Cultures will be done within one week of discharge in patients with positive cultures. Treatment effectiveness will be based on resolution of leukocytosis and pain and normalization of temperature.

Progress: This study was terminated due to other committments by the principal investigator. No patients were entered.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/18	Status: Terminated

Title: Impact of Health and Military Readiness of a Tri-Cycle Oral Contraceptive Regimen

Start Date: 15 Nov 85	Est Completion Date: Nov 86	
Department: OB/GYN		Facility: MAMC
Principal Investigator:	CPT Kathryn D. Parks, MC	
Associate Investigators:	MAJ Gary Nickel, MC	
Key Words: contraception, oral, tri-cycle, military readiness		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $300.00	Periodic Review: Mar 87

Study Objective: To determine the effects of a tri-cycle oral contraceptive regimen on blood pressure, hematocrit, fasting blood sugar, serum lipids, weight, military readiness, and duty performance. The effect on duty performance will be evaluated by the subject.

Technical Approach: Patients will be screened for historical or medical contraindications. Nonsmokers <35 y/o with normal GYN examination will be studied. Excluded will be patients with hypertension, diabetes mellitus, elevated lipids, history of thromboembolic disease, myocardial infarction, angina pectoris, or cerebral vascular accident, known or suspected cancer of the breast or sex organs, migraine headaches, epilepsy, psychiatric disorder, or gallbladder disease. Half the patients will be given 35 mg/day estrogen oral contraceptive in the usual fashion and the other half will be given one tablet daily for 84 days, followed by a 7-day withdrawal period, repeating the cycle for a year. On entrance and at 6 and 12 months, weight, blood pressure, fasting blood sugar, hematocrit, and lipid profiles will be evaluated. On entrance each patient will have a PAP smear, a bimanual examination of the pelvis, and a breast exam. At each of the four evaluation periods the volunteer will complete a questionnaire regarding her perception of the effects the pill had on duty performance, convenience, etc, as well as side effects. Three months after the study period each volunteer will be evaluated for weight, blood pressure, fasting blood sugar, hematocrit, and lipid profile to demonstrate return to prestudy levels.

Progress: Two patients were entered in the protocol. One withdrew due to a change of duty station. There was an inadequate number of patients who agreed to participate in this study to complete it before the principal investigators was reassigned. Therefore, it was terminated.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 85/11	Status: Completed

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:	COL Gary L. Treece, MC LTC I. Keith Stone, MC
Key Words: Estrogen, renal, calcium, parathyroid, postmenopausal	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $3700.00	Periodic Review: Nov 86

Study Objective: 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.

Technical Approach: Twenty chronically estrogen deficient postmenopausal women will be placed on an approximate 400 mg/day calcium diet for one week prior to testing. Serum PTH, cAMP, SMA 20, and calcitonin will be done. Urine protein, creatinine, calcium, phosphorous, and cAMP will be collected after a 12-hr fast. Assays will be collected before and at six weeks after instituting therapy with Premarin at a dose of of 0.625 mg, qd, or 1.25 mg, qd. After 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 $(OH)_2D_3$, 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.

NOTE: Because a fall in total calcium and serum proteins was noted during the study, it was postulated that ionized calcium does not change with estrogen treatment. Therefore, the protocol was amended in November 1986 to add ionized calcium determinations.

Progress: Nineteen postmenopausal women were evaluated. Serum total calcium decreased after treatment with the low dose estrogen, but not with the higher dose and was accompanied by a fall in serum protein and albumin, serum phosphate, plasma cyclic AMP, the chloride/phosphate ratio, TRP, and TMP/GFR. Ca/Cr ratio fell with both dose regimens. Intact PTH and serum calcitonin were not affected by either dose. Total urinary cyclic AMP and nephrogenous cyclic AMP increased after both doses. The results suggest that, in contrast to the effect of conjugated equine estrogens (CEE) at the level of bone, where reduced PTH-mediated bone resorption is observed, CEE increases bioactivity of PTH at the level of the kidney without changing its immunoreactive concentration. This may be an important and adjunctive mechanism whereby estrogen treatment restores calcium balance in the postmenopausal woman.

A paper will be presented at the American College of OB/GYN in October 1987 and a paper is being submitted for publication.

Detail Summary Sheet

Date: 30 Sep 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Oct 86

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 gases, maternal pain perception, newborn weight and neonatal problems will also be noted.

Progress: No patients have been entered due to time and manpower 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 87	Protocol No.: 83/12	Status: Completed

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:	COL Edward E. Dashow, MC LTC Fred H. Coleman, 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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Oct 86

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: This study has been completed. A paper has been accepted for publication by Obstetrics and Gynecology.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/56	Status: Completed

Title: A Comparative Study of Treatment of UTI in Obstetric Patients Utilizing Three Different Dosage Regimens of Augmentin

Start Date: Apr 86	Est Completion Date: Indefinite
Department: OB/GYN	Facility: MAMC
Principal Investigator: MAJ Andrew Robertson, MC	
Associate Investigator: COL Patrick Duff, MC	
Key Words: UTI, obstetric, Augmentin	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jul 87

Study Objective: To compare three different regimens of Augmentin for the treatment of UTI in obstetric patients.

Technical Approach: Patients who have either asymptomatic bacteriuria or acute cystitis caused by an organism sensitive to Augmentin will be eligible. All patients will have repeat urine cultures within 3 days of the conclusion of therapy and again at approximately 30 days after therapy. Patients who have either relapses or reinfections will be treated with a conventional 10 day course of antibiotic, selected on the basis of culture and sensitivity results.

Patients (30/group) will be randomly assigned to:

Group A: single dose of Augmentin (250 mg Amoxicilin plus 125 mg clavulanic acid) - 8 tablets

Group B: Augmentin, 1 tablet, q 8 h for 3 days

Group C: Augmentin, 1 tablet, q 8 h for 10 days.

Progress: Eighty-three (83) patients were evaluated. Initial cure rates were 86% (Group A), 90% (Group B), and 100% (Group C). Subsequent infections (relapse and reinfection) developed in 24% (Group A), 8% (Group B), and 8% (Group C). Differences in treatment successes and recurrent infection rates between the groups were not statistically significant. No patient developed pyelonephritis. The investigators conclude that the combination of amoxicillin-clavulanic acid provides acceptable initial therapy for obstetric patients with lower urinary tract infections. Regardless of the duration of therapy, these individuals need long-term surveillance for recurrent infections.

A paper has been submitted for consideration for publication.

Detail Summary Sheet

Date: 30 Sep 87 Protocol No.: 86/51 Status: Terminated

Title: Objective Measurement of Thyroid Volume During Pregnancy

Start Date: Mar 86 Est Completion Date: Jun 87

Department: OB/GYN Facility: MAMC

Principal Investigator: CPT Karen L. Southmayd, MC

Associate Investigators: COL Gary L. Treece, MC
MS Jackie McAdams, DAC

Key Words: thyroid, volume, pregnancy

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $400.00 Periodic Review: Jun 87

Study Objective: To objectively measure thyroid gland size and volume using ultrasonography of the thyroid intrapartum and postpartum in 10 otherwise healthy pregnant women to determine whether or not the thyroid enlarges during pregnancy.

Technical Approach: Pregnant women with a negative personal and family history of thyroid disease, >18 years, will have baseline thyroid function tests (T_4, T_3U, T_3 by RIA, TSH, and thyroid antibodies), history and physical exam performed as early as possible during the pregnancy. Each subject will have four ultrasonic examinations of the thyroid for the determination of thyroid size and volume, once in each trimester of pregnancy (at least six weeks apart) and again six weeks postpartum. Repeat thyroid function tests will be obtained 6 weeks postpartum to detect postpartum thyroid dysfunction. Patients who develop postpartum thyroid dysfuntion will be excluded from the analysis of thyroid size and volume. Thyroid gland size and volume will be determined by ultrasonically measuring the length of each lobe of the thyroid and the cross-sectional areas of multiple sections of each lobe at 0.5 cm intervals and calculating the volume by means of integration formulas. The volume of each lobe will be added to determine the total thyroid volume. Each patient will serve as her own control, with the data for thyroid gland volume summed and averaged for each trimester and postpartum and compared using multiple t-tests. The measured thyroid gland volumes in the pregnant (and postpartum) subjects will also be compared to thyroid gland volumes measured in 10 normal control men and women. The control women will be age and weight matched. Data will also be compared to that recorded in the literature.

Progress: This protocol was terminated due to difficulty in obtaining patients willing to enter the study.

Detail Summary Sheet

Date: 30 Sep 87	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: LTC I. Keith Stone, MC	
Associate Investigator: MAJ Leslie W. Yarbrough, VC	
Key Words: Residents, proficiency, reproductive tracts, rabbits	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $400.00
	Periodic Review: Jan 87

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: Twelve sessions were conducted in FY 87. 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 87	Protocol No.: 87/73	Status: On-going

Title: Effect of Continuous versus 13 Day Provera Supplementation to Premarin Treatment on Serum Lipids in Postmenopausal Women

Start Date: 15 Apr 87	Est Completion Date: Sep 88
Dept/Svc: OB/GYN	Facility: MAMC
Principal Investigator:	CPT Michael Yancey, MC
Associate Investigators:	LTC Keith Stone, MC MAJ Charles Hannan, MS CPT Karl Friedl, MS Thomas Kettler, B.S., DAC
Key Words:	postmenopausal, lipids, provera, premarin

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $8670.00	Periodic Review N/A

Study Objective: To determine if there are any significant differences in the effect of continuous progestogen treatment compared to a standard regimen of intermittent progestogen treatment in postmenopausal women receiving estrogen therapy.

Technical Approach: Sixty non-smoking, postmenopausal women will be entered into 3 groups, all of which will receive conjugated estrogens plus either 13 day Provera treatment at 10 mg qd, continuous Provera at 5 mg qd, or continuous Provera at 10 mg qd. Fasted blood samples will be drawn one week apart, prior to the initiation of treatment and again on days 13 and 26 of each treatment cycle in the 1st, 3rd, and 6th months. Post-heparin lipase activities will also be measured in blood samples obtained 10 min after infusion of 30 IU heparin/kg body weight. If significant decreases in HDLC exceeding a 25% change are detected in the first 10 women in any group after the first 3 months of treatment, the study will be terminated at that point. Serum lipid analysis will include total cholesterol, triglyceride, HDL-cholesterol, and HDL2-cholesterol and enzymatic methods, and apolipoportein A-I and A-II will be measured by RIA kits. Hepatic triglyceride lipase and lipoprotein lipase activities will be measured by hydrolysis of 3H-triolein and differentiated by protamine sulfate inhibition. Provera will be measured by an in-house assay which uses antibody and labeled 6a-methyl-17a-hydroxyprogesterone acetate. SHBG will be measured by SHBG DHT-binding assay. Estrogens and insulin may also be measured by specific RIAs after review of the results from other assays. Individual variables will be initially tested in 3-way analysis of variance and significant differences will then be pinpointed with a multiple range test. Univariate correlations will be examined for SHBG and HDLC, serum Provera and each of the lipid varibles. Covariates including age, body weight, adiposity, and former smoking, drinking, and exercise histories may also be considered.

Progress: Twenty-two patients have been enrolled in 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

DEPARTMENT OF PEDIATRICS

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/66	Status: Ongoing

Title: A Study of Fecal Overload in Adolescents

Start Date: 17 Apr 87	Est Completion Date: 31 Jan 88
Dept/Svc: Pediatrics/ Adolescent	Facility: MAMC
Principal Investigator:	COL Thomas S. Charbonnel, MC
Associate Investigators:	COL Robert D. Karl, MC LTC Dan C. Moore, MC CPT Scott McClean, MC
Key Words: fecal, overload, adolescents	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0- / Periodic Review: N/A

Study Objective: To determine if fecal overload is a common cause of abdominal pain in adolescents; to determine if the scoring method of plain abdominal film devised by Barr, et al, is an accurate and easy way for a primary care physician to diagnose this condition, given minor suggestive findings in the history and physical; and to determine if treatment of this condition is effective in eliminating the symptom of abdominal pain.

Technical Approach: Inclusion criteria: children having at least four episodes of abdominal pain lasting at least one minute over a two month or longer period of time, plus one or more of the following: constipation, frequency of stools less than every other day, straining during defecation, large stools, rectal or abdominal pain during defecation, blood either on stool or on wiping paper, hard or pellet-like stools, diet severely lacking in fiber, intermittent crampy character to the pain, palpation of fecal material in the abdomen, large amount of stool in the rectum, or anal fissures.

A history and physical exam will be obtained and a flat plate abdominal film will be obtained and read according to the scoring system devised by Barr, et al. If the score is >10, the patient will be entered in the study. Sixty subjects will be randomized to either Ducolax (two 5 mg tablets at bedtime) or a placebo. The patient will be followed up in two to three weeks. Relief of symptoms will be evaluated by questioning. A repeat abdominal film will be obtained and read in the same manner as the pretreatment film. The treatment will be judged successful and appropriate, if the symptoms are gone and the score falls below 10 or in the case of those initially having a score of 10-12, a drop of 4 or more points.

Progress: No patients have been entered due to complications in obtaining the drug and the placebo.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 84/73	Status: On-going

Title: Prophylactic Intravenous Immunoglobin in High Risk Neonates

Start Date: 17 Aug 84	Est Completion Date: Sep 87
Department: Pediatrics	Facility: MAMC
Principal Investigator:	MAJ Jose Garcia, MC
Associate Investigators:	LTC C. Gilbert Frank, MC CPT Glenn D. Jordan, MC
Key Words:	immunoglobin, neonates, high risk, prophylactic
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-
	Periodic Review: Nov 86

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: Three (3) children have entered the study. One child expired prior to completion of the study, secondary to intraventricular hemorrhage. Two children have completed the study and all appropriate laboratory studies and documentations have been forwarded to WRAMC for ongoing evaluation.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/68	Status: On-going

Title: Antenatal Phenobarbital: Prophylactic Efficacy for the Prevention of Neonatal Intracerebral Hemorrhage (ICH)

Start Date: Sep 86	Est Completion Date: May 89
Dept/Svc: Pediatrics	Facility: MAMC
Principal Investigator:	MAJ Jose Garcia, MC
Associate Investigators:	CPT Glenn D. Jordan, MC LT Fred Guyer, M.D., USPHS
Key Words:	intracerebral hemorrhage, prophylactic, phenobarbital

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $50.00	Periodic Review: Jul 87

Study Objective: To assess the putative benefit of antenatal administration of phenobarbital in ICH prophylaxis.

Technical Approach: Mother-infant dyads <30 weeks gestation who present with either premature labor or ruptured membranes will be studied in a randomized, double-blind, placebo-controlled trial. Subjects will be given an initial dose of either 1000 mg, I.V. over 60 minutes or a placebo. Subsequent patient management will be in accordance with standard patient care. If the delivery does not occur within 24 hours of initial drug administration, a maintenance dose of the drug will be given every 24 hours until delivery or until labor is successfully arrested. After delivery each infant will receive a cranial ultrasound on at least three occasions (within 12 hours of birth, at 72 hours, and at 7 days). A sample of cord blood will be obtained at delivery and samples of each infant's blood will be drawn on days 3 and 7 for serum drug levels. Length of time pre- and postadministration of phenobarbital to delivery will be analyzed. Data from mothers on steroids will be analyzed separately.

Progress: Due to time constraints, no patients have been entered in this study.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/35	Status: Completed

Title: Urine and CSF Latex Agglutination: Predictive Value for Subsequent Culture-Proven Sepsis/Meningitis on a General Pediatrics Service

Start Date: 21 Feb 86	Est Completion Date: Mar 87	
Department: Pediatrics		Facility: MAMC
Principal Investigator: CPT Jeffrey W. Glassheim, MC		
Associate Investigator: COL Marvin S. Krober, MC		
Key Words: sepsis, meningitis, latex agglutination, predictive		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Feb 87

Study Objective: To determine the sensitivity/specificity of the latex agglutination test on urine and cerebrospinal fluid for the presence of antigens from the four leading etiologic agents for pediatric sepsis and/or meningitis and assess predictive value for disease that is later proven by positive cultures of either CSF or blood.

Technical Approach: Approximately 100 infants, one week to 24 months with a minimum rectal temperatures of 40°C, will be studied per month. Excluded from the patient population will be patients who were previously admitted to the NICU and any patients currently present in the NICU carrying a diagnosis of R/O sepsis/meningitis. Any patient with a positive chest x-ray for pulmonary infiltrate(s) will be analyzed separately from the main patient pool.

Inpatients with an admitting diagnosis of R/O sepsis/meningitis or febrile seizures will have the following specimens obtained: urine for latex (catheter, clean-catch, or bagged); CSF for latex (usual aseptic technique for LP) - PRN as per clinical judgment; CSF for culture/sensitivity - PRN as per clinical judgment; blood for culture/sensitivity (usual sterile technique); CBC to include differential white blood cell count. These procedures will be in addition to the remainder of a complete sepsis work-up which also includes urine C&S, and chest x-ray. Negative cultures will be considered "final" at 72 hours for the purposes of this study. Latex studies will be performed in the usual manner. In accordance with the Chief of Microbiology Service, the same pool of laboratory technicians will perform all latex/culture studies, thus effecting a "standardization" of procedure. All outpatients from the emergency room or Family Practice that have been sent to Pediatrics for further evaluation/work-up who do not get admitted will have the identical procedures performed. Statistical analysis will consist of the calculation of sensitivity/specificity for each of the four etiologic agents' latex results, which will lead to the calculation of the predictive value.

Progress: Approximately 30 patients were entered in this study. Preliminary analysis of data did not appear to show a good correlation between latex agglutination and subsequent culture results. A manuscript is in preparation.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/32	Status: Terminated

Title: Response to Combination Meningococcal Vaccine in Children

Start Date: 16 Jan 87	Est Completion Date: Apr 88	
Department: Pediatrics		Facility: MAMC
Principal Investigator: MAJ Kip Hartman, MC		
Associate Investigator: COL Marvin Krober, MC		
Key Words: vaccine, meningococcal, safety, antigenicity		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A

Study Objective: To conduct a safety and antigenicity study of a new meningococcal vaccine in the pediatric patient who is to be splenectomized or who is already splenectomized.

Technical Approach: 0.3 cc's of the combination polysaccharide-protein vaccine will be given to immunocompromised children ages 1-18. Routine doses of acetominophen will be administered at the time of immunization and again if a temperature of 101°F occurs in the ensuing 48 hours. Ten cc's of whole blood will be drawn pre-immunization, two weeks post-immunization, six weeks post-immunization, and six months post-immunization and an initial throat culture for meningococcus will be obtained. After removal of serum, it will be analyzed by a serum bactericidal test. Two cc's of whole blood will be analyzed by Wright's stained smear for Howell-Jolly bodies in the splenectomized patients. Antigenicity will be measured by a bactericidal test and response will be defined as a >4-fold increase in antibody titer. Children will be seen at 24 hours post-immunization and temperature will be recorded at 6 and 24 hours and the vaccination site will be examined and children/parents will be questioned regarding adverse reactions. If the temperature is <101°F at 24 hours, the parents will record two subsequent 12-hourly temperatures. If the temperature is >101°F at 24 hours, the parents will continue to administer acetaminophen and record the child's temperature prior to administration through the next 24 hours. A telephone inquiry will be made at 48 hours to record adverse reactions. In order to compare antibody responses, the procedure outlined above will be followed in a control group of well children ages 1-18 years, who will be traveling to areas of endemic disease or are household and day-care center contacts of those developing disease.

A two-factor analysis of variance for repeated measures will be used to detect differences in antibody titer from baseline to 2 weeks, 6 weeks, and 6 months post-immunization and between groups. If a difference exists, pairwise comparisons will be used to detect which time periods are different.

Progress: The vaccine was unavailable from WRAIR; therefore testing of the vaccine was not initiated at MAMC.

Date: 30 Sep 87	Protocol No.: 87/94	Status: On-going

Title: Surgical Resuscitation: The Role of Blood Substitutes

Start Date: 17 Jul 87	Est Completion Date: May 89	
Department: Pediatrics		Facility: MAMC
Principal Investigator: MAJ Kip Hartman, MC		
Associate Investigators: MAJ Michael D. Hayre, VC Lorrie Langdale, M.D.		
Key Words: blood, substitutes, LEBH, swine model		
Accumulative MEDCASE Cost: -0-	Est Accumulative** OMA Cost: -0-	Periodic Review: N/A

Study Objectives: To assess the immediate and delayed biophysiologic response to interval small volume infusions of liposome encapsulated bovine hemoglobin (LEBH) in Microswine™; to assess the efficacy and physiologic response to LEBH transfusion in a total exchange transfusion model and in a resuscitation from normovolemic anemia model; and to document the effects of single unit infusion in non-human primates, paralleling the Microswine™ studies.

Technical Approach: To assess safety and immune response in a single unit infusion, each animal will receive an infusion of 200 ml of the test solution. Test solutions will be 5% albumin in phosphate buffered saline (6 controls), liposomes without hemoglobin encapsulation (6 controls), and LEBH (6). Animals will be infused at 14 days in the same manner and then euthanized at 4 weeks and a necropsy performed. All measurements during both time frames will be repeated at the same intervals. Alterations in the hepatic, renal, pulmonary and hematology systems (measured by serologic function studies and changes in morphology) will be documented. The immune response to low dose infusion of LEBH will be evaluated by ELISA. To document the effects of single dose infusion in non-human primates, 10 adult *Macaca nemestrina* will undergo the same procedures when the Microswine study is completed.

To assess the efficacy, physiology, and immune response in a large dose transfusion, four animals will undergo a total exchange transfusion with LEBH to Hct=0%. Two animals will serve as controls, undergoing exchange transfusion with 5% albumin phosphate buffered saline toward Hct=0%. After induction of normovolemic anemia, six animals will undergo plasma exchange with LEBH and six control animals will be autotransfused with packed red cells. Alterations in the hepatic, renal, pulmonary and hematology systems (measured by serologic function studies and changes in morphology) will be documented. The immune response to large dose infusion and delayed challenge with LEBH will be evaluated by ELISA.

Progress: The study has not been implemented. The investigators are awaiting the funding which has been approved.

**to be funded by a proposed VA/DoD grant

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/50	Status: On-going

Title: Antibody Response to Measles-Mumps-Rubella Vaccine in Children with Concurrent Upper Respiratory Infection

Start Date: 27 Feb 87	Est Completion Date: Mar 88	
Department: Pediatrics		Facility: MAMC

Principal Investigator: COL Marvin S. Krober, MC

Associate Investigators: Dr. Marchetti, University of Hawaii
Catherine Yokan, M.D., DAC
Carl Stracener, M.D., DAC

Key Words: vaccine, measles-mumps-rubella, concurrent URI, antibody response, safety, efficacy

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

Study Objective: To determine whether or not afebrile upper respiratory infections interfere with successful immunization with combined measles-mumps-rubella vaccine (MMR).

Technical Approach: Fifty children with upper respiratory infections and 50 well controls between 15 and 24 months of age will be entered in the study when they present for routine MMR immunization. Pertinent history and physical findings will be recorded and the children will be given the standard MMR. Blood will be drawn and repeat samples obtained at eight weeks. The paired samples will be assayed for serologic response to the immunization. Patients shown to be immune on the initial sample will be excluded from further analysis. For those initially susceptible, antibody responses will be compared in geometric mean titers and in percent of vaccine failures (no rise in titer) to determine whether or not upper respiratory infections resulted in a failure of response or a diminution of response.

Progress: The implementation of this study has been delayed due to problems with the site of immunization at MAMC and also to problems with the reference laboratory. The investigators expect to begin entering patients into the study within a month.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/82	Status: Terminated

Title: Neuromotor Status of Infants with Non-Organic Failure to Thrive (NOFIT)

Start Date: 15 Aug 86	Est Completion Date: Jan 88
Department: Pediatrics	Facility: MAMC
Principal Investigator:	MAJ Ernest F. Krug, MC
Associate Investigators:	Mary T. Arnold, O.T. Kristie Bjornson, R.P.T. Patricia Hoppa, R.N., C.P.N.P. Janis Kathrein, R.P.T. W.R. Peterson, M.D.
Key Words:	NOFIT, neuromotor status, natural history

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Dec 86

Study Objective: To better define the natural history of motor development in infants with the diagnosis of non-organic failure to thrive (NOFIT).

Technical Approach: The study will assess developmental changes in NOFIT infants prospectively over 12 months from initial diagnosis. The Movement Assessment of Infants (MAI) will be administered by a trained therapist at regular intervals from diagnosis to document neurodevelopmental status in four major areas. Information and scores will be recorded for tone, primitive reflexes, automatic reactions, and volitional movements as outlined in the MAI. Patients <5 mos, 14 days with no previously diagnosed neuromotor abnormalities will receive a neuromotor assessment to consist of Bayley Scales of Infant Development: Motoro Scale, Peabody Developmental Motor Scales, and Movement Assessment of Infants. Testing will be repeated at 4.5 to 6.5 months, 8.5 to 10.5 months, and 11.5 to 12.5 months. The Gessell Developmental Screening Inventor will be added to the testing procedure at the 11.5 - 12.5 testing. Data will then be collected and analyzed. Therapists will periodically rate a child independently during an evaluation to maintain some measure of inter-rater reliability.

Progress: No patients were entered on this protocol. There were delays in obtaining a therapist to assist with the study. By the time the therapist was obtained, the principal investigator had received orders to be reassigned and the study was terminated.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/16	Status: On-going

Title: Higher Cortical Functioning in School Aged Children with Headache

Start Date: 21 Nov 86	Est Completion Date: Jan 89	
Department: Pediatrics		Facility: MAMC
Principal Investigator: MAJ William McClintock MC		
Associate Investigator: CPT Barry S. Anton, MSC, USAR		
Key Words: headache, muscle contraction, migraine, siblings		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A

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

Technical Approach: Three groups of school aged children between the ages of six and twelve years will be studied.

Group 1: Ten children with muscle contraction headaches (intermittent - at least one headache every two months for one year).
Group 2: Ten children with migraine headaches (intermittent - at least one headache every two months for one year).
Group 3: Ten siblings of children from gourp 1 or group 2 with no history of headache or other medical condition (controls).

Subjects in the two experimental groups will have no history of progressive neurologic disease or other serious medical condition. A complete history (including onset of headache, frequency, cause, intensity, location and character of pain, associated symptoms, and relief factors), family history of headache, physical exam (blood pressure, cardiovascular exam, HEENT exam, fundoscopic exam, listening for bruits), neurological examination (cranial nerve exam, musculo-skeletal exam, sensory and motor exam, gait, reflex and cerebellum) will be conducted on each patient. In addition, neurophyschological assessment of each patient will be undertaken. The neuropsychological examination will include the following standardized test instruments: Wechsler Intelligence Scale for Children - Revised, Wide Range Achievement Test - Revised, Trail Making Test, Bilateral Name Writing, Word Fluency Test, Bilateral Finger Agnosia, Token Test for Children, Grooved Pegboard, Digit Symbol Test (oral and written), and Child Behavior Checklist. Tests will be given to all children in the same sequence. In order to assess current medical status and screen for medical disorders that might affect neuropsychological test results, medical records of all subjects will be thoroughly reviewed. A parent of each child will be asked to complete a problem check list and a detailed medical history questionnaire.

Progress: Ten subjects have been entered in the study.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/100	Status: On-going

Title: Thyroid Size in Children and Adolescents

Start Date: 21 Aug 87	Est Completion Date: Dec 88	
Department: Pediatrics		Facility: MAMC
Principal Investigator: LTC Dan Moore, MC		
Associate Investigators: None		
Key Words: thyroid, size, children, manually, ultrasound		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A

Study Objective: To establish normal dimensions + 2 standard deviations (SD) for thyroid lobe length and width in children and adolescents. A goiter would then be defined as thyroid gland exceeding 2 SD of these dimensions.

Technical Approach: During the course of a routine physical examination, thyroid glands of 300 normal children and adolescents aged 6-20 years (20 at each age, 10 of each sex) will be measured in the following manner. With the neck extended, the thyroid isthmus is located with the index finger. The medial aspect of each lobe is followed to the apparent tip of each lobe. The upper tip of each lobe is located as the patient swallows with the index finger over each tip. The apparent inferior border of each lobe is located as the patient swallows with the index finger over the inferior portion of the gland. The lateral borders of the gland will be located with the index fingers placed medial to the sternocleidomastoid muscle as the gland moves as the patient swallows. The length will be measured as the distance from the apparent tip of each lobe to the apparent inferior border of each lobe. The width will be measured as the distance from the lateral borders of the gland. Means and SD will be calculated for length of each lobe and mid-isthmus width. For validation of measurement accuracy, 30 patients (2 each age, 1 each sex) will have the same measurements determined by thyroid ultrasound.

Progress: Twenty-six (26) children have been entered in the study.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/14	Status: Completed

Title: Cortisol Response in Febrile Children

Start Date: 21 Nov 86	Est Completion Date: Jul 87	
Department: Pediatrics		Facility: MAMC
Principal Investigator: CPT David A. Nickels, MC		
Associate Investigators: LTC Dan C. Moore, MC		
Key Words: cortisol response, fever, adrenal insufficiency		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $1500.00	Periodic Review: N/A

Study Objective: To delineate specifically the cortisol response in normal children to the stress of fever.

Technical Approach: Approximately 100 children with a fever >101°F will be entered in the study. On the initial visit, height, weight, history, and physical exam will be obtained. No patients will be given antipyretics until seen by the physician. Laboratory evaluation for the specific febrile illness as deemed appropriate by the examining physician will be performed. Each patient enrolled in the study will have the temperature rechecked and recorded just prior to having serum cortisol level drawn. The patient will be recalled at a future date when recovered from the presenting febrile illness for a cortisol level done at approximately the same time of day as the initial cortisol level. The average rise in cortisol will be calculated and a relationship to the height of temperature and type of illness will be sought. These data will be applied to children with adrenal insufficiency in an attempt to delineate more appropriate dosing recommendations during times of stress.

Progress: 105 children were entered in the study.

Cortisol response was unrelated to height of temperature but there were significant differences between diseases. Five diagnoses were represented with sufficient number to permit analysis by disease category. The greatest MAG (magnitude of change) occurred with pneumonia; one patient with meningitis had a similar MAG. Overall, MAG for pneumonia, FEU (fever of unexplained origin), and otitis were significantly higher than upper respiratory infection and strep pharyngitis. Basal cortisols were not significantly different. The investigators conclude that height of temperature is not a reliable predictor of cortisol response in febrile illness and that cortisol stress response varies with disease process. Current recommendations to double or triple replacement hydrocortisone are sufficient only for simple febrile illnesses such as strep pharyngitis and upper respiratory infection but are subtherapeutic for infections such as pneumonia, meningitis, and FUE which imply more diffuse and widespread involvement. A 4-5 fold increase appears appropriate for these conditions.

A manuscript is being prepared for submission for publication.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/97	Status: Terminated

Title: Associations Between IVH and Prolonged QT-Interval in Premature Neonates

Start Date: 19 Sep 86	Est Completion Date: Mar 87	
Department: Pediatrics		Facility: MAMC
Principal Investigator:	CPT Juan A. Rivera-De Leon	
Associate Investigators:	MAJ Jose Garcia, MC MAJ William McClintock, MC	
Key Words:	IVH, prolonged QT Interval, association, neonates	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $3000.00	Periodic Review: Oct 86

Study Objective: To study the possible direct effect of IVH on QT-interval in premature neonates and to study the role of Ca++ and Mg++ levels on prolonged QT-interval in premature neonates.

Technical Approach: Subjects will be 50 neonates <1500 gms and/or 32 weeks gestation with and/or without IVH. Patients with severe congenital malformations which are themselves life-threatening will be ineligible. Control group will be patients with no IVH and no EKG abnormalities. A lead-II EKG will be performed to determine QT-interval; the QTc=measured QT-interval over the square root of the R-R-interval of the same lead. Blind analysis of the EKG will be done by a pediatric cardiologist. Ionized Ca++ levels will be drawn after EKG monitoring, only if abnormal. Cranial ultrasound analysis will be performed by a neonatologist when a radiologist is not available. Mg++ levels will be drawn during one of the routine blood drawings and followed per clinical indication. If needed, a second ionized Ca++ level will be drawn. EKG will be done by the end of the first day, third day, and prior to discharge. 2D Echo will be performed by a neonatologist on days that a radiologist is not available, i.e., first and discharge days. Routine electrolytes to include Ca++ and Mg++ levels will be drawn per the infant's condition or if the EKG is abnormal. Two major groups will consist of prolonged QT-interval and normal QT-interval. Two minor groups will consist of presence of IVH and absence of IVH. Each of the major and minor groups will be correlated to the Mg++ and Ca++ levels. Infants with prolonged QT-interval will be followed by a cardiologist and in the NICU follow-up clinic. Infants with IVH will be followed by a neurologist and in the NICU follow-up clinic. Data analysis: t-test.

Progress: No patients were entered in this study and it was terminated due to the reassignment of the principal investigator.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/51	Status: On-going

Title: Optimum Penicillin Dosage for Treatment of Streptococcal Pharyngitis

Start Date: 27 Feb 87	Est Completion Date: Feb 88	
Department: Pediatrics		Facility: MAMC
Principal Investigator:	COL Conrad L. Stayton, MC	
Associate Investigators:	COL Thomas Charbonnel, MC COL Marvin Krober, MC COL Michael Weir, MC CPT Nicholas Themelis, MC	
Key Words:	streptococcal pharyngitis, penicillin, efficacy, compliance, hematuria	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $500.00	Periodic Review: N/A

Study Objective: To determine the relative efficacy of different dosage regimens of penicillin in the treatment of streptococcal pharyngitis; to ascertain compliance on the different regimens; and to find the incidence of hematuria after illness.

Technical Approach: Children between the ages of 3 and 18 years with clinical symptoms of sore throat and with throat culture or streptococcal latex agglutination rapid screening test positive for Group A beta hemolytic streptococci will be entered in the study. Approximately 300 children will be randomized to receive penicillin VK in one of three regimens: 1000 mg once daily, 500 mg twice daily, or 250 mg four times daily. Throat cultures and urine specimens will be obtained at two days. A urine sample will be obtained on the last day of a 10 day treatment plan. Two to three days after the treatment has been completed, the children will be examined and the throat will again be cultured and the urine checked for presence of blood and penicillin. Pill counts will be used as a second measure of compliance. Subjects will have a final examination and throat culture done two weeks after completing antibiotic treatment. Comparison will be made between the three treatment groups in: percentages with persistent positive throat cultures; percentages with recurrence of positive culture with or without symptoms; amount of unused medicine; percentage still taking penicillin at ten day followup (as evidenced by presence of penicillin in the urine sample); and percentage with hematuria.

Progress: Twenty-four patients have been entered in the study.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 85/52	Status: Terminated

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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jul 87

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 Personnel Resources 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: A total of 55 patients were enrolled in this study. It has been terminated because the investigators were unable to enroll children in the abusive group due to parental objections.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87799	Status: On-going

Title: Rapid Detection of Infectious Mononucleosis by Enzyme Immunoassay

Start Date: 21 Aug 87	Est Completion Date: Aug 88	
Department: Pediatrics		Facility: MAMC
Principal Investigator:	COL Michael R. Weir, MC	
Associate Investigators:	COL Thomas Charbonnel, MC COL Marvin S. Krober, MC	
Key Words:	mononucleosis, detection, rapid, enzyme immunoassay	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A

Study Objective: To evaluate the performance characteristics (reliability, accuracy, ease of use) of the Ventrescreen Mono Test for use in detecting infectious mononucleosis heterophil antibodies in finger tip blood and venipuncture samples.

Technical Approach: Approximately 100 patients suspected of having infectious mononucleosis after a thorough history and physical examination will be entered in the study. A fingerstick capillary tube blood sample will be obtained and used for the performance of the Ventrescreen Mono Test at the time of entry. Venous blood samples will be obtained from a single venipuncture at the time of entry as follows: 3 cc for CBC with differential; 3 cc for rapid slide testing for heterophil antibodies in the conventional manner; 1 cc for the performance of the Ventrescreen Mono Test; and 6 cc to be evaluated for viral capsid antigen IgM and VCA IgG.

The Ventrescreen Mono Test will be compared to the conventional heterophil antibody rapid slide test using a standard two-by-two table. Any samples with a discrepancy will undergo Epstein-Barr virus serology. Five samples in positive agreement and five samples in negative agreement will undergo EBV serology as controls.

Progress: Eight patients have been entered in 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

DEPARTMENT OF RADIOLOGY

Detail Summary Sheet

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

Title: Magnetic Resonance Investigational Study Protocol

Start Date: 19 Jun 87	Est Completion Date: Jun 88	
Department: Radiology		Facility: MAMC
Principal Investigator:	CPT James D. Winthrop, MC	
Associate Investigators:	COL Robert D. Karl, MC MAJ Craig S. Hammes, MC	
Key Words:	magnetic resonance imaging, software, surface coils	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A

Study Objective: To estimate the sensitivity (the incidence of true positive results) and specificity (the incidence of true negative results) of magnetic resonance (MR) as a diagnostic procedure.

Technical Approach: Included in the study will be inpatients and outpatients with suspected medical disorders, where definitive diagnosis is likely, who have had or are scheduled for other imaging modalities. Patients with mechanical or electrically activated implants such as cardiac pacemakers, neurostimulators, or biostimulators will be excluded. Patients with aneurysm clips will be excluded unless the physician is certain that the clips are not magnetically active.

The subject accrual period will be ongoing until all supplements related to the the MR system configuration and intended clinical indication are attained.

Prior to performing the imaging study, the investigators will review the patient's medical history and existing physical exam results, verify eligibility, and record the results on a study form. Subjects will serve as their own controls. Investigators will determine the subjects' final clinical diagnoses by compiling the results of other diagnostic procedures. These results will be compared to the MR results. Efficacy will be measured by comparing the accuracy (estimating sensitivity and specificity) of MR to the final clinical diagnosis. Short-term safety exposure to MR will be assessed by compiling complication and adverse reaction results.

Statistical analysis will include a description of the subject's baseline characteristics, identification of complications and adverse reactions, and summarization of the efficacy parameters. Analysis of the efficacy parameters will include a comparison of the MR results to the final clinical diagnosis and other diagnostic results.

Progress: Successful clinical imaging has been completed in 157 patients. Three patients suffered from claustrophobia, with two successfully completing the imaging on a second attempt. No other adverse reactions were reported.

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 SURGERY

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/07	Status: Suspended

Title: General Surgery Stapling Familiarization Lab (Swine Model)

Start Date: 17 Oct 86	Est Completion Date: Oct 87	
Dept/Svc: Surgery/General		Facility: MAMC
Principal Investigator:	COL Charles A. Andersen, MC	
Associate Investigators:	COL Stanley C. Harris, MC LTC Richard Hall, MC MAJ Stephen Smith, MC	
Key Words: familiarization lab, stapling, general surgery, swine		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $500.00	Periodic Review: N/A

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

Technical Approach: For each laboratory session, two animals will be anesthetized by veterinary personnel using ketamine HCl 20 mg/kg body weight and atropine .088 mg/kg body weight, IM, as a pre-anesthetic. The animals will then be intubated endotracheally and surgical anesthesia will be induced and maintained using a mixture of Halothane and nitrous oxide.

Once a surgical level of anesthesia has been achieved, the abdominal cavity will be entered via a midline incision. A demonstration of stapling techniques (under the direct supervision of staff surgeons and representatives from the staple manufacturer) will be performed on the animal by the surgical residents. After the demonstration, all animals will be euthanatized without being allowed to recover from anesthesia.

Progress: One training session was held during FY 87. The protocol has been suspended pending further revisions by the principal investigator.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/88	Status: On-going

Title: Method of Determining in Dogs the Vascularity of Transposed Patellar Tendons Used in ACL Reconstructions Utilizing Fluorescein Dye, with Correlation to Viability

Start Date: 15 Aug 86	Est Completion Date: Aug 87	
Dept/Svc: Surgery/Orthopedics		Facility: MAMC
Principal Investigator: CPT Brian Barnard, MC		
Associate Investigator: CPT Robert Arciero, MC		
Key Words: patellar tendons, vascularity, fluorescein dye, dogs		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $400.00	Periodic Review: Dec 86

Study Objective: To determine whether the patellar tendon graft utilized in ACL reconstructions is vascularized at the time of transposition and whether the transposed graft maintains its circulation, i.e., remains viable.

Technical Approach: Preoperatively, the animals will be weighed and examined for general physical abnormalities as well as examination of the knees to include ROM, ligamentous laxity, thigh circumference, and x-rays. Six experimental and six control animals will be studied. After being anesthetized, a midline incision will be made under tournequet control to identify the patella-patellar tendon complex. The central 1/3 of the PT will be harvested with an attached wedge of bone taken proximally from the patella and distally from the proximal tibia. The attachment of the fat pad to the PT graft will be reinforced and the free ends of the graft will be tagged with sutures placed through drill holes in the bone. The intercondylar notch will be exposed and the ACL will be resected from its femoral and tibial attachments. Boney canals will be created to allow isocentric placement of the graft. At this point the tournequet will be deflated and fluorescein will be injected. After 10 minutes, photos will be obtained of the graft using the fluorescence camera. The patellar bone wedge will be passed into the femoral canal and fixated. The tibial component will be passed and prior to final fixation, an exam of the knee to include ROM and stability will be performed. When no instability is detected, yet motion is not impeded, the graft will be secured. The defect in the patellar tendon and the skin will be closed and the surgical site covered with a cast with the knee bent at 45°. The cast will be kept on for 7-10 days. The animals will be sacrificed on a weekly basis beginning at the third postop week in order to obtain 2 control and 2 study knees per week. Before sacrifice, the animals will be anesthetized and examined to check for knee motion and laxity. After sacrifice, the hind limb will be disarticulated at the hip, decalcified, and sectioned for radiographic and histologic examination.

Progress: The control animals have been studied. Further work on this study was delayed due to a rotation at the University of Washington by the principal investigator.

Detail Summary Sheet

Date: 30 Sep 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Mar 87

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; or with evidence of tumor outside the testis by any other diagnostic means, or with 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: One patient was entered in this study in FY 87.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/86	Status: On-going

Title: An 18-Month Double-Blind, Multicenter Study to Compare the Efficacy and Safety of the Antiandrogen RU 23908 in Combination with Leuprolide with that of Leuprolide in Patients with Carcinoma of the Prostate (Stage D_2), Followed by an Extended Treatment Period to Evaluate the Long-Term Safety and Tolerance of RU 23908

Start Date: 15 Aug 86	Est Completion Date: Sep 88	
Dept/Svc: Surgery/Urology		Facility: MAMC
Principal Investigator: COL William D Belville, MC		
Associate Investigator: COL Irwin B. Dabe, MC		
Key Words: prostate, carcinoma, RU 23908, leuprolide		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Aug 87

Study Objectives: To compare the safety and efficacy of the antiandrogen RU 23908 in combination with leuprolide with that of leuprolide plus placebo in the treatment of patients with prostatic carcinoma (Stage D_2). Difference in time to progression, survival, clinical response, pain and performance will be assessed as well as long-term safety of RU 23908 in the same patient population.

Technical Approach: This is a multicenter study with two parts. Part A is a randomized, double-blind, parallel comparison between the combination of leuprolide plus antiandrogen RU 23908 and leuprolide plus placebo. Patients 18-85 years of age presenting with newly diagnosed stage D_2 carcinoma of the prostate and a life expectancy of at least 3 months will be eligible. Patients who have undergone orchiectomy, received previous hormonal or systemic chemotherapy, with rapidly progressing fatal illness other than carcinoma of the prostate, who have undergone previous hypophysectomy or adrenalectomy, or with another neoplasm, sensitivity to any contrast agent in a radiological evaluation, or severe hepatic or renal dysfunction will be excluded. Patients will be treated for 18 months. Patients who do not respond to treatment will be unblinded. Those receiving RU 23908 will be given the option to continue or to receive other treatment. Patients receiving placebo will be withdrawn from the the study.

Progress: Five subjects were entered in this study at MAMC in FY 87. The combined therapy appears to be as effective as standard therapy. No toxicity has been evidenced at MAMC; however, there has been a small number of reports of interstitial pneumonitis at other institutions.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/85	Status: On-going

Title: Vocal Function Following Carbon Dioxide Laser Surgery

Start Date: 19 Jun 87	Est Completion Date: Dec 93	
Dept/Svc: Otolaryngology/Surgery		Facility: MAMC
Principal Investigator: LTC Don B. Blakeslee, MC		
Associate Investigators: Kenton L. Yockey, MA/CCC Guity Nevissi, M.D.		
Key Words: vocal function, surgery, carbon dioxide laser		
Accumulative MEDCASE Cost: -0-**	Est Accumulative OMA Cost: -0-**	Periodic Review: N/A

Study Objective: To determine if vocal fold dysfunction is directly related to the depth of the surgically created ulcer of the vocal fold.

Technical Approach: Phase I: Direct laryngostroboscopy will be performed on 12 dogs. The recurrent laryngeal nerves and the external branches of the superior laryngeal nerves will be stimulated and phonation will be videorecorded for 8-12 seconds. A surgical wound will be created by removing a 4x4 mm segment from the midportion of a vocal cord by CO_2 laser dissection with the nonoperated cord serving as the control. The wound will be observed under magnification and photographed to confirm the accuracy of the resection, and the specimen will be histologically examined to verify the exact segments removed. After a six-week healing period, the larynges will be re-examined and laryngeal form and function will be restudied. Function studies will include symmetry of wave form, measurement of subglottic pressure, air flow, sound pressure, and electroglottography. Fundamental frequency, jitter, shimmer, noise-to-harmonics ratio, and intensity will be analyzed on a PM pitch analyzer. The animals will then be euthanized and one vocal fold from each larynx will be removed for histologic examination to include gross anatomy of the body and the cover, fibroblast activity, foreign body, and inflammatory reaction.

Phase II: 24 adult patients with vocal dysfunction secondary to vocal fold lesions, who have failed appropriate medical management, will undergo preoperative studies utilizing the GLIMPES station, which uses a videocamera in conjunction with a microphone, an electroglottograph, an intraoral pressure tube, a transducer, and an accelerometer and its associated electronics to record fundamental frequency, jitter, shimmer, noise-to-harmonics ratio, and intensity. The patient will then undergo excision of the vocal fold lesion by CO_2 laser with specimens obtained for histopathology. The depth of of each incision will be documented and recorded. Each patient will be studied again using the GLIMPES station at 3, 6, and 12 months after surgery.

Progress: This study has not been implemented. The investigators are awaiting a decision on a joint VA/DoD** grant to fund the study.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/38	Status: On-going

Title: Bioreactivity of Blood Vessel Prostheses After Implantation

Start Date: 16 Jan 87	Est Completion Date: Jan 89	
Dept/Svc: Surgery/General		Facility: MAMC
Principal Investigator:	CPT Jon C. Bowersox, MC	
Associate Investigators:	COL Charles A. Andersen, MC John B. Sharefkin, M.D.	
Key Words: bioreactivity, prostheses, blood vessel, fibronectin		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $1386.00	Periodic Review: N/A

Study Objective: To quantitate the levels of fibronectin on the luminal surfaces of blood vessel grafts after removal from patients for indications such as single limb thrombosis or infection; to determine the distribution of fibronectin; and to measure the extent of vascular endothelial cell spreading and attachment on the graft surfaces.

Technical Approach: Fibronectin assay by ELISA: Specimens will be incubated in a polycarbonate immunoassay chamber, first with rabbit anti-human fibronectin antibody and then with alkaline phosphatase-conjugated goat anti-rabbit IgG. Samples will then be incubated with nitrophenylphosphate and an ELISA reader used to determine relative concentrations of the reaction product. Positive controls of the enzymatic detection system will be prepared by reacting the phosphate substrate directly with secondary antibody conjugate. A standard curve will be constructed from serial dilutions of human fibronectin incubated with either nonimplanted graft material or NIH reference standard polyethylene. This assay will also be performed using monoclonal antibodies against the human fibronectin cell-binding domain. Cell attachment studies: Human saphenous vein endothelial cells (SVEC) in near confluent monolayers will be exposed to ^{3}H-thymidine in M199 for 24 hours and the resulting radiolabeled cells harvested. Specific radiolabeling activity will be determined by quantitating equal cell aliquots with a hemocytometer and a scintillation counter. All samples will be standardized so that equal aliquots can be incubated with graft material, after which samples of both the attached cells and the reaction supernatant will be quantitated with a scintillation counter. Cell spreading: SVEC will be prepared as described above except that ^{3}H-thymidine uptake will be omitted. Following incubation with the graft material, cells will be fixed, stained with Wright's stain, and quantitated by light microscopy. Immunohistochemical examination of graft surfaces: Prepared sections of the graft material will be subjected to antibody staining. After incubating the specimens first with rabbit anti-human fibronectin and then with rhodamineconjugated goat anti-rabbit IgG, they will be examined by epi-illumination light microscopy.

Progress: This study has not implemented due to scheduling conflicts and other commitments of the principal investigator.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/39	Status: On-going

Title: Effects of Cell Attachment Peptides on Endothelial Cell Binding to Synthetic Blood Vessel Grafts

Start Date: 16 Jan 87	Est Completion Date: Jun 88
Dept/Svc: Surgery/General	Facility: MAMC
Principal Investigator: CPT Jon C. Bowersox, MC	
Associate Investigator: COL Charles Andersen, MC	
Key Words: cell attachment peptides, endothelial cell binding, synthetic blood vessel grafts	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $1220.00	Periodic Review: N/A

Study Objective: To determine the effects of the cell attachment peptides on endothelial cell seeding (attachment and retention).

Technical Approach: Crosslinking cell attachment peptides tc graft material: The synthetic cell attachment peptides arginine-glycine-aspartic acid (RGD) and RGD + serine-cysteine (RGDCS) will be used in this study. A reaction will be started by dissolving RGDCS in DMSO containing 10 mM SADP (N-succininmidyl-4-azidophenyl-1, 3 dithiopropionate) . After 30 minutes, the reaction will be terminated and DMSO removed by dialysis. PTFE and Dacron graft material will be cross reacted with RGDCS-SADP and activated by exposure to light. The efficiency of the crosslinking reaction will be determined by using ^{3}H-RGDCS peptides prepared by borohydride reduction.

Determining endothelial cell attachment efficiency to grafts: Graft material prepared as described above will be placed in immunoassay chambers and cell attachment will be quantitated using human saphenous vein endothelial cells. To determine the specificty of the attachment reaction for cell attachment peptides, RGD and RGDCS will be added to the attachment medium containing the endothelial cells.

The major difficulty in completing this study will lie in effectively crosslinking attachment peptides to graft materials. Heterobifunctional crosslinking reagents are the most versatile class of linkers available; if the initially chosen molecule is ineffective, additional crosslinkers will be utilized.

The reactivity of these grafts toward platelets and fibrin will be compared with those coated with the intact fibronectin molecule.

Progress: This study has not implemented due to scheduling conflicts and other commitments of the principal investigator.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/57	Status: Ongoing

Title: Urinary Retention as an Indicator of Prostate Carcinoma

Start Date: 20 Mar 87	Est Completion Date: Jan 88
Dept/Svc: Surgery/ Urology	Facility: MAMC
Principal Investigator:	CPT Rodney Davis, MC
Associate Investigators:	COL William D. Belville, MC COL Victor J. Kiesling, Jr, COL LTC John A. Vaccaro, MC
Key Words:	carcinoma, prostate, urinary retention, indicator

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

Study Objective: To determine the incidence of adenocarcinoma of the prostate in males who present with acute urinary retention.

Technical Approach: Fifty consecutive patients > 18 years of age presenting with acute urinary retention will be evaluated. A record will be maintained on each subject to include documentation of the results of the findings on physical examination of the prostate and the examiner's initial clinical impression of a benign or malignant gland. Following initial evaluation and stabilization, all patients will undergo standard transperineal needle biopsy of the prostate. Biopsy material will be evaluated for the presence or absence of malignancy. The results of the prostate biopsy will be correlated with the initial examiner's clinical impression and any subsequent prostatic tissue obtained by a definitive surgical procedure.

Progress: Thirty-nine consecutive patients ranging in age from 47-81 underwent perineal needle biopsy. Of those seven patients with palpably abnormal prostate glands, all had biopsies positive for cancer. Of the remaining 32 patients with palpably normal glands, all biopsies save one were negative. Therefore, acute urinary retention by itself would not seem to indicate prostate cancer in the elderly male.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 85/49	Status: Completed

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 Investigators:

COL Richard A. Camp, MC	MAJ Charles Hannan, MSC
COL Thomas J. Parr, MC	MAJ Gary Price, MSC

Key Words: synovial fluid, changes, arthroscopy

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $1300.00	Periodic Review: Jul 87

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: Preliminary data indicate a high correlation between certain types of knee problems and certain parameters gathered from the analysis. A paper was presented at the 1986 Annual Meeting of the Society of Military Orthopaedic Surgeons. The investigator is in the process of completing data analysis.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/94	Status: On-going

Title: A Prospective Evaluation of Testicular Shielding in Preventing Hypogonadism in Prostate Cancer Patients Receiving External Beam Radiotherapy

Start Date: Sep 86	Est Completion Date: May 87
Dept/Svc: Surgery/General	Facility: MAMC

Principal Investigator: CPT Christopher P. Evans, MC

Associate Investigators: COL Victor J. Kiesling, MC
COL Donald H. Kull, MC
COL Stephen R. Plymate, MC
MAJ Pushpa M. Patel, MC

Key Words: prostate cancer, hypogonadism, testicular shielding

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $1500.00	Periodic Review: Oct 86

Study Objective: To assess a possible protective effect on testicular function of a lead testicular shield during the radiation treatment period.

Technical Approach: Twenty male prostate cancer patients >18 years will be randomized into two groups to wear a lead gonadal shield during radiation therapy or to wear no shield during the therapy. Patients with prior radiation or hormonal therapy will be excluded. Prior to entry blood will be drawn for basal FSH, LH, testosterone, TeBG, prolactin, and estradiol levels. An LHRH stimulation test will be done with 30 and 60 minute levels drawn. Blood will again be drawn during mid-course of therapy and at 1 and 12 weeks post-therapy for these same determinations. Comparison of group results will be performed by standard statistical methodology.

Progress: Five patients have been enrolled and have completed all required blood work.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87758	Status: On-going

Title: Patency of Double J Ureteral Stents

Start Date: 20 Mar 87	Est Completion Date: Mar 88	
Dept/Svc: Surgery/Urology		Facility: MAMC
Principal Investigator:	MAJ Charles W. Fox, Jr, MC	
Associate Investigators:	COL William Belville, MC COL Stanton F. Brown, MC COL Robert D. Karl, MC COL Victor J. Kiesling, MC LTC John A. Vaccaro, MC	
Key Words:	ureteral stents, patency, cystography (nuclear and retrograde), lasix renography	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $35.00	Periodic Review: N/A

Study Objective: To establish the lasix diuretic renogram half disappearance time for renal units which have indwelling double J silicone ureteral catheters; to compare the ability of standard retrograde cystography and nuclear cystography in determining patency of double J silicone ureteral catheters in obstructed renal units; and to correlate the half time of disappearance of radionuclide with patency evaluations done by standard retrograde cystography and nuclear cystography.

Technical Approach: Twenty patients requiring an indwelling ureteral catheter will undergo retrograde cystography, nuclear cystography, and lasix renography prior to placement of the catheter. Patients will receive post-instrumentation antibiotics to decrease the risk of infection. The same tests will be repeated at 2 weeks post-catheter placement and every 4 weeks after that until the catheter is removed. Four weeks following removal, patients will be studied again.

The Nuclear Medicine Service will calculate the half life on lasix renography and evaluate the nuclear cystogram for demonstration of reflux into the renal pelvis which would be listed as a positive test. The Urology Service will interpret the retrograde cystogram. A positive test will be demonstration of reflux into the renal pelvis.

Progress: Fourteen subjects have been studied. Preliminary results indicate that nuclear cystogram is more sensitive than retrograde cystogram in showing reflux in stented renal units. The lasix renogram half disappearance time for stented renal units is proving to not be obstructed (>20 minutes), nor is it normal (<10 minutes). This is proving to be invaluable clinical evidence.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/50	Status: On-going

Title: Ultrasonic Imaging of Veins Throughout Pregnancy and Early Post-Partum

Start Date: Mar 86	Est Completion Date: Sep 88	
Dept/Svc: Surgery/Vascular Surgery		Facility: MAMC
Principal Investigator:	Nancy N. Greenfield, R.N., M.S., DAC	
Associate Investigators:	COL William L. Benson, MC Linda K. Bickerstaff, M.D., DAC	
Key Words:	DVT, pregnancy, early post-partum, ultrasound	
Accumulative MEDCASE Cost: $16,990.00	Est Accumulative OMA Cost: -0-	Periodic Review: Mar 87

Study Objective: To map out changes occurring in the veins throughout normal pregnancy and identify patients at risk for or having deep venous thrombosis (DVT).

Technical Approach: Thirty patients aged 18-30, assumed to have a normal uncomplicated pregnancy with no history of DVT or a complicated pregnancy in the past, will be studied. Fifteen patients will be first pregnancy and 15 patients will be in a second or later pregnancy. Ultrasonic imaging of the deep venous system from the common femoral vein as far distal as can be imaged (attempt will be made to image the calf vessels) will be done. Recording of the images will be made on video. These studies will be done serially at 3, 6, 7, 8, and 9 months and again 6 weeks post-partum.

Progress: The imager which is necessary to implement the study was not received until September 1987. Classes on use of the imager have been scheduled.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/55	Status: On-going

Title: Technetium-99m Stannous Pyrophosphate Myocardial Scintigraphy in the Diagnosis of Rabbit Myocardial Contusion

Start Date: 20 Mar 87	Est Completion Date: May 87
Dept/Svc: General Surgery	Facility: MAMC
Principal Investigator:	CPT Robert L. Hall, MC
Associate Investigators:	COL Robert C. Karl, MC LTC James Jones, MC CPT George Hodges, MC CPT Mark R. Nyreen, MC
Key Words:	myocardial contusion, diagnosis, scintigraphy, 99m technetium stannous pyrophosphate

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $131.00	Periodic Review: N/A

Study Objective: To determine if 99m technetium pyrophosphate scintigraphy will accurately diagnose acute myocardial contusion in the rat model.

Technical Approach: Ten large adult SPF Sprague-Dawley rats will be anesthetized and connected to a 3-lead ECG. While anesthetized, the rats will receive a controlled mediastinal-directed blow sufficient to induce cardiac injury yet allow the rat to survive. Prior studies on four rats will have determined the exact procedures to be used to give consistent injuries. Technetium pyrophosphate will be injected intravenously into the rat. Two hours after injection, the rat will undergo nuclear scanning. After completion of the scan, a thoracotomy will be performed and the heart and great vessels will be harvested. The harvested heart will be inspected for gross evidence of injury. Histopathological findings will be identified and noted. The accuracy of the nuclear medicine scan will be determined by comparing the scan results with confirmed pathological evidence of injury. Four additional rats will serve as controls and undergo all procedures except the injury.

It is anticipated that the results derived from this protocol will be clear cut and will lead to obvious conclusions. However, if instances arise where the data suggest ambiguity as to whether subtle or minor changes occurred compared to controls, then the potential implications of such changes will be analyzed to determine if it would be of interest in the context of the project to examine them by detailed mathematical statistical analysis.

Progress: The model of injury for the myocardial contusion has been established.

Detail Summary Sheet

Date: 30 Sep 87	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 Cost: -0-	Est Accumulative OMA Cost: $1600.00	Periodic Review: Feb 87

Study Objective: To provide training to general surgery, emergency medicine, and family practice residents and, specifically, to teach proper management of the initial one hour following major trauma.

Technical Approach: During a laboratory session involving goat surgery, each student in the group will be directly involved in a hands-on performance of a venous cutdown, a cricothyroidotomy, a tube thoracostomy, peritoneal lavage, and pericardiocentesis. This course will be conducted 3-4 times/year at MAMC.

Progress: Three ATLS courses were presented with approximately 16 students per class.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 84/23	Status: Terminated

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 Everette Hart, MC
Associate Investigators:	COL Waylon Black, MC LTC David W. Moore, MC CPT James B. Erhardt, CPT Dale B. Smith, MC
Key Words:	sinusitis, sepsis, foreign bodies, nasal cavity

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $500.00	Periodic Review: Feb 87

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 demonstrate 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 films or CT scan demonstrate 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 ne the ethmoid and sphenoid sinuses will be concurrently culture 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: Dr. Hart assumed the role of principal investigator for this protocol in February 1987. However, several months later, when the staff reviewed the workload versus information that could be obtained, it was decided that there would be too few patients entered in the future to justify further extension. Only four patients were entered in the study. No patients were entered in the study in FY 87.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/31	Status: On-going

Title: Stapedius Reflex for Evaluation of the Perforated Tympanic Membrane

Start Date: 1 Jun 87	Est Completion Date: Dec 87	
Dept/Svc: Surgery/Otolaryngology		Facility: MAMC
Principal Investigator: CPT Michael A. Jaindl, MC		
Associate Investigators: LTC Carl M. Loovis, MS CPT Robert Wright, MS		
Key Words: tympanic membrane, perforated, stapedius reflex		
Accumulative MEDCASE Cost: $6895.00	Est Accumulative OMA Cost: -0-	Periodic Review: N/A

Study Objective: To examine the stapedius reflex in patients with perforations of the tympanic membrane and correlate size of perforation with presence of reflex.

Technical Approach: Patients who have been identified with a tympanic membrane perforation or PE tube in place will be examined and the location and size of the perforation documented. A pure tone audiogram and stapedius reflex testing will then be performed. The stapedius reflex testing will be done using a Model 310 audiometer with test frequencies of 1, 5, and 10 KHz and probe tones of 200 and 500 Hz and 1 KHz. The amplitude of each respone will be recorded. The strength of the test signal will be increased and the resultant reflex amplitude will be observed and recorded in order to document presence or absence of rollover. Finally, a continuous test signal will be presented to test for reflex decay. Any patient with evidence of rollover or reflex decay will be included in the study and referred for further noninvasive tests to rule out presence of an acoustic or cerebellopontine angle tumor.

The data will be analyzed to attempt to correlate size of perforation with presence and amplitude of stapedius reflex. Calculations will be presented that demonstrate the acoustics of the stapedial reflex as generally understood today. Calculations will also be presented that support the observation that a stapedius reflex can be measured in the presence of a perforation depending on the size of the perforation. Chi square analysis will be used to correlate reflex amplitude and size of perforation.

All patients with perforations will be followed. If the perforation closes, the patient will be reevaluated using the same procedure to document presence of stapedius reflex.

Progress: This study has not been implemented becasue the essential equipment has not yet been received.

Italics

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/42	Status: On-going
Title: Efficacy of Behavioral Testing as a Screening Device for Military Children at High Risk for Hearing Loss		
Start Date: 27 Feb 87	Est Completion Date: Jan 89	
Dept/Svc: Surgery/Audiology		Facility: MAMC
Principal Investigator:	LTC Carl F. Loovis, MS	
Associate Investigators:	CPT Randy Bennett, MC CPT Robert Wright, MS	
Key Words: hearing loss, children, behavioral testing		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $200.00	Periodic Review: N/A

Study Objective: To devise a time efficient, effective, and practical procedure for the early identification of childhood hearing loss and to develop a behavioral screening method that is simple, accurate, and brief enough to act as a primary filter.

Technical Approach: Thirty infants 4.5 - 12 months of age will be tested. The subjects will be children with congenital prenatal infections, elevated bilirubin, low birth weight, with suspected craniofacial abnormalities, *H. influenza* meningitis, or other NICU graduates or whose parents have expressed concern. Screening for narrow band and speech detection will be performed using a conventional 2-channel clinical audiometer. Screening for speech will be performed using a monitored live voice peaked on a VU meter uttering the child's name alternately with the nonsense syllables "pa-pa-pa". The screening level criterion for a "pass" for narrow band will be 40 db and 30 db KHz for threshold estimate for speech. Response authentication will be performed by an examiner in the control booth and an observer seated facing the mother and child. Infants will be given a tympanometric exam on each visit and any child with middle ear pressure in excess of negative 100 mm H_2O in either ear will be screened out. The subjects will return at a later date for auditory brainstem response testing. A questionnaire will be filled out by a parent to establish whether there is parental concern about deafness. All subjects will be divided into two categories, "pass" or "fail" behavioral screening criteria. All will be evaluated by ABR, a definitive means of establishing the integrity of the basal portion of the cochlea. A matrix will be developed, plotting "pass/fail" according to the two different measures. A statistical value for specificity and sensitivity will be determined to evaluate the effectiveness of the behavioral procedure in predicting hearing loss as determined by the ABR. Trends pointing to the greater predictability of hearing loss by etiology using the behavioral technique will be sought.

Progress: Seven infants have been tested. Results on this limited number of subjects indicate that behavioral testing is as effective as the brainstem response audiometry.

Detail Summary Sheet

Date: 30 Sep 87	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:	MAJ Kevin J. Chismire, MC
COL Stanley C. Allison, MC	MAJ Leslie P. Fox, MC
COL Stanley C. Sollie, MC	MAJ Paul H. Ryan, MC
LTC John C. Goodin, MC	MAJ Anthony R. Truxal, 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 Cost: -0-	Est Accumulative OMA Cost: $200.00
	Periodic Review: Apr 87

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 150 IOL's were implanted in FY 87 with no adverse reactions. IOL's have withstood the test of time and most 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.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 85/51	Status: Completed
Title: The Transconjunctival Oxygen Monitoring System as a Predictor of Carotid Stenosis		
Start Date: 19 Apr 85	Estimated Completion Date: Jn 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 Cost: -0-	Est Accumulative OMA Cost: $650.00	Periodic Review: Aug 87

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 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.

Progress: Twenty patients were entered in this study. The data suggest that the measurement of coujunctival oxygen may be a useful predictor of the severity of carotid disease, since the lowest values were obtained in patients diagnosed with >80% bilateral stenosis or with unilateral internal carotid artery occlusion. It was not a useful indicator of moderate stenosis and conjunctival oxygen outcome was not consistent in the small number of CEA's studied.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/29	Status: On-going

Title: The Clinical Study of Intraocular Lens Implant and the Use of Viscoat™, Phase II

Start Date: 17 Jan 86	Est Completion Date: Jan 88	
Dept/Svc: Surgery/Ophthalmology		Facility: MAMC
Principal Investigator:	LTC Thomas M. Mader, MC	
Associate Investigators:	MAJ Kevin J. Chismire, MC MAJ Leslie P. Fox, MC MAJ Lawrence J. White, MC	
Key Words: IOL, Viscoat, adverse effects, other surgeries		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Apr 87

Study Objective: To collect data for reports of potential adverse reactions or complications which may have been undetected in a pilot study with a smaller patient population and to evaluate certain indications including corneal transplant surgery, retinal detachment surgery, glaucoma filtering surgery, and other more specific procedures.

Technical Approach: Viscoat is a sterile non-pyrogenic, viscoelastic solution used to maintain anterior chamber depth which exhibits IOL coating properties and effectively protects the ocular tissue, as shown in Phase I of this study of 200 consecutive patients. In Phase II, additional investigators will be added to the study and non-consecutive patients will be used to provide a sufficient number of patients in certain surgical procedure categories, such as corneal transplant, glaucoma surgery, and retinal detachment. The preoperative condition of each patient will be recorded with particular reference to corneal abnormalities, previous anterior segment disease, and intraocular pressure level. Intraoperative conditions will be evaluated and recorded as to the ocular status before Viscoat is injected. Viscoat will be introduced and the amounts introduced aspirated from the eye will be recorded, along with the effectiveness in facilitating anterior segment surgery. At 1-3 and 4-15 days postoperatively, the corneal appearance, anterior segment inflammation (iritis), and intraocular pressure level will be examined and recorded. In order to monitor the safety of Viscoat, a table will be generated that summarizes the occurrence of both adverse reactions and postoperative complications.

Progress: Approximately 150 patients have been treated with Viscoat with no adverse reactions.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/21	Status: On-going

Title: Home Intravenous Hyperalimentation in Treatment of Lymphoma

Start Date: Nov 86	Est Completion Date: Sep 87	
Dept/Svc: Surgery/General		Facility: MAMC
Principal Investigator: CPT Robert Martindale, MC		
Associate Investigators:		
Pamela Charney, R.D.	COL Charles A. Andersen, MC	
LTC Howard Davidson, MC	COL John Redmond, MC	
MAJ Lauren K. Colman, MC	COL Irwin B. Dabe, MC	
Key Words: lymphoma, hyperalimentation, intravenous, home		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A:

Study Objective: To determine if addition of home intravenous hyperalimentation in patients treated with aggressive, curative-intent chemotherapy regimens for lymphoma can reduce the incidence of chemotherapy complications, specifically mucositis, weight loss and infection; and to study whether patients treated with hyperalimentation are able to stay closer to full intended doses.

Technical Approach: Ten subjects ranging from 18-75 years will be studied. Medications to be used for chemotherapy will already have been determined. Patients will receive Nystatin Swish and Swallow or Mycelex Troches, generic mylanta, Benydryl, and Lidocaine Gel mouthwash, and Septra. Intravenous hyperalimentation solution based on metabolic requirements as determined by the BEE method with addition of appropriate stress factor will start within one week of first chemotherapy. TPN will be given according to the same schedule as chemotherapy. TPN will be temporarily withheld if patient's weight gain is >5 pounds above entry weight. Patients will be given either the total estimated caloric requirement or one half the total estimated and adjusted weekly as needed. Hyperalimentation will be given at night so as not to itself deter patients from oral alimentation. For patients who receive MACOP-B, the body weight changes, TLC, and albumin values, as well as the number of days hospitalized, number of days with fever, number of days with severe stomatitis, and percentage of full dose chemotherapy administered will be compared to those same values and parameters in a historical control group of seven patients who received MACOP-B. For patients who receive m-BACOD or PROMACE-Cytabom, the control group will be historical controls as reported in Phase II SWOG studies of each of the regimens. Analysis will be performed by calculating means of each parameter in the two groups compared, then using chi-square analysis.

Progress: Three patients have been entered in the study with no adverse effects reported.

Detail Summary Sheet

Date: 30 Sep 87	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: MAJ Charles Morrow, MC	
Associate Investigators: COL Thomas J. Parr, MC MAJ Jonathan P. Bacon, MC	
Key Words: hip replacement, biologic ingrowth, non-cemented	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Aug 87

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. Preoperative 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-prothesis 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 protheses 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 additional patients were entered at MAMC in FY 87 for a total of 45 patients. Patient entry has been completed and the investigators are continuing to collect follow-up data.

The principal investigator has been changed to MAJ Morrow due to the retirement of COL Parr.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/95	Status: Completed
Title: Youth Soccer Injuries in a Training Camp		
Start Date: 19 Sep 86	Est Completion Date: Jan 87	
Dept/Svc: Surgery/ Orthopedics		Facility: MAMC
Principal Investigator: COL Thomas J. Parr, MC		
Associate Investigators: Nathan J. Smith, M.D. Douglas D. Backous, B.S.		
Key Words: soccer, youth, injuries, training camp		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A

Study Objective: To document sports injuries and health problems among young soccer players attending a professionally run soccer camp, to test the hypothesis that soccer is a safe sport for young athletes, and to identify factors which may lead to an increased risk of injury.

Technical Approach: This is a retrospective study of routine data collected by physicians during a training camp for young soccer players. The camp consisted of seven one-week sessions. Since maturation varies among individuals of the same chronological ages, the maturation level was assessed in male and female participants by measuring grip strength with a hand dynamometer. Health records for each attendee were screened for previous injuries and health problems prior to camp. Age, sex, height, and weight will be taken from the camp registry. Skill level assessment was done routinely by the coaches. A registered athletic trainer diagnosed and recorded injuries. Two physicians made biweekly visits to further verify diagnoses.

Progress: This prospective study of injuries encountered by boys (681) and girls (458) 7-17 years of age revealed an incidence of 10.6/1000 hours in girls and 7.3/1000 hours in boys, with an increased incidence at age 14. Seventy percent of injuries involved the lower extremities. Contusions represented 35.2%, muscle strains 27.8%, ligament sprains 19.4%, and fracture and dislocations 2%. The ankle was the most frequent site of injury in both sexes, with a high incidence of quadriceps strains also noted in boys. The boys with the highest incidence of injury were over 65" in height but with a weak grip strength of <25 kg. Pubertal maturity does not appear to be an important discriminator of who will be injured playing soccer. Instead, injuries might be more effectively reduced by matching participants according to some parameter of muscular development, since this generally lags behind pubertal and skeletal maturity in the developing adolescent.

A manuscript has been submitted to the American Journal of Diseases of Children.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/43	Status: Terminated

Title: Nitrofurantoin and Pediatric Pulmonary Function

Start Date: 21 Mar 86	Est Completion Date: Mar 87
Dept/Svc: Surgery/Urology	Facility: MAMC
Principal Investigator:	CPT Leonard G. Renfer, MC
Associate Investigators:	COL William D. Belville, MC
	COL Victor J. Kiesling, MC
	COL William A. Madden, MC
	CPT Russell R. Moores, MC
	CPT Thomas A. Rozanski, MC
Key Words:	pulmonary function, pediataric, nitrofurantoin

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $15.00	Periodic Review: Jun 87

Study Objective: To evaluate the effect of nitrofurantoin on pediatric pulmonay function.

Technical Approach: Children, ages 6 to 16, presenting with an uncomplicated lower urinary tract infection will be treated with nitrofurantoin, when indicated, and evaluated in a prospective fashion using pulmonary function tests before and after therapy. Patients on both short and long term therapy will be evaluated. Nitrofurantoin therapy will be given 5-7 mg/kg q.i.d for 10 days. All children will be evaluated initially with a urinalysis, urine culture, and PFT's. Patients will be seen in follow-up in 12 to 14 days and the studies will be repeated. A final assessment with urine culture and PFT's will be done one month after treatment.

All patients will undergo routine urologic evaluation. Any child requiring long term suppressive therapy will be evaluated every other month with urine culture and PFT's.

Progress: Due to other research commitments by Dr. Rozanski, the principal investigator was changed in July to Dr. Renfer. Due to complications of having patients referred from Pediatrics, it was later decided to terminate the study. No patients were entered in this study.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/100	Status: On-going

Title: Effects of Androgen Depletion on Human Prostate Tumor Cell Growth in the Athymic Balb/c Mouse

Start Date: Sep 86	Est Completion Date: Sep 87
Dept/Svc: Surgery/Urology	Facility: MAMC

Principal Investigator: CPT Thomas A. Rozanski, MC

Associate Investigators:

COL William D. Belville, MC
COL Stephen R. Plymate, MC
Richard Ostenson, M.D.
Stephen Loop, M.S.

Key Words: prostate tumor, androgen depletion, cell growth, mouse

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $7021.00	Periodic Review: Oct 86

Study Objective: To study the effects of androgen depletion on prostate tumor growth using the athymic Balb/c mouse and human prostate tumor cell line ALVA-31 as the model.

Technical Approach: Surgical castration will be performed under light halothane anesthesia with aseptic technique. GnRH will be used in doses of 25 to 100 µg and administered as daily intraperitoneal injections or implanted slow-release microcapsules. Flutamide will be administered intraperitonealy on a daily basis. Varying doses will be used to determine optimal effect. Tumor cells will be injected subcutaneously into the posterior flank and volume measured 3 times/wk. Approximately 40 animals will be studied at a time and various hormone manipulations will be compared using normal or castrated animals as controls. Eight animals per group will be studied. Serum hormone levels will be measured in order to assure castration levels of testosterone, along with monitoring of various other hormone levels before, during, and after treatments. Testosterone and GRH receptors will be isolated from tumor nodules by radioactive iodine binding and dextran/ charcoal techniques. Biochemical studies will attempt to characterize the receptors and determine relationships between receptor numbers and activity before and after hormonal manipulations.

Progress: Approximately 200 mice have been studied. Androgen depletion was accomplished by surgical orchiectomy or the daily intraperitoneal administration of gonadotrophin releasing hormone (GnRH). Orchiectomy alone resulted in a greater than 50% reduction in prostate tumor growth. The administration of LHRH agonists at doses of 25, 50, and 100 µg resulted in equivalent suppression of prostate tumor growth. ALVA-31 prostate tumor cells cultured in varying concentrations of LHRH agonist resulted in a suppression of tritiated thymidine uptake in a dose related manner. These data demonstrate the inhibition of tumor growth by androgen depletion and a possible direct effect of the LHRH agonist on the growth of the tumor cell itself. As an offshoot of this work, ALVA-31 tumor cells were exposed to hematoporphyrin *in vitro*, which demonstrated a marked effect of photodynamic therapy on the tumor cell.

An abstract from this study won the Best Resident Research Award at both the Kimbrough Urologic Seminar in October 1986 and the Northwest Urologic seminar in November 1986.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/84	Status: On-going
Title: Intraoperative Monitoring of Recurrent Laryngeal Nerve Function in Swine		
Start Date: 15 Aug 86	Est Completion Date: May 87	
Dept/Svc: Surgery/Otolaryngology		Facility: MAMC
Principal Investigator: CPT Dale B. Smith, MC		
Associate Investigators: LTC Donald B. Blakeslee, MC MAJ Edward Woody, MC MAJ Leslie W. Yarbrough, MC CPT Margaret Richardson, MC		
Key Words: recurrent laryngeal nerve, intraoperative, swine		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $800.00	Periodic Review: Aug 87

Study Objective: To demonstrate the effectiveness and sensitivity of an endolaryngeal monitoring device to allow documentation of true vocal cord function during intraoperative electrical stimulation of the recurrent laryngeal nerve and to correlate histologic damage with intraoperative stimulation patterns and post-op recovery rates by the introduction of various stages of nerve damage.

Technical Approach: Five 10-20 kg pigs will be anesthetized and intubated with a 7.0 mm customized double-ballooned endotracheal tube. The sensing balloon will be inflated between the vocal cords and connected to a Hewlett-Packard monitor. Various system settings will be investigated to identify the most suitable balloon inflation volume, graphic sensitivity, and stimulator amperages. Once these parameters are identified, the laryngeal innervation will be exposed using surgical approaches commonly used in human cases. Various degrees of nerve damage will be induced in a unilateral recurrent laryngeal nerve (RLN) by pressure loaded calipers and confirmed by histologic examination of identically damaged nerves which are motor to the strap muscles in the area. Stimulation of the damaged RLN will be recorded graphically, immediately after nerve damage and in the reopened surgical wound on post-op days seven and ten. Additional histologic specimens from damaged strap nerves will be harvested at these times. The wounds will then be allowed to undergo complete healing. The pigs will undergo sedation and endoscopic laryngeal exams and squeal recordings to monitor the laryngeal recovery. The frequency of these exams will be dictated by the speed of recovery.

Progress: Eight animals have been studied. The degree of injury was correlated with perioperative nerve stimulation patterns. The piglet proved an adequate model for laryngeal research.

An abstract was presented at the Annual Meeting of the Otolaryngology, Head and Neck Surgery Meeting in September 1987.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/85	Status: On-going
Title: Device for Intraoperative Identification of Recurrent Laryngeal Nerve		
Start Date: 15 Aug 86	Est Completion Date: Indefinite	
Dept/Svc: Surgery/Otolaryngology		Facility: MAMC
Principal Investigator: CPT Dale B. Smith, MC		
Associate Investigators: COL Charles A. Andersen, MC LTC Donald B. Blakeslee, MC LTC David Moore, MC MAJ Peter Greenman, MC		
Key Words: laryngeal nerve, identification, balloon device		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jan 87

Study Objective: To determine the effectiveness of using an endolaryngeal monitoring device to assist in identification of laryngeal nerves and the prevention of intraoperative nerve damage.

Technical Approach: This protocol will be implemented if animal studies in #86/84 are successful. Patients requiring general anesthesia for surgical procedures involving risk of injury to laryngeal nerves will undergo a pre-op laryngeal exam and voice analysis. Intubation with a double-cuffed endotracheal tube will be done at surgery. The upper most cuff (sensing balloon) will lie at the level of the true vocal cord and will be intermittently inflated while connected to a Hewlett-Packard arterial pressure monitor through a pressure transducer. Electrical stimulation of the laryngeal nerves with resultant true vocal cord motion will be confirmed by graphic display. Post-operative laryngeal exam will be conducted and any anatomic or vocal impediment will be noted. Patients will be followed until normal laryngeal function returns. Statistical analysis will be done of change in operative morbidity using the device. Possible correlation between required stimulation amperage, graphic pattern, and type and duration of laryngeal impediment will be studied. Further analysis will attempt to correlate the findings in the swine study with this human clinical trial.

Progress: Forty patients have been entered in the study.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/89	Status: On-going

Title: The Effect of a Veterans Administration Geriatric Assessment and Rehabilitation Unit on Elderly Surgery Patients from an Army Medical Center

Start Date: 19 Jun 87	Est Completion Date: Dec 90
Dept/Svc: Surgery/General	Facility: MAMC
Principal Investigator: MAJ Stephen B. Smith, MC	
Associate Investigators: David Silverman, M.D., ALVAMC Kenneth Mostow, ALVAMC	
Key Words: geriatric, surgery, assessment, rehabilitation	

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

Study Objective: To determine if frail, elderly surgery patients treated in the Geriatric Assessment and Rehabilitation Unit (GARU) at American Lake VA Medical Center (ALVAMC) will have better outcomes with improved cost-benefit and cost-effectiveness than those receiving the standard care at Madigan Army Medical Center (MAMC).

Technical Approach: The study population will consist of 160 frail, elderly (>65) patients who have had surgery at MAMC with one or more medical or functional problems that will interfere with discharge. Persons with severe dementia or terminal phase disease will be excluded. The patients will be enrolled five days after surgery and randomly assigned to either remain at MAMC and receive the usual care or be tranferred to ALVAMC and treated at the newly created GARU. The GARU utilizes an interdisciplinary team trained in geriatrics to provide specialty care to frail elderly patients at risk of institutionalization. Before randomization, study patients will be interviewed to obtain base-line data regarding demographic background, medical and social history, and physical and mental function, and a relative or close friend will be interviewed to confirm this information. The patients will be reassessed to include patient and proxy interview at discharge and at 3 and 12 months after discharge. Standardized and validated instruments will be used to measure changes in the physical and mental functioning of both groups to include the Personal Self-Maintenance Scale, the Instrumental Activities of Daily Living Scale, the Kahn-Goldfarb Mental Status Questionnaire, and the Yesavage Depression Scale. Data will also be collected to determine the cost of the health care provided to both groups from their admission for surgery until one year after discharge. Data analysis will be performed primarily with descriptive statistics. Means and standard deviations will be calculated for pre- and post-test variables, such as placement location at discharge and changes in functional and mental status. Death rates and cost will also be analyzed.

Progress: This study has not been implemented. The investigators are awaiting a decision on the submission of a joint VA/DoD grant.

**To be funded by a joint VA/DoD grant.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/16	Status: On-going

Title: Teaching Program for Practical Microsurgery

Start Date: 15 Nov 85	Estimated Completion Date: Open-ended
Dept/Svc: Surgery/Orthopaedic	Facility: MAMC
Principal Investigator: LTC Bruce R. Wheeler, MC	
Associate Investigators:	COL Thomas Griffith, MC
COL Richard A Camp, MC	MAJ Stephen D. Clift, MC
COL Jackie Finney, MC	MAJ Leslie W. Yarbrough, VC
Key Words: microsurgery, teaching program, laboratory animals	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $690.00
	Periodic Review: Mar 87

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

Technical Approach: A schedule of one or two afternoons per week will be set aside for teaching sessions. Sessions will begin with lectures, followed by practical exercises in anatomy and step-by-step instruction in the surgical techniques. Staff and residents from the Orthopaedic, Plastic Surgery, and Thoracic Surgery Services will train in the following procedures:

(1) reimplantation of extremities
(2) re-anastomosis of peripheral vessels and nerves
(3) repair of avulsion wounds
(4) graft transplants
(5) free cutaneous, myocutaneous and composite tissue transfer for traumatic lesions and reconstructive procedures
(6) re-anastomosis of facial nerve lesions

The training will begin with small vessels and nerves in cadaver specimens of small laboratory animals. When the anatomy of the area is learned as well as the use of the microsurgical instruments and the operating microscope, then microsurgical procedures in living rats, guinea pigs, and rabbits can be learned.

Progress: Six training sessions were held in FY 87.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 85/92	Status: Terminated
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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 86

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: Five patients were entered in this study. The associate investigator, who was gathering the data, had to moved to another area and the study was terminated.

D E T A I L S H E E T S

F O R

P R O T O C O L S

DIRECTORATE OF NUTRITION CARE

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/43	Status: On-going

Title: Advance Liquid Diet Evaluation

Start Date: 27 Feb 87	Est Completion Date: Mar 89	
Unit: Directorate of Nutrition Care		Facility: MAMC
Principal Investigator: LTC Annetta J Cooke, SP		
Associate Investigators: Dianne Engell, Ph.D. USA Natick Research Center		
Key Words: diet, liquid, dental, acceptability, cost		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A

Study Objective: To determine whether commercially produced dental liquid products are acceptable to patients who are placed on a dental liquid diet for jaw injuries and/or other dental problems.

Technical Approach: This is a multi-institutional study. The study population will be 75 patients (total) who will be on a liquid diet because of a dental problem or jaw injury. The test diet has been developed by the Food Engineering Directorate at the US Army Research, Development, and Engineering Center. It is a three-meal/day diet containing approximately 2500-3100 calries/day. Protein, carbohydrate and fat make up, respectively, 12%, 25%, and 43% of the daily caloric intake, depending on the consumption of supplements such as juices and milk. The subjects will be tested for four days. They will receive the test diet and the current hospital diet on alternate days. A repeated measures design will be used so that each patient will evaluate both diets and thus serve as his own control. The two conditions will be counterbalanced; half the patients will receive the test diet first and half will receive the current diet first. The participants will complete a questionnaire three times a day to cover all meal and snack periods to rate products on acceptability, appearance, flavor, consistency, texture, ease of sipping, variety, and portion size. A questionnaire will be developed specifically for each meal. On the days the subjects receive the test liquid items, they will also fill out a second questionnaire to estimate the amount of each new meal and between-meal product they have consumed. To validate the intake estimate, dietitians will measure the amount of each product before and after the patient has consumed as much as he wants. Dietitians will be asked to evaluate the products on characteristics such as ease of prepartaion, time requirements, and variety of products.

Progress: No patients have been entered at MAMC. The investigators have had a very difficult time finding patients for the four-day test. To date, two days is the longest period of time that the dental liquid meals have been required by patients.

D E T A I L S H E E T S

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PREVENTIVE MEDICINE SERVICE

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/92	Status: Completed

Title: Correlates of Smoking Behaviors Among Soldiers and Family Members

Start Date: Nov 86	Est Completion Date: May 87	
Service: Preventive Medicine		Facility: MAMC
Principal Investigator: LTC Dale A. Carroll, MC		
Associate Investigators: COL Frederick J. Erdtmann, MC MAJ Wayne M. Lednar, MC		
Key Words: smoking behaviors, soldiers, families, correlates		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $400.00	Periodic Review: N/A

Study Objective: To perform an observational study of Fort Lewis soldiers and their families to correlate descriptive data with smoking status.

Technical Approach: Data will be collected on approximately 500 active duty soldiers at Fort Lewis by means of a questionnaire. Data will be collected on an infantry battalion and on a random sample of spouses of these soldiers via telephone interviews. If there is significant agreement between family smoking data provided by the spouse and the soldier, the results of the random sample will be used to describe the concordance of smoking status between spouses. If significant agreement is not obtained, the remainder of the spouses will receive a questionnaire by mail with a follow-up questionnaire for no response, and, if necessary, a telephone interview if still no response has been obtained. Descriptive data obtained will include demographic data, influence of peers, concordance of smoking status between spouses, standard smoking history data and impact of the Army Smoking Cessation Program on smoking prevention and cessation.

Progress: Of the 499 subjects studied, the overall smoking prevalence was 45% with the highest prevalence among the older soldiers; those with less than a high school education; mid-level enlisted personnel (E/4-E/6); and those with >9 years of active duty service. Smoking soldiers were more likely to be married to smokers, have more friends who smoke, and have a higher smoking prevalence in their duty section. Seventy-three percent of smokers reported that Army smoking policies had little or no impact on their smoking and 83% intend to quit within the next year. Intentions to quit are associated directly with the smoker's perception of how harmful cigarettes are to his health and his reported likelihood of contracting a smoking related disease in the next 12 months and knowledge regarding smoking related diseases. Smoking programs should be directed at young soldiers of low and mid-level enlisted ranks. Rather than target smoking cessation programs to segments with the highest prevalence of cigarette use, programs should be directed to smoking personnel interested and motivated to quit. Smokers with low intentions should receive a program to raise their awareness of smoking risks and increase their confidence in the ability to quit. Ex-smokers who have quit within the past six months are at high risk for relapse and shouuld receive support and follow-up. An abstract from this protocol was presented at the Annual Preventive Medicine Symposium.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/21	Status: On-going

Title: Data Collection for the Selected Cancers Among Vietnam Veterans Study

Start Date: 15 Nov 85	Est Completion Date: Jun 89	
Service: Preventive Medicine		Facility: MAMC
Principal Investigator:	COL Frederick J. Erdtmann, MC	
Associate Investigators:	Linda S. Heuser, M.A., Hutchinson CRC Thomas L. Vaughan, M.D., Hutchinson CRC	
Key Words: cancer, vietnam veterans, Agent Orange		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Feb 87

Study Objective: To evaluate the risk associated with exposure to Agent Orange among veterans of the Armed Forces in Vietnam.

Technical Approach: This is a multicenter study, funded by the U.S. Centers for Disease Control. Males diagnosed between 1 Oct 85 and 30 Nov 88 with birth dates between 1929 and 1953 as having soft tissue sarcomas (excluding Kaposi's sarcoma), certain bone and cartilage sarcomas, lymphomas, nasal cancers, nasopharyngeal cancers, and primary liver cancers will be studied. Subjects must be identified within one month of diagnosis and interviewed within three months of diagnosis. The patient or the next-of-kin will be sent a letter and a fact sheet explaining the study and requesting participation. This letter will be followed by a telephone call and a time for a telephone interview will be scheduled. The vital status of all interviewed patients will be checked every six months and a physician will interview the next-of-kin on those patients who have died since being interviewed. This interview will be done in order to compare the information provided by the next-of-kin with that originally obtained from the patient. The interview will obtain information about patients' jobs, medical illnesses, personal habits, and other information related to general health. Tissue blocks and/or a set of six slides will be requested from pathologists and sent to a pathology panel for independent review. If the patient is a Vietnam veteran, information will also be obtained from military records about previous chemical exposures in Vietnam. The CDC will also request information about chemical exposure from from the military. Controls will be matched for age and vital status. Controls will be contacted in the same manner as other subjects. Once an interview is edited for completeness, it will be sent to the CDC where requests for information from military records and data analysis will be done.

Progress: The investigators are still entering patients. Six patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/84	Status: Suspended

Title: Effects of an Employee Fitness Program on Back Injuries and Absenteeism

Start Date: 19 Jun 87	Est Completion Date: Dec 89	
Servicec: Preventive Medicine		Facility: MAMC
Principal Investigator: MAJ Wayne M. Lednar, MC		
Associate Investigators: Richard A Deyo, M.D., M.P.H. Seattle V.A. Medical Center		
Key Words: employee fitness, back injuries, absenteeism		
Accumulative MEDCASE Cost: -0-**	Est Accumulative OMA Cost: -0-**	Periodic Review: N/A

Study Objective: To determine if a worksite exercise program can improve aerobic fitness, reduce recurrences of back pain, back-related absenteeism, and overall work loss; to determine the factors that influence the individual decision to participate in and comply with an exercise regimen; to determine the overall costs of a work-based exercise program; and to determine the net cost or savings from the employer's perspective.

Technical Approach: The program will be implemented as a randomized controlled trial at MAMC and two V.A. facilities. Approximately 750 employees with prior back problems will be enrolled. Patients will be randomized to a supervised and individualized exercise program, conducted at the worksite, including back and general aerobic conditioning, or to a control group that receives no exercise. The baseline evaluation will include a questionnaire which will elicit demographic data, job information, physical activity, days of limited activity, and back pain history. Physiologic and psychological status will be determined at entry, 5 wk, 6 mth, and 1 yr with functional status determined at entry, 6 mth, and 1 yr. A sub-study will be conducted to address the problem of compliance and develop compliance-enhancing techniques. This sub-study will consist of interviewing subjects who decline to enter the exercise study regarding their reasons for not participating, interviewing subjects who drop out of the study about their reasons for dropping out, and having a sample of 120 potentially eligible subjects evaluate the questionnaire. The resulting compliance-enhancing strategies will be implemented in year two of the study. Costs will be assessed by asking patients to maintin a diary of cost for mecidal care, by having the subjects complete the medical costs section of Fries' Health Assessment Questionnaire at six months and one year, and by maintaining a record of health care costs and continuation-of-pay compensation paid by the employer for the subjects. Costs of the exercise program and costs of time excused from work will also be included.

Progress: This study has been suspended until the principal investigator staffs the protocol through the appropriate Ft Lewis units as stipulated by the Institutional Review Board.

**to be funded by joint VA/DoD grant

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86793	Status: Completed

Title: Assessing Potential Predictor Variables of Overweight in a Military Population

Start Date: Nov 86	Est Completion Date: May 87	
Service: Preventive Medicine		Facility: MAMC
Principal Investigator:	MAJ Rene J. Sanchez, MC	
Associate Investigators:	COL Frederick J. Erdtman, MC MAJ Wayne M. Lednar, MC	
Key Words:	overweight, military, predictor variables, AR 600-9	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $350.00	Periodic Review: N/A

Study Objective: To cross-sectionally describe the weight for height status of soldiers at Fort Lewis using the new AR 600-9 standards and to assess the association of selected behavioral and familial predictor variables with overweight in a military population.

Technical Approach: Five hundred active duty soldiers from an infantry battalion at Fort Lewis with at least one year of active duty in the Army will be given a structured questionnaire which will obtain information on health practices (such as drinking, smoking, and planned and normal everyday activities), weight history, opinions as to influences on weight control, daily stress, methods of relaxation, and personal methods of modifying unhealthy behavior. Prior to administering the questionnaire, soldiers will be weighed and height will be recorded noting the type of uniform worn. Weight and height values for one year earlier will be retrieved from personnel or weight control records. The results will be compared with similar groups in the civilian population.

Progress: The survey questionnaire was administerd to 399 of the 436 soldiers in a battalion. Analysis of the data showed that overall overweight status distribution of the battalion was comparable to that of a similarly aged civilian population. However, the trend of increasing obesity with increasing age was reversed in the study population with the highest obesity found among the lowest ranking enlisted personnel. Four of the nine predictor variables were found to be significantly associated with obesity among the soldiers. Of these four, three exhibited trends completely opposite to that trend observed in civilian populations (i.e., the obesity predictor variable was more prevalent among the leaner soldiers). These were: lower self-control, lower social support, and lack of a self-imposed weight threshold. Early age of obesity onset was the only associated factor exhibiting the expected trend of increasing prevalence among increasingly obese soldiers. The presence of the Army Weight Control Program is postulated as possibly explaining the observed differences in association of predictor variable with obesity among soldiers.

A paper from this study was presented at the Preventive Medicine Symposium at Walter Reed Army Institute of Research, May 1987.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/116	Status: On-going

Title: A Clinical Efficacy Study Comparing Gram Stain and Culture to Enzyme Immunoassay for the Diagnosis of Gonococcal Urethritis in Men

Start Date: 18 Sep 87	Est Completion Date: Dec 87
Service: Preventive Medicine	Facility: MAMC
Principal Investigator: CPT LeRoy Southmayd, MC	
Associate Investigators:	MAJ Charles Hicks, MC, WRAMC
COL Edmund C. Tramont, MC, WRAIR	CPT Jeff Lennox, MC, WRAMC
LTC John W. Boslego, MC, WRAIR	Michael Goerss, M.D., MAMC
LTC Rodney Michael, MC, MAMC	Carrie Gilreath, MAMC
Key Words: urethritis, gonococcal, diagnosis, gram stain, culture, enzyme immunoassay	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-
Periodic Review: N/A	

Study Objective: To evaluate the efficacy of the enzyme immunoassay system (EIA) for the diagnosis of gonorrhea.

Technical Approach: Approximately 300 males, 18-65 years of age, with a clinical diagnosis of acute urethritis will be enrolled in the study. A medical history, including recent antimicrobials, and physical exam will be obtained. Two urethral swab specimens will be obtained. Culture, gram stain and EIA will be done on one specimen and EIA only will be done on the second specimen. To avoid experimental bias, the test sequence will be alternated according to odd/even numbers.

The EIA test will be performed such that the EIA results will be available for all patients within two hours of initial registration, thus being available within a reasonable time for theoretical application toward diagnosis. Cultures will be processed per the usual routine. Cultures will be considered positive when there is growth of typical *N. gonorrhoea* colonies which are oxidase positive, show characteristic gram staining, and are positive with Phadebact tests. A positive gram stain will be defined as the presence of GNID or GNED with characteristic morphology. EIA definitions: true positive - a positive EIA with either a positive gram stain, a positive culture, or a known GC contact; true negative: a negative EIA with a negative gram stain and a negative culture; false positive: a positive EIA with a negative gram stain, a negative culture, and no recent GC contact; and false negative: a negative EIA with either a positive gram stain or a positive culture. Sensitivity, specificity, and positive and negative predictive values will be calculated from the EIA subsets in the standard manner. EIA results will be compared independently to both culture and gram stain.

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

D E T A I L S H E E T S

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ACTIVE DUTY STUDENTS

STUDENT DETACHMENT, HSC

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87795	Status: On-going

Title: Early Mobilization: Its Effects on Grade Two and Single Ligament Grade 3 Lateral Ankle Injuries

Start Date: 17 Jul 87	Est Completion Date: Dec 87	
Unit: Student Detachment, Health Services Cmd		Facility: MAMC
Principal Investigator: MAJ Joseph R. Dettori, AMSC		
Associate Investigators: LTC Bruce Wheeler, MC CPT Bradley D. Pearson, PT		
Key Words: ankle, injuries, lateral, grade 2, early mobilization		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $1160.00	Periodic Review: N/A

Study Objective: To determine if the management of Grade 2 and single ligament Grade 3 ankle sprains in active duty personnel by early ankle mobilization can return soldiers back to full duty quicker than delayed ankle mobilization and to determine if cheaper forms of early ankle mobilization management (ace wraps) are as successful as more expensive forms of early mobilization management such as air splints.

Technical Approach: Patients will be randomized to a control group (plaster immobilization) and two experimental groups (ace wrap and air splint). Subjects will undergo an initial assessment to include ankle arthrography to delineate the extent of injury. Group 1 will receive plaster immunobilization (controls) and will perform isometric exercises in the cast hourly, for one week. Group 2 will receive an ace wrap and perform active range of motion (AR), with the wrap removed, at least three times per day and resis ve exercises with rubber tubing three times per day plus ice and elevation throughout the day, as permitted, for one week. Group 3 will receive an air splint and therapy the same as in Group 2. Phase two will consist of three treatments in the Physical Therapy clinic over a one week period. All three groups will perform strengthening exercises for 10 minutes, proprioceptive exercise on a balance board for ten minutes, single legged toe rasies (maximum of 20), and home exercise instruction for AROM with resistive exercises with rubber tubing and toe raises. Phase III will consist of five treatment sessions over a period of two weeks. Each group will participate in functional ankle exercises and home exercises with rubber tubing and AROM. The measures to be utilized in this study will be swelling, AROM, gait, strength, height/weight, point tenderness, anterior drawer test, pain, work status, ability to run, and ability to complete the functional ankle program without pain. All data except for muscle strength will be collected prior to intervention and weekly thereafter. A final measurement to include muscle strength will be performed at the end of Phase 3.

Progress: Twenty-three (23) subjects have been entered in the study with six completing the entire course of 5 weeks. Approximately 1/2 of the subjects have a Grade III tear (all were initially diagnosed as Grade II) confirmed by arthrogram.

Detail Summary Sheet

Date: 30 Sep 87	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:	Lynette S. Chandler, Ph.D.	
COL Carl Plonsky, MC	Margon B. Holm, Ph.D.	
LTC Glenn Tripp, MC	Catherine Yokan, M.D.	
Key Words: movement deficits, infants, Chandler Movement Assessment of Infants - Screening Test		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Aug 87

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 reliability. 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: Norms were previously established for 2 to 8 month old infants. After numerous comments from volunteers and professionals regarding the ease of use of the screening test and face validity for both examiners and parents, the investigators screened 33 infants from 8-12 months in FY 87 in order to establish norms for 8 to 12 month old infants.

An article has been accepted for publication in Pediatrics.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 85/15	Status: Completed

Title: Physiologic Correlates of Neurological 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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 86

Study Objective: To analyze the physiologic responses of neonates to neurological assessment procedures.

Technical Approach: Thirty medically stable newborns will be studied in two groups of 15 each: (a) full-term group (39-41 weeks gestation) and (b) preterm group (32-34 weeks gestation). 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, will 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).

Due to a successfully completed pilot study, the protocol was amended in Jan 86 to include 40 more children with the addition of blood pressure measurement to the procedures. The title of the protocol was changed from "Neurobehavioral Assessment" to "Neurological Assessment."

Progress: Twenty subjects were studied in each age group. While the neurological assessment was physiologically and behaviorally destablizing to both age groups, preterm subjects had a higher heart rate, a greater increase in blood pressure, decreased peripheral oxygenation, and higher frequencies of finger splay, arm salute, hiccoughs, and yawns than full-term infants. Both groups demonstrated greater physiological and behavioral stress during the neuromotor component of the neurological assessment process. Respiratory rate was the least sensitive physiological measure. An abstract has been accepted for presentation at the 1988 American Physical Therapy Association Annual Conference.

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 87	Protocol No.: 86/65	Status: On-going

Title: CCG 105: Treatment of Newly Diagnosed Acute Lymphoblastic Leukemia in Children with an Intermediate Prognosis

Start Date: 16 May 86	Est Completion Date: Indefinite
Department: Pediatrics	Facility: MAMC
Principal Investigator: MAJ Kip Hartman, MC	
Associate Investigator: LTC Allen R. Potter, MC	
Key Words: leukemia, lymphoblastic, intermediate prognosis	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jul 87

Study Objective: To minimize therapy in good prognosis patients without altering their prognosis and to improve the proportion of all patients cured of leukemia in each category, without seriously compromising the quality of their life span.

Technical Approach: Patients defined as having intermediate prognosis ALL will be randomized to one of four treatment arms, which differ substantially during the first six months of therapy and then share the same maintenance program. The treatment will not be less than two years. Regimen 1 A will utilize vincristine, daunomycin, prednisone, L-asparaginase, and IT methotrexate for induction; consolidation will utilize cyclophosphamide, 6-mercaptopurine, cytosine arabinoside, IT methotrexate, and cranial radiation; interim maintenace will use 6-mercaptopurine and methotrexate; delayed intensification will be vincristine, dexamethasone, adriamycin, L-asparaginase, cyclophosphamide, 6-thioguanine, cytosine arabinoside, and IT methotrexate; maintenance will consist of vincristine, prednisone, 6-mercaptopurine, and methotrexate. Regime 1B will utilize vincristine, prednisone, L-asparaginase, and IT methotrexate for induction; 6-mercaptopurine, IT methotrexate, and cranial radiation for consolation; 6-mercaptopurine and methotrexate for interim maintenance; delayed intensification and maintenance will be the same as Regimen 1A. Regimen 1C will have induction, consolidation, and maintenance as in Regimen A but with no interim maintenance and delayed intensification. Regimen 1D will have induction, consolidation, and maintenance as in Regimen 1B but without interim maintenance and delayed intensification. Regimens 2A, 2B, 2C, and 2D will correspond to Regimens 1A, 1B, 1C, and 1D, respectively, but with no cranial radiation, and maintenance will be with IT methotrexate.

Progress: No patients were entered in this protocol.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/44	Status: On-going

Title: CCG-107: Treatment of Newly Diagnosed Acute Lymphoblastic Leukemia and Acute Undifferentiated Leukemia in Infants Less than 12 Months of Age

Start Date: 21 Mar 86	Est Completion Date: Indefinite
Dept/Svc: Pediatrics	Facility: MAMC
Principal Investigator: MAJ Kip Hartman, MC	
Associate Investigator: LTC Allen R. Potter, MC	
Key Words: leukemia, lymphoblastic, acute, undifferentiated	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Mar 87

Study Objective: To subdivide childhood acute lymphoblastic leukemia into homogeneous subgroups (stages) in which specific biologic and therapeutic hypotheses can be tested; to minimize therapy in good prognosis patients without altering their prognosis; and to improve the proportion of all patients cured of leukemia in each category, without seriously compromising the quality of their life span.

Technical Approach: Patients <12 months with newly diagnosed acute lymphoblastic leukemia will receive intensive induction therapy consisting of vincristine, daunomycin, prednisone, L-asparaginase, IT cytosine arabinoside, and IT methotrexate. Following remission induction, patients will receive consolidation therapy consisting of 3 very high dose, protracted (24 hr), systemic infusions of methotrexate with high dose citrovorum factor rescue, and IT cytosine arabinoside. Consolidation therapy will also include 6 mercaptopurine and vincristine. This phase will be followed by an interim maintenance therapy of 6-mercaptopurine and methotrexate. Four months following diagnosis, patients will receive intensification with dexamethasone, vincristine, daunomycin, L-asparaginase, and IT methotrexate for 4 weeks (reinduction) and 6-thioguanine, vincristine, methotrexate, and tapered dexamethasone with citrovorum factor rescue for 3 weeks (reconsolidation). Maintenance therapy (96 weeks) consists of 6-mercaptopurine and methotrexate with periodic vincristine/prednisone pulses as well as IT methotrexate

Progress: No subjects entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No: 87/93	Status: On-going

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

Start Date: 17 Jul 87	Est Completion Date: Jul 92
Deparatment: Pediatrics	Facility: MAMC
Principal Investigator: MAJ Kip Hartman, MC	
Associate Investigators: None	
Key Words: ALL, high risk, chemotherapy	

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

Study Objective: To improve the treatment results for children with acute lymphoblastic leukemia (ALL) who possess poor prognostic features; to prevent the development of central nervous system (CNS) leukemia in these patients using a treatment regimen which includes both systemic high dose chemotherapy and intrathecal chemotherapy, but avoids cranial radiation; and to determine whether there is a difference in the outcome of poor prognosis patients with and without lymphomatous features treated on an identical treatment regimen.

Technical Approach: Previously untreated high risk patients with acute lymphoblastic leukemia will be treated. The induction phase of therapy will be 28 days in length and consist of treatment with vincristine, L-asparaginase, prednisone, daunomycin, and allopurinol. CNS therapy will consist of intrathecal cytosine arabinoside and methotrexate as well as the use of a high dose, protracted systemic methotrexate infusion. Consolidation therapy will begin 7-10 days following completion of induction therapy and will last 35 days. Chemotherapy will consist of vincristine, prednisone, and 6-mercaptopurine. CNS prophylaxis for patients during consolidation will include both intravenous high dose methotrexate and intrathecal Ara-C. A 12-week intensification phase will begin 7-10 days after the last day of consolidation. Chemotherapy will consist of cyclophosphamide, L-asparaginase, vincristine, daunomycin, and prednisone. CNS treatment will include periodic intrathecal methotrexate and cytosine arabinoside as well as systemic high dose Ara-C. Maintenance therapy will begin 7-10 days after the last day of consolidation. Chemotherapy will consist of prednisone, vincristine, 6-mercaptopurine, L-asparaginase, and daunomycin. CNS treatment will include periodic intrathecal chemotherapy with methotrexate and Ara-C as well as systemic high dose methotrexate and high dose Ara-C. The chemotherapy will be given over a 24 week cycle, which will be repeated 4 times, after which all chemotherapy ceases. The first year off study, patients will have a physical exam and CBC every month and bone marrow and lumbar puncture every 4 months. The second year, they will have physical exam and CBC every 3 months and bone marrow and lumbar puncture every 6 months. The third and subsequent years off study, patients will receive routine followup per institutional guidelines.

Progress: One patient has been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/31	Status: On-going

Title: CCG 323P: Cyclic Combination Chemotherapy for Newly Diagnosed Stage III Neuroblastoma Age 2 Years or Older at Diagnosis and Newly Diagnosed Stage IV Neuroblastoma All Ages

Start Date: 17 Jan 86	Est Completion Date: Indefinite
Department: Pediatrics	Facility: MAMC
Principal Investigator: MAJ Kip Hartman, MC	
Associate Investigators: LTC Allen Potter, MC	
Key Words: neuroblastoma, Stages III & IV, chemotherapy, cyclic	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jan 87

Study Objective: To evaluate the effect of melphalan in newly diagnosed untreated Stage IV neuroblastoma; to evaluate the effect on the toxicity in Stage III neuroblastoma age 2 years and older and in Stage IV neuroblastoma of alternating cycles of vincristine-cyclophosphamide-DTIC and intravenous melphalan; and to continue to evaluate front-end prognostic factors other than age at diagnosis in Stage III neuroblastoma 2 years of age and older and Stage IV.

Technical Approach: After satisfying the eligibility criteria as listed in the protocol, patients with Stage III neuroblastoma age 2 years and older at diagnosis or with Stage IV (except IV-S) neuroblastoma, all ages, will be treated with two courses of cyclophosphamide and DTIC for 22 weeks. After a total of 22 weeks of therapy, if the patient has a complete remission, partial remission, or stable disease with no progression, alternating cycles of melphalan and vincristine/cyclophosphamide/DTIC chemotherapy will be continued for the full 105 weeks. Patients with progressive disease after a minimum of four chemotherapy pulses (12 weeks) will be removed from the study and will be candidates for alternative therapy. Patients experiencing progressive disease prior to week 22 may receive XRT at the discretion of the PI and radiotherapist and continue on therapy to week 22.

Progress: One patient was entered in this study in FY 87 for a total of two entries.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/112	Status: On-going

Title: CCG 461: Intergroup National Wilms' Tumor Study 4

Start Date: 18 Sep 87	Est Completion Date: Sep 97	
Department: Pediatrics		Facility: MAMC
Principal Investigator: MAJ Kip Hartman, MC		
Associate Investigators: None		
Key Words: Wilms' tumor, chemotherapy, favorable histology, clear cell carcinoma, stages I-IV		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A

Study Objective: To gain a better understanding of the Wilms' tumor by gathering detailed information regarding gross and histologic morphology and to correlate this information with treatment and clinical outcome; to test treatment hypotheses by randomized, prospective clinical trials according to stage and histological grade of disease; to refine methods of treatment according to histology and stage; to identify children and families at high risk for cancer, and to study the late consequences of successful treatment given for Wilms' tumor.

Technical Approach: The hypothesis being tested is that simplified yet intensified treatment using agents known to be effective will prove to be better or at least no worse than regimens on previous protocols. Intensification will be achieved through shortening the interval between drug cycles, in the process giving more therapy up front and giving as much, if not more, of the drugs over the same time interval, except for vincristin in Stage II/FH (favorable histology). Simplification will be achieved through administering all drugs in single injections at each cycle rather than five daily doses of actinomycin-D and three daily doses of adriamycin as in previous protocols. After surgery, Stage I/FH and anaplastic tumors and Stage II/FH will receive actinomycin-D and vincristine in either the standard schedule or on a pulsed, intensive schedule. Stage III/FH will receive actinomycin D, vincristine, and doxorubicin on a standard schedule plus radiation therapy. High risk (clear cell sarcoma, all stages, and Stage IV/FH) patients will receive pulsed, intensive chemotherapy with actinomycin-D, vincristine, and dactinomycin plus radiotherapy if the primary tumor would qualify as Stage II were there no metastasis.

Progress: No patients entered in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87776	Status: On-going

Title: CCG-521: Treatment of Newly Diagnosed Advanced Hodgkins Disease (Pathologic Stages III_1 AS_{macro}, III_1A Macromediastinum, III_2A, IIIB, IVA, IVB)

Start Date: 15 May 87	Est Completion Date: May 92	
Department: Pediatrics		Facility: MAMC
Principal Investigator: MAJ Kip Hartman, MC		
Associate Investigators: None		
Key Words: Hodgkins, newly diagnosed, chemotherapy, radiotherapy		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A

Study Objective: To improve the proportion of patients with advanced Hodgkin's Disease who are cured; to compare the relapse free survival and survival in advanced Hodgkin's disease in children utilizing an eight-drug (twelve cycle MOPP/ABVD) combination chemotherapy regimen versus a four drug (six cycle ABVD) chemotherapy regimen followed by low dose (2100 cGy rad) regional radiation therapy; and to compare the concurrent and long term toxicity of the two regimens.

Technical Approach: Patients less than 21 years of age, with newly diagnosed Hodgkin's disease, pathologically staged as III_1 AS_{macro}, III_1A macromediastinum, III_2A, IIIB, IVA, or IVB will be randomized to either Regimen A or Regimen B.

The drugs used in Regimen A are mustard, vincristine, prednisone, procarbazine (MOPP) and adriamycin, bleomycin, vinblastine, and DTIC (ABVD). Six courses of therapy will be given. Each course consists of alternating 28-day cycles of MOPP and ABVD. Each cycle of MOPP consists of two pulses of chemotherapy of mustard and vincristine given seven days apart and a fourteen day administration of prednisone and procarbazine. Each cycle of ABVD consists of two pulses of chemotherapy given two weeks apart. Treatment will be terminated at the end of the six courses of chemotherapy or upon disease progression.

Regimen B will consist of six cycles of ABVD. Each cycle consists of two pulses of chemotherapy given two weeks apart. All patients will receive six cycles of chemotherapy unless progressive disease is noted or unacceptable toxicity occurs. Regional irradiation of 2100 cGy in 12 fractions will then be given.

Progress: No patients have been entered in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/45	Status: On-going

Title: CCG 631: Intergroup Rhabdomyosarcoma Study - III
NCI Protocol #: INTERG-0032

Start Date: 21 Mar 86	Est Completion Date: Feb 92	
Dept/Svc: Pediatrics		Facility: MAMC
Principal Investigator: MAJ Kip Hartman, MC		
Associate Investigators: LTC Allen Potter, MC		
Key Words: rhabdomyosarcoma, chemotherapy, radiotherapy		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Mar 87

Study Objective: To compare various forms of treatment of rhabdomyosarcoma and to determine: if various combinations of vincristine, dactinomycin, adriamycin, cyclophosphamide, cis-platin, and VP-16, with or without radiation therapy, will improve survival rates in both favorable and unfavorable histology tumors that have been completely or grossly, but incompletely, removed; if patients with localized orbit and head tumors will do well with vincristine and dactinomycin therapy limited to one year; patients with localized prostate, bladder, vagina, or uterus tumors can be treated successfully with cis-platin, adriamycin, vincristine, cyclophosphamide, and dactinomycin to avoid radical surgery and preserve the involved organ. Other objectives are to use second and third operations to see if the tumor is gone and, if not, to see if any remaining tumor can be surgically removed; to add other combinations of drugs when only partial response is obtained from the initial treatment; to use XRT and IT drugs to treat tumors extending or at risk of extension into the brain or spinal cord; and to do various studies of drug sensitivity and tumor typing on the removed tumor tissue to find new drugs for treatment and new ways of diagnosing cancer.

Technical Approach: Patients will be catogorized as: Group I: localized disease, completely resected; Group II: total gross resection with evidence of regional spread; Group III: incomplete resection with gross residual disease; and group IV: distant metastatic disease present at onset. Patients will then be subcategorized into groups according to favorable or unfavorable histology and location of disease and treated with one of 8 regimens containing various combinations of actinomycin-D, adriamycin, cisplatinum, cyclophosphamide, cytosine arabinoside, DTIC, hydrocortisone, leucovorin, vincristine sulfate, methotrexate, and VP-16, with or without the addition of radiation therapy and surgery.

Progress: No patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/67	Status: On-going

Title: CCG-8602: Idarubicin for Remission Induction in Patients with Leukemia in Children in Second or Subsequent Marrow Relapse

Start Date: 17 Apr 87	Est Completion Date: May 91	
Department: Pediatrics		Facility: MAMC
Principal Investigator: MAJ Kip Hartman, MC		
Associate Investigators: None		
Key Words: leukemia, marrow relapse, idarubicin		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A

Study Objective: To refine the determination of the maximal tolerated dose of intravenous idarubicin given by a weekly x 3 and by a daily x 3 schedule in children with leukemia; to determine the pharmacokinetics of intravenous idarubicin and idarubicinol in children with acute leukemia treated with two schedules, weekly x 3 and daily x 3; and to determine the effects of drug scheduling of idarubicin on remission induction rates for children with acute lymphoblastic leukemia and acute non-lymphoblastic leukemia.

Technical Approach: This is a randomized Phase II study employing two different dosing schedules of idarubicin, given IV. Children who have had a second or subsequent marrow relapse will be treated with a weekly x 3 schedule or a daily x 3 schedule. Since the maximal tolerated dose (MTD) has been reported as both 40 mg/m^2 and as 30 mg/m^2, when given IV in equally divided doses daily for three days, the MTD for dosing on the daily schedule will be further refined and the MTD for a weekly schedule in children determined. A dose intermediate between the reported MTD's will be selected to evaluate first. If toxicity is acceptable, the dosages of drug given each week or each day will be escalated after three evaluable patients have been treated. Subsequent escalations in dose will also require acceptable toxicity in three evaluable patients. The dose will not be escalated in individual patients. Each patient will receive only one dosage throughout their treatment. Once the MTD for each schedule is determined, the dose will be used in six additional patients to confirm acceptable toxicity. If acceptable toxicity is confirmed, additional patients will be entered at this dose level to assess remission induction rates. Remission induction rates will be determined at 21 days from initiation of therapy. If remission is not obtained following the three doses of idarubicin, if the leukemia has not responded, and if toxicity from the first course was acceptable, patients will be treated with a second course of the drug, using the same dose and schedule. Remission status will again be evaluated 21 days from the start of the second course of treatment. For patients attaining a complete remission, maintenance therapy will be at the discretion of the investigator caring for the patient.

Progress: No patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/68	Status: On-going

Title: CCG 8603: Phase I Study of the Combination of 5 Days Intravenous 5-Fluorouracil (NSC-19893) and 6 days of High Dose Oral Leucovorin (NSC-3590) in Pediatric Patients

Start Date: 17 Apr 87	Est Completion Date: May 91	
Department: Pediatrics		Facility: MAMC
Principal Investigator: MAJ Kip Hartman, MC		
Associate Investigators: None		
Key Words: IV 5-FU, oral high dose leucovorin, combination		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $3000.00	Periodic Review: N/A

Study Objective: To determine the maximally tolerated dose of 5-fluorouracil (5-FU) administered as a daily x 5 bolus dose in combination with high dose oral folinic acid (leucovorin) in pediatric patients with cancer; to investigate the effects of 5-FU in combination with high dose folinic acid on the inhibition and recovery of thymidylate synthase in leukemic cells; and to determine the pharmacokinetics of oral folinic acid in pediatric patients.

Technical Approach: Patients with leukemia and solid tumors, ages 1-21 years, will be studied. Leucovorin will be administered orally at 0, 1, 2, and 3 hours daily for six days, commencing 24 hours prior to the first dose of 5-FU. Patients will be treated by IV bolus infusion over 15 minutes of 5-FU for five days (days 2-6), within one hour after the fourth dose of leucovorin each day. Second and subsequent courses will be administered no more frequently than three weeks or when the patient has recovered from the toxic effects of the therapy. The daily dose for leucovorin will be 500 mg/m^2 divided into four equal doses. The starting dose of 5-FU will be 300 mg/m^2/day.

The maximum tolerated dose (MTD) will be investigated for leukemia and solid tumors separately. For each of these two disease categories, three evaluable patients will be required at each dose level examined. Dose escalation will proceed at 25% of the previous dose until a dose is reached at which there is evidence of Grade III or IV toxicity which is attributable to the treatment. Three patients will then be enrolled at the penultimate dose and evaluated. If there is no evidence of life threatening toxicity among these three patients, this dose will be considered the MTD. If evidence of such toxicity is noted, the dose level will be reduced in single steps by the original increments and three evaluable patients enrolled. The first dose at which no life threatening toxicities are noted will be considered the MTD.

Progress: No patients have been enrolled at MAMC.

D E T A I L S H E E T S

F O R

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FRED HUTCHINSON CANCER RESEARCH CENTER GROUP PROTOCOLS

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 83/30	Status: Completed

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

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 allogenetic, 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 87 at MAMC. One patient entered in FY 84 and had fairly severe side effects to the chemotherapy with multiple admissions for infection and leukopenia.

Group-wide, all patients have suffered nausea, vomiting, mucositis, and pancytopenia. All of these side-effects were expected. Hepatitis was seen in some patients. Whether this represents a side effect of the drugs or of the blood transfusions is not clear. One case of ITP and one case of Guillian-Barre syndrome have been seen.

Detail Summary Sheet

Date: 30 Sep 87	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: MAJ Thomas M. Baker, MC		
Associate Investigators:		
COL Irwin B. Dabe, MC	LTC Howard Davidson, MC	
COL Friedrich H. Stutz, MC	MAJ Alfred H. Chan, MC	
LTC James E. Congdon, MC	MAJ Timothy J. O'Rourke, MC	
Key Words: non-Hodgkin's lymphoma, intermediate, high-grade		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: May 87

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 theapy. 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: No new patients were entered at MAMC in FY 87. Six patients have been entered in previous years. In one patient, second cycle CHOP post-radiotherapy caused neutropenic fever. the patient recovered and subsequent doses were reduced. Group-wide results show a complete remission of 75% in limited disease and 56% in extensive disease. Survival to three years is 50% in HBI arm (mostly Stage IVB patients).

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 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 86

Study Objective: To determine the efficacy of cis-platinum diamminedichloride in patients whose advanced malignancies have been resistant to higher priority methods of treatment.

Technical Approach: All patients with measurable gynecological cancer, who have failed higher priority therapies, will be offered cis-platinum as a Phase II drug to determine its efficacy. The drug is given at 50 mg/M^2 intravenously every three weeks as toxicity permits. Patients who respond or who demonstrate disease will continue to receive the agent until progression has occurred.

Progress: No new patients were entered at MAMC in FY 87. Three were entered in previous years.

Group-wide data indicate that cis-platinum has marked activity as first-line chemotherapy of squamous cell carcinoma of the cervix, endometrial cancer, and mixed mesodermal sarcomas of the uterus, and is active as second-line therapy of advanced ovarian adenocarcinoma and mixed mesodermal sarcoma of the uterus at the dose and schedule tested. The drug appears to be inactive as second-line therapy against endometrial carcinoma and vulvar carcinoma, and is inactive as first or second-line therapy of leiomyosarcoma of the uterus. It may have limited activity in the therapy of cervical adenocarcinomas.

Detail Summary Sheet

Date: 30 Sep 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 86

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/M^2 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: One patient was entered at MAMC in FY 87.

Group-wide, VP-16 appears to have minimal activity against ovarian adenocarcinoma and insignificant activity against squamous cell carcinoma of the cervix and endometrial adenocarcinoma at the dose and schedule tested. VP-16 appears to be inactive in advanced or recurrent non-squamous cell carcinoma of the cervix. Insufficient numbers of cases have been entered into other tumor categories to indicate any trends.

Detail Summary Sheet

Date: 30 Sep 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 86

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/M^2 slow I.V. push weekly. If no toxicity has has occurred after 4 doses, the dosage will be increased to 75 mg/M^2 weekly. Patients will continue to receive the agent until progression occurs.

Progress: No patients entered at MAMC.

Groupwide results thus far show complete and partial remissions in carcinoma of the cervix have been 19%, which is encouraging enough for future studies, possibly in combination with other drugs. One complete remission lasted 38 months. The other relapsed at 8 months after entry into the study.

Complete and partial remissions in carcinoma of the ovary were 15%. Almost all of these patients had received prior chemotherapy. One complete remission relapsed at 32 months; the other relapsed at 15 months after entry.

One partial remission in 17 patients with endometrial adenocarcinoma was observed. One complete response and one partial in 27 patients with non-squamous cervix were observed. Activity appears negligible at the dose and schedule tested.

Detail Summary Sheet

Date: 30 Sep 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 86

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/M^2, 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 87. One patient was entered in FY 83, exhibited no response to ICRF and died from disease in FY 84.

Group-wide results thus far show that ICRF appears to have moderate activity in squamous cell carcinoma of the cervix and no significant activity in epithelial tumors of the ovary, endometrial carcinoma, and non-squamous cell carcinoma of the cervix at the dose and schedule tested despite induction of significant myelosuppression.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 83/21	Status: Completed

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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 86

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/M^2 I.V. once every 28 days. Patients will continue to receive the agent until progression occurs.

Progress: No patients entered at MAMC.

Group-wide results indicate that AMSA at the doses and schedule utilized has negligible activity in patients with cervical carcinoma previously treated with radiation and chemotherapy.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 83/22	Status: Completed

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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 86

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.

Group-wide results indicate that Yoshi 864, at the dose schedule used in this study, is not an active drug in the treatment of patients with advanced epithelial ovarian cancer or advanced squamous cell carcinoma of the uterine cervix, recurring after previous treatment with chemotherrapy.

Detail Summary Sheet

Date: 30 Sep 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Mar 87

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: No patients were entered in this study at MAMC in FY 87. In previous years, two patients had been entered. Both expired from their disease.

Group-wide, tamoxifen did not reveal any activity in patients with advanced or recurrent adenocarcinoma or adenosquamous carcinoma of the endometrium of unknown hormonal receptor status, progressing after heavy pretretment with hormonal therapy with progestational agents and/or chemotherapy.

Tamoxifen shows definite activity as second-line treatment for epithelial ovarian carcinoma, with overall response rate of approximately 18% and a 10% complete response rate. Durations of response range from 7 to 12 months. Toxicity is minimal. An additional 38% of patients exhibit stable disease, although durations are considerably shorter.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 83/23	Status: Completed

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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 86

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/M^2 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.

Group-wide results show that there is no activity with this drug in ovarian or cervical cancer in previously treated patients. Substantial skin adverse effects and occasional central nervous system adverse effects have been noted with this drug.

Detail Summary Sheet

Date: 30 Sep 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 86

Study Objective: To determine the efficacy of DHAD in patients whose advanced malignancies have been resistant to higher priority methods of treatment.

Technical Approach: All patients with measurable gynecological cancer who have failed higher prior therapies will be offered DHAD as a Phase II drug to determine its efficacy. The drug will be given as 12 mg/M^2 I.V. every three weeks. Patients will continue to receive the agent until progression or adverse effects prohibit further therapy.

*This protocol was closed to uterus/MMT patient entry in August 1987.

Progress: No new patients were entered in FY 87 at MAMC. In previous years three patients had been entered. All died of their disease.

Group-wide, the data indicate minimal activity of DHAD in patients with ovarian cancer who have previously received doxorubicin. In patients with previously treated advanced carcinoma of the cervix, this drug also shows minimal activity. DHAD has minimal activity in patients with nonsquamous carcinoma of the cervix.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 82/30	Status: On-going

Title: GOG #26-O: A Phase II Trial of Aziridinylbenzoquinone (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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Feb 87

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/M^2 given every three weeks. Patients will continue to receive the agent until progression or adverse effects prohibit further therapy.

Progress: No patients entered in FY 87. One patient entered at MAMC during FY 84 with no response to AZQ; death by cancer of cervix.

Group-wide data thus far indicate that AZQ has little if any activity as a salvage agent in either epithelial ovarian cancer or squamous cell carcinoma of the cervix.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 83/25	Status: Completed

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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 86

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/M^2 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.

Group-wide data showed that the drug has minimal efficacy and a poor therapeutic index due to its significant neurotoxocity.

Detail Summary Sheet

Date: 30 Sep 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review Nov 86

Study Objective: To determine the efficacy of aminothiadiazole in patients whose advanced malignancies have been resistant to high priority methods of treatment.

Technical Approach: All patients with measurable gynecological cancer who have failed higher prior therapies will be offered aminothiadiazole as a Phase II drug to determine its efficacy. The drug will be given as 125 mg/M^2 I.V. once a week. Patients will continue to receive the agent until progression or adverse effects prohibit further therapy.

Progress: No entries in FY 87. One patient was entered in FY 85 and died from squamous cell carcinoma of the cervix.

Detail Summary Sheet

Date: 30 Sep 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jan 87

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: One patient was entered on the protocol in FY 87 and died of the disease. No other patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jul 87

Study Objective: To determine the efficacy of Teniposide in patients whose advanced malignancies have been resistant to high priority methods of treatment.

Technical Approach: Teniposide will be administered at a dosage of 100 mg/M^2 every week. The patients will be followed for toxicites to the drug and the drug dosages will be modified according to the severity of the toxicities. Response to the drug will be followed. Progression of disease and/or excessive toxicities will terminate the study for the patient.

Progress: No new patients entered in FY 87. Two patients were entered at MAMC in previous years. One patient has died of disease and the other has progression of disease.

Group-wide data show that teniposide produced only modest activity in previously treated patients with epithelial ovarian cancer at the dose and schedule used. Teniposide displays only modest activity in patients with squamous cell carcinoma of the cervix.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 84/65	Status: Terminated

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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jul 87

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/M^2 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 were entered at MAMC in FY 87. One patient was entered at MAMC in FY 86. None had been entered in previous years.

The protocol was terminated by the SWOG Group Headquarters.

Detail Summary Sheet

Date: 30 Sep 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 86

Study Objective: To determine the efficacy of ifosfamide plus mesna in patients whose advanced malignancies have been resistant to higher priority methods of treatment.

Technical Approach: All eligible patients who have failed higher priority therapies will be offered ifosfamide plus mesna as a Phase II drug regimen to determine its efficacy. Ifosfamide will be given at a dosage of 1.8 g/M^2 daily for five days and mesna will be given 400 mg/M^2 t.i.d every four weeks. Patients will be followed for toxicities to the drug and the drug dosage will be modified according to the severity of the toxicities. Response to the drug will be followed; progression of disease and/or excessive toxicities will terminate the study for the patient.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	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
Deptartment: 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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 86

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/M^2 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 87	Protocol No.: 86/75	Status: On-going

Title: GOG 26W: A Phase II Trial of Echinomycin (NSC #526417) in Patients with Advanced Pelvic Malignancies

Start Date: 20 Jun 86	Est Completion Date: Indefinite
Department: OB/GYN	Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC	
Associate Investigators: COL William L. Benson, MC	
Key Words: malignancies, pelvic, advanced, echinomycin, Phase II	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jul 87

Study Objective: To screen for activity of new agents or drug combinations in patients with advanced malignancies. Its intent is to determine the efficacy of chemotherapeutic agents in patients whose advanced malignancies have been resistant to high priority methods of treatment.

Technical Approach: Echinomycin will be administered at a dosage of 1500 mcg/m every 4 weeks. An adequate trial is defined as receiving one dose of drug and alive at four weeks. Patients receiving one dose of drug and demonstrating progression $\leq$ 4 weeks from study entry will be considered evaluable for response and toxicity. Each patient will remain on study and continue to receive drug until disease progression or adverse effects prohibit further therapy.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/62	Status: On-going

Title: GOG 26Y: A Phase II Trial of Vinblastine (NSC 049842) in Patients with Advanced Pelvic Malignancies

Start Date:	Est Completion Date:	
Department: OB/GYN		Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigators: COL William L. Benson, MC		
Key Words:		
Accumulative MEDCASE Cost:	Est Accumulative OMA Cost:	Periodic Review: N/A

Study Objective: To screen for activity of new agents or drug combinations in patients with advanced malignancies. Its intent is to determine the efficacy of chemotherapeutic agents in patients whose advanced malignancies have been resistant to high priority methods of treatment.

Technical Approach: Vinblastine will be administered at a dosage of 9 mg/m^2, I.V. push, on day 1 every three weeks with dose escalation to 12 mg/m^2 if minimal or no toxicity. An adequate trial is defined as receiving one course of therapy and alive for evaluation at three weeks. Patients will remain on study until progression of disease or adverse effects prohibit further therapy.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 81/12	Status: On-going

Title: GOG #33: A Clinical Pathologic Study of Stages I and II Carcinoma of the Endometrium

Start Date: 21 Nov 80	Est Completion Date: Nov 83	
Department: OB/GYN		Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: carcinoma, lymph node, aortic, pelvic, metasteses		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A**

Study Objectives: To determine the incidence of pelvic and aortic lymph node metastases associated with Stages I and II adenocarcinoma of the endometrium and the relationship of the node metastases to other important prognostic factors. These findings will then be used as a guide for treatment protocols.

Technical Approach: Patients will receive standard treatment; this protocol is only for data collection purposes. Patients with histologically proven endometrial carcinoma, clinical FIGO Stages I (grades 2 and 3) and Stage II (all grades) who have undergone total abdomonial hysterectomy, bilateral salpingo-oopherectomy, selective pelvic and para-aortic lymphadenectomy, and peritoneal cytology sampling are eligible. The following histologic types of endometrial carcinoma are acceptable: adenocarcinoma, adenocarcinoma with squamous metaplasia, adenoacanthoma, and adenosquamous carcinoma. Patients who have received preoperative radiotherapy are ineligible. Pathologic evaluation will include: (a) peritoneal washing will be evaluated for malignant cells; (b) the uterus will be evaluated in regard to location of tumor, depth of myometrial invasion, differentiation of tumor, size of uterus; (c) the adnexae will be evaluated for presence of metastasis (d) the lymph nodes (total number indicated) will be evaluated as to metastasis and location and number of lymph nodes involved. After surgery, all patients will be entered into the appropriate protocol or receive appropriate treatment if no protocol is available.

Progress: This protocol is closed to patient entry. No patients were entered in FY 87. In previous years, eight patients were entered on the protocol. Three of the eight patients had recurrence of endometrial cancer and died.

**This protocol was reactived in October 1986. It was mistakenly closed in FY 84 when it was closed to patient entry. However, the GOG continues to collect data on the patients who have survived; therefore, it must remain open and be reviewed periodically.

Preliminary group-wide data indicate that this study could define the surgical procedure required for optimal evaluation of endometrial cancer.

Detail Summary Sheet

Date: 30 Sep 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 86

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 87. Eight subjects were entered in previous years. The protocol is closed to patient entry. The investigators are continuing to collect data.

Detail Summary Sheet

Date: 30 Sep 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jul 87

Study Objective: To determine the incidence of pelvic and aortic lymph node metastases associated with Stages I and II uterine sarcomas, the relationship of these node metastases to other important prognostic factors such as mitotic index of the tumor, and the complication rate of the procedures. These findings will then be used as a guide for treatment protocols.

Technical Approach: Patients with histologically proven uterine sarcoma clinical Stages I or II who undergo total abdominal hysterectomy, bilateral salpingo-oophorectomy, selective pelvic and para-aortic lymphadenectomy, peritoneal cytology sampling and omentectomy (optional) as described in the protocol are eligible. Patients who have had prior preoperative adjuvant pelvic radiation or chemotherapy will be ineligible. The following pathologic evaluation will be done:

a. Peritoneal cytology will be evaluated for malignant cells.
b. The uterus will be evaluated at least in regard to: (1) location of tumor; (2) depth of myometrial invasion; (3) differentiation of tumor; (4) size of uterus; (5) number of mitoses per 10 HPF; (6) histologic type of tumor.
c. The adnexa will be evaluated for presence of metastasis.
d. The lymph nodes will be evaluated as to metastasis and location and number of involved lymph nodes.

After surgical staging, patients may be transferred to an appropriate treatment protocol if all criteria are met. If no protocol is available, further treatment will be at the discretion of the physician.

Progress: No new patients were entered at MAMC in FY 87. Six patients have been entered in previous years.

Group-wide data show that the distribution by cell type shows dominance of mixed mesodermal tumors as found in earlier sarcoma protocols. There is a trend toward tumor size being a significant factor. No significant serious adverse effects have been encountered. The findings obtained from this study will be used as a guide for treatment protocols.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 81/35	Status: On-going

Title: GOG 41: Surgical Staging of Ovarian Carcinoma

Start Date: 16 Jan 81	Est Completion Date: Jan 86	
Department: OB/GYN		Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigator: COL William Benson, MC		
Key Words: surgical staging, ovarian carcinoma, intraperitoneal structures, retroperitoneal lymph nodes, direct examination, cytologic sampling, biopsy		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A**

Study Objective: To determine the spread of ovarian carcinoma to intraperitoneal structures and retroperitoneal lymph nodes by direct examination, cytologic sampling, and biopsy; to establish a surgical protocol for patients entered into GOG ovarian cancer treatment protocols; to determine the complication rate of the procedures.

Technical Approach: This protocol is being performed as a statistical protocol on patients who have surgery as standard treatment. Eligible patients will be those who have Stages I, II, or III ovarian carcinoma. Patients undergoing total abdominal hysterectomy, bilateral or unilateral salpingo-oophorectomy, bivalving of the other ovary, selective pelvic and para-aortic lymphadenectomy, omental biopsy, or peritoneal cytology sampling will be studied. They will not be given any preoperative treatment, but will be subjected to a complete and thorough evaluation before surgery. All patients will be explored and the steps for surgery will be as standard surgery dictates. Specific observations will be made as to the findings. If fluid is not present, washings will be taken from the inside of the abdomen to study cells. A thorough examination of all structures from the diaphragm to the pelvic floor will be carried out. After surgical staging, patients will be transferred to the appropriate treatment protocol or to standard treatment if no protocol is available.

Progress: This protocol was closed to patient entry in FY 84. Sixteen patients were entered at MAMC.

**This protocol was reactived in October 1986. It was mistakenly closed in FY 84 when it was closed to patient entry. However, the GOG continues to collect data on the patients who have survived; therefore, it must remain open and be reviewed periodically.

This study demonstrates the value of omentectomy, lymph node excisions, and diaphragm biopsy in epithelial ovarian tumors. Still to be determined is the value of these procedures in sex cord-stromal and germ cell tumors. Results of this study will be used as a guide in future treatment protocols.

Detail Summary Sheet

Date: 30 Sep 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 86

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 87. Two patients were entered at MAMC in previous years. The protocol is closed to patient entry.

Group-wide data show that VAC is an active regimen. Six to nine courses will prevent recurrence in the majority of women with malignant germ cell tumors of the ovary.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 81/43	Status: On-going

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

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 primary stage III or IV, recurrent or residual endometrial adenocarcinoma, adenoacanthoma, or adenosquamous carcinoma, whose potential for cure by radiation therapy or surgery alone or in combination is very poor, are eligible. Patients who have received previous chemotherapy are ineligible. Patients will be randomized to: (1) Adriamycin, 60 mg/M^2 IV, q 3 wks x 8 courses. Responders will have follow-up only. Those with progression will be transferred to Protocol #26 or (2)Adriamycin, 60 mg/M^2 IV, q 3 wks x 8 courses plus cyclophosphamide 500 mg/M^2 IV q 3 weeks x 8 courses. Responders will receive follow-up only. Those with progression will be transferred to Protocol #26. 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: No patients were entered in FY 87. The protocol has been closed to patient entry. Five subjects were entered at MAMC. Four patients died from disease and one is alive with disease.

**This protocol was reactived in May 1987. It was mistakenly closed in FY 85 when it was closed to patient entry. However, the GOG continues to collect data on the patient who has survived; therefore, it must remain open and be reviewed periodically.

Group-wide data show that the combination of adriamycin plus cyclophosphamide appears to offer no advantage over adriamycin alone in the management of endometiral carcinoma. Progestins appear to be less active than previously thought in the treatment of endometrial carcinoma.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 81/70	Status: On-going

Title: GOG #49: A Surgical-Pathologic Study of Women with Invasive Carcinoma of the Cervix Stage I_B and Randomly Assigned Radiation Therapy Versus No Further Therapy in Selected Patients, Phase III

Start Date: 20 Mar 81	Est Completion Date: Mar 86
Department: OB/GYN	Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC	
Associate Investigator: COL William Benson, MC	
Key Words: carcinoma, cervix, radiation versus no further therapy	

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

Study Objective: To determine by observations of the 5-year survival and disease free interval, the validity of current FIGO staging of the histopathologic prognostic factors of size of lesion, location of lesion, depth of invasion of tumor in millimeters, histology and grade, growth pattern, and site and number of positive lymph nodes in Stage I_B carcinoma of the cervix; to rapidly accumulate prospectively significant surgical pathologic data which would expedite development of further protocols; to determine morbidity of primary radical surgical therapy; to determine if radiation therapy will improve survival in selected patients with positive nodes.

Technical Approach: Patients with primary, previously untreated histologically confirmed invasive Stage I_B carcinoma of the cervix will be eligible. Patients must have undergone exploratory laparotomy, peritoneal fluid sampling, bilateral pelvic and para-aortic lymphadenectomy and radical hysterectomy to be eligible for the randomized portion of the study. Those with negative pelvic nodes will receive no further therapy and be followed for 5 years. Patients with positive pelvic nodes, unilateral metastasis, <3 positive pelvic nodes, no parametrial involvement, and clear vaginal margins will be randomized to receive no further therapy (follow-up for 5 years) or whole pelvic radiation with follow-up of 5 years. Those with positive para-aortic nodes on paraffin section will be entered on other GOG protocols as appropriate.

Progress: This protocol has been closed to patient entry. No patients were entered at MAMC in FY 87. Eight patients were previously entered on this protocol at MAMC.

**This protocol was reactived in October 1986. It was mistakenly closed in FY 84 when it was closed to patient entry. However, the GOG continues to collect data on the patients who have survived; therefore, it must remain open and be reviewed periodically.

There are no conclusions regarding the randomized portion of this study due to poor group-wide accrual. The surgical staging part of this study must await further follow-up to confirm the prognostic significance of several clinical and pathological factors.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 81/105	Status: On-going

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

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 patients entered in FY 87. Six patients were entered in previous years. The study has been closed to patient entry.

**This protocol was reactived in May 1987. It was mistakenly closed in FY 85 when it was closed to patient entry. However, the GOG continues to collect data on the patients who have survived; therefore, it must remain open and be reviewed periodically.

Group-wide data show that no significant advantage can be demonstrated for CAP over CP in this patient population when using an equitoxic dose schedule.

Detail Summary Sheet

Date: 30 Sep 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 86

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, granulosatheca 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 87. Previously, two patients have entered.

Detail Summary Sheet

Date: 30 Sep 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Feb 87

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: One new patient was entered in FY 87. In previous years, six patients have been entered.

Detail Summary Sheet

Date: 30 Sep 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 86

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: No new entries at MAMC in FY 87. In previous years, five patients have been entered.

The protocol has been closed to patient entry. Although it is inconclusive from group-wide data analysis that hydroxyurea with radiotherapy is superior to misonidazole with radiotherapy, it appears that hydroxyurea is the more appropriate potentiator in patients with bulky cervix cancer.

Detail Summary Sheet

Date: 30 Sep 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Dec 86

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 in FY 87. One patient was entered previously. The protocol is closed to patient entry.

Group-wide results indicate that the standard MAC regimen is more effective and less toxic than MBP.

Detail Summary Sheet

Date: 30 Sep 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 86

Study Objective: To determine if cis-diamminedichlorplatinum, cisplatin, given in an adjuvant setting will decrease the risk of geographic failure or improve the survival rate 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: 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 will be eligible. Patients will undergo preoperative clinical staging, utilizing lymphangiography, computerized axial tomography, and/or sonography as well as traditional methods. Subsequently, 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. 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 4 weeks, or survival of 8 weeks after radiation therapy for the no-further-treatment regimen.

Progress: No entries at MAMC in FY 87. Previously one patient has been entered. The protocol is closed to patient entry.

Group-wide data indicate that scalene node biopsy is of limited value. Even in this young patient population with favorable performance status, post radiation systemic therapy was not feasible.

Detail Summary Sheet

Date: 30 Sep 87 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 Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Nov 86

Study Objective: To determine if the addition of BCG to doxorubicin plus cyclophosphamide plus cisplatin improves remission rate, remission duration, or survival in suboptimal Stages III and IV ovarian adenocarcinoma; to determine the frequency and duration of true complete remission using these regimens as judged at second-look laparotomy.

Technical Approach: Eligibility: Patients with established suboptimal Stage III or Stage IV ovarian epithelial cancer. Patients must have optimal surgery for ovarian cancer, with at least an exploratory laparotomy and appropriate tissue for histologic evaluation. Patients with measurable or nonmeasurable disease will be evaluated. Patients with histologically confirmed serous adenocarcinoma, mucinous adenocarcinoma, clear-cell adenocarcinoma, endometrioid adenocarcinoma, undifferentiated carcinoma, or mixed epithelial carcinoma will be eligible. Patients who have received previous chemotherapy or radiotherapy will be ineligible. Patients will be randomized to receive either doxorubicin, cyclophosphamide, and cisplatin every 3 weeks for 8 courses; or the above regimen plus BCG (days 8 & 15 for 8 courses). Patients with complete response will have a second look laparotomy and will be taken off therapy if complete response is confirmed. Patients who have partial response of stable disease will be considered for a second look if, in the opinion of the investigator, significant tumor reduction may have been achieved. If residual tumor is detected, patients will be taken off study and placed on GOG #61. Patients with progressive disease at any time will be removed from the chemotherapy on this study, but will be followed.

Progress: No patients were entered in FY 87. Six patients were entered in previous years. The protocol has been closed to patient entry.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 82/09	Status: On-going

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

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 87. Four patients were entered at MAMC in previous years. The protocol is closed to patient entry.

**This protocol was reactived in May 1987. It was mistakenly closed in FY 85 when it was closed to patient entry. However, the GOG continues to collect data on the patients who have survived; therefore, it must remain open and be reviewed periodically.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/38	Status: Completed

Title: GOG 62: Data Collection Form for Extravasation Injury with Doxorubicin

Start Date: Feb 86	Est Completion Date: Indefinite
Department: OB/GYN	Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC	
Associate Investigator: COL William Benson, MC	

Key Words: extravasation, doxorubicin, data collection

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Feb 87

Study Objective: To record clinical observations and treatment of doxorubicin (Adriamycin) extravasation for the purpose of the future development of standardized descriptors and/or protocol for method of treatment.

Technical Approach: Eligible patients will be those on a GOG study with gynecologic malignancy undergoing chemotherapy who have incurred an extravasation injury during doxorubicin administration, who return within 72 hours of receiving doxorubicin with signs and symptoms of extravasation. Patients experiencing an extravasation injury with a chemotherapy agent other than doxorubicin and those experiencing a doxorubicin "flare" rather than true extravasaation injury will be excluded. Treatment for extravasation will be initiated immediately and follow MAMC guidelines. Information to be recorded will be venipuncture site, course of chemotherapy, amount extravasated, concentration of drug, initial dilution of drug, type of needle used, method of administration, condition of veins, number of venipuncture attempts, nurse's experience administering chemotherapy, amount and severity of pain at needle site, amount of swelling, color and dimension of infiltration site, lesion evaluation, and description of chemotherapy given.

Progress: No patients were entered on this protocol at MAMC. It was closed to patient entry in July 1987.

Detail Summary Sheet

Date: 30 Sep 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Mar 87

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: No entries at MAMC in FY 87. In previous years five subjects had been entered.

Detail Summary Sheet

Date: 30 Sep 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Feb 87

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 nonkeritinizing 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 thearpy 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/M^2, and cyclophosphamide, 750 mg/M^2, IV every 21 days. Patients with previous irradiation will receive vincristine, 2 mg, doxorubicin, 40 mg/M^2, and cyclophosphamide, 600 mg/M^2, 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/M^2. Patients in whom tumor progression occurs on this regimen will be treated with VP-16, 100 mg/M^2 (no previous irradiation) or 80 mg/M^2 (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 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jul 87

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: No new entries at MAMC in FY 87. In previous years, two patients have been entered. The protocol has been closed to patient entry.

Detail Summary Sheet

Date: 30 Sep 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Feb 87

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 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Feb 87

Study Objective: To evaluate the biologic behavior of ovarian tumors of low malignant potential; to evaluate the effectiveness of chemotherapy against this disease (initially, a Phase II study of melphalan); and to evaluate the response rate to cisplatin in melphalan failures.

Technical Approach: Patients without prior chemotherapy or radiotherapy who have had adequate surgical staging will be eligible. Patients with no grossly visible residual disease will receive no treatment and be followed for 5 years if there is no subsequent disease. If there is no grossly visible clinically apparent residual for 12 months, the patients will have second look surgery and then proceed to melphalan treatment (5 days every four weeks) or follow-up (complete response). With progression after melphalan, patients will proceed to third look and cis-platin treatment (once every three weeks for eight weeks) or follow-up. If there is no evidence of response after three courses of 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 was entered in FY 87. Two patients have been entered in previous years.

Detail Summary Sheet

Date: 30 Sep 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jan 87

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 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jan 87

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* $\leq$ 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 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jan 87

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 87	Protocol No.: 87/11	Status: On-going

Title: GOG 76A: Master Protocol for Phase II Drug Studies in Treatment of Advanced or Recurrent Squamous Cell Carcinoma of the Cervix

Start Date: 17 Oct 86	Est Completion Date: Indefinite
Dept/Svc: OB/GYN	Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC	
Associate Investigators: COL William L. Benson, MC	
Key Words: master protocol, phase II, carcinoma, cervix, squamous cell, advanced, recurrent	

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

Study Objective: To identify new active drugs in the control of advanced or recurrent squamous cell carcinoma of the cervix so that combinations of cytotoxic drugs can be formed which might lead to an improved complete remission rate.

Technical Approach: In order that attractive new cytotoxic or other chemotherapeutic agents receive as fair a trial as possible, this study constitutes a Phase II design in a population of patients who have had no prior cytotoxic drug therapy. A rejection type design will be used involving an average sample size of 25 evaluable patients per drug studied, allowing for agents found to be ineffective to be rapidly replaced by other agents. The study will be done in a non-randomized fashion.

Patients with histologically confirmed advanced, persistent, or recurrent squamous cell carcinoma of the cervix with documented disease progression after local therapy who are considered incurable will be eligible. All patients must have measurable disease consisting of abdominal, pelvic, or other masses which can be defined in at least two dimensions by palpation, x-ray, or ultrasound. Patients with another malignancy (prior or concomitant) other than the skin (excluding melanoma) will be ineligible.

Patients who receive one or more courses of the drug and live for at least three weeks will be evaluable for response. Patients who receive one or more courses of the drug, regardless of subsequent survival, will be evaluable for adverse effects.

Each drug will be studied on a separate protocol. Specific details for treatment with each drug will be given in the protocol dealing with the particular agent to be studied.

Progress: One patient has been entered on the cis-platin/5FU protocol (76G).

**Continuing review will be done on individual protocols.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/12	Status: On-going

Title: GOG 76D: A Phase II Trial of Dibromodulcitol (DBD, NSC #104800) in Patients with Advanced Squamous Cell Carcinoma of the Cervix

Start Date: 17 Oct 86	Est Completion Date: Indefinite
Department: OB/GYN	Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC	
Associate Investigators: COL William L. Benson, MC	
Key Words: carcinoma, squamous cell, cervix, dibromodulcitol	

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

Study Objective: To identify new active drugs in the control of advanced or recurrent squamous cell carcinoma of the cervix so that combinations of cytotoxic drugs can be formed which might lead to an improved complete remission rate.

Technical Approach: Dibromodulcitol, 180 mg/m^2 p.o., will be taken in a single dose days 1-10 and repeated every four weeks until progression of disease or adverse effects prohibit futher therapy.

Progress: No patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/81	Status: On-going

Title: GOG 76 F: A Phase II Trial of Gallium Nitrate (NSC 15200) Patients with Advanced Squamous Cell Carcinoma of the Cervix

Start Date: 15 May 87	Est Completion Date: Indefinite
Department: OB/GYN	Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC	
Associate Investigators: COL William L. Benson, MC	
Key Words: carcinoma, cervix, squamous, gallium nitrate	

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

Study Objective: To identify new active drugs in the control of advanced or recurrent squamous cell carcinoma of the cervix so that combinations of cytotoxic drugs can be formed which might lead to an improved complete remission rate.

Technical Approach: Gallium nitrate will be given as a slow IV infusion of 30-60 minutes at a dose of 750 mg/m^2 once every three weeks until progression or adverse effects prohibit further therapy.

Progress: No patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87780	Status: On-going

Title: GOG 76 G: A Phase II Trial of Cisplatin - 5-Fluorouracil Carcinoma of the Cervix

Start Date: 15 May 87	Est Completion Date: Indefinite
Department: OB/GYN	Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC	
Associate Investigators: COL William L. Benson, MC	
Key Words: carcinoma, cervix, cisplatin, 5-FU	

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

Study Objective: To identify new active drugs in the control of advanced or recurrent squamous cell carcinoma of the cervix so that combinations of cytotoxic drugs can be formed which might lead to an improved complete remission rate.

Technical Approach: Patients will be initially treated with a a 50 mg/m^2 infusion of cis-platin on day 1. Subsequent to that, they will receive a 24-hour infusion, days 1-5, of 5-FU at a dose of 1000 mg/m^2 per day. The regimen will be repeated every 21 days until progression or adverse effects prohibit further therapy.

Progress: One patient has been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 84/29	Status: Completed

Title: GOG #77: A Randomized Study of Carboplatin (CBDCA-NSC #241240) Versus CHIP (NSC #256927) In Advanced Carcinomma of the Cervix

Start Date: 20 Jan 84	Est Completion Date: Indefinite
Department: OB/GYN	Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC	
Associate Investigators: COL William L. Benson, MC	
Key Words: carcinoma, cervix, carboplatin vs CHIP	

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

Study Objective: To determine the objective response rate of squamous cell carcinoma of the cervix to Carboplatin and to CHIP; to determine in a randomized study whether Carboplatin or CHIP has a superior (statistically significant) objective response rate in cervical carcinoma; and to assess and compare toxicity (gastrointestinal and renal) of Carboplatin and CHIP.

Technical Approach: Patients who have histologically confirmed, locally advanced, recurrent, persistent, or metastatic squamous cell carcinoma of the cervix resistant to curative treatment with surgery or radiotherapy will be eligible. Patients will be randomized to one of the following regimens.

Regimen I: Carboplatin will be given 400 mg/M^2 as a 15 min IV infusion once every four weeks.

Regimen II: CHIP will be given 300 mg/M^2 as a 2 hr infusion once every four weeks.

Both treatments will continue until disease progresses or until toxicity prohibits further therapy. Survival status will continue to death.

Progress: Three patients were entered at MAMC.

**This protocol was reactived in October 1986. It was mistakenly closed in FY 84 when it was closed to patient entry. However, the GOG continues to collect data on the patients who have survived; therefore, it must remain open and be reviewed periodically.

The protocol was closed at MAMC in July 1987 upon the death of the third subject.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 84/74	Status: On-going

Title: GOG 78: Evaluation of Adjuvant VP-16, Bleomycin and Cis-** platin (BEP) Therapy in Totally Resected Choriocarcinoma, Endodermal Sinus Tumor, Embryonal Carcinoma and Grade 3 Immature Teratoma of the Ovary, Pure and Mixed with Other Elements

Start Date: 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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 86

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. Per addendum of Jan 87: to evaluate the acute and chronic toxicity of this chemotherapy on gonadal and reproductive function.

Technical Approach: Patients with totally resected Stage I choriocarcinoma, endodermal sinus tumor, or embryonal carcinoma of the ovary with negative peritoneal washings, normal (or falling at a rate that does not suggest residual disease) serum AFP and beta-HCG levels, and adequate bone marrow, renal, and hepatic function will be studied. Stages II and III will also be eligible if all gross tumor is resected. After recovery from surgery, patients will receive 3 cycles of VBP therapy. Patients who show evidence of progression while on VBP therapy will be candidates for GOG Protocol 26. Patients completing three cycles of treatment clinically free of disease will undergo reassessment laparotomy. Patients with recurrent disease at reassessment laparotomy will be candidates for GOG Protocol 26. To be evaluable a patient will receive at least one week of chemotherapy and live another two weeks. Each patient will remain on study until adverse effects prohibit further therapy or until evidence of progression is noted.

**Per addendum of Jan 86: the title has been changed as shown above; vinblastin has been replaced by VP-16; Grade 3 immature teratoma has been added for entry and evaluation.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 86

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/M^2, 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: No entries at MAMC in FY 87. Two patients were entered on this protocol in FY 86 with no adverse side effects.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/59	Status: Completed

Title: GOG 80: Cytoreductive Surgery and PAC Chemotherapy vs PAC Chemotherapy for Advanced Stage Epithelial Ovarian Carcinoma After Previous Debulking (Primary Stage III and Only Stage IV with Malignant Pleural Effusion, Phase III

Start Date: 18 Apr 86	Est Completion Date: Indefinite
Department: OB/GYN	Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC	
Associate Investigator: COL William Benson, MC	
Key Words: carcinoma, previous debulking, surgery, chemotherapy	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0- Periodic Review: Jul 87

Study Objective: To compare the complete surgical response rate to combination chemotherapy for patients treated with or without attempted primary cytoreductive surgery; to evaluate the influence of attempted primary cytoreductive surgery on the survival of patients with advanced stage epithelial ovarian cancer; to determine the feasibility of optimal tumor resection in patients with advanced stage epithelial ovarian cancer; and to compare the morbidity associated with attempted primary cytoreductive surgery and primary chemotherapy.

Technical Approach: Regimen I: Surgery will be performed with an attempt made to remove as much tumor as possible. Following recovery from surgery, the patient will be treated with adriamycin, cytoxan, and cisplatin every three weeks for eight cycles. Patients with no clinical evidence of disease will then have second-look laparotomy. If there is persistent disease, patient will be entered on another appropriate GOG protocol. If there is no evidence of disease, patients will have clinical follow-up for 5 years.

Regimen II: Patients will receive chemotherapy as in Regimen I, without surgery. Patients with disease progression after 3 cycles of chemotherapy will have exploratory laparotomy with attempted maximal cytoreduction and entered on another appropriate GOG protocol. Patients with stable disease or clinical response will receive 5 more cycles of chemotherapy, following which they will have exploratory laparotomy. If gross disease is found, they will have attempted resection of residual tumor and will be entered on an appropriate GOG protocol. If there is no evidence of disease, patients will have clinical follow-up for 5 years.

Progress: No patients entered on this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/08	Status: On-going

Title: GOG 81/A: Master Protocol for Hormonal Treatment of Advanced or Recurrent Carcinoma of the Endometrium

Start Date: 18 Oct 85	Est Completion Date: Oct 93	
Department: OB/GYN		Facility: MAMC
Principal Investigator:	COL Roger B. Lee, MC	
Associate Investigators:	COL William L. Benson, MC	

Key Words: carcinoma, endometrium, advanced, recurrent, hormonal therapy, medroxyprogesterone acetate, master protocol

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

Study Objective: To determine the relative efficacy of two dose schedules of oral MPA in the management of advanced or recurrent endometrial carcinoma; to examine the relationship between the levels of estrogen and progesterone receptors in the neoplasm and subsequent response to progestin therapy; and to determine whether patients who respond to therapy with progestins will respond to therapy with anti-estrogens when they relapse on progestins.

Technical Approach: This is a master protocol established in order to study patients being treated with medroxyprogesterone acetate (MPA) for advanced or recurrent endometrial carcinoma. The protocol will be divided into sections to study MPA in patients with various estrogen and progesterone receptors:

- 81B: positive estrogen and progesterone receptors
- 81C: negative estrogen and progesterone receptors
- 81D: positive receptors for etiher estrogen or progesterone, but not both
- 81E: unknown estrogen and progesterone receptors

Section 81F will study Tamoxifen salvage in patients responsive to MPA in sections B-E. The treatment regimens in sections B-E will be the same with only the receptors studied being different.

Treatment I: medroxyprogesterone acetate 200 mg p.o. daily

Treatment II: medroxyprogesterone acetate 1000 mg p.o. daily

Continue until evidence of disease progression. A course will be considered as every 4 weeks.

Each patient must have a serum sample drawn after one month on therapy to document compliance and absorption.

Progress: No patients have been entered in any of the sections to this protocol.

**Continuing review will be done on individual protocols.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/09	Status: On-going

Title: GOG 81/B: A Phase I-II Trial of Medroxyprogesterone Acetate (MPA) in Patients with Advanced or Recurrent Endometrial Carcinoma Positive for Estrogen and Progesterone Receptors

Start Date: 18 Oct 85	Est Completion Date: Indefinite
Department: OB/GYN	Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC	
Associate Investigators: COL William L. Benson, MC	
Key Words: endometrial carcinoma, medroxyprogesterone acetate, positive estrogen and progesterone receptors	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0- Periodic Review: Nov 86

Study Objective: To determine the relative efficacy of a high versus a low dose schedule of oral medorxyprogesterone acetate in treatment of advanced or recurrent endometrial carcinoma and to determine the response rate to progestins in patients positive for estrogen and progesterone receptors.

Technical Approach: Patients will be randomized to:

Treatment I: medroxyprogesterone acetate 200 mg p.o. daily
or
Treatment II: medroxyprogesterone acetate 1000 mg p.o. daily

Therapy will continue until evidence of disease progression. A course will be considered as every 4 weeks. Each patient will have a serum sample drawn after one month on therapy to document compliance and absorption. Treatment will be continued until there is evidence of disease progression or the patient experiences unacceptable adverse effects.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/10	Status: On-going

Title: GOG 81/C: A Phase I-II Trial of Medroxyprogesterone Acetate (MPA) in Patients with Advanced or Recurrent Endometrial Carcinoma Negative for Estrogen and Progesterone Receptors

Start Date: 18 Oct 85	Est Completion Date: Indefinite
Department: OB/GYN	Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC	
Associate Investigators: COL William L. Benson, MC	
Key Words: carcinoma, endometrial, medroxyprogesterone acetate, negative estrogen and progesterone receptors	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 86

Study Objective: To determine the relative efficacy of a high versus a low dose schedule of oral medorxyprogesterone acetate in treatment of advanced or recurrent endometrial carcinoma and to determine the response rate to progestins in patients negative for estrogen and progesterone receptors.

Technical Approach: Patients will be randomized to:

Treatment I: medroxyprogesterone acetate 200 mg p.o. daily
or
Treatment II: medroxyprogesterone acetate 1000 mg p.o. daily

Therapy will continue until evidence of disease progression. A course will be considered as every 4 weeks. Each patient will have a serum sample drawn after one month on therapy to document compliance and absorption. Treatment will be continued until there is evidence of disease progression or the patient experiences unacceptable adverse effects.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/II	Status: On-going

Title: GOG 81/D: A Phase I-II Trial of Medroxyprogesterone Acetate (MPA) in Patients with Advanced or Recurrent Endometrial Carcinoma Positive for Either Estrogen or Progesterone Receptors but Not Both

Start Date: 18 Oct 85	Est Completion Date: Indefinite
Department: OB/GYN	Facility: MAMC
Principal Investigator:	COL Roger B. Lee, MC
Associate Investigators:	COL William L. Benson, MC

Key Words: carcinoma, endometrial, medroxyprogesterone acetate, positive for either estrogen or progesterone receptors but not both

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 86

Study Objective: To determine the relative efficacy of a high versus a low dose schedule of oral medorxyprogesterone acetate in treatment of advanced or recurrent endometrial carcinoma and to determine the response rate to progestins in patients positive for either estrogen or progesterone receptors.

Technical Approach: Patients will be randomized to:

Treatment I: medroxyprogesterone acetate 200 mg p.o. daily
or
Treatment II: medroxyprogesterone acetate 1000 mg p.o. daily

Therapy will continue until evidence of disease progression. A course will be considered as every 4 weeks. Each patient will have a serum sample drawn after one month on therapy to document compliance and absorption. Treatment will be continued until there is evidence of disease progression or the patient experiences unacceptable adverse effects.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/12	Status: On-going

Title: GOG 81/E: A Phase I-II Trial of Medroxyprogesterone Acetate (MPA) in Patients with Advanced or Recurrent Endometrial Carcinoma with Unknown Estrogen or Progesterone Receptors

Start Date: 18 Oct 85	Est Completion Date: Indefinite
Department: OB/GYN	Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC	
Associate Investigators: COL William L. Benson, MC	
Key Words: carcinoma, endometrial, medroxyprogesterone acetate, estrogen or progesterone receptors, unknown	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 86

Study Objective: To determine the relative efficacy of a high versus a low dose schedule of oral medroxyprogesterone acetate in the management of advanced or recurrent endometrial carcinoma; to examine the relationship between the levels of estrogen and progesterone receptors in the neoplasm and subsequent response to progestin therapy; and to determine whether patients who respond to therapy with progestins will respond to therapy with anti-estrogens when they relapse on progestins.

Technical Approach: Patients will be randomized to:

Treatment I: medroxyprogesterone acetate 200 mg p.o. daily
or
Treatment II: medroxyprogesterone acetate 1000 mg p.o. daily

Therapy will continue until evidence of disease progression. A course will be considered as every 4 weeks. Each patient will have a serum sample drawn after one month on therapy to document compliance and absorption. Treatment will be continued until there is evidence of disease progression or the patient experiences unacceptable adverse effects.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/13	Status: On-going

Title: GOG 81/F: A Phase I-II Trial of Tamoxifen Citrate in Patients with Advanced or Recurrent Endometrial Carcinoma Responsive to Progestins

Start Date: 18 Oct 85	Est Completion Date: Indefinite
Department: OB/GYN	Facility: MAMC
Principal Investigator:	COL Roger B. Lee, MC
Associate Investigators:	COL William Benson, MC
Key Words: carcinoma, endometrial, tamoxifen citrate, progestins	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0- Periodic Review: Nov 86

Study Objective: To determine whether patients with endometrial carcinoma who have responded to medroxyprogesterone acetate and then progressed will respond to a second hormonal manipulation in the form of tamoxifen citrate.

Technical Approach: Patients must have developed progression of disease on MPA after initial response and must have been off MPA for at least three weeks with no evidence of disease response to withdrawal of MPA unless there is rapid progression, in which case tamoxifen will begin immediately.

Patients will receive tamoxifen, 20 mg p.o., daily. Treatment will be continued until there is evidence of disease progression. An adequate trial is defined as at least one month of therapy.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/23	Status: Completed

Title: GOG 82: A Phase III Trial Comparing Combination Chemotherapy (CAP) with Whole Abdominal Radiation Therapy for Stage III Optimal Epithelial Ovarian Cancer with No Gross Residual Disease or Gross Residual Disease <1 CM**

Start Date: 17 Jan 86	Est Completion Date: Indefinite
Department: OB/GYN	Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC	
Associate Investigators: COL WILLIAM Benson, MC	
Key Words: epithelial ovarian cancer, chemotherapy, radiation	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jan 87

Study Objective: To compare survival and progression free interval of patients with epithelial ovarian cancer, treated with adjuvant whole abdominal and pelvic irradiation or combination chemotherapy; to determine the influence of grade, histology, and treatment in patterns of failure; and to compare the acute and late sequelae of adjuvant radiation therapy and chemotherapy.

Technical Approach: Patients will be stratified to no gross residual cancer or gross residual < 1 CM. After optimal cytoreductive surgery, patients will be randomized to :

Regimen 1: cyclophosphosphamide, doxorubicin, and cisplatin every three weeks for eight courses

or

Regimen II: 3000 cGy total abdominal irradiation by open field technique with an additional 1980 cGy to the pelvis. The total maximum pelvic dose will be 4980 cGy. The total treatment time will be 6-7 weeks. Each patient will be followed one month after the completion of adjuvant treatment, then every three months for the first two years, every six months for the third, fourth, and fifth years, and yearly after the fifth year. Follow-up assessment will include a history, physical examination, x-rays, and blood counts.

**Amendment Mar 86: protocol was amended to include patients with gross residual disease of one centimeter or less. This change necessitated a change in the title to add "or Gross Residual Disease <1 Cm."

Progress: No entries at MAMC in FY 87. One patient was entered on the protocol in FY 86 and subsequently died of disease.

SWOG closed the protocol to entry in Jul 87.

Detail Summary Sheet

Date: 30 Sep 87	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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 86

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: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87725	Status: On-going

Title: GOG 84: Evaluation of a Shortened Course of Vincristine, Dactinomycin and Cyclophosphamide (VAC) as Adjuvant Therapy for Immature Teratoma of the Ovary, Stage I, Grade 2, Completely Resected (Phase II)

Start Date: 21 Nov 86	Est Completion Date: Indefinite	
Department: OB/GYN		Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigators: COL William L. Benson, MC		
Key Words: ovary, immature teratoma, VAC, shortened course, adjuvant therapy, post-surgery		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A

Study Objective: To evaluate vincristine, dactinomycin, and cyclophosphamide (VAC) given in a shortened course as adjuvant chemotherapy for Stage I Grade 2 immature teratomas of the ovary following removal of all gross tumor.

Technical Approach: Previously untreated patients with histologically confirmed immature teratomas of the ovary, Stage I, Grade 2, that has been completely resected will be eligible. Following recovery from surgery, patients will receive vincristine in a single dose of 1.5 mg/^{2} IV every two weeks for 12 courses. Dactinomycin will be given 1.2 mg/m^2 IV every four weeks for 6 courses. Cyclophosphamide will be given 750 mg/m^2 IV every four weeks for six courses. If progression is noted during chemotherapy, patients will be transferred to an appropriate GOG protocol. After completion of therapy, patients will undergo a reassessment laparotomy. Those with progression of disease will be transferred to an appropriate GOG protocol. Those who have no evidence of disease will be followed on no futher therapy. If recurrence develops, the patient will be entered on the appropriate GOG protocol.

Progress: No patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/89	Status: On-going

Title: GOG 85: A Randomized Comparison of Hydroxyurea versus 5-FU Infusion and Bolus Cisplatin as an Adjunct to Radiation Therapy in Patients with Stages II-B, III, and IV-A Carcinoma of the Cervix and Negative Para-aortic Nodes

Start Date: 15 Aug 86	Est Completion Date: Indefinite	
Dept/Svc: OB/GYN		Facility: MAMC
Principal Investigator: COL Roger E. Lee, MC		
Associate Investigators: COL William Benson, MC		
Key Words: carcinoma, cervix, chemotherapy, radiation		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Dec 86

Study Objective: To determine whether hydroxyurea or the combination of 5-FU and cisplatin is superior as a potentiator of radiation therapy in advanced cervical carcinoma and to determine the relative toxicities of hydroxyurea versus the combination of 5-FU and cisplatin when given concurrently with radiation therapy.

Technical Approach: Patients with invasive squamous cell, adenocarcinoma, or adenosquamous carcinoma of the cervix, Stages II-B, III, and IV-A, who meet the eligibility requirements as listed in the protocol, will undergo clinical staging as permitted by FIGO rules. All patients will undergo surgical staging to include extraperitoneal sampling of the para-aortic lymph nodes, peritoneal cytology, and intraperitoneal exploration. Patients with cancer confined to the pelvis will receive pelvic irradiation and will be randomly assigned to receive either concomitant 5-FU and cisplatin or hydroxyurea. Patients with disease outside the pelvis are not eligible for this protocol. The study will continue as long as treatment protocols remain activated. The patients will be followed for two years and then every six months for three additional years.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/14	Status: On-going

Title: GOG 86/A: Master Protocol for Phase II Drug Studies in Treatment of Recurrent Carcinoma of the Endometrium

Start Date: 18 Oct 85	Est Completion Date: Oct 87	
Department: OB/GYN		Facility: MAMC
Principal Investigator:	COL Roger B. Lee, MC	
Associate Investigators:	COL William L. Benson, MC	
Key Words: carcinoma, endometrium, recurrent, master protocol		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A**

Study Objective: To identify additional active agents, by studying single new drugs, in patients with advanced or recurrent endometrial carcinoma not previously exposed to chemotherapy. Sections relating to specific agents will be sequentially incorporated into this protocol as the use of each agent is approved by the Institutional Review Board.

Treatment of advanced or recurrent carcinoma of the endometrium has been studied only in a relatively small number of cases. To date, only hormonal therapy with progestins or tamoxifen and the cytotoxic drug adriamycin have been shown to be conclusively active. This study seeks to identify additional active agents by studying single new drugs in patients with advanced or recurrent endometrial carcinoma not previously exposed to chemotherapy. Approximately 30 evaluable patients will be accrued for each drug studied to allow for reasonable estimates of response rates.

Technical Approach: Specific treatment regimens will be given for each protocol as that section is submitted for approval. The principal parameters employed to evaluate the efficacy of each agent will be: the frequency and duration of objective response; the frequency and severity of observed adverse effects; survival time for all patients; and duration of progression-free interval for all patients. Anticipated annual accrual group-wide is approximately 40 patients (0-5 at MAMC). See section 2.0 of the master protocol for patient eligibility and exclusions. Consent forms will be provided for the use of each agent as the protocol for that agent is submitted for approval.

Progress: No entries at MAMC.

**Continuing review will be performed for individual protocols.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/15	Status: Completed

Title: GOG 86/B: A Phase II Trial of Hexamethylmelamine (NSC #13875) in Patients with Advanced or Recurrent Endometrial Carcinoma

Start Date: 18 Oct 85	Est Completion Date: Oct 87	
Department: OB/GYN		Facility: MAMC
Principal Investigator:	COL Roger B. Lee, MC	
Associate Investigators:	COL William L. Benson, MC	
Key Words: carcinoma, endometrial, recurrent, hexamethylmelamine		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 86

Study Objective: To identify additional active agents, by studying single new drugs, in patients with advanced or recurrent endometrial carcinoma not previously exposed to chemotherapy.

Technical Approach: Patients will receive hexamethylmelamine, 280 mg/M^2 orally daily, on days 1-14 of each 4 week course. Each day's dose will be given in 4 divided doses after meals and at bedtime. An adequate trial will be at least one drug course and follow-up totaling 4 weeks. The drug will be continued until there is documentation of disease progression or unacceptable adverse effects.

Progress: No entries at MAMC. This protocol was closed to patient entry by GOG in December 1986.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/26	Status: On-going

Title: GOG 86D: A Phase II Trial of Methotrexate (NSC 740) in Patients with Advanced or Recurrent Endometrial Carcinoma

Start Date: 21 Nov 86	Est Completion Date: Indefinite
Department: OB/GYN	Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC	
Associate Investigators: COL William L. Benson, MC	
Key Words: carcinoma, endometrial, methotrexate, phase II	

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

Study Objective: To identify additional active agents, by studying single new drugs, in patients with advanced or recurrent endometrial carcinoma not previously exposed to chemotherapy.

Technical Approach: Patients will receive methotrexate, 40 mg/m^2 IV, once weekly for a total of 12 weeks. After 12 weeks, patients with stable or responding disease will be continued on the same dosage every other week until there is documentation of disease progression or unacceptable side effects.

An adequate trial is defined as at least four weeks of therapy. Patients who die of progressive disease before this will be considered treatment failures and considered to have a progressive disease response. Patients who have toxicity before the four weeks and who are removed from the study will be considered evaluable for toxicity but not response.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/27	Status: On-going

Title: GOG 86E: A Phase II Trial of Vincristine (VCR) Given as a Weekly Intravenous Bolus in Advanced or Recurrent Endometrial Carcinoma

Start Date: 21 Nov 86	Est Completion Date: Indefinite	
Department: OB/GYN		Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigators: COL William L. Benson, MC		
Key Words: carcinoma, endometrial, vincristine, phase II		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A

Study Objective: To identify additional active agents, by studying single new drugs, in patients with advanced or recurrent endometrial carcinoma not previously exposed to chemotherapy.

Technical Approach: Vincristine will be given as an IV bolus at a dose of 1.4 mg/m^2 (maximum dose 2.0 mg) weekly for four weeks. Patient response will be evaluated on the fifth week. Responders (complete or partial remission or stable disease) will be treated on the fifth week and then continued on treatment every two weeks until progression of disease or the development of unacceptable adverse effects.

An adequate trial is defined as at least four weeks of therapy. Patients who die of progressive disease before this will be considered treatment failures and considered to have a progressive disease response. Patients who have toxicity before the four weeks and who are removed from the study will be considered evaluable for toxicity but not response.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/101	Status: On-going

Title: GOG 86F: A Phase II Trial of Mitomycin-C (NSC #26980) in Patients with Advanced Endometrial Carcinoma

Start Date: 21 Aug 87	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, endometrial, advanced, mitomycin-C	

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

Study Objective: To identify additional active agents, by studying single new drugs, in patients with advanced or recurrent endometrial carcinoma not previously exposed to chemotherapy.

Technical Approach: Patients will receive mitomycin-C, 20 mg/m^2 IV, every six weeks for two doses and then 10 mg/m^2 every six weeks thereafter, except for those patients at high risk for myelosuppression. No treatment course will be started until the white blood count is >100,000/mcl. Therapy will continue until there is documentation of disease progression or unacceptable adverse effects.

An adequate trial is defined as at least one drug course. Patients who receive at least one drug dose and follow-up adequate to permit assessment of response will be considered fully evaluable. Patients whose follow-up is inadequate to permit response assessment will be considered evaluable for toxicity only.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/24	Status: On-going

Title: GOG 87A: Master Protocol for Phase II Drug Studies in the Treatment of Recurrent or Advanced Uterine Sarcomas

Start Date: 17 Jan 86	Est Completion Date: Indefinte
Department: OB/GYN	Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC	
Associate Investigators: COL William L. Benson, MC	
Key Words: sarcoma, uterine, recurrent, master protocol, drugs	

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

Study Objective: To identify new agents and combinations for treating this malignancy and to allow the best possible chance for a new cytotoxic agent to demonstrate activity. This study constitutes a Phase II design in a population of patients who have had no prior drug therapy.

Technical Approach: The study design will involve treating an average sample size of 30 evaluable patients per drug studied for each of the following cell type categories:

Mixed mesodermal tumor
Leiomyosarcoma
Other sarcomas

Patients will have had no prior drug therapy. Since this is a Phase II study, no randomization is involved. The principal parameters employed to evaluate the efficacy of each agent are:

The frequency and duration of objective response.
The frequency and severity of observed adverse effects.
Survival time for all patients.
Duration of progression-free interval for all patients.

In order to estimate the true response rate and be 90% certain that the estimate is within +15%, 30 evaluable patients per histologic category will be needed (group wide). Reviews will be held at least twice yearly. Consequently, on at least two occasions, early termination can be considered if the results do not warrant conducting the study to completion. Although the exact number of patients accessioned cannot be forecasted at this time, the relatively slow accrual rates guarantee that inactive agents will be expeditiously recognized. The active phase of this study for each drug should be approximately:

Mixed mesodermal tumor - 1 to 1 1/4 years
Leiomyosarcoma - 3 years
Other sarcomas - 6 years

Progress: No entries at MAMC.

**Continuing review will be done on individual protocols.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/25	Status: On-going

Title: GOG 87B: A Phase II Trial of Ifosfamide (NSC #109724) and the Uroprotector, Mesna (NSC #25232), in the Treatment of Recurrent or Advanced Uterine Sarcomas

Start Date: 17 Jan 86	Est Completion Date: Indefinite
Department: OB/GYN	Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC	
Associate Investigators: COL William L. Benson, MC	
Key Words: sarcoma, uterine, recurrent, ifosfamide, mesna	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jan 87

Study Objective: To allow the best possible chance for a new cytotoxic agent to demonstrate activity. This study constitutes a Phase II design in a population of patients who have had no prior drug therapy. The study design will involve treating an average sample size of 30 evaluable patients for mixed mesodermal tumor, leiomyosarcoma, and other sarcomas. This will allow agents found to be ineffective to be rapidly replaced by other agents.

Technical Approach: Ifosfamide will be given in an initial dose of 1.8 g/M^2 daily for five days except those patients who have received prior pelvic radiation therapy. These patients will start at an initial dose of 1.5 g/M^2 daily for five days, once every four weeks. Mesna will be 20% of the ifosfamide dose, given three doses daily, at the completion of ifosfamide administration and four and eight hours after ifosfamide in order to reduce the urothelial toxicity of ifosfamide. Dosage will be modified according to adverse effects.

Ad adequate trial is defined as receiving one course of treatment and living four weeks for an additional tumor measurement. Toxixity, however, may be assessed as soon as the patient receives the drug. Each patient will remain on study and continue to receive the drug until the disease progresses or until adverse effects prevent further treatment.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/102	Status: On-going

Title: GOG 87C: A Phase II Trial of Hydroxyurea, Dacarbazine (DTIC) and Etoposide (VP-16) in Patients with Advanced or Recurrent Uterine Sarcomas

Start Date: 21 Aug 87	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: sarcoma, uterine, recurrent, hydroxyurea, DTIC, VP-16	

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

Study Objective: To identify new agents and combinations for treating this malignancy; to allow the best possible chance for a new cytotoxic agent to demonstrate activity. This study constitutes a Phase II design in a population of patients who have had no prior drug therapy. The study design will involve treating an average sample size of 30 evaluable patients for mixed mesodermal tumor, leiomyosarcoma, and other sarcomas. This will allow agents found to be ineffective to be rapidly replaced by other agents.

Technical Approach: The treatment regimen combines hydroxyurea, a chemotherapeutic agent with a known cell-cyle synchronizing effect with DTIC, an antimetabolite, and VP-16, a premitotic inhibitor.

On Day 1, Hydroxyurea, 500 mg capsules, will be given p.o. every 6 hours with no restrictions on diet or activity. On Day 2, VP-16, 100 mg/m^2, diluted in 250 cc NS will be infused over one hour beginning at exactly 24 hours after the start of hydroxyurea, followed by DTIC, 700 mg/m^2, diluted in 500 cc D_5W, infused over four hours. On Day 3, VP-16, 100 mg/m^2, diluted in 250 cc NS will be infused over one hour. On Day 4, VP-16, 100 mg/m^2, dilutes in 250 cc NS will be infused over one hour. Premedication with antiemetic regimens will be given on Day 2. The treatment course will be administered every four weeks, if toxicity permits and will continue for 12 courses unless progression occurs.

An adequate trial is defined as receiving one course of treatment and living four weeks. If the patient suffers progressive disease before four weeks elapse, this indicates treatment failure. Patients will remain on study and continue to receive therapy for 12 months unless there is progression or adverse effects which prohibit further therapy. Patients who die of drug-related complications prior to having their disease re-evaluated will be considered inevaluable for response but evaluable for toxicity.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/103	Status: On-going

Title: GOG 87D: A Phase II Trial of VP-16 (NSC #141540) in Patients with Advanced Uterine Sarcoma

Start Date: 21 Aug 87	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: sarcoma, uterine, advanced, VP-16	

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

Study Objective: To identify new agents and combinations for treating this malignancy; to allow the best possible chance for a new cytotoxic agent to demonstrate activity. This study constitutes a Phase II design in a population of patients who have had no prior drug therapy. The study design will involve treating an average sample size of 30 evaluable patients for mixed mesodermal tumor, leiomyosarcoma, and other sarcomas. This will allow agents found to be ineffective to be rapidly replaced by other agents.

Technical Approach: Patients will receive VP-16, 125 mg/m^2 IV, daily for three days every three weeks except for those patients at high risk for myelosuppression. No treatment course will be started until the white blood count is >3000/mcl and platelets are >100,000/mcl.

An adequate trial is defined as at least one course. Patients who receive at least one drug dose and follow-up adequate to permit assessment of response will be considered fully evaluable. Patients whose follow-up is inadequate to permit response assessment will be considered evaluable for toxicity only. The therapy will be continued until there is documentation of disease progression or unacceptable adverse effects.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/90	Status: On-going

Title: GOG 88: A Randomized Study of Radical Vulvectomy and Bilateral Groin Dissection versus Radical Vulvectomy and Bilateral Groin Radiation

Start Date: 15 Aug 86	Est Completion Date: Indefinite
Dept/Svc: OB/GYN	Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC	
Associate Investigators: COL William Benson, MC	
Key Words: vulvectomy, radical, groin dissection, groin radiation	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0- Periodic Review: Dec 86

Study Objective: To evaluate the comparative efficacy and morbidity of groin radiation therapy in lieu of groin dissection for selected patients with invasive squamous cell carcinoma of the vulva and to monitor patterns of recurrence and survival of patients treated with groin radiation therapy in lieu of groin dissection.

Technical Approach: Patients with invasive squamous cell carcinoma of the vulva who meet eligibility criteria as listed in the protocol will be randomized between radical vulvectomy and groin dissection and radical vulvectomy and groin radiation therapy. Complete clinical and radiographic evaluation will be performed prior to randomization. Needle aspiration cytology will be performed if there is concern over groin node status.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/13	Status: On-going

Title: GOG 90: Evaluation of Cisplatin, Etopside, and Bleomycin (BEP) Induction Followed by Vincristine, Dactinomycin, and Cyclophosphamide (VAC) Consolidation in Advanced Ovarian Germ Cell Tumors

Start Date: 17 Oct 86	Est Completion Date: Indefinite
Department: OB/GYN	Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC	
Associate Investigators: COL William L. Benson, MC	
Key Words: tumors, ovarian, germ cell, BEP induction, VAC	

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

Study Objective: To evaluate the effect of induction chemotherapy with cisplatin plus etoposide plus bleomycin (BEP) followed by consolidation with vincristine plus dactinomycin plus cyclophosphamide (VAC) in previously untreated patients with advanced ovarian germ cell tumors.

Technical Approach: After adequate recovery from surgery, if done, previously untreated patients will be treated by three courses of BEP followed by three courses of VAC. Patients exhibiting disease progression on either phase will be taken off study. Patients who had previous VAC or similar regimens will be treated with four courses of BEP. After recovery from BEP therapy, reassessment laparotomy will be performed in patients with negative markers who are clinically free of disease. Progressing patients will be removed from the study. Patients with no evidence of disease at second look will be followed. Patients with persistent disease at second look will be removed from the study.

An adequate trial is defined as receiving two courses of the drug and living at least six weeks. Each patient will remain on study until adverse effects prohibit further therapy or until evidence of progression of disease.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/104	Status: On-going

Title: GOG 92: Treatment of Selected Patients with Stage 1B Carcinoma of the Cervix After Radical Hysterectomy and Pelvic Lymphadenectomy: Pelvic Radiation Therapy Versus No Further Therapy

Start Date: 21 Aug 87	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, cervix, pelvic radiation vs no therapy	

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

Study Objective: To determine the value of adjunctive pelvic radiation in the treatment of Stage 1_B carcinoma of the cervix but with selected high-risk factors; to determine the recurrence-free interval, survival and patterns of failure in those patients; and to determine the morbidity of adjunctive pelvic radiation following radical hysterectomy.

Technical Approach: All patients with Stage 1_B cancer of the cervix who have been treated by radical hysterectomy and pelvic node dissection and found to have cancer confined to the cervix and who have a large tumor and/or lymph or blood vessel invasion in the cervix will be eligible to enter the study. Patients will be randomized to one of two groups. One group will receive external radiation therapy to the pelvis and the other group will receive no further therapy. Patients assigned to receive the radiation therapy will receive the therapy daily for 4 to 6 weeks. Both groups of patients will be required to have check-ups every three months for three years and then every six months for two more years.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/48	Status: On-going

Title: GOG 94: A Phase II Study of the Treatment of Papillary Serous Carcinoma of the Endometrium Stages I and II and Maximally Debulked Advanced Endometrial Carcinoma with Total Abdominal Radiation Therapy

Start Date: 27 Feb 87	Est Completion Date: Indefinite
Department: OB/GYN	Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC	
Associate Investigator: COL William Benson, MC	
Key Words: carcinoma, endometiral, papillary serous, radiation	

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

Study Objective: To determine the survival and progression-free interval of patients with maximally debulked advanced endometrial carcinoma treated with abdominal radiation and to determine the progression-free interval and site of recurrence in patients with Stage I or II papillary serous carcinoma of the endometrium treated with abdominal radiation therapy with pelvic boost.

Technical Approach: Following surgery, the whole abdomen will be irridiated with opposed fields to a total dose of 3000 cGy in 20 fractions of 150 cGy each. If the treatment is not tolerated because of GI symptoms or leukopenia, the daily fraction will be decreased to 125 cGY per day. Whole abdominal radiation will require four to five weeks.

Following whole abdominal radiation, the pelvis will be boosted to a midplane dose of 980 cGy at 180 cGy per fraction for eleven treatments. The combined whole abdominal radiation and the total pelvic field radiation will require a total time of approximately six to seven weeks.

Patients will be followed quarterly for the first two years after completion of therapy and semi-annually for an additional three years.

Patients will continue on protocol until disease progression or adverse effects necessitates removal from the study. An adequate trial will consist of receipt of any protocol therapy.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/28	Status: On-going

Title: GOG 95: Randomized Clinical Trial for the Treatment of Women with Selected Stage IC and II (A,B,C,) and Selected Stage IAi & IBi and IAii & IBii Ovarian Cancer, Phase III

Start Date: 21 Nov 86	Est Completion Date: Indefinite	
Department: OB/GYN		Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC		
Associate Investigators: COL William L. Benson, MC		
Key Words: cancer, ovarian, chemotherapy, staged, cyclophosphamide, cisplatin, P32		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A

Study Objective: In definitively staged patients who have tumor involving one or both ovaries with pelvic extension and/or malignant ascites and/or positive peritoneal washings and in those Stage IAi and IBi patients with poorly differentiated tumors and stage IAii and IBii (all grades) to: compare the progression-free interval and overall survival of the two treatment regimens; determine the patterns of relapse for each form of therapy; and define the relative toxicities of the two treatment approaches.

Technical Approach: The study design will be a randomized comparison between the standard adjuvant treatment (P32) and an experimental arm of short term intensive adjuvant combination chemotherapy with cyclophosphamide/cisplatin. One to two weeks following surgery, P32 therapy will be started. Fifteen millicuries of chromic phosphate suspension mixed in 500 cc of normal saline will be infused into the peritoneal cavity via the peritoneal dialysis catheter after a technetium scan or abdominal x-rays with contrast material has demonstrated adequate distribution. In order to facilitate distribution of the P32, the patient will be turned every 15 minutes to the left side, onto the back, in Trendelenburg and reverse Trendelenburg positions, onto the right side and so on for two hours following the infusion.

Chemotherapy will consist of cyclophosphamide, 1 mg/m^2 I.V., on day 1 plus cisplatin, 100 mg/m^2 IV, on day 1 administered one hour after cyclophosphamide. Cycles of combination chemotherapy will be repeated every three weeks depending upon the time to recovery of the blood counts to pretreatment level. Cycles of chemotherapy will be repeated for a total of three cycles. Patient follow-up will continue until death, loss of follow-up, or termination of the study. Patients will remain on study until disease progression or adverse effects dictate otherwise. An adequate trial is defined as receipt of at least one course of therapy and one follow-up visit.

Progress: Two patients have been entered on the study at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/40	Status: On-going

Title: GOG 97: Phase III Randomized Study of Cyclophosphamide (NSC #26271) and Cisplatin (NSC #119875) in Patients with Suboptimal Stage III and Stage IV Epithelial Ovarian Carcinoma Comparing Intensive and Non-intensive Schedules

Start Date: 16 Jan 87	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, epithelial, cyclophosphamide, cisplatin, intensive vs non-intensivve	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-
	Periodic Review: N/A

Study Objective: To determine response rate, response duration and survival in suboptimal Stages III and IV ovarian carcinoma treated with Cytoxan and cisplatin administered by two different schedules, one intense and the other standard; to determine the relative toxicities of the two schedules; the therapeutic index of the two schedules; to evaluate if dose intensity is directly correlated with tumor response, response duration, and survival; to examine quality of life through the use of the FLIC questionnaire, and examine the ability of CA-125 levels to predict tumor response.

Technical Approach: Following optimal initial surgery, patients will be stratified according to whether or not measurable disease is present. They will then be randomized to cyclophosphamide, 1000 mg/m^2 and cisplatin 100 mg/m^2 every 21 days for four courses or to cyclophosphamide, 500 mg/m^2 and cisplatin 50 mg/m^2, every 21 days for eight courses. Patients with partial response, stable disease, or increasing disease will then go off study. Patients with no clinical evidence of disease will have second look surgery. Those with residual disease will go off study. Those with no evidence of disease will be followed every month for six months, then every three months for four years, and yearly thereafter. The FLIC quality of life evaluation will be completed by the patient when the consent form is signed, prior to each course of therapy, and six weeks after the last course of therapy or at the time of the second reassessment, whichever comes first. CA-125 levels will be recorded prior to admission, immediattely after the intitial course of therapy, after each course, on completion of therapy and at each follow-up for three years.

Adequate trial to evaluate response is defined as receiving one course of therapy and living three weeks for repeat lesion measurement. Adequate trial to evaluate toxicity is defined as receiving one course of therapy and receiving any follow-up information for observation of toxicity.

Progress: One patient was entered at MAMC in FY 87.

Detail Summary Sheet

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

Title: GOG 99: A Phase III Randomized Study of Adjunctive Radiation Therapy in Intermediate Risk Endometrial Adenocarcinoma

Start Date: 19 Jun 87	Est Completion Date: Indefinite
Department: OB/GYN	Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC	
Associate Investigators: COL William L. Benson, MC	
Key Words: adenocarcinoma, endometrial, adjunctive radiation	

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

Study Objective: To determine if patients with intermediate risk endometrial adenocarcinoma who have no spread of disease to the lymph nodes benefit from postoperative pelvic radiotherapy and to evaluate how the addition of pelvic radiotherapy will alter the site and rate of cancer recurrence in these intermediate risk patients.

Technical Approach: Patients with primary histologically confirmed Grade 2 or 3 endometrial adenocarcinoma (endometrioid, villoglandular, mucinous and adenosquamous) and clear cell carcinoma will be eligible. Patients must have had a total abdominal hysterectomy, bilateral salpingo-oophorectomy, selective pelvic and para-aortic node sampling, pelvic washings and found to be surgical Stage 1 with myometrial invasion. Following surgery, patients will be randomized to no additional treatment of pelvic radiation therapy to begin no later than eight weeks after surgery. Those randomized to radiation therapy will be treated with AP and PA parallel ports with each port being treated each day. A daily tumor dose of 180 cGy will be given to a total dose of 5040 cGY in approximately six weeks. Each patient will be followed with regular visits occurring every three months for the first two years, every six months for the third, fourth and fifth years, and yearly thereafter.

Progress: Two patients were entered at MAMC in FY 87.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/105	Status: On-going

Title: GOG 100: Monoclonal Antibody Against Free Beta HCG to Predict Development of Persistent Gestational Trophoblastic Disease (PGTD) in Patients with Hydatidiform Mole

Start Date: 21 Aug 87	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: PGTD, hydatidiform mole, free beta HCG, monoclonal antibody	

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

Study Objective: To measure the serum concentration of free beta HCG and total beta HCG in patients with molar pregnancies in order to determine whether the ratio of free beta HCG to total beta HCG may be of value in predicting which molar pregnancies will undergo spontaneous remission and which will subsequently develop into persistent gestational trophoblastic disease.

Technical Approach: Patients with gross and microscopically verified diagnosis of hydatidiform mole, either classic (true) or partial (incomplete), obtained by evacuation of the uterus with uterine conservation will be eligible. Patients will have a pelvic ultrasound within two weeks of evacuation and the first serum will be drawn within 48 hours (prior to if at all possible) of evacuation for beta HCG and free beta HCG determinations. Following histologic confirmation of the hydatidiform mole (within one week of evacuation) the patient will be placed on study. Serum samples will be obtained weekly until a negative assay is attained or until a plateau or rise in titer is observed. All patients will remain on study for a minimum of twelve weeks after primary evacuation of the molar pregnancy. After spontaneous remission, patients will have beta HCG titers monthly for six months (free beta HCG assay is not necessary). After persistent disease, the patient will remain on study until remission. The principle parameters employed to investigate the prediction of which molar pregnancies will undergo spontaneous remission and which will subsequently develop into persistent trophoblaastic disease are free beta HCG, total HCG concentration, ratio of free beta HCG to total HCG, and remission of disease as determined by weekly titers.

Progress: No patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/106	Status: On-going

Title: GOG 101: A Phase II Evaluation of Pre-operative Chemoradiation for Advanced Vulvar Cancer

Start Date: 21 Aug 87	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: cancer, vulvar, chemoradiation, pre-operative	

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

Study Objective: To determine: the feasibility of using preoperative chemoradiotherapy to obviate the need for pelvic exenteration for patients with advanced vulvar cancer involving the proximal urethra, bladder, anal canal, or rectum; the feasibility of allowing a less extensive vulvar and vaginal resection in patients with a T3 primary tumor by using preoperative chemoradiotherapy; the survival rate for patients with Stage III or IV-A disease associated with this technique of therapy; the morbidity of a combined chemoradiosurgical approach to advanced vulvar cancer and to attempt to improve survival in patients with N3 groin nodes.

Technical Approach: Patients with primary, previously untreated, histologically confirmed invasive squamous or adenocarcinoma of the vulva clinically determined to be Stage III or IV will be treated with chemoradiation therapy according to the sub-stage.

Regimen I: Patients with T4 or unresectable T3 primary tumor and NO or N1 groin nodes will receive a split course of radiation therapy to the vulva by AP-PA fields. Twice daily fractions of cGY will be given on days 1-4 and 1'-4'; once daily fractions 180 cGY will be given on days 5, 8-12 and 5', 8'-12'. A 1 1/2 to 2 1/2 week split will be allowed between the two courses. Total midplane dose will be 4560 cGY.

During the twice daily radiation (days 1-4 and 1'-4'), patients will receive concurrent chemotherapy of 5-FU, 1000 mg/m^2 over 24 hours, allopurinol, 300 mg p.o., and cisplatin, 50 mg/m^2 IV, (days 1 and 1' only). Four to eight weeks following completion of chemoradiotherapy, patients considered to have resectable disease without the need for an exenterative procedure will undergo excision of the area previously replaced by primary tumor. An inguinal/femoral lymphadenectomy will also be performed.

Regimen II: The same as Regimen I with the addition of radiation to the inguinal/femoral and low pelvic lymph nodes. Total dose will be the same.

Progress: No patients have been entered at MAMC.

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 87	Protocol No.: 81/33	Status: On-going

Title: NCI #7602: All Stage I_C and II (A, B, C) and Selected Stage I_{Aii} and I_{Bii} 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 Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jan 87

Study Objective: To define the natural history of patients treated with surgery plus either chemotherapy or radioisotope; to study the effect of various potential prognostic factors on the natural history of patients treated by each form of therapy; to determine the patterns of relapse for each form of therapy; to establish the value of various staging parameters on the stage of disease and its natural history.

Technical Approach: All patients with common epithelial ovarian cancer are eligible, if after definitive staging procedures the patient is zoned to be in Stages 2_A, 2_B, 2_C, 1_{Aii}, 1_{Bii}, or 1_{Ai} or 1_{Bi} 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 II_B, II_C, 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: No new entries in FY 87 at MAMC. The protocol was closed to new patient entry in September 1986. Two patients were entered in previous years and are still in follow-up.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 81/102	Status: Completed

Title: NCI #I80-12: 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:	MAJ Thomas Baker, MC
Associate Investigators:	COL Irwin B. Dabe, MC COL F. H. Stutz, MC LTC Lauren K. Colman, MC LTC Alan Mease, MC
Key Words:	delta-9-tetrahydrocannabinol, guidelines

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jul 87

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/m^2 p.o., will be administered 6-8 hours prior to the administration of chemotherapy and for 12 hours thereafter. Should the 5 mg/m^2 dose prove to be ineffective, and in the absence of significant side effects, the dose may be escalated to 7.5 mg/m^2. Any untoward side effects will be reported to the NCI.

Progress: A total of 18 patients was entered at MAMC. Drowsiness was the only reported side effect.

The protocol was closed in July 1987 because the drug was released by the FDA.

D E T A I L S H E E T S

F O R

P R O T O C O L S

PUGET SOUND ONCOLOGY CONSORTIUM

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87771	Status: On-going

Title: PSOC 507: 5-FU, Cisplatin and VP-16 in the Treatment of Sub-optimal Stage III-IV Ovarian Cancer

Start Date: 17 Apr 87	Est Completion Date: Apr 90	
Dept/Svc: Medicine/Hematology		Facility: MAMC
Principal Investigator: LTC Howard Davidson, MC		

Associate Investigators:

COL Irwin B. Dabe, MC	
COL Roger B. Lee, MC	MAJ David Dunning, MC
LTC Lauren K. Colman, MC	MAJ Ruben Sierra, MC
MAJ Thomas M. Baker, MC	CPT David R. Bryson, MC

Key Words: cancer, ovarian, sub-optimal stages III-IV, 5-FU cisplatin, VP-16

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

Study Objective: To determine the response rate and side effects in patients with ovarian cancer to a combination chemotherapy regimen of 5-FU, Cisplatin, and VP-16.

Technical Approach: Patients with a histologically confirmed diagnosis of ovarian cancer and disease that is either measurable by physical exam or CT scan or evaluable (CA-125 >100 is considered evaluable disease) will be eligible. Patients will be stratified based on measurable or evaluable disease and prior or no prior treatment.

5-FU by continuous infusion of 800 mg/m^2 per day will be given for four consecutive days (days 1-4).

Cisplatin, 100 mg/m^2 will be administered in 1000 ml D_5NS with 37.5 g mannitol IV over 1-2 hours on day 1. The starting dose for patients with serum creatinine 1.8-2.2 mg/dl will be 50 mg/m^2 on day 2. Those >65 or with extensive prior chemo or radiation therapy will start at 75 mg/m^2.

VP-16, 75 mg/m^2, will be administered in 250 ml D_5W over 1 hour on days 1-3. Patients >65 years or with extensive prior chemo or radiation therapy will start at 55 mg/m^2.

Drug alteration or removal from the study will be made for each course, based on the toxicity encountered.

Treatment will be repeated every 21 days. Patients with rapidly progressive disease after one cycle or progression after two cycles will be considered treatment failures and removed from the study.

An adequate trial is defined as at least one complete cycle of therapy showing some biologic activity (Grade 1 or greater toxicity) from drug(s) or two cycles with appropriate dose escalation if no toxicity is observed in the first cycle.

Progress: One patient was entered in FY 87 at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/79	Status: On-going

Title: PSOC 615: Intraperitoneal Consolidation Therapy Following Second-Look Operation in Ovarian Cancer

Start Date: 15 May 87	Est Completion Date: Indefinite
Department: OB/GYN	Facility: MAMC
Principal Investigator: COL Roger B. Lee, MC	
Associate Investigators: COL William L. Benson, MC	
Key Words: cancer, ovarian, P-32, cis-platinum, 5-FU, surgery	

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

Study Objective: To examine the effect of intraperitoneal therapy on disease free survival in patients with no disease or minimal residual disease following second-look surgery and to document the complication rate associated with the use of intraperitoneal chromic phosphate or chemotherapy in patients previously treated with systemic chemotherapy.

Technical Approach: Following standard induction chemotherapy, patients with Stage IIb, IIc, or III epithelial carcinoma of the ovary will have second-look laparotomy in the standard fashion. The second look procedure will include resection of any remaining female genital organs (ovaries, tubes, or uterus). If the patient has no evidence of gross persistent disease greater than 1.0 cm at the time of second look, a Tenckhoff catheter will be inserted.

If the pathologic findings from the second look procedure show no evidence of persistent tumor, the patient will receive 15 millicuries of intraperitoneal P-32 in 1000-1500 ml of normal saline, with appropriate rotation of position to assure proper distribution of the P-32.

If the patient has positive disease within the peritoneal cavity, she will receive chemotherapy with cisplatin (100 mg/m^2) and 5-FU (1000 mg/m^2) through the Tenckhoff catheter every three weeks for a maximum of four doses unless there are unacceptable side effects.

Progress: One patient was entered in FY 87 at MAMC.

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 87	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:	LTC Howard Davidson, MC
Associate Investigators:	COL Friedrich Stutz, MC LTC H. Irving Pierce, MC Suresh B. Katakkar, M.D., DAC
Key Words:	adenocarcinoma, gastric, adjuvant FAM vs surgery
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0- / Periodic Review: Jun 87

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/M^2 IV days 1 & 8, 29 & 36
adriamycin, 30 mg/M^2 IV days 1 & 29
mitomycin-C, 10 mg/M^2 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 87 at MAMC. One entry in FY 84 at MAMC on the observation arm.

Group-wide: Of 67 patients evaluated for toxicity, there was one fatal cardiac toxicity which occurred in a patient receiving adjuvant FAM therrapy. Two other patients experienced life-threatening thrombocytopenia while 27 patients had severe toxicities. The moderate "cardiac other" toxicites were pericardial effusion (1 patient), elevated PIP/LVET (1 patient), and ejection fraction of .47 (1 patient), and clinically mild coronary heart failure (1 patient). The miscellaneous other toxicity was pulmonary fibrosis.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 78747	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: Jan 88	
Dept/Svc: Medicine/Oncology		Facility: MAMC
Principal Investigator:	LTC Howard Davidson, MC	
Associate Investigators:	COL Friedrich Stutz, MC LTC James E. Congdon, MC LTC H. Irving Pierce, MC Suresh B. Katakkar, M.D., DAC	
Key Words: Hodgkin's disease, stages III and IV, MOPP #6		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jul 87

Study Objective: To attempt to increase the complete remission rate induced with MOP-BAP (nitrogen mustard, vincristine, procarbazine, prednisone, adriamycin, and bleomycin) alone utilizing involved field radiotherapy in patients with Stages III and IV Hodgkin's disease achieving partial remission at the end of 6 cycles; and to determine if immunotherapy maintenance with levamisole or consolidation with low dose involved field radiotherapy will produce significantly longer remission durations over a no further treatment group when complete remission has been induced with 6 cycles of MOP-BAP in Stages III & IV Hodgkin's.

Technical Approach: Patients (>15 yrs) must have histologic diagnosis of Hodgkin's disease; no prior chemotherapy. Patients with a history of congestive heart failure, valvular heart disease, or serious obstructive or restrictive pulmonary disease will be excluded. Normal marrow patients will receive six cycles of MOP-BAP. Impaired bone marrow patients will receive six cycles of MOP-BAP with dose modifications. Complete Remission (CR) patients with prior radiotherapy will be randomized to Treatment 3 (no treatment) or Treatment 4 (levamisole). CR patients without prior radiotherapy will receive Treatment 5 (radiotherapy). Partial remission (PR) patients without prior radiotherapy or residual bone marrow involvement will receive Treatment 6 (radiotherapy). PR patients with prior radiotherapy or those with residual bone marrow involvement will receive Treatment 7 (4 additional cycles of MOP-BAP); after ten total cycles of MOP-BAP, patient will continue study on MOP-BAP therapy at the discretion of the investigator.

Progress: No new patients entered at MAMC in FY 87. Seven patients were entered in previous years.

Group-wide: Of 396 previously untreated patients evaluated for response, 79% achieved a complete response in either portion of the protocol. A total of 12 fatal toxicities has been seen. Five fatal toxicities (three due to infections and two to cardiovascular problems) were on the low dose arm and seven were on the high dose arm (all related to infection).

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 7996	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: LTC Howard Davidson, MC	
Associate Investigators: COL Irwin B. Dabe, MC LTC James E. Congdon, MC	
Key Words: carcinoma, breast, combined modality therapy	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jul 87

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: No new patients entered at MAMC in FY 87. Twenty-six patients were entered in previous years.

Group-wide: No fatal toxicities have been reported in the premenopausal patients. Two treatment related deaths (fungal pneumonia on CMFVP and interstitial pneumonitis on CMFVP plus tamoxifen) have been reported in the ER positive post-menopausal patients.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 81780	Status: Completed

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: COL Irwin B. Dabe, MD		
Associate Investigators: COL Friedrich H. Stutz, MC LTC Lauren K. Colman, MC		
Key Words: CML, intermittent busulfan, with or without Vitaman A		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Dec 86

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; therefore is was closed at MAMC in Apr 87 when it was closed to patient entry by SWOG.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 82713	Status: Completed

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	LTC James E. Conaton, MC
COL Irwin B. Dabe, MC	MAJ Thomas Baker, MC
LTC Lauren K. Colman, MC	MAJ Alfred H. Chan, MC

Key Words: melanoma, surgical excision, vitamin A		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Feb 87

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 patient was entered at MAMC in 1982 who was taken off study due to light-headedness and a metallic taste in the mouth. Therefore, this protocol was closed at MAMC when it was closed to patient entry in March 1987 by SWOG.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 83705	Status: Completed

Title: SWOG 8107: Mamanqement 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	
COL Irwin B. Dabe, MC	MAJ Alfred H. Chan, MC	
LTC James E. Congdon, MC	MAJ Timothy J. O'Rourke, MC	
Key Words: melanoma, disseminated, combination chemotherapy		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review Feb 87

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 metasses 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: One new patient in FY 87. This patient was taken off protocol due to progression of disease. Nausea and vomiting were noted as side effects. Two patients were entered previously. Both died of disease with no untoward reactions to the treatment.

SWOG closed the protocol to patient entry in Dec 86 due to sufficient accrual of patients.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/06	Status: On-going

Title: SWOG 8206: Trial Chlorozotocin and 5-FU in Metastatic Islet Cell Carcinoma, Phase II

Start Date: 15 Oct 85	Est Completion Date: Sep 87
Dept/Svc: Medicine/Oncology	Facility: MAMC

Principal Investigator: MAJ Thomas M. Baker, MC

Associate Investigators:

COL Irwin B. Dabe, MC	MAJ David Dunning, MC
LTC Howard Davidson, MC	MAJ Michael D. Stone, MC
MAJ Lauren K. Colman, MC	CPT David R. Bryson, MC

Key Words: carcinoma, islet cell, metastatic, chlorozotocin, 5-FU

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jan 87

Study Objective: To study the response of functioning and non-functioning islet cell carcinoma to Chlorozotocin (CTZ) and 5-fluorouracil (5-FU) and to determine the toxicity of CTZ and 5-FU when given in combination.

Technical Approach: Patients with prior chemotherapy will be ineligible, but those with prior radiation therapy are eligible. Patients will receive CTZ and 5-FU at intervals of 6 weeks.

Induction therapy will consist of the following for a period of 4 courses: Good risk - CTZ, 175 mg/M^2 IV day 1 and 5-FU, 800 mg/M^2 IV, 24 hour infusion, days 1-4. Poor risk - CTZ, 75 mg/M^2 IV day 1 and 5-FU, 600 mg/M^2 IV 24 hour infusion, days 1-4.

Maintenance therapy will consist of: Good risk - CTZ, 100 mg/M^2 IV day 1 and 5-FU, 600 mg/M^2 bolus IV days 1 and 8, every 6 weeks. Poor risk - CTZ, 50 mg/M^2 IV day 1 and 5-FU, 400 mg/M^2 bolus IV days 1 and 8, every 6 weeks.

An adequate trial is one course of therapy in the presence of progressive disease. Therapy with CTZ and 5-FU will be continued in the presence of stable disease or a response until increasing disease is documented. Therapy with CTZ and 5-FU will be continued for a maximum of 18 months in the presence of a complete response.

Progress: No entries at MAMC.

The study is now closed to poor risk patients due to poor accrual.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 85/07	Status: Terminated
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: COL Irwin B. Dabe, MC		
Associate Investigators:		
COL F.H. Stutz, MC	MAJ Timothy O'Rourke, MC	
LTC Howard Davidson, MC	MAJ Michael D. Stone, MC	
MAJ Thomas Baker, MC	CPT David Bryson, MC	
Key Words: multiple myeloma, aclacinomycin A		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Feb 87

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/M_2 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 was entered at MAMC (FY 85) who subsequently expired from hypercalcemia, renal failure, and congestive heart failure associated with his multiple myeloma.

This protocol was suspended in November 1985 by the SWOG in order to study the benefit/risk ratio due to unexpected toxicities. The protocol was terminated by the SWOG in Feb 87 due to drug toxicity.

Detail Summary Sheet

Date: 30 Sep 87	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 William D. Belville, MC	MAJ Alfred E. Chan, MC
COL Irwin B. Dabe, MC	MAJ Timothy J. O'Rourke, MC
COL Friedrich H. Stutz, MC	MAJ Michael D. Stone, MC
Key Words: cancer, bladder, BCG immunotherapy, adriamycin	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0- Periodic Review: Feb 87

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 chemotherpy. Patients who develop tumor recurrence following treatment will be eligible for crossover to the other treatment arm.

Progress:

No patients entered at MAMC in FY 87. Three patients were entered at MAMC during FY 84. All three are being followed with only mild side effects reported (mild leukopenia to intravesical adriamycin and a local reaction to intradermal BCG).

The protocol was closed to new patient entry in December 1985 due to sufficient patient accrual.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 83/60	Status: Completed

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 Irwin B. Dabe, MD	MAJ Thomas M. Baker, MC
COL Friedrich H. Stutz, MC	MAJ Alfred H. Chan, MC
LTC James E. Congdon, MC	MAJ Timothy J. O'Rourke, MC
Key Words: prostate, adenocarcinoma, chemo-endocrine therapy	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Dec 86

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 adeqaute trial. When a total of 300 mg/M^2 adriamycin in good risk or 200 mg/M^2 in poor risk patients has been given, it will be discontinued and cyclophosphamide will be given alone at a dose of 1000 mg/M^2 (good risk) or 750 mg/M^2 (poor risk) every three weeks. Cyclophosphamide will be discontined 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: No entries at MAMC in FY 87. One patient was entered in FY 84, but has been lost to follow-up.

The protocol was closed to patient entry in December 1986 by SWOG.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 8221	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 James M. Baker, MC
COL Irwin B. Dabe, MC	MAJ Alfred H. Chan, MC
COL Donald Kull, MC	MAJ Timothy J. O'Rourke, MC
COL Friedrich H. Stutz, MC	MAJ Michael D. Stone, MC

Key Words: cancer, bladder, irradiation, cystectomy		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Feb 87

Study Objective: To compare survival and pelvic recurrence rates in patients with transitional cell bladder cancer treated with radical surgery alone versus patients treated with preoperative irradiation with 2,000 rads followed by cystectomy.

Technical Approach: Patients eligible to be entered, must have histologically proven transitional cell carcinoma of the urinary bladder, and must have one of the following characteristics:

1. Evidence of muscle invasion.
2. Rapidly recurring superficial high-grade tumors and/or diffuse carcinoma in situ not amenable to transurethral resection and/or intravesical chemotherapy.

Patients will be randomized to receive either surgery with radical cystectomy or radiation therapy plus radical cystectomy. Patients will be seen in follow-up every three months following the cystectomy. Patients with either local or distant recurrence will be removed from the study. Five-year survival rates and two-year recurrence rates will be the major objectives of this study.

Progress: No entries in FY 87. One patient was entered during FY 84 and was randomized to cystectomy alone and tolerated the procedure well. Patient was lost to follow-up in FY 86.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 83/55	Status: Completed

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 Irwin B. Dabe, MC	MAJ Thomas M. Baker, MC
COL Friedrich H. Stutz, MC	MAJ Alfred H. Chan, MC
LTC James E. Congdon, MC	MAJ Timothy J. O'Rourke, MC

Key Words: breast disease, progesterone receptor, tamoxifen		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Dec 86

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/M^2 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 with 86% of patients experiencing mild or no toxicity.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 83761	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 Irwin B. Dabe, MC	MAJ Thomas M. Baker, MC
COL Friedrich H. Stutz, MC	MAJ Alfred H. Chan, MC
LTC James E. Congdon, MC	MAJ Timothy J. O'Rourke, MC
Key Words: multiple myeloma, chemotherapy, radiotherapy	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0- Periodic Review: Jun 87

Study Objective: To compare the effectiveness of two intermittent pulse schedules of VMCP (vincristine, melphalan, cyclophosphamide, and prednisone) and VBAP (vincristine, BCNU, ardiamycin and prednisone) for induction of remission in previously untreated patients with multiple myeloma. Results will also be compared with other combination regimens in previous SWOG studies. In patients proven to achieve remission, to compare the value of 12 months of chemo-immunotherapy maintenance (VMCP + levamisole) vs a consolidation program consisting of sequential half-body radiotherapy plus vincristine and prednisone followed by unmaintained remission. In patients who only achieve improvement, to determine whether sequential half-body radiotherapy plus vincristine and prednisone will increase the remission rate. To determine whether sequential half-body radiotherapy plus vincristine and prednisone can serve as an effective form of induction therapy for patients who fail to respond to chemotherapy or suffer early relapse.

Technical Approach: Patients with previously untreated multiple myeloma will be stratified as to tumor mass status and then randomized to induction therapy on VMCP alternated every three wks with VBAP for a minimum of 6 months to a maximum of one yr or to VMCP for 3 cycles followed by 3 cycles of VBAP, repeated every 3 3 wks, for a minimum of 6 months to a maximum of one year. Upon completion of induction, patients with documented 75% regression with chemotherapy alone will be randomized to receive VMCP + levamisole, repeated every 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, vincristine and prednisone for six weeks.

Progress: No patients were entered at MAMC in FY 87. Five patients have been entered in the study at MAMC and three are still being followed on this study. Two patients had prolonged mild to moderate thrombocytopenia after upper half-body radiotherapy.

The study was closed to patient entry, 15 Mar 87, due to sufficient patient accrual.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 83/68	Status: Completed

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 Irwin B. Dabe, MC	MAJ Timothy J. O'Rourke, MC	
COL Friedrich H. Stutz, MC	MAJ Michael D. Stone, MC	
Key Words: neoplasms, germinal cell, extragonadal, chemotherapy		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Feb 87

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 metastic 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. The protocol was closed by SWOG to patient entry, 15 Oct 86, due to slow accrual.

Detail Summary Sheet

Date: 30 Sep 87	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 Irwin B. Dabe, MC	MAJ Thomas M. Baker, MC	
COL Friedrich H. Stutz, MC	MAJ Alfred H. Chan, MC	
LTC James E. Congdon, MC	MAJ Timothy J. O'Rourke, MC	
Key Words: cancer, breast, operable, node negative, chemotherapy		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jul 87

Study Objective: To assess the impact of short-term intensive chemotherapy with CMEP 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 hispathological 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: One patient was entered in FY 87 for a total of eleven entries.

Groupwide: One patient had fatal toxicity (WBC of 200 followed by pneumonia and pulmonary emboli) and 15 had life-threatening toxicity (mainly hematologic).

Detail Summary Sheet

Date: 30 Sep 87	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	Est Completion Date: Oct 86
Dept/Svc: Medicine/Hematology	Facility: MAMC

Principal Investigator: MAJ Thomas M. Baker, MC

Associate Investigators:

COL Irwin B. Dabe, MC	MAJ Timothy O'Rourke, MC
COL Fredrich H. Stutz, MC	MAJ Michael Stone, MC
LTC Howard Davidson, MC	CPT David Bryson, MC

Key Words: Toxicity, patterns, prophylaxis

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jan 87

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: One patient was entered in FY 87. Two patients were entered in FY 86. One patient expired from disease.

Group-wide, 201 eligible patients have been entered in the study. The accrual goal of 240 eligible patients should be reached in early 1988.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87787	Status: On-going

Title: SWOG 8309: Autologous Marrow Transplantation for the Treatment of Non-Hodgkin's Lymphoma, Phase II-Pilot

Start Date: 19 Jun 87	Est Completion Date: May 90
Dept/Svc: Medicine/Hematology	Facility: MAMC

Principal Investigator: MAJ Thomas M. Baker, MC

Associate Investigators:

COL Irwin B. Dabe, MC	MAJ David Dunning, MC
LTC Howard Davidson, MC	MAJ Ruben Sierra, MC
LTC Lauren K. Colman, MC	CPT David R. Bryson, MC

Key Words: non-Hodgkin's lymphoma, marrow transplantation, autologus

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

Study Objective: To determine the therapeutic potential of high-dose cyclophosphamide and total body irradiation followed by autologous marrow transplantation in patients with an otherwise poor prognosis for cure in the following disease categoris: lymphoblastic lymphoma, Burkitt's lymphoma, or diffuse undifferentiated lymphoma presenting with central nervous system (CNS) involvement or in relapse after intial therapy; diffuse histiocytic lymphoma presenting with CNS/and or marrow involvement or in relapse after initial therapy; and favorable histology lymphomas with recurrent disease after initial therapy.

Technical Approach: Patients as stated in the study objective will be eligible. Bone marrow will be collected and stored until the proper time for implantation as determined by disease category and availability of a transplant bed. Patients will receive a preparative regimen of chemo/radiation therapy consisting of cyclophosphamide (60 mg/kg/day) on two successive days, followed by a day of rest and then fractionated total body irradiation (200 rad/day) for six days, followed on the last day of irradiation by the infusion of the bone marrow. After transplant, patients will receive methotrexate, 12 mg/m^2 intrathecally, on days 32, 46, 60, 74, 88, and 102. Platelets will be transfused to prevent bleeding and an attempt will be made to keep the circulating platelet level >20,000/µl at all times. Infection prophylaxis will be determined by the physician and can include any reasonable form, including laminar air flow isolation, prophylactic granulocytes, or prophylactic antibiotics. Patients with stable disease or a partial or complete remission will be followed until definite evidence of disease progression, at which time they will be taken off study.

Progress: No patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 85762	Status: Completed

Title: SWOG 8310: Evaluation of Aziridinylbenzoquinone (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 Irwin B. Dabe, MC	MAJ Timothy O'Rourke, MC
COL F.H. Stutz, MC	MAJ Michael D. Stone, MC
LTC Howard Davidson, MC	CPT David Bryson, MC

Key Words: AZQ, refractory relapsing myeloma

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: 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/M^2 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.

SWOG closed the protocol to patient registration on 1 Oct 86.

Detail Summary Sheet

Date: 30 Sep 87	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 Irwin B. Dabe, MC	MAJ Timothy J. O'Rourke, MC
COL Friedrich H. Stutz, MC	MAJ Michael D. Stone, MC
Key Words: cancer, breast, ER+, metastatic, chemotherapy	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jan 87

Study Objective: To determine if combination hormonal therapy with aminoglutethimide and hydrocortisone + megestrol acetate, agents thought to have different mechanisms of action, offers an improved response rate with prolonged response duration and increased survival over the sequential use of each agent in ER+ patients who have progressed after responding to primary hormonal treatment with tamoxifen; to assess the relative toxicities of megestrol acetate and medical adrenalectomy, and the value of progesterone receptors in predicting subsequent responses to a variety of hormonal therapies.

Technical Approach: Patients who have had an adequate trial of tamoxifen and have achieved at least a partial response or maintained stable disease for 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., q.i.d., given alone until there is documented evidence of disease progression; Arm II - aminoglutethimide, 250 mg p.o., b.i.d., for 2 weeks, then 250 mg p.o., q.i.d., plus hydrocortisone, 20 mg p.o. upon rising, 20 mg p.o. at 1700 hrs, and 60 mg p.o. at bedtime, daily for 2 weeks, then reduced to 10 mg given on the same schedule; 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 patients were entered at MAMC in FY 87. One patient was entered at MAMC in FY 86 with no adverse effects reported.

Group-wide, toxicity has been moderate on megestrol acetate. Severe or life threatening toxicites were reported in 23% of the patients on the aminoglutethimide arms of the study.

Detail Summary Sheet

Date: 30 Sep 87	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 Irwin B. Dabe, MC	MAJ Timothy J. O'Rourke, MC
COL Friedrich H. Stutz, MC	MAJ Michael D. Stone, MC
Key Words: carcinoma, breast, ER-, adjuvant, multiple drug	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jul 87

Study Objective: To compare through a randomized prospective study the recurrence rates and disease-free intervals for postoperative axillary node positive estrogen receptor negative breast cancer patients given adjuvant therapy with either short term intense chemotherapy (FAC-M) or one year standard chemotherapy (CMFVP); to compare the effect of these two adjuvant therapies on survival; to compare the relative toxicity of the two therapies; to compare the quality of life of patients with operable breast cancer randomized to receive one year of CMFVP or a short intensive regimen of FAC-M x 4 courses; and to compare a multiple item questionnaire for assessing quality of life.

Technical Approach: Women who have histologically proven breast cancer with axillary lymph node metastasis and negative estrogen receptors will be entered 14-21 days post-lumpectomy or within 14-42 days postmastectomy and randomly assigned to receive: Arm I - a tapering course of oral prednisone for 6 weeks, weekly IV vincristine for 10 weeks, weekly IV methotrexate, and weekly IV 5-FU plus daily oral cyclophosphamide for a total of one year; or Arm II - four cycles of adriamycin (IV day 1), cyclophosphamide (IV day 1), 5-FU (IV days 1 and 8), and methotrexate (IV day 22). Each cycle will be five weeks and total duration of therapy in this arm is approximately 20 weeks. Questionnaires to compare quality of life will be completed at 72 hours prior to chemotherapy.

Added to this protocol will be a sub-study to determine the prognostic significance of circulating human mammary epithelial antigens. This will involve blood tests prior to chemotherapy and then once every three months.

Progress: No patients were entered in FY 87. Three have been entered in previous years. One patient had more than usual leukopenia requiring substantial dose reduction and one receiving FAC-M developed left arm weakness, which resolved despite continued therapy on schedule.

Group-wide, toxicity has been worse on FAC-M (66%) than on CMFVP (55%).

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 84/61	Status: Completed

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 Irwin B. Dabe, MC	MAJ Alfred H. Chan, MC
COL Friedrich H. Stutz, MC	MAJ Timothy J. O'Rourke, MC
MAJ Thomas M. Baker, MD	MAJ Michael D. Stone, MC

Key Words: cancer, lung, non-small cell, combined modality

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

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: No entries in FY 87. One patient was entered at MAMC in FY 85 with decreased hearing secondary to cis-platinum and possible herpes zoster after radiation. This patient expired of disease in March 1986. The protocol was closed to patient entry by SWOG on 1 Oct 86.

Group-wide: Forty-four patients werre entered. There was a 52% response to initial chemotherapy, (5% complete remission). After chest radiation there was a 79% response (39% complete remission). Drug toxicity: 1 death and 2 life-threatening leukopenias, one case of mitomycin pneumonitis and two of nephropathy; neutron toxicity included two episodes of pneumonitis (1 fatal) and two of severe fibrosis with late respiratory failure in the first five patients treated. A change of characteristics of the cyclotron used resulted in substantially less toxicity in remaining patients.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 84/07	Status: Completed

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 Irwin B. Dabe, MC	MAJ Alfred H. Chan, MC
COL Friedrich H. Stutz, MC	MAJ Timothy J. O'Rourke, MC
MAJ Thomas M. Baker, MD	MAJ Michael D. Stone, MC

Key Words: sarcoma, refractory, vinblastine, cis-platinum

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Feb 87

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. Cis-Platinum 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. The protocol was closed to patient entry, 1 Oct 86, due to sufficient accrual of subjects.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 84/37	Status: Completed

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 Irwin B. Dabe, MC	MAJ Alfred H. Chan, MC
COL Friedrich H. Stutz, MC	MAJ Timothy J. O'Rourke, MC
LTC Howard Davidson, MD	MAJ Michael D. Stone, MC

Key Words: leukemia, lymphocytic, chronic, fludarabine phosphate

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Apr 87

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/M^2 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. The protocol was closed to patient entry on 15 Jun 87.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/88	Status: On-going

Title: SWOG 8406: Evaluation of Esorubicin (4'Deoxydoxorubicin NSC-267269) in Malignant Lymphoma, Phase II

Start Date: 19 Jun 87	Est Completion Date: Jun 1990
Dept/Svc: Medicine/Hematology	Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

COL Irwin B. Dabe, MC	MAJ David Dunning, MC
LTC Lauren K. Colman, MC	MAJ Ruben Sierra, MC
MAJ Thomas M. Baker, MC	CPT David R. Bryson, MC

Key Words: lymphoma, malignant, esorubicin

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

Study Objective: To determine the response rate and response duration of malignant lymphoma treated with Esorubicin (4'deoxydoxorubicin) and to define the qualitative and quantitative toxicities of Esorubicin administered in a Phase II study.

Technical Approach: Patients with a pathologically verified histologic diagnosis of malignant lymphoma refractory to prior chemo or radiation therapy will be eligible. Good risk patients with no prior nitrosourea or mitomycin-C therapy, good tolerance to other prior chemotherapy, and no prior extensive pelvic or mediastinal irradiation will receive Esorubicin at an initial dose of 30 mg/m^2, every 21 days. Poor risk patients with prior nitrosourea or mitomycin-C therapy, severe myelosuppression from other previous chemotherapy or prior extensive pelvic or mediastinal irradiation will receive Esorubicin at an initial dose of 25 mg/m^2, every 21 days. Esorubicin will be given by rapid IV infusion. Dose adjustments will be made on the basis of myelosuppression. Esorubicin will be discontinued in the event of clinically detectable evidence of congestive heart failure or in the event of a decrease in the ejection fraction as measured by MUGA scan of >10% or below the lower limits of normal. A MUGA scan will be done after a total cumulative dose of 150 mg/m^2. If the ejection fraction is above the lower limits of normal, a MUGA scan will be required at a cumulative dose of 250 mg/m^2 and then before every other cycle. An adequate trial is defined as at least two courses of Esorubicin.

Progress: No patients have been entered at MAMC.

Group-wide: The preliminary analysis of this study indicates that Esorubicin is clearly active in non-Hodgkin's and Hodgkin's lymphoma. The early results in Hodgkin's disease are encouraging. Toxicity seems to be limited to myelosuppression with approximately 25% of patients having life-threatening complications. Side effects, including gastrointestinal and hair loss, have not been severe. Although the response rate is substantially higher for good risk patients than for low risk patients, similar degrees of serious toxicity were seen in both groups.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 85/43	Status: On-going

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 Irwin B. Dabe, MC	MAJ Timothy O'Rourke, MC
COL F.H. Stutz, MC	MAJ Michael D. Stone, MC
LTC Howard Davidson, MC	CPT David Bryson, MC

Key Words: fludarabine phosphate, refractory, multiple myeloma

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Apr 87

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/M^2,* IV daily times five, repeated every 3 weeks. Poor risk patients will receive 12 mg/M^2. 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.

*Group-wide: This study was suspended in September 1985 to review the results on the first 16 patients. There were no responses, but no substantial myelosuppression; therefore, the decision was reached by SWOG to reopen the study in October 1985 at a dose of 18 mg/m^2.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 85/44	Status: Suspended

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 M. Baker, MC

Associate Investigators:

COL Irwin B. Dabe, MC	MAJ Timothy O'Rourke, MC
COL F.H. Stutz, MC	MAJ Michael D. Stone, MC
LTC Howard Davidson, MC	CPT David Bryson, MC

Key Words: IV, every 28 days, non-amenable to surgery

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Apr 87

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 within six weeks will be eligible. Patients will receive DTIC, 850 mg/M^2 IV, every 28 days. Poor risk will receive 650 mg/M^2. An adequate trial will be defined as two cycles of therapy with evidence of increasing disease. Patients with stable disease or in PR or CR will continue on therapy until increasing disease or relapse occurs.

Progress: No entries at MAMC.

This study is temporarily closed to patient entry for evaluation by the study coordinator.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/53	Status: On-going

Title: SWOG 8412: Carboplatin/Cyclophosphamide versus Cisplatin/ Cyclophosphamide in Patients with Measurable and Non-Measurable (Sub-Optimal) Disease Stages III and IV Ovarian Cancer, Phase III

Start Date: 21 Mar 86	Est Completion Date: Mar 88	
Dept/Svc: Medicine/Hematology		Facility: MAMC
Principal Investigator: LTC Howard Davidson, MC		
Associate Investigators:		
COL Irwin B. Dabe, MC	MAJ David Dunning, MC	
LTC Lauren K. Colman, MC	MAJ Michael D. Stone, MC	
MAJ Thomas M. Baker, MC	CPT David R. Bryson, MC	
Key Words: ovarian cancer, stages III and IV, chemotherapy		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Apr 87

Study Objective: To determine the efficacy (as determined by percentage of pathologically proven complete response) of carboplatin plus cyclophosphamide as compared to cisplatin plus cyclophosphamide in suboptimally resected Stages III and IV ovarian carcinoma; to evaluate the comparative toxicities of the two drug regimens; and to prospectively evaluate the power of human tumor clonogenic assay to predict objective clinical response to combination chemotherapy with cyclophosphamide plus one of two platinum compounds.

Technical Approach: Patients will be stratified by Stage II vs Stage IV disease, measurable versus nonmeasurable, suboptimal disease, and institution and randomized to one of the following: Arm I: cisplatin, 100 mg/M^2 IV in 1/2-1 liter NS, 1 mg/min, following prehydration with at least 1 liter NS over 1 hr, Day 1, plus cytoxan, 600 mg/M^2 IV, Day 1; or Arm II: carboplatin, 300 mg/M^2, IV, Day 1 plus cytoxan, 600 mg/M^2 IV, Day 1. Courses will be repeated every four weeks as tolerated. All patients will receive at least two courses of therapy (an adequate trial) before being removed from the study due to progression. Six courses of therapy will constitute the remission induction phase of the protocol, after which they will be re-evaluated. All patients in clinical or complete remission will undergo second-look exploratory laparotomy to document complete remission. Patients found to be free of disease at time of surgical reevaluation will have all chemotherapy discontinued, but will remain on study and be followed. Patients with residual tumor detected at re-evaluation will go off study.

Progress: No patients entered in FY 87 at MAMC. One patient was entered at MAMC in FY 86 who suffered high frequency hearing loss from the cis-platinum.

Group-wide eleven patients have been evaluated for toxicity with one life-threatening thrombocytopenia noted. Other toxicities reported include one moderate case of chills and one mild gastrointestinal problem.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86707	Status: On-going

Title: SWOG 8417/19: Evaluation of Two Consolidation Regimens in the Treatment of Adult Acute Lymphoblastic Leukemia, Ph II

Start Date: 18 Oct 85	Est Completion Date: Sep 87
Dept/Svc: Medicine/Oncology	Facility: MAMC
Principal Investigator: LTC Lauren K. Colman, MC	
Associate Investigators:	MAJ Thomas M. Baker, MC
COL Irwin B. Dabe, MC	MAJ Michael D. Stone, MC
LTC Howard Davidson, MC	CPT David R. Bryson, MC
Key Words: leukemia, lymphoblastic, consolidation regimens	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jan 87

Study Objective: To compare the effects on remission duration and survival of two consolidation regimens: the L-10-M consolidation used in SWOG 8001 versus a regimen employing daunomycin, cytosine, arabinoside, 6-thioguianine and escalating methotrexate/L-asparaginase in patients with adult lymphoblastic leukemia and to compare the toxicities of the two consolidation regimens.

Technical Approach: Patients will begin remission induction with vincristine, prednisone, adriamydin, methotrexate, cyclophosphamide, and adriamycin (36 days to complete therapy). On or about day 30, patients will have an Ommaya reservoir placed in the frontotemporal area of the skull. After completion of therapy there will be a 14 day rest period. Following completion of induction therapy, patients will have a bone marrow performed. Those patients failing to achieve an A_1 marrow status will be taken off study. Patients with complete remission will be randomized to one of the following consolidation regimens: ARM I (L-10-M): methotrexate and Ara-c given IV daily x 5 on days 1, 36, and 71; Ara-C (IV) and 6-thioguanine (PO) every 12 hr for 12 doses on days 15, 50, and 85; methotrexate (IT, days 15, 17, 57, and 59); vincristine (IV) and prednisone (PO) days 50 and 57; L-asparaginase (IV beginning day 99 and given 3 times weekly for a total of 6 doses), and cyclophosphamide (IV day 110 following last dose of L-asparaginase. Arm II: daunomycin (IV days 1-3), Ara-C (IV continuous infusion days 1-5), 6-thioguanine (PO every 12 hr days 1-5), followed by a 21-28 day rest period. Methotrexate (IV ev - ery 10 days from 28-98, L-asparaginase (IM every 10 days 29-99. After a 2-week rest period, maintenance therapy will begin with vincristine, prednisone, adriamycin, 6-mercaptopurine, methotrexate IT, methotrexate PO, dactinomycin, vincristine, prednisone, BCNU, cyclophosphamide, 6-mercaptopurine, and methotrexate. This cycle will be repeated every 21 wk for 36 mth or until relapse. An adequate trial will be the completion of remission induction therapy.

Progress: No patients were entered at MAMC in FY 87. Four patients were entered in FY 86. Three have expired from their disease. No adverse effects reported. Group-wide, of 37 patients evaluated for toxicity, there have been no fatal toxicities.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 85/45	Status: Completed

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 Irwin B. Dabe, MC	MAJ Timothy O'Rourke, MC
COL F.H. Stutz, MC	MAJ Michael D. Stone, MC
LTC Howard Davidson, MC	CPT David Bryson, MC
Key Words: mesothelioma, diffuse, unresectable, cis-platinum	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: 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 cis-platinum, 100 mg/M^2, 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. The protocol was closed to patient entry on 1 Oct 86.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 85/46	Status: Completed

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 Irwin B. Dabe, MC	MAJ Timothy O'Rourke, MC
COL F.H. Stutz, MC	MAJ Michael D. Stone, MC
MAJ Thomas Baker, MC	CPT David Bryson, MC

Key Words: cancer, lung, small cell, chemotherapy, radiation

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review Oct 85: continue

Study Objective: To determine the overall and complete response rates to the combination of cyclophosphamide, VP-16 (etopside) and cis-platinum followed by vincristine plus prophylactic 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 approxmately 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: No entries in FY 87 at MAMC. Four patients were entered in FY 85 with no unexpected toxicities. Two expired of the disease and two are off study.

The protocol was closed to patient entry on 27 Sep 85. Group-wide, the response rate to this regimen was 56%, only 6% complete responses. The radiation increased these percentages only slightly. Response duration was nine months (median) for complete response and five months for partial response. Median survival was nine months for complete response and 6 months overall. Myelosuppression, as anticipated, was the major toxicity, with 21% of patients requiring admittance for neutropenic fever; 9% died of sepsis while neutropenic. The regimen is not considered superior to standard therapy, e.g., Cytoxan, Adriamycin, and Vincristine.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 85/56	Status: Completed

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 Irwin B. Dabe, MC	MAJ Timothy O'Rourke, MC
COL F.H. Stutz, 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 Cost: -0-	Est Accumulative OMA Cost: -0- Periodic Review: Jun 87

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/M^2 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. The protocol was closed to patient entry in June 1987 due to sufficient accrual of subjects.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 85/77	Status: Completed

Title: SWOG 8494: A Comparison of Leuprolide with Flutamide and Leuprolide in Previously Untreated Patients with Clinical Stage D_2 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	MAJ Michael D. Stone, MC
COL Irwin B. Dabe, MC	CPT David Bryson, MC
Key Words: cancer, prostate, untreated, leuprolide, flutamide	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jan 87

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 (D_2) 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 D_2, 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. The protocol was closed to patient entry in July 1987.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/33	Status: On-going

Title: SWOG 8501 (INT-0051): Intraperitoneal Cis-Platinum/Intravenous Cyclophosphamide vs Intravenous Cis-Platinum/Intravenous Cyclophosphamide in Patients with Non-Measurable (Optimal) Disease Stage III Ovarian Cancer, Phase III Intergroup

Start Date: 16 Jan 87	Est Completion Date: Dec 89
Dept/Svc: Medicine/Hematology	Facility: MAMC

Principal Investigator: MAJ Thomas M. Baker, MC

Associate Investigators:

LTC Irwin B. Dabe, MC	MAJ David Dunning, MC
LTC Howard Davidson, MC	MAJ Ruben Sierra, MC
MAJ Lauren K. Colman, MC	CPT David R. Bryson, MC

Key Words: cancer, ovarian, cis-platinum, cyclophosphamide, intraperitoneal, intravenous

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

Study Objective: To perform a Phase III randomized trial of intermediate dose intraperitoneal cis-platinum plus intravenous cyclophosphamide versus intermediate dose intravenous cis-platinum and cyclophosphamide for optimal Stage III ovarian cancer; to evaluate the comparative toxicities of the two regimens; and to determine, in the setting of a prospective randomized trial, if the human tumor clonogenic assay with a wide range of drug concentration testing can accurately predict pathologic complete response to two-drug combination therapy in the setting of systemic and intraperitoneal drug administration.

Technical Approach: Only patients with epithelial neoplasms will be eligible. Patients will be stratified by residual disease (<0.5 cm vs residual disease >0.5 cm but < 2 cm indivudual tumor masses) and performance (status 0-1 versus 2). They will be randomized to Arm I or Arm II. Arm I: IV cisplatin, 100 mg/m^2 plus IV cyclophosphamide, 600 mg/m^2 every 28 days for six courses. Arm II: IP cisplatin, 100 mg/m2 plus IV cyclophosphamide, 600 mg/m^2, every 28 days for six courses. Patients with partial or no response will go off study. Those with clinical complete response will undergo second look laparotomy. Those with residual tumor at second look laparotomy will be taken off study and entered in an appropriate protocol. Those with pathologic complete response will be followed by observation only until evidence of progression of disease appears. All patients who receive any amount of chemotherapy will be evaluable for toxicity. Patients who receive at least two courses of therapy will be evaluable for response and survival.

Progress: One patient was entered at MAMC in FY 87. Of 25 patients evaluated for toxicity by the SWOG study coordinator, one complained of metallic taste of unknown degree and mild chronic anxiety and one had severe dehydration. One life-threatening leukopenia was reported and another patient had grade 4 alopecia.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 85/78	Status: Completed

Title: SWOG 8503: Combination Chemotherapy of Intermediate and High Grade Non-Hodgkin's Lymphoma with ProMACE-Cytabom, Phase II

Start Date: 23 Aug 85	Est Completion Date: Jul 87
Dept/Svc: Medicine/Oncology	Facility: MAMC

Principal Investigator: *LTC Howard Davidson, MC*

Associate Investigators:

COL Irwin B. Dabe, MC	MAJ Michael D. Stone, MC
MAJ Thomas M. Baker, MC	CPT David Bryson, MC

Key Words: lymphoma, non-Hodgkin's, chemotherapy, ProMACE-Cytabom

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Feb 87

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, etopside, 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 etopside 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. The protocol was closed to patient entry by SWOG in January 1987.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/26	Status: Completed

Title: SWOG 8504: Evaluation of Menogaril (NSC-269148) in Renal Cell Carcinoma, Phase II

Start Date: 17 Jan 86	Est Completion Date: Dec 87	
Dept/Svc: Medicine/Hematology		Facility: MAMC
Principal Investigator: MAJ Thomas M. Baker, MC		
Associate Investigators:		
COL Irwin B. Dabe, MC	MAJ David Dunning, MC	
LTC Lauren K. Colman, MC	MAJ Michael D. Stone, MC	
LTC Howard Davidson, MC	CPT David R. Bryson, MC	
Key Words: carcinoma, renal cell, menogaril		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jan 87

Study Objective: To determine the response rate and remission duration of advanced renal cell carcinoma when treated with menogaril by one hour infusion every 28 days and to define the qualitative and quantitative toxicities of menogaril administered in a Phase II study.

Technical Approach: Patients will not have received prior chemotherapy. Patients may have received surgery, radiation or hormonal therapy as part of the treatment of their primary disease. The initial dose level for all patients will be menogaril 200 mg/M^2 over one hour in 500 ml of 5% Dextrose in water. Courses of menogaril will be administered every 28 days provided the patient has a total absolute granulocyte count >2,000/µl and platelet count is >100,000/µl. Menogaril treatment will continue until progression of disease. An adequate trial will be two doses requiring a total duration of observation of 8 weeks. Patients will be removed from the study with 25% increase in the size of measured lesion or the appearance of new lesions or unacceptable stable disease after one or more courses of therapy or unacceptable toxicity.

Progress: No entries at MAMC. The protocol was closed to patient entry in January 1987.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/107	Status: On-going

Title: SWOG 8507: Maintenance versus No Maintenance BCG Immunotherapy of Superficial Bladder Cancer, Phase III

Start Date: 21 Aug 87	Est Completion Date: Aug 90
Dept/Svc: Medicine/Hematology	Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

COL William D. Belville, MC	MAJ Thomas M. Baker, MC
COL Irwin B. Dabe, MC	MAJ David M. Dunning, MC
COL Victor Kiesling, MC	MAJ Ruben D. Sierra, MC
LTC Lauren K. Colman, MC	CPT Denis P. Bouvier, MC

Key Words: cancer, bladder, BCG immunotherapy

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

Study Objective: To compare the effectiveness of intravesical and percutaneous BCG immunotherapy given on a maintenance versus no maintenance schedule with respect to disease-free interval and rate of tumor recurrence in patients with transitional cell carcinoma of the bladder; to assess the toxicity of maintenance and no maintenance BCG immunotherapy; and to assess the association of intermediate strength PPD skin test reactivity with disease-free status in patients treated with BCG immunotherapy.

Technical Approach: Patients will be stratified according to prior chemotherapy, disease type, and PPD skin test conversion. One week following a standard transurethral resection, BCG, 120 mg lyophilized BCG organisms will be diluted in 50.5 cc of sterile, preservation-free saline. Fifty cc will be administered intravesically and 0.5 cc will be administered percutaneously. The BCG adminstration will be repeated weekly for a total of six weeks. Patients will then be randomized to the BCG maintenace or no maintenance arms. The BCG maintenance arm will consist of weekly intravesical and percutaneous BCG immunotherapy administrations repeated for three consecutive weeks at three months, six months, and every six months thereafter for a total treatment period of 36 months. Documented tumor recurrence or positive random biopsy is not an indication for withdrawal from the study since many patients require six months for a complete response. Patient removal from the study will be determined by the type of tumor. Any patient with progression of disease, defined by an increase in tumor grade or stage beyond the highest previous grade or stage or an increase in the number or frequency or recurrences will be removed from the study

Progress: One patient was entered in the study at MAMC in FY 87.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/27	Status: On-going

Title: SWOG 8509: Evaluation of Menogaril (NSC-269148) in Adenocarcinoma of the Prostate, Phase II

Start Date: 17 Jan 86	Est Completion Date: Dec 87	
Dept/Svc: Medicine/Hematology		Facility: MAMC

Principal Investigator: MAJ Thomas M. Baker, MC

Associate Investigators:

COL Irwin B. Dabe, MC	MAJ David Dunning, MC
LTC Lauren K. Colman, MC	MAJ Michael D. Stone, MC
LTC Howard Davidson, MC	CPT David R. Bryson, MC

Key Words: adenocarcinoma, prostate, menogaril

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jan 87

Study Objective: To assess the antitumor activity of menogaril in patients with advanced adenocarcinoma of the prostate and to define the qualitative and quantitative toxicities of menogaril administered in a Phase II study.

Technical Approach: Patients may not have received prior chemotherapy. Prior hormonal or immunotherapy is permitted. All patients must have a pretreatment total absolute granulocyte count >2000/µl and platelet >100,000/µl. Menogaril, 200 mg/M^2, will be administered IV in 500 ml of 5% Dextrose in water over one hour on day 1. Courses of menogaril will be repeated every 28 days. An An adequate trial will consist of two doses requiring a total duration of observation of 8 weeks. Patients will be taken off study with 25% increase in the size of measured lesion, the appearance of new lesions, unacceptable stable disease after one or more courses of therapy, unacceptable toxicity, or patient's refusal to continue treatment.

Progress: No entries at MAMC.

This study was temporarily closed in July 1986 due to a fatal myelosuppressive toxicity. It was reopened in May 1987 with reduced doses after review of the data. There has been sufficient activity observed to justify second stage accrual.

The toxicity data are complete for only seven patients, including the previously mentioned death due to myelosuppression. Severe and life-threatening myelosuppression was observed in three additional patients. There were no other severe or life-threatening toxicities. Other toxicity was mild angioneurotic edema which is considered questionable with respect to its relationship to the treatment.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87709	Status: On-going

Title: SWOG 8510: Intra-Arterial Cis-Platinum and Radiation Therapy in Primary Brain Tumors; A Phase II Randomized Study Comparing Sequential and Combined Treatments

Start Date: 17 Oct 86	Est Completion Date: Oct 89
Dept/Svc: Medicine/Hematology	Facility: MAMC

Principal Investigator: MAJ Thomas M. Baker, MC

Associate Investigators:

COL Irwin B. Dabe, MC	MAJ David Dunning, MC
LTC Howard Davidson, MC	MAJ Ruben Sierra, MC
MAJ Lauren K. Colman, MC	CPT David R. Bryson, MC

Key Words: tumor, brain, cis-platinum, intra-arterial, radiation

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

Study Objective: To assess the toxicity and response to therapy of intra-arterial cis-platinum administered in two schedules, sequential and concomitant, with radiation therapy in the treatment of patients with primary malignant gliomas and to determine the time to progression and overall survival in these patients.

Technical Approach: Patients must have a histologically confirmed diagnosis of primary malignant glioma (Kernohan's astrocytoma, Grade 3 or 4, or WHO classification glioblastoma and gliobalastoma multiforme with no prior chemo or radiotherapy. Chemotherapy will be initiated 7-28 days after surgery. Patients will be randomized to: Arm I - Sequential chemotherapy and radiation therapy. Cis-platinum, 150 mg (adjusted for size and creatinine clearance) intra-arterial administration, Day 1. Three weeks later, the dose will be repeated followed by a three week rest. The entire intracranial contents will then receive 4500 cGY at 180 cGy per fraction, five fractions per week, followed by a boost of 180 cGy daily fractions for six fractions (per week). Total dose will be 5580 cGy. Arm II: Concomitant chemotherapy and radiation therapy. Cis-platinum will be given on Day 1 as in Arm I. Radiation therapy will be initiated within 24-48 hours after the first dose of intra-arterial chemotherapy. The total dose is 5580 cGy as outlined for Arm I. The second dose of intra-arterial cisplatinum will be given three weeks following the first chemotherapy dose (concomitant with radiation therapy). Following the completion of two cycles of cis-platinum and the prescribed radiation therapy, patients will receive no further therapy and will be followed.

Progress: No patients have been entered at MAMC. Group-wide, only seven patients have been evaluated for toxicity. No life-threatening or fatal toxicities have been observed.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/71	Status: On-going

Title: SWOG 8514: Randomized Comparison of Cis-Platin + 5 Fluorouracil versus CBDCA + 5-Fluorouracil versus Methotrexate in Advanced Squamous Cell Carcinoma of the Head and Neck, Phase III

Start Date: 20 Jun 86	Est Completion Date: Jun 1989
Dept/Svc: Medicine/Hematology	Facility: MAMC

Principal Investigator: MAJ Thomas M. Baker, MC

Associate Investigators:

COL Irwin B. Dabe, MC	MAJ David Dunning, MC
LTC Lauren K. Colman, MC	MAJ Michael D. Stone, MC
LTC Howard Davidson, MC	CPT David R. Bryson, MC

Key Words: carcinoma, squamous cell, head & neck, chemotherapy

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Aug 87

Study Objective: To determine and compare the response rate (complete and partial), duration of response, and survival time of patients treated with two combination chemotherapy regimens: (Arm I) cis-platin + 5-FU, (Arm II) CBDCA - 5-FU, with Arm III (single agent methotrexate).

Technical Approach: Patients may not have received prior chemotherapy for recurrent disease. Patients who have received induction chemotherapy only are eligible. Patients may have received prior radiotherapy (not within past 6 months).

Arm I: (every 21 days)
cis-platinum, 100 mg/M^2, IV, pre and post-treatment hydration
5-FU 1000 mg/M^2 continuous IV infusion x 4 days

Arm II: (every 21 days)
CBDCA 300 mg/M^2, IV, no hydration required
5-FU 1000 mg/M^2 continuous IV infusion x 4 days

Arm III: methotrexate 40 mg/M^2, IV bolus every week.

In patients achieving disease regression, the duration of disease regression will be measured from the start of chemotherapy to the first sign of progression or relapse.

Patients will be removed from the study if there is progression of disease after at least four weeks of treatment, if there is unacceptable toxicity, or if the patient does not want to continue treatment.

Progress: One patient was entered at MAMC. No fatal toxicities have been reported by SWOG. The incidence of moderate to life-threatening toxicity has been greatest on the CDDP+5-FU arm (93%) compared with 62% on CBDCA+5-FU and 63% on methotrexate.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/80	Status: On-going

Title: SWOG 8516: A Phase III Comparison of CHOP versus m-BACOD versus ProMACE-CytaBOM versus MACOP-B in Patients with Intermediate or High-Grade Non-Hodgkin's Lymphoma

Start Date: 15 Aug 86	Est Completion Date: Jul 89	
Dept/Svc: Medicine/Hematology		Facility: MAMC
Principal Investigator: MAJ Thomas M. Baker, MC		
Associate Investigators:		
COL Irwin B. Dabe, MC	MAJ David Dunning, MC	
LTC Lauren K. Colman, MC	MAJ Michael D. Stone, MC	
LTC Howard Davidson, MC	CPT David R. Bryson, MC	
Key Words: non-Hodgkin's, CHOP, m-BACOD, ProMACE-CytaBOM, MACOP-B		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Dec 86

Study Objective: To compare in a randomized group-wide setting the complete response rate, response duration, and survival of patients with intermediate and high grade non-Hodgkin's lymphoma treated with one of four combination chemotherapy regimens: CHOP, m-BACOD, ProMACE-CytaBOM, or MACOP-B; and to compare the toxicities of each regimen in this patient population.

Technical Approach: Patients with prior chemotherapy or radiotherapy are ineligible. Arm I (CHOP every 3 weeks for 8 consecutive cycels): cyclophosphamide (IV), doxorubicin (IV), vincristine (IV) and prednisone (PO). Arm II (m-BACOD every 3 weeks x 10): cyclophosphamide (IV), doxorubicin (IV), vincristine (IV), bleomycin (IV), dexamethasone (PO), methotrexate (IV), and calcium leukovorin rescue after each MTX dose. Arm III (Pro-MACE-CytaBOM every 21 days, treated until complete remission plus 2 additional cycles): cyclophosphamide (IV), doxorubicin (IV), VP-16 (IV), prednisone (PO), ara-C (IV), bleomycin (IV), vincristine (IV), methotrexate (IV), calcium leukovorin rescue after each MTX dose, and trimetheprim-sulfamethoxazole (PO). Arm IV (MACOP-B will be given over 12 weeks): methotrexate (IV), calcium leucovorin rescue after each MTX bolus, doxorubicin (IV), cyclophosphamide (IV), vincristine (IV), bleomycin (IV), prednisone (PO), and trimethoprim-sulfa (PO). Patients with documented progressive disease may be taken off study at any time; however patients will preferably be be restaged upon completion of the treatment program to assess response. Patients with less than a complete response at restaging will be taken off study. Patients whose clinical disease has disappeared and who appear to be in complete remission will undergo a complete and thorough laboratory and radiographic search for evidence of persistent lymphoma approximately one month after completion of therapy. If complete remission is confirmed, the patient will be observed with no further therapy.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/96	Status: On-going

Title: SWOG 8519: Phase II Evaluation of Methyl-Glyoxal Bis-Guanylhydrazone (MGBG) in Patients with Advanced Bladder Cancer

Start Date: 17 Jul 87	Est Completion Date: July 1990
Dept/Svc: Medicine/Hematology	Facility: MAMC

Principal Investigator: MAJ Thomas M. Baker, MC

Associate Investigators:

COL Irwin B. Dabe, MC	MAJ David Dunning, MC
LTC Howard Davidson, MC	MAJ Ruben Sierra, MC
LTC Lauren K. Colman, MC	CPT Denis Bouvier, MC

Key Words: cancer, bladder, advanced, MGBG

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

Study Objective: To determine response rate and remission duration with weekly intravenous therapy using MGBG in patients with metastatic carcinoma who have failed on higher priority protocols and to define the qualitative and quantitative toxicity of this regimen.

Technical Approach: Patients must have a histologically confirmed diagnosis of metastatic transitional cell carcinoma of the urothelium. Only patients with one prior systemic chemotherapy or immunotherapy regimen are eligible. Patients with up to two prior intravesicle regimens are acceptable. Patients with prior radiotherapy are eligible if the disease has progressed and measurable sites of disease exist outside of the previous radiation field.

An initial dose of MGBG, 600 mg/m^2, will be given as an IV infusion over 90 minutes. Treatment will be repeated every week until disease progression.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/44	Status: On-going

Title: SWOG 8530: Efficacy of Prednisone in Refractory and Relapsing Multiple Myeloma and Measurement of Glucocorticoid Receptors, Phase II

Start Date: 27 Feb 87	Est Completion Date: Feb 90	
Dept/Svc: Medicine/Hematology		Facility: MAMC

Principal Investigator: MAJ Thomas M. Baker, MC

Associate Investigators:

COL Irwin B. Dabe, MC	MAJ David Dunning, MC
LTC Howard Davidson, MC	MAJ Ruben Sierra, MC
LTC Lauren K. Colman, MC	CPT David R. Bryson, MC

Key Words: myeloma, refractory, glucocorticoid receptors

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

Study Objective: To estimate the response rate and duration with high dose prednisone in patients with refractory myeloma and to measure glucocorticoid receptors in multiple myeloma.

Technical Approach: Patients must have had prior chemotherapy or hormonal therapy for myeloma with progression of disease. Fasting blood glucose must be $\leq$160 mg% and stool guaiac must be negative.

Therapy: Prednisone, 100 mg po, every other day for two weeks followed by 50 mg po every other day for ten weeks.

Each patient will receive three months of therapy to be considered evaluable for response. If no response is observed after three months of therapy, the patient will be removed from the study.

Therapy may be continued after three monhts of treatment with 50 mg PO every other day, providing the toxicities remain acceptable and the patient remains responsive to therapy.

Progress: No entries at MAMC.

Of 40 patients accrued group-wide, two instances of life-threatening thrombocytopenia have been reported, though one may be unrelated to treatment. The other severe toxicity reported was hyperglycemia. Other toxcities include malaise, blurred vision, weight gain, muscle cramps, bruising, and insomnia.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/10	Status: On-going

Title: SWOG 8562: High-Dose Cisplatin in Hypertonic Saline for the Treatment of Metastatic or Recurrent Malignant Melanoma, Phase II-Pilot

Start Date: 17 Oct 86	Est Completion Date: Oct 89
Dept/Svc: Medicine/Hematology	Facility: MAMC

Principal Investigator: MAJ Thomas M. Baker, MC

Associate Investigators:

COL Irwin B. Dabe, MC	MAJ David Dunning, MC
LTC Howard Davidson, MC	MAJ Ruben Sierra, MC
MAJ Lauren K. Colman, MC	CPT David R. Bryson, MC

Key Words: melanoma, cisplatin, high-dose, hypertonic saline

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

Study Objectives: To estimate the response rate and duration of response to high-dose cisplatinum in hypertonic saline in recurrent and/or metastatic melanoma; to assess qualitative and quantitative toxicities of this treatment program; and to measure time to progression of disease and survival of patients.

Technical Approach: Subjects must have biopsy-proven metastatic melanoma with measurable disease and no prior chemotherapy. Patients will be hospitalized the night before the start of chemotherapy. An infusion of normal saline at 250 cc/hr with potassium chloride, 20 meq/L, will be started 12 hours prior to each dose of cisplatin and continued for 12 hours after each dose. The maintenance hydration will be continued until the patient is taking po fluids well. Furosemide, 20 mg, will be given intravenously 20-30 minutes before each dose of cisplatin. Daily serum electrolytes, calcium, magnesium, BUN, and creatinine will be checked.

Therapy: Cisplatin, 100 mg/m^2, days 1 and 8. The cisplatin will be reconstituted in 250 ml of 3% saline and infused over 30 minutes.

Courses will be repeated at four-week intervals until dose-limiting toxicity is reached or there is progression of disease.

Progress: No entries at MAMC.

Of 15 patients entered group-wide, one patient had life-threatening granulocytopenia, thrombocytopenia, and leukopenia. Other toxicities include severe cold sweats, moderate edema, and moderate or severe ototoxicity.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/108	Status: On-going

Title: SWOG 8571: Induction Chemotherapy with High-Dose Cyclophosphamide for Poor Prognosis, Disseminated Breast Cancer with Radiation Therapy in Complete Responders, Phase II Pilot

Start Date: 21 Aug 87	Est Completion Date: Aug 90
Dept/Svc: Medicine/Hematology	Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

COL Irwin B. Dabe, MC	MAJ David M. Dunning, MC
LTC Lauren K. Colman, MC	MAJ Ruben D. Sierra, MC
MAJ Thomas M. Baker, MC	CPT Denis P. Bouvier, MC

Key Words: breast cancer, cyclophosphamide, radiation therapy

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

Study Objective: To define toxicity and response rate to a brief, intensive program of combination chemotherapy (FUVA); to determine feasibility, toxicity, and effect on response quality of high-dose cyclophosphamide consolidation; and to assess response duration and survival resulting from this approach.

Technical Approach: Patients with recurrent or disseminated breast cancer with estrogen receptor cytosol protein <4 or primary tumors which were estrogen receptor positive but failed to respond to hormonal therapy will be eligible. Patients will have had no previous chemotherapy for disseminated or recurrent breast cancer other than prior adjuvant chemotherapy provided the interval between its discontinuation and recurrence or dissemination is >6 months. Patients will have had no prior exposure to doxorubicin.

Induction chemotherapy (FUVA) will start on day 1 and will consist of 5-FU by continuous infusion, 1000 mg/m^2/day, for three days; Adriamycin, 25 mg/m^2, by rapid infusion on days 1 and 3; and vinblastine, 2 mg/m^2, by rapid IV infusion on days 1 and 3. Treatment will be repeated every 21 days for four cycles. Intensification chemotherapy will start four weeks after cycle #4 of FUVA and will consist of cyclophosphamide, 60 mg/kg/day, on two successive days. Patients with complete response will have whole brain irradiation plus four cycles of FUVA (as in induction) starting eight weeks after cyclophosphamide intensification therapy. Radiation treatment will be delivered through parallel opposed lateral ports to deliver a midplane, central axis dose of 3600 cGy at 180 cGy/day, 20 total fractions, five days per week. Partial responders will be given FUVA (as in induction) for four cycles starting eight weeks after intensification.

Progress: No entries at MAMC.

Toxicity has been severe, particularly on high dose Cytoxan, as expected. Eleven of 13 patients evaluated group-wide have been reported to have grade four hematologic toxicity.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 86/72	Status: On-going

Title: SWOG 8573: Treatment of Limited Small Cell Lung Cancer with Concurrent Chemotherapy, Radiotherapy, and Intensification with High Dose Cyclophosphamide, Phase II Pilot

Start Date: 20 Jun 86	Est Completion Date: Jun 89
Dept/Svc: Medicine/Hematology	Facility: MAMC
Principal Investigator: LTC Lauren K. Colman, MC	
Associate Investigators:	MAJ Thomas M. Baker, MC
COL Irwin B. Dabe, MC	MAJ David Dunning, MC
LTC Howard Davidson, MC	CPT David R. Bryson, MC
Key Words: cancer, small cell lung, chemotherapy, radiotherapy	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0- Periodic Review: Jun 87

Study Objective: To estimate the response rate and survival of patients with limited small cell lung cancer when treated with concurrent chemo-radiotherapy followed by chemotherapy and late intensification with high dose cyclophosphamide and to assess the toxicity of this treatment program.

Technical Approach: Patients treated previously with chemotherapy or radiotherapy are ineligible, except if radiation was given for localized, controlled skin cancer. Only patients with limited disease (confined to one hemithorax, mediastinal, hilar or supraclavicular area which could be encompassed within a single radiation therapy port, or an ipsilateral pleural effusion) will be eligible. Patients will be taken off study for non-response or increasing disease after induction therapy, increasing disease at any time, inability to tolerate the lowest prescribed dose of chemotherapy, or to deliver the radiotherapy within the allowable time.

Induction (days 1-36):
VP-16, 60 mg/M^2, days 1-5, 22-26
CDDP, 50 mg/M^2, days 1,8,22, & 29
Chest XRT - 4500 rads (180/day) days 1-36

Consolidation (days 64-92):
VP-16, 60 mg/M^2, days 64-66 & 85-87
CDDP, 50 mg/M^2, days 64 & 85
Adriamycin, 50 mg/M^2, days 64 & 85
Vincristine, 2 mg, days 64,71,85, and 92

Late intensification (days 113-141):
cyclophosphamide 50 mg/kg, days 113-115
Brain XRT, 3000 rads, 200/day, days 120-141

Progress: Two patients were entered in FY 87 for a total of three entered at MAMC. Group-wide, of 29 patients entered, myelosuppression was the only life-threatening toxicity reported to date. Other toxicities reported were weakness, fatigue, and electrolyte imbalance.

Detail Summary Sheet

Date: 30 Sep 87	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

Principal Investigator: MAJ Thomas M. Baker, MC

Associate Investigators:

COL Irwin B. Dabe, MC	LTC Howard Davidson, MC
COL William H. Gernon, MC	MAJ Timothy J. O'Rourke, MC
COL F.H. Stutz, MC	MAJ Michael D. Stone, MC
LTC Don Blakeslee, MC	CPT David R. Bryson, MC

Key Words: carcinoma, head and neck, squamous, chemotherapy, radiotherapy, surgery

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jun 87

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: Two patients were entered in FY 87 for a total of three patients entered at MAMC.

Group-wide: As expected, the chemotherapy followed by radiation arm has had a higher incidence of severe and life-threatening toxicity; 38% versus 12% on the radiation only arm. No fatal toxicities have been reported. The life-threatening toxicities were all hematologic, occurring during chemotherapy.

Detail Summary Sheet

Date: 30 Sep 87	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
Principal Investigator: MAJ Thomas Baker, MC	
Associate Investigators:	MAJ Timothy O'Rourke, MC
COL Irwin B. Dabe, MC	MAJ Michael D. Stone, MC
COL F.H. Stutz, MC	MAJ Jens A. Strand, MC
LTC Howard Davidson, MC	CPT David Bryson, MC
Key Words: adenocarcinoma, colon, surgical, levamisole, 5-FU	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jun 87

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 c rative section will be eligible. The patients with modified Dukes B_2 (serosal penetration) or B_3 (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 was entered in FY 87 for a total of six entries at MAMC.

Group-wide: During the first cycle of treatment with 5-FU plus levamisole, one Duke's C patient experienced life-threatening thrombocytopenia and stomatitis along with fatal toxicity due to leukopenia. Two others had life-threatening leukopenia, one had life-threatening stomatitis, and one Duke's B patient had life-threatening leukopenia. Three Duke's C patients on 5-FU plus levamisole experienced life-threatening toxicities post cycle one: one due to diarrhea, one due to an allergic reaction, and one due to a skin reaction. No life-threatening or fatal toxicities were experienced either during or post cycle one for patients on levamisole alone. Other toxicities were fatigue, taste or smell perversion, eye irritation, and muscle ache.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/117	Status: On-going

Title: SWOG 8592: Evaluation of Low-Dose Ara-C versus Supportive Therapy Alone in the Treatment of Myelodysplastic Syndromes, Phase III. (ECOG EST 4483)

Start Date: 18 Sep 87	Est Completion Date: Apr 90
Dept/Svc: Medicine/Hematology	Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

COL Irwin B. Dabe, MC	MAJ David Dunning, MC
LTC Lauren K. Colman, MC	MAJ Ruben Sierra, MC
MAJ Thomas M. Baker, MC	CPT David R. Bryson, MC

Key Words: myelodysplastic syndromes, Ara-C, supportive therapy

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

Study Objective: To compare the benefit of low-dose Ara-C therapy versus supportive care in patients with myelopdyplastic syndromes. The endpoints will be transfusion requirements, incidence of bleeding and infectious complications, time to progression and leukemia transformation, frequency of leukemic transformation and survival from diagnosis. Also, to determine the frequency, extent, and duration of response to this regimen in these patients, to assess the toxicity of a 21 day course of low-dose Ara-C, and to correlate patient response with presenting clinical characteristics and marrow cytogenetic and morphological features.

Technical Approach: Stratification factors include morphologic type and prior chemotherapy for other malignancies or autoimmunodisease excluding prednisone, oxymethalone, and pyridoxine. Patients will be randomized to one of two treatment arms: (I) Supportive therapy only with red cell and platelet trnsfusions for symptoms or to maintain hematocrits >25%. Patients with progressive disease of at least 2 months duration will be switched to the low-dose Ara-C arm of the study. (II) Therapy with low-dose ara-C, 10 mg/m^2, subcutaneously every 12 hours for 21 days after which patients with a complete or partial response will receive no further therapy and will be followed monthly with a blood count, and a bone marrow aspirate and a biopsy one month after therapy and then every three months during the first year. During subsequent years, a bone marrow aspirate and biopsy will be obtained every six months. Patients with stable disease or documented progression after eight weeks of therapy will be considered treatment failures and will be followed as in the supportive therapy arm. Patients who respond to Ara-C with at least a four-week documented complete or partial response and then relapse will be retreated with a 21 day course of Ara-C at the time of relapse or progression. Low dose Ara-C may be repeated as long as the patient continues to demonstrate a response.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87722	Status: On-going

Title: SWOG 8594: A Phase III Trial of Cis-Platin Alone or in Combination with Doxorubicin, Vinblastine, and Methotrexate in Advanced Bladder Cancer (SEG/NCI #GU-305)

Start Date: 21 Nov 86	Est Completion Date: Oct 89
Dept/Svc: Medicine/Hematology	Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

LTC Irwin B. Dabe, MC	MAJ David Dunning, MC
MAJ Thomas Baker, MC	MAJ Ruben Sierra, MC
MAJ Lauren K. Colman, MC	CPT David R. Bryson, MC

Key Words: cancer, bladder, cis-platin, doxorubicin, vinblastine, methotrexate, alone, combination

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

Study Objective: To determine if cisplatin in combination with doxorubicin, vinblastine, and methotrexate is more effective than cisplatin alone in the treatment of patients with advanced bladder cancer in terms of objective response rate, response duration, and survival.

Technical Approach: Patients must have histologically proven advanced bladder carcinoma not curable by surgery or radiation therapy. Patients will be stratified according to performance status and history of prior radiation therapy. Patients will be randomized to Regimen A or Regimen B with cycles repeated every 28 days.

Regimen A: cisplatin, 70,g/m^2 IV by 70 minute infusion

Regimen B: methotrexate, 30 mg/m^2 IV - days 1, 15, and 22
vinblastine, 3 mg/m^2 IV - days 2, 15, and 22
adriamycin, 30 mg/m^2 IV - day 2
cisplatin, 70 mg/m^2 IV by 70 minute infusion, day 2

Patients will be hydrated with D_5 1/2 NS IV at 150 ml/hour for 10-15 hours before and 24 hours after cisplatin treatment. Patients will receive therapy until evidence of progression or for a maximum of six cycles. Patients with evidence of disease progression on cis-platin alone may be crossed over to Regimen B at the discretion of the investigator.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/72	Status: On-going

Title: SWOG 8597: Randomized Phase III Intergroup Study of Supradiaphragmatic Irradiation in Stage II-A Seminoma (RTOG 8514/Intergroup 0055)

Start Date: 17 Apr 87	Est Completion Date: Apr 1990
Dept/Svc: Medicine/Hematology	Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

COL William D. Belville, MC	MAJ Thomas M. Baker, MC
COL Irwin B. Dabe, MC	MAJ David Dunning, MC
COL Donald H. Kull, MC	MAJ Ruben Sierra, MC
LTC Lauren K. Colman, MC	CPT David R. Bryson, MC

Key Words: seminoma, stage II-A, supradiaphragmatic irridiation

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

Study Objective: To compare the recurrence rates and the patterns of recurrence in Stage II A seminomas treated with either infradiaphragmatic irradiation only or infradiaphragmatic irradiation followed by supradiaphragmatic irradiation; to assess the tolerance to salvage chemotherapy and the salvage rate in relapsing patients; and to examine the effect of the treatment on gonadal function.

Technical Approach: Patients with Stage II-A seminoma (<5 cm nodal disease), no prior malignancies other than skin cancer, no prior radio or chemotherapy, and no evidence of disease spread beyond the abdomen will be randomized to: (1) intradiaphrgmatic irradiation with 25.00 Gy (1.50-1.80 Gy/day) plus boost to gross tumor to 35.00 Gy; or (2) infradiaphragmatic irrdiation with 25.00 Gy (1.50-1.80 Gy/day) plus supradiaphragmatic irradiation with 25.00 Gy (1.75-2.00 Gy/day). Treatment will be given four or five times a week. Allowing for treatment related reactions or other factors that could interrupt treatment, the overall duration of the radiotherapy course should not exceed 45 days for patients on arm 1 and 65 days for patients on arm 2. Patients who relapse will receive chemotherapy determined by the physician for salvage. Data regarding tolerance to salvage chemotherapy will be collected systematically on all relapsing patients.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/109	Status: On-going

Title: SWOG 8598 (RTOG-85-01): Prospective Trial for Localized Cancer of the Esophagus: Comparing Radiation as a Single Modality to the Combination of Radiation Therapy and Chemotherapy, Phase III, Intergroup

Start Date: 21 Aug 87	Est Completion Date: Aug 90
Dept/Svc: Medicine/Hematology	Facility: MAMC

Principal Investigator: LTC Lauren K. Colman, MC

Associate Investigators:

COL Irwin B. Dabe, MC	MAJ David M. Dunning, MC
LTC Howard Davidson, MC	MAJ Ruben D. Sierra, MC
MAJ Thomas M. Baker, MC	CPT Denis P. Bouvier, MC

Key Words: cancer, esophagus, radiation therapy versus radiation plus chemotherapy

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

Study Objective: To determine the role of chemotherapy for a potentially curable subset of patients with squamous cell cancer of the esophagus. Specifically, to determine if the combination of chemotherapy and radiation will add to the overall survival and cure of patients treated with the combination when compared to patients treated by radiation alone. To determine if the patterns of recurrence for patients treated with chemotherapy plus radiation differs from those patients treated with radiation alone.

Technical Approach: Patients with squamous cell or adenocarcinoma of the thoracic esophagus, no evidence of disseminated cancer, negative bone scan, and WBC >4,000/mm, platelets >100,000/mm, creatinine <1.5 mg%, BUN <22 mg%, and/or creatinine clearance >60 cc/min are eligible. Patients will be stratified according to weight loss, lesion size, and histology. Patients will be randomized to arms I or II.

(I) Cisplatinum, 75 mg/m^2 the first day of weeks 1, 5, 8, and 11, 5-FU, 1000 mg/m^2 96-hr continuous fusion, weeks 1, 5, 8 and 11; Radiotherapy, 2 Gy five days a week for three weeks followed by boost of 2 Gy five days a week for five weeks

(II) 2 Gy for five days a week for five weeks followed by a boost of 2 Gy five days a week for 1.4 weeks

If 12 weeks after therapy is completed, tumor remains in the esophagus or there is recurrence, the patient has failed therapy but continues to be followed for survival. Patients with no evidence of tumor upon esophagoscopy and esophagram will be considered response to therapy and followed until relapse or death.

Progress: No entries at MAMC. Group-wide, four cases have been evaluated for toxicity with grade 3 the worst degree of toxicity reported.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87745	Status: On-going

Title: SWOG 8600: A Randomized Investigation of High-Dose Versus Standard Dose Cytosine Arabinoside with Daunorubicin in Patients with Acute Non-Lymphocytic Leukemia

Start Date: 27 Feb 87	Est Completion Date: Feb 90
Dept/Svc: Medicine/Hematology	Facility: MAMC

Principal Investigator: LTC Lauren K. Colman, MC

Associate Investigators:

COL Irwin B. Dabe, MC	MAJ David Dunning, MC
LTC Howard Davidson, MC	MAJ Ruben Sierra, MC
MAJ Thomas M. Baker, MC	CPT David R. Bryson, MC

Key Words: leukemia, non-lymphocytic, cytosine arabinoside, high dose vs standard dose with daunorubicin

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

Study Objective: To compare, among patients with acute nonlymphocytic leukemia, the rate of complete remission produced by induction regimens of either standard dose cytosine arabinoside and daunorubicin or high-dose cytosine arabinoside and daunorubicin; to compare the duration of complete remission and of disease-free survival among patients who receive one of the three combinations of induction and consolidation regimens listed below; to determine the comparative toxicities of these three programs, and to determine the feasililibty of implementing a predetermined approach to supportive care for these patients in a multi-institutional cooperative group setting.

Technical Approach: Patients will be stratified according to age and institution. Induction therapy will consist of standard dose Ara-C plus daunorubicin (Arm I) or high dose Ara-C + daunorubicin (Arm II). Patients requiring a second cycle of induction will receive the same doses as cycle 1, following the recovery of hematologic toxicities.

Consolidation chemotherapy will begin when bone marrow and blood counts have recovered or on day 28 after the last induction cycle. Patients initially randomized to Arm I will be randomized to Arm III (high dose, one cycle only) or Arm IV (standard dose, two cycles). Patients initially randomized to Arm II (high dose) will be assigned to Arm III. Following the completion of consolidation, no further therapy will be given and patients will be followed only. Supportive care will include a predetermined antibiotic regimen determined by the physician.

Progress: No entries at MAMC. Group-wide, among 51 patients evaluated for induction toxicity, one patient in each treatment arm died of infection. All but one of the remaining patients in each arm had life-threatening hematologic toxicity.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/34	Status: On-going

Title: SWOG 8605: Cyclophosphamide, Ara-C Infusion and Vincristine for Relapsed or Refractory Extensive Small Cell Lung Cancer: A Phase II Study of the Southwest Oncology Group, Phase II Pilot

Start Date: 16 Jan 87	Est Completion Date: Dec 89
Dept/Svc: Medicine/Hematology	Facility: MAMC

Principal Investigator: MAJ Thomas M. Baker, MC

Associate Investigators:

LTC Irwin B. Dabe, MC	MAJ David Dunning, MC
LTC Howard Davidson, MC	MAJ Ruben Sierra, MC
MAJ Lauren K. Colman, MC	CPT David R. Bryson, MC

Key Words: cancer, lung, small cell, relapsed, refractory, cyclophosphamide, Ara-C, vincristine

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

Study Objective: To determine the maximum tolerated dose of cyclophosphamide, cytosine arabinoside (Ara-C) and vincristine in a specific treatment schedule for patients with relapsing or refractory extensive small cell lung cancer, to obtain a qualitative and quantitative assessment of toxicity at each dose level, and to estimate the efficacy of the combination at the maximal tolerated dose.

Technical Approach: Induction chemotherapy: Cycle 1, cyclophosphamide, 500 mg/M, IV over 1 hour, Day 1, plus vincristine 2 mg, day 14, plus Ara-C, 250 mg/M/hour, every 12 hours continuous infusion (total dose 3 gm/M), beginning 3 hours after completion of cyclophosphamide infusion. If no Grade IV toxicity is observed, the dose of cyclophosphamide will be escalated for each course by 250 mg/M to a maximum of 1,000 mg/M. Therefore, cycle 2 (day 22) will have cyclophosphamide increased to 750 mg/M, Cycle 3 (day 43) increased to 1000 mg/M and other drugs the same as Cycle 1. Cycle 4 (day 64) will be the same as Cycle 3. Prophylactic whole brain irradiation (3,000 cGy in 15 fractions, 200 cGy/fraction) will be given three weeks after Cycle 4 (day 85) to patients with a complete or partial remission. Patients presenting with brain metastasis will receive therapeutic brain irradiation beginning on day 1 of protocol treatment. For patients presenting with a solitary brain metastasis the dose will be 30 Gy in 10 fractions for two weeks. Irradiation will be adjusted for bulky or poorly responsive lesions and will be boosted by 3 Gy for multiple metastases. Late intensification: Day 169 repeat one cycle of induction chemotherapy at the previous maximum acceptable dose and Day 337 the same as day 169.

Progress: One patient was entered at MAMC in FY 87.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/110	Status: On-going

Title: SWOG 8616: Intergroup Phase III Randomized Study of Doxorubicin and Decarbazine with or without Ifosfamide and Mesna in Advanced Soft Tissue and Bone Sarcoma (INT-#0072)

Start Date: 21 Aug 87	Est Completion Date: Aug 90	
Dept/Svc: Medicine/Hematology		Facility: MAMC

Principal Investigator: LTC Lauren K. Colman, MC

Associate Investigators:

COL Irwin B. Dabe, MC	MAJ David M. Dunning, MC
LTC Howard Davidson, MC	MAJ Ruben D. Sierra, MC
MAJ Thomas M. Baker, MC	CPT Denis P. Bouvier, MC

Key Words: sarcoma, soft tissue, bone, doxorubicin, decarbazine ifosfamide, mesna

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

Study Objective: To determine if the addition of ifosfamide to doxorubicin and dacarbazine significantly changes the response rate, survival, and toxicity.

Technical Approach: Patients with histologically documented metastatic or unresectable sarcoma will be eligible. Metastatic osteogenic (OGS), Ewing's (ES), and rhabdomyosarcoma (RMS) will be assigned to Arm II (doxorubicin/DTIC plus ifosfamide) and will be analyzed separately. Kaposis sarcoma and mesothelioma will be excluded. Patients will have had no prior chemotherapy for sarcomas and no prior doxorubicin. Patients will be stratified by stage, grade, and radiotherapy history. Patients will be randomized to receive either doxorubicin/DTIC or doxorubicin/DTIC + ifosfamide. Doxorubicin, 15 mg/m^2, will be given by continuous infusion, Days 1-4. DTIC, 250 mg/m^2, will be given by continuous infusion, Days 1-4. Ifosfamide, 2500 mg/m^2, will be given by continuous infusion, Days 1-3. Mesna will be infused continuously Days 1-4 to counteract urotoxicity. Each regimen will be given every 21 days. OGS, ES, and RMS patients will be removed from study and crossed to a standard regimen after four cycles if response is documented. Complete responders will continue combination chemotherapy for six cycles after documentation of response. Partial response and stable disease patients will continue treatment at the highest tolerable dose for a least two cycles after the maxiumum response or until disease progression. Patients with rapid disease progression will be removed from the study. Otherwise, there will be a minimum of two cyles of chemotherapy before removal.

Progress: One patient was entered at MAMC in FY 87.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/46	Status: Completed

Title: SWOG 8622: Evaluation of Echinomycin in Advanced Colorectal Cancer. Phase II.

Start Date: 27 Feb 87	Est Completion Date: Feb 90
Dept/Svc: Medicine/Hematology	Facility: MAMC

Principal Investigator: MAJ Thomas M. Baker, MC

Associate Investigators:

LTC Irwin B. Dabe, MC	MAJ David Dunning, MC
LTC Howard Davidson, MC	MAJ Ruben Sierra, MC
MAJ Lauren K. Colman, MC	CPT David R. Bryson, MC

Key Words: cancer, colorectal, echinomycin

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

Study Objective: To determine the antitumor activity of echinomycin in patients with colorectal carcinoma by determination of the response rate and remission duration and to define the qualitative and quantitative toxicities of this drug in a phase II study.

Technical Approach: Patients must have a biopsy proven adenocarcinoma arising from the colon or rectum, with measurable disease, to be eligible for this study. Patients may not have received prior chemotherapy. Patients with surgery or prior radiotherapy to less than 25% of the bone marrow-bearing areas are eligible.

Patients will receive echinomycin, 1.2 mg/m^2 IV, over 15-30 minutes once every week for four weeks, followed by a two week rest period. Treatment will continue on this schedule provided patients have WBC $\geq$3,500/µl and platelet count $\geq$100,000/µl. Patients failing to achieve a complete or partial response or stable disease after one course of therapy will be removed from the study. One four-week treatment period followed by the two-week rest period will constitute one course of therapy. Courses of therapy will be continued until patients demonstrate evidence of progressive disease or there is unacceptable toxicity.

Progress: No entries at MAMC. This study was closed by SWOG in September 1987 due to sufficient patient accrual.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/60	Status: On-going

Title: SWOG 8624: A Phase III Randomized Trial of Combination Therapy for Multiple Myeloma. (1) Comparison of VMCP/VBAP to VAD or VMCPP/VBAPP for Induction; (2) Alpha-2b Interferon or No Therapy for Maintenance; and (3) Alpha-2b Interferon + Dexamethasone for Incomplete or Non-Responders

Start Date: 20 Mar 87	Est Completion Date: Sep 90	
Dept/Svc: Medicine/Hematology		Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

COL Irwin B. Dabe, MC	MAJ David Dunning, MC
LTC Lauren K. Colman, MC	MAJ Ruben Sierra, MC
MAJ Thomas M. Baker, MC	CPT David R. Bryson, MC

Key Words: myeloma, multiple, VMCP, VBAP, VAD, VMCPP, VBAPP, alpha-2b interferon, dexamethasone

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

Study Objective: To compare the effectiveness in achieving remission of the three regimens; to determine if interferon alpha-2b prolongs remission duration and survival compared to no maintenance therapy for patients achieving remission; to determine if dexamethasone plus interferon alpha-2b will enable patients achieving only improvement with the chemotherapy induction to achieve remission, and to study various proposed prognostic factors in multiple myeloma.

Technical Approach: Agents to be used are Adriamycin (A), BCNU (B), cyclophosphamide (C), dexamethasone (D), melphalan, (M), prednisone (P), vincristine (V), and alpha-2b interferon. Patients previousy untreated with chemotherapy with the diagnosis of multiple myeloma are eligible. Patients will be stratified as to tumor mass, prior radiation therapy, and risk category. Patients will be randomized to induction therapy as follows: Arm I - VMCP alternating with VBAP every 3 weeks; Arm II - VAD every 3 weeks; or Arm III - VMCPP alternating with VBAPP every 3 weeks. Induction therapy on arms I and III will be given for a minimum of 9 cycles and a maximum of 18 cycles. Arm II (VAD) induction therapy will be given for a minimum of 6 cycles and a maximum of 9 cyles. Arms I and III will require a minimum of 9 cycles of induction therapy and Arm II a minimum of 6 cycles before beginning maintenance therapy. Supplemental treatment with transfusions, dialysis, and radiation therapy may be given at the discretion of the investigator. At the appropriate time, responding patients will be randomized for maintenenace to alpha-b interferon or no maintenance. Evaluable patients failing to achieve 75% tumor regression will be ineligible for remission maintenence but will be registered on a non-randomized trial of dexamethasone plus alpha 2b interferon to determine if this therapy can convert the patient to a remission status.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/47	Status: On-going

Title: SWOG 8691: A Randomized Comparison of Deoxycoformycin versus Alpha-Interferon in Previously Untreated Patients With Hairy Cell Leukemia

Start Date: 27 Feb 87	Est Completion Date: Feb 90	
Dept/Svc: Medicine/Hematology		Facility: MAMC
Principal Investigator: LTC Howard Davidson, MC		
Associate Investigators:		
COL Irwin B. Dabe, MC	MAJ David Dunning, MC	
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MAJ Thomas M. Baker, MC	CPT David R. Bryson, MC	
Key Words: hairy cell leukemia, deoxycoformycin, alpha interferon		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A

Study Objective: To compare deoxycoformycin (dCF) versus alpha-interferon (α-IFN) in terms of relative efficacy in hairy cell leukemia patients who have not had splenectomy and to evaluate toxicities of both.

Technical Approach: Patients will be stratified according to performance status and randomized to either Arm I or Arm II.

Arm I: α-IFN, $3x10^6$ IU, subcutaneously, 3 times a wk for 6 mon.

Complete or partial remissions will continue treatment for 6 more months. Non-responders will be crossed over to dCF. After the second 6 months of treatment, if either a complete or partial remission has been achieved, therapy will be discontinued and the patient will be observed on a monthly basis to document duration of response.

Arm II: dCF, IV, every two weeks for 6 months.

Performance status 0, 1, or 2 patients will receive 4 mg/m^2 and status 3 patients will receive 2 mg/m^2 and escalated as permitted by toxicity (maximum 4 mg/m^2). If a complete remission is achieved, 2 additional doses of dCF will be given and then treatment will be stopped and the patient observed at monthly intervals. If a complete or partial remission has not been achieved by 6 months, the patient will be crossed over to the α-IFN arm. If a partial remission is achieved, dCF will be continued. When a complete remission is documented, 2 additional doses of dCF will be given and then treatment will be stopped. At 12 months on either therapy, if the best response is a partial remission, therapy will be discontinued and the patient will be observed at monthly intervals.

Progress: No entries at MAMC. Group-wide, five patients have been evaluated for toxicity. One patient in each treatment arm had life-threatening hematologic toxicity.

Detail Summary Sheet

Date: 30 Sep 87	Protocol No.: 87/111	Status: On-going

Title: SWOG 8694: (CALGB-8582), A Comparison of Pentostatin (NSC-377523) in Splenectomized Patients with Active Hairy Cell Leukemia

Start Date: 21 Aug 87	Est Completion Date: Aug 90
Dept/Svc: Medicine/Hematology	Facility: MAMC

Principal Investigator: COL Irwin B. Dabe, MC

Associate Investigators:

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Key Words: leukemia, hairy cell, splenectomized, pentostatin

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

Study Objective: To compare the frequency of response between pentostatin and alpha-interferon treatment in patients with hairy cell leukemia who following splenectomy manifest active or progressive disease; to compare time to response, response duration, and toxicity of these two treatments; and to determine if pentostatin salvages nonresponders to alpha-interferon treatment and if alpha-interferon salvages nonresponsder to pentostatin treatment.

Technical Approach: Patients will have had splenectomy at least 3 months prior to treatment, with no prior treatment with pentostatin or interferon. Patients will be randomized to either interferon or pentostatin.

Interferon ($2x10^6$ IU/m^2) will be given by injection (s.c.) 3 times a week. Patients will be assessed at 3 months but will continue interferon treatment. Patients will be assessed at 6 months and those with complete (CR) or partial remission (PR) or stable disease (SD) will continue treatment for 6 months more. Non-responders will be crossed over to pentostatin. Patients will be assessed at 12 months, and those with CR, PR, or SD will be followed with no further therapy. If progression occurs, patients will be retreated with interferon.

Pentostatin, 4 mg/m^2, will be given IV on days 1 and 15, and repeated every 4 weeks with dosage adjusted for performance status. Patients will be assessed at 3 months and the pentostatin will be reduced to once every 4 weeks. At the 6 month assessment, patients with CR, PR, or SD will continue treatment for 6 more months. Non-responders will be crossed over to interferon. Patients will be assessed at 12 months and those with CR, PR, of SD will be followed with no further therapy. If progression occurs, patients will be retreated with pentostatin.

Progress: No entries at MAMC. Group-wide, one death has been reported, presumably from a fungal infection. No post-mortem was performed, and it is not clear if this death was treatment related.

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