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Department of Clinical Investigation

Annual Research Progress Report



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Madigan Army Medical Center

Tacoma, Washington 98431-5454

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ANNUAL PROGRESS REPORT

30 September 1989

DEPARTMENT OF CLINICAL INVESTIGATION

MADIGAN ARMY MEDICAL CENTER

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Nancy J. Whitten

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This report covers all research protocols that were administratively or technically supported by the Department of Clinical Investigation, Madigan Army Medical Center, during FY 89. Included in the individual reports are title, investigators, funding, objective, technical approach, and progress for FY 89. Also included in the report are personnel rosters for the Department, funding information, and presentations and publications emanating from Madigan Army Medical Center during this period.

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ANNUAL RESEARCH PROGRESS REPORT

FISCAL YEAR 1989

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

In conducting the research described in this report, the investigators adhered to the "Guide for 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, preparation, and editing 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 the Commander and other Headquarters personnel. Without the support of these individuals, productivity would have been much less. In addition, the Clinical Investigation Activity at Health Services Command has increasingly been responsive to our problems and needs, and we would like to thank them for their support in the last year. This report is a summary of the activities which have taken place in the research arena at Madigan Army Medical Center during fiscal year 1989.

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

UNIT SUMMARY FY 89

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

	MANPOWER	
DESCRIPTION	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 MacMILLAN, JAMES G., D.V.M., MAJ, VC	O4	64C9B
C, Microbiology Svc van HAMONT, JOHN E. CPT, MS	O3	68A9B
C, Biochemistry Service HANNAN, Charles J., Ph.D., MAJ, MS	O4	68C9C
C, Biological Research Svc HOOP, RITA C., M.S., CPT, MS	O2	68C00
NCOIC (OCT 88 - Feb 89) SGT CAMPBELL, Naomi	E5	91T2R
NCOIC (Mar 89 - Sep 89) SGT SPAHN Shelley		
OR TECH (Oct 88 - Dec 88) SGT ROBBINS, John L.	E5	91D2R
OR TECH (Jul - Sep 89) SGT WILLIAMS, Gary L.	E5	91D20
Med Lab Spec SP4 GONZALEZ/RESTO, Alexander	E4	92B10
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Vet Animal Spec (OJT) PV4 DEVOL Kenneth A	E4	91T10
Med Tech KETTLER, Thomas M.	GS9	0644
Med Tech MATEJ, Louis A.	GS9	0644
Med Tech WRIGHT, JAMES	GS9	0644
Computer Programmer Analyst (temp) PATIENCE, TROY	GS9	0334
Edit Asst/Steno WHITTEN, Nancy J.	GS6	1087
Sec/Steno HOUGH, Eugenia R.	GS5	0318
Maintenance Worker KAEO, Curtis	WG7	4749

FUNDING FY 89

MEDCASE Equipment	66,177.00
Capital Equipment	9,247.00
Civilian Salaries	188,939.00
Military Salaries	559,982.00
Consumable Supplies	94,109.00
Contractual Services	8,958.00
TDY	177.00
TOTAL	$927,589.00

GRANTS: AMOUNT: $78,577.00 Source: NIH

FOR: Protocol - The Effects of Head Rotation and Hyperoxygenation-Suction Sequences During Endotracheal Suctioning of Newborn Infants

PRINCIPAL INVESTIGATOR: LTC Barbara S. Turner, AN

HSC #89033 MAMC #89/11

3. Progress

During FY 89 there were 283 active protocols that received administrative and/or technical support during the year. Of these, 215 are presently ongoing; 51 were completed; and 17 were terminated.

There were 80 publications from approved research studies and 80 papers were presented at regional, national, or international meetings.

4. Fellowship/Residency Program Support

During FY 89, the Department of Clinical Investigation supported research conducted by Fellows/Residents in the following GME training programs:

Fellowship Programs	#protocols
Child Psychology	1
Endocrinology	3
Hematology/Oncology	2
Maternal/Fetal Med	1
Pulmonology	3

Residency Programs	# protocols
Emergency Medicine	3
Family Practice	2
General Surgery	3
Internal Medicine	8
OB/GYN	8
Oral Maxillofacial Surg	1
Orthopedic Surgery	1
Otolaryngology	2
Pediatric Dentistry	3
Preventive Medicine	1
Public Health	2
Urology	3

The Department of Clinical Investigation also supported research for three medical interns as part of their training.

In addition, the Department of Clinical Investigation supported a research protocol for the US Army/Texas Wesleyan University Program in Anesthesia Nursing and 5 protocols that fulfilled the research requirement for five graduate degrees in Nursing at the University of Washington.

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

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Madigan Army Medical Center
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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 1989:

YANCEY, Michael K. CPT, MC	Effect on Serum Lipids and Lipoproteins of Continuous or Cyclic Medroxyprogesterone Acetate Treatment in Postmenopausal Women

OTHER NOMINEES WERE:

BOWERSOX, Jon C. CPT, MC	Response of Human Venous Endothelial Cells to Seeding on Extracellular Matrices
ELG, Steven A. CPT, MC	Evaluation of Serum Haptoglobin Levels in Patients with Adnexal Masses
FOX, Charles W. CPT, MC	Determination of Indwelling Ureteral Stent Patency: Comparison of Standard Contrast Cystography, Nuclear Cystography, and Lasix Renography

PUBLICATIONS

FISCAL YEAR 89

DEPARTMENT OF CLINICAL INVESTIGATION

Backous DD, Farrow JA, Friedl KE	Assessment of Pubertal Maturity in Boys Using Height and Grip Strength. Clin Res 37(1): 167, 1989
Buckley WE, Yesalis CE, Friedl KE, Anderson WA, Streit AL, Wright JE	Estimated Prevalence of Anabolic Steroid Use Among Male High School Seniors. JAMA 260(23): 3441-45, 1988
Friedl KE, Hannan CJ, Schadler PW, Jacob WH	Atropine Absorption After Intramuscular Administration with 2-Pralidoxime Chloride By Two Automatic Injector Devices. J Pharmaceutical Sciences 78(9): 1989
Friedl KE, Jones RE, Hannan CJ, Plymate SR	Exogenous Androgen Administration Is Not Associated With Impaired Insulin Secretion or Impaired Glucose Tolerance. Clin Res 37(1): 1989
Friedl KE, Jones RE, Hannan CJ, Plymate SR	The Administration of Pharmacological Doses of Testosterone or 19-Nortestosterone To Normal Men is Not associated with Increased Insulin Secretion or Impaired Glucose Tolerance. J Clin Endo Metab 68 (5): 971-75, 1989
Friedl KE, Yesalis CE	Self-Treatment of Gynecomastia in Bodybuilders Who Use Anabolic Steroids. Physician Sports Med 17 (3): 67-79, 1989
Garden GA, Hannan CJ, Spencer CA, Plymate SR	The Effect of Sex Hormone Binding Globulin (SHBG) on the Pituitary Testicular Axis in Hyperthyroid Men. Steroids 52(4): 385-86, 1988
Hannan CJ, Kettler TM, Dabe IW, Clark TS	Delta-aminolevulinic Acid in Plasma by Free Amino Acid Analysis. Clinical Chemistry 35(9): 1998, 1989

Hayre MD, Robbins JR	What's Your Diagnosis? Skin Lesions in Pigs. Lab Animal 18(2): 19-20, 1989
Jones RE, Plymate SR	Docosahexaenoic Acid Regulates Fatty Acid:CoASH Ligase Activity in Human Spermatozoa Through Negative Cooperativity. J Andrology 10(1): 44, 1989
Kiel DP, Baron JA, Plymate SR, Chute CC	Sex Hormones and Lipoproteins in Men. Amer J Med 87(1): 35-39, 1989
Moore WV	Editorial - Anabolic Steroid Use in Adolescence. JAMA 260(23): 3484-86, 1988
Nestler JE, Barlascini CO, Matt DW, Steingold KA, Plymate SR, Clore JN, Blackard WG	Suppression of Serum Insulin by Diazoxide Reduces Serum Testosterone Levels in Obese Women with Polycystic Ovary Syndrome. J Clin Endo Metab 68(6): 1027-32, 1989
Plymate SR, Jones RE, Matej LA, Friedl KE	Regulation of Sex Hormone Binding Globulin (SHBG) Production in Hep G2 Cells by Insulin. Steroids 52(4): 339-40, 1988
Plymate SR, Tenover JS, Bremner WJ	Circadian Variation in Testosterone, Sex Hormone Binding Globulin, and Calculated Non-Sex Hormone Globulin-Bound Testosterone in Healthy Young and Elderly Men. J Androl 10(5): 366-71, 1989
Sterling Dan	Citation - High Schools Not Immune. USA Today, p 16, Dec 1988
Yesalis CE, Herrick RT, Buckley WE, Friedl KE, Brannon D, Wright JE	Self-Reported Use of Anabolic-Androgenic Steroids by Elite Power Lifters. Physician Sports Med 16 (12): 91-99, 1988
Yesalis CE, Streit AL, Vicary JR, Friedl KE, Brannon D, Buckley W	Anabolic Steroid Use: Indications of Habituation Among Adolescents. J Drug Educa 19(2): 103-16, 1989

DEPARTMENT OF EMERGENCY MEDICINE

Cloonan CC	The "Civilianization" of the Army Medical Department. Military Medicine 153: 538, 1988
Eitzen EM, Seward PN	Arthropod Envenomations in Children. Pediatr Emer Care 4(4): 266-72, 1988
Gibson DE, Moore GP, Pfaff JA	Camphor Ingestion. Amer J Emer Med 7(1): 41-43, 1989
Hurley WT, Saglio SD, Henley CE, Gatrell CB	Evaluation of a Rapid Theophylline Test Strip Assay in the Emergency Department Setting. Ann Emer Med 17(10): 1029-33, 1988
Moore GP, Hurley WT, Pace SA	Hereditary Angioedema. Ann Emer Medicine 17(10): 1082-86, 1988

DEPARTMENT OF MEDICINE

Elam MP, Laird JR, Johnson S, Stratton JR	Swallow Syncope Associated with Complete Atrioventricular Block - A Case Report and Review of the Literature. Mil Med 154(9): 465-66, 1989
Jeffers DJ, Cooper GS, Noel GL	Assessing Interviewing Skills of Residents Using Multiple Brief Videotaped Interviews. Clinical Research 37(2): 808, 1989
Jones RE, Plymate SR	Phosphatidylcholine Synthesis in Human Spermatozoa. J Androl 10(5): 346-50, 1989
Koenig KG, Lindberg JS, Zerwekh JE, Williams PK, Cushner HM, Copley JB	Utility of Free 1,25(OH)2D3 Measurements in Renal Failure. Clinical Research 37(2): 453, 1989
Kollef MH, Dunn TL	Pulmonary-Embolism Masquerading as Pulmonary Arteriovenous Malformation on Computerized Tomography. South Med J 82(7): 924-26, 1989
Roth BJ, O'Meara T, Cragun WH	Serum Effusion Albumin Gradient in the Evaluation of Pleural Effusions. Amer Rev Resp Dis 139(4): 359, 1989

Tapp DC, Wortham WG, Addison JF, Hammonds DN, Barnes JL, Venkatachalam MA	Food Restriction Retards Body Growth and Prevents End-Stage Renal Pathology in Remnant Kidneys of Rats Regardless of Protein Intake. Lab Invest 60(2): 184-95, 1989
Vincent DS, Cooper GS, Jeffers DJ	A Match Made in Heaven - The Introduction of Meta Analysis to a Journal Club. Clinical Research 37(2): 816, 1989

DEPARTMENT OF NURSING

Wiswell TE, Turner BS, Bley JA, Fritz DL, Hunt RE	Determinants of Tracheobronchial Histologic Alterations During Conventional Mechanical Ventilation. Pediatrics 84(2): 304-11, 1989

DEPARTMENT OF OB/GYN

Brady WK, Duff P	Rheumatic Heart Disease in Pregnancy. Clin Obstet Gynecol (32)1:21-40, 1989
Brady WK, Duff P, Schilhab JC, Herd M	Reliability of a Rapid Latex Fixation Test for Detecting Group B Streptococci in the Genital Tract of Parturients at Term. Obstetrics and Gynecology 73(4): 678-81, 1989
Christian SS, Duff P	Is Universal Screening for Hepatitis B Infection Warranted in all Prenatal Populations?. Obstet Gynecol 74(2): 259-261, 1989
Duff P	Antibiotics in Treatment of Chorioamnionitis. Amer J Obstet Gynecol 160(1): 271, 1989
Duff P	Prenatal Screening for HIV Infection: Purpose, Priorities, Protocol, and Pitfalls. Obstet Gynecol 74(3): 403-404, 1989
Duff P, Brady WK	On Improving the Lecture. Obstet Gynecol 73(6): 1050, 1989
Elg S, Lee RB, Stones C, Webber PJ, Benson WL	Evaluation of Serum Haptoglobin Levels in Patients with Adnexal Masses. Mil Med 154(5): 234-236, 1989.

Harlass FE, Duff P, Brady WK, Read JA	Hydrops Fetalis and Premature Closure of the Ductus Arteriosus: A Review. Ob Gyn Survey 44(7): 541-43, 1989
Harlass FE, Magelssen DJ	Benefits of Posturethropexy Bladder Conditioning. Journal Repro Med 33(12): 961-63, 1988
Kopelman JN, Duff P, Read JA	Randomized Comparison of Oral Terbutaline and Ritodrine for Preventing Recurrent Preterm Labor. J Repro Med 34(3): 225-30, 1989
Lee RB, Kelly J, Elg SA, Benson WL	Pregnancy Following Conservative Surgery and Adjunctive Chemotherapy for Stage-III Immature Teratoma of the Ovary. Obstet Gynecol 73(5): 853-55, 1989
Magelssen DJ	Voiding Abnormalities in Women. Amer Uro-Gynecol Soc Quar Rpt 6(4): 1988
Magelssen DJ	Urinary Tract Infections in Women. IN: Patient Education Booklet, Norwich Eaton, 1989
Yancey M, Magelssen DJ, Demaurez A, Kelly J, Lee RB	The Clinical Significance of Endometrial Cells on Cervical Cytology. Gynecologic Oncology 32: Feb 1989

DEPARTMENT OF PEDIATRICS

Hartman KR, Mancojohnson M, Rawlings JS, Bower DR, Marlar RA	Homozygous Protein-C Deficiency and Purpura Fulminans - Early Treatment With Warfarin. Pediatric Research 25(4): 270, 1989
Jordan GD, Jarrett RV, Garcia J, Frank CG, Pettett PG	Central Nervous System Air Embolism in Respiratory Distress Syndrome: Considerations for Patient Survival. Amer J Perinatol 6(1): 80-83, 1989
Kaufmann CR, Rivara FP, Maier RV	Pediatric Trauma - Need for Surgical Management. Journal of Trauma 29(8): 1120-1126, 1989
Kelly PC, Blake WW, Davis JR	Tandem-Y/6 Translocation With Partial Deletion 6 (P23->PTER). Clinical Genetics 35(3): 204-07, 1989

Kelly PC, Cohen ML, Walker WO, Caskey OL, Atkinson AW	Self-Esteem in Children Medically Managed for Attention Deficit Disorder. Pediatrics 83(2): 211-16, 1989
Keniston RC, Reyna T, Becker W, Weir MR, Enriquez JI, Duncan F	Prognostic Value of Underproteinized Plasma Pyridoxal 5'- Phosphate Concentrations. IN: Clinical and Physiological Applications of Vitamin B-6, JE Leklem, RD Reynolds (ed.), Alan R. Liss, Inc, New York, 1988
Moore DC	Body Image and Eating Behavior in Adolescent Girls. Amer J Dis Child 142(10): 1114-18, 1988
Nickels DA, Moore DC	Serum Cortisol Responses in Febrile Children. Pediatr Infec Dis J 8(1): 16-19, 1989
Pearl W, Weir MR, Stafford EM, Gregory G, Imai W, Schydlower M	Ethnic Differences in Adolescent Electrocardiograms. International Pediatrics 4(1): 49-52, 1989
Rawlings JS, Krober MS, Aamodt LW	Imaging Case of the Month: Neonatal Herpes Simplex Virus Pneumonia. American Journal Perinatology 6(3): 304-06, 1989
Stafford EM, Weir MR, Pearl W, Imai W, Schydlower M, Gregory G	Sexual Maturity Rating: A Marker for Effects of Pubertal Maturation on the Adolescent Electrocardiogram. Pediatrics 83(4): 565-69, 1989
Stephan MJ, Stevens EL, Wenstrup RJ, Greenberg CR, Gritter HL, Hodges GF, Guller B	Mucopolysaccharidosis I: Presenting with Endocardial Fibroelastosis of Infancy. Amer J Dis Child 143(7): 782-84, 1989
Weir MR	Atypical Idiopathic Hypercalciuria in an Adolescent. J Adolescent Health Care 9(6): 498-500, 1988
Weir MR	Intravascular Injuries from Intramuscular Penicillin. Clinical Pediatrics 27(2): 85-90, 1988
Weir MR, Duncan NO	Acute Suppurative Adenoiditis. Amer J Dis Child 143(9): 97-98, 1989

Weir MR, Stafford EM, Gregory G, Lawson MA, Pearl W	The Relationship Between Sexual Maturity Rating, Age, and Increased Blood Pressure in Adolescents. J Adoles Health Care 9(6):465-69, 1988
Weir MR, Weir TE	Are Hot Ears Really Hot?. Amer J Dis Child 143(7): 763-64, 1989

PREVENTIVE MEDICINE SERVICE

Brandt C	Health Promotion and Disease Prevention Survey of US Army Retirees. Thesis, MPH, University of Washington, 1989

DEPARTMENT OF PSYCHIATRY

Parkison SC, Kelly PC,	Multidisciplinary Treatment of Encopretic Children. IN: Casebook of Child & Ped Psych, MC Roberts, CE Walker, Guilford Press, New York, pp 298-318, 1989

DEPARTMENT OF SURGERY

Arciero RA, Leung KYK, Pierce JH	Spontaneous Unstable Burst Fracture of the Thoracolumbar Spine in Osteoporosis - A Report of Two Cases. Spine 14(1): 114-17, 1989
Beck RA, Blakeslee DB	The Changing Picture of Facial Fractures - 5-Year Review. Arch Otolaryngol H&N Surg 115(7): 826-29, 1989
Bowersox JC, Andersen CA	Acute Effects of Intravenous Lipid Emulsion Infusion on Plasma Fibronectin. Nutrition Research 9(8): 867-71, 1989
Kiesling VJ, Tank ES	Postoperative Intussusception in Children. Urology 33(5): 387-89, 1989
Mooney MJ, Carter PL	Routine Cholecystectomy in the Morbidly Obese. Mil Med 154(8): 489-511, 1989

Moul JW, Davis R, Vaccaro JA, Sihelnik SA, Belville WD, McLeod DG	Acute Urinary Retention Associated with Prostatic-Carcinoma. J Urology 141(6): 1375-1377, 1989
Mukherjee D, Inahara T	Endarterectomy as the Procedure of Choice for Atherosclerotic Occlusive Lesions of the Common Femoral Artery. Amer J Surg 157: 498-500, 1989
Piatt JH	Trauma Case for Diagnosis - Atlanto-Occipital Dislocation. Military Medicine 154(9): 455-57, 1989
Piatt JH, Goodkin R	Barbiturates in Severe Head Injury. J Neurosurgery 70(3): 501-02, 1989
Piatt JH, Hoffman HJ	Cor Pulmonale: A Lethal Complication of Ventriculoatrial CSF Diversion. Child's Nerv Syst 5(1): 29-31, 1989
Renfer LG, Kelley J, Belville WD	Inverted Papilloma of the Urinary Tract: Histogenesis, Recurrence and Associated Malignancy. J Urol 140(4): 832-34, 1988
Rozanski TA, Kiesling VJ, Vaccaro JA, Belville WD	Elective Cholecystectomy During Major Urological Surgery. J Urology 141(6): 1295-1297, 1989
Smith DB, Arnold JE, Fox B, Blakeslee DB	Hereditary Carcinoma Syndromes Associated with Benign Head and Neck Tumors. H & N Jr for the Sci Special H & N 11(3): 247-51, 1989
Smith DB, Woody EA, Richardson M, Olsen HL, Blakeslee DB	A Device for the Intraoperative Identification of the Recurrent Laryngeal Nerve in Piglets. Otolaryngology H&N Surg 100(2): 137-45, 1989
Wilson WJ	Intraoperative Autologous Transfusion in Revision Total Hip Arthroplasty. J Bone Joint Surg 71(1): 8-14, 1989

PRESENTATIONS

FISCAL YEAR 89

DEPARTMENT OF CLINICAL INVESTIGATION

Friedl KE, Jones RE, Hannan CJ, Plymate SR	Exogenous Androgen Administration is not Associated With Impaired Insulin Secretion or Impaired Glucose Tolerance.	American Federation for Clinical Research, Western Region, Carmel, CA, February 89
Hannan CJ, Kettler TM, Friedl KE, Plymate SR	Plasma Homovanillic Acid (HVC) Changes During Testosterone or Nandrolone Administration in Humans.	1988 Annual Meeting of the Society of Neuroscience, Toronto, CN, November 88
Hoop RC, Jones RE	Regulation of SHBG Concentration by Peptide and Steroid Hormones.	71st Annual Meeting of The Endocrine Society, Seattle, WA, June 89
Jones RE, Plymate SR	Docosahexaenoic Acid Regulates Fatty Acid: CoASH Ligase Activity in Human Spermatozoa Through Negative Cooperativity.	American Society of Andrology, New Orleans, LA, April 89
Lampe TE, Veith RC, Plymate SR, Risse SC, Koepikin H, Cubberley L, Raskind MA	The Effects of TRH on Blood Pressure and Plasma Norepinephrine May Distinguish AD and Normal Men.	Second International Symposium on Familial Alzheimer's Disease, May 89
Plymate SR, Paulsen CA	Relationship of Serum Inhibin Levels to FSH and Sperm Production in Normal Men and Men with a Varicocele.	71st Annual Meeting of The Endocrine Society, Seattle, WA, June 89
Plymate SR, Petra PH, Que B, Hoop RC	Regulation of Sex Hormone Binding Globulin (SHBG) Production Pre and Post-Translational Mechanisms.	5th Annual Army Regional Meeting, American College of Physicians, San Francisco, CA, October 88

Tenover JS, Zeitner ME, Plymate SR	Effects of 24-Week Administration of a 5-Alpha Reductase Inhibitor (MK-906) on Serum Levels of Testosterone (T), Free T, and Gonadotropins in Men.	The Endocrine Society, Seattle, WA, June 89
van Hamont JE, Wright JR	Analysis of Ureaplasma Urealyticum Serovar Antigens with Monoclonal Antibodies.	NW Branch American Society for Microbiology, Seattle, WA June 89

DEPARTMENT OF DENTISTRY

Allinder JR	Pulpotomy in the Primary Dentition: A Clinical Evaluation of Two Techniques	American Academy of Pediatric Dentistry, May 89

DEPARTMENT OF EMERGENCY MEDICINE

Burkle FM, Pimentel L, Friedl KE	Countertransference Dangers in Emergency Medicine	6th World Conference on Disaster and Emergency Medicine, Hong Kong, HK, September 89
Moore GP, Pace SA, Busby W	Comparison of Intraosseous, Intramuscular, and Intravenous Administration of Succinylcholine.	National Scientific Assembly of Society for Academic Emergency Medicine, San Diego, CA, May 89

DEPARTMENT OF FAMILY PRACTICE

Blount BW	Lightning Injuries	Uniformed Services Chapter of the American Academy of Family Physicians, March 89
Blount BW	Metal Fume Fever in the Military	Uniformed Services Chapter of the American Academy of Family Physicians, March 89

Blount BW	Clinical Precepting and Bedside Rounds	Uniformed Services Chapter of the American Academy of Family Physicians, March 89
Magelssen DJ, Henley Ce	Correlation Between Faculty Development and Organizational Systems Behavior in Military Medical Centers	Society of Teachers for Family Medicine, October 88

DEPARTMENT OF MEDICINE

Jeffers DJ	The Reliability of Two Methods for Assessing Resident Problem Solving and Interviewing Techniques.	Advances in Internal Medicine, American College of Physicians, San Francisco, CA, October 88
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MacHaffie B	An Eight Year Old Girl With Intracerebral Hemorrhage and Mycotic Abscesses and Growth Hormone Deficiency - Case Report	7th Annual Meeting of the NW Society for Developmental and Behavioral Pediatrics, Portland, OR, April 89

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

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DEPARTMENT OF CLINICAL INVESTIGATION

Detail Summary Sheet

Date: 30 Sep 89 | Protocol No.: 87/86 | Status: Completed

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, phenylethylamine-induced, age specific, γ-endorphin, rats

Accumulative MEDCASE Cost: -0- | Est Accumulative OMA Cost: -0- | Periodic Review: Oct 88

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 project was proposed for a joint VA-DoD grant, but was not funded. Limited experiments were done on 30 rats using DCI funding. The data are being analyzed and prepared for publication.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 87/94 Status: Terminated

Title: Surgical Resuscitation: The Role of Blood Substitutes
Start Date: 17 Jul 87 Est Completion Date: May 89
Department: Pediatrics Facility: MAMC
Principal Investigator: CPT Rita C.Hoop, MS
Associate Investigators: MAJ Kip Hartman, MC
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: Oct 88

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, liposomes without hemoglobin encapsulation, and LEBH (6 animals/group). 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 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, 4 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, 6 animals will undergo plasma exchange with LEBH and 6 controls will be autotransfused with packed red cells. Alterations in the hepatic, renal, pulmonary and hematology systems will be documented. The immune response to large dose infusion and delayed challenge with LEBH will be evaluated by ELISA.

Progress: The particular blood substitute which was tested in rats in a previous protocol was found to be toxic, causing a precipitous drop in heart rate. No work was done on this protocol in FY 89 due to the nonavailability of an acceptable, nontoxic blood substitute product. Therefore, the protocol was terminated.

**Funded by a joint VA/DoD grant.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 83/83 Status: Completed

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
COL Gary L. Treece, MC
MAJ Stanley P. Liebenberg, VC
CPT Karl E. Friedl, MSC
Mina J. Garrison, B.S., M.T.
Louis A. Matej, B.S., M.T.

Key Words: Hep G2 cells, testosterone, estradiol, PRL, insulin

Accumulative MEDCASE Cost: -0-

Est Accumulative OMA Cost: $500.00

Periodic Review: Sep 89

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

Technical Approach: The investigators had originally planned to use beagles for this study, but with the ban on the use of dogs in 1983 the protocol was restructured to an *in vitro* study using the human hepatoma cell line, Hep G2.

The human hepatoma cell line, Hep G2, was grown to confluence in Dulbecco's Minimum Essential Median (DMEM) with 10% fetal calf serum (FCS). Additions of T_4, insulin, estradiol, and testosterone will be done daily for three days with DMEM without FCS, and media 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 will be harvested and counted in each flask. SHBG production will be normalized for cell number. Each hormone addition will be performed in triplicate per experiment.

Progress: The information gained from this study was used as the basis for several other studies as well as the publication and presentation listed below.

PUBLICATION: J Clin Endocrinol Metab 67:460, 1988.

PRESENTATION: Amer Fed Clin Res, Western Region, February 1988 (abstract #130, Clinical Research, Feb 88).

The study has shown that insulin and prolactin inhibit SHBG production and that testosterone, T_4, and estradiol stimulate SHBG production *in vitro*. These findings suggest that insulin and prolactin may be important factors in the regulation of SHBG production *in vivo*.

Detail Summary Sheet

Date: 30 Sep 89 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., Univ Washington
Richard E. Berger, M.D., Univ Washington
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: Sep 89

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 scheduled for varicocele repair, (2) infertile men without varicoceles; (3) fertile men scheduled for varicocele repair, 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, 2 sperm penetration assays at least 4 weeks apart, and 2 LH/RH stimulation tests performed. Blood samples will be drawn every 15 min for 2 hrs after the injection of the LH/RH. Following repair of the varicocele, seminal fluid analyses every 2-4 wks, sperm penetration assay at 6 and 12 months after the varicocele ligation, and LH/RH at 6 and 12 months after the varicocele ligation will be performed.

Progress: Approximately 100 additional subjects were entered in this study in FY 89 for a total enrollment of 260.

The data accrued to this date support the concepts that inhibin interacts with FSH in a negative feedback fashion in normal men and Sertoli cell function (as assessed by serum inhibin levels) is directly related to quantitatively normal spermatogenesis. The disappearance of these correlations and the decrease in sperm production in the presence of a varicocele suggest gonadal damage associated with a varicocele regardless of fertility status.

More patients will be studied if the University of Washington Reproductive Genetics Laboratory is funded to continue performing the sperm penetration assays.

A manuscript is being prepared for submission to the Journal of Clinical Endocrinology and Metabolism.

PRESENTATION: 71st Meeting of the Endocrine Society, Seattle, WA, June 1989

Detail Summary Sheet

Date: 30 Sep 89 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: Oct 88

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

Technical Approach: Blood from second trimester pregnancy plasma will be purified and amino acid sequencing will be performed. Once sequencing has been completed, the appropriate cDNA probe will be obtained from a cDNA library obtained from Hep G2 cells. The cDNA probe will be tritiated and the studies using insulin, growth hormone, prolactin, estradiol, and testosterone will be performed on the Hep G2 cell cultures with subsequent cDNA hybridization. When these experiments are complete, media will be assayed by RIA or DCC binding assay for SHBG, and RNA will be extracted from the cells. Basically, the cells will be placed in freshly constituted homogenization buffer and disrupted using a polytron homogenizer. The extracts will be left overnight at 4°C and then centrifuged at 2000g for 30 mins. The precipitate pellet will be washed and dissolved in 50 mM tris buffer pH 5 containing 10% SDS and extracted twice with phenylmethylchloride. RNAs will then be precipitated with ethanol dissolved in 10% SDS. Following this, northern blot analysis using 10 mg of RNA will be performed by electrophoresis on 1% agarose formaldehyde gels. Following northern blot analysis, the RNA will be hybridized using either ^{3}H or ^{32}P 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: Studies using growth hormone have been completed and a paper has been submitted for publication. Affinity labeling of SHBG has been started and an oligonucleotide probe is being used to extract a full length cDNA from a Hep G2 library. The investigators are continuing to perform studies using other hormones.

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

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 87/30 Status: Completed

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 Nemestrina)*

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
Philip 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: Oct 88

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

Technical Approach: Six male pigtail macaques, preconditioned to a primate restraining chair, will have in-dwelling catheters implanted 48 hours before the study. The primates will be placed in a restraining chair and allowed to recover for 24-48 hrs. After recovery, tritiated labelled testosterone and estradiol will be infused for 6 hours following a bolus to give a constant rate of tritiated labelled testosterone or estradiol per 2 ml of infusate per hour. Blood samples will be collected every 10 min and every hour the plasma will be separated and the red cells resuspended in physiologic buffer and reinfused 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 4 weeks of rest. Then they will be infused with SHBG for a 3 hr period, followed by infusion of an antibody to SHBG, 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: Since this study was initiated, the SHBG gene has been found to have 95% homology with androgen binding protein which is produced by Sertoli cells of the testes. Therefore, the protocol was amended (Apr 89) to allow the investigators to perform a testicular biopsy on 3 of the animals and inject testosterone, 20 mg IM weekly and 5 µg leuprolide daily for 2 weeks. At the end of the 2 weeks, a second testicular biopsy will be performed, the RNA will be extracted, run on an agarose gel, transferred to nitrocellulose paper, and probed with an alkaline phosphatase-labelled 24 mer oligonucleotide and a biotin-labelled complete sequence cDNA for SHBG.

The study has been completed and a paper has been submitted to the Journal of Steroid Biochemistry. Other papers are planned on the addendum to the study.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/20 Status: On-going

Title: Studies on the Production and Glycosylation of SHBG by HepG2 Cells Using ^{35}S-Labelled Methionine

Start Date: 11 Dec 87 Est Completion Date: Jun 89

Department: Clinical Investigation Facility: MAMC

Principal Investigator: COL Stephen R. Plymate, MC

Associate Investigators:	Benito Que, M.D.
MAJ Charles J. Hannan, MS	Thomas M. Kettler, B.S., M.T.
CPT Karl E. Friedl, MS	Louis A. Matej, B.S., M.T.
Philip H. Petra, M.D.	James R. Wright, B.A. M.T.

Key Words: HepG2, ^{35}S methionine, SHBG, steroids, peptides

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $602.00	Periodic Review: Oct 88

Study Objective: To determine the effects of previously identified steroid and peptide hormones which have been shown to affect sex hormone binding globulin (SHBG) levels, *in vivo* and *in vitro* in the HepG2 cell culture, on production, secretion, and glycosylation of SHBG and to determine the effects of these agents on production of the messenger ribonucleic acid (mRNA) for SHBG in this cell culture system.

Technical Approach: HepG2 cells will be grown to confluence in 25 cm^2 flasks. Confluent cells will then be either continuously labelled with ^{35}S-methionine for 4 hours or pulse labelled for 10 minutes in methionine free media. In the case of the pulse labeling, the label will be chased with a 20,000 fold excess of methionine for three hours following the initial pulse. Flasks will be pretreated with either basal media, T_4, estradiol, testosterone, or insulin in the concentrations which we have shown in a previous study to have the greatest stimulatory or inhibitory effects on SHBG production by these cells. Following the initial labeling of the cells with ^{35}S methionine, both the supernate and cell lysate will be subjected to specific immunoprecipitation. Following the immunoprecipitation, cells from these same flasks that have not been lysed will be lysed and subjected to dot-blot analysis using a specific cDNA probe from a HepG2 library for the SHBG mRNA. When all data have been collected, differences in synthesis versus processing will be assessed between the various treatments using the ANOVA method.

Progress: Immunoprecipitation confirmed the studies on insulin and estradiol controls of SHBG in HepG2 cells. The investigators are currently proceeding with the cDNA portion of the study.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/42 Status: Completed

Title: Protocol for the Study of Sex Steroid Effects on Lipid Metabolism

Start Date: 18 Mar 88 Est Completion Date: Apr 89

Department: Clinical Investigation Facility: MAMC

Principal Investigator: COL Stephen R. Plymate, MC

Associate Investigators:	MAJ Charles Hannan, MS	Stephen Babirak, M.D.
	CPT Karl Friedl, MS	John D. Brunzell, M.D.
	CPT Curtis J. Hobbs, MC	Tom Kettler, B.S.
	CPT Rita Hoop, MS	Louis Matej, B.S.

Key Words: testosterone enanthate, testolactone, vascular disease

Accumulative MEDCASE Cost: -0-	Est accumulative OMA Cost: $2800.00	Periodic Review: N/A

Study Objective: The regulation of enzymes that metabolize lipids is in part under the control of gonadal steroids. The objective of this protocol is to study the regulation of these enzymes and their products in order to aid in the understanding of the pathogenesis of vascular disease and to help further evaluate the risk factors associated with steroid replacement.

Technical Approach: Twelve healthy young males, 20-40 years, with normal liver profile, CBC, UA, EKG, LDL, HDL, and TG will be studied. A complete physical examination, including measurement of testicular size, a liver function test, and a CBC will be done prior to treatment as well as three fasting blood samples drawn at least three days apart for TG, HDL_2, HDL_3, LDL, total cholesterol, Apo proteins AI and II, Apo B, Apo CIII, LH, FSH, T, SHBG, and E_2. Subjects will also submit three semen samples and two four-hour urine samples for urinary measurements of LH and FSH. Anthropomorphic measurements will be made by caliper measurements and tape measurements of the neck and waist. A needle fat biopsy will be taken from the buttock of each man and analyzed for aromatase, lipase, and lipase mRNA by cDNA hybridization. These studies, except for semen analysis, CBC, liver function tests, and fat biopsy, will be repeated at 2, 4, 6, and 10 weeks. Semen analyses will be repeated at 6 and 10 weeks. CBC's, liver function tests, and fat biopsy will be repeated at 6 weeks. After the two-week baseline period, six subjects will be randomized to receive testosterone enanthate, 200 mg im, each week for 6 weeks and six subjects will be randomized to receive testosterone enanthate, 200 mg im, each week plus testolactone, 250 mg po qid, for six weeks. Subjects will be interviewed and have a physical examination at 2, 4, and 6 weeks of the study and at 4 weeks post-study.

Progress: All patients have been entered. Final data analysis is in progress. Preliminary results of this study were presented at the American Federation of Clinical Research (Western Section) in Feb 89.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/12 Status: On-going

Title: Alzheimer's Disease: Physiologic Responses to TRH Infusion
Start Date: 20 Jan 89 Est Completion Date: Dec 90
Department: Clinical Investigation Facility: MAMC
Principal Investigator: COL Stephen R. Plymate, MC
Associate Investigators: Steven Risse, M.D.
Daniel Dorsa, Ph.D. Murray Raskind, M.D.
Thomas Lampe, M.D. Richard Veith, M.D.
Key Words: Alzheimer's, TRH-mediated & plasma NE responses, males
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: N/A

Study Objective: To compare TRH-mediated pressor and plasma norepinephrine responses of male Alzheimer's disease (AD) patients with those of age-matched healthy elderly males, healthy young adult males, and male Huntington's disease (HD) patients; and to further clarify the potential role of the sympathetic nervous system (SNS) in mediating TRH pressor effects.

Technical Approach: AD subjects will meet DSM-III criteria for primary degenerative dementia and NINCDS criteria for probable AD. Subjects with a history of alcoholism, COLD, hypertension, diabetes mellitus, myocardial infarction, or other criteria as listed in the protocol will be excluded. Subjects will be maintained free of any medications that could influence SNS activity and/or blood pressure for at least two weeks before and during participation. Six groups of 20 subjects (mild AD, moderate AD, severe AD, HD, normal elderly, and normal young) will participate in this study. Responses of plasma NE and systolic and diastolic BP to two infusions (0.1 mg of TRH; normal saline) will be determined. The order of administration will be randomized and counterbalanced and the two infusions will be separated by an interval of 4-7 days. Two baseline blood samples will be obtained 35 and 40 min after the IV line is established. A sample for measurement of baseline thyroid indices will be obtained during the first baseline sampling. Immediately after obtaining the second baseline sample, infusions will be administered in a rapid bolus. Samples for plasma NE measurement will be obtained at 1, 2, 4, 5, 8, 12, 18, and 30 min after infusion. As each NE sample is being drawn, blood pressure will be determined. In view of the unresolved but potential role of arginine vasopressin (AVP) in TRH pressor response, plasma AVP levels will be determined in 10 healthy young normals before and after TRH infusion. If a response is evident, plasma AVP will be measured in other study groups. Baseline plasma NE and systolic and diastolic BP will be calculated as the mean of the two baseline measurements of each parameter before each infusion. Two sets of analyses will be conducted: (1) the maximum change in principal study parameters produced by each infusion and (2) responses over time.

Progress: Thirty patients were entered in the study in FY 89.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/73 Status: On-going

Title: 5 Alpha Reductase Inhibitors and Prostate Carcinoma in Athymic Nude Mice

Start Date: 28 Jul 89 Est Completion Date: Dec 89

Department: Clinical Investigation Facility: MAMC

Principal Investigator: COL Stephen R. Plymate, MC

Associate Investigators:	Steve Loop, M.S.
LTC Robert E. Jones, MC	Louis A. Matej, B.S.
Jerry Brooks, Ph.S.	Richard Ostenson, M.D.
Leonard James, M.S.	Joyce S.(Lisa) Tenover, M.D.

Key Words: prostate carcinoma, inhibition, 5α reductase, mice

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $7500.00	Periodic Review: N/A

Study Objective: To determine the *in vivo* and *in vitro* effects of the inhibition of 5α reductase activity on human prostate tumors.

Technical Approach: Cell lines to be used are ALVA 31, 41, 101, and DU-145. Androgen receptor status will be determined according to a method developed by Plymate and Matej. To determine the 5α reductase activity in these tumors, they will be grown in nude mice. For the *in vivo* studies, each of the four tumors will be implanted into one of four groups of nude mice (intact, castrated, castrated and T replaced, castrated and DHT replaced). Group 5 will consist of intact nontumor implanted mice. Five to six animals will be used per set. Within each of the five groups, each drug and a placebo will be tested with a set of animals at each of two drug doses and for each of the test drugs, 4-MA and MK-906. The dose of the drug used will first be established as that dose which provides a 75% or greater reduction in serum DHT levels. This dose and a dose 5 times this will be used. The animals will be treated for a two week period of time with the drug being given by a daily injection. The initial dose of 4-MA will be 500 µg per day. For the initial dose response studies, two injections will be given followed by blood sampling. Following this, injections into mice implanted with tumors will be given on a daily basis for two weeks.

MEASUREMENTS: Tumor size will be measured at 0, 7, and 14 days. Following sacrifice of the animals, the tumor will be weighed and volume determined by water displacement. Testosterone and DHT measurements will be performed on trunk blood and extracted tumor. Prostate Specific Antigen and prostatic acid phosphatase will also be performed on trunk blood.

DATA ANALYSIS PLAN: Statistics will be performed using the Statview Statistical Program. One way analysis of variance will be used to examine differences between treatments.

Progress: Both *in vitro* studies and xerographs of the *in vivo* studies have shown a dose response or these tumors to 4MA as the reductase inhibitor.

Detail Summary Sheet

Date: 30 Sep 89 | Protocol No.: 88/70 | Status: On-going

Title: Characterization of Serovar-Specific Ureaplasmal Antigens by Analysis with Monoclonal Antibodies

Start Date: 19 Aug 88 | Est Completion Date: Oct 90

Department: Clinical Investigation | Facility: MAMC

Principal Investigator: CPT John E. van Hamont, MS

Associate Investigators: None

Key Words: *Ureaplasma urealyticum*, antigens, serovar-specific

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $3700.00	Periodic Review: Sep 89

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

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

Progress: Monoclonal antibodies were prepared against ureaplasma reference strains I, II, III, IV, V, VI, VII, VIII, XII, XIII by fusion of P3X63-Ag8.653 myeloma cells with activated splenocytes from BALB/C mice. Ureaplasma-specific clones were screened against antigens of 11 of the 14 reference strains to assess interstrain antigen distribution. Three species-specific monoclonal antibodies were identified. A prototype reverse-capture antibody inhibition ELISA was established as a possible means of screening future clinical specimens.

PRESENTATION: van Hamont JE and Wright JR: Analysis of *Ureaplasma urealyticum* Serovar Antigens With Monoclonal Antibodies. American Society for Microbiology, Northwest Regional Meeting, Seattle, WA, July 1989

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 89 Protocol No.: 88/39 Status: On-going

Title: Pulpotomy in the Primary Dentition: A Clinical Evaluation of Two Techniques

Start Date: 18 Mar 88 Est Completion Date: Mar 91

Unit: Dental Clinic #3 Facility: MAMC

Principal Investigator: COL Gerald R. Aaron, DC**

Associate Investigators: MAJ James R. Allinder, DC
Peter K. Domoto, D.D.S., M.P.H.
John M. Davis, D.D.S., M.S.D.

Key Words: electrosurgical, formocresol, children

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $100.00 Periodic Review: May 89

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

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

Progress: One additional patient entered in FY 89 for a total of six patients. The six month return rate has been only 50%. Preliminary results suggest that there is no difference in the techniques. PRESENTATION: American Academy of Pediatric Dentistry, May 1989.

** Replaced Dr. Allinder as PI in Sep 89

Detail Summary Sheet

Date: 30 Sep 89	Protocol No.: 89/46	Status: On-going

Title: The Effect of Point-of-Use Water Conditioning Systems on Community Fluoridated Water

Start Date: 10 Apr 89	Est Completion Date: Dec 89
Department: Dentistry	Facility: MAMC
Principal Investigator:	MAJ Michael D. Brown, DC
Associate Investigator:	COL Gerald R. Aaron, DC
Key Words:	fluoridation, community systems, water conditioners
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $575.00
	Periodic Review: N/A

Study Objective: To determine the effect of point-of-use water conditioning systems on the fluoride concentration in community fluoridated water.

Technical Approach: Point-of-use water conditioning systems are defined as those systems installed in the proximity of the sink that condition the water used for cooking and drinking. A sampling apparatus will be constructed that connects, in parallel, the following types of point-of-use water conditioning systems: faucet water filter, under sink water filter, reverse osmosis type under sink filter, and distillation unit. Samples will be collected in polyethylene bottles before and after conditioning.

Phase 1 will be a pilot study to determine the accuracy of the tests performed by the Water Treatment Plant, Ft Lewis, WA, and to provide data necessary to determine sample size. Water will be collected from the Ft Lewis water system and submitted to the treatment facility for determination of fluoride concentration. Variation in fluoride levels from the same sample would indicate the range of accuracy of the test facilities. Additionally, samples of known concentration will be prepared using medical grade distilled water and fluoride tablets.

Phase 2 will be the collection of the conditioned water samples. The sample size will be based on the standard deviation determined from Phase 1. These samples will be submitted in coded containers as described above. These samples will be taken pre- and post-conditioner and the results tabulated. Results will be considered clinically significant if they result in the modification of supplemental fluoride dosage as described by the American Dental Association.

Progress: No subjects have been entered. The materials for the study are in the process of being purchased and assembled.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/57 Status: On-going

TITLE: The Reliability of Cephalometric Evaluation in Genioplasty: A Retrospective Study

Start Date: 10 May 89 Est Completion Date: Apr 90

Department: Dentistry Facility: MAMC

Principal Investigator: MAJ Carlton J. Floyd, DC

Associate Investigator: COL Douglas D. Boyd, DC

Key Words: genioplasty, evaluation, cephalometric, tissue changes

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

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

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

Progress: The records of patients for two of the past five years have been reviewed. Preliminary findings indicate that the procedure has been performed on 22 patients, primarily as a secondary procedure after mandibular advancement. Complications were few outside of the expected postsurgical paresthesia. Post operative clinical and radiographic follow-up indicate considerable stability and unlimited resorption as a result of the procedure.

Detail Summary Sheet

Date: 30 Sep 89 | Protocol No.: 88/46 | Status: Completed

Title: A Comparison of Dental Needs of Abused and Neglected Children and Nonabused/Neglected Children in the Military Population

Start Date: 15 Apr 88 | Est Completion Date: Nov 88

Unit: Dental Activity | Facility: MAMC

Principal Investigator: CPT Patrice E. Greene, DC

Associate Investigators: COL Gerald R. Aaron, DC
LTC Timothy Davis, MS

Key Words: dental exam, questionnaire, dental history

Accumulative MEDCASE Cost: -0- | Est Accumulative OMA Cost: $200.00 | Periodic Review: May 89

Study Objective: To compare the dental needs of children ages 2-12 who are confirmed by MAMC Social Work Services as abuse and neglect cases to a control group who have not been confirmed as abuse and neglect cases but who are from a similar socioeconomic background.

Technical Approach: Approximately 100 children confirmed to be abuse/neglect cases by the Social Work Service, MAMC, will be consecutively studied. A parent or legal guardian will complete a questionnaire designed to obtain information on length of time in service, location of previous assignments, length of time at previous and present assignments, sponsor's rank, educational level of the parents, the child's dental history, use of military and civilian dental care facilities, parent's opinion of the child's present dental needs, and response to and critique of the military family members dental plan. The dentist will complete a dental screening exam that determines the dental needs of the child. Dental status of the children will be reported to the parents. One hundred non-abused/non-neglected control subjects, matched for age, sex, race, and similar socioeconomic background, will be studied in the same fashion as the study subjects. Data will be analyzed using the chi square test.

Progress: 11 additional children were entered in the study group in FY 89 for a total of 49 entries. Getting parents to agree to participation in the study group proved to be more difficult than expected. Therefore, the investigator decided to close the study in May 1989 due to her reassignment. Approximately 1500 children were screened in the control group. The data are now being analyzed, after which a paper will be written for submission for presentation at a national dental association meeting.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/33 Status: Completed

Title: Use of an Inexpensive Caries Activity Test to Compare the Acidogenicity of Dental Plaque of 6-8 Year Old School Children

Start Date: 23 Jan 89 Est Completion Date: Apr 89

Department: Dentistry Facility: MAMC

Principal Investigator: MAJ William C. Horton, DC

Associate Investigators: COL Gerald R. Aaron, DC
COL Lawrence H. Shire, DC

Key Words: caries, acidogenicity, plaque, fluoridated water

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $480.00 Periodic Review: N/A

Study Objective: To test the reliability of the Cariostat caries activity test in a large American population and to compare the acidogenicity of dental plaque of 6-8 year old children who have fluoridated water at home with that of children without fluoridated water at home.

Technical Approach: During Children's Dental Health Month, the Pediatric Dentistry Service conducts screening exams of the Ft Lewis and Tillicum elementary school children. This screening consists of a visual exam with tongue blade, mirror, and hand-held light, and the results are recorded. The children are given oral hygiene instructions, a fluoride rinse, and a personalized letter to parents advising them of their child's oral health status.

For purposes of this study, approximately 750 first and second grade students will be given a short questionnaire two days prior to the screening for their parents to complete. On screening day, these students will return the questionnaires, be examined and given the caries activity test. All other steps of the screening will remain the same. Test vials from the caries activity test will be collected and incubated for 48 hours at 37°C. The tests will be blinded and read at 48 hours per manufacturer's instructions. Data will be analyzed using the chi square test or other tests appropriate to the data obtained by the questionnaire.

Progress: 568 subjects were entered. Data analysis is in progress. Preliminary results indicate a high degree of correlation between plaque acidogenicity as measured by the caries activity test and dental caries as found by dental examination. The role of home use fluoride-containing products is not clear. The caries activity test may prove beneficial for mass screening situations where a small number of quickly trained personnel can identify high risk patients.

Detail Summary Sheet

Date: 30 Sep 89 | 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: Jan 89

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: 26 patients were entered in FY 89 for a total of 62 entries. The investigators have developed a simple method for obtaining a sample of the blood incidental to dental procedures which is relatively free from saliva. Without purposefully causing bleeding, they will continue to collect samples until 100 have been obtained and then compare the data with the blood samples previously collected.

Detail Summary Sheet

Date: 30 Sep 89	Protocol No.: 88/38	Status: Completed

Title: A Comparison of the Cariogenicity of Plaque from Mother-Infant Pairs Using a Caries Activity Test

Start Date: 18 Mar 88	Est Completion Date: Nov 88
Unit: Dental Clinic #3	Facility: MAMC
Principal Investigator: MAJ Mark Rogow, DC	
Associate Investigators: COL Lawrence H. Shire, DC Peter K. Domoto, D.D.S., M.P.H.	
Key Words: history, questionnaire, caries bacterial activity test	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $150.00	Periodic Review: May 89

Study Objective: To compare the caries risk of mothers in the permanent dentition and their infants in the early primary dentition stage and to compare the caries risk predicted by this test and the mother's past caries experience.

Technical Approach: Mothers and their infants 8-15 months of age will be asked to participate. Each mother will complete a dental record for her infant and for herself and a questionnaire to elicit information regarding the child's health, perinatal history, antibiotic use, present prescription medicine, fluoride supplements, dental care, and breast feeding history. The mother and the infant will then have a dental examination and a caries bacterial activity test will be performed. Decayed, missing, and filled teeth of both mother and infant will be recorded. Test vials will be incubated for 48 hrs and read in a blinded fashion at 24 and 48 hrs, with the 48-hr reading used as the final test score. The test results will be determined by comparing the color of the test vial and four reference color vials, using fluorescent illumination. The tests will be scored on a scale of 0 for blue, 1 for green, 2 for yellow-green, and 3 for yellow, with 0.5, 1.5, and 2.5 used for vials which are intermediate in color between the reference vials. Subjects whose test results indicate a high risk of caries will be notified by mail. The chi square test will be used for data analysis.

Progress: Twenty-eight additional mother-infant pairs were entered in the study in FY 89 for a total of 102 pairs entered. Patient entry has been completed. No correlation was found between the infant and mother test scores; mother's test score and decayed, missing, filled teeth; or environmental factors and caries activity test screen.

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

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DEPARTMENT OF EMERGENCY MEDICINE

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/75 Status: On-going

Title: Determination of Endotracheal Tube Placement Site in a Porcine Animal Model Simulating Emergency Department Intubation

Start Date: 15 Sep 89 Est Completion Date: Sep 90

Department: Emergency Medicine Facility: MAMC

Principal Investigator: MAJ Richard G. Foutch, MC

Associate Investigator: CPT Mark D. Magelssen, MC

Key Words: intubation, endotracheal, esophageal detectordevice

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $340.00 Periodic Review: N/A

Study Objective: To investigate a simple, noninvasive means (an esophageal detector device or EDD) for determination of endotracheal tube placement that might significantly improve the performance of emergency airway management.

Technical Approach: The animals will be appropriately anesthetized and monitored according to currently accepted standards. Either the trachea or esophagus will be intubated, the tube secured in place, and the animal ventilated through the tube using 100% O_2 via a bag-valve device. Tube placement will be confirmed in all instances by bronchoscopy. An airway manager (another physician or a nurse anesthetist) will determine tube placement, using one of three methods randomly determined by drawing a card. The accuracy and time required to arrive at this decision will be recorded. The three methods are: commonly used clinical methods; end-tidal CO_2 measurement; and the EDD which consists of a 50 cc syringe with a 15 mm tracheal tube fitting that exploits the anatomical difference between the esophagus (normally closed) and the trachea (permanently held open). Air easily withdrawn without resistance indicates tracheal placement; resistance met with creation of a vacuum indicates esophageal placement. If minimal resistance is met without creation of a vacuum, the EDD will be checked for airtightness, and the procedure repeated. If the test is still unclear, it will be recorded as indeterminate and the airway manager will be asked to determine ET tube placement using accepted clinical methods. A second tube will then be placed (leaving the first tube in the other lumen), and the animal will be adequately ventilated. A second airway manager will test the EDD and identify the tube location. Stomach pressure will be recorded simultaneously. Tracheal ventilation will be stopped and the esophageal tube will be bagged for 20 breaths. Stomach pressure will be recorded every 15 seconds. At the end of the esophageal ventilation period, both tubes will be tested with the EDD and the results recorded. Power analysis indicates 30 animals as an adequate minimum number. ANOVA will be used to evaluate both time and accuracy of the three methods among the various levels of expertise of the participants.

Progress: This study was approved in September 1989 and has not been implemented.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 82/25 Status: On-going

Title: Emergency Room Procedure Training
Start Date: Feb 82 Est Completion Date: Feb 87
Department: Emergency Medicine Facility: MAMC
Principal Investigator: LTC Cloyd B. Gatrell, MC
Associate Investigators: COL Frederick Burkle, MC
LTC Samuel T. Coleridge, MC
MAJ Steven C. Dronen, MC
MAJ Stanley P. Liebenberg, VC
MAJ Matthew M. Rice, MC
MAJ Mel D. Robinson, MC
Key Words: Training techniques, invasive & life-saving procedures
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $1360.00 Periodic Review: Oct 88

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: Three training sessions were held on this protocol in FY 89.

The protocol was amended in Jun 89 to permit a one-time training session using a ferret so that the emergency room residents could practice using a model that is similar to pediatric intubation. A separate protocol will be presented at a later date that is specifically aimed at pediatric intubation.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/62 Status: On-going

Title: A Pilot Study on the Safety and Efficacy of Nifedipine in the Treatment of Biliary Colic

Start Date: 15 Jul 88 Est Completion Date: Jun 89

Department: Emergency Medicine Facility: MAMC

Principal Investigator: LT John H. Mastalski, MC, USNR

Associate Investigators: CPT Lee E. Payne, MC, USAF

Key Words: biliary colic, nifedipine, placebo, efficacy, safety

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $200.00 Periodic Review: Sep 89

Study Objective: To determine the safety and efficacy of nifedipine, 10 mg orally, for the treatment of acute biliary colic in the emergency room.

Technical Approach: Fifty patients, ages 18-70 years, seen in the Emergency Room with a clinical diagnosis of biliary colic or ultrasound proven cholelithiasis will be studied. Only those patients with ultrasound proven cholelithiasis will be included in the data analysis. Patients with hypotension, heart block greater than first degree, hepatitis, jaundice, any evidence of choledocholithiasis, temperature >101, any evidence of choleangitis/cholecystitis or pregnancy will be excluded. A history will be taken and physical exam done on patients presenting with right upper quadrant pain. Initial vital signs will be recorded. The patient will complete a visual analogue scale to grade the pain. The patient will then be placed on a cardiac monitor and dynamap continuous blood pressure monitor. An IV will be established and lab work completed. Chest x-rays and abdominal films will be performed as needed. Nifedipine or a placebo will be given by a double blind protocol. The patient will be monitored over a one-hour period with pain evaluation and blood pressure recordings every 15 minutes. If the patient has equivocal improvement in pain over an hours time, an anticholinergic will be used as deemed necessary by the treating physician. A surgical consultation will be made as needed. A biliary ultrasound and surgical consultation will be made on patients with the diagnosis of biliary colic. Results of the surgical consultation will be recorded for each patient. Patients will be evaluated for pain relief, blood pressure response, vital sign changes, ECG changes, and side effects. Chi square analysis will be used to determine if nifedipine given orally is significantly better than placebo in alleviating the pain of biliary colic.

Progress: Thirty subjects have been enrolled in this study; an equal number of placebo responders and nifedipine responders. Preliminary results indicate that nifedipine may not be any more effective than placebo for the pain of biliary colic.

Detail Summary Sheet

Date: 30 Sep 89	Protocol No.: 89/56	Status: Terminated

Title: Needleless Local Anesthesia for Intravenous Catheter Insertion and Minor Suturing

Start Date: 19 May 89	Est Completion Date: Nov 89
Department: Emergency Medicine	Facility: MAMC
Principal Investigator: CPT Annette R. Nathan, MC	
Associate Investigator: LTC Matthew M. Rice, MC	
Key Words: MadaJet, syringe, needle, catheter, suturing	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $1.00	Periodic Review: N/A

Study Objective: To determine if the MadaJet is effective in achieving local anesthesia for suturing and reducing the pain of intravenous catheter insertion; and to document its effect on intravenous catheter insertion success rates.

Technical Approach: Part I of the study will be done on 20 volunteers to determine if analgesia is produced by injection of saline solution versus lidocaine. In Part II, 150 patients requiring intravenous (IV) catheters will be randomly assigned to no anesthesia, 0.1cc of 2% lidocaine injected with the MadaJet, or the lidocaine injected with a syringe and needle. The number of attempts until successful insertion and the size of the catheter will be recorded, and the difficulty in inserting the IV catheters will be assessed by the person inserting the catheter. In Part III, 100 patients requiring minor suturing for extremity lacerations will be randomized to have the lidocaine injected with a syringe and needle or with the MadaJet. After one minute, adequacy of analgesia will be determined and additional lidocaine injected if necessary. Any patients requiring a second IV catheter at a later time during the study period, will be asked to compare the pain associated with both IV insertions. The volumes of lidocaine and the number of injections will be recorded in both groups. In Part II, the following groups will be compared: MadaJet, syringe and needle, no analgesia, patients with prior IV insertions, patients requiring two insertions. In Part III, the MadaJet group will be compared to the syringe and needle group. Patient comparison of prior suturing with present suturing, the number of IV attempts required, and the assessment of difficulty by the person inserting the IV catheter will be evaluated. A visual analogue scale will be used to measure patient perception of local pain.

Progress: Fifty-four subjects were entered; 22 in Part I, 29 in Part II, and 3 in Part III. Local anesthesia with a syringe and needle was superior to the MadaJet in two areas: the pain reported by patients and the ease of insertion of the IV catheter as reported by medical personnel. In addition the MadaJet produced significant soreness and discomfort for several days after the injection of lidocaine or sterile saline. Due to this discomfort, the study was terminated after three patients because of ethical concerns.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/16 Status: On-going

Title: Occult Sinusitis in the Symptomatic Asthma Patient

Start Date: 20 Jan 89 Est Completion Date: Jul 89
Department: Emergency Medicine Facility: MAMC
Principal Investigator: MAJ James I. Stubblefield, MC
Associate Investigators: Lee E. Payne, MC
Rush A. Youngberg, M.D., DAC
Key Words: sinusitis, occult, asthma, symptomatic, x-rays

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

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

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

Progress: Sixty-nine (69) subjects were entered in FY 89; 28 have returned for part 2 of the study. A data base has been established, but it is still too early for conclusions.

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 89 Protocol No.: 88/23 Status: Terminated

Title: A Study of an Intervention Involving Screening, Patient, and Provider Education in an Attempt to Reduce the Incidence of Preterm Delivery

Start Date: 15 Jan 88 Est Completion Date: Dec 88

Department: Family Practice Facility: MAMC

Principal Investigator: CPT Bruce Greenburg, MC

Associate Investigators:

COL John A. Read, MC
MAJ John P. Kugler, MC
MAJ William K. Brady, MC
CPT Arthur H. Herpolsheimer, MC
MAJ Charles E. Henley, MC
CPT Rebecca A. Rush, MC

Key Words: preterm delivery, intervention, education, screening

Accumulative MEDCASE Cost: -0-

Est Accumulative OMA Cost: $300.00

Periodic Review: Mar 89

Study Objective: To implement a screening questionnaire to attempt to identify patients at high risk for premature delivery; to implement an intervention program for those identified at high risk in an attempt to prevent premature delivery; and to attempt to identify the presence of specific risk factors for premature delivery for active duty pregnant patients.

Technical Approach: Approximately 2000 patients will be studied in each of two groups (intervention and nonintervention comparison). A high risk screen will be completed, which will elicit information regarding weight; height; birth control; scale of how much the patient desires the pregnancy; alcohol and tobacco consumption; history of premature delivery, uterine anomalies, induced abortion, and present pregnancy. Patients determined by the screening standards to be high risk will be entered in an intervention program that consists of watching a videotape which will provide patients with instructions on nutrition, premature risks, and the signs and symptoms of premature labor; weekly cervical exams at 20 weeks; and standard premature labor therapy for any patient diagnosed to be in premature labor. Patients considered low risk by the screening standards will receive routine OB care with rescreening at 26 weeks. Those who are redefined as high risk will be entered in the intervention program. Physician and nursing staff will be given inservices on the early identification of the high risk patient and the diagnosis of premature labor. The intervention group and the comparison group will be assessed by income status, race, maternal age, and parity. The outcome variable will be the percent of premature deliveries for each group. The intervention will also be assessed in its totality along with other possible occurrences that could affect outcome such as new and more effective tocolytics. Therapies available during the intervention period will be compared with therapies during the comparison period.

Progress: This protocol was terminated in Feb 89 because the principal investigator had not provided the revisions to the Department of Clinical Investigation as required by the IRB.

Detail Summary Sheet

Date: 30 Sep 89 | Protocol No.: 84/69 | Status: Completed

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: MAJ Charles E. Henley, MC

Associate Investigators:

LTC David W. Roberts, MC	Craig S. Scott, Ph.D.
Daniel J. Erickson, M.D.	Steven C. Macdonald, M.P.H.
William Neighbor, M.D.	Douglas C. Schaad, M.Ed.
Robert L. Van Citters, M.D.	Marcia Hunt, B.A.

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

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Dec 88

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

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

Progress: Data collection is completed and data analysis is in progress at the University of Washington.

Detail Summary Sheet

Date: 30 Sep 89 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 Henley, MC
Associate Investigators:
Philip Rakestraw, Ph.D. Barbara Simpson, M.S.W.
Carol Milner, Ph.D. CPT Ellen Pinholt, MC
Key Words: geriatrics, trainees, evaluation

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: May 89

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. 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 begin with the residents doing a workup of either a depression or a dementia case by their usual format, and the patient interactions will be evaluated by a preceptor. The simulated patient will be asked to rate a resident's performance on measures of interpersonal skills, communication, and professional manners. 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 and the performance using the "usual" workup between the professionals and residents. 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 protocol was submitted for a joint VA/DoD grant which was not approved. The investigators are conducting a pilot study and Phase I of the study while other avenues of funding are explored. No subjects have been entered.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/14 Status: On-going

Title: Antepartum GBS Screening

Start Date: 9 Dec 88 Est Completion Date: Aug 89
Department: Family Practice Facility: MAMC
Principal Investigator: CPT Michael J. Murray, MC
Associate Investigators: MAJ W. Kim Brady, MC
CPT John Schilhab, MS
Key Words: group B streptococci, last trimester, vaginal, rectal
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $2000.00 Periodic Review: N/A

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

Technical Approach: The first 500 women, ages 14-45, who are followed from 26 weeks to delivery and who give informed consent will be studied. Women presenting with ROM prior to presentation to labor and delivery and in whom amniotic fluid bacteriostatic quality might interfere in the detection of GBS will be excluded. The vaginal introitus and rectum will be cultured at 26, 30, 34, and 38 weeks and prior to delivery. Blood agar with gentamicin will be used as the culture media. Any gram positive cocci will be definitively identified using the catalase test (GBS beta hemolytic) bacitracin disc (GBS resistant), and CAMP test (GBS positive). No treatment will be given until the time of delivery.

Each of the interval cultures will be compared to the colonization status of the patient at the time of presentation in labor. The negative and positive predictive values will be calculated. The time of presentation will be recorded in order to assess the percentage of patients who would deliver prior to six hours and thus not benefit from rapid latex fixation testing.

Progress: 240 subjects were entered in FY 89. Thus far, the negative predictive value of GBS culture at 24 weeks is high (>90%) and the positive predictive value of GBS rectal carriers screened at initial OB visit appears to be high on subsequent culture. The investigators anticipate that the study will be completed in April 1990.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/66 Status: On-going

Title: Treatment of Exercise Induced Friction Blisters. Benzoin vs Padding

Start Date: 16 Jun 89 Est Completion Date: Aug 89

Department: Family Practice Facility: MAMC

Principal Investigator: LTC Roland J. Weisser, MC

Associate Investigators: Ray Howard
Lydia E. Weisser

Key Words: friction blisters, draining, padding, benzoin

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $57.00	Periodic Review: N/A

Study Objective: To determine the most practical and efficient method for treating exercise induced friction blisters of the feet by comparing two treatment regimens that are commonly used by military physicians.

Technical Approach: Approximately 140 new military trainees will be studied. Upon arrival each trainee is given a physical, which includes a slide-tape presentation on the prevention of blisters. The trainees also receive twice daily foot inspections and are referred for medical evaluation when signs of blister formation appear. Those trainees referred with blister formation will be asked to participate in the study. Subjects will be asked to fill out a form stating their opinion of the degree of disability and pain caused by the blister. Medical personnel will describe the lesion using established objective parameters. The subjects will then be randomized to treatment consisting of draining the blister with a needle and encircling it with a protective patch in a ring configuration or to treatment consisting of draining the blister with a needle and replacing the blister fluid with an equal amount of tincture of benzoin. The lesion will then be encircled by a protective patch in a ring configuration. Follow-up evaluations will be conducted at 24, 48, and 72 hours and will include both objective and subjective patient evaluations. The subjects will also be evaluated at 7 and 14 days to monitor final resolution of the lesions and associated symptoms.

Progress: This study has not been started. The investigators had planned to use ROTC cadets at Ft Lewis for summer camp. However, the protocol did not receive final approval from all the units involved in time to utilize this population. An addendum was approved in September 1989 to allow the principal investigator to use the trainee population of trainees in the Cascade Wolfpack training exercise.

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

F O R

P R O T O C O L S

DEPARTMENT OF MEDICINE

Detail Summary Sheet

Date: 30 Sep 89	Protocol No.: 89/55	Status: On-going

Title: Multicenter Clinical Evaluation of Penicillin Skin Testing

Start Date: 19 May 89	Est Completion Date: Jun 90
Dept/Svc: Medicine/Allergy	Facility: MAMC
Principal Investigator at MAMC: COL William P. Andrade, MC	
Project Principal Investigator: LTC James S. Brown, MC, FAMC	
Key Words: PPL, fresh pen G, penicilloate (MDM-A), penicilloate (TS-Sullivan), penilloate (MDM-B)	

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

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

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

Progress: No patients have been entered in the study, which is still being coordinated between the various medical centers.

Detail Summary Sheet

Date: 30 Sep 89 | Protocol No.: 88/79 | Status: On-going

Title: Salicylate Overdose: Quantitation of Renal Excretion with Forced Alkaline Diuresis

Start Date: 16 Sep 88 | Est Completion Date: Jan 90

Dept/Svc: Medicine | Facility: MAMC

Principal Investigator: CPT Matthew S. Bachinski, MC

Associate Investigators: MAJ Howard M. Cushner, MC
CPT Donna L. Mercado, MC
CPT Thomas Peller, MC
CPT Bernard J. Roth, MC
CPT LeRoy Southmayd, MC

Key Words: salicylate, overdose, renal excretion, diuresis

Accumulative MEDCASE Cost: -0- | Est Accumulative OMA Cost: $1900.00 | Periodic Review Sep 89

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

Technical Approach: Patients as stated above will be admitted to the ICU and followed, receiving the standard of care plus: baseline labs for SGOT, SGPT, LDH, bilirubin, calcium, magnesium and phosphorus; history taken to quantify as closely as possible the amount of aspirin ingested and the time of ingestion; IV D5W with 150 mEq $NaHCO_3$/L at 50-150 cc per hour; weight every 12 hours; chest x-ray each day; calcium and magnesium every 12 hours; labs to include arterial blood gas, electrolytes, BUN, creatinine, and serum salicylate level, every 6 hours; urine collection every 6 hours for dipstick pH, volume measurement, urine salicylate level and sodium determination. IV infusion rate will be adjusted to patient size and age. Pulmonary edema will be monitored by chest x-ray and physical examination; arterial blood gases, electrolytes, calcium, and magnesium will be monitored and adjustments made to maintain chemical homeostasis. Patients will be treated until serum salicylate is <30 mg/dl. Patients' normal outpatient medications not containing aspirin will be allowed.

Progress: Three subjects were entered in FY 89.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/47 Status: On-going

Title: Investigation into Thyroid Function Abnormality Associated with Hexabrix, a New Intravenous Iodine-Containing Contrast Agent

Start Date: 15 Apr 88 Est Completion Date: Jun 88

Dept/Svc: Medicine/Endocrine Facility: MAMC

Principal Investigator: CPT Brenda K. Bell, MC

Associate Investigators: MAJ Jennifer Nuovo, MC
CPT Patrick Gorman, MC

Key Words: Hexabrix, Hypaque 76, cardiac catheterization

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $1800.00	Periodic Review: Sep 89

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

Technical Approach: Subjects with no evidence of thyroid function abnormality and patients with goiter undergoing cardiac catheterization, with the administration of Hexabrix or Hypaque contrast material, will be studied. Patients will be examined for the presence of goiter or nodular thyroid disease and a baseline thyroid function test, including TSH and T_3 by RIA, will be done. The thyroid function tests will be repeated at three days and at one month after administration of the contrast agent. The amount of contrast agent administered will be used to calculate the milligrams of iodine that the patient was administered.

Progress: MAJ Nuovo was the original principal investigator for this protocol. CPT Bell was appointed the new principal investigator upon the resignation of MAJ Nuovo.

Originally, 21 subjects were entered in the study, but complete data is available on only four subjects. There was a major problem with patients forgetting the one month thyroid function tests. Since the data was incomplete and several months passed when no work was done on the project, CPT Bell and the other investigators will scrap the previous data and start over using the same plan.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 87/118 Status: Terminated

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: Oct 88

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 study was terminated due to difficulty in scheduling investigators to obtain baseline data. No patients were entered.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/04 Status: On-going

Title: Sequential Cisplatin and High Dose Ara-C in the Treatment of Resistant Adenocarcinomas: A Phase II Study

Start Date: 21 Oct 88 Est Completion Date: May 90

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: CPT Denis P. Bouvier, MC

Associate Investigators: COL Irwin B. Dabe, MC
LTC Howard Davidson, MC
MAJ Everado Cobos, MC
MAJ Mark H. Kozakowski, MC
CPT Kenneth A. Bertram, MC

Key Words: adenocarcinoma, Cis-platinum, Ara-C, sequential

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

Study Objective: To assess the responsiveness of resistant adenocarcinomas to the synergistic interaction of sequentially administered Cis-Platinum and high dose Ara-C.

Technical Approach: A minimum of 20 patients, 20-65 years of age, with histologic diagnosis of adenocarcinoma of the colon, rectum, lung, stomach, or pancreas, unresectable, and refractory to conventional therapy will be entered. The therapy will consist of CDDP, 100 mg/M^2, by CIV over 24 hours on day 1 followed by Ara-C, 2 gm/M^2, over two hours after CDDP on day 2. Antiemetics will be given as follows: Decadron, 20 mg, IVP pre med, days 1 and 2; Inapsine, 2.5 mg, IVP pre med, days 1 and 2; Torecan, 20 mg PO, premed Days 1 and 2; Inapsine infusion 2.5 mg/hr for 12 hours then 0.8 mg/hr for remainder of chemotherapy. Two such cycles will be given at a 21 day interval. The second cycle will be delayed if any of the following are noted on the laboratory data obtained 48 hours prior to cycle 2: WBC <1500, platelet <100,000, nephrotoxicity, or M/B elevated creatinine compared to prestudy. Patients will be considered evaluable for response if they complete both cycles of the protocol and if they have submitted to prestudy testing and at least one course of poststudy testing. Prestudy tests will consists of CBC, chemistry panel, serum magnesium, CXR, CT scan, tumor markers CEA, noninvasive vascular studies of the LE, and audiogram. Intrastudy evaluations will consist of CBC, chemistry panel, serum magnesium, and serum CEA weekly. CBC, 909, calcium, albumin, magnesium, and PO_4 will be done 48 hours prior to therapy. Post study will include CBC, chemistry panel, and serum magnesium monthly and CT scan and serum CEA one month after cycle 2 and then every three months. Patients will be followed until death or censorship. Response rate will be defined as the number of patients who have achieved a complete response or a partial response divided by the total number evaluable for response.

Progress: Seven subjects have been entered. To date, responses have been disappointing with nondurable partial response the best response. Toxicity has been significant but not unexpected.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/34 Status: On-going

Title: Performance of Hemoccult II and Hemoccult SENSA

Start Date: 17 Mar 89 Est Completion Date: 1 Oct 89
Dept/Svc: Internal Medicine/Medicine Facility: MAMC
Principal Investigator: CPT Carole A. Buckner, MC
Associate Investigators: MAJ Michael F. Lyons, MC
MAJ Amy M. Tsuchida, MC
Key Words: Hemoccult II, Hemoccult SENSA, sensitivity, specificity
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: N/A

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

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

Progress: To date, 74 subjects have been enrolled with 53 subjects completing the evaluation. Ten patients have had positive fecal occult blood tests. Of these, 7 had adenomas, one had a hyperplastic polyp, and one had Duke's D carcinoma of the colon. Of the 43 patients with negative fecal occult blood tests, 14 had adenomas, 11 had hyperplastic polyps, nine had hemorrhoids, 10 had normal exams, two had inflammatory bowel disease, 5 had diverticula, and one had colitis. Twenty-one patients had neoplasms. Hemoccult II was sensitive in 23.8% of the tests with the rate being 31.6% in Hemoccult SENSA. However, there appears no difference in specificity; Hemoccult II was 90.4% and Hemoccult SENSA was 91.3%.

An abstract is being prepared for presentation at the William Beaumont Seminar in October 1989 and for the Air Force Society of Physicians Meeting in March 1990.

Detail Summary Sheet

Date: 30 Sep 89	Protocol No.: 89/27	Status: On-going

Title: Correlation Between Mean Platelet Volume and Bleeding Time and Assessment of Mean Platelet Volume as a Marker of Hemorrhagic Tendency in Thrombocytopenic Patients

Start Date: 17 Feb 89	Est Completion Date: Mar 90
Dept/Svc: Medicine/Internal Medicine	Facility: MAMC
Principal Investigator: CPT Valerie A. Carregal, MC	
Associate Investigator: Denis P. Bouvier, MC	
Key Words: mean platelet volume, bleeding time, thrombocytopenia	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $535.00	Periodic Review: N/A

Study Objective: To examine the association between the size of platelets (mean platelet volume) and the bleeding time in a group of thrombocytopenic patients and to examine the association between the number and size of the platelets with the appearance of a hemorrhagic tendency.

Technical Approach: Two hundred and fifty (250) adult thrombocytopenic patients will be entered. Pregnant patients and those with congenital bleeding disorders, abnormal coagulation parameters, taking anticoagulants or antiaggregating agents, or who have received a platelet transfusion within two weeks prior to the study will be excluded.

Before entry CBC, platelet counts, mean platelet volume (MVP), bleeding time, and physical exam for evidence of hemorrhage will be performed. The type of hemorrhage will be noted - none, petechia, ecchymosis, epistaxis, GI, GU, vaginal, etc. Data to be recorded include: age, sex, type of disease, platelet count, MPV, bleeding time, and type of hemorrhage.

Blood samples will be obtained using normal procedures, collected in standard EPTA tubes, and processed within one hour of resection. All thrombocytopenic samples identified on Coulter counter will be correlated with phase microscopy counts. Quality control and calibration of the Coulter counter will be established daily.

All subjects will have a bleeding time performed prior to any platelet transfusions. The modified IVY method using a Simplate II blade will be used to measure the bleeding time.

Student's t test, discriminant analysis, and sensitivity and specificity indices will be used to analyze data.

Progress: Forty-five subjects have been entered.

Detail Summary Sheet

Date: 30 Sep 89 | Protocol No.: 87/98 | Status: Terminated

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: LTC William H. Cragun, MC**
Associate Investigator: CPT Marin H. Kollef, MC
Key Words: COLD, airflow, Ibuprofen, placebo
Accumulative MEDCASE Cost: -0- | Est Accumulative OMA Cost: $350.00 | Periodic Review: Oct 88

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: Data collection was completed on two subjects at MAMC. Two studies from other institutions were reported that confirmed that Ibuprofen had no effect on airflow in patients with COLD. Therefore, the protocol was terminated.

**Replaced Dr. Kollef as principal investigator, July 1988.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/85 Status: Completed

Title: Free 1,25 $(OH)_2D_3$ Measurements in Nephrotic Patients with and without Chronic Renal Failure

Start Date: 16 Sep 88 Est Completion Date: Oct 88

Dept/Svc: Medicine/Nephrology Facility: MAMC

Principal Investigator: MAJ Howard Cushner

Associate Investigators: None

Key Words: nephrotic syndrome, normal renal function, renal insufficiency, free 1,25 $(OH)_2D_3$

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $122.00	Periodic Review N/A

Study Objective: To evaluate vitamin D binding protein and free 1,25 $(OH)_2D_3$ levels in patients with nephrotic syndrome to determine if there is a reduced circulating level of vitamin D binding protein due to urine losses and if there is an alteration in binding of vitamin D with this protein in this disorder.

Technical Approach: Patients with nephrotic syndrome followed in the Nephrology Clinic at MAMC will be identified by chart review. Five patients with nephrotic syndrome and normal renal function, and five patients with nephrotic syndrome and renal insufficiency will be studied. A 27 cc blood sample will be obtained and assayed for total 1,25 dihydroxyvitamin D, percent free 1,25 dihydroxyvitamin D, and vitamin D binding protein. Free total 1,25 vitamin D concentrations will be calculated.

Progress: Five subjects were entered in FY 89 for a total of 8 subjects. The study has been completed. Both total and free 1,25 $(OH)_2D_3$ decreased with decreasing renal function, while vitamin D binding protein and percent free did not. Vitamin D binding protein levels were not altered in this patient population. Total and free 1,25 $(OH)_2D_3$ levels were highly correlated ($r=0.968$, $P<0.0001$). The investigators conclude that in these patients total 1,25 $(OH)_2D_3$ accurately reflects vitamin D status.

PRESENTATION: Koenig KG, Lindberg S, Zerwekh JE, Williams PK, Cushner HM, Copley JB: Utility of Free 1,25$(OH)_2D_3$ Measurements in Renal Failure Patients. American Federation for Clinical Research, February 1989.

Detail Summary Sheet

Date: 30 Sep 89 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 Howard Davidson, MC **

Associate Investigators:

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

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

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Sep 89

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 days 1-3, 29-31, and 57-59. There will be no radiotherapy.

Group II: Limited NSCLC, no prior radiotherapy, will be treated with cis-platinum, 100 mg/M^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 radiotherapy is completed for patients achieving clinical partial or complete remission.

Group III: Extensive NSCLC will receive the same regimen as Group 1. Response rate will be defined as number of patients who achieve a complete or partial response divided by the total number of patients evaluable for response (completed at least four weeks of the treatment program). Patients will be evaluable for toxicity if they received at least one dose of chemotherapy.

Progress: Five patients were entered in FY 89 for a total of 20 subjects. There was virtually no nephrotoxicity, but all patients except those who died early experienced ototoxicity. Peripheral neuropathy and/or orthostatic hypotension were moderate to severe in three patients. All patients had a decrease in hemoglobin (median decrease of 2.0 g% for chemo only patients and 4.2 g% for chemo plus radiation).

**Replaced COL Irwin B. Dabe, MC, Sep 89

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/18 Status: On-going

Title: Urinalysis as a Screening Exam for NGU in Males Attending an STD Clinic

Start Date: 20 Jan 89 Est Completion Date: Apr 89

Dept/Svc: Internal Med/Medicine Facility: MAMC

Principal Investigator: CPT Roberta Ficke, MC

Associate Investigators:

MAJ Margot Krauss, MC
CPT John E. van Hamont, MS
CPT Sheri E. Nottestad, MC
Jonathan Burg, M.D.

Key Words: leukocyte esterase, WBC, chlamydia, ureaplasma

Accumulative MEDCASE Cost: -0-

Est Accumulative OMA Cost: 1458.00

Periodic Review: N/A

Study Objectives: To determine the sensitivity and specificity of urine analysis (UA), specifically leukocyte esterase (LE) and white cells (WBC's), as an indicator of nongonococcal urethritis (NGU) in males presenting to a sexually transmitted diseases (STD) clinic; to document prevalence of chlamydia and ureaplasma in these patients; and to determine the number of WBC's on urinalysis which is significant for NGU when taken three hours after last void.

Technical Approach: Population: 200 Males, 18-25 years, with or without complaints of urethral discharge and/or dysuria. Subjects will be grouped as: (a) symptomatic - dysuria, urethral itching or discharge; (b) asymptomatic - absence of complaints listed above (this group will consist mainly of patients presenting with scabies, venereal warts, or asymptomatic contacts). Participants will complete a questionnaire which solicits information on symptoms, number of sexual partners in last 6 months, history of contact with persons with STD, and treatment history for STD. Those in Group A will have a urethral swab for urethral smear and GC culture. Both groups will have a swab done for chlamydia culture and will have a UA and ureaplasma cultures. Patients of both groups will be treated with standard therapy for any positive results. Patients from the symptomatic group will be treated for NGU despite lack of objective evidence. Patients with a previously negative evaluation who are not treated initially and who later develop a positive culture will be contacted and appropriately treated. NGU will be defined as a positive urethral gram stain, chlamydia culture, UA, or positive ureaplasma concomitant with a positive UA or gram stain. When the urine is the only positive culture, then any associated positive UA or gram stain will be considered indicative of urinary tract infection. LE results will not be used as criteria for diagnosing NGU. The prevalence of chlamydia and ureaplasma in both groups will be calculated. Logistic regression will be performed on a small portion of the data to determine appropriate cut off values for the WBC/LE assay. Chi square analysis will be employed to combine WBC and traditional methods of NGU diagnosis. Sensitivity and specificity of LE/WBC assay as a predictor of NGU will be determined.

Progress: Twelve patients have been entered in this study.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/19 Status: Completed

Title: Effect of Hydrochlorothiazide on Postural Blood Pressure Changes

Start Date: 11 Dec 87 Est Completion Date: Jun 89

Dept/Svc: Medicine/Internal Facility: MAMC

Principal Investigator: CPT Joel T. Fishbain

Associate Investigators:

LTC Robert Harvey, MC MAJ Howard Cushner, MC

CPT Thomas Peller, MC CPT Leroy Southmayd, MC

Key Words: blood pressure, postural, changes, hydrochlorothiazide

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $150.00	Periodic Review: Mar 89**

Study Objective: To assess the effect of hydrochlorothiazide on postural change in blood pressure and pulse.

Technical Approach: 50-80 patients diagnosed as hypertensive, confirmed by 5-day blood pressure recordings, will have a baseline history and physical examination. Prior to initiating thiazide, the patients will have a 24-hour urine and a fasting 908, and creatinine clearance will be calculated. Within one day of the urine collection and after five minutes of rest in a prone position, orthostatic changes will be assessed by taking three blood pressure measurements and a one minute pulse rate. These measurements will be repeated after two minutes in a sitting and then a standing position. The patient will be weighed (fasting) and placed on 25 mg of hydrochlorothiazide. The 24-hour urine collection, the 909, and the blood pressure and pulse measurements as described above will be repeated at three weeks and three months. All patients will be given identical encouragement to observe and restrict sodium intake, increase activity at least five days per week, and, when appropriate, lose weight and discontinue smoking. Pretreatment, three week, and three month orthostatic blood pressure and pulse measurements will be compared. Changes in pulse rate, systolic blood pressure, diastolic blood pressure, and mean arterial pressure will be compared using the paired T test. If there are significant differences, the lab values will be studied to determine correlation.

Progress: Approximately 15 patients have been entered in this study at MAMC with 4 additional patients entered at Ft Leonard Wood, Mo. The data are being analyzed and the investigators anticipate that a paper will be finalized by May 90.

**On continuing review, CPT Fishbain stated that he had been unable to continue 24-hour urine collections because the patients had problems returning the urines within 24 hours of BP measurements. The protocol was revised to state that spot urinalyses and chem 20's would be done the day of BP measurements as an estimate of volume status. This was done by utilizing the patient's specific gravity, BUN, creatinine, and uric acid levels to estimate the patient's volume status. A revised consent form was also submitted an approved.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/43 Status: On-going

Title: The Effects of Testosterone Replacement in Hypogonadal, Malnourished Patients with Chronic Obstructive Pulmonary Disease (COPD)

Start Date: 17 Mar 89 Est Completion Date: Oct 89

Dept/Svc: Pulmonary/Medicine Facility: MAMC

Principal Investigator: MAJ Bruce S. Grover, MC

Associate Investigators: COL Stephen R. Plymate, MC
MAJ Jonathan P. Kushner, MC

Key Words: COPD, testosterone, hypogonadal, malnourished

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $65.00	Periodic Review: N/A

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

Technical Approach: Twenty male patients ≥40 years will have baseline spirometry, maximum inspiratory and expiratory pressures, maximum voluntary ventilation, 6 minute walking distance, triceps skin fold, midarm muscle circumference, testosterone and lipoprotein profiles, electrolytes, liver function test, ABG, total lymphocyte count, hematocrit, transferrin, albumin, nitrogen balance, creatinine height index, anergy panel, % ideal body weight, and % usual body weight. A clinical assessment (history and physical exam) will be done and a diet history taken. Patients will be allowed to continue usual medications and activities and exercise will be unrestricted. If either total or free testosterone is low, the patient will be admitted to the hospital for five days. A dietary regimen will be initiated with a regular diet, supplemented on Day 3 with Pulmocare, one can three times a day. Calorie counting will be performed to assess nitrogen balance on Days 2 and 5. An interview and patient log will be used to count calories. Patients will be randomized to either testosterone enanthate, 100 mg/ml, or placebo injections. Injections will be given on Day 3 and then once a week for four doses. On Day 5 repeat studies will include: ABG, 24 hr urine urea nitrogen, calorie count, weight, change in weight, and testosterone profile. At the end of weeks 2 and 4 all baseline tests will be repeated except for ABG.

This protocol was amended in Sep 89 in order to determine the relationship of testosterone to pulmonary function, as measured by FEV_1, DL_{CO}, and MIP. Initial testosterone (free and total), SHBG, and estradiol will be determined. The investigators will then determine if there is a linear fall in testosterone as FEV_1 falls and if low testosterone is related to weight loss or steroid use. These determinations will then be used to determine entry into the main part of the study.

Progress: Initial determinations have been done on eight patients, but none was entered into the main study.

Detail Summary Sheet

Date: 30 Sep 89 | Protocol No.: 88/44 | Status: Completed

Title: Redundant Care of Internal Medicine Patients in Subspecialty Clinics

Start Date: 18 Mar 88 | Est Completion Date: May 88

Dept/Svc: Medicine/Internal | Facility: MAMC

Principal Investigator: LTC Robert C. Harvey, MC**

Associate Investigators: CPT Patrick D. Gorman, MC
CPT Steven C. Hahn, MC

Key Words: multi-clinic/single clinic visits, resources

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Sep 89

Study Objective: To evaluate redundant subspecialty clinic visits in the internal medicine patient population and estimate the impact on resources in terms of potential excessive visits.

Technical Approach: This will be a retrospective chart review of patients receiving care in the Internal Medicine Clinic at MAMC. Two groups, defined as multi-clinic and single clinic visits, will be studied. The first group will consist of patients receiving care solely in the Internal Medicine Clinic by a single care provider for the entire case management without involvement of physicians in other areas. Referrals for evaluation or recommendation of care, subspecialty oriented procedures and follow-up, and patients seen for less than one year will be excluded. The second group will consist of patients who receive care in the Internal Medicine Clinic and are also seen in the subspecialty clinics for internal medicine problems. Approximately 300 charts will be reviewed. Demographics, epidemiology (diagnosis, duration, and therapy), number of patient visits for the past four years, length of time as a patient in the Internal Medicine Clinic, and manner of referral will be assessed. Appropriateness of the visit and the reason for overlap between clinics will also be assessed for multi-clinic visit patients. Patients in the two groups will be matched demographically and epidemiologically. At the conclusion of the review, baseline characteristics of the patient population will be described. Appropriate statistical techniques will be applied to determine differences in staff, housestaff, quantity of medical problems or medications, and referral patterns. Categorical data analysis (descriptive and inferential) will be performed as warranted.

Progress: Data were collected on approximately 200 patients. There was a significant amount of redundancy between the Internal Medicine Service and subspecialty clinics caused by referrals and misdirection of patients from outside the Service. A paper is being prepared for submission for publication.

**Replaced Dr. Gorman as principal investigator, August 1988.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/49 Status: On-going
Title: Steroid Transport Across the Blood-Cerebrospinal Fluid Barrier in the Adult Rat: Kinetics and Effects of Sex Hormone Binding Globulin
Start Date: 21 Apr 89 Est Completion Date: Nov 89
Dept/Svc: Endocrinology/Medicine Facility: MAMC
Principal Investigator: CPT Curtis J. Hobbs, MC
Associate Investigators: COL Stephen R. Plymate, MC
MAJ Charles J. Hannan, MS
Key Words: steroids, CSF, androgen, kinetic, rat model
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $780.00 Periodic Review: N/A

Study Objective: To examine the transport of steroid hormones in a bidirectional fashion across the blood-cerebrospinal fluid barrier of the rat and to assess the influence of sex hormone binding globulin (SHBG) on such transport.

Technical Approach: Male Sprague-Dawley rats will undergo cannulation of the lateral ventricle. After a 3-day recovery period, the animals will be anesthetized and the femoral vein cannulated to allow blood sampling and injection of radiolabeled testosterone (^{3}H-T) and immobilized to facilitate puncture and sampling from the cisterna magna. Phase I: At time zero ,1 µl of lactated Ringer's solution containing 25,000 CPM (counts per min) of ^{3}H-T will be introduced via the intraventricular catheter. At 5 min intervals (for 45 min) 10 µl samples of CSF (via the cisterna magna catheter) and 100 µl samples of blood (via the femoral catheter) will be withdrawn for scintillation counting. CPM will be plotted versus time from initial injection. Data points will be generated until equilibrium between the two compartments is achieved. Stage 2: identical to Stage 1 except that ^{3}H-T will be injected via the femoral catheter. Stage 3: A quantity of ^{3}H-T identical to that in Stage 1 will be coadministered intraventricularly with an excess of unlabeled testosterone to allow demonstration of saturable kinetics if present. Stage 4: Identical to Stage 3 except that labeled and unlabeled testosterone are injected via the femoral catheter. Stage 5: Identical to Stage 1 except that SHBG is administered intrafemorally 5 minutes prior to the intraventricular injection of ^{3}H-T. Stage 6: Identical to Stage 2 except that SHBG is administered intrafemorally 5 min prior to the intraventricular injection of ^{3}H-T. At each stage, samples will be analyzed by HPLC to demonstrate recovery of intact ^{3}H-T. Data will be analyzed using the StatView 2 Program for MacIntosh computer systems.

Progress: To date, data from 28 animals demonstrated that following femoral vein infusion of ^{3}H-T, initial uptake and distribution of testosterone into the CSF and clearance of ^{3}H-T from the venous pool were delayed by the prior femoral vein administration of SHBG; following administration of ^{3}H-T via the cisterna magna, initial clearance from the CSF and uptake and distribution into the venous pool were enhanced by the prior administration of SHBG; and no differences were noted between control and SHBG infused animals in ^{3}H-T distribution in the steady state.

Detail Summary Sheet

Date: 30 Sep 89	Protocol No.: 89/67	Status: On-going

Title: The Effect of Androgens on Glucose Tolerance

Start Date: 16 Jun 89	Est Completion Date: Apr 90
Dept/Svc: Endocrinology/Medicine	Facility: MAMC
Principal Investigator:	CPT Curtis J. Hobbs, MC
Associate Investigators:	COL Stephen R. Plymate, MC
	LTC Robert E. Jones, MC
	CPT Brenda K. Bell, MC
Key Words: IVGTT, testosterone enanthate, nandrolone decanoate	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $4500.00
	Periodic Review: N/A

Study Objective: To determine whether the administration of supra-physiological doses of androgens impair glucose tolerance as measured by the tolbutamide modified Intravenous glucose tolerance test.

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

Technical Approach: Twenty-three subjects have been enrolled. Four subjects have dropped out due to conflicts with work schedules. All subjects have been randomized and injections are on schedule. Subjects 1 and 2 have completed the first phase of the protocol. Baseline studies have been collected on all subjects and entered into a database. No results are currently available with regard to the effect of androgens on glucose tolerance. Insulin assays have not yet been performed. All subjects, except one, have had their first IVGTT.

Detail Summary Sheet

Date: 30 Sep 89	Protocol No.: 88/49	Status: On-going

Title: Methotrexate in the Treatment of Steroid Dependent Chronic Obstructive Pulmonary Disease (COPD)

Start Date: 15 Apr 88	Est Completion Date: Oct 89	
Dept/Svc: Medicine/Pulmonary		Facility: MAMC
Principal Investigator: CPT Thomas W. Irvine, MC**		
Associate Investigators:	MAJ Samuel G. Joseph, MC	
COL William P. Andrade, MC	CPT Bruce S. Grover, MC	
LTC W. Hal Cragun, MC	CPT Mary P. Horan, MC	
Key Words: double-blind, crossover, placebo		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $770.00	Periodic Review: Sep 89

Study Objective: To demonstrate a statistically significant reduction in the cortisone requirements of COPD patients who cannot successfully be weaned below 10 mg/day despite trials on $\geq$2 occasions.

Technical Approach: In a double-blind, crossover method, patients 40-70 years of age will be studied. At the time of entry each patient will have required 10 mg/day of prednisone, therapeutic levels of theophyllines, and inhaled beta agonist at least three times per day for the preceding year. Patients will be randomly assigned to receive either methotrexate or placebo for 12 weeks (Period 1.) At the end of Period 1, patients will be crossed over to the other drug (Period 2). During the first week of each period, patients will take one pill every 12 hrs x 3 doses/week, and, during weeks 2-12, they will take 2 pills every 12 hrs x 3 doses/week. During the entire study, patients will keep a daily diary, recording cortisone usage and subjective rating of COLD symptoms. Laboratory data on entry will include chest x-ray, spirometry, DL_{CO}, creatinine, SGOT, CBC, differential CBC, and pregnancy test if appropriate. Patients will be seen every three weeks for collection of diaries, directed examination, pulmonary function tests, a review of adverse reactions, and laboratory assessment to include creatinine, SGOT, CBC, and differential CBC. DL_{CO} will be performed at entry and at the end of each 12-week period. Chest x-rays will be obtained upon entry and exit from the study. Trough theophylline levels will be obtained at entry and at the end of each 12 week period and the frequency of inhalant usage will be noted at entry and at the end of each 12 week period. Data analysis will be performed using Student's two-tailed t-test to determine the effect of methotrexate upon cortisone usage. In addition, analysis will be done to compare symptom scores, pulmonary functions, WBC; SGOT; theophylline levels; presence or absence of positive allergy skin tests; prior dosage of steroid as determinant of response; and adverse occurrences.

Progress: No patients have been entered. CPT Irvine has just been appointed the principal investigator on this study. He will begin to enter patients after he has time to study the protocol.

**Replaced CPT Horan, September 1989.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/51 Status: On-going

Title: Comparison of Oral Cefpodoxime Proxetil (U-76,252; CS-807) and Cefaclor (Ceclor) in the Treatment of Acute Community Acquired Pneumonia

Start Date: 21 Apr 89 Est Completion Date: Apr 92

Dept/Svc: Pulmonary/Medicine Facility: MAMC

Principal Investigator: CPT Thomas W. Irvine, MC

Associate Investigators: LTC Hal W. Cragun, MC

Key Words: cefpodoxime proxetil, cefaclor, randomized, blinded

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $150.00	Periodic Review: N/A

Study Objective: To compare the efficacy and safety of orally administered cefpodoxime proxetil and cefaclor (Ceclor) in the treatment of lower respiratory tract infections caused by pathogens sensitive to these two antibiotics.

Technical Approach: This is a randomized, double-blind, double-dummy, multicenter study. Patients will be selected based on signs and symptoms of community acquired pneumonia caused by organisms expected to be susceptible to the agents. A total of approximately 135 (20 at MAMC) outpatient or hospitalized patients meeting the following criteria will be entered: male or nonpregnant/nonbreast-feeding females, ≥18 years of age, body weight at least 90 pounds. Patients must exhibit one of the following (1) cough or oral temperature >100° C plus a purulent sputum and infiltrate on chest x-ray. Any therapy that might assist recovery will be initiated. Patients will be randomized to take either cefpodoxime proxetil, 200 mg active or placebo tablet taken with food every morning and evening or Cefaclor, two 250 mg active or placebo capsules taken every eight hours on an empty stomach. A complete chemistry panel, complete urinalysis, CBC, platelets, cultures, and disk sensitivities of sputum samples will will be obtained on enrollment, at 7-10 days and at the end of therapy. The cultures and disk sensitivities will also be obtained 1-2 weeks post-therapy. A chest x-ray will be obtained on enrollment, at the end of therapy, and 1-2 weeks post-therapy. Statistical analyses will be done of all cases and separately for evaluable cases only. Tests will be computed to detect differences in efficacy and safety between the experimental and comparator drugs. Clinical and bacteriological response rates will be estimated as will the incidence of adverse drug experiences. Categorical data analysis procedures will be utilized to analyze success ratios between treatment regimens incorporating factors such as pretreatment MIC values and investigator effects. Some analyses of the evaluable cases may also be done on subsets partitioned according to physical parameters (pulse, respiration, side effects), laboratory parameters, bacteriologic and clinical outcomes.

Progress: No patients have been entered. The principal investigator is awaiting HSC approval.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/62 Status: On-going

Title: Determination of the Sensitivity and Specificity of Light Reflection Rheography for the Diagnosis of Deep Venous Thrombosis in the Lower Extremity

Start Date: 16 Jun 89 Est Completion Date: Jun 90

Dept/Svc: Medicine/Internal Medicine Facility: MAMC

Principal Investigator: MAJ Duane J. Jeffers, MC

Associate Investigators: COL Charles A. Andersen, MC
MAJ Dipankar Mukharjee, MC
SGT Charles Adams
Nancy N. Greenfield, M.S.
Michael Bertoglio, B.S.

Key Words: light reflection rheography, duplex scanning, DVT

Accumulative MEDCASE Cost: $6000.00 | Est Accumulative OMA Cost: $760.00 | Periodic Review: N/A

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

Technical Approach: Two hundred (200) adult subjects referred for evaluation of suspected lower extremity DVT will be studied.

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

Progress: Nine patients have been entered. Light reflection rheography and duplex scanning have been performed on each patient with no adverse reactions.

Detail Summary Sheet

Date: 30 Sep 89 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: Jan 89

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 μC of (3H) will be present in each individual assay. The samples will be centrifuged at 2800g for 10 minutes at room temperature, the seminal plasma supernatant will be discarded, and the sperm pellet will be resuspended in an isotonic buffer. This sperm mixture will be recentrifuged and washed twice prior to use. After the final centrifugation, the pellet will be diluted in a potassium enriched buffer to achieve a sperm density of $2x10^8$/ml. The assay mixture will contain palmitic acid, ATP, Mg++ and CoASH and will be initiated by the addition of the washed sperm preparation. Time and protein dependency curves will be run to determine the length of incubation needed to achieve first order kinetics in the measurement of initial velocities. Both Lineweaver-Burk plots and hyperbolic best-fit will be used to calculate approximate Km values for each substrate. Temperature, pH curves, and rates with alternate substrates will also be run. Enzyme location/latency will be determined by assaying separate cell fractions prepared by sonication and differential centrifugation of the isolated sperm. The effects of sulfhydryl reagents, albumin, and detergents will be studied to assist in estimation of latency.

Progress: At the present time, the investigators are attempting to purify sperm plasma membranes and to complete autoradiographic experiments. Results of preliminary studies can be found in the following articles.

Jones, Plymate: Biol Reprod 39:76, 1988
Jones, Plymate: Ann NY Acad Sci 513:571, 1987
Jones, Plymate: J Andrology 7:323, 1986

Detail Summary Sheet

Date: 30 Sep 89 | 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, molecular size, functional relationship, hepatic/mitochondrial forms

Accumulative MEDCASE Cost: -0- | Est Accumulative OMA Cost: 708.00 | Periodic Review: Sep 89

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 purificatior step.

Progress: Technical problems preventing neutralization of acrosomal protease have interfered with purification. The investigators are trying new agents/techniques to solve the purification problem. No further progress was made on this study in FY 89.

Detail Summary Sheet

Date: 30 Sep 89 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: Oct 88

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 transferase, acyl CoA:1-acyl-sn-glycero-3-phosphocholine O-acyl transferase will be screened by coincubating human sperm with labelled fatty acids, CoASH, ATP, Mg^{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-phosphatidyl choline. The conversion of lyso-phosphatidyl choline to phosphatidyl choline will be chromatographed. This assay will be optimized for pH, ionic strength, substrate levels and amount of enzyme before kinetic constants are determined. For carnitine-dependent transacylation, D,L-palmitoyl carnitine and lyso-phosphatidyl choline will be coincubated with washed sperm, delipidated and the products chromatographed as above. If the amount of lyso-phosphatidyl choline declines while phosphatidyl choline increases, a carnitine dependent mechanism will be presumed to exist. Alternatively, carnitine dependency could be screened by using ^{3}H-palmitoyl carnitine to look for labelled phosphatidyl choline formation. The effect of 22:6 on 16:0 incorporation into phospholipids will be assessed by incubating unlabeled 22:6 with ^{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: This protocol has demonstrated that fresh human spermatozoa can incorporate palmitic and docosahexaenoic acid into exogenous and endogenous lysophosphatides. See summary of protocol #88/83. Presented at the 1988 Meeting, Amer Soc Andrology, Jones, Plymate: J Androl 9:41, 1988. A manuscript has been accepted for publication in the Journal of Andrology.

Detail Summary Sheet

Date: 30 Sep 89 | Protocol No.: 88/26 | Status: On-going

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

Start Date: 15 Jan 88 | Est Completion Date: Jun 89

Dept/Svc: Medicine/Endocrinology | Facility: MAMC

Principal Investigator: LTC Robert E. Jones, MC

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

Key Words: fatty acids, lipid synthesis, ligase activity, sperm

Accumulative MEDCASE Cost: $40,000 | Est Accumulative OMA Cost: $2,000.00 | Periodic Review: Jan 89

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

Technical Approach: The incorporation of palmitic (16:0) and docosahexaenoic acids (22:6) into neutral or phospholipids will be measured by incubating whole, fresh sperm with ^{3}H-16:0 and ^{14}C-22:6. Total lipids will be extracted using the method of Bligh and Dyer. The chloroform phase will be taken to dryness under N_2 at 42°C and subsequently reconstituted in a minimal volume of chloroform. The chloroform mixture will be applied to a silicic acid column and subsequentially eluted with 20 ml chloroform followed by 20 ml of methanol. The chloroform fractions containing neutral lipids will be combined, evaporated, and repeatedly extracted to remove the free fatty acids. Both the methanol and chloroform eluates will be counted, and an aliquot of each will be chromatographed on silica gel G to ensure complete separation. Incorporation rates will be expressed as nmoles fatty acid incorporated/10^6 sperm or nmoles phospholipid P/hour. After extracting the sperm with 0.1% Triton X100, ligase activity will be measured. Both 16:0 and 22:6 will be used as substrates in the incubations. Ligase activity will be expressed as nmoles acyl CoA formed/min/mg protein. The seminal plasma concentrations of these compounds will be measured using an enzymatic spectrophotometric technique. These parameters will be considered separately in relationship to ligase activity and lipid synthesis. Semen samples will be handled and analyzed according to the current WHO guidelines. Morphology will be assessed on fixed smears, and motility will be objectively quantified with an automated semen analyzer. With the exception of the sperm density, the semen quality will be blinded to the person performing the biochemical analyses. Incorporation rates and the distribution of the fatty acid labels and ligase activity will be correlated with sperm morphology and motility of the semen sample using either linear regression or chi-square analyses.

Progress: The investigators have been perfecting lipid isolation techniques, but progress has not been made due to difficulty in procurement of the sperm motility analyzer.

Detail Summary Sheet

Date: 30 Sep 89	Protocol No.: 88/83	Status: On-going
Title: Influence of Calcium on Phosphatidylcholine Synthesis in Human Spermatozoa		
Start Date: 16 Sep 88	Est Completion Date: Sep 89	
Dept/Svc: Medicine/Endocrine		Facility: MAMC
Principal Investigator: LTC Robert E. Jones, MC		
Associate Investigators: COL Stephen R. Plymate, MC MAJ Charles Hannan, MC		
Key Words: free fatty acids, lyso-phosphatidylcholine		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $2444.00	Periodic Review Sep 88

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

Technical Approach: Semen samples will be centrifuged at 650g for 15 minutes and washed twice in an isotonic buffer. The sperm pellet will be resuspended at a concentration of $2x10^8$ in the isolation buffer. Approximately $1x10^7$ sperm will be used per assay. The incubation buffer conditions will be identical to those previously established in the DCI lab. In brief, the incubation mixture contains 20 mM ATP, 20 mM $MgCl_2$, 50 µM LPC, 10 µM fatty acid, 5mM dithiothreitol, 0.1 mM coenzyme A, and 280 mM Tris. The reaction is initiated with the addition of washed spermatozoa. After one hour, the phospholipids are extracted and separated by thin layer chromatography. Enzymatic rates are calculated as nmoles fatty acids incorporated into phosphatidylcholine/10^7 sperm/hour. The investigators have shown that there are two types of substrate blanks in this system. The first, a coenzyme A blank, assess ligase and acyl transferase activity and consequently provides data on the activities of these two enzymes while the second, the LPC blank, yields information on the generation of acyl acceptors presumably through the activity of phospholipases. By using either 16:0 or 22:6 as acyl substrates and utilizing the LPC blank, the phospholipase A_1 can be differentiated from A_2, Because LPC is added to the incubations, the LPC blanks become all the more critical in determining the possibility of calcium control of this pathway. The concentration of calcium in the incubations will be 1.7 mM, and the concentration of A23187, a calcium ionophore, will range from 10-30 µM. If an effect is seen which suggests ligase modulation, ligase activity will be specifically addressed using both whole sperm or a Triton x 100 extract of sperm. The rates of acyl substrate utilization will be compared by an ANOVA, rates obtained with and without LPC will be compared with a Student's t test. Ligase activity will be assessed using kinetic techniques previously described (Biol Reprod 39:76, 1988).

Progress: Incubations of sperm with A23187 demonstrated that this calcium ionophore suppressed docosahexaenoic acid (22:6) incorporation into phosphatidylethanolamine (PE) using endogenous lysophosphatidylcholine as the acyl acceptor. The rate of fatty acid incorporation into phospholipids was greater for PE than phosphatidylcholine. A paper has been accepted for publication.

Detail Summary Sheet

Date: 30 Sep 89	Protocol No.: 88/84	Status: On-going

Title: *In Vivo* and *In Vitro* Comparisons for Sex Hormone Binding Globulin (SHBG) Production in Morbid Obesity

Start Date: 15 Sep 88	Est Completion Date: Sep 89
Dept/Svc: Medicine/Endocrine	Facility: MAMC
Principal Investigator:	LTC Robert E. Jones, MC
Associate Investigators:	COL Preston L. Carter, MC COL Stephen R. Plymate, MC MAJ Jonathan Kushner, MC CPT Rita C. Hoop, MS
Key Words:	morbid obesity, SHBG, hepatic tissue, L-thyroxine

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $4750.00	Periodic Review Sep 89

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

Technical Approach: Subjects: 5 morbidly obese subjects undergoing a vertical banded gastroplasty (VBG) and 5 lean, age and sex matched controls undergoing and elective cholecystectomy.

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

Progress: No subjects have been entered in this study.

Detail Summary Sheet

Date: 30 Sep 89 | Protocol No.: 88/71 | Status: On-going

Title: Hepatitis B Vaccine (Recombivax) - Abbreviated Schedule Vaccination Trial

Start Date: 19 Aug 88 | Est Completion Date: Mar 90

Dept/Svc: Medicine | Facility: MAMC

Principal Investigator: CPT Robert J. Kazragis, MC

Associate Investigators: LTC Ronald H. Cooper, MC

Key Words: hepatitis B, vaccine, conventional vs reduced dose

Accumulative MEDCASE Cost: -0- | Est Accumulative OMA Cost: $3785.00 | Periodic Review: Sep 89

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

Technical Approach: Subjects: 75, male/female, ages 18-45

Exclusion criteria: history of hepatitis or positive hepatitis B serology, chronic disease or immunosuppressive condition or malignancy; pregnancy; prior vaccination with hepatitis B virus vaccine or receipt of hepatitis B immune globulin within 12 months.

Evaluations before entry: medical history form and interview; hepatitis B surface antigen and antibody, hepatitis B core antibody, serum alanine and aspartate aminotransaminase levels, and a completed blood count.

The subjects will be randomized to one of three arms:

10 µg dose Recombivax IM at 0,4, and 7 weeks
2 µg dose Recombivax ID at 0, 4, and 7 weeks
1 µg dose Recombivax ID at 0, 4, and 7 weeks

HBsAg, anti-HBs, and anti-HNc will be followed at days 0, 30, 60, 90, 180, and 360.

Individuals who fail to achieve a protective level of anti-HBs will be revaccinated at one year with 10 µg IM, Recombivax.

Data analysis: Chi-square analysis of geometric mean titers of anti-HBs and comparison of antibody titers and response rates to previously published studies.

Progress: Approximately 60 participants have been randomized and vaccinated with with one of the regimens. Anti-HB's have been collected at 30, 60, 90, and 180 days. Preliminary data at 90 days shows percent seroconversion of 85.7%, 74.4%, and 80.0% for 10 µg IM, 1 µg ID, and 2 µg ID, respectively.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/78 Status: Terminated

Title: The Regression of Left Ventricular Hypertrophy by Echocardiographic Criteria in Patients Treated for Poorly Controlled Hypertension in an Intensive Stepped Care Approach versus the Usual Clinic Setting, Utilizing the Same Antihypertensive Regimen

Start Date: 16 Sep 88 Est Completion Date: Jun 90

Dept/Svc: Medicine/Pulmonary Facility: MAMC

Principal Investigator: CPT Lynn M. Keenan, MC

Associate Investigators:

MAJ Howard M. Cushner, MC MAJ Alice M. Mascette, MC

MAJ Kim Havas, ANC CPT Mark P. Elam, MC

Key Words: hypertrophy, hypertension, intensive/routine setting

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $4000.00	Periodic Review: N/A

Study Objective: To determine if the regression of left ventricular hypertrophy (LVH) occurs with the treatment of hypertension in patients followed in an intensive setting as opposed to the usual setting and to evaluate whether there is a critical level of blood pressure (BP) control that is necessary in order to achieve regression of LVH in the setting of hypertension.

Technical Approach: Sixty patients ages 30-70 treated at MAMC for poorly controlled hypertension with LVH by echocardiographic criteria will be evaluated by screening history and physical, SMA-20 (to include potassium, CO_2, and chloride), urine analysis and blood pressure. Subjects will be randomized to be followed by their primary care physician using his routine procedures or to be followed intensely with evaluations every four weeks. Blood pressures will be obtained consistently by the same investigator with the same blood pressure cuff with the patient seated at rest for five minutes. All patients will be tapered off previous medications over a period of weeks as hydrochlorothiazide and lisinopril are added. In order to achieve good blood pressure control, lisinopril will be started at 5 mg qd and increased as necessary to 40 mg qd. Hydrochlorothiazide will be started at 25 mg qd and increased to 50 mg qd. If necessary, Catapres will be added. The goal of BP control is systolic BP <140 and diastolic BP <90. Patients will receive follow-up SMA-20 at weeks 1 and 4 and at the end of the study. Blood pressures will be followed by monthly visits in the intensive care group versus less often in the usual care group. Differences in left ventricular wall thickness will be compared with a t test. One statistical significance of regression in left ventricular wall thickness and BP control for the intensive versus usual care patients will be assessed.

Progress: This protocol was terminated due to logistical problems with personnel when attempting to implement the study. No patients were entered.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 87/01 Status: Completed

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 Mark H. Kozakowski, MC**

Associate Investigators:	MAJ David Dunning, MC
COL Irwin B. Dabe, MC	MAJ Ruben Sierra, 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: Jan 89

Study Objective: To evaluate a treatment schedule in terms of therapeutic effectiveness: response rate, survival, and toxicity 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: No additional patients were entered in FY 89. A total of 29 patients was entered in previous years.

Although this regimen was well tolerated, overall objective response rate was low at 13% in this group of patients. When this protocol was discussed by the staff of the Oncology Service, they decided not to enter additional patients.

A paper was presented at the ACP/4th Annual Army Regional Meeting in October 1987 and at the Annual Meeting of the American Society for Clinical Oncology in May 1988.

Pro Ann Meet Am Soc Clin Oncol 7:142A, 1988

**Replaced MAJ Ruben Sierra, MC, August 1988.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/63 Status: On-going

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

Start Date: 15 May 89 Est Completion Date: Oct 90

Dept/Svc: Medicine/Hematology Facility: MAMC

Principal Investigator: MAJ Mark H. Kozakowski, MC

Associate Investigators:

COL Michael J. Carlon, MC	CPT Denis P. Bouvier, MC
COL John A. Read, MC	CPT Sheri E. Nottestad, MC
MAJ W. Kim Brady, MC	CPT Randal D. Robinson, MC
MAJ Everardo Cobos	CPT Donna S. Whittaker, MC

Key Words: lupus anticoagulant, pregnancy, fetal wastage

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $1087.00	Periodic Review: N/A

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

Technical Approach: Approximately 1500 pregnant females between 18 and 35 years of age without known coagulopathy will be studied.

Before entry a physical exam, including detailed obstetric history and thromboembolic disease history; prothrombin (PT) and partial thromboplastin time (PTT); and anticardiolipin antibody (ACA) will be done. Subjects with a prolonged PTT will undergo evaluation to include 1:1 mixing study and platelet neutralization procedure; Russell viper venom test if 1:1 mixing study is consistent with the lupus anticoagulant.

Subjects who have a normal PTT will be followed for the remainder of the pregnancy and have a PTT and ACA drawn at the time of delivery. If the PTT is prolonged, the 1:1 mixing study and platelet neutralization procedure will be repeated and then performed again at the time of delivery. If a fetal death or spontaneous abortion occurs, anticardiolipin antibody will be done.

A prolonged PTT and a correctable platelet neutralization procedure at any stage will constitute the presence of the lupus anticoagulant. The frequency of the lupus anticoagulant in pregnancy will be calculated as well as the frequency of spontaneous abortion when the lupus anticoagulant is present.

Progress: The investigators have just completed revisions requested by the IRB and are ready to proceed with the study.

Detail Summary Sheet

Date: 30 Sep 89 | Protocol No.: 87/65 | Status: On-going

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: LTC Rodney A. Michael, MC**

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

Key Words: pyelonephritis, trimethoprim-sulfamethoxazole, days

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jul 89

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

Technical Approach: All patients will initially receive intravenous TMP/SMX every 12 hours for at least six doses and until afebrile. Thereafter, patients will receive oral TMP/SMX twice daily and continue oral therapy as outpatients. Group A will receive 14 days of therapy and Group B will receive 7 days of therapy. All subjects will have a physical exam and a symptom assessment before the institution of therapy and daily while in the hospital. Urine samples will be obtained before therapy and daily thereafter during the hospital stay. Quantitative aerobic bacterial cultures will be performed on all specimens. Antibody coated bacteria testing will be performed on all initial specimens which grow $\geq 10^3$ 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 calendar which they were given at discharge. At two weeks following the end of therapy, patients will return to provide a clean-catch midstream urine specimen for culture and urinalysis. Appropriate statistical techniques will be used to compare the baseline characteristics of the patient population and to analyze the adverse effects and clinical laboratory data. Categorical data analysis of the efficacy data will be performed as warranted.

Progress: No new patients were entered in this study in FY 89. The available data are being analyzed. Many data sheets are incomplete. The study is on hold until a decision is made if the study will be continued.

**Replaced Dr. Vogel as the PI, Jul 89.
*Replaced Dr. Gorman as PI, Aug 88.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/55 Status: Terminated

Title: Double Blind, Multicenter, Placebo Controlled Clinical Trial to Evaluate the Efficacy and Safety of HA-1A Human Monoclonal Antibody in Patients with Severe Gram-negative Sepsis/Gram-negative Septic Shock

Start Date: 20 May 88 Est Completion Date: May 89

Dept/Svc: Medicine/Infectious Disease Facility: MAMC

Principal Investigator: LTC Rodney A. Michael, MC

Associate Investigators:	MAJ Samuel Joseph, MC
LTC Ronald H. Cooper, MC	MAJ Anthony Sado, MC
LTC William Cragun, MC	CPT Mary Horan, MC
MAJ Bruce Grover, MC	CPT Bernard Roth, MC

Key Words: Gram-negative sepsis, HA-1A, efficacy, mortality

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

Study Objective: To determine: the efficacy of HA-1A monoclonal antibody in reducing the mortality and direct morbidity of gram-negative sepsis; the impact on patient benefit and laboratory parameters/clinical signs associated with sepsis; and the safety and potential for immunogenicity of HA-1A.

Technical Approach: In a multicenter, double-blind, parallel group study, severely ill patients with a clinical diagnosis of severe gram-negative sepsis or gram-negative septic shock will be randomized to receive either a single intravenous infusion of 100 mg of HA-1A human monoclonal IgM antibody or a human albumin placebo. Prior to enrollment, each patient will undergo a physical exam, a medical history will be taken, and an APACHE II score will be calculated. Samples for clinical chemistry, clinical hematology, and urinalysis will be obtained 4 hrs prior to infusion, at 12 and 24 hr, and 3, 5, 7, 14, and 28 days after infusion until death or at least one documented normal set of values is obtained. Blood for bacteriological cultures will be obtained within the 24 hours prior to enrollment and subsequently as dictated by the clinical course. Additional body sites and fluids will be cultured as dictated by clinical status to document all suspected foci of infection. Chest x-rays will will be done within 12 hours of infusion, either pre or post infusion. HA-1A antibody concentration will be measured prior to and at 1 and 2 hr and 28 days after infusion. The mortality rate will be the primary efficacy variable (although other efficacy parameters will be measured) and will be estimated in the control group following the entry of 10 confirmed gram-negative placebo patients. This will determine the time of 3 interim analyses and the overall sample size. All statistical tests will be based on 2-sided alternative hypotheses, since no prior assumptions will be made that HA-1A treatment is superior to that of placebo.

Progress: This protocol was terminated by the sponsoring company due to sufficient accrual before any patients were entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/53 Status: On-going

Title: Single Patient Protocol for Treatment of Systemic Mycoses with Itraconazole (R51,211)

Start Date: 21 Apr 89 Est Completion Date: Apr 90
Dept/Svc: Medicine/Infectious Diseases Facility: MAMC
Principal Investigator: LTC Rodney A. Michael, MC
Associate Investigators: None
Key Words: mycosis, refractory, standard drugs, Itraconazole

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

Study Objective: To treat a patient with severe systemic mycosis refractory to all standard therapies or unable to take these drugs because of drug toxicity.

Technical Approach: A complete physical examination with related medical history, clinical assessment of the disease, description of the lesions, and, if possible, photographs of the lesions will be done prior to treatment. If appropriate, serology, chest x-ray, CT scan and other diagnostic tests or procedures will be done. Biochemistries to include liver function tests and electrolytes, CBC with differential, and urinalysis will be done prior to entry. The patient must have a positive culture and/or histologic findings which identify the pathogen. Patients will be re-examined at Week 3, Month 1, and monthly thereafter. Cultures and other microbiologic tests, serology, x-rays, etc., will be repeated at appropriate intervals during the study. Biochemistries, CBC/diff and urinalysis will be repeated at Week 2, Month 1, and monthly thereafter.

The patient will be initiated on 100 mg q.d. with a meal and maintained on that dose for at least one month. If the patient is unchanged or worsening, the dose may be increased in 100 mg increments to a maximum of 400 mg/day. Doses greater than 200 mg will be given on a b.i.d. basis. If the patient is improving, dose will be continued for duration of therapy. The optimal duration of treatment is unknown, but a treatment course of about one year is planned. Results will be classed as healed (cured), markedly improved, moderately/slightly improved, unchanged, deteriorated, or unevaluable for statistical analysis.

No systemic antifungal medication may be used concurrently. However intrathecal amphotericin-B may be used if there is CNS involvement. Drugs that reduce gastric acidity must be delayed for at least two hours after itraconazole is given. Rifampin should not be used during the treatment period.

Progress: The patient is currently taking Itraconazole, 400 mg q.d. There was evidence of progression with 200 mg q.d.. The patient has completed approximately 5 1/2 months of treatment and a reassessment is in progress.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/70 Status: Completed

Title: Non-comparative Study of Fluconazole in Patients With Serious Mycoses Who Cannot Be Treated With Conventional Antifungal Therapy

Start Date: 28 Jul 89 Est Completion Date: Sep 89

Dept/Svc: Medicine/Infectious Diseases Facility: MAMC

Principal Investigator: LTC Rodney A. Michael, MC

Associate Investigators: None

Key Words: candidiasis, fluconazole, safety, efficacy

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

Study Objective: To provide an alternative to conventional antifungal therapy in a patient with documented systemic (peritoneal) candidemia, who is currently being dialyzed and in whom conventional therapy (amphotericin B) is undesirable due to its nephrotoxic potential.

Technical Approach: The usual adul- dosage is 400 mg oral loading dose, followed by 200 mg once daily. If oral therapy cannot be used, fluconazole may be given intravenously at an infusion rate of 50 mg/hour until the entire dose has been delivered. Dosage will be adjusted for renal dysfunction or creatinine clearance <50 ml/min. If the initial regimen fails, the dosage may be increased up to 400 mg daily. Treatment will continue for two weeks after the resolution of clinical symptoms, but for a minimum of three weeks and a maximum of eight weeks. If response is incomplete, an extended duration of up to 12 months may be done with the approval of the clinical monitor.

The investigator will assess the patient to include fluconazole's influence on the course of the disease and any potential side effects or toxicity. The assessment will also include objective and subjective information which may assist in the evaluation of the safety and efficacy of fluconazole therapy. Physical parameters of infection (temperature, vital signs, etc) and laboratory measures (i.e., cultures, antigen detection tests, CBC's, tissue and fluid examinations, radiographs, and nuclear medicine studies) will be recorded prior to, during, and at the end of therapy, as well as for a 2-4 week follow-up period. Serum fluconazole concentration will be measured bi-weekly. Efficacy of treatment will be based on the clinical and microbiologic evaluations as follows: (1) Clinical - cure, improved, failure; (2) Microbiologic cure, failure, indeterminate. Treatment failure will be defined as persisting positive blood, body fluid, or tissue cultures, taken on or after the seventh day of treatment of evidence of clinical deterioration or continued sepsis attributable to candidiasis by the seventh day of therapy.

Progress: The patient successfully completed treatment with IV fluconazole for Candida peritonitis. There was clinical and microbiological evidence of response.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/74 Status: Completed

Title: Compassionate Use of Ciprofloxacin Intravenous in the Treatment of a Patient With an Infection Refractory to Currently Marketed Antibiotics

Start Date: 15 Sep 89 Est Completion Date: Sep 90

Dept/Svc: Medicine/Infectious Diseases Facility: MAMC

Principal Investigator: LTC Rodney A. Michael, MC

Associate Investigators: None

Key Words: *Enterobacter aerogenes*, ciprofloxacin, intravenous

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

Study Objective: To provide effective antibiotic therapy to a patient with bacteremia, peritonitis, and pneumonia due to a multiply resistant pathogen, *Enterobacter aerogenes*.

Technical Approach: Prior to onset of ciprofloxacin treatment, a full clinical, bacteriological, and laboratory examination will be performed for the patient. Ciprofloxacin will be administered intravenously, in general at a daily dose of 400 mg (i.e., 200 mg approximately every 12 hours); IV dosing may be followed by oral administration as soon as the patient is able to take oral medication.

Antimicrobial effectiveness will be evaluated by means of conventional clinical and laboratory determinations, including cultures of all infected sites, before, during, and after therapy. safety of drug treatment will be monitored by careful clinical observations, including evaluation of possible central nervous system effects, and by tests of renal, hepatic, and hematopoietic function.

Progress: This patient died on the second day of therapy. Death was caused by apparent cardiovascular collapse related to ongoing septicemia.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/30 Status: Completed

Title: Investigation of the Serum-Effusion Albumin Gradient to Aide in the Differential Diagnosis of Pleural Effusions

Start Date: 19 Feb 88 Est Completion Date: Sep 88

Dept/Svc: Medicine/Pulmonary Facility: MAMC

Principal Investigator: CPT Bernard J. Roth, MC

Associate Investigators: LTC William Cragun, MC
LTC Thomas O'Meara, MC

Key Words: transudate, exudate, thoracentesis

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $303.00 Periodic Review: N/A

Study Objective: To evaluate the serum-effusion albumin gradient in patients with pleural effusions of varying etiologies in order to determine its efficacy in distinguishing transudates from exudates.

Technical Approach: A thoracentesis will be performed on patients with radiographic evidence of a pleural effusion. Albumin, total protein, glucose, and LDH levels will be determined on the fluid as well as cell count with cytospin differential, culture for bacteria, fungi and tuberculosis, and cytology. If the fluid appears milky, triacylglycerol and cholesterol levels will be determined. Total protein, LDH, glucose, and albumin levels will be determined on a simultaneously drawn serum sample. If the fluid is exudative by Light's criteria (effusion-serum protein ratio >0.5, effusion LDH >200 IU, or effusion-serum LDH ratio >0.6) and etiology is not evident from the above evaluations, a pleural biopsy will be performed, if clinically indicated. The evaluation of each patient will be reviewed and a clinical assignment of likely etiology, transudative versus exudative, will be made. This will be supported by pathology and pulmonary pressures whenever available. The following categories will be established: (1) patients with transudates secondary to congestive heart failure, either prior to or after diuretic therapy; (2) patients with exudates secondary either to infection or malignancy, and (3) miscellaneous (hypoalbuminemia, chylous, pseudochylous, etc.). The discriminating power of the serum-effusion albumin gradient will be compared to that of Light's criteria. A serum-effusion albumin >1.1 will be defined as a transudate.

Progress: 36 additional subjects were entered in FY 89 for a total of 61 subjects. CONCLUSION: Although Light's criteria for exudates are very sensitive, an albumin gradient of 1.2 or less tends to be more specific, especially in cases of chronic congestive heart failure.

A paper was presented to the Washington State Chapter of the American College of Physicians (FY 88) and at the National Meeting of the American Thoracic Society, May 1989. A paper has been submitted for consideration for publication in the Annals of Internal Medicine.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: #88/36 Status: Terminated

Title: Diurnal Variability of Corticotropin-Releasing Hormone, Corticotropin, and Cortisol in Pregnant Women

Start Date: 18 Mar 88 Est Completion Date: Oct 88

Dept/Svc: Medicine/Endocrinology Facility: MAMC

Principal Investigator: MAJ William R. Sheldon, MC

Associate Investigators: None

Key Words: CRH, ACTH, cortisol, hemoglobin, hematocrit

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $1690.00	Periodic Review: N/A

Study Objective: To determine if a diurnal variation exists in the secretion of corticotropin releasing hormone (CRH) of placental origin and of adrenocorticotropin hormone (ACTH) and cortisol measured simultaneously in maternal blood during the third trimester of pregnancy.

Technical Approach: Six patients in the third trimester of an uncomplicated pregnancy will be studied. Two nonpregnant women with normal menstrual periods and on no medications will be studied in the same manner as the pregnant subjects in order to establish that the normal diurnal variation in ACTH and cortisol can be clearly seen under the experimental conditions. Subjects will be admitted to the hospital the evening prior to the study. At least one hour before the first blood sample is drawn, an IV line will be placed in a forearm vein and infused with 0.9% saline at a rate sufficient to keep the line open throughout the study. Samples of blood will be drawn every two hours starting at 0800 hours and ending at 0600 hours the next morning. The samples will be assayed for hCRH, ACTH, and cortisol, using standard RIA kits. At the end of the study, the hemoglobin and hematocrit will be measured on each subject. Analysis of variance will be used for the statistical analysis of the data.

Progress: Progress was made in developing the assay for corticotropin-releasing hormone. The protocol was terminated due to logistical problems with carrying out the design of the study. No patients were entered.

Detail Summary Sheet

Date: 30 Sep 89 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: Sep 89

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 89. Eight patients have previously been studied and additional patients are being sought. The investigators plan to rerun the TSH determinations using the highly sensitive TSH assays, and, also, to complete the development of a urinary T_3 and T_4 assay.

Detail Summary Sheet

Date: 30 Sep 89 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: Sep 89

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: No additional patients were entered in FY 89. In previous years, four patients have been entered. Patient recruitment is continuing; however entry has been hampered by the rarity of the patients meeting the entry criteria. The available blood/urine remains frozen for batch analysis when patient recruitment is complete.

Detail Summary Sheet

Date: 30 Sep 89 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: Sep 89

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 additional patients were entered in this study at MAMC in FY 89. One patient was entered prior to FY 88. Eight subjects have been entered Army-wide.

Subject recruitment is very difficult for this protocol. Recruitment will continue until 12 patients have been entered Army-wide.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 87/59 Status: On-going

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: MAJ Amy M. Tsuchida

Associate Investigators:
MAJ Marshall E. McCabe, MC
LTC Thomas F. O'Meara, MC*
CPT Gregory E. Schlepp, MC**
LTC Michael H. Walter, MC
Gari Sisk, R.N.

Key Words: ulcer, duodenal, healing, recurrence, Ranitidine

Accumulative MEDCASE Cost: -0-

Est Accumulative OMA Cost: -0-

Periodic Review: Jun 89

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 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 original principal investigator and time constraints on Dr. Tsuchida. Patient recruitment will begin on this protocol with the next few months.

**Original PI
*Interim PI (May - Aug 88)

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/34 Status: On-going

Title: Use of Dipentum in Patients with Ulcerative Colitis Who Are Sensitive to Azulfidine

Start Date: 19 Feb 88 Est Completion Date: Mar 89

Department/Service: Gastrointestinal Facility: MAMC

Principal Investigator: MAJ Amy M. Tsuchida, MC

Associate Investigators: LTC Michael H. Walter, MC**

Key Words: colitis, ulcerative, Dipentum, Azulfidine

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Sep 89

Study Objective: To ascertain the efficacy of Dipentum in the treatment of active ulcerative colitis in emergency instances in patients for whom sulfasalazine is contraindicated and to ascertain the potential side effects of Dipentum.

Technical Approach: In an open, uncontrolled trial, patients will have a complete physical, the diagnosis and extent of colitis will be determined, and disease severity classified. Baseline hemoglobin, white blood cell count with differential, including inspection of Heinz bodies, reticulocyte count, mean corpuscular volume, prothrombin time, platelet count, glucose-6-phosphodehydrogenase activity, SGOT, SGPT, glucose, alkaline phosphatase, bilirubin, total protein, albumin, globulin, blood urea nitrogen, serum creatinine and sedimentation rate, and chemical and microscopic urinalysis will be determined and repeated on days 14 and 28. Treatment will be conducted on a graduated dose regimen as follows: Days 1-4, 250 mg, Days 5-8, 250 mg twice a day; days 9-12, 250 mg three times a day; and days 13 and thereafter, 250 mg four times a day. After two weeks of treatment, the investigator may discretionally increase or decrease the dose by up to 50% should conditions warrant such a change. At the completion of a 60 day course of Dipentum, the patient will be examined and colitis activity will be classified as remission, mild, or severe. Patients whose disease state has improved, those whose disease is slightly improved and the physician feels will continue to improve with further therapy, and those who by virtue of Dipentum treatment have been able to reduce the dose of steroids and/or other drugs for ulcerative colitis, will be continued on Dipentum treatment. Patients will return at two weeks after the completion of treatment for a physical examination and a repeat of the laboratory work to determine progress of disease and the presence of any side effects. Patients who continue on Dipentum beyond the 60 days will be examined at bi-monthly intervals. During each office or telephone interview, possible side effects will be elicited. A series of signs and symptoms will be evaluated to include date of onset, cessation, management, and follow-up.

Progress: One patient was entered in this study on a compassionate-use basis in FY 88.

**Original PI

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/54 Status: On-going

Title: Sucralfate, Aluminum, and Calcium

Start Date: 19 May 89 Est Completion Date: Jun 89
Dept/Svc: Medicine, Internal Facility: MAMC
Principal Investigator: CPT John H. Vockroth, MC
Associate Investigators: MAJ Michael F. Lyons, MC
MAJ Amy Tsuchida, MC
Key Words: sucralfate, urine aluminum, urine calcium, diet
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $2516.00 Periodic Review: N/A

Study Objective: To confirm the observed increases in serum and urine aluminum demonstrating that there is a significant amount of aluminum absorption during treatment with sucralfate and to determine if there is an increased urinary calcium excretion or change in serum osteocalcin level during treatment with sucralfate.

Technical Approach: Approximately ten subjects, >18 years of age without a history of significant medical illness, to include peptic ulcer, renal, and metabolic diseases, and with no previous treatment with aluminum-containing antacids or sucralfate will be studied.

Subjects will be given a dietary instruction sheet and will record their diet for two consecutive three-day periods. On the third day of the diet, serum sodium, potassium, chloride, BUN, creatinine, phosphate, albumin, magnesium, calcium osteocalcin, parathyroid hormone, and aluminum levels will be measured. Urine collection will begin after the morning void and will be completed before the first dose of sucralfate. Subjects will then be given sucralfate, 1 gm p.o. 30 minutes before each meal and at bedtime for three days. During the third day of the treatment period, serum sodium, potassium, chloride, BUN, creatinine, phosphate, albumin, magnesium, calcium, osteocalcin, parathyroid hormone, and aluminum levels will be measured and patients will begin to collect a 24 hour urine after the morning void for calcium, phosphate, creatinine, and aluminum levels. All samples will be frozen and run on the same machine after it has been calibrated. Evaluation of compliance to diet and medication will be assessed at the end of the study period.

Data will be analyzed as paired results (before and during testing) assessing a difference between paired data with Student's t-test.

Progress: All clinical work has been completed and statistical analysis has begun. Ten patients were entered.

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 89 Protocol No.: 89/61 Status: Completed

Title: Effect of an Emergency Department Visit for Treatment of Minor Illness/Injury on Subsequent Sleep Cycle and Performance Cycle

Start Date: 16 May 89 Est Completion Date: Sep 89

Department: Nursing Facility: MAMC

Principal Investigator: LTC Jacqueline Brick, AN

Associate Investigators: MAJ Vicky M. Sheldon, AN

Key Words: ER visit, sleep, performance, normal activities

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

Study Objective: To determine the effect of an emergency department visit for minor illness or injury on subsequent sleep cycle and/or performance cycle.

Technical Approach: One hundred patients, ages 18-55, will be studied. Patients with a chronic sleep disorder or on regular, prescribed sleep medications will be excluded as will persons admitted to the hospital for continued medical treatment.

The study will consist of a descriptive subjective survey. Upon release from medical care, consenting subjects will be given a packet containing a demographic data questionnaire, a Verran-Synder-Halpern Sleep Scale, and a subject performance evaluation. At 0600 the next morning or upon first awakening, the subject will complete the demographic data questionnaire and the sleep scale questionnaire. At the end of the day, the subject will complete the performance scale. The demographic questionnaire contains items covering age, gender, marital status, sleep habits, time of emergency department visit, length of visit, and medication upon discharge. The Verran-Synder-Halpern Sleep Scale will elicit information regarding amount of sleep during the previous day, difficulty falling asleep, number of times the subject awoke during the night, and how the patient felt upon awakening in the morning. The performance scale will elicit information on degree of difficulty of accomplishing normal activities from normal to unable to perform normal activities.

Central tendencies, frequencies, mean and standard deviations, and variability of responses will also be determined. Pearson's correlation will be utilized to determine if a correlation exists between the quality/quantity of sleep and performance and the time and length of the emergency department visit.

Progress: LTC Brick is in the process of writing a thesis. The findings indicate that a positive correlation exists between sleep disturbances pre and postvisit as well as in sleep effectiveness. There was an overall decrease in the quality of sleep following the visit. No change in performance was reported by the subjects. The recommendation is made that emergency nurses consider including stressor effects on sleep patterns in discharge instructions.

Detail Summary Sheet

Date: 30 Sep 89	Protocol No.: 89/20	Status: Completed
Title: The Effect of Nonprocedural Positioning During Endotracheal Suctioning of the Newborn on Intracranial Pressure		
Start Date: 20 Jan 89	Est Completion Date: 30 Mar 89	
Department: Nursing	Facility: MAMC	
Principal Investigator: Helene F. Brodeur, R.N., USAR		
Associate Investigators: None		
Key Words: positioning, suctioning, ICP, physiologic, behavioral		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A

Study Objective: To examine the effect of nonprocedural positioning during suctioning and observe its effect on intracranial pressure (ICP) in the sick, extremely premature infant.

Technical Approach: An experimental, repeated measures design will be followed in which the subjects will function as their own controls. Five to ten premature infants from birth to 6 days of age (gestational age 24-32 weeks), intubated and mechanically ventilated, will be studied. The Ladd ICP sensor will be applied on the infant's anterior fontanel 15 minutes prior to beginning the study. Suctioning will be done according to MAMC NICU protocol as deemed necessary by the NICU staff. During one of the suctioning procedures, as designated by the toss of a coin, a third individual will implement the nonprocedural positioning which will consist of placing the infant in a supine, horizontal position, and encapsulating the infant's head very gently and maintaining it midline with the trunk while the other hand places the infant's lower extremities in soft flexion. The infant's arms will be stabilized in soft flexion and midline. The positioning will be maintained for five minutes after completion of suctioning. Each subject will be observed on two separate occasions within 5 days of birth and at least two hours apart with one suctioning episode done with nonprocedural positioning and the other as is routinely done without positioning. Baseline data (blood pressure, heart rate, oxygen saturation, ICP, and neonatal behavior using the NIDCAP assessment tool) will be gathered on each infant 15 minutes prior to, during, and 15 minutes following the suctioning procedure. A demographic data sheet will be completed to obtain background information such as apgar, birthweight, mode of delivery, brief prenatal history, neonatal history, ventilator settings, blood gas results, gestational age, and age in hours at the time of the study. Because of the small sample size, descriptive statistics will be used for data analysis.

Progress: One subject was entered in the study. Because of time constraints and difficulty in obtaining subjects who met the criteria, the study was limited to a single case study. Results indicated that nonprocedural positioning had an overall favorable effect on ICP associated with the suctioning procedure. Heart rate and oxygen saturation as well as behavioral responses did not appear to benefit from nonprocedural positioning.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/40 Status: Completed

Title: Certified Registered Nurse Anesthetists Attitudes Toward Graduate Education

Start Date: 23 Feb 89 Est Completion Date: Sep 89

Department: Nursing Facility: MAMC

Principal Investigator: CPT Keith A. Krause, AN

Associate Investigators:

CPT Larry J. Stinbrink, AN 1LT Timothy O. Bollenbacher, AN

CPT James A. Stutts, AN 2LT Robert B. Ryder, AN

Key Words: necessity, intent, motivation, questionnaire

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $1134.00 Periodic Review: N/A

Study Objective: To identify certified registered nurse anesthetists (CRNA's) attitudes towards master's degree preparation.

Technical Approach: The CRNA Educational Attitude Questionnaire, consisting of three parts, will serve as the survey instrument. Section one consists of demographic and professional data items which will be used to correlate with answers from sections two and three. Section two consists of general statements about master's degree education and intent to obtain a master's degree. Individuals with a master's degree or Ph.D. preparation will not respond to questions concerning intent to obtain a master's degree. Section three consists of two open ended questions which ask the respondent to list and prioritize at least three factors which would personally serve as motivators for them to obtain a master's degree. One question is designed for individuals who currently possess at least a master's degree and the second is designed for those without a master's degree. The data will be entered into a correlation matrix. Basic nursing degree, age, sex, years in practice, marital status, and possibly other demographic factors will be correlated with attitudes toward advantages of a master's degree, current employment situation and opportunities, and the intent to obtain a master's degree. After trends have been identified, a one way analysis of variance to test for significant differences between associate, diploma, and baccalaureate prepared nurses will be computed. Characteristics of the sample, descriptive statistics, and pertinent inferential statistics will be reported.

Progress: 405 questionnaires were returned. The typical respondent was a 40 year old individual with a baccalaureate degree. Overall, respondents were undecided concerning the advantages of master's preparation, although all groups agreed with the AANA proposal that future students should graduate with a master's degree. All groups agreed that employers fail to provide incentives to attend a master's program, and a majority of respondents disagreed that a master's degree should be an employment requirement. The study indicates that the majority of practicing CRNA's have no intent to seek a master's degree and will maintain that position due to lack of inducements and negative barriers. The data from this study was used to prepare a thesis by the investigators as a requirement of the US Army Anesthesia Nursing Course.

Detail Summary Sheet

Date: 30 Sep 89	Protocol No.: 89/44	Status: Completed

Title: Potassium Chloride Supplementation via Feeding Tube: Evaluation by Patient Tolerance and Serum Analysis

Start Date: 17 Mar 89	Est Completion Date: Jun 89
Department: Nursing	Facility: MAMC
Principal Investigator:	CPT Mary S. McCarthy, AN
Associate Investigators:	MAJ Debra Savinske, AN Eleanor Bond, R.N., Ph.D. Margaret Heitkemper, R.N., Ph.D.
Key Words:	feeding tube, KCL, administration schedule, GI distress

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

Study Objective: To quantify gastrointestinal symptom distress related to potassium chloride (KCl) administration by feeding tube and to evaluate subjective and objective patient response to KCl supplementation by feeding tube when administered first by one and then an alternate common nursing technique.

Technical Approach: Ten patients, 18-60 years, without underlying GI or renal disease who are receiving continuous tube feedings and KCl supplementation for the clinical diagnosis of hypokalemia will be studied. Subjects will serve as their own controls. Two trials will be conducted on each subject using the same technical procedure and manipulating only the length of time the feeding is interrupted. One method will consist interrupting tube feeding for five minutes while KCl is given; the other method will consist of interrupting feeding for 30 minutes, administration of KCl, and delaying resumption of the feeding for an additional 30 minutes. Subjective response to KCl supplementation will be measured before and after each of the methods of administering KCl, using a questionnaire designed to evaluate gastrointestinal symptom distress. One hour after administration of the KCl, blood samples will be drawn for measurement of serum potassium level. Results obtained from these measurements will be used as an objective measure of therapy. The Mann-Whitney U Test will be used for the comparison of paired data in this non-parametric design.

Progress: Data from four patients were analyzed. The study confirmed findings of subjective distresses related to nasogastric tube feedings reported by other researchers. A sore nose and throat and being deprived of chewing, testing, and swallowing food were consistently ranked as distressing by three of the four patients. Gastrointestinal distress was occasionally present in the form of nausea, abdominal distention, and cramping and was usually perceived as slightly or moderately distressing. It did not appear to be related to KCl administration. Likewise, serum potassium concentration did not appear to be influenced by the method of medication administration. It is recommended that critical care nurses address the problem of distress related to nasogastric tube feeding while assisting patients with adjustment to tube feeding and that they insure proper dilution and flushing of hypertonic oral electrolyte solution in order to enhance patient tolerance and therapeutic resporse.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/51 Status: Completed
Title: Positioning of Premature Infants in Car Seats and Effects on Ventilation
Start Date: 15 Apr 88 Est Completion Date: Dec 88
Department: Pediatrics Facility: MAMC
Principal Investigator: 1LT Pamela S. Smith, AN
Associate Investigators: MAJ Jose Garcia, MC
2LT Alice Hofer, AN
Key Words: BP, pulse, respiration, oxygen saturation, 3 angles
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $15.00 Periodic Review: May 89

Study Objective: To test the hypothesis that premature infants weighing less than 3 kg are at risk for ventilatory compromise while restrained in infant car seats.

Technical Approach: Fifteen infants born before 36 wks gestation will be studied. Information will be recorded from a routine heelstick spun hematocrit done 48 hours prior to the data collection. Theophylline levels will be recorded from routine samples on those infants who are on theophylline. A complete nursing assessment will be performed to include temperature, pulse, respiration, BP, height, weight, and chest circumference. The study will begin 30 min after the infants have been fed. The infants will have been prefitted for the car seat to prevent excessive handling during the testing phase. The test period will comprise 90 min: 30 min to collect baseline data, 30 min in the car seat, and 30 min for recovery. Each infant will be tested at the same hour on three consecutive days, utilizing a different angle of inclination each day (95/110/140°). Baseline and recovery data will be collected with the infants in prone position. Data to be collected include pulse, respiration, blood pressure, oxygen saturation, color, activity status, position, and nursing interventions required for apnea or bradycardia episodes. During the testing phase infants will be placed in a car seat, with attention given to maintaining proper position for a patent airway. The child will be placed in the car seat under an Ohio Neonatal Warmer with temperature probe attached. A cardiorespiratory monitor will be attached to the child. and an oximeter probe will be attached to a hand or a foot to monitor oxygen saturation. A polaroid photo will be taken to ensure that the infants are positioned in the same fashion each day. Data throughout the three test phases will be collected in two minute intervals, using a stopwatch for accurate timing. Two investigators will be recording data during the testing in order to verify accuracy. The Freidman test will be used for data analysis.

Progress: Four additional infants were entered in FY 89; 13 total entries. Based on the data from this study it is recommended that parents be advised not to use the 95° position for a premature infant, the car seat should face the rear and when possible an adult should be seated next to the infant to observe for lateral slouch. Foam inserts would provide better body mechanics and head positioning. A paper has been submitted for publication.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/11 Status: On-going
Title: The Effects of Head Rotation and Hyperoxygenation-Suction Sequences During Endotracheal Suctioning of Newborn Infants
Start Date: 18 Nov 88 Est Completion Date: May 90
Department: Nursing Facility: MAMC
Principal Investigator: LTC Barbara S. Turner, AN
Associate Investigators: None
Key Words: endotracheal suctioning, newborns, head rotation
Accumulative MEDCASE Cost: -0-** Est Accumulative OMA Cost: -0-** Periodic Review: N/A

Study Objective: To compare left, right, and non-rotation of the head; to compare 2 vs 3 hyperoxygenation suction sequences (HSS); and to examine the interaction effects of head rotation and the number of HSS during intubation and ventilation of term and preterm infants. The parameters to be studied are oxygenation, secretion recovery, intracranial pressure (ICP), and heart rate.

Technical Approach: Seventy newborn infants without tracheal malformations will be studied and serve as their own controls during 4 consecutive endotracheal suctioning procedures (ETS) within a 6 to 12 hour period. Infants will be randomized to one of the following: head turned to right, midline, and left with 3 HSS; head turned to right and left with 2 HSS; and head not turned with 2 HSS and 3 HSS. Analysis of variance for repeated measures will be used to determine the effect of head rotation and the number of HSS on oxygen saturation, secretion recovery, heart rate, and ICP. Scheffe's S Test will be used to evaluate a posteriori contrasts among the means. Baseline oxygenation will be the 5-minute period immediately prior to suctioning; the during-suction period will begin with the initial increase in inspired oxygen concentration and end with the return of oxygen to baseline levels; and the post suctioning time period will be the 5-minute period that begins when the oxygen returns to baseline concentration. Secretion recovery will be analyzed by subtracting the presuction catheter weight and the mucus trap weight from respective post-suction weights. ICP will be analyzed in the same manner as oxygenation. Pearson's correlation coefficient will be used to correlate the variables that define the acuity of illness with oxygenation, secretion recovery, heart rate, and ICP. If more than one of the variables is significantly related, an attempt will be made to quantify the nature of that relationship using multiple regression analysis.

Progress: Fifteen subjects were entered in FY 89 for a total of 28 entries. The two protocols using head rotation resulted in significantly lower and longer levels of hypoxemia. ETS produced a significant rise in ICP beginning with the first pass of the catheter and peaking at the second pass. A third pass produced a rise in ICP that was less than that on the second pass. Significant differences were found in ICP between head rotation and non-head rotation. Overall, there were no significant differences in the weight of secretions recovered. However, HSS with head rotation recovered more secretions than without. Four presentations were given from this data.

**Funded by an NIH grant.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/28 Status:On-going

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

Start Date: 17 Feb 89 Est Completion Date: 30 May 94

Department: Nursing Facility: MAMC

Principal Investigator: LTC Barbara S. Turner, AN

Associate Investigators: None

Key Words: premature infants, endotracheal suctioning, hyperoxygenation, levels, MRB vs ventilator

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

Study Objectives: To compare two methods of hyperoxygenation delivery [manual resuscitation bag (MRB) and a ventilator]; to compare two levels of hyperoxygenation; and to examine the interaction effects of the delivery methods and levels of hyperoxygenation during endotracheal suctioning of premature infants.

Technical Approach: Forty premature infants <38 weeks of gestational age and <21 postnatal days, that have been orally intubated and mechanically ventilated for routine treatment will be studied. This will be a within-subject, randomized block design study with repeated measures in which selected physiologic parameters will be monitored during a controlled endotracheal suctioning procedure in a convenience sample of premature infants. The independent variables will be level of hyperoxygenation (FIO_2 increased 10% and 20%) and method of delivery (MRB and ventilator). The dependent variables will to be measured are oxygenation, intracranial pressure, carbon dioxide tension, heart rate, and secretion recovery. Other physiologic variables to be monitored are mean airway pressure, PO_2/FIO_2 ratio, respiratory rate; and mean arterial pressure (if there is an indwelling arterial line already in place. Subjects will serve as their own controls during 4 consecutive endotracheal suctioning procedures within a 6-12 hour time period, administered at 1.5 to 3 hour intervals. Each of the following endotracheal suctioning protocols will be implemented in each infant in a random order: 10% increase over baseline FIO_2 by MRB; 20% increase over baseline FIO_2 by MRB; 10% increase over baseline FIO_2 by ventilator; and 20% increase over baseline FIO_2 by MRB.

Progress: No subjects have been entered in this study. The principal investigator is awaiting determination of an NIH funding request before implementation of the study.

**Potentially to be funded by an NIH grant.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/79 Status: On-going

Title: The Breast Feeding Experiences of Military Women

Start Date: 15 Sep 89 Est Completion Date: Jan 90
Department: Nursing Facility: MAMC
Principal Investigator: CPT Joan K. VanderLaan, AN
Associate Investigator: LTC Lorna R. Imbruglio, AN
Key Words: Problems, satisfactions, support, suggestions
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $332.00 Periodic Review: N/A

Study Objective: To establish an empirical data base on the breast feeding experiences of active duty military women to include rate who initiated breast feeding, duration of breast feeding, factors military women identify as supportive, detrimental, or perceived to potentially improve the breast feeding experience.

Technical Approach: Approximately 50 active duty women who have indicated breast feeding as their choice of infant feeding method will be mailed a questionnaire not later than three months following delivery of the child. Women who leave active duty before return to work will be excluded from the study.

The questionnaire will include questions to elicit information on breast feeding history, the decision to breast feed, preconceptions about breast feeding as a military mother, supplemental bottle feeding, age of child when subject returned to work, age of child when mother ceased breast feeding, day care of child upon return to work, problems or discomforts upon returning to work, effect on work performance, support received from supervisors/coworkers, type of duty assignment (office, field), shift worked, length and reasons for separations from the child due to military duties, information on Physical Training testing after child was born, feelings regarding closeness to child or importance of breast feeding for working mothers, pleasures associated with breast feeding, and demographics on both mother and child. The mothers will be asked to comment on improvements in the system or to comment on information that could assist a military working mother to make a decision when contemplating breast feeding her child. Data will be coded and analyzed using the Statistical Package for Social Sciences. Descriptive statistics will be used to group the data.

Progress: Revisions required by the IRB have been completed and the questionnaires are being prepared for mailing.

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

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DEPARTMENT OF OB/GYN

Detail Summary Sheet

Date: 30 Sep 89 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: Oct 88

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

Technical Approach: One hundred patients with known twin gestation at 20-26 weeks gestation confirmed by ultrasound will be entered in a randomized double blind study. All patients will be advised to stop working, abstain from intercourse, and institute maximum bed rest at home (a minimum of 8 hours of bed rest during the day in addition to the normal hours of sleep). All patients will undergo the following baseline laboratory studies: EKG, glycosylated hemoglobin, one hour glucose challenge test, endocervical/vaginal cultures for Group B streptococci, *Chlamydia trachomatis* and *N. 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 mg orally every 4 hours while awake (0600-2200 hrs), from the time of entry into the study until 37 weeks gestation. The control group of patients will receive a placebo and will undergo the same laboratory and clinical testing. Chi-square/ Fisher Test and T-test will be used to analyze the data.

Progress: An additional 10 patients were entered in FY 89 for a total of 40 patients entered.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 87/05 Status: Completed

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: Oct 88

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, blood samples will be obtained on 25 term women with chorioamnionitis 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: The study has been completed and a manuscript has been accepted for publication in Obstetrics and Gynecology.

Plasma concentrations of fibronectin were measured in early labor and at the time of delivery in 30 normal parturients and compared to concentrations in 30 healthy nonpregnant control women. The mean plasma concentrations of fibronectin in women in early labor and at delivery were 400±104 and 410±147 µg/mL, respectively (not significant). Both of these values were higher than the mean fibronectin concentration in controls (283±81 µg/mL). The investigators conclude that plasma concentrations of fibronectin are higher in pregnant women than in nonpregnant controls and that they remain relatively constant during uncomplicated term labor.

Detail Summary Sheet

Date: 30 Sep 89 | 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: Sep 89

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 hr 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. Serial ultrasounds with biometric measurements will be performed at 28 and 34-36 weeks to assess fetal growth. Serial umbilical artery doppler FVW studies will be done at entry into the study, at 2 weeks, and again when scheduled ultrasounds are done. This information will be compared to the respective patient's thromboxane/prostacyclin data and clinical outcome.

Progress: Fifty-four patients have been entered, all in FY 89. Since this is a double blind study, no data are available. When 75 subjects have been studied, an independent individual will review the incidence of preeclampsia and compare groups. If significance is present, the study will be terminated.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 87/115 Status: On-going

Title: Treatment of Bacterial Vaginosis in Pregnancy

Start Date: 18 Sep 87 Est Completion Date: Oct 88
Department: OB/GYN Facility: MAMC
Principal Investigator: MAJ W. Kim Brady, MC**
Associate Investigators: COL Patrick Duff, MC
David A. Eschenbach, Univ Washington
Key Words: vaginosis, bacterial, pregnancy, treatment
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Sep 89

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 Gram stain and a summary of labor and delivery will be abstracted from their charts. 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: After studying approximately 100 patients utilizing amoxicillin as the study agent, there was no statistically significant difference between the response of the amoxicillin placebo groups, with approximately 50-55% of the patients in each group experiencing resolution of their infection. This protocol was revised in August 1988 to compare topical 2% clindamycin cream with a placebo. In FY 89, 117 subjects were enrolled for a total enrollment of 122. Data are still being collected.

**Dr. Brady replaced Dr. Duff as the principal investigator in Sep 89.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 85/20 Status: Terminated

Title: Microsurgical Technique
Start Date: 16 Jan 85 Estimated Completion Date: Indefinite
Department: OB/GYN Facility: MAMC
Principal Investigator: MAJ John W. Cassels, MC
Associate Investigators: COL Richard P. Belts, MC
LTC I. Keith Stone, MC
MAJ Leslie W. Yarbrough, VC
Key Words: Residents, proficiency, reproductive tracts, rabbits
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $400.00 Periodic Review: Oct 88

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: This protocol has been suspended since September 1988, so no training sessions were held in FY 89. The protocol was terminated in September 1989.

Dr. Stone, the original principal investigator, PCS'd in August 1988 and Dr. John Cassels took over this protocol as the principal investigator. The protocol was suspended until it was rewritten to bring it more in line with current format and standards.

Dr. Cassels has determined that this type of training protocol is not necessary at the present time in the Department of OB/GYN. If it is determined at a later dates that this type of training protocol is necessary, it will be rewritten and submitted as a new protocol.

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Gordon O. Downey, MC

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

Key Words: hysterectomy, infection, cefamandole

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jan 89

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: LTC Gordon Downey was named the principal investigator on this protocol in August 1988 upon Dr. Lee's retirement.

Four patients were entered in this study in previous years. No eligible patients agreed to enter the study in FY 89.

Detail Summary Sheet

Date: 30 Sep 89 | 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: LTC Gordon O. Downey, MC

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

Key Words: ovarian carcinoma, prior chemotherapy, interferon, cis-platinum, intraperitoneal, efficacy, toxicity

Accumulative MEDCASE Cost: -0- | Est Accumulative OMA Cost: -0- | Periodic Review: May 89

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 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 89	Protocol No.: 89/17	Status: On-going

Title: Surgical Management of the Bowel and Urinary Tract in Gynecologic Surgery (Swine Model)

Start Date: 20 Jan 89	Est Completion Date: Indefinite
Department: OB/GYN	Facility: MAMC
Principal Investigator:	LTC Gordon O. Downey, MC
Associate Investigators:	COL Richard P. Belts, MC
	LTC David Magelssen, MC
	MAJ John W. Cassels, MC
Key Words: surgery, gynecologic, management, swine model	

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

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

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

Progress: Seven training procedures were held in FY 89.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/35 Status: Terminated

Title: Comparison of Endometrial Biopsy Specimens Using a Plastic Curette (Pipelle) versus a metal Curette (Novak)

Start Date: 15 Mar 88 Est Completion Date: Aug 88

Department: OB/GYN Facility: MAMC

Principal Investigator: CPT Katherine S. Foley, MC

Associate Investigators: COL William L. Benson, MC
COL James L. Kelley, MC
CPT Mark Brissette, MC
CPT Neil W. Rawlins, MC

Key Words: hysterectomy, fragmentation, adequacy, accuracy

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Jun 89

Study Objective: To compare the reliability of Pipelle curettes and Novak curettes when used to perform endometrial biopsies.

Technical Approach: Sixty gynecological patients scheduled for vaginal or abdominal hysterectomy will be randomly assigned to have a biopsy with either the Pipelle or the Novak curette. The biopsies will be performed in the operating room after the administration of anesthesia. Specimens will be processed in the usual fashion. Specimens from the hysterectomy will be used as controls. An OB/GYN staff member and two pathologists will grade the specimens from the biopsies and the hysterectomy without the knowledge of the biopsy instrument used.

Student's t test will be used to analyze the weight and degree of fragmentation. Chi square analysis will be used to determine the diagnostic accuracy and adequacy of the specimen.

Progress: Seven additional patients were entered in FY 89 for a total enrollment of 15.

The protocol was terminated due to the reassignment of CPT Foley. No other individual wished to continue this study. The literature already contains all the information that was obtained in the patients studied.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/48 Status: Completed

Title: The Course of Labor in Primiparous Patients Undergoing Vaginal Birth After Cesarean Section

Start Date: 3 Apr 89 Est Completion Date: Jun 89

Department: OB/GYN Facility: MAMC

Principal Investigator: MAJ Frederick E. Harlass, MC

Associate Investigator: COL Patrick Duff, MC

Key Words: cesarean, dystocia, primiparous, nulliparous, oxytocin

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

Study Objective: To define the labor characteristics of the patient who is undergoing a trial of labor after a single previous lower transverse cervical cesarean section. Specifically, to determine if primiparous women who have had a cesarean section for dystocia have a subsequent labor pattern more characteristic of a nulliparous or primiparous patient and the frequency of oxytocin augmentation in these patients.

Technical Approach: The charts of 100 patients, gestational age 37-42 weeks, will be reviewed. Information obtained will include: age, gravity, parity, estimated gestational age, length of the first and second stages of labor, weight of the previous and current infant, usage of oxytocin, and Apgar scores at 1 and 5 minutes. Each study patient will be matched to two control patients. Control factors will be age, race, and conduction anesthesia. One control patient will be nulliparous and the other will be primiparous. The primiparous patient will have undergone a previous vaginal delivery. The next two deliveries meeting these criteria, who appropriately match the study patient in terms of the three control factors, that appear within the delivery log following the study patient will be selected as the controls. Data will be collected anonymously using descriptive factors to match subjects and controls. Continuous data analysis by Student's t-test, ANOVA, and chi-square analysis will be used as appropriate.

Progress: A paper has been accepted for publication in Obstetrics and Gynecology. This paper won the MAMC Fellow's Research Award, 1989.

The investigators conclude that primiparous women who have had a previous cesarean section for dystocia subsequently have a course of labor similar to that of nulliparous patients. No statistically significant differences were noted in gestational age, fetal weight, maternal age, or epidural anesthesia between the groups. Patients who had had a cesarean section in the latent phase of labor had a longer first stage of labor than other groups. All study patients had a longer first stage of labor than primiparous controls. Primiparous controls had a shorter second stage than other groups. These differences remained significant when differences in fetal weight were considered. There was no correlation between oxytocin augmentation and length of each phase of labor.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/24 Status: On-going

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

Start Date: 15 Jan 88 Est Completion Date: Jun 88

Department: OB/GYN Facility: MAMC

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

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

Key Words: maternal/neonatal morbidity, spontaneous/forceps delivery, cranial ultrasound, cord gases

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $480.00	Periodic Review: N/A

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

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

Progress: A total of 253 subjects have been entered in this study.

A paper reporting preliminary results has been accepted for presentation at the Armed Forces Division of the American College of Obstetricians and Gynecologists. There was no significant difference in the mean gestational age, mean infant birth weight, lengths of the first and second stages, Apgar scores, umbilical cord pH values, or the occurrence of neonatal trauma. The use of outlet forceps in nulliparous patients resulted in an increased incidence of third and fourth degree perineal lacerations and a significant decrease in hematocrit. No significant differences in maternal morbidity were observed among multiparous patients in either group.

**Replaced Dr. Yancey as principal investigator, Sep 89.

Detail Summary Sheet

Date: 30 Sep 89	Protocol No.: 89/26	Status: On-going

Title: Pulmonary Function in Pregnant Women Receiving Magnesium Sulfate Infusions

Start Date: 17 Feb 89	Est Completion Date: Mar 89
Department: OB/GYN	Facility: MAMC
Principal Investigator:	CPT Arthur Herpolsheimer, MC
Associate Investigators:	MAJ W. Kim Brady, MC CPT Michael Yancey, MC Marugan R. Pandian, Ph.D.
Key Words: pregnant, magnesium sulfate, pulmonary function	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $4.36	Periodic Review: N/A

Study Objective: To evaluate the effects of magnesium sulfate infusion on the pulmonary function of pregnant women.

Technical Approach: Twenty females of reproductive age will be studied. Patients admitted to the Obstetric Service at MAMC who require treatment with magnesium sulfate infusion for preeclampsia or premature labor will undergo determination of baseline serum magnesium levels and pulmonary function tests with a DeVilriss Surveyor I Spirometer permitting measurement of FVC, FEV_1, PEF, and FEF_{25-75}. Additionally, maximal inspiratory pressure and maximal expiratory pressure will be measured. An intravenous infusion of magnesium sulfate will then be delivered according to current department protocol. Determination of pulmonary function will be repeated two hours later and a second determination of serum magnesium level will be obtained. Differences within the treatment group will be analyzed by the chi-square and Student's t test as appropriate.

Progress: Nineteen subjects have been entered. The protocol is completed with the exception of the assays of the magnesium sulfate.

Detail Summary Sheet

Date: 30 Sep 89 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

Department: OB/GYN Facility: MAMC

Principal Investigator: LTC David J. Magelssen, MC***

Associate Investigators: COL Patrick Duff, MC**
LTC Keith Stone, MC
CPT Timothy J. Boley, MC*

Key Words: hysterectomy, Cefazolin, cefotetan, prophylaxis

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $600.00 Periodic Review: Jun 89

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: Thirty-five patients were entered in this study in FY 89 for a total of 172 entries. No adverse reactions to the medications have been reported.

***Replaced Dr. Duff as PI, Jun 89
**PI, Jul 88 - Jun 89
*Original PI

Detail Summary Sheet

Date: 30 Sep 89	Protocol No.: 88/28	Status: On-going

Title: The Urethral Cytology of Patients with Urethral Syndrome

Start Date: 19 Feb 88	Est Completion Date: May 88	
Department: OB/GYN		Facility: MAMC
Principal Investigator: LTC David J. Magelssen, MC**		
Associate Investigator: CPT Kevin P. Sargeant, MC		
Key Words: urethral syndrome, present/absent, cytology		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $30.00	Periodic Review: Jun 89

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

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

Progress: Four new patients were entered in this study in FY 89 for a total of 22 entries.

**Replaced Dr. Sargeant as PI, Jul 88

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/54 Status On-going

Title: Intraoperative Autotransfusion During Cesarean Section
Start Date: 20 May 88 Est Completion Date: Dec 88
Department: OB/GYN Facility: MAMC
Principal Investigator: MAJ Douglas A. Milligan, MC**
Associate Investigators: COL Patrick Duff, MC
CPT Michael K. Yancey, MC
Key Words: Haemonetic cell-saver, goats, pulmonary emboli
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $1275.00 Periodic Review: May 89

Study Objective: To explore the potential use for autologous intraoperative blood transfusion in obstetrical cases in which the blood has been contaminated with amniotic fluid debris.

Technical Approach: Phase I. Washed and unwashed blood specimens that have been contaminated with amniotic fluid debris from five patients who underwent cesarean section will undergo analysis. Parameters will include microscopic analysis of buffy coat smears, utilizing stains for mucin, fat, and fetal squamous cells, microbiologic cultures, and fetal erythrocyte counts. Descriptive statistics will document the content of the specimens.

Phase II. Group I: Five pregnant goats will be used as controls. A cesarean section will be performed on each animal. Amniocentesis will be performed and as much amniotic fluid removed as possible. Blood contaminated with amniotic fluid will be suctioned from the abdominal cavity and reinfused back into the animal after it has been diluted with an equal volume of amniotic fluid, which will be determined by a drop in hematocrit to 50% of a venous sample. ECG, mean arterial pressure, pulmonary capillary wedge pressure, and central venous pressure will be continuously monitored. After 48 hours, the animals will be given euthanasia and necropsied. Histological specimens will then be obtained to determine the presence or absence of pulmonary emboli.

Group II: Five pregnant goats will be used in this group. The procedures will be identical to those of Group I except the blood and amniotic fluid will be filtered with a Haemonetic cell-saver prior to reinfusion.

The analysis of patient samples will be descriptive. The animal data will be evaluated in terms of the principal outcome measure: presence of pulmonary emboli.

Progress: Phases II and III of this protocol were terminated on continuing review in May 89 because the investigators were unable to complete the protocol while the sheep were pregnant due to technical and scheduling difficulties. Phase I of the study was approved for continuation. Blood specimens have been obtained from two patients.

**Replaced Dr. Yancey as the PI, May 89.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/22 Status: On-going

Title: Preterm Delivery Prevention

Start Date: 17 Feb 89 Est Completion Date: Jun 90
Department: OB/GYN Facility: MAMC
Principal Investigator: MAJ Douglas A. Milligan, MC
Associate Investigators: COL Patrick Duff, MC
MAJ W. Kim Brady, MC
MAJ Glenn Jordan, MC
Key Words: Unasyn, Augmentin, tocolytic therapy, 7 days vs term
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $5960.00 Periodic Review: N/A

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

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

Progress: No patients have been entered in this study. Data collection will commence as soon as collection of data on previously approved studies is completed.

Detail Summary Sheet

Date: 30 Sep 89	Protocol No.: 89/23	Status: On-going

Title: Prophylactic Antibiotics in the Management of Preterm Rupture of the Membranes

Start Date: 17 Feb 89	Est Completion Date: Jun 90
Department: OB/GYN	Facility: MAMC
Principal Investigator:	MAJ Douglas A. Milligan, MC
Associate Investigators:	COL Patrick Duff, MC MAJ W. Kim Brady, MC MAJ Glenn Jordan, MC
Key Words: PPROM, Unasyn, Augmentin	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $3574.00	Periodic Review: N/A

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

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

Differences between treatment groups will be analyzed by the chi-square test and the t test, as appropriate.

Progress: No patients have been entered in this study. Data collection will commence as soon as collection of data on previously approved studies is completed.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/50 Status: On-going

Title: Objective Measurement of Thyroid Volume During Pregnancy

Start Date: 3 Apr 89 Est Completion Date: Nov 90
Department: OB/GYN Facility: MAMC
Principal Investigator: CPT Montgomery E. Thorne, Jr., MC
Associate Investigators: COL Gary L. Treece, MC
MAJ W. Kim Brady, MC
Key Words: thyroid volume, pregnancy, ultrasonography
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $465.00 Periodic Review: N/A

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

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

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

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

Progress: Nine patients have been enrolled with the initial ultrasound performed for eight of the subjects and the second trimester ultrasound performed for one of the subjects.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/25 Status: On-going

Title: CT Pelvimetry as a Predictor of Successful Vaginal Birth After Cesarean Section

Start Date: 17 Feb 89 Est Completion Date: Mar 90

Department: OB/GYN Facility: MAMC

Principal Investigator: CPT Kevin C. Turner, MC

Associate Investigators: COL Sankaran S. Babu, MC
COL John A Read, MC
MAJ W. Kim Brady, MC

Key Words: CT pelvimetry, pelvis, cesarean section

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $2082.00 Periodic Review: N/A

Study Objective: To evaluate computed tomographic examination of the pelvis as a predictor of successful vaginal delivery in women who have had prior cesarean sections.

Technical Approach: Two hundred pregnant patients with a history of one or more prior cesarean sections without an indication for repeat cesarean section will be studied. Patients will be admitted to Labor and Delivery for delivery of the fetus only when indicated and the labor and delivery course will not be changed. Each will have a set for standard labs obtained and a peripheral IV access will be obtained and IV fluids administered throughout labor. Internal fetal monitors will be placed, to include fetal scalp lead and intrauterine pressure catheter. Labor and delivery management will be performed in the usual manner. Once committed, the patients will be managed in the same fashion as all trial of labor patients. This may include medical augmentation of labor followed eventually by vaginal or cesarean delivery. Postpartum, the patient will be counselled and enrolled in the study following written informed consent. CT pelvimetry will be performed during the patients postpartum hospital course (within 72 hours of delivery). Statistical analysis comparing pelvimetry parameters will be made between two groups of patients--those who successfully delivered vaginally versus those who ultimately required a repeat cesarean section. Efficacy of CT pelvimetry will be evaluated with respect to it specificity, sensitivity, predictive value, and efficiency in determining success of trial of labor in patients with history of prior cesarean section.

Progress: The new CT scan was received by Radiology in July 1989 at which time the principal investigator was able to implement the study. Twelve patients have been entered.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 87/73 Status: Completed

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

Department: 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 May 89

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. Serum lipid analysis will include total cholesterol, triglyceride, HDL-cholesterol, and HDL2-cholesterol and enzymatic methods, and apolipoprotein 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 variables. Covariates including age, body weight, adiposity, and former smoking, drinking, and exercise histories may also be considered.

Progress: No further subjects were enrolled in FY 89. Sixty-one subjects were enrolled in previous years. Although optimal hormonal replacement regimen has not yet been determined, this study provides evidence that a continuous regimen with 5 mg of medroxyprogesterone acetate can provide a favorable lipid profile while maintaining a state of amenorrhea in the majority of patients. The study has been accepted for presentation at the Fertility & Sterility conference in Nov 89 and a paper has been submitted for publication.

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 89 Protocol No.: 88/72 Status: Terminated

Title: Antibiotic Prophylaxis of Recurrent Otitis Media

Start Date: 19 Aug 88 Est Completion Date: Aug 89
Department: Pediatrics Facility: MAMC
Principal Investigator: LTC Thomas R. Babonis, MC
Associate Investigators: COL Thomas S. Charbonnel, MC
COL Dan C. Moore, MC
COL Marvin S. Krober, MC
COL Michael R. Weir, MC
LTC Janet Rowe, MC
CPT Amy M. Taylor, MC
Key Words: otitis media, prophylaxis, recurrent, children
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Sep 89

Study Objective: To determine relative efficacy of low dose sulfisoxazole, high does sulfisoxazole, or erythromycin in prophylaxis for recurrent otitis media.

Technical Approach: Children 12 months to 12 years of age with a history of 3 or more episodes of acute otitis media in the previous 6 months or 5 or more episodes in the previous 12 months will be considered for entry. Children with immune deficiency, cleft palate, ventilating tubes, serious otitis media, and other chronic illnesses will be excluded. The subjects will be evaluated by history, physical examination and tympanogram. Physical examination will include ears, pneumatic otoscopy, nose, throat, palate, lymph nodes. Subjects will be randomly assigned to receive either sulfisoxazole, 35 mg/kg/day as a single dose; sulfisoxazole, 75 mg/kg/day in two doses; erythromycin ethylsuccinate, 20 mg/kg/day in two doses, or placebo in two doses. After 3 months, the subjects will again be randomly assigned to receive one of the 3 remaining medications. These assignments will be made before the study begins using paired random numbers. All subjects will be seen at monthly intervals with otoscopy, tympanometry, side effects to medication, and history of ear problems during the preceding month recorded. Outcome measurements will include the incidence of symptomatic ear infections, and abnormal otoscopy and tympanograms on each treatment regimen. The presence of risk factors will be correlated with the overall effectiveness of prophylaxis. Data analysis: Each population will be compared in a 2x2 chi square as initial vs final and the results combined. Then a 2x4 chi square comparing each medication will be used to determine differences between medications; 2x2 chi square tables will be used for post hoc tests. The units will be months with otitis vs months without otitis.

Progress: Patient entry was severly limited by the general notion of parents that an antibiotic was always preferable to no antibiotic. Also, the follow-up length of the study decreased the compliance rate tremendously. Therefore, the protocol was terminated due an insufficient number of patients.

Detail Summary Sheet

Date: 30 Sep 89 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: May 89

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: Samples were obtained from 26 additional patients in FY 89 for a total of 53 entries. No additional patient enrollment is planned. Serologic studies will be done within the next six months and results prepared for submission for publication.

Detail Summary Sheet

Date: 30 Sep 89	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 Marvin Krober, MC**
Associate Investigators:	COL Thomas Charbonnel, MC COL Conrad L. Stayton, 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: May 89

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 follow-up (as evidenced by presence of penicillin in the urine sample); and percentage with hematuria.

Progress: In November 1988, the protocol was revised to authorize 80 additional subjects; 70 additional patients were entered in FY 89 for a total of 149 entries. Patient entry is completed. Preliminary analysis shows twice daily therapy to be optimal. Urine studies for compliance remain to be done within the next three months. Publication of the results should follow shortly thereafter.

**COL Conrad Stayton original PI; changed to COL Krober, Jul 88.

Detail Summary Sheet

Date: 30 Sep 89 | Protocol No.: 88/25 | Status: On-going

Title: Ceftriaxone for Outpatient Management of Suspected Occult Bacteremia

Start Date: 15 Jan 88 | Est Completion Date: Jul 89

Department: Pediatrics | Facility: MAMC

Principal Investigator: COL Marvin S. Krober, MC

Associate Investigator: MAJ Edward M. Eitzen, MC

Key Words: bacteremia, occult, ceftriaxone, outpatient

Accumulative MEDCASE Cost: -0- | Est Accumulative OMA Cost: 3000.00 | Periodic Review: Jan 89

Study Objective: To determine if ceftriaxone given in a single injection per day will clear existing bacteremia and eradicate established subclinical focal infections.

Technical Approach: Subjects (approximately 400) will be sick febrile children 3 months to 3 years of age with fever ≥39.5° C of unknown origin and WBC ≥15,000. Children with a temperature ≥40.3° C, rectally, will be entered regardless of WBC value. Only children who have no evidence of a specific viral infection will be considered. Children who have clinical evidence of focal infection warranting early antimicrobial treatment, CSF analysis consistent with meningitis, symptoms of a nonspecific upper respiratory illness, and antibiotic therapy or DPT immunization within the preceding 48 hr will be excluded. All children who meet the criteria will have a urinalysis and urine cultures and chest x-rays. Patients will be randomized to receive oral Augmentin, 40 mg/kg/day, in divided doses or ceftriaxone in a single IM injection, 75 mg/kg/day. A comprehensive data form, including all pertinent clinical, laboratory, and demographic information will be completed at the time the child is entered in the study. Patients will be re-evaluated within 24 hours with particular attention to the development of focal infection and/or therapeutic adverse reactions. If the patient is still sick and febrile at 24 hours, blood cultures will be repeated and each patient will continue to receive the initial treatment. Each patient will subsequently be seen daily with the blood culture repeated and treatment continued until the patient is afebrile and clinically improved for 24 hr. All patients who have positive blood cultures will be re-examined and repeat blood cultures will be obtained. Subsequent management will be determined by the examining pediatrician. Preliminary analysis will characterize age, gender, race, magnitude of fever, and duration of fever prior to therapy. Evaluations will consist of the presence of focal infection and persistence of bacteremia on follow-up (chi square analysis) and decrement in body temperature and functional status (Wilcoxon rank sum test). The functional status of the patient will be quantified via a scoring system of behavioral characteristics: irritability, consolability, and presence or absence of social smile.

Progress: Eight additional patients were entered at MAMC in FY 89. Enrollment in this multicenter study is expected to be completed by the spring of 1990.

Detail Summary Sheet

Date: 30 Sep 89	Protocol No.: 89/76	Status: On-going

Title: Protective Role of Pyridoxine in Gentamicin Nephrotoxicity

Start Date: 15 Sep 89	Est Completion Date: Sep 90	
Department: Pediatrics		Facility: MAMC
Principal Investigator:	COL Marvin S. Krober, MC	
Associate Investigators:	COL Michael Weir, MC LTC Jose D Masi, MC	
Key Words: nephrotoxicity, gentamicin, pyridoxine, rabbits		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $3135.00	Periodic Review: N/A

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

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

BMDP and SPSS will be used to analyze data. If there are striking differences between the renal pathology of the various animals, the pathology will be scored for rank testing versus PLP, creatinine, gentamicin levels, and B6 dose.

Progress: This study has only recently been approved. The animals have been ordered and the study will be implemented as soon as they are received.

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Joseph P. McCarty, MC**
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: Oct 88

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

Technical Approach: Three groups of school aged children between the ages of six and twelve years will be studied.

Group 1: Ten children with muscle contraction headaches (intermittent - at least one headache every two months for one year).
Group 2: Ten children with migraine headaches (intermittent - at least one headache every two months for one year).
Group 3: Ten siblings of children from group 1 or group 2 with no history of headache or other medical condition (controls).

Subjects in the two experimental groups will have no history of progressive neurologic disease or other serious medical condition. A complete history (including onset of headache, frequency, cause, intensity, location and character of pain, associated symptoms, and relief factors); family history of headache; physical exam; neurological examination and neurophyschological assessment will be conducted on each patient. The neuropsychological examination will include the following standardized test instruments: Wechsler Intelligence Scale for Children (Revised), Wide Range Achievement Test - Revised, Trail Making Test, Bilateral Name Writing, Word Fluency Test, Bilateral Finger Agnosia, Token Test for Children, Grooved Pegboard, Digit Symbol Test (oral and written), and Child Behavior Checklist. Tests will be given to all children in the same sequence. In order to assess current medical status and screen for medical disorders that might affect neuropsychological test results, medical records of all subjects will be thoroughly reviewed. A parent of each child will be asked to complete a problem check list and a detailed medical history questionnaire.

Progress: Twenty-eight additional patients were entered in FY 89 for a total of 37 entries. No conclusions have been derived to date and the investigators feel that additional patients should be entered in order to derive any statistical significance.

**Replaced Dr. McClintock, Oct 88.

Detail Summary Sheet

Date: 30 Sep 89 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: Sep 89

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: 45 additional patients were entered in FY 89 for a total enrollment of 90 patients.

The thyroid ultrasound aspect of this study continues to be suspended due to the workload in the Department of Radiology. The investigators are continuing to collect patient data on age, height, weight, thyroid measurement, and pubertal stage.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/06 Status: Terminated

Title: Comparison of Growth Response of Two Commercially Available Recombinant Preparations of Growth Hormone

Start Date: 16 Oct 87 Est Completion Date: Oct 92

Department: Pediatrics Facility: MAMC

Principal Investigator: LTC Dan C. Moore, MC

Associate Investigator: None

Key Words: growth response, Humatrope, Protropin

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

Study Objective: To compare two commercially available growth hormone preparations in equal doses to determine if there is a significant difference in growth response and antigenicity.

Technical Approach: This is a randomized, double-blind study of prepubertal children, who have never received growth hormone, with <5 cm/yr growth velocity and <10 ng/ml peak growth hormone after administration of 2 pharmacologic stimuli (Arm I); and prepubertal children who have been on growth hormone for at least two years who are beyond the typical catch-up growth phase (Arm II). Baseline data will include age, sex, pretreatment growth velocity, height, weight, growth hormone antibodies, bone age, serum T_4, and concurrent hormone therapy. Patients will be randomized to receive either Humatrope or Protropin, 0.06 mg/kg/dose sq 3 times a week for 6 months. After 6 months, the alternate hormone preparation will be given in the same dosage. At 6 and 12 months, data collection will include height, weight, growth velocity, bone age, growth hormone antibodies, T_4, pubertal stage, and change in concurrent hormone therapy. At 12 months, the patients will be continued on the hormone which has been most effective. A minimum of 35 children will be studied in each arm of the study.

The initial response to growth hormone will be compared using a logistic regression with manufacturer as dependent and all other data as independent variables. The coefficients of the independent variables will provide information about the relative weight of each variable. Failure to show a difference will not show comparability, but will indicate that very large samples are necessary to show a difference. Repeated measures ANOVA will be used to compare the crossover aspect of the study. Group differences may or may not be significant; a significant interaction term is indicative or preparation differences at the dose used. Paired and unpaired t-test will be used as post-hoc tests. A difference in annualized growth velocity of >0.5 cm/yr will be considered as a difference in effectiveness.

Progress: One patient was entered in this study at MAMC in FY 88. The study was to be done in conjunction with Children's Hospital in Seattle, WA. The funds for the study at Children's were withdrawn. The protocol was terminated at MAMC because the patient population was not large enough to support the study.

Detail Summary Sheet

Date: 30 Sep 89 | Protocol No.: 88/18 | Status: On-going

Title: Attitudes Towards Body Weight and Eating in Children

Start Date: 11 Dec 87 | Est Completion Date: Dec 88
Department: Pediatrics | Facility: MAMC
Principal Investigator: LTC Dan C. Moore, MC
Associate Investigators: None
Key Words: children, body weight, eating, attitudes, 10-12 yrs

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Oct 88

Study Objective: To determine the degree to which female children ages 10-12 years are concerned about weight and body size.

Technical Approach: A minimum of 300 female children ages 10-12 seen in the Pediatric Clinic will be asked to participate. After assent, the subjects' weight and height will be recorded and they will complete a questionnaire before leaving the clinic. The questionnaire will elicit information the subject's satisfaction with and self perception of height, weight, and appearance; desire to gain or lose weight; dieting history; eating habits; and worries about becoming too fat or thin. Responses will be analyzed descriptively, then analyzed by ANOVA, test or proportions, and Duncan's multiple range (SPSS) to detect significant differences by height, weight, or age in feelings about weight, body shape, and eating/weight loss behaviors.

Progress: 126 subjects have been enrolled. Preliminary data indicate that a significant proportion of preteen girls are concerned about body weight and eating. Some have already experienced behaviors usually associated with eating disorders in adolescents. Adolescent attitudes toward body weight and eating may have their roots in childhood.

Patient entry has been temporarily suspended by the principal investigator while he further evaluates the data to determine if more subjects are necessary.

PRESENTATION: Triservices Pediatric Meeting, March 1989.

Detail Summary Sheet

Date: 30 Sep 89	Protocol No.: 88/07	Status: On-going

Title: Quantitation of Dysmorphic Features for Syndrome Identification

Start Date: 16 Oct 87	Est Completion Date: Oct 89
Department: Pediatrics	Facility: MAMC
Principal Investigator: LTC Glenn C. Tripp, MC	
Associate Investigators: COL Michael Weir, MC Gentry Yeatman, M.D.	
Key Words: syndrome, identification, dysmorphic features, image analysis, computerized	

Accumulative MEDCASE Cost: $40,000.00	Est Accumulative OMA Cost: -0-	Periodic Review: Sep 89

Study Objective: By careful measurement of facial features and ratios of these features of normal and syndromic children or photographs of them, to explore the limits of normal and attempt to identify clearly significant syndromic deviations.

Technical Approach: Initial data will be obtained from measurements of facial photographs of children without a pre-existing diagnosis of a malformation syndrome. Initial sampling will include 100 randomly selected children from each of the following groups: 6 and 18 months and 3.5 and 6.5 years. Samples will be representative of the major ethnic groups. These data will subsequently be compared to known craniofacial malformation syndromes for patients seen clinically and from case reports and series. The study will also use a computer-based image analysis system for normal patients, syndromic patients, and literature reports of syndromes. The images will be digitalized and distances and areas will be recorded. Where available, absolute sizes will be recorded, but ratios of suspect features to apparently normal features will be the principal data element. The focus of the data analysis will be to identify cut points to distinguish normal features from borderline and from clearly abnormal features. Features explored will involve location, size, and shape of facial/cranial features and may be expanded to hand and foot segment/lower segment ratios.

Dimensions and ratios will be compared across ethnic groups by ANOVA. If no differences occur, groups will be combined. Similar analysis will be used to compare syndromes with the normal groups.

Progress: Problems with photographic and digitalizing equipment have dominated work thus far. The time spent on this protocol in the last year has been in an effort to solve the technical and logistical problems. No patients were entered in FY 89. Twenty patients were entered in FY 88.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/71 Status: On-going

Title: Comparison of Effectiveness of Lidocaine HCL vs Hyaluronidase in the Early Treatment of Soft Tissue Extravasation Injuries in Swine *(Sus scrofa)*

Start Date: 28 Jul 89 Est Completion Date: Oct 89

Department: Pediatrics Facility: MAMC

Principal Investigator: COL Michael R. Weir, MC

Associate Investigators: None

Key Words: extravasation, Renografin, hyaluronidase, lidocaine

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $614.00	Periodic Review: N/A

Study Objective: To determine if lidocaine HCl is a superior therapeutic agent in the treatment of soft tissue extravasation when compared to more traditional therapy.

Technical Approach: The agents which produce cell death by direct cellular toxicity when extravasated include such drugs as Adriamycin, methotrexate, and Renografin. This study will focus on the efficacy of lidocaine HCl versus hyaluronidase as a primary therapeutic agent in the treatment of soft tissue extravasation injury produced by the subcutaneous infusion of Renografin.

One pig will be used to attempt to create an extravasation injury. If this attempt is successful, then an extravasation injury will be created in three additional pigs.

Each animal will have its flank closely shaven. Renografin will be injected subcutaneously into two areas of the flank in order to create the extravasation injury. X-rays will be used to determine the distribution of the Renografin. After the injury has been created, one injection site on each pig will be infused with normal saline and the other site injected with either hyaluronidase alone, lidocaine HCl alone, or a combination of lidocaine HCl and hyaluronidase. In this manner, each pig will serve as its own control. Lesions will be monitored daily for the presence or absence of blister formation and these results photographed and recorded. Measurements will include necrosis and induration. The data will be analyzed by comparing the daily induration and blister or ulcer size to healing or to scar.

Progress: The original protocol was to be performed using rabbits with three groups of three rabbits each. However, the investigators were unable to produce an extravasation injury in the rabbit after attempting this in three different sites. The skin of the rabbit is not nearly as adherent to the subcuticular tissues as human skin. Since the skin of the pig is more closely analogous to human skin in this regard, the investigators revised the protocol (Sep 90) to use pigs with one in each group in a pilot study. The pigs have been ordered and the study will continue when the pigs are received.

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 PSYCHIATRY

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/32 Status: On-going

Title: Evaluation of Changes in Steroid Metabolism and Mental Status During an Acute Episode of Intermittent Porphyria

Start Date: 17 Mar 89 Est Completion Date: Jul 89

Department: Psychiatry Facility: MAMC

Principal Investigator: Timothy S. Clark, Ph.D., DAC**

Associate Investigators:

COL Irwin B. Dabe, MC LTC Kenneth A. Zych, MS

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

Key Words: porphyria, acute, steroid metabolism, mental status

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $786.00 Periodic Review: N/A

Study Objective: To determine the degree of correlation between psychological changes and the production of 5-beta reduced steroids during the acute and recovery phases of an episode of acute intermittent porphyria (AIP)

Technical Approach: Only one or two subjects are expected during the study period due to the rarity of the condition. Baseline blood samples and a control psychiatric evaluation will be done during a period when the patient is not in the midst of an acute porphyria attack. The study will follow a subject from admission for AIP until the resolution of symptoms. Morning, noon, and evening venous blood samples will be obtained each day. A brief neuropsychiatric evaluation will also be done at these times. To reduce the practice effect on the patient's performance, instruments will be used which have alternate forms. For instruments that have no alternate forms, instruments which are not susceptible to practice effects will be used. The following seven instruments will be used: Spokes Test, Finger Tapping, Grip Strength, Letter Cancellation Task; Porteus Mazes; Face-hand Test; and Pain Scale. Chemical analyses will include serum PBG and delta-aminolevulinate and serum beta and alpha reduced steroids by gas chromatography/mass spectrometry. The specific steroid ratios (beta/alpha) to be examined are metabolic products of testosterone (etiocholanolone to androsterone), cortisol (tetrahydrocortisol to allotetrahydrocortisol) and progesterone (5-beta-pregnan-17 alpha-ol-3,20-dione to 5 alpha-pregnan-17 alpha-ol-3,20-dione).

The control day tests will be compared to the acute episode tests by multiple analysis of variance with repeated measures. Correlation coefficients will be calculated between the measure of the beta/alpha steroid ratios and the neuropsychiatric variables.

Progress: One patient entered the study, but failed to complete the protocol. However, the samples obtained were analyzed and resulted in the publication below.

PUBLICATION: Delta-aminolevulinic Acid in Free Plasma by Free Amino Acid Analysis. Hannan, et al: Clin Chem 35(9):1998, 1989

**Replaced MAJ Hannan as PI, Sep 89

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/77 Status: Completed

Title: Self-Report of Attention Deficit Hyperactivity Disorder (ADHD)

Start Date: 16 Sep 88 Est Completion Date: 30 Jun 89

Department: Psychiatry Facility: MAMC

Principal Investigator: CPT Jeffrey E. Hansen, MS

Associate Investigators: Thomas Clingan, M.D., DAC

Key Words: ADHD, self-report, instrument, development

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

Study Objective: To develop a children's self-report instrument for ADHD.

Technical Approach: The experimental group will consist of 25 male ADHD children. The control group will consist of 25 normal children. All children will be between 6 and 12 years of age and have an IQ score of at least 70. Experimental and control groups will be matched on the basis of IQ. The Hansen Self-Report Scale (HSRS) will be administered to all children. This is a scale constructed by the principal investigator. To represent the construct of ADHD, items were chosen to parellel as closely as possible the specific DSM III-R criteria for ADHD. The 20 item HSRS was arranged in a true-false format. Most of the items were taken from the previously validated Revised Conners Teacher Rating Scale (CTRS) [Conners; 1969; 1973], the Revised Parent Symptom Questionnaire (PSQ) [Conners 1973 and 1978] and the Child Behavior Checklist (Achenbach and Edelbroch, 1983), and rewritten for administration to children. Parents of all children will be administered the PSQ and teachers will be administered the CTRS. The ADHD children will be administered the Slosson Intelligence Test (SIT) and the HSRS and then seen by a pediatrician, who is blinded to the results of these tests. The pediatrician will conduct an intake/assessment and collect the PSQ from the parents and the CTRS from the school. Normal subjects will not be seen by the pediatrician but will be given the SIT and the HSRS.

The following statistical procedures will be used to analyze the data: Multiserial correlation: concurrent validity, construct validity, internal reliability; Multiple Sample Chi Square: Differences between groups.

This protocol was revised in Nov 88 to drop the conduct problem control group, increase the number to 25 in the normal control group, change the minimum age to 6, and change the minimum IQ score to 70.

Progress: 22 male ADHD children and 25 control subjects were studied. The data suggest that children between 6 and 12 are able to understand the concepts involved in rating ADHD.

A paper has been written which was submitted for the Fellow's Research Award at MAMC and will be submitted for publication.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/69 Status: On-going

Title: Treatment Use of Anafranil in Obsessive Compulsive Disorder

Start Date: 28 Jul 89 Est Completion Date: Jul 90
Department: Psychiatry Facility: MAMC
Principal Investigator: MAJ John R. Tarr, MC
Associate Investigators: COL Richard L. Schneider, MC
LTC Deborah L. Hickey, MC
Key Words: obsessive compulsive disorder, Anafranil, treatment
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: N/A

Study Objective: To provide Anafranil for the treatment of patients with Obsessive Compulsive Disorder (OCD) who meet protocol criteria and to obtain additional data on the drug's safety.

Technical Approach: This will be an open-label, long-term treatment protocol of Anafranil providing for flexible dosage up to a maximum of 250 mg daily for adults and 200 mg daily for minors. A fixed schedule of titration is provided as a guideline for increasing the dose. The protocol will be conducted by Board Certified psychiatrists throughout the United States. The duration of each patient's treatment participation will depend upon his/her clinical response and tolerance of Anafranil. The protocol will remain active until the drug has FDA approval and is marketed.

Patient enrollment will be considered on a case-by-case basis as determined by an eligibility criteria checklist. Patients 10-65 with a history of primary psychiatric diagnosis of OCD by the following diagnostic criteria: either obsessions or compulsion; one year by history; normal laboratory findings; electrocardiogram without clinically significant abnormalities. Female patients of childbearing age must not be pregnant and a pregnancy test will be required. Patients with depressive symptoms, panic disorder, or phobic disorders may be entered only if the OCD is the primary diagnosis. Nursing mothers or patients with a history of seizures, drug/alcohol abuse, cardiac disturbances, diabetes, hyperthyroidism, or other psychiatric disorders that are the primary diagnosis will not be eligible to be treated on this protocol. The use of other drugs concurrently with Anafranil will be closely monitored.

Progress: The investigator is awaiting HSC approval and the the receipt of the drug from the sponsor before entering one patient that is eligible for the study at this time.

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 89 Protocol No.: 87/07 Status: On-going

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 Preston L. Carter, MC
COL Richard A. Hall, MC
COL Stanley C. Harris, MC
MAJ Stephen B. Smith, MC
Key Words: familiarization lab, stapling, general surgery, swine
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $500.00 Periodic Review: Oct 88

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

Technical Approach: For each laboratory session, two animals will be anesthetized (ketamine HCl 20 mg/kg body weight and atropine .088 mg/kg body weight, IM) as a pre-anesthetic. The animals will then be intubated endotracheally and surgical anesthesia will be induced and maintained using a mixture of Halothane and nitrous oxide.

Once a surgical level of anesthesia has been achieved, the abdominal cavity will be entered via a midline incision. A demonstration of stapling techniques (under the direct supervision of staff surgeons and representatives from the staple manufacturer) will be performed on the animal by the surgical residents. After the demonstration, all animals will be euthanatized without being allowed to recover from anesthesia.

Progress: Multiple techniques and applications were performed during the two training labs that were held in FY 89. Four animals were used.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/24 Status: On going

Title: Serum Angiotensin Converting Enzyme (SACE) in HIV Patients

Start Date: 17 Feb 89 Est Completion Date: Aug 89
Dept/Svc: Surgery/Otolaryngology Facility: MAMC
Principal Investigator: CPT Richard A. Beck, MC
Associate Investigator: LTC Rodney A. Michael, MC
Key Words: HIV positive, SACE, lymphadenopathy, T_4 cell count
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $2050.00 Periodic Review: N/A

Study Objective: To determine if SACE levels are abnormal in patients with HIV infection and if SACE levels are correlated with other manifestations of HIV infection.

Technical Approach: Approximately 60 HIV positive patients followed by the Infectious Disease Service, 18-60 years of age, will be studied. Semiannual examination of all HIV patients followed at MAMC is performed by the Infectious disease Service. This evaluation includes a physical exam and laboratory studies. During this routine evaluation, a determination of a SACE level will be done along with the other standard laboratory studies. A matched (for age and sex) control group of HIV seronegative subjects will also have a SACE level determined. The results of the SACE will be analyzed in relation to the HIV serology. Correlations of SACE with lymphadenopathy, T_4 cell count, the presence of opportunistic infection, and delayed hypersensitivity response will be examined for statistical significance.

Progress: SACE levels have been obtained on 21 subjects. Due to a change of reference laboratory contract after the study was initiated, nine subjects will require repeat measurement. Preliminary results suggest that elevated SACE values correlate with lymphadenopathy.

Detail Summary Sheet

Date: 30 Sep 89 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: Sep 89

Study Objectives: To compare the safety and efficacy of the antiandrogen RU 23908 in combination with leuprolide to 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, performance, and long-term safety of RU 23908 will be assessed 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: The consent form for this study was amended in March 1988 to add the risk of interstitial pneumonitis as a side effect of RU 23908 since a 3.1% incidence of this complication was reported study-wide.

The study was closed to patient entry in September 1988 since the required number of subjects had been enrolled. Seven subjects were enrolled at MAMC with no complications. Monitoring of subjects is still in progress.

The protocol was amended in May 1989 to allow patients who have not objectively progressed at Month 18 the option to continue the same treatment they are on under double-blind conditions.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/03 Status: On-going

Title: A Multicenter, Observer-Blind, Randomized Study of the Safety, Efficacy, and Tolerance of Two Dosage Regimens of Cefpirome (HR 810) in the Treatment of Patients with Urinary Tract Infections

Start Date: 21 Oct 88 Est Completion Date: Indefinite

Dept/Svc: Surgery/Urology Facility: MAMC

Principal Investigator: COL William D. Belville, MC

Associate Investigator: LTC Rodney A. Michael MC

Key Words: urinary, infections, Cefpirome, randomized

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

Study Objective: To assess the safety, efficacy, and tolerance of two dosage regimens of Cefpirome in the treatment of adult hospitalized patients with urinary tract infections.

Technical Approach: This is an observer-blind, randomized group study in which no less than 180 evaluable patients will be enrolled. A minimum of 50 patients will be enrolled at each study site. Patients will be hospitalized adults (either sex) with acute pyelonephritis or complicated upper and lower urinary tract infections requiring parenteral antibiotic therapy. Patients will be randomized to receive Cefpirome, either 0.5 gm q 12 hrs or 1 gm q 12 hrs. Treatment will be administered for a minimum of 5 days and will not exceed 14 days. Susceptibility of the organism to Cefpirome will be determined by disc sensitivity and by determination of the minimum inhibitory concentrations. If sensitivity is not indicated, therapy will not be instituted or continued unless the patient shows obvious clinical improvement. Urine and blood cultures will be obtained for the isolation, identification and sensitivity testing of the causative pathogen(s) not more than 48 hours prior to initiation of therapy. Cultures will be taken between 2 and 4 days after the initiation of treatment and at 5 to 9 days and 4 to 6 weeks after completion of antibiotic treatment.

To determine the similarity of treatment groups, selected background variables will be examined to compare all patients eligible for efficacy analyses. The clinical and bacteriologic responses for the two dose groups will be compared overall and for each organism. The overall comparison will account for the investigators as strata. Dose group by investigator interactions will be assessed. The incidence of adverse reactions for the treatment groups will be compared. Laboratory data for the dose groups will be compared after classifying the data as clinically normal or abnormal. Tabulations will be prepared for physical examination, vital signs, and concomitant medication information.

Progress: No patients have been entered in this study. The investigators will implement this study when patient entry is complete on studies already in progress.

Detail Summary Sheet

Date: 30 Sep 89	Protocol No.: 89/42	Status: On-going

Title: A Phase III, Multicenter, Double-Blind, Parallel Group, Prospective Randomized, Comparative Study of Cefpodoxime Proxetil (CS-807, U-76,252) and Cefaclor in the Treatment of Outpatients with Uncomplicated Urinary Tract Infections

Start Date: 16 Jun 89	Est Completion Date: Jun 90
Dept/Svc: Surgery/Urology	Facility: MAMC
Principal Investigator: COL William D. Belville, MC	
Associate Investigator: LTC Rodney Michael, MC	
Key Words: cefpodoxime proxetil, cefaclor, UTI, safety, efficacy	

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

Study Objective: To evaluate the safety and efficacy of cefpodoxime proxetil, compared with cefaclor in the treatment of outpatients with uncomplicated urinary tract infections (UTI).

Technical Approach: Approximately 25 medical centers will enroll 24 patients each in a controlled, randomized, double-blind parallel group study. Patients will be randomized in a 2:1 fashion to receive cefpodoxime proxetil or cefaclor, respectively, for a maximum of 7 days. In order to maintain the double-blind nature of the study, a double-dummy dosing technique will be utilized in which patients will receive medication four times daily. Patients receiving cefpodoxime proxetil will receive a 100 mg tablet every 12 hours and three placebo capsules per day. Patients receiving cefaclor will receive one 250 mg capsule every 8 hours and two placebo tablets twice a day. Each patient will receive a total of two tablets and three capsules daily. Medication will be taken under fasting conditions (1-2 hours prior to eating). A complete medical history, physical exam, laboratory safety tests, pregnancy test (if applicable), and microscopic exam of the urine will be performed at Visit 1. Patient's signs and symptoms including frequency, urgency, back pain, dysuria, costovertebral angle tenderness, nocturia, fever, chills, and hematuria will also be evaluated. Patients will have urine collected for culture prior to initiation of therapy unless it is in the best interest of the patient to initiate treatment immediately. Patients will be evaluated at day 3-5 during treatment, including urine and blood cultures, and again at the end of treatment, 5-9 days post-treatment, and 4-6 weeks post-treatment.

Progress: Twelve patients have been entered in this study.

Detail Summary Sheet

Date: 30 Sep 89	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 Kevin J. Chismire, MC**	
Associate Investigators:	MAJ Bruce D. Bellin, 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
LTC Thomas H. Mader, MC	CPT Lawrence E. Hannon, MC
Key Words: intraocular lenses, implantation	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $200.00	Periodic Review: Jul 89

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 240 IOL's were implanted in FY 89 with no adverse reactions. IOL's have withstood the test of time, are considered safe for most patients, and are no longer considered investigational. However, the protocol will remain open in order to use updated lenses that are awaiting FDA approval.

**Replaced LTC Mader as the PI, July 1989.

Detail Summary Sheet

Date: 30 Sep 89 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/Orthopedic Facility: MAMC
Principal Investigator: MAJ Michael Q. Cosio, MC**
Associate Investigators:

COL Richard A Camp, MC	LTC Robert J. Kenevan, MC
COL Jackie Finney, MC	LTC Bruce E. Wheeler, MC
COL Thomas Griffith, MC	MAJ Stephen D. Clift, MC

Key Words: microsurgery, teaching program, laboratory animals

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $690.00	Periodic Review: Sep 89

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

Technical Approach: A schedule of one or two afternoons per week will be set aside for teaching sessions. Sessions will begin with lectures, followed by practical exercises in anatomy and step-by-step instruction in the surgical techniques. Staff and residents from the Orthopedic, Plastic Surgery, and Thoracic Surgery Services will train in the following procedures:

(1) reimplantation of extremities
(2) re-anastomosis of peripheral vessels and nerves
(3) repair of avulsion wounds
(4) graft transplants
(5) free cutaneous, myocutaneous and composite tissue transfer for traumatic lesions and reconstructive procedures
(6) re-anastomosis of facial nerve lesions

The training will begin with small vessels and nerves in cadaver specimens of small laboratory animals. When the anatomy of the area is learned as well as the use of the microsurgical instruments and the operating microscope, then microsurgical procedures in living rats, guinea pigs, and rabbits can be learned.

Progress: Five residents have been certified in performing end-to-end arterial repairs of the femoral artery using microvascular techniques. Additional equipment is being acquired to improve the program.

**MAJ Cosio replaced LTC Wheeler as the principal investigator in Sep 89.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/47 Status: Completed

Title: The Effect of Not Rinsing Hands After Pre-surgical Scrubbing on Post Operative Bacterial Counts from Surgeon's Hands

Start Date: 12 Jan 89 Est Completion Date: Mar 89

Dept/Svc: Surgery/Orthopedics Facility: MAMC

Principal Investigator: CPT James A. Dahl, MC

Associate Investigator: COL Bruce Wheeler, MC

Key Words: presurgical scrubbing, chlorhexidine, nonrinsing

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $122.00 Periodic Review: N/A

Study Objective: To determine if there is a difference in the number of bacteria which can be cultured from a surgeon's hands postoperatively depending on whether the hands are rinsed or not following presurgical scrubbing with a chlorhexidine containing scrub.

Technical Approach: Approximately 60 surgical procedures will be studied. Prior to each operative procedure, each investigator will scrub in his regular fashion with Hibiclens scrub. He will then rinse off one hand and forearm with water and leave the foam on the other. He will then gown and glove in the usual manner and proceed with the surgery. At the conclusion of the surgery, the gown and gloves will be removed and the surgeon will rub his fingers together in separate sterile bowls containing 40-50 cc of tryptic soy broth. The contents of these bowls will then be poured into labeled centrifuge tubes and transferred to the laboratory to be spun down, and the particulate matter at the bottom of the tubes will be cultured for bacterial colony counts. The first 2-3 cultures will be grown to isolation to estimate the bacterial flora involved. The surgeons will alternate which hand is to be rinsed in a random fashion. At the conclusion of the study, the data will be analyzed, using the Wilcoxon signed-rank test, to compare bacterial colony counts with the length of the operation and whether or not the Hibiclens was rinsed off.

Progress: Fifty procedures were studied. There was a significant difference ($p<.005$) in the number of bacterial colonies isolated from the rinsed hands versus the unrinsed hands (the former being greater). There also seemed to be a trend towards larger bacterial counts following longer case; however, the difference was not significant. Neither one of the surgeons noted any evidence of dermatitis during the course of the study. These results suggest that not rinsing after the chlorhexidine scrub can lead to lower bacterial counts on the surgeon's hands and less chance of wound contamination should glove puncture occur. Cases in which glove puncture occurred were excluded from the study.

Detail Summary Sheet

Date: 30 Sep 89 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: Sep 89

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 45 physicians receiving training.

Detail Summary Sheet

Date: 30 Sep 89	Protocol No.: 89/78	Status: On-going

Title: Immunohistochemical Detection of Phosphotyrosine as a Predictor of Recurrence and Long-Term Survival in Breast Cancer Patients by CPT Ismail Jatoi, MC

Start Date: 15 Sep 89	Est Completion Date: Jul 90
Dept/Svc: Surgery/ General	Facility: MAMC
Principal Investigator:	MAJ Ismail Jatoi, MC
Associate Investigators:	COL Preston L. Carter, MC COL James L. Kelley, MC CPT Leonard N. Howard, MC CPT John E. van Hamont, MS
Key Words: breast cancer, phosphotyrosine, predictor	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $1150.00	Periodic Review: N/A

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

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

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

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/57 Status: On-going

Title: Evaluation of Ankyloglossia: A Prospective Study

Start Date: 20 May 88 Est Completion Date: Apr 91
Dept/Svc: Surgery/ Otolaryngology Facility: MAMC
Principal Investigator: CPT Ray E. Jensen, MC
Associate Investigators:
COL Gerald R. Aaron, DC MAJ Jose D. Masi, MC
LTC Don B. Blakeslee, MC Mark J. Stephan, M.D., DAC
MAJ Newton O. Duncan, MC Kenton L. Yockey, M.A., DAC
Key Words: natural history, criteria for intervention & treatment
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Sep 89

Study Objective: To better define the natural history of congenital ankyloglossia in order to establish appropriate criteria for intervention and treatment.

Technical Approach: This will be a non-randomized prospective study of congenital ankyloglossia to include objective diagnosis with management based on multi-disciplinary input from otolaryngology, speech pathology, dentistry, and pediatrics. Electron microscopy will be included for completeness. Hereditary patterns will be investigated and reported when available. Indications will be speech disorders, swallowing problems, dental problems, and cosmetic/functional abnormalities all directly related to ankyloglossia. Consultations will be obtained on all patients from speech pathology, developmental pediatrics, and dentistry. Speech recordings will be obtained pre and post-treatment.

Twenty-five patients <3 years will be entered and observed. Twenty-five patients $\geq$ 3 years will be entered and considered for surgical repair if indicated. Periodic review of subject files will take place as needed to direct appropriate management and case gathering. Follow-up for surgical patients will be at two weeks post-operation and at 1 and two years for all patients. After a two to three year period, cases will be compiled and an attempt made to draw conclusions from the gathered data. Type of data analysis will be based on type of data obtained.

Progress: This protocol was suspended in December 1988 because the principal investigator had not made revisions required by the IRB. A revised copy of the protocol was submitted in August 1989 and reviewed and approved by the IRB in September 1989. Approximately 20 patients have been entered in the study.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/31 Status: Terminated

Title: Photodynamic Therapy of Human Prostate Cancer *in Vitro*
Start Date: 19 Feb 88 Est Completion Date: Aug 88
Dept/Svc: Surgery/Urology Facility: MAMC
Principal Investigator: COL Victor J. Kiesling, MC**
Associate Investigators:
COL William Belville, MC Richard Ostenson, M.D., ALVAMC
CPT Thomas A. Rozanski, MC Stephen Loop, M.S., ALVAMC
Key Words: cell line, prostate, ALVA-31, HPD, phototherapy

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $1205.00	Periodic Review: N/A

Study Objective: To study the effect of photodynamic therapy on the primary human prostate tumor cell line ALVA-31, using the hematoporphyrin derivative (HPD) as the photosensitizing agent.

Technical Approach: Tumor cells from a primary human prostate cancer cell line which originated from a radical prostatectomy specimen and which has been maintained in continuous culture for over 3 years will be used in this study. Tumor cells will be suspended in media and placed on a 96-well plate using 10,000 cells/well. HPD will be diluted with tissue culture media into various concentrations, ranging from 0.3 to 40.0 µg/ml. The cells will be incubated with the HPD for varying periods of time prior to light exposure with a 750 watt halogen-tungsten lamp. Light passes through a plate of heat absorbing glass and a red filter prior to irradiating the cells. Each plate will be set up with 3 treatment groups: cells exposed to light only without prior HPD treatment; cells treated with HPD and kept covered during the light exposure; and cells treated with HPD and exposed to light. Following light exposure, the tumor cells will be incubated with tritiated thymidine, used as a measure of cell growth. This process measures the effect of HPD phototherapy on the viability of the prostate tumor cells. Preliminary studies, using 8 different doses of HPD and incubating cells with HPD for 2 hr prior to light exposure at 30 sec and 2 and 6 min demonstrated an obvious dose-response relationship to both increasing the dose (concentration) of HPD and increasing the duration of light exposure. These experiments will be repeated as well as devising a more complete response curve with the above mentioned variables.

Progress: Using tritiated thymidine uptake, a dose response relationship in cell toxicity with respect to time of light exposure and to increasing concentration of HPD was demonstrated in the ALVA 31 human prostate tumor cell line. Further studies planned on this protocol were not completed due to the retirement of Dr. Kiesling and to difficulties in coordinating the study with American Lake VA Medical Center. Preliminary results were presented by Dr. Rozanski at the Kimbrough Urological Society in Nov 87 and at the Northwest Urological Society in Dec 87.

**Replaced CPT Rozanski as the principal investigator, Jul 88.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 87/21 Status: Terminated

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: Nov 88

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. Chemotherapy medications will already have been determined. Patients will receive Nystatin Swish and Swallow or Mycelex Troches, generic mylanta, Benadryl, and Lidocaine Gel mouthwash, and Septra. An I.V. hyperalimentation solution based on metabolic requirements as determined by the BEE method with the 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 a 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. Body weight changes, TLC, albumin values, number of days hospitalized, number of days with fever, number of days with severe stomatitis, and percentage of full dose chemotherapy in patients who receive MACOP-B 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: Four patients were entered in the study with no adverse effects reported. This method of treatment proved to be very beneficial in completing chemotherapy regimers. The protocol was terminated because CHAMPUS would no longer provide the funds.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/40 Status: On-going

Title: Clinical and Radiographic Evaluation of Base Wedge Osteotomies of the First Metatarsal

Start Date: 18 Mar 88 Est Completion Date: Mar 89

Dept/Svc: Surgery/Podiatry Facility: MAMC

Principal Investigator: CPT Ernest L. Mollohan, MS

Associate Investigators: MAJ Richard O. Jones, MS

Key Words: periosteum, stripping/nonstripping, x-rays

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Sep 89

Study Objective: To assess the effects on bone healing of stripping or not stripping the periosteum when performing base wedge osteotomies of the first metatarsal, utilizing ASIF fixation.

Technical Approach: A minimum of 100 patients with signs and symptoms within the realm of diagnosis of hallux abducto valgus, requiring surgical intervention, will have base wedge osteotomies of the first metatarsal performed. Patients will be randomized to have the periosteum stripped or not stripped prior to ASIF fixation. All patients will be placed in below the knee casts with crutch ambulation. Periosteum will be cut with sharp dissection in all cases, whether for complete exposure of metatarsal shaft or for measuring wedge osteotomy. Axial, lateral, and medial oblique x-rays will be obtained at 2, 6, 12, and 26 weeks postsurgery. Radiographs will be compared for boney union.

Progress: A total o f 64 patients has been entered in this study. The investigator is in the process examining the data to determine if the number of subjects is sufficient for statistical significance.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 86/85 Status: Completed
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: LTC David W. Moore, MC**
Associate Investigators: COL Charles A. Andersen, MC
LTC Donald B. Blakeslee, MC
MAJ Peter Greenman, MC
CPT Dale B. Smith, MC
Key Words: laryngeal nerve, identification, balloon device
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Sep 89

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 was implemented after animal studies on safety and efficacy of the device proved 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: Thirty-five (35) patients were entered in this protocol. The device has proven reliable, safe, and effective.

Dr. Dale Smith, the original principal investigator, who is now stationed at Fort Sill, OK, is in the process of submitting the protocol through the proper channels to conduct an expanded multicenter study.

A paper was presented at the American Academy of Otolaryngology Head and Neck Surgery Meeting in September 1988.

**LTC Moore replaced Dr. Smith the PI, Aug 88.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/05 Status: On-going

Title: An Epidemiological Study of Nasopharyngeal Cancer

Start Date: 21 Oct 88 Est Completion Date: Jan 92
Dept/Svc: Surgery/Otolaryngology Facility: MAMC
Principal Investigator: MAJ Michael R. Morris, MC**
Associate Investigators: LTC Donald B. Blakeslee, MC
Thomas L. Vaughan, M.D.
Fred Hutchinson Cancer Research Center
Key Words: cancer, nasopharyngeal, formaldehyde, exposure
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: N/A

Study Objective: To test the hypothesis that occupational and residential exposure to formaldehyde increases the risk of nasopharyngeal cancer; to determine if any increase in risk is modified by smoking status, dietary intake of beta-carotene and vitamin C, and other potential risk factors; and to identify other medical, environmental, and lifestyle factors associated with risk of the disease in a low-incidence population.

Technical Approach: Eligible cases will be all persons aged 18-74 years who develop nasopharyngeal cancer between 1 Jan 87 and 30 Jun 91, who reside in areas covered by six population-based cancer registries in the United States. A random digit dialing technique will be used to select one control per case from among residents of the same area in which each case resides. Subjects will be interviewed by phone using a standardized questionnaire and interviewer manual to determine occupational and residential histories, along with other factors suspected to be associated with risk of nasopharyngeal cancer, including medical, tobacco, alcohol, chemical exposure, and dietary histories. Blood specimens will be collected from nasopharyngeal cancer cases and controls. These specimens will be analyzed for histocompatibility type as well as antibodies to Epstein-Barr virus. Using exposure assessment methods already developed in a preliminary study, indices of formaldehyde exposure, both from home and workplace sources, will be calculated. Both stratified and multivariate analysis will be used to estimate relative risks of nasopharyngeal cancer in relation to the various environmental factors considered.

Progress: Madigan is participating in this study only as a referring institution. The patient will be made aware of the study and given instructions on who to contact for participation if the patient wishes to take part in the study. No patients at Madigan Army Medical Center have entered the study.

**Replaced LTC Blakeslee at PI, Apr 89

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/01 Status: On-going

Title: Effects of Common Arthroscopic Irrigating Solution on Adult Rabbit Articular Cartilage Proteoglycan Synthesis: An *In Vivo* Study and An Animal Model to Simulate Arthroscope Induced Trauma

Start Date: 21 Oct 88 Est Completion Date: Jan 89

Dept/Svc: Surgery, Orthopedics Facility: MAMC

Principal Investigator: CPT Jerome J. Perra, MC

Associate Investigators: COL Bruce Wheeler, MC
MAJ Charles J. Hannan, MS

Key Words: synthesis, proteoglycan, irrigating, rabbit

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $1720.00 Periodic Review: N/A

Study Objective: To assess the effects of commonly used arthroscopic irrigating solutions on articular cartilage proteoglycan synthesis using an animal model to simulate arthroscope-induced trauma to the articular surface which violates the lamina splendins.

Technical Approach: One control and three experimental groups of 10 adult male New Zealand white rabbits, weighing 2.0-3.0 kg, will be properly anesthetized. Both knee joint capsules will be exposed by surgical dissection and a small arthrotomy created in the capsule. A series of superficial lacerations 1.0 mm in depth will be made across the condyles with a controlled depth device. After repair of the arthrotomy, the knees will be irrigated continuously for two hours, using normal saline, Ringer's lactate, sterile H_2O, or nothing (control group). After the irrigation is completed, the incision will be closed. Twenty-four hours after irrigation the animals will be re-anesthetized and infused intravenously with 200 µc of $^{35}SO_4$. One hour later the cartilage from the right knee will be excised and two hours post infusion the cartilage from the left knee will be excised. The samples will be blotted, weighed, and washed three times in distilled water for one hour and then overnight to remove unincorporated radioactivity. Samples will be placed in Aquasol for 24 hours and counted in a liquid scintillation spectrometer. The scintillant will be aspirated and counted separately to ensure that only incorporated $^{35}SO_4$ is being counted. Counts/minute/gram cartilage will be plotted against time and graphed linearly. The one hour and two hour counts will be plotted against time and forced through the origin. Data with correlation coefficient <0.8 will be rejected. Standard deviations will be calculated and the means of the different groups compared using the Mann-Whitney non-parametric test.

Progress: Twenty five rabbits have been tested using all three fluids. Serum samples have been collected to correlate counts to serum concentration of isotope. Some variability in data has been noted between groups and also within each group. No control animals have been tested.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/15 Status: Completed

Title: The Posterolateral Approach to the Lumbosacral Spine: An Anatomic Study

Start Date: 20 Jan 89 Est Completion Date: Sep 89

Dept/Svc: Surgery/Neurosurgery Facility: MAMC

Principal Investigator: MAJ Joseph H. Piatt, Jr., MC

Associate Investigators: Robert Goodkin, M.D.
Sandra Goodkin (medical artist)

Key Words: spine, lumbosacral, posterolateral, nerve roots

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $750.00	Periodic Review: N/A

Study Objective: Radiculopathy due to degenerative disease of the lumbar spine almost always requires a midline operative approach. The posterolateral approach to the lumbosacral spine is occasionally used for lateral fusions. Because spinal fusion is generally the domain of the orthopedist, it is the osteology and myology of that region that has been described with the greatest care. The anatomic relationships of the nerve roots have received relatively scant attention. Therefore, the investigators plan to investigate the lumbosacral spine in order to prepare a more precise description of the osseous, ligamentous, and vascular relationships of the nerve roots than any previously published.

Technical Approach: The physician investigators will conduct gross anatomic dissections of the lumbosacral spine utilizing cadavers. Three male and three female cadavers will be use to provide 12 posterolateral lumbosacral spine dissections. Abundant and detailed photographic records will be made. The medical artist will prepare illustrations of the surgical approach and diagrams of selected anatomic relationships from the photographs and from the dissections. Special attention will be directed to relationships and anomalies of the following structures: the transverse processes, articular facets, pedicles, and bodies of the lower lumbar vertebrae, the alae of the sacrum, the crests of the ilium, the intervertebral discs, the iliolumbar ligaments, the segmental arteries, and the ganglia and extraforaminal courses of the L3, L4, and L5 spinal nerve roots.

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

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/29 Status: On-going

Title: Suprarenal Inferior Vena Cava Narrowing in Pigs and Right Solitary Kidney Viability

Start Date: 17 Feb 89 Est Completion Date: Jun 89

Dept/Svc: Surgery/Urology Facility: MAMC

Principal Investigator: CPT McKay L. Platt, MC

Associate Investigators: LTC John A. Vaccaro, MC
LTC Barbara Turner, MC

Key Words: kidney, survivability, vena caval narrowing

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $870.00	Periodic Review: N/A

Study Objective: To determine the degree of suprarenal inferior vena caval (SR-IVC) narrowing that will allow for right renal survivability.

Technical Approach: Fifteen pigs will be operated to accomplish narrowing of the SR-IVC by tying the vena cava around Hegar dilators of known diameter; to resect the left kidney; and to measure the IVC pressure proximal and distal to the narrowing by means of a manometer. Five groups of pigs will be defined based on the degree of vena cava narrowing, with three pigs in each group. The control group will undergo left renal resection and measurement of the IVC pressure but no IVC narrowing. Groups will be defined as narrowing to 5, 8, 11, and 14 mm diameter and none for the control group. Serum creatinine will be drawn from an indwelling catheter every other day postoperatively to assess renal function. Pigs will be euthanized four weeks postoperatively and renal vein and inferior vena caval thrombosis will be assessed.

An addendum to this protocol was approved at the same time as the protocol to allow LTC Turner to describe histopathologic changes in the tracheal epithelium in the 4 weeks following the initial surgery. The trachea will be exposed at necropsy and the location of the tip of the endotracheal tube and the cuff area of the endotracheal tube will be marked by placing ligatures in the tracheal wall prior to removal of the heart and lungs. The trachea, bronchi, and lungs will be fixed by inflation and the external diameter of the trachea will be measured and recorded. The ID:OD ratio of trachea to endotracheal tube will be determined. Following fixation, the trachea and bronchi will be dissected and removed. Serial transverse sections (N=10) will be taken from the trachea at the locations marked by ligatures. Two sections will be examined with a scanning electron microscope. The remaining sections will be embedded in paraffin and stained with the periodic acid schiff reaction, hematoxylin, and eosin. All slides will be scored and loss of intraepithelial mucus, surface cilia, submucosal hemorrhage, polymorphonuclear leukocytic infiltration, epithelial erosion, and necrosis will be assessed. Total injury scores will be calculated for each of the areas examined and described using descriptive statistics.

Progress: Ten pigs have been studied.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/56 Status: On-going

Title: Idiopathic Hematuria with Hypercalciuria in Adults: Incidence, Pathogenesis, and Treatment

Start Date: 20 May 88 Est Completion Date: May 89

Dept/Svc: Surgery/Urology Facility: MAMC

Principal Investigator: CPT Leonard G. Renfer, MC

Associate Investigators: COL Victor J. Kiesling, MC
MAJ Howard M. Cushner, MC

Key Words: hematuria, hypercalciuria, HCTZ vs no treatment

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: 2000.00	Periodic Review: Sep 89

Study Objective: To identify that proportion of patients with idiopathic hematuria that have hypercalciuria and to monitor the response of the hematuria to hydrochlorothiazide (HCTZ)in both normocalciuric and hypercalciuric patients.

Technical Approach: Patients ≥ 18 years of age with idiopathic hematuria will be studied for hypercalciuria. Specifically, patients with hematuria >2 RBC/hpf on spun sample will undergo IVP/cytoscopy/urine C&S. If these studies fail to identify the source of persistent hematuria, the patients will undergo the following studies: 24-hr urine specimen for calcium, protein, creatinine, and uric acid, SMA-20, complete blood count with ESR, PTT/PT, and sickle index (if patient is black).

Patients with normal studies will be divided into control and treatment groups. The treatment group will be treated with HCTZ, 50 mg b.i.d., for 8 weeks. Seven days prior to the initiation of therapy, the patient will begin testing urine dipstick for blood daily and continue for the remainder of the study period. Clinic follow-up for both controls and treatment groups will be at 2, 4, and 8 weeks after initiation of therapy as well as 2 and 4 weeks after termination of therapy. A repeat 24 hr urine collection to assess for response of calcium excretion, the SMA-20 for serum electrolytes, and a separate spot urine sample for urine calcium/urine creatinine ratio will also be performed at each visit.

Patients with the diagnosis of hypercalciuria will be randomized into control and treatment groups with treatment and monitoring as for the subjects with normal studies.

Control groups will receive no treatment , but have follow-up and diagnostic tests as described for the treatment group.

Progress: Nine patients were entered in the study in FY 89 for a total of 13 patients studied. Most of the patients have normocalciuria and it appears that HCTZ has no effect on hematuria.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/10 Status: Completed

Title: Clinical Comparison of Prostatic Needle Aspiration and Prostatic Core Sampling Using the Biopty Gun

Start Date: 18 Nov 88 Est Completion Date: Oct 89

Dept/Svc: Surgery/Urology Facility: MAMC

Principal Investigator: CPT Leonard G. Renfer, MC

Associate Investigators: COL James L. Kelley, MC
COL Victor J. Kiesling, MC

Key Words: prostate, needle aspiration, core sampling, Biopty Gun

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $2445.00	Periodic Review: N/A

Study Objective: To compare transrectal fine needle aspiration to transrectal biopty tissue core sampling of the prostate in the following areas: (1) feasibility and patient comfort in an outpatient setting under local anesthesia and (2) accuracy, including assessment of sensitivity, specificity, and efficiency.

Technical Approach: Approximately 100 patients with palpably suspicious prostates will be studied. An appropriate medical history, including medications, allergies, and urine culture, will be obtained. Sampling will first be accomplished with two separate needle aspirations from each prostatic lobe. Following this, 4 tissue cores from each prostatic lobe will be obtained using the Bard Biopty instrument. All patients will receive 500 mg of Ciprofloxacin immediately after the procedure as well as 12 hours later. All patients will be observed for at least two hours post-procedure. The first voided specimen will be checked for hematuria. Patients will be asked to grade degree of discomfort for both sampling techniques. Complications, including fever, infection, and hematuria, will be monitored. A urine culture will be obtained one week post-biopsy.

A positive core biopsy will be considered proof of malignancy, regardless of aspiration result. All inadequate or negative tissue core results will require repeat samplings in two months. On subsequent samplings, a positive core biopsy will be considered proof of malignancy. If the core sampling is inadequate, the procedure will be repeated in 2 months. If the core biopsy is negative and the aspiration is positive, inadequate, or suspicious, the procedure will be repeated in 2 months. If the core biopsy is negative and the aspiration is negative, routine close urologic follow-up will be maintained.

Sensitivity, specificity, and average comfort scores for each procedure will be calculated.

Progress: The Biopty Gun was more sensitive and better tolerated than transrectal needle aspiration.

A paper has been submitted for consideration for publication.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/02 Status: Terminated

Title: Effect of Ipratropium Bromide on Patients with Rhinitis

Start Date: 21 Oct 88 Est Completion Date: Mar 89
Dept/Svc: Surgery, Otolaryngology Facility: MAMC
Principal Investigator: CPT Ronald E. Schwartz, MC
Associate Investigators: COL W. Pierre Andrade, MC
LTC Don B. Blakeslee, MC
MAJ Newton O. Duncan, MC
Key Words: rhinitis, subclasses, ipratropium bromide, placebo
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: N/A

Study Objective: To determine the efficacy of the drug ipratropium bromide in the treatment of rhinitis; to determine if the response to ipratropium bromide differs between the subclasses of rhinitis; and to establish a distinct patient subpopulation that would benefit most from treatment with this drug.

Technical Approach: Fifteen patients, skin test positive, and 15 patients, skin test negative, will be entered in the study. Patients will be randomized to receive either a placebo or an aerosol canister of ipratropium bromide. The dose schedule will be 40 µg in each nostril 4x/day. Patients will be given a questionnaire in order to rate symptoms of rhinorrhea, sneezing, and nasal blockage prior to entering the study. They will be told to use the medication supplied to them to the exclusion of all other medicines that they usually use to control symptoms of rhinitis. Patients will be instructed in the use of an intranasal applicator and will demonstrate proficiency before beginning the study. They will be instructed to spray two times into each nostril four times per day. Patients will use the canister for three weeks and keep a daily scorecard of symptoms. After three weeks, patients will return the canister and be immediately entered into the other wing of the study. Weeks 1 and 4 will be considered wash out periods and reported symptoms will not be used for statistical analysis. Patients will have one scheduled appointment for evaluation during each of the three-week arms as well as an evaluation at the conclusion of the study. During these evaluations, the patient will undergo a complete head and neck exam and will report any side effects experienced. Data will be analyzed using repeated measures analysis of variance.

Progress: The IRB determined that the investigator would need to obtain an IND number in order to perform this study. The protocol was terminated because the investigator was unable to obtain this number before he was reassigned to a one year rotation to the health facility at Yakima Firing Range.

Detail Summary Sheet

Date: 30 Sep 89 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: Sep 89

Study Objective: To determine if frail, elderly surgery patients treated in the Geriatric Assessment and Rehabilitation Unit (GARU) at American Lake VA Medical Center (ALVAMC) will have better outcomes with improved cost-benefit and cost-effectiveness than those receiving the standard care at Madigan Army Medical Center (MAMC).

Technical Approach: The study population will consist of 160 elderly (>65) patients who have had surgery at MAMC with one or more medical or functional problems that will interfere with discharge. Persons with severe dementia or terminal phase disease will be excluded. The patients will be enrolled five days after surgery and randomly assigned to either remain at MAMC and receive the usual care or be transferred to ALVAMC and treated at the newly created GARU. The GARU utilizes an interdisciplinary team trained in geriatrics to provide specialty care to frail elderly patients at risk of institutionalization. Before randomization, study patients will be interviewed to obtain baseline data regarding demographic background, medical and social history, and physical and mental function, A relative or close friend will be interviewed to confirm this information. The patients will be reassessed to include patient and proxy interview at discharge and at 3 and 12 months after discharge. Standardized and validated instruments will be used to measure changes in the physical and mental functioning of both groups to include the Personal Self-Maintenance Scale, the Instrumental Activities of Daily Living Scale, the Kahn-Goldfarb Mental Status Questionnaire, and the Yesavage Depression Scale. Data will also be collected to determine the cost of the health care provided to both groups from their admission for surgery until one year after discharge. Data analysis will be performed primarily with descriptive statistics. Means and standard deviations will be calculated for 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: Twenty-three additional patients were entered in this study in FY 89 for a total of 28 entries. Preliminary analysis has gave no cause for terminating the project because of adverse outcomes among either the experimental or the control group.

**Funded by a joint VA/DoD grant.

Detail Summary Sheet

Date: 30 Sep 89 | Protocol No.: 88/41 | Status: On-going

Title: Urinary D-Lactate as an Indicator of Bowel Ischemia

Start Date: 18 Mar 88 | Est Completion Date: Aug 88
Department/Service: Surgery/General | Facility: MAMC
Principal Investigator: CPT Barbara L. Tylka, MC
Associate Investigators: COL Charles A. Andersen, MC
CPT Jon C. Bowersox, MC
Key Words: ischemia, bowel, urinary D-lactate levels
Accumulative MEDCASE Cost: -0- | Est Accumulative OMA Cost: $400.00 | Periodic Review: Sep 89

Study Objective: To determine whether urinary D-lactate levels can be used as non-invasive indicators of bowel ischemia in critically ill patients.

Technical Approach: Patients ≥18 years of age with hypovolemia, Ogilvie's syndrome, or a hemodynamically significant cardiac event requiring pressor support will be studied. Daily urine samples will be collected for analysis of urinary D-lactate until discharge from the ICU or CCU or death. The D-lactate concentration will be determined via the enzymatic conversion of D-lactate to pyruvate by the enzyme D-lactate dehydrogenase. To correct for variations in urine concentration, the urine creatinine will also be measured and results expressed as the D-lactate/creatinine ratio. If operative intervention is deemed necessary on clinical grounds, the bowel will be examined at surgery or, in the event of death, at autopsy for evidence of ischemia. The determination of ischemia will be made by the operating surgeon and any resected specimens will be examined by the pathologist. Subjects discharged from the ICU or CCU without operative intervention will be considered to not have experienced any clinically significant bowel ischemia and will form the control population. Based on previous studies, it is estimated that 20-30 patients, with a minimum of 10 with clinically proven bowel ischemia, will be required to determine a difference in urinary D-lactate levels between control and ischemic populations. Results will be analyzed by Student's paired t-test.

Progress: Three controls and three patients with bowel ischemia were entered in FY 88. No further patients have been entered due to logistical problems with the laboratory and other commitments of the principal investigator. Hopefully, these problems can be overcome and the project completed in FY 90.

Detail Summary Sheet

Date: 30 Sep 89 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: LTC John A. Vaccaro, MC ***

Associate Investigators: COL Donald H. Kull, MC
COL Stephen R. Plymate, MC
COL Victor J. Kiesling, MC**
MAJ Rahul N. Dewan, MC
MAJ Pushpa M. Patel, MC
CPT Christopher P. Evans, MC

Key Words: prostate cancer, hypogonadism, testicular shielding

Accumulative MEDCASE Cost: -0- | Est Accumulative OMA Cost: $1500.00 | Periodic Review: Sep 89

Study Objective: To assess a possible protective effect on testicular function of a lead testicular shield during the radiation treatment period.

Technical Approach: Twenty prostate cancer patients >18 years will be randomized into two groups to wear a lead gonadal shield during radiation therapy or to wear no shield during the therapy. Patients with prior radiation or hormonal therapy will be excluded. 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: Four additional subjects were enrolled in the study in FY 89 for a total of seven entries.

The protocol has been approved at WRAMC and will be conducted as a joint study in order to accrue sufficient subjects.

MAJ Rahul N. Dewan, Chief, Radiation Therapy, was added as an associate investigator.

***Replaced Dr. Kiesling as the PI, Sep 89
**Replaced Dr. Evans as the PI, Dec 87

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/68 Status: On-going

Title: Effects of Testosterone on PSA Levels in Normal Males

Start Date: 28 Jul 89 Est Completion Date: Jun 90
Dept/Svc: Surgery/Urology Facility: MAMC
Principal Investigator: LTC John A. Vaccaro, MC
Associate Investigators: COL William D. Belville, MC
COL Victor J. Kiesling, MC
COL Stephen R. Plymate, MC
Key Words: prostate specific antigen, FSH, LH, testosterone
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $450.00 Periodic Review: N/A

Study Objective: To determine if a rise in prostate specific antigen will occur after administration of parenteral testosterone in young males.

Technical Approach: Serum testosterone, FSH, and LH values have already been determine on the sera from 48 patients who were given testosterone injections for infertility. Specimens were drawn just before and one week after an IM testosterone injection and were appropriately frozen. These sera will be thawed and submitted for prostate specific antigen analysis and these values will be compared to serum testosterone levels before and after testosterone injection.

Progress: Twenty-one of the serum samples have been studied.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 85/65 Status: Completed

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 William J. Wilson, MC***
Associate Investigators: COL Thomas J. Parr, MC*
MAJ Jonathan P. Bacon, MC
MAJ Charles Morrow, MC**
Key Words: hip replacement, biologic ingrowth, non-cemented
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Sep 89

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) $\geq$ 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 can not 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-prosthesis contact, AP and lateral radiographs will be made to profile the undersurface of the femoral collar. These same radiographs will be made at the 1, 3, 6, 12, 18, and 24 month evaluations. Evaluation of the device will be based on the incidence and severity of complications. The results will be presented according to a number of baseline and operative factors (e.g., primary diagnosis, age, sex, bone quality, operative complications) to determine if there are particular subgroups of the target population at high risk for certain complications. The incidence of complications will be compared to published results on follow-up of patients with cemented and non-cemented prostheses to determine if the risk of complications is equivalent to the published results. The Harris Hip Score and the Charnley Modified D'Aubigne Scale will be used to evaluate the effectiveness of the device.

Progress: All 40 subjects entered at MAMC have completed the 24 month follow-up as stated in the protocol; 76% of these patients had a good to excellent rating on the Harris Hip Scale. The mean score at 24 months was 85 (out of a possible 100 points).

***MAJ Wilson replaced MAJ Morrow as the PI, Aug 88.
**MAJ Morrow replaced COL Parr as the PI, Aug 87.
*Original PI.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/19 Status: Terminated

Title: Correlation of the Vocal Fold Vibratory Pattern to the Post-Operative Surgical Wound in the Porcine Model

Start Date: 20 Jan 89 Est Completion Date: Apr 89

Dept/Svc: Surgery, Otolaryngology Facility: MAMC

Principal Investigator: Kenton L. Yockey, DAC**

Associate Investigators: LTC Don B. Blakeslee, MC
MAJ Philemon Anderson, MC

Key Words: scar formation, vibratory dysfunction, pig model

Accumulative MEDCASE Cost: $18,369.00 Est Accumulative OMA Cost: $10,676.00 Periodic Review: N/A

Study Objective: To demonstrate the histological correlation between scar formation and vibratory dysfunction and to describe the amount of scar formation in the three layers of the vocal fold following surgery.

Technical Approach: Twelve juvenile pigs will undergo suspension microlaryngoscopy to confirm normal anatomy and to surgically excise a portion of the right true vocal fold. A lesion will be created by removing a 4x6 mm segment in the midportion of the fold. The lesions will be distributed (three each) through the epithelial cover, through the transitional layer, into the muscular body, and in the mucosa (Reinke's space). The left vocal fold will be left intact to act as a control. Tissue removal from the right fold will be verified by Pathology. The vocal folds will be allowed to heal for 4-6 weeks. Each animal will then, after placement of an oral endotracheal tube, have a distal tracheotomy performed and an endotracheal tube passed to deliver the oxygen/-anesthetic gas mixture. A second tracheotomy will be performed through which a cuffed tracheotomy tube will be directed cranially with the tip before the glottis in order to pass air through the larynx to simulate phonation. A Hilger Nerve Stimulator will be used to excite the exposed internal branch of the superior laryngeal nerves and the recurrent laryngeal nerves, bilaterally. The nerve stimulation will adduct the fold and complete the simulation of phonation. A microphone will be placed 15 cm from the vocal folds in order to provide frequency control for the stroboscope which will be used to provide a record of the vibratory cycle in normal vocal folds. A 0° rigid laryngeal telescope will be positioned 2 cm from the vocal folds to record supraglottic images. Subglottic stroboscopy will be performed and stroboscopic images will be recorded with videotape. The healed right vocal fold of the pig will be excised for serial section.

Progress: This protocol was terminated after the reassignment of Dr. Blakeslee, who had applied for a USAMRDC grant. It was determined that he should have the protocol approved at his present duty station (FAMC) and performed there.

**Mr. Yockey replaced Dr. Blakeslee as the principal investigator, Mar 89.

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

F O R

P R O T O C O L S

PHYSICAL MEDICINE AND REHABILITATION SERVICE

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/35 Status: Completed

Title: Interexaminer Reliability Using a Knee Ligament Arthrometer on Chronic Anterior Cruciate Ligament (ACL) Deficient Knees

Start Date: 24 Feb 89 Est Completion Date: Apr 89

Dept/Svc: Physical Med & Rehab Svc Facility: MAMC

Principal Investigator: CPT William J. Tatu, SP

Associate Investigators: COL Bruce R. Wheeler, MC
MAJ Joseph R. Dettori, SP
MAJ Nelson E. Wiegman, MC
CPT Jerome J. Perra, MC

Key Words: knee, ligament, arthrometer, displacement

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

Study Objective: To determine interexaminer reliability with a knee ligament arthrometer.

Technical Approach: The portable knee ligament arthrometer, model KT-1000, MEDmetric, will be used. Four separate examiners will measure 20 patients in groups of four. Each examiner will take three measurements on each patient and record the average of the three measurements. The sequence for the four examiners will be done in a random fashion and rotated after the first group of patients. Measurement technique will follow the instructions given on a videotape that came with the KT-1000. Each examiner will preview the tape and practice the application of the device The examiners will consist of one staff orthopedist, two orthopedic residents, and one physical therapist. Examiners will position subjects supine with both legs placed on a thigh support. Knee angle will be 20-30 degrees of flexion. Foot and thigh supports will control rotation of the limb. Examiners will record A-P laxity to the nearest 0.5 mm for the 89 newton (20 lb) and maximal anterior displacement forces. Maximal displacement will also be documented. This number will be taken during a maximal anterior excursion force by the examiner. The highest number displayed by the indicator dial will be recorded. Examiners will perform measurements on the unaffected limb first, consistent with normal clinical practice.

Progress: Statistical analysis using interclass correlation coefficients revealed relatively low interrater reliability coefficients for normal and ACL deficient knees at all displacement values. A test was used to compare displacement measurements. There were significant differences between the involved and uninvolved knees at all displacement values. The authors conclude that the knee arthrometer is very reliable at recognizing chronic ACL deficient knees. However, clinicians will experience difficulty in reproducing results obtained from other practitioners.

The results of this study were presented in a poster presentation at the Mary L. Hamrick AMSC Research Course, Jul/Aug 89.

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

F O R

P R O T C O L S

PREVENTIVE MEDICINE SERVICE

Detail Summary Sheet

Date: 30 Sep 89	Protocol No.: 88/80	Status Completed

Title: Health Promotion and Disease Prevention Needs Assessment of the Army Retirees in the Pacific Northwest

Start Date: 16 Sep 88	Est Completion Date: Dec 88
Service: Preventive Medicine	Facility: MAMC
Principal Investigator: CPT Cynthia A. Brandt, MC	
Associate Investigators: LTC K. Mills McNeill, MC CPT Margot R. Krauss, MC	
Key Words: retirees, disease prevention, health promotion	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $520.00	Periodic Review Sep 89

Study Objective: To identify and quantify the health promotion and disease prevention needs of the Army retiree personnel as measured by the prevalence of health risk behaviors as well as preventive behaviors.

Technical Approach: This is a descriptive cross-sectional study utilizing a self-administered mailed questionnaire. Questionnaires will be mailed to a randomly selected sample of 400 Army retirees residing within the "catchment area" defined as a 40 mile radius of MAMC. An equivalent number of subjects will be selected from zip codes not in this area. The age range is expected to be from approximately 40 to 85 years of age. Patients who would require surrogate respondents will be excluded.

The questionnaire will contain questions to elicit demographic data as well as data concerning hospital usage, general health of the subject, diet and alcohol use, daily activities, and safety and preventive measures such as seat belt use and immunizations

Descriptive statistics will include prevalence of behavioral risk factors of the total sample with 95% confidence intervals, comparison will be made to general population data available, and comparison of the "catchment area" group with the other geographical groups of retirees, to identify differences in the core users of Madigan as regards behavioral risk factors. Secondary analysis may include looking for evidence of a cohort effect, a relationship of the year entered service and behavioral risk factors, or length of service and behavioral risk factors.

Progress: Questionnaires were sent to 600 Army retirees, with an 84% (504 retirees) response rate. Overall, the behavioral risk factors in this population suggest the need for health promotion targeted at alcohol use and misuse and smoking cessation for enlisted retirees in conjunction with increased emphasis on these behaviors in the current health promotion programs for the active duty soldiers.

A thesis has been written using this data and the paper is to be presented at the Health Promotion Meeting at USUHS in Oct 89.

Detail Summary Sheet

Date: 30 Sep 89 | Protocol No.: 86/21 | Status: Completed

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: CPT Margot R. Krauss, MC**

Associate Investigators: COL Frederick J. Erdtmann, MC
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: May 89

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. The patient or the next-of-kin will be sent a letter/fact sheet explaining the study and requesting participation, and then 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 of 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 the military. Controls will be matched for age and vital status. Completed interviews will be sent to the CDC to acquire information from military records. Data analysis will be done at CDC.

Progress: Approximately 250 patients were studied. An increased risk of non-Hodgkin's lymphoma was found among Vietnam veterans relative to men who did not serve in Vietnam, but no increased risk was found for the other five cancers. Of particular interest, is the finding of no increased risk for sarcoma, a group of cancers that has been of great concern among Vietnam veterans. There was no indication that the pattern of distribution of the cancers found was related to the pattern of Agent Orange use in Vietnam. A manuscript is being written.

**Replaced COL Erdtmann as the PI, Aug 88.

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

F O R

P R O T O C O L S

1ST SPECIAL FORCES GROUP

FT LEWIS, WA

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/29 Status: Terminated

Title: Special Operations Medical NCO Sustainment Training

Start Date: 19 Feb 88 Est Completion Date: Feb 91
Unit: 1st Special Forces Group Facility: MAMC
Principal Investigator: CPT Dustin Frazier, MC
Associate Investigators: CPT Jeffrey S. Macintire, VC
Key Words: venous cutdown, needle thoracentesis tube thoracostomy, pericardiocentesis, cricothyroidotomy, peritoneal lavage

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: May 89

Study Objective: To provide annual Advanced Trauma Life Support-type surgical training for 18D Special Forces medical sergeants as required by Special Operations Command Regulation 350-9.

Technical Approach: Having received formal training at the 18D MOS qualification course, medical NCO's will be afforded the opportunity to conduct sustainment training on no less than an annual basis in accordance with SOCOM Reg 350-9.

Combat Trauma Management Lab The purpose of this lab is to refresh skills in aseptic emergency surgical techniques. Personnel will be divided into groups of 4 with each group under the supervision of an instructor. Each soldier will perform each of the following surgical exercises:

venous cutdown	needle thoracentesis
tube thoracostomy	pericardiocentesis
cricothyroidotomy	peritoneal lavage

These procedures will be performed in the manner described in the Academy of Health Sciences Advanced Trauma Life Support Program.

One adult goat will be used per group. Four people will be in each group. All procedures will be done under general anesthesia. All animals will be euthanized at the end of the training procedure by lethal injection of T-61 veterinary euthanasia solution.

Progress: The purpose of this protocol is to provide an opportunity for Special Operations medics to practice ATLS skills in the event they are unable to attend the annual instruction provided locally by the Academy of Health Sciences. To date, the protocol has not been utilized.

Upon review of a policy letter from SOCOM, it was determined that this protocol was in contradiction to SOCOM policy and the protocol 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

CHILDRENS CANCER STUDY GROUP PROTOCOLS

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 86/65 Status: Completed

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: Edythe A. Albano, M.D.***

Associate Investigators: LTC Allen R. Potter, MC*
MAJ Kip R. Hartman, MC**

Key Words: leukemia, lymphoblastic, intermediate prognosis

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 88

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 maintenance 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.

*Original PI
**Replaced Dr. Potter as PI, Dec 86
***Replaced Dr. Hartman as PI, Aug 88

Detail Summary Sheet

Date: 30 Sep 89	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	
Department: Pediatrics		Facility: MAMC
Principal Investigator: Edythe A. Albano, M.D.**		
Associate Investigator: MAJ Kip R. Hartman, MC*		
Key Words: ALL, high risk, chemotherapy		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 88

Study Objective: To improve the treatment results for children with acute lymphoblastic leukemia (ALL) who possess poor prognostic features; to prevent the development of central nervous system (CNS) leukemia in these patients using a treatment regimen which includes both systemic high dose chemotherapy and intrathecal chemotherapy, but avoids cranial radiation; and to determine whether there is a difference in the outcome of poor prognosis patients with and without lymphomatous features treated on an identical treatment regimen.

Technical Approach: Previously untreated high risk patients with acute lymphoblastic leukemia will be treated. The induction phase of therapy will be 28 days in length and consist of treatment with vincristine, L-asparaginase, prednisone, daunomycin, and allopurinol. CNS therapy will consist of intrathecal cytosine arabinoside, methotrexate, and a high dose, protracted, systemic methotrexate infusion. Consolidation therapy will begin 7-10 days following completion of induction therapy and will last 35 days and will consist of vincristine, prednisone, and 6-mercaptopurine. CNS prophylaxis during consolidation will include both I.V. high dose methotrexate and intrathecal Ara-C. A 12-week intensification phase will begin 7-10 days after the last day of consolidation and will consist of cyclophosphamide, L-asparaginase, vincristine, daunomycin, and prednisone. CNS treatment will include periodic intrathecal methotrexate and cytosine arabinoside as well as systemic high dose Ara-C. Maintenance therapy will begin 7-10 days after the last day of consolidation and will consist of prednisone, vincristine, 6-mercaptopurine, L-asparaginase, and daunomycin. CNS treatment will include periodic intrathecal chemotherapy with methotrexate and Ara-C as well as systemic high dose methotrexate and high dose Ara-C. The chemotherapy will be given over a 24 week cycle, which will be repeated 4 times, after which all chemotherapy ceases. The first year off study, patients will have a physical exam and CBC every month and bone marrow and lumbar puncture every 4 months. The second year, they will have physical exam and CBC every 3 months and bone marrow and lumbar puncture every 6 months. The third and subsequent years off study, patients will receive routine follow-up per institutional guidelines.

Progress: No patients entered in FY 89. One patient was entered in FY 87 and one in FY 88. Both are in the follow-up stage. The study is closed to patient entry.

**Replaced Dr. Hartman as PI, Aug 88
*Original PI

Detail Summary Sheet

Date: 30 Sep 89 | Protocol No.: 88/63 | Status: On-going

Title: CCG 144: Treatment of Acute Lymphoblastic Leukemia in Average Risk Patients

Start Date: 15 Jul 88 | Est Completion Date: Jul 93

Department: Pediatrics | Facility: MAMC

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

Associate Investigator: MAJ Kip R. Hartman, MC*

Key Words: chemotherapy, protracted intravenous, intrathecal

Accumulative MEDCASE Cost: -0- | Est Accumulative OMA Cost: -0- | Periodic Review: Nov 88

Study Objective: To compare the efficacy of high dose, protracted intravenous methotrexate infusions versus intrathecal methotrexate as CNS preventive therapy for children with average risk lymphoblastic leukemia and to determine if there is a difference in the hematologic remission duration achieved using these different treatment approaches.

Technical Approach: Newly diagnosed average risk patients will be randomly allocated to receive one of two forms of CNS preventive therapy; either high dose protracted systemic methotrexate infusions or intrathecal methotrexate administered periodically during induction, consolidation, and maintenance. Systemic therapy will be identical for all patients. To insure similarity in the two treatment groups, patient randomization will be stratified to the prognostically significant variables of age and initial white blood cell count. Approximately 80 randomized patients will be required. It is anticipated that the required number of patients will be accrued within a 12-18 month period.

The induction phase for both arms will 28 days in length and will include chemotherapy in both groups with vincristine, l-asparaginase, prednisone, daunomycin, and allopurinol as well as the methotrexate and citrovorum factor rescue.

Consolidation (35 days in length) will begin 10 days after induction therapy is completed and will include vincristine, prednisone, and 6-mercaptopurine in addition to the methotrexate.

Maintenance therapy will begin 10 days after the consolidation phase is completed and will be divided into 6 cycles of therapy, each 22 weeks in length. In addition to the methotrexate, chemotherapy will include prednisone, vincristine, 6-mercaptopurine, and l-asparaginase, daunomycin given on a staggered schedule.

Patients who have an M_3 bone marrow after completing as least 28 days of therapy or who manifest progressive disease will be removed from the study.

Progress: No patients entered in FY 89. One patient entered in FY 88 is in the follow-up stage. The study is closed to patient entry.

**Replaced Dr. Hartman as PI, Aug 88
*Original PI

Detail Summary Sheet

Date: 30 Sep 89 | Protocol No.: 88/14 | Status: On-going

Title: CCG 213: Treatment of Newly Diagnosed Acute Non-lymphoblastic Leukemia for Children Greater than One Month but Less than 21 Years of Age

Start Date: 11 Dec 87 | Est Completion Date: Jan 94

Department: Pediatrics | Facility: MAMC

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

Associate Investigator: MAJ Kip R. Hartman, MC*

Key Words: ANLL, chemotherapy, sub-protocol/AMOL, chemotherapy

Accumulative MEDCASE Cost: -0- | Est Accumulative OMA Cost: -0- | Periodic Review: Nov 88

Study Objective: To improve the duration of complete remission in children with acute non-lymphocytic leukemia (ANLL).

Technical Approach: Induction will consist of two or three 14-day cycles of Denver Therapy (VP 16-213, daunomycin, Ara-C, 6-thioguanine, and dexamethasone) followed by two or three 14-day cycles of DNM/Ara-C (daunomycin and Ara-C) or given in the reverse order depending on randomization. If bone marrow is M1, ANC $\geq$750, and platelet count $\geq$75,000 after two cycles, the patient will start the alternate re imen. Patients with M1 marrow after the first regimen of induction or M1 or M2A marrow at any time after completion of induction will have a bone marrow transplant if a suitable donor is available and the patient/family wishes to pursue this course of action. At the end of induction, patients with remission and no donor will be entered in a consolidation phase which will consist of 2 cycles of high-dose Ara-C and L-asparaginase, followed by two cycles of 6thioguanine, vincristine, ara-C 5-azacytidine, and cyclophosphamide, and then one cycle of VP 16-213, daunomycin, Ara-C, dexamethasone, and 6-thioguanine. Those with remission and no donor will then be randomized to no further therapy or eighteen 28-day cycles of 6-thioguanine, vincristine, Ara-C, 5-azacytidine, and cyclophosphamide. Those who have failed therapy will be taken off study. Intrathecal Ara-C prophylaxis will be given on day 0 of each cycle except for the regimen using high-dose Ara-C.

Children $\leq$2 years of age with acute monoblastic/monocytic leukemia will also be treated on this protocol using a 4-week induction phase of chemotherapy, followed by a four week consolidation phase of chemotherapy plus radiation therapy for CNS prophylaxis or involvement. The maintenance phase will consist of four 3-month chemotherapy courses plus radiation therapy for CNS prophylaxis or involvement. Drugs to be used are VM-26, VP-16, cyclophosphamide, intrathecal Ara-C, vincristine, prednisone, daunomycin, and 6-thioguanine. Patients will be taken off study if they are not in complete remission by Weck 8 of the study.

Progress: One patient has entered this study. The patient has completed therapy and is being followed.

**Replaced Dr. Hartman as PI, Aug 88
*Original PI

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/09 Status: On-going

Title: CCG CCG-321P4: "6 in 1" Chemotherapy for Children with Newly Diagnosed Advanced Stage Neuroblastoma

Start Date: 18 Nov 88 Est Completion Date: Indefinite

Department: Pediatrics Facility: MAMC

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

Associate Investigators: None

Key Words: vincristine, cisplatin, cyclophosphamide, Adriamycin imidazole carboxamide, VM-26, efficacy, maximum dose

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

Study Objective: To explore the novel "6 in 1" regimen in patients between 1 and 16 years of age with previously untreated advanced stage neuroblastoma. To assess the toxicity of this regimen and determine a maximum acceptable regimen by stepwise modification in cohorts of 5-10 patients.

Technical Approach: Patients will receive cycles of vincristine, cisplatin, cyclophosphamide, imidazole carboxamide (DTIC), Adriamycin, and VM-26, administered over 36 hours every 3-4 weeks for 8 cycles or until tumor progression. Patients will be evaluated for response following cycles 4 and 8 (weeks 12 and 24). Patients for whom surgical resection of residual primary tumor seems feasible will undergo such surgery after 4 or 8 cycles. Upon completion of chemotherapy, sites of original bulky tumor will be irradiated to 2000 rads or, at institutional option, patients may undergo ablative therapy with bone marrow rescue. Patients with progressive disease at any point after initiation of therapy will proceed to alternate therapy.

The initial cohort will receive a schedule that is more intense than that received by the ad hoc patients. The primary outcome index will be the mortality rate occurring in the first four cycles of treatment (approximately 3 months from start of treatment). If two or more deaths occur, then evaluation of the treatment schedule will be stopped with a conclusion of unacceptable mortality. Pending the outcome of this initial cohort and patient accrual, a second cohort of 10 patients will receive a schedule that will be an intensification or a reduction of this initial schedule. Efficacy will be assessed by comparison to historical experience of recent CCSG studies in this group.

The intended total duration of the study is two years of accrual and 6 to 12 months of follow-up to evaluate the outcome results.

Progress: No patients entered in this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 86/31 Status: Completed

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: Edythe A. Albano, M.D.***

Associate Investigators: LTC Allen R. Potter, MC*
MAJ Kip R. Hartman, MC**

Key Words: neuroblastoma, Stages III & IV, chemotherapy, cyclic

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jan 89

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: Two patients were entered in this study. Both completed therapy and are no longer being followed.

*Original PI
**Replaced Dr. Potter as PI, Dec 86
***Replaced Dr. Hartman as PI, Aug 88

Detail Summary Sheet

Date: 30 Sep 89 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: Edythe A. Albano, M.D. (Aug 88)
Associate Investigator: MAJ Kip R. Hartman, MC (Original PI)
Key Words: Wilms' tumor, chemotherapy, favorable histology, clear cell carcinoma, anaplastic, stages I-IV
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Sep 89

Study Objective: To compare the relapse-free and overall survival percentages of patients with: (1) Stages 1 and 2 favorable histology (FH) and Stage 1 anaplastic Wilms' tumor (Ana), using conventional versus pulse intensive (P/I) chemotherapy with vincristine and actinomycin D; (2) Stages 3 and 4 FH, and stages 1-4 clear cell sarcoma of the kidney using conventional versus P/I vincristine, actinomycin D, and Adriamycin plus radiation therapy; (3) Stages 2-4 Ana treated with vincristine, actinomycin D, and Adriamycin versus the same 3 drugs plus cyclophosphamide, and radiation therapy; and (4) Stages 2-4 FH and Stage 1-4 clear cell sarcoma of the kidney treated for 6 versus 14 months after nephrectomy.

Technical Approach: All patients will be ≤16 years of age, have had no prior chemo- or radiation therapy, will have undergone nephrectomy, and will meet other criteria as stated in the protocol.

Patients will be randomized as follows:

Stage I/FH & Stage I Ana	A + V (24 wks) or P/I A + V (18 wks)
Stage II/FH	A + V (22 vs 65 wks) or P/I A + V (60 wks)
Stages III & IV FH & clear cell (I-IV)	A + V + D (26 vs 65 wks) plus RT or P/I A + V + D (24 vs 54 wks) plus RT
Stages II-IV Ana	A + V + D (65 wks) plus RT or A + V + D + C (65 wks) plus RT

A = actinomycin D V = vincristine
D = doxorubicin (Adriamycin) C = cyclophosphamide
RT = radiation therapy

Progress: A revised version of this protocol was approved in Sep 89. The main changes were to define specific parameters to be studied as opposed to a general information gathering protocol, a reduction in the length of treatment, and the addition of an arm to treat Stages 2-4 anaplastic tumor. Changes were made based on information gained in studies by other investigators as well as the information gained from this study to date. One patient has been entered (Aug 89) in the study at MAMC.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/08 Status: On-going

Title: CCG 503: A Randomized Trial of COMP - Cyclophosphamide (NSC 26271), Vincristine (NSC 67574), Prednisone (NSC 10023), and Methotrexate (NSC 740) versus COMP & DAUNO (Cyclophosphamide, Vincristine, Methotrexate, Prednisone, Daunomycin (NSC 82151)) for Treatment of Non-localized, Nonlymphoblastic, Non-Hodgkin's Lymphoma Combined With a Study of Disease Characterization, Phase III, Groupwide

Start Date: 21 Oct 88 Est Completion Date: Indefinite

Department: Pediatrics Facility: MAMC

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

Associate Investigators: None

Key Words: lymphoma, COMP vs COMP + daunomycin, toxicity

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

Study Objective: To improve the prognosis of children with disseminated nonlymphoblastic lymphomas by adding daunorubicin to COMP; to compare toxicity of this regimen with COMP alone; to examine the relationships between response to therapy, anatomic presentation, and histopathologic group; to improve the outcome for those patients with CNS disease at diagnosis or at risk for CNS relapse because of disease adjacent to the meninges; and to evaluate the relationship between cell surface markers, disease characteristics, and clinical course.

Technical Approach: Following initial evaluation, those patients without CNS or marrow involvement will be randomized to either COMP/ (cyclophosphamide, methotrexate, vincristine, prednisone) alone or to COMP plus daunorubicin. Patients with bone marrow or CNS involvement will be non-randomly assigned to COMP+DAUNO. The duration of chemotherapy for both regimens will be 18 months. Therapy will continue past 18 months if a minimum of 15 maintenance cycles has not been completed and will continue until the completion of 15 maintenance cycles. Radiation treatment will be given only to those patients with nervous system involvement, testicular involvement, bone involvement, or disease adjacent to the meninges.

Progress: One patient was entered in this study in FY 89 and died of the disease.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 87/76 Status: On-going

Title: CCG-521: Treatment of Newly Diagnosed Advanced Hodgkin's 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: Edythe A. Albano, M.D.**

Associate Investigator: MAJ Kip R. Hartman, MC*

Key Words: Hodgkin, newly diagnosed, chemotherapy, radiotherapy

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Dec 88

Study Objective: To improve the proportion of patients with advanced Hodgkin's Disease who are cured; to compare the relapse free survival and survival in advanced Hodgkin's disease in children utilizing an eight-drug (twelve cycle MOPP/ABVD) combination chemotherapy regimen versus a four drug (six cycle ABVD) chemotherapy regimen followed by low dose (2100 cGy rad) regional radiation therapy; and to compare the concurrent and long term toxicity of the two regimens.

Technical Approach: Patients <21 years with newly diagnosed Hodgkin's disease, pathologically staged as 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.

**Replaced Dr. Hartman as PI, Aug 88
*Original PI

Detail Summary Sheet

Date: 30 Sep 89 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

Department: Pediatrics Facility: MAMC

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

Associate Investigators: LTC Allen R. Potter, MC*
MAJ Kip R. Hartman, MC**

Key Words: rhabdomyosarcoma, chemotherapy, radiotherapy

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Dec 88

Study Objective: To compare various forms of treatment of rhabdomyosarcoma and to determine: if various combinations of vincristine, dactinomycin, adriamycin, cyclophosphamide, cis-platin, and VP-16, with or without radiation therapy, will improve survival rates in both favorable and unfavorable histology tumors that have been completely or grossly, but incompletely, removed; if patients with localized orbit and head tumors will do well with vincristine and dactinomycin therapy limited to one year; patients with localized prostate, bladder, vagina, or uterus tumors can be treated successfully with cis-platin, adriamycin, vincristine, cyclophosphamide, and dactinomycin to avoid radical surgery and preserve the involved organ. Other objectives are to use second and third operations to see if the tumor is gone and, if not, to see if any remaining tumor can be surgically removed; to add other combinations of drugs when only partial response is obtained from the initial treatment; to use XRT and IT drugs to treat tumors extending or at risk of extension into the brain or spinal cord; and to do various studies of drug sensitivity and tumor typing on the removed tumor tissue to find new drugs for treatment and new ways of diagnosing cancer.

Technical Approach: Patients will be categorized as: Group I: localized disease, completely resected; Group II: total gross resection with evidence of regional spread; Group III: incomplete resection with gross residual disease; and group IV: distant metastatic disease present at onset. Patients will then be subcategorized into groups according to favorable or unfavorable histology and location of disease and treated with one of 8 regimens containing various combinations of actinomycin-D, adriamycin, cisplatinum, cyclophosphamide, cytosine arabinoside, DTIC, hydrocortisone, leucovorin, vincristine sulfate, methotrexate, and VP16, with or without the addition of radiation therapy and surgery.

Progress: No patients have been entered at MAMC.

*Original PI
**Replaced Dr. Potter as PI, Dec 86
***Replaced Dr. Hartman as PI, Aug 88

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/13 Status: On-going

Title: CCG 921: Unfavorable Medulloblastoma and Intracranial Primitive Neuroectodermal Tumors (PNET), Malignant Ependymoma, Ependymoblastoma, Pineoblastoma, and Central Neuroblastoma

Start Date: 11 Dec 87 Est Completion Date: Jan 94

Department: Pediatrics Facility: MAMC

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

Associate Investigator: MAJ Kip R. Hartman, MC*

Key Words: blastoma, intracranial primitive neuroectodermal tumors, children, chemotherapy, radiotherapy

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Oct 88

Study Objective: To define a more effective treatment for high risk medulloblastoma and other primitive neuroectodermal tumors of childhood.

Technical Approach: Patients <21 years old will have resection, intraoperative staging, and histopathologic assessment. If extent of disease evaluation demonstrates residual tumor >1.0x1.5 cm^2 in Stage T_{1-2} tumors or Stage T_{3-4} tumors and/or neuraxis or metastatic extension of tumor (M_{1-4}), patients will be randomized to receive either Control Regimen A or Experimental Regimen B.

Regimen A: Standard radiation therapy plus vincristine once a week for 8 weeks followed by a 28-day rest period and then vincristine, prednisone, and CCNU maintenance chemotherapy given every 42 days for eight courses.

Regimen B: 8-drugs-in-1-day chemotherapy (cisplatin, procarbazine, CCNU, vincristine, cyclophosphamide, methylprednisolone, hydroxyurea, and cytosine arabinoside) for 2 courses on days 0 and 14. A rest period of 14 days will be followed by an extent-of-disease evaluation, then standard craniospinal radiation, and then 8-drugs in-1-day maintenance every 42 days for up to 8 courses. Patients will be followed for toxicity, time, sites of relapse, and survival for five years.

The end-point of this study will be time to disease recurrence or progression, as defined by both neuroradiological and clinical assessments, and overall survival.

Progress: No patients have been entered in this study at MAMC.

**Replaced Dr. Hartman as PI, Aug 88
*Original PI

Detail Summary Sheet

Date: 30 Sep 89 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: Edythe A. Albano, M.D.**

Associate Investigator: MAJ Kip R. Hartman, MC*

Associate Investigators: None

Key Words: leukemia, marrow relapse, idarubicin

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Dec 88

Study Objective: To refine the determination of the maximal tolerated dose of intravenous idarubicin and to determine the pharmacokinetics of intravenous idarubicin and idarubicinol in children with acute leukemia when treated with two schedules, weekly x 3 and daily x 3; and to determine the effects of scheduling of idarubicin on remission induction rates for children with acute lymphoblastic leukemia and acute non-lymphoblastic leukemia.

Technical Approach: Children who have had a second or subsequent marrow relapse will be randomized to a weekly x 3 schedule or a daily x 3 schedule. Since the maximal tolerated dose (MTD) has been reported as both 40 mg/m^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 treatment. Once the MTD for each schedule is determined, the dose will be used in six additional patients to confirm acceptable toxicity. If acceptable toxicity is confirmed, additional patients will be entered at this dose level to assess remission induction rates. Remission induction rates will be determined at 21 days from initiation of therapy. If remission is not obtained following the three doses of idarubicin, the leukemia has not responded, and toxicity from the first course was acceptable, patients will be treated with a second course of the drug, using the same dose and schedule. Remission status will again be evaluated 21 days from the start of the second course of treatment. For patients attaining a complete remission, maintenance therapy will be at the discretion of the investigator.

Progress: No patients have been entered at MAMC.

**Replaced Dr. Hartman as PI, Aug 88
*Original PI

Detail Summary Sheet

Date: 30 Sep 89 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: Edythe A. Albano, M.D.**

Associate Investigator: MAJ Kip R. Hartman, MC*

Key Words: IV 5-FU, oral high dose leucovorin, combination

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $3000.00 Periodic Review: Dec 88

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.

**Replaced Dr. Hartman as PI, Aug 88
*Original PI

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

F O R

P R O T O C O L S

FRED HUTCHINSON CANCER RESEARCH CENTER GROUP PROTOCOLS

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 83/47 Status: Completed

Title: FHCRC #152: Combined Modality Treatment for Non-Hodgkin's Lymphomas of Intermediate and High-Grade Malignancy

Start Date: 18 Feb 83 Est Completion Date: Jan 85

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

COL Irwin B. Dabe, MC
COL Friedrich H. Stutz, MC
LTC James E. Congdon, MC
MAJ Thomas M. Baker, MC
MAJ Alfred H. Chan, 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: Sep 89

Study Objective: To compare in patients with extensive (stage III and IV), aggressive (intermediate and high-grade malignancy) non-Hodgkin's lymphoma (NHL) the response rate, duration, and survival after treatment with: (1) combined cyclophosphamide, adriamycin, vincristine, and prednisone (CHOP) chemotherapy combined with total body irradiation (TBI), or (2) CHOP chemotherapy combined with upper and lower hemibody irradiation (HBI); and to determine the response rate, duration and survival of patients with limited (stage I, II, and certain stage III and IV), aggressive NHL treated with CHOP chemotherapy with local radiotherapy.

Technical Approach: After appropriate tests to determine the extent of the lymphomas, patients will receive 4 cycles of multi-agent chemotherapy to include Cytoxan, adriamycin, Oncovin and prednisone. At the end of 4 cycles of chemotherapy, given 4 wks apart, patients will be restaged to determine the extent of remaining disease. If there is at least a 50% reduction in the observed disease, the patients will proceed to Phase II consisting of radiation therapy. All patients will receive prednisone every other day by mouth and vincristine IV every other week. Those patients with disease involving <50% of the body will receive limited radiation therapy to sites of known lymphoma involvement.

Those patients with extensive disease will be randomized to receive either low dose total body radiation or low dose sequential hemibody radiation therapy. At the completion of Phase II, all patients will receive 4 more cycles of CHOP with the intervals lengthened to 8 weeks. At the end of Phase III, if there is no evidence of remaining disease, patients will be taken off therapy and observed.

Progress: Six patients were entered in this study at MAMC (none in FY 89). All patients have passed the three-year follow-up period and the study has been closed at MAMC.

Group-wide results show a complete remission of 75% in limited disease and 56% in extensive disease. Survival to three years is 50% in the HBI arm (mostly Stage IVB patients).

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

F O R

P R O T O C O L S

GYNECOLOGY ONCOLOGY GROUP PROTOCOLS

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 82/73 Status: On-going

Title: GOG #26A: Master Protocol for Phase II Drug Studies in Treatment of Advanced, Recurrent Pelvic Malignancies

Start Date: 20 Nov 81 Est Completion Date: Indefinite

Department: OB/GYN Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

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

Key Words: advanced malignancy, refractory to prior therapy

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Sep 89

Study Objective: To implement a master protocol to screen for activity and efficacy of new agents or combinations in patients with advanced or recurrent pelvic malignancies, resistant to higher priority methods of treatment.

Technical Approach: A "rejection" type design will be used with a fixed sample size of 25 evaluable patients/disease site/drug or combination studied. The design allows replacement of ineffective regimens by newer agents or combinations. Sections relating to specific agents will be sequentially incorporated into this protocol as these agents are studied. Continuing review will be done for each separate protocol.

To be eligible, patients must have histologically confirmed, advanced, recurrent, persistent, metastatic, or local gynecologic cancer with documented disease progression; lesions that are measurable and can be followed for tumor response; abdominal, pelvic, or other masses which can be defined in at least two dimensions by palpation or by x-ray; a GOG performance Grade 0, 1, or 2 (Karnofsky scale 30-100); free of clinically significant infection; off previous chemotherapy for at least 3 weeks; recovered from effects of recent surgery, radiotherapy, or chemotherapy; passed the nadir blood counts from previous therapy and a granulocyte count $\geq 1500/mm^3$, platelet count $\geq 100,000/mm^3$, BUN ≤ 25 mg%, creatinine ≤ 1.5 mg%, bilirubin ≤ 1.1 mg, SGOT ≤ 5 IU. Patients receiving myelosuppressive agents will have adequate bone marrow function as described above. Exception to the general requirement for normal liver function will be secondary to documented metastatic tumor to the liver or as noted in the section dealing with that particular agent. Patients with all primary disease sites of gynecologic malignancies are eligible. Each disease site will be accumulated as a separate study sample. For a particular drug study, the allowable disease site(s) may be further qualified. Ascites and pleural effusion alone are not considered measurable for purposes of the study. A steady rise in the titers of alpha-fetoprotein and beta-HCG will be taken as evidence of disease progression in germ cell tumors of the ovary.

Progress: No new patients were entered in this group of protocols in FY 89. Protocols 26 D, 26 O, and 26 FF were closed to patient accrual in FY 89 due to sufficient numbers of patients.

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Gordon O. Downey, MC

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

Key Words: advanced malignancy, refractory to prior therapy

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Nov 88

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 in FY 89. Three patients were entered in previous years.

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Gordon O. Downey, MC

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

Key Words: pelvic malignancies, advanced, resistant

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Nov 88

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: No patients were entered in this study at MAMC in FY 89. 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 89 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: LTC Gordon O. Downey, MC

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

Key Words: pelvic malignancies, advanced, DHAD

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Nov 88

Study Objective: To determine the efficacy of DHAD in patients whose advanced malignancies have been resistant to higher priority methods of treatment.

Technical Approach: All patients with measurable gynecological cancer who have failed higher prior therapies will be offered DHAD as a Phase II drug to determine its efficacy. The drug will be given as 12 mg/M^2 I.V. every three weeks. Patients will continue to receive the agent until progression or adverse effects prohibit further therapy.

This protocol was closed to uterus/MMT patient entry in Aug 87.

Progress: No new patients were entered in FY 89 at MAMC. In previous years three patients had been entered. All died of their disease.

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Gordon O. Downey, MC

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

Key Words: malignancies, advanced, AZQ

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 88

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 89. 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 89 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: LTC Gordon O. Downey, MC

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

Key Words: pelvic malignancies, advanced, aminothiadiazole

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review Nov 88

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 89. One patient was entered in FY 85 and died from squamous cell carcinoma of the cervix.

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Gordon O. Downey, MC

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

Key Words: pelvic malignancies, advanced, Teniposide

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Dec 88

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 toxicities to the drug and the drug dosages will be modified according to the severity of the toxicities. Response to the drug will be followed. Progression of disease and/or excessive toxicities will terminate the study for the patient.

Progress: No new patients entered in FY 89. Two patients were entered in previous years and died of the disease.

Detail Summary Sheet

Date: 30 Sep 89 | 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: LTC Gordon O. Downey, MC

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

Key Words: ifosfamide, mesna, advanced pelvic malignancies

Accumulative MEDCASE Cost: -0- | Est Accumulative OMA Cost: -0- | Periodic Review: Dec 88

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 89 | 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: LTC Gordon O. Downey, MC

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

Key Words: malignancies, pelvic, advanced, echinomycin, Phase II

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Dec 88

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 89 Protocol No.: 88/58 Status: On-going

Title: GOG 26X: A Phase II Trial of Gallium Nitrate (NSC #15200) in Patients with Advanced Pelvic Malignancies

Start Date: 20 May 88 Est Completion Date: Indefinite

Department: OB/GYN Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

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

Key Words: pelvic malignancy, advanced, gallium nitrate

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Dec 88

Study Objective: To screen for activity of new agents or drug combinations in patients with advanced malignancies. Its intent is to determine the efficacy of chemotherapeutic agents in patients whose advanced malignancies have been resistant to high priority methods of treatment.

Technical Approach: Gallium nitrate will be given as a slow intravenous infusion over 30-60 minutes at a dose of 750 mg/m^2. The dose will be repeated once every three weeks.

Patients will be hydrated with at least three liters of fluid the day prior to treatment. An additional 500 cc normal saline will be infused in the two hours prior to administration of gallium nitrate. Hydration of three liters of fluid orally or intravenously will be continued during the first 24 hours after therapy.

Patients receiving concurrent radiotherapy are ineligible for this study.

An adequate trial will be defined as receiving one course of therapy and living three weeks. Each patient will continue receiving gallium nitrate until disease progression or death or until adverse effects prohibit further therapy.

Progress: No patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 89 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: 20 Mar 87 Est Completion Date: Indefinite

Department: OB/GYN Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

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

Key Words: pelvic malignancy, advanced, vinblastine

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Dec 88

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 89 Protocol No.: 88/59 Status: On-going

Title: GOG 26Z: A Phase II Trial of Leuprolide Acetate (IND #29308) in Patients with Advanced Epithelial Ovarian Carcinoma

Start Date: 20 May 88 Est Completion Date: Indefinite

Department: OB/GYN Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

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

Key Words: carcinoma, ovarian, epithelial, leuprolide acetate

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $7200.00	Periodic Review: Dec 88

Study Objective: To screen for activity of new agents or drug combinations in patients with advanced malignancies. Its intent is to determine the efficacy of chemotherapeutic agents in patients whose advanced malignancies have been resistant to high priority methods of treatment.

Technical Approach: Patients must have biopsy-proven epithelial ovarian cancer according to the criteria of Scully (Human Pathology 1:73, 1970). Patients with tumors of low malignant potential are not eligible. Patients must have a life expectancy of at least two months.

Leuprolide acetate will be administered at a dosage of 1 mg as a daily subcutaneous injection until disease progression.

A minimum trial will be defined as receiving a minimum of eight weeks of therapy. Patients who develop bowel obstruction, toxic side effects, or refuse therapy in these first eight weeks will not be considered fully evaluable for response. Patients will receive therapy until progression or until adverse effects prohibit further therapy.

Progress: No entries in FY 89. One patient entered at MAMC in FY 88 and died of disease.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/67 Status: On-going

Title: GOG 26-DD: A Phase II Trial of Amonafide (NSC #308847) in Patients with Advanced Pelvic Malignancies

Start Date: 19 Aug 88 Est Completion Date: Indefinite

Department: OB/GYN Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

Associate Investigators: None

Key Words: malignancy, pelvic, advanced, chemotherapy, amonafide

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Dec 88

Study Objective: To screen for activity of new agents or drug combinations in patients with advanced malignancies. Its intent is to determine the efficacy of chemotherapeutic agents in patients whose advanced malignancies have been resistant to high priority methods of treatment.

Technical Approach: Patients must have normal renal and hepatic function. Patients will be entered as nonrandomized cases. Amonafide will be administered as a slow intravenous infusion over an hour at an initial dose of 300 mg/m^2 daily for five days. A serial dose escalation up to 450 mg/m^2 will be used in patient without toxicity after each cycle of therapy until a Grade 1 hematologic toxicity occurs.

All patients will receive therapy until disease progression or until adverse effects prohibit further therapy.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/82 Status: On-going

Title: GOG 26-EE: A Phase II Trial of Didemnin B (NSC #325319) in Patients with Advanced Pelvic Malignancies

Start Date: 16 Sep 88 Est Completion Date: Indefinite

Department: OB/GYN Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

Associate Investigators: None

Key Words: malignancy, pelvic, advanced, chemotherapy, didemnin-B

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Dec 88

Study Objective: To screen for activity of new agents or drug combinations in patients with advanced malignancies. Its intent is to determine the efficacy of chemotherapeutic agents in patients whose advanced malignancies have been resistant to high priority methods of treatment.

Technical Approach: Patient must demonstrate a normal prothrombin time to be eligible for this protocol. Didemnin B will be administered at a dosage of 4.2 mg/m^2 every four weeks. The dosage will be calculated using the GOG standard monogram. Prophylaxis against nausea and vomiting using metoclopramide, diphenhydramine, and dexamethasone will be required. Dose modifications will be will be permitted.

An adequate trial is defined a *receiving one dose of drug* and alive at four weeks. Patients receiving one dose of Didemnin B and demonstrating progression more than or equal to four weeks from study entry will be considered evaluable for response and progression. Toxicity, however, may be assessed as soon as drug is given. Each patient should remain on study and continue to receive drug until disease progression or adverse effects prohibit further therapy.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/68 Status: Completed

Title: GOG 26-FF: A Phase II Trial of Taxol (NSC #125973) in Patients With Advanced or Recurrent Ovarian Carcinoma

Start Date: 19 Aug 88 Est Completion Date: Indefinite

Department: OB/GYN Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

Associate Investigators: None

Key Words: carcinoma, ovarian, Taxol, efficacy

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Dec 88

Study Objective: To screen for activity of new agents or drug combinations in patients with advanced malignancies. Its intent is to determine the efficacy of chemotherapeutic agents in patients whose advanced malignancies have been resistant to high priority methods of treatment.

Technical Approach: Patients who meet the criteria listed in the master protocol (26A) will be administered Taxol as a 24-hour continuous infusion at an initial dose of 170 $mg/m^2/24$ hours, once every three weeks. The dose will be reduced to 135 $mg/m^2/24$ hours for high-risk patients (those who have received pelvic radiation in addition to first line chemotherapy). Dexamethasone, diphenhydramine, and ranitidine will be given prior to Taxol administration to prevent allergic reaction. Vital signs, including blood pressure, pulse, respiration, and temperature will be taken every 15 minutes during the initial two hours of infusion and then every hour thereafter until one hour after completion of the infusion. Cardiac monitoring is required during the infusion. An adequate trial is defined as receiving one course of therapy and alive for evaluation at three weeks. Each patients should 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 89 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: LTC Gordon O. Downey, MC

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

Key Words: carcinoma, lymph node, aortic, pelvic, metastases

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 88

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 abdominal hysterectomy, bilateral salpingo-oophorectomy, selective pelvic and para-aortic lymphadenectomy, and peritoneal cytology sampling are eligible. The following histologic types of endometrial carcinoma are acceptable: adenocarcinoma, adenocarcinoma with squamous metaplasia, adenoacanthoma, and adenosquamous carcinoma. Patients who have received preoperative radiotherapy are ineligible. Pathologic evaluation will include: (a) peritoneal washing will be evaluated for malignant cells; (b) the uterus will be evaluated in regard to location of tumor, depth of myometrial invasion, differentiation of tumor, size of uterus; (c) the adnexa will be evaluated for presence of metastasis (d) the lymph nodes (total number indicated) will be evaluated as to metastasis and location and number of lymph nodes involved. After surgery, all patients will be entered into the appropriate protocol or receive appropriate treatment if no protocol is available.

Progress: This protocol is closed to patient entry. No patients were entered in FY 89. In previous years, eight patients were entered on the protocol. Four patients are still being followed.

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Gordon O. Downey, MC

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

Key Words: sarcoma, uterine, pathologic study

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Dec 88

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 89. Six patients have been entered in previous years, with three of them still being followed.

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Gordon O. Downey, MC

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

Key Words: germ cell, ovary, adjuvant, chemotherapy

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 88

Study Objective: To evaluate the effect of combined prophylactic vincristine, dactinomycin, and cyclophosphamide (VAC) chemotherapy in patients with endodermal sinus tumor, embryonal carcinoma, immature teratoma (Grades 2 and 3), choriocarcinoma, and malignant mixed germ cell tumors of the ovary, Stages I and II, after total removal of all gross tumor; to evaluate the role of serum markers, especially alpha-feto-protein and human chorionic gonadotropin (beta-HCG), when these are present in predicting response and relapse; to determine the role of restaging laparotomy in determining response, predicting relapse, and planning further therapy.

Technical Approach: Patients with histologically confirmed malignant germ cell tumors of the ovary, Stage I or II, if previously untreated and completely resected, (excluding patients with pure dysgerminoma) will be eligible. Patients with Grade 2 or 3 immature teratoma are eligible. After adequate recovery from required surgery, patients will receive 6 courses of VAC chemotherapy. If progression is noted during chemotherapy, patients will be transferred to the appropriate protocol. Patients with no evidence of disease after 6 courses will then undergo a restaging laparotomy. Those showing evidence of progression will be transferred. If laparotomy reveals no evidence of disease, patients will receive an additional 3 courses of VAC and then be followed on no further therapy.

Progress: No new entries in FY 89. Two patients were entered at MAMC in previous years. The protocol is closed to patient entry.

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Gordon O. Downey, MC

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

Key Words: adenocarcinoma, ovarian, chemotherapy

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Dec 88

Study Objective: To determine, in optimal Stage III ovarian adenocarcinoma, if the addition of adriamycin to cyclophosphamide plus cis-platinum improves progression-free interval, frequency of negative second-look laparotomy and survival. This protocol replaces GOG #25.

Technical Approach: Eligible patients are those more than six weeks post-operative with proven primary Stage III ovarian adenocarcinoma confined to the abdominal cavity and its peritoneal surfaces with residual tumor masses after surgery no larger than 1 cm in diameter. Patients with prior chemo- or radiotherapy are ineligible. Patients will be randomized to cyclophosphamide plus Platinol every three weeks for eight courses or to cyclophosphamide and Platinol plus adriamycin every three weeks for eight courses. After eight courses those with less than clinically complete response will go off study and be followed for survival; those with clinically complete response will have second-look surgery to validate the complete response or to remove residual tumor masses. Patients will then be followed for approximately five years for survival rates.

Progress: No patients were entered in FY 89. Six patients were entered in previous years. The study has been closed to patient entry. Three patients died of the disease, one has been lost to follow-up, and two are currently being followed on this protocol.

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Gordon O. Downey, MC

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

Key Words: cervix, negative para-aortic nodes, chemotherapy

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Nov 88

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 89. In previous years, five patients have been entered. One died of the disease and four are being followed. The protocol has been closed to patient entry.

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Gordon O. Downey, MC

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

Key Words: carcinoma, cervix, stages II_B, III, IV_A, pathologic

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Dec 88

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 89. In previous years five subjects were entered. Data are still being collected on one patient.

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Gordon O. Downey, MC

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

Key Words: cervix, carcinoma, radiation, lymphadenectomy, hysterectomy

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Dec 88

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: One patient entered at MAMC in FY 86 and is still being followed.

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Gordon O. Downey, MC

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

Key Words: tumor, ovarian, natural history, melphalan, cisplatin

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Dec 88

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: Four new patients were entered in FY 89 for a total of eight entries. Six are presently being followed.

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Gordon O. Downey, MC

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

Key Words: melanoma, vulva, hemivulvectomy, clinicopathologic

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Jan 89

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. The 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 89 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: LTC Gordon O. Downey, MC

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

Key Words: carcinoma, vulvar, lymphadenectomy, hemivulvectomy

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Jan 89

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 $\leq$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 89 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

Department: OB/GYN Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

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

Key Words: master protocol, phase II, carcinoma, cervix, squamous cell, advanced, recurrent

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Dec 88

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 for 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 was entered on the echinomycin (76H) protocol in FY 89; one patient was entered on the cis-platin/5-FU protocol (76G) in FY 87, and one patient was entered in the mitomycin-C protocol (76J) in FY 88. Section 76F was closed in December 1988 due to sufficient accrual of patients.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 87/81 Status: Completed

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: LTC Gordon O. Downey, MC

Associate Investigators: COL William Benson, MC
COL Roger B. Lee, 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 were entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/06 Status: On-going

Title: GOG 76H: A Phase II Trial of Echinomycin (NSC #526417) in Patients with Advanced Squamous Cell Carcinoma of the Cervix

Start Date: 21 Oct 88 Est Completion Date: Indefinite

Department: OB/GYN Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

Associate Investigators: None

Key Words: cervix, carcinoma, squamous cell, echinomycin

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: The population will consist of patients who have had no prior cytotoxic drug therapy. 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.

Echinomycin will be administered at a dosage of 1500 mcg/m^2 every four weeks. An adequate trial is defined as receiving one dose of drug and alive at four weeks. Patients receiving one dose of Echinomycin 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: One patient has been entered in this study. The study was closed to patient entry in August 1989.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No. 88/52 Status: On-going

Title: GOG 76J: A Phase II Trial of Mitomycin-C (NSC#26980) in Patients with Advanced Squamous Cell Carcinoma of the Cervix

Start Date: 15 Apr 88 Est Completion Date: Indefinite

Department: OB/GYN Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

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

Key Words: carcinoma, cervix, squamous cell, mitomycin-C

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Dec 88

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 receive mitomycin-C, 20 mg/M^2, intravenously 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. In patients at high risk for myelosuppression, no treatment course will start until the WBC is >3000/mcl and the platelets are >100,000/mcl. The dose level will be reduced in these patients according to nadir counts, length of time myelosuppression is prolonged, and previous radiotherapy history.

A dose reduction will be mandated in all patients in whom the adverse effects exceed a grade 2 level. Should serum creatinine exceed 2.0 mg/dl, drug therapy will be discontinued.

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. The drug will be continued until there is documentation of disease progression or unacceptable adverse effects.

Progress: No entries in FY 89. One patient was entered in the study at MAMC in FY 87 and died of the disease.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 84/74 Status: On-going

**Title: GOG 78: Evaluation of Adjuvant VP-16, Bleomycin and Cisplatin (BEP) Therapy in Totally Resected Choriocarcinoma, Endodermal Sinus Tumor, Embryonal Carcinoma and Grade 3 Immature Teratoma of the Ovary, Pure and Mixed with Other Elements

Start Date: 17 Aug 84 Est Completion Date: Jul 89

Department: OB/GYN Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

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

Key Words: ovary, embryonal carcinoma, choriocarcinoma, endodermal sinus tumor, vinblastine, bleomycin, cisplatin

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Dec 88

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; vinblastine 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 89 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: LTC Gordon O. Downey, MC

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

Key Words: carcinoma, endometrium, advanced, recurrent, hormonal therapy, medroxyprogesterone acetate, master protocol

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Dec 88

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 if 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
81D: positive for either estrogen or progesterone receptors 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 each section will be the same with only the receptor studied being different.

Treatment I: medroxyprogesterone acetate 200 mg p.o. daily
Treatment II: medroxyprogesterone acetate 1000 mg p.l. daily

Progress: No patients at MAMC have been entered in any of the sections to this protocol. All sections of the protocol that were open at MAMC have been closed. This master protocol will remain open until GOG decides if more drugs will be studied.

Group-wide, 193 patients are presently evaluable for response on the combined trials. Sufficient activity is evident in each regimen to warrant completion of the study. Treatment comparisons will be undertaken in final analysis.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 86/09 Status: Completed

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: LTC Gordon O. Downey, MC

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

Key Words: endometrial carcinoma, medroxyprogesterone acetate, positive estrogen and progesterone receptors

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

Study Objective: To determine the relative efficacy of a high versus a low dose schedule of oral medroxyprogesterone 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 89 | Protocol No.: 86/10 | Status: Completed

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: LTC Gordon O. Downey, MC

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

Key Words: carcinoma, endometrial, medroxyprogesterone acetate, negative estrogen and progesterone receptors

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

Study Objective: To determine the relative efficacy of a high versus a low dose schedule of oral medroxyprogesterone 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. One course will be considered as every four weeks. Each patient will have a serum sample drawn after one month on therapy to document compliance and absorption. Treatment will be continued until evidence of disease progression or the patient experiences unacceptable adverse effects.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 89 | Protocol No.: 86/11 | Status: Completed

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: LTC Gordon O. Downey, MC

Associate Investigators: COL William Benson, MC
COL Roger B. Lee, 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: N/A

Study Objective: To determine the relative efficacy of a high versus a low dose schedule of oral medroxyprogesterone 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 evidence of disease progression or the patient experiences unacceptable adverse effects.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 86/12 Status: Completed

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: LTC Gordon O. Downey, MC

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

Key Words: carcinoma, endometrial, medroxyprogesterone acetate, estrogen or progesterone receptors, unknown

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

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 evidence of disease progression or the patient experiences unacceptable adverse effects.

Progress No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 86/13 Status: Completed

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: LTC Gordon O. Downey, MC

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

Key Words: carcinoma, endometrial, tamoxifen citrate, progestins

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

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 89 | 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: LTC Gordon O. Downey, MC

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

Key Words: carcinoma, ovarian, endometrial, simultaneous

Accumulative MEDCASE Cost: -0- | Est Accumulative OMA Cost: -0- | Periodic Review: Dec 88

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 89 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

Department: OB/GYN Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

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

Key Words: carcinoma, cervix, chemotherapy, radiation

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Dec 88

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 89 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: LTC Gordon O. Downey, MC

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

Key Words: carcinoma, endometrium, recurrent, master protocol

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Dec 88

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.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 87/27 Status: Ongoing

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: LTC Gordon O. Downey, MC

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

Key Words: carcinoma, endometrial, vincristine, phase II

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Nov 88

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 89 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: LTC Gordon O. Downey, MC

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

Key Words: carcinoma, endometrial, advanced, mitomycin-C

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Dec 88

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 89 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: Indefinite

Department: OB/GYN Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

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

Key Words: sarcoma, uterine, recurrent, master protocol, drugs

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Jan 89

Study Objective: To identify new agents and combinations for treating this malignancy and to allow the best possible chance for a new cytotoxic agent to demonstrate activity. This study constitutes a Phase II design in a population of patients who have had no prior drug therapy.

Technical Approach: The study design will involve treating an average sample size of 30 evaluable patients per drug studied for each of the following cell type categories:

Mixed mesodermal tumor
Leiomyosarcoma
Other sarcomas

Patients will have had no prior drug therapy. Since this is a Phase II study, no randomization is involved. The principal parameters employed to evaluate the efficacy of each agent are:

The frequency and duration of objective response.
The frequency and severity of observed adverse effects.
Survival time for all patients.
Duration of progression-free interval for all patients.

In order to estimate the true response rate and be 90% certain - that the estimate is within ±15%, 30 evaluable patients per histologic category will be needed (group wide). Reviews will be held at least twice yearly. Consequently, on at least two occasions, early termination can be considered if the results do not warrant conducting the study to completion. Although the exact number of potential subjects cannot be forecast at this time, the relatively slow accrual rates guarantee that inactive agents will be expeditiously recognized. The active phase of this study for each drug should be approximately:

Mixed mesodermal tumor - 1 to 1 1/4 years
Leiomyosarcoma - 3 years
Other sarcomas - 6 years

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Gordon O. Downey, MC

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

Key Words: sarcoma, uterine, recurrent, hydroxyurea, DTIC, VP-16

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Dec 88

Study Objective: To identify new agents and combinations for treating this malignancy and to allow the best possible chance for a new cytotoxic agent to demonstrate activity. This study constitutes a Phase II design in a population of patients who have had no prior drug therapy. The agents to be studied in protocol are hydroxyurea, dacarbazine (DTIC), and etoposide (VP-16).

Technical Approach: The treatment regimen combines hydroxyurea, a chemotherapeutic agent with a known cell-cycle synchronizing effect with DTIC, an antimetabolite, and VP-16, a premitotic inhibitor.

On Day 1, Hydroxyurea, 500 mg capsules, will be given p.o. every 6 hours with no restrictions on diet or activity. On Day 2, 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, diluted in 250 cc NS will be infused over one hour. Premedication with anti emetic regimens will be given on Day 2. The treatment course will be administered every four weeks, if toxicity permits and will continue for 12 courses unless progression occurs.

An adequate trial is defined as receiving one course of treatment and living four weeks. If the patient suffers progressive disease before four weeks elapse, this indicates treatment failure. Patients will remain on study and continue to receive therapy for 12 months unless there is progression or adverse effects which prohibit further therapy. Patients who die of drug-related complications prior to having their disease re-evaluated will be considered inevaluable for response but evaluable for toxicity.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Gordon O. Downey, MC
Associate Investigators: COL William Benson, MC
COL Roger B. Lee, MC
Key Words: sarcoma, uterine, advanced, VP-16
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Dec 88

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 89 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

Department: OB/GYN Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

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

Key Words: vulvectomy, radical, groin dissection, groin radiation

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Dec 88

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 89 Protocol No.: 87/13 Status: On-going

Title: GOG 90: Evaluation of Cisplatin, Etoposide, and Bleomycin (BEP) Induction Followed by Vincristine, Dactinomycin, and Cyclophosphamide (VAC) Consolidation in Advanced Ovarian Germ Cell Tumors

Start Date: 17 Oct 86 Est Completion Date: Indefinite

Department: OB/GYN Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

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

Key Words: tumors, ovarian, germ cell, BEP induction, VAC

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Dec 88

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 89 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: LTC Gordon O. Downey, MC

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

Key Words: carcinoma, cervix, pelvic radiation vs no therapy

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Dec 88

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 entries in FY 89 at MAMC. One patient was entered in FY 88, who is still being followed.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/36 Status: On-going

Title: GOG 93: Evaluation of Intraperitoneal Chromic Phosphate Suspension Therapy Following Negative Second-Look Laparotomy for Epithelial Ovarian Carcinoma (Stage III)

Start Date:19 May 89 Est Completion Date: Indefinite
Department: OB/GYN Facility: MAMC
Principal Investigator: LTC Gordon O. Downey, MC
Associate Investigators: None
Key Words: carcinoma, ovarian, epithelial, IP chromic phosphate
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $2416.00 Periodic Review: N/A

Study Objective: To evaluate the role of intraperitoneal chromic phosphate (^{32}P) suspension therapy in patients with Stage III epithelial ovarian carcinoma who have no detectable evidence of disease at the second-look laparotomy and to evaluate disease free survival, sites and frequency of relapse, and the morbidity from intraperitoneal ^{32}P therapy.

Technical Approach: Patients with primary histologically confirmed epithelial carcinoma of the ovary who are in complete clinical remission, with no persistent or recurrent cancer, and initial FIGO Stage III will be eligible. Patients with distant metastatic disease, previous pelvic or abdominal radiation therapy, previous or concomitant malignancies other than of skin (excluding melanoma), and borderline malignancy of the ovary will be ineligible.

Patients will be randomized to one or two regimens. Regimen I will consist of 15 millicuries of intraperitoneal chromic phosphate suspension therapy, preferably within 10 days (but no more than six weeks) after second-look laparotomy. Patients will be randomized before second-look laparotomy and a dialysis catheter will be inserted during second-look laparotomy in those patients randomized to receive ^{32}P. Patients will be rotated every 10 minutes (left side to back to right side) for two hours to facilitate distribution of the ^{32}P. Anterior and lateral scans of the abdominal cavity will be done to evaluate adequate distribution in the peritoneal cavity of the ^{32}P and to confirm that loculation has not occurred. Data collection will continue until disease progression or death.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Gordon O. Downey, MC

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

Key Words: carcinoma, endometrial, papillary serous, radiation

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Dec 88

Study Objective: To determine the survival and progression-free interval of patients with maximally debulked advanced endometrial carcinoma treated with abdominal radiation and to determine the progression-free interval and site of recurrence in patients with Stage I or II papillary serous carcinoma of the endometrium treated with abdominal radiation therapy with pelvic boost.

Technical Approach: Following surgery, the whole abdomen will be irradiated with opposed fields to a total dose of 3000 cGy in 20 fractions of 150 cGy each. If the treatment is not tolerated because of GI symptoms or leukopenia, the daily fraction will be decreased to 125 cGY per day. Whole abdominal radiation will require four to five weeks.

Following whole abdominal radiation, the pelvis will be boosted to a midplane dose of 980 cGy at 180 cGy per fraction for eleven treatments. The combined whole abdominal radiation and the total pelvic field radiation will require a total time of approximately six to seven weeks.

Patients will be followed quarterly for the first two years after completion of therapy and semi-annually for an additional three years.

Patients will continue on protocol until disease progression or adverse effects necessitates removal from the study. An adequate trial will consist of receipt of any protocol therapy.

Progress: No entries at MAMC in FY 89. Two patients were entered in FY 88. Both died of the disease.

Detail Summary Sheet

Date: 30 Sep 89 | 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: LTC Gordon O. Downey, MC

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

Key Words: cancer, ovarian, chemotherapy, staged, cyclophosphamide, cisplatin, P32

Accumulative MEDCASE Cost: -0- | Est Accumulative OMA Cost: -0- | Periodic Review: Nov 88

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: One patient was entered in the study at MAMC in FY 89. Two patients were entered at MAMC in FY 88. One of these patients died of the disease.

Detail Summary Sheet

Date: 30 Sep 89 | 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: LTC Gordon O. Downey, MC

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

Key Words: carcinoma, ovarian, epithelial, cyclophosphamide, cisplatin, intensive vs non-intensive

Accumulative MEDCASE Cost: -0- | Est Accumulative OMA Cost: -0- | Periodic Review: Jan 89

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, immediately after the initial course of therapy, after each course, on completion of therapy and at each follow-up for three years.

Adequate trial to evaluate response is defined as receiving one course of therapy and living three weeks for repeat lesion measurement. Adequate trial to evaluate toxicity is defined as receiving one course of therapy and receiving any follow-up information for observation of toxicity.

Progress: One patient was entered at MAMC in FY 89. One patient was entered in FY 87.

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Gordon O. Downey, MC

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

Key Words: adenocarcinoma, endometrial, adjunctive radiation

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Dec 88

Study Objective: To determine if patients with intermediate risk endometrial adenocarcinoma who have no spread of disease to the lymph nodes benefit from postoperative pelvic radiotherapy and to evaluate how the addition of pelvic radiotherapy will alter the site and rate of cancer recurrence in these intermediate risk patients.

Technical Approach: Patients with primary histologically confirmed Grade 2 or 3 endometrial adenocarcinoma (endometrioid, villoglandular, mucinous and adenosquamous) and clear cell carcinoma will be eligible. Patients must have had a total abdominal hysterectomy, bilateral salpingo-oophorectomy, selective pelvic and para-aortic node sampling, pelvic washings and found to be surgical Stage 1 with myometrial invasion. Following surgery, patients will be randomized to no additional treatment of pelvic radiation therapy to begin no later than eight weeks after surgery. Those randomized to radiation therapy will be treated with AP and PA parallel ports with each port being treated each day. A daily tumor dose of 180 cGy will be given to a total dose of 5040 cGY in approximately six weeks. Each patient will be followed with regular visits occurring every three months for the first two years, every six months for the third, fourth and fifth years, and yearly thereafter.

Progress: No patients entered at MAMC in FY 89. Two patients were entered FY 87. Both are still being followed.

Detail Summary Sheet

Date: 30 Sep 89 | 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: LTC Gordon O. Downey, MC

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

Key Words: PGTD, hydatidiform mole, free beta HCG, monoclonal antibody

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Dec 88

Study Objective: To measure the serum concentration of free beta HCG and total beta HCG in patients with molar pregnancies in order to determine whether the ratio of free beta HCG to total beta HCG may be of value in predicting which molar pregnancies will undergo spontaneous remission and which will subsequently develop into persistent gestational trophoblastic disease.

Technical Approach: Patients with gross and microscopically verified diagnosis of hydatidiform mole, either classic (true) or partial (incomplete), obtained by evacuation of the uterus with uterine conservation will be eligible. Patients will have a pelvic ultrasound within two weeks of evacuation and the first serum will be drawn within 48 hours (prior to if at all possible) of evacuation for beta HCG and free beta HCG determinations. Following histologic confirmation of the hydatidiform mole (within one week of evacuation) the patient will be placed on study. Serum samples will be obtained weekly until a negative assay is attained or until a plateau or rise in titer is observed. All patients will remain on study for a minimum of twelve weeks after primary evacuation of the molar pregnancy. After spontaneous remission, patients will have beta HCG titers monthly for six months (free beta HCG assay is not necessary). After persistent disease, the patient will remain on study until remission. The principle parameters employed to investigate the prediction of which molar pregnancies will undergo spontaneous remission and which will subsequently develop into persistent trophoblastic disease are free beta HCG, total HCG concentration, ratio of free beta HCG to total HCG, and remission of disease as determined by weekly titers.

Progress: No patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Gordon O. Downey, MC

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

Key Words: cancer, vulvar, chemoradiation, pre-operative

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Dec 88

Study Objective: To determine: the feasibility of using preoperative chemoradiotherapy to obviate the need for pelvic exenteration for patients with advanced vulvar cancer involving the proximal urethra, bladder, anal canal, or rectum; the feasibility of allowing a less extensive vulvar and vaginal resection in patients with a T3 primary tumor by using preoperative chemoradiotherapy; the survival rate for patients with Stage III or IV-A disease associated with this technique of therapy; the morbidity of a combined chemoradiosurgical approach to advanced vulvar cancer and to attempt to improve survival in patients with N3 groin nodes.

Technical Approach: Patients with primary, previously untreated, histologically confirmed invasive squamous or adenocarcinoma of the vulva clinically determined to be Stage III or IV will be treated with chemoradiation therapy according to the sub-stage.

Regimen I: Patients with T4 or unresectable T3 primary tumor and NO or N1 groin nodes will receive a split course of radiation therapy to the vulva by AP-PA fields. Twice daily fractions of 150 cGY will be given on days 1-4 and 1'-4'; once daily fractions of 180 cGY will be given on days 5, 8-12 and 5', 8'-12'. A 1 1/2 to 2 1/2 week split will be allowed between the two courses. Total midplane dose will be 4560 cGY.

During the twice daily radiation (days 1-4 and 1'-4'), patients will receive concurrent chemotherapy of 5-FU, 1000 mg/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.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/60 Status: On-going

Title: GOG 102A: Master Protocol for Phase II Intraperitoneal Drug Studies in Treatment of Minimal Residual Ovarian Malignancies Documented at Second-Look Surgery

Start Date: 20 May 88 Est Completion Date: Indefinite

Department: OB/GYN Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

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

Key Words: chemotherapy, intraperitoneal, Cis-platin, 5-FU

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Dec 88

Study Objective: To determine the activity of various drugs or biologic response modifiers (BRM's) alone or in combination when used by the intraperitoneal route in patients who have persistent minimal residual disease epithelial ovarian malignancies after standard therapy and to evaluate further the toxicity (systemic and local) of drugs and BRM's or combinations used.

Technical Approach: Eligible patients: those with primary histologically documented epithelial carcinoma of the ovary; partial or incomplete responses to combination chemotherapy or minimal residual disease ($\leq$1.0 cm maximum tumor diameter) at second-look surgery; a history of complete response followed by a recurrence with no nodule >1 cm in diameter, GOG performance grade of 0, 1, or 2; at least three weeks from last treatment with chemotherapy or radiation, WBC $\geq$3000, platelet count >100,000, serum creatinine >2.0 mg%, and bilirubin and SGOT $\geq$ two times normal.

Ineligible patients: those with borderline tumors; leptomeningeal or cerebral metastases; current evidence of disease outside the peritoneal cavity; serious infection, septicemia, or pneumonia; major or extensive intra-abdominal adhesions or other factors - which would impair surgical placement of the intraperitoneal catheters; prior whole abdominal radiation therapy; or other specific criteria as detailed in the individual sections of the protocol.

Chemotherapy will start within 12 weeks of second-look surgery. The drug or drugs will be administered intraperitoneally through an implantable peritoneal dialysis catheter. The catheter will be placed at the time of second-look laparotomy or at a subsequent operation. Ovarian tumor tissue will be studied for sensitivity against various chemotherapeutic agents utilizing *in vitro* clonogenic assays. Patients who receive one or more courses of drug and live at least three weeks will be evaluable for response. Patients who receive one or more courses of drug are evaluable for adverse effects regardless of subsequent survival.

Progress: No patients entered in this master protocol at MAMC. Section B of this protocol was closed in Jan 89.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/61 Status: Completed

Title: GOG 102B: Intraperitoneal Administration of Cisplatin (NSC #119875) and 5-Fluorouracil (NSC #19893) in Residual Ovarian Carcinoma (Phase II)

Start Date: 20 May 88 Est Completion Date: Indefinite

Department: OB/GYN Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

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

Key Words: chemotherapy, intraperitoneal, cisplatin, 5-FU

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

Study Objective: To determine the activity of the combination of cisplatin and 5-fluorouracil (5-FU) when used by the intraperitoneal route in patients who have persistent minimal residual disease epithelial ovarian malignancies after standard therapy and - to evaluate further the toxicity (systemic and local) of this combination of drugs.

Technical Approach: Eligible patients will be those who meet the criteria as set forth in the master protocol (102-A). Every - three weeks the subjects will receive a total dose of 100 mg of cisplatin and 2000 mg of 5-FU for a total of eight treatments (not per m^2). Patients will be premedicated at the discretion of the physician and will be hydrated with D_5 - 1/2 NS with 20 mEq KCl at 500 cc/hr for two hours or at 250 cc/hr for four hours prior to treatment. Chemotherapy will continue through eight cycles unless disease progression is documented or unacceptable toxicity occurs. At the completion of eight cycles, patients will undergo surgical evaluation.

An adequate trial is defined as having received one cycle and the patient is alive three weeks thereafter. Patients receiving one dose of therapy and demonstrating progression in three weeks or less from study entry will be considered evaluable for response and toxicity.

Progress: No patients entered at MAMC.

This protocol was closed to patient entry in January 1989.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/07 Status: On-going

Title: GOG 102-C: Intraperitoneal Administration of Cisplatin (NSC #119875) and Recombinant Alpha 2 Interferon in Residual Ovarian Carcinoma

Start Date: 21 Oct 88 Est Completion Date: Indefinite

Department: OB/GYN Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

Associate Investigators: None

Key Words: carcinoma, ovarian, intraperitoneal, chemotherapy

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

Study Objective: To determine the activity of cis-platin and recombinant alpha 2 interferon when used by the intraperitoneal route in patients who have persistent minimal residual disease epithelial ovarian malignancies after standard therapy, and to evaluate further the toxicity (systemic and local) of this combination of drugs.

Technical Approach: Every three weeks, subjects will receive a total dose of 50 mg/m^2 of cis-platin and 25 x 10^6 units of Interferon for a total of eight treatments. Chemotherapy will continue through eight cycles unless disease progression is documented or unacceptable toxicity occurs. At the completion of eight cycles, patients will undergo surgical re-evaluation.

Immediately prior to infusion of the interferon, patients will be premedicated with Tylenol to be continued every four hours for the first 24 hours. Interferon will be infused over one hour. That night, IV hydration with $D_5$1/2NS plus potassium chloride will be started and will be continued until discharge. Twelve to eighteen hours after the administration of interferon (the next morning) cis-platin will be administered intraperitoneally. One hour prior to drug administration, patients will receive anti-emetic premedication and immediately prior to cis-platin infusion Mannitol will be administered IV.

An adequate trial is defined as two cycles of therapy and alive at three weeks thereafter. Patients receiving two doses of therapy and demonstrating progression six weeks or less from study entry will be considered evaluable for response and toxicity.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/81 Status: On-going

Title: GOG 106: Evaluation of the Serum Marker, CA-125, in the Management of Carcinoma of the Endometrium

Start Date: 16 Sep 88 Est Completion Date: Indefinite

Department: OB/GYN Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

Associate Investigators: None

Key Words: serum marker, CA-125, carcinoma, endometrium

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Dec 88

Study Objective: To evaluate the sensitivity of CA-125 for endometrial carcinoma; to correlate CA-125 levels with surgical-pathologic criteria (stage, grade, sites); to evaluate the efficacy of CA-125 in monitoring response to therapy (surgery, radiation, chemo, hormonal) in endometrial carcinoma; and to evaluate the efficacy of CA-125 in predicting survival and/or recurrence in endometrial cancer.

Technical Approach: Patients with endometrial carcinoma who are eligible for designated concurrently active GOG treatment protocols for endometrial cancer will be eligible. Specific protocols are selected to obtain a population of patients with tumor burdens and risks for recurrence appropriate to accomplish the study objectives. Serum for CA-125 will be collected according to a schema individually developed for each treatment protocol to be consistent with the regimen and anticipated findings. The collection schedules developed will follow the general schema below, modified as appropriate.

1. prior to surgery, if surgery is needed
2. prior to initiation of therapy
3. prior to each chemotherapy treatment
4. monthly during hormonal therapy
5. prior to initiation of postoperative radiation and at two week intervals during therapy
6. at the completion of therapy
7. at regular follow-up intervals, approximately every three months for the first year, every four months the second year, and every six months thereafter, on patients who are free of disease
8. in patients who progress, follow-up blood samples will not be required after progression is well documented and sera at those time points has been obtained

The duration of this study will be determined by the designated concurrently active GOG treatment protocols with five years of follow-up thereafter.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/37 Status: On-going

Title: GOG 107: A Randomized Study of Doxorubicin (NSC 123127) versus Doxorubicin Plus Cisplatin (NSC 119875) in Patients with Primary Stage III and IV, Recurrent Endometrial Adenocarcinoma

Start Date: 17 Mar 89 Est Completion Date: Indefinite
Department: OB/GYN Facility: MAMC
Principal Investigator: LTC Gordon O. Downey, MC
Associate Investigators: None
Key Words: adenocarcinoma, endometrial, chemotherapy, randomized
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: N/A

Study Objective: To determine: whether the addition of cisplatin to doxorubicin offers significant improvement in the frequency of objective response; the duration of progression-free interval; and the length of survival as compared to doxorubicin alone.

Technical Approach: Patients will be randomized to either Regimen I or Regimen II.

Regimen I: doxorubicin 60 mg/m^2 IV every three weeks to a maximum total dose of no greater than 500 mg/m^2.

Regimen II: doxorubicin 60 mg/m^2 IV every three weeks plus cisplatin, 50 mg/m^2 IV, every three weeks, to be continued to a maximum total dose of doxorubicin of 500 mg/m^2.

Each regimen will require both dose escalation and dose reduction in accordance with adverse effects observed on the previous course of therapy.

Patients who reach maximum doxorubicin dose will undergo a complete re-evaluation. All therapy will then be stopped and the patient followed on no further therapy until progression of disease is documented. Further therapy at that point will be at the discretion of the investigator.

Patients on no further treatment will be followed every three months for the first two years, then every six months for three years, and annually thereafter.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/52 Status: On-going

Title: GOG 108: Ifosfamide (NSC #109724) and the Uroprotector Mesna (NSC 113891) With or Without Cisplatin (NSC 119875) in Patients With Advanced or Recurrent Mixed Mesodermal Tumors of the Uterus

Start Date: 21 Apr 89 Est Completion Date: Indefinite

Department: OB/GYN Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

Associate Investigators: None

Key Words: mesodermal tumor, uterus, Ifosfamide, Mesna, Cisplatin

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

Study Objective: To confirm reported high response rates of advanced or recurrent mixed mesodermal tumors of the uterus to Ifosfamide/Mesna; to determine the toxicity and whether the addition of Cisplatin to Ifosfamide/Mesna improves response rates or survival in patients with these tumors.

Technical Approach: Patients will be randomized to either Regimen I or to Regimen II.

Regimen I: Ifosfamide 1.5 $g/m^2/d$ IV for 5 days plus Mesna 120 $mg/^2$ IV bolus 15 minutes prior to Ifosfamide, first day only; then 1.5 $g/m^2/d$ infusion over 5 days; repeated every 21 days.

Regimen II: cisplatin 20 $mg/m^2/d$ IV for five days before administration of Ifosfamide as given in Regimen I; repeated every 21 days.

The Ifosfamide starting dose will be 1.2 g/m^2 if the patient has had prior radiotherapy.

One course of chemotherapy and living three weeks for repeat lesion measurement will be the minimal trial to evaluate response.

One course (or part of one course) of therapy and receiving any follow-up information for observation of toxicity will be the minimal trial to evaluate toxicity.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 89	Protocol No.: 89/38	Status: On-going

Title: GOG 8803: Flow Cytometrically Determined Tumor DNA Content In Advanced Epithelial Ovarian Cancer

Start Date: 17 Mar 89	Est Completion Date: Indefinite
Department: OB/GYN	Facility: MAMC
Principal Investigator: LTC Gordon O. Downey, MC	
Associate Investigators: None	
Key Words: tumor ploidy, cell proliferation, DNA	

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

Study Objective: To determine if ploidy and cell proliferation: (1) can be correlated to accepted tumor and host factors, including patient age, tumor histology, and grade, stage, and amount of residual disease; (2) can be correlated to tumor response, second look laparotomy findings, relapse, and survival; and (3) are consistent between primary and metastatic sites and stable before and after combination chemotherapy.

Technical Approach: Pre-chemotherapy paraffin-embedded ovarian tumor blocks will be obtained from patients with advanced (Stage III or IV) epithelial ovarian cancer who were previously entered on GOG protocols 47, 52, or 60. To be eligible patients must have received enough chemotherapy on protocol to be considered evaluable for response and have adequate follow-up information including second look laparotomy findings (if done) or time to progression, as well as follow-up after negative second look laparotomy and survival. If possible, blocks will be analyzed from both the primary ovarian tumor as well as 1 to 3 metastatic sites to look at the inter-tumor variability. When one or more of the blocks has been obtained, specimens for flow cytometric determination of tumor cell DNA content and, if possible, cell cycle distribution will be prepared by a modification of the method described by Hedley, et al (Cytometry 6:327-33, 1985).

Progress: Blocks are being submitted to GOG for analysis.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/39 Status: On-going

Title: GOG 8809: Flow Cytometrically Determined Tumor DNA Content in Ovarian Tumors of Low Malignant Potential

Start Date: 17 Mar 89 Est Completion Date: Indefinite

Department: OB/GYN Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

Associate Investigators: None

Key Words: DNA, flow cytometry, extent, recurrence, survival

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

Study Objective: To determine if the DNA content of borderline ovarian tumors (carcinoma of low malignant potential) can be correlated with extent/stage of tumor, potential for recurrence, and patient survival.

Technical Approach: This study proposed to determine the DNA content in paraffin-embedded tumor specimens in patients with any stage of disease entered on GOG Protocol #72. These data will be correlated with stage of disease at entry, as well as recurrence/ progression of disease. Specimens of recurrent tumor will also be analyzed to determine the effect of treatment on DNA content.

At least one representative paraffin-embedded ovarian tumor specimen from the pretreatment laparotomy must be available as well as follow-up information including second look laparotomy findings (if done) or time to progression and follow-up after negative second look laparotomy and survival.

When one or more of the blocks has been obtained, specimens for flow cytometric determination of tumor cell DNA content and, if possible, cell cycle distribution will be prepared by a modification of the method described by Hedley, et al (Cytometry 6:327-33, 1985).

Progress: Blocks are being submitted to GOG for analysis.

Detail Summary Sheet

Date: 30 Sep 89	Protocol No.: 89/41	Status: On-going

Title: GOG 8810: Flow Cytometrically Determined DNA Content in Endometrial Carcinoma

Start Date: 17 Mar 89	Est Completion Date: Indefinite
Department: OB/GYN	Facility: MAMC
Principal Investigator: LTC Gordon O. Downey, MC	
Associate Investigators: None	
Key Words: DNA, flow cytometry, aneuploid, adenocarcinoma	

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

Study Objective:To determine the DNA content of primary, recurrent, and metastatic endometrial adenocarcinoma and to identify whether the presence of aneuploid cell populations is related to histologic cell type, histologic grade, or stage of disease; to determine if tumor ploidy is related to the probability of lymph node or distant metastasis, extended progression free interval, or five year survival; and to determine whether tumor ploidy is consistent when primary tumors are compared with their metastases.

Technical Approach: The investigators will study the DNA content of primary, recurrent, and metastatic endometrial adenocarcinomas of patients entered on GOG Protocol ##, using nuclei obtained from conventionally processed paraffin blocks. At least one paraffin block containing endometrial adenocarcinoma obtained at D&C or hysterectomy must be available. If metastatic tumor was histologically confirmed in that patient, then one paraffin block of metastatic tumor also would be highly desirable.

When one or more of the blocks has been obtained, specimens for flow cytometric determination of tumor cell DNA content and, if possible, cell cycle distribution will be prepared by a modification of the method described by Hedley, et al (Cytometry 6:32733, 1985).

Progress: Blocks are being submitted to GOG for analysis.

Detail Summary Sheet

Date: 30 Sep 89	Protocol No.: 89/72	Status: On-going

Title: GOG 8902: Correlation of Specific HPV Types and Amplification and Expression of the C-MYC Gene with the Behavior of Squamous Carcinoma of the Cervix

Start Date: 28 Jul 89	Est Completion Date: Indefinite
Department: OB/GYN	Facility: MAMC
Principal Investigator: LTC Gordon O. Downey, MC	
Associate Investigators: None	
Key Words: HPV, amplification, expression, c-myc gene, carcinoma	

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

Study Objective: To determine if HPV (human papilloma virus) types correlate with lymph node metastasis, survival, and other pathologic factors such as histologic diagnosis, grade, capillary-like space invasion, etc, in Stage I carcinoma of the cervix; to determine if c-myc gene amplification and overexpression correlate with lymph node metastasis, survival, and other pathologic factors in Stage I carcinoma of the cervix; and to determine if HPV type, c-myc amplification and overexpression are independent or interrelated prognostic factors for cervical cancer.

Technical Approach: Paraffin blocks from evaluable patients with cervical cancer (squamous, adenocarcinoma, or adenosquamous carcinoma) who were entered on GOG Protocol 49 will be obtained. There must also be adequate follow-up information on these patients. The blocks should correspond to the slides from the primary tumor and lymph node metastasis that were originally reviewed for entry onto Protocol 49. If these particular blocks are not available, another representative block from the tumor will be used.

An H&E section and six sections for PCR (polymerase chain reaction) analysis will be prepared from each paraffin block. Analysis will be performed for HPV's 6, 11, 16, 18, 31, 33, 35, and c-myc gene sequences. HPV DNA will be extracted from the paraffin blocks and analyzed. Positive controls, negative controls, and controls to measure the sensitivity of the test will be included in each test. PCR analysis will be performed using oligomer primers complementary to sequences 100 base pairs apart within the third exon of the c-myc gene. PCR will be performed under conditions wherein the amount of amplified product is linearly related to complementary DNA in starting material. The amplified DNA sequences will be subjected to electrophoresis. In situ hybridization using ^{3}H labelled antisense RNA probes for c-myc transcript will be performed to correlate c-myc expression with cellular morphology in tissue sections. A c-myc sense probe and ribosomal RNA antisense will be used as negative and positive hybridization controls, respectively.

Progress: Blocks are being submitted to GOG for analysis.

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

F O R

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NATIONAL CANCER INSTITUTE PROTOCOLS

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Gordon O. Downey, MC

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

Key Words: cancer, ovarian, natural history

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Jan 89

Study Objective: To define the natural history of patients treated with surgery plus either chemotherapy or radioisotope; to study the effect of various potential prognostic factors on the natural history of patients treated by each form of therapy; to determine the patterns of relapse for each form of therapy; to establish the value of various staging parameters on the stage of disease and its natural history.

Technical Approach: All patients with common epithelial ovarian cancer are eligible, if after definitive staging procedures the patient is zoned to be in Stages 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 89 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.

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

F O R

P R O T O C O L S

PEDIATRIC ONCOLOGY GROUP

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/77 Status: On-going

Title: POG Protocol #8850 (CCSG #7881): Evaluation of Vincristine, Adriamycin, Cyclophosphamide, and Dactinomycin With or Without the Addition of Ifosfamide and Etoposide in the Treatment of Patients with Newly Diagnosed Ewing's Sarcoma or Primitive Neuroectodermal Tumor off Bone, A Phase III Intergroup Study

Start Date: 18 Aug 89 Est Completion Date: Indefinite

Department: Pediatrics Facility: MAMC

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

Associate Investigators: None

Key Words: standard vs addition of VP-16 and ifosfamide

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

Study Objective: To determine the event-free survival (EFS) and survival of patients with Ewing's sarcoma and primitive neuroectodermal tumor (PNET) of the bone who are treated with etoposide and ifosfamide in combination with standard therapy; and to compare their EFS and survival rates with those of patients treated with standard therapy alone.

Technical Approach: Patients with newly diagnosed ($\leq$ 1 month) Ewing's sarcoma, PNET of bone, or a diagnosis compatible with primitive sarcoma of bone will be eligible. Patients will be randomized to one of two treatment regimens. One regimen will use drugs according to the standard regimen (vincristine, adriamycin, actinomycin D, and cyclophosphamide) and the other will add VP-16 and ifosfamide. Mesna will be given to prevent bleeding from the bladder. Patients will be treated with chemotherapy for 9 weeks and then evaluated. Those who have a response to treatment will be treated for 6 additional weeks with chemotherapy and radiation therapy and/or surgery. The necessity and extent of surgery will be determined based on the response to therapy and the site of the lesion. Patients will receive radiation therapy to the site of the primary lesion and to all sites of metastases which were present at the time of diagnosis, unless there has been complete resection of the primary lesion with a documented tumor-free margin of $\leq$ 1 cm. At the end of this treatment period, patients will again be evaluated, and those who have shown a marked response to treatment will continue chemotherapy for another 34 weeks. Patients with no response or recurrent or progressive disease at any of the evaluation points will go off study.

Progress: One patient was entered in this study at MAMC in FY 89.

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

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PUGET SOUND ONCOLOGY CONSORTIUM

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Gordon O. Downey, MC

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

Key Words: cancer, ovarian, P-32, cis-platinum, 5-FU, surgery

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Dec 88

Study Objective: To examine the effect of intraperitoneal therapy on disease free survival in patients with no disease or minimal residual disease following second-look surgery and to document the complication rate associated with the use of intraperitoneal chromic phosphate or chemotherapy in patients previously treated with systemic chemotherapy.

Technical Approach: Following standard induction chemotherapy, patients with Stage IIb, IIc, or III epithelial carcinoma of the ovary will have second-look laparotomy in the standard fashion. The second look procedure will include resection of any remaining female genital organs. If the patient has no evidence of gross persistent disease greater than 1.0 cm at the time of second look, a Tenckhoff catheter will be inserted.

If the pathologic findings from the second look procedure show no evidence of persistent tumor, the patient will receive 15 millicuries of intraperitoneal P-32 in 1000-1500 ml of normal saline, with appropriate rotation of position to assure proper distribution of the P-32.

If the patient has positive disease within the peritoneal cavity, she will receive chemotherapy with cisplatin (100 mg/m^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: No patients entered at MAMC in FY 89. One patient was entered in FY 87 at MAMC and is in the follow-up phase of 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

SOUTHWEST ONCOLOGY GROUP PROTOCOLS

Detail Summary Sheet

Date: 30 Sep 89 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: Sep 89

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 $\leq$25 mg%; serum creatinine $\leq$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 89 at MAMC. One entry in FY 84 at MAMC on the observation arm.

Group-wide: 190 patients have been entered. Seven patients on the observation arm had major deviations because they received treatment and two patients on the FAM arm refused treatment; 29 patients were taken off FAM due to toxicity or refusal of further FAM treatment because of side effects. Of the 80 patients evaluated for toxicity, there was one fatal cardiac toxicity. The Grade 3 "Cardiac other" toxicities were pericardial effusion (1), elevated PIP/LVET (1), an ejection fraction of .47 (1 patient), and clinically mild coronary heart failure (1). Two patients experience Grade 4 thrombocytopenia while 33 patients had severe, but not worse, toxicities. The miscellaneous toxicities were moderate pulmonary fibrosis and moderate microangiopathic-hemolytic anemia.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 78/47 Status: On-going

Title: SWOG 7808, Combination Modality Treatment for Stages III and IV Hodgkin's Disease, MOPP #6

Start Date: 11 Aug 78 Est Completion Date: 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: Sep 89

Study Objective: To attempt to increase the complete remission rate induced with MOP-BAP (nitrogen mustard, vincristine, procarbazine, prednisone, adriamycin, and bleomycin) alone utilizing involved field radiotherapy in patients with Stages III and IV Hodgkin's disease achieving partial remission at the end of 6 cycles; and to determine if immunotherapy maintenance with levamisole or consolidation with low dose involved field radiotherapy will produce significantly longer remission durations over a no further treatment group when complete remission has been induced with 6 cycles of MOP-BAP in Stages III & IV Hodgkin's.

Technical Approach: Patients (≥15 yrs) must have histologic diagnosis of Hodgkin's disease; no prior chemotherapy. Patients with a history of congestive heart failure, valvular heart disease, or serious obstructive or restrictive pulmonary disease will be excluded. Normal marrow patients will receive six cycles of MOP-BAP. Impaired bone marrow patients will receive six cycles of MOP-BAP with dose modifications. Complete Remission (CR) patients with prior radiotherapy will be randomized to Treatment 3 (no treatment) or Treatment 4 (levamisole). CR patients without prior radiotherapy will receive Treatment 5 (radiotherapy). Partial remission (PR) patients without prior radiotherapy or residual bone marrow involvement will receive Treatment 6 (radiotherapy). PR patients with prior radiotherapy or those with residual bone marrow involvement will receive Treatment 7 (4 additional cycles of MOP-BAP); after 10 total cycles of MOP-BAP, patient will continue study on MOP-BAP therapy at the discretion of the investigator.

Progress: No new patients entered at MAMC in FY 89. Seven patients were entered in previous years. Three patients have died of their disease and the other four are being followed. The study is closed to patient entry.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 79/96 Status: Ongoing

Title: SWOG 7827: Combined Modality Therapy for Breast Carcinoma, Phase III

Start Date: 21 Sep 79 Est Completion Date: Sep 81

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: 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: Sep 89

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: Two patients entered at MAMC in FY 89 for a total of 35 entries.

The ER negative arms of this study have been closed. Toxicities for both arms of the ER positive study have been similar with no fatal toxicities reported. Toxicities for the two CMFVP arms are similar with Grade 4 toxicities being leukopenia and infections. Toxicity on the tamoxifen arm has been mostly mild.

Detail Summary Sheet

Date: 30 Sep 89 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 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: cancer, bladder, BCG immunotherapy, adriamycin

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Sep 89

Study Objective: To compare the effectiveness of intravesical BCG immunotherapy with intravesical Adriamycin in chemotherapy with respect to disease-free interval and two-year recurrence rate; to compare the toxicity of topical immunotherapy and chemotherapy; and to obtain experience regarding disease-free interval and the recurrence rate in patients who develop tumor recurrence and are then crossed over to the alternative treatment arm.

Technical Approach: Following a standard transurethral resection, patients will be stratified by the presence or absence of documented carcinoma *in situ* and as to prior chemotherapy and then randomized to receive BCG immunotherapy or Adriamycin chemotherapy. Patients who develop tumor recurrence following treatment will be eligible for crossover to the other treatment arm.

Progress: The protocol was closed to new patient entry in FY 88. Three patients were entered at MAMC during FY 84 with some patients still being followed

Group-wide, 230 patients were evaluated for toxicity. The severity of the toxicities is roughly equal for the two treatments. For patients in whom carcinoma *in situ* was present, there is strong evidence that BCG is superior to ADR with respect to response and progression-free survival. There is also strong evidence that BCG is superior to ADR with respect to relapse-free survival for patients *in whom carcinoma in situ* was absent.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 84/19 Status: On-going

Title: SWOG 8221: Treatment of Advanced Bladder Cancer with Preoperative Irradiation and Radical Cystectomy Versus Radical Cystectomy Alone, Phase III

Start Date: 18 Nov 83 Est Completion Date: Oct 85

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

COL William Belville, MC	MAJ Thomas M. Baker, MC
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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: Sep 89

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 89. One patient was entered during FY 84 and was randomized to cystectomy alone and tolerated the procedure well. The patient was lost to follow-up in FY 86.

This protocol was temporarily closed, 2/1/88, because of slow accrual, the availability of a higher-priority competing study (SWOG 8710), and sufficient data for answering the primary question is potentially available. When data collection has been completed, the study will be analyzed.

Detail Summary Sheet

Date: 30 Sep 89 | Protocol No.: 83/61 | Status: On-going

Title: SWOG 8229/30: Combined Modality Therapy for Multiple Myeloma, VMCP-VBAP for Remission Induction Therapy: VMCP + Levamisole vs Sequential Half-Body Radiotherapy + Vincristine-Prednisone for Patients Who Fail to Achieve Remission Status with Chemotherapy Alone, Phase III

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

Dept/Svc: Medicine/Oncology | Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

COL 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: Sep 89

Study Objective: To compare the effectiveness of two intermittent pulse schedules of VMCP (vincristine, melphalan, cyclophosphamide, and prednisone) and VBAP (vincristine, BCNU, adriamycin and prednisone) for induction of remission in previously untreated patients with multiple myeloma. Results will also be compared with other combination regimens in previous SWOG studies. In patients proven to achieve remission, to compare the value of 12 months of chemo-immunotherapy maintenance (VMCP + levamisole) vs a consolidation program consisting of sequential half-body radiotherapy + vincristine and prednisone followed by unmaintained remission. In patients who only achieve improvement, to determine whether sequential half-body radiotherapy plus vincristine and prednisone will increase the remission rate. To determine if sequential half-body radiotherapy plus vincristine and prednisone can serve as an effective form of induction therapy for patients who fail to respond to chemotherapy or suffer early relapse.

Technical Approach: Patients with previously untreated multiple myeloma will be stratified as to tumor mass status and randomized to induction therapy on VMCP alternated every 3 wks with VBAP for a minimum of 6 months to a maximum of one yr or to VMCP for 3 cycles followed by 3 cycles of VBAP, repeated every 3 wks, for a minimum of 6 months to a maximum of one year. Upon completion of induction, patients with documented 75% regression with chemotherapy alone will be randomized to receive VMCP + levamisole, repeated every 3 wks or to sequential half-body radiotherapy and concomitant vincristine and prednisone. Partial responders or nonresponders following induction therapy will receive sequential half-body radiotherapy, vincristine, and prednisone for 6 wks.

Progress: No new patients entered at MAMC in FY 89; 5 patients were entered in previous years. The study is closed to patient registration, but the data collection has not been completed. Group-wide, the radiotherapy is not superior and quite possibly could be inferior to VMCP alone with respect to survival and is the more toxic of the two regimens.

Detail Summary Sheet

Date: 30 Sep 89 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
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LTC James E. Congdon, MC
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MAJ Alfred H. Chan, 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: Sep 89

Study Objective: To assess the impact of short-term intensive chemotherapy with CMFP to prevent disease recurrence and prolong survival in node negative patients with any size estrogen receptor negative tumors and node negative patients with estrogen receptor positive tumors whose pathological size is $\geq$3 cm; to assess the impact of surgical procedure, estrogen receptor status, menopausal status and tumor size; to develop guidelines referable to histopathological features of node negative tumors which are reproducible and to assess their prognostic impact for disease-free survival and survival; to assess the value to CEA in predicting recurrence and survival rates; to assess the natural history of a subgroup with node negative, estrogen receptor positive small tumors (3 cm).

Technical Approach: Patients will have laboratory evaluations to ensure that there is no evidence of disseminated disease. They will be stratified into a number of treatment groups based on the site of tumor, estrogen receptor status, age, and menopausal status. Patients with primary tumors less than 3 cms in diameter who are estrogen receptor positive will be followed by close observation only to determine the natural history of their tumor. All other patients who have a somewhat greater likelihood of relapse will be randomized to receive either close observation only or 6 cycles of systemic chemotherapy. The chemotherapy will consist of 4 agents: cyclophosphamide, methotrexate, 5-fluorouracil, and prednisone given for six 28 day cycles. The dosage of the individual agents will be determined by body height and weight.

Progress: No patients were entered in FY 89. Eight patients have been entered at MAMC in previous years. The protocol was closed to patient entry in May 88, but data collection has not been completed.

Preliminary group-wide data indicate that this has proven to be a positive study; the CMFP arm has shown superior disease free survival.

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Howard Davidson, MC

Associate Investigators:

COL Irwin B. Dabe, MC	MAJ Timothy O'Rourke, MC
COL Friedrich H. Stutz, MC	MAJ Michael Stone, MC
MAJ Thomas M. Baker, MC	CPT David Bryson, MC

Key Words: Toxicity, patterns, prophylaxis

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Sep 89

Study Objective: To compare combination chemotherapy (FOMi/CAP: 5-FU, vincristine, and mitomycin-C alternating with cyclophosphamide, Adriamycin, and cis-platinum) plus radiotherapy to radiotherapy alone for patients with limited, non-small cell lung cancer (NSCLC) in a randomized study with stratification for known important prognostic factors with regard to response rate, response duration, and survival duration; to determine the toxicity of radiotherapy plus FOMi-CAP relative to radiotherapy alone for patients with limited NSCLC; to evaluate the responsiveness of smaller tumor burdens (less than metastatic disease) to FOMi-CAP; to determine the pattern of relapsing disease in each treatment arm and in subgroups of patients determined by histology and response to FOMi/CAP; and to determine if prophylactic brain irradiation will decrease the chances for brain metastasis and influence toxicity or survival.

Technical Approach: Patients will be randomized to four treatment arms: (1) radiation alone to the chest; (2) radiation therapy to the chest and prophylactic radiation to the brain; (3) chemotherapy with FOMi/CAP followed by radiation therapy to the chest (those patients showing some response will receive two additional cycles of chemotherapy after completion of radiation therapy); (4) same treatment as in #3 with the addition of concomitant prophylactic brain irradiation to 3750 rads.

Progress: No entries in FY 89. Three patients were entered at MAMC in previous years. Two of the patients have expired of the disease and one patient is still in follow-up at MAMC. The study was closed to patient entry in March 1988.

Group-wide data show that none of the regimens has been highly toxic. A significant difference has been shown among the four arms. A difference has been noted in favor of the two arms not receiving prophylactic cranial irradiation. Final analysis of the data is in progress.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 87/87 Status: Completed

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: LTC Howard Davidson, MC

Associate Investigators:

COL Irwin B. Dabe, MC
LTC Lauren K. Colman, MC
MAJ Thomas M. Baker, MC
MAJ David Dunning, MC
MAJ Ruben Sierra, 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: Sep 89

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 categories: lymphoblastic lymphoma, Burkitt's lymphoma, or diffuse undifferentiated lymphoma presenting with central nervous system (CNS) involvement or in relapse after initial 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. This study was closed to patient entry, 5/1/89.

Groupwide: 35 patients have been evaluated for toxicity. Leukopenia, thrombocytopenia, and granulocytopenia are generally Grade 4. One fatal toxicity was seen due to sepsis four days after marrow transplantation.

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Howard Davidson, MC

Associate Investigators:
COL Irwin B. Dabe, MC
COL Friedrich H. Stutz, MC
MAJ Thomas M. Baker, MC
MAJ Timothy J. O'Rourke, MC
MAJ Michael D. Stone, MC

Key Words: cancer, breast, ER+, metastatic, chemotherapy

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Sep 89

Study Objective: To determine if combination hormonal therapy with aminoglutethimide and hydrocortisone + megestrol acetate, agents thought to have different mechanisms of action, offers an improved response rate with prolonged response duration and increased survival over the sequential use of each agent in ER+ patients who have progressed after responding to primary hormonal treatment with tamoxifen; to assess the relative toxicities of megestrol acetate and medical adrenalectomy, and the value of progesterone receptors in predicting subsequent responses to a variety of hormonal therapies.

Technical Approach: Patients who have had an adequate trial of tamoxifen and have achieved at least a partial response or maintained stable disease for 6 months with documented disease progression and clear-cut bone scan evidence of cortical bone metastases will be randomized to: Arm I - megestrol acetate given alone until there is documented evidence of disease progression; Arm II - aminoglutethimide plus hydrocortisone; or Arm III - megestrol acetate plus aminoglutethimide and hydrocortisone. An adequate trial of each arm will consist of at least eight weeks of daily therapy in the absence of documented evidence of disease progression. Patients in Arms I and II with documented progressive disease after an adequate trial will be crossed over to the other treatment arm. The only exception to crossover will be patients who develop life threatening brain, liver, or pulmonary metastases who require systemic chemotherapy. Patients randomized to Arm III will go off study at the time of disease progression.

Progress: No patients were entered at MAMC in FY 89. One patient entered at MAMC in FY 86 has died of the disease.

Group-wide: One treatment-related death reported on the combination arm from bacteremia secondary to leukopenia. Fourteen of 51 patients on the combination arm had toxicities of ≥ 3, compared to 7 of 59 on the aminoglutethimide arm and 3 of 60 on the megestrol acetate arm. Miscellaneous other toxicities were lethargy/fatigue, edema/fluid retention, shortness of breath, ataxia, and bone pain/flare reaction.

Detail Summary Sheet

Date: 30 Sep 89 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: Sep 89

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 89. Three have been entered in previous years. Two the these patients have died of progressive breast cancer.

Group-wide: The percentage of patients experiencing severe or worse toxicities have been similar for the two arms.

The quality of life component of this study was discontinued in January 1989 because of poor compliance in completing questionnaires.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/16 Status: On-going

Title: SWOG 8325: Combination Chemotherapy with O,P'-DDD and Cis-Platinum in Metastatic Adrenal Carcinoma, Phase II

Start Date: 11 Dec 87 Est Completion Date: Oct 90

Dept/Svc: Medicine/Hematology Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

COL Irwin B. Dabe, MC
COL Gary L. Treece, MC
LTC Lauren K. Colman, MC
MAJ Thomas M. Baker, MC
MAJ David M. Dunning, MC
MAJ Ruben D. Sierra, MC
CPT Denis P. Bouvier, MC

Key Words: carcinoma, adrenal, metastatic, O,P'-DDD, cis-platinum

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $365.00	Periodic Review: Oct 88

Study Objective: To study the responsiveness of adrenocortical carcinoma to combination chemotherapy consisting of cis-platinum and Mitotane (O,P'-DDD); to study the prognostic features of patients with metastatic and/or resectable adrenal carcinoma receiving chemotherapy; and to document the toxicity of chemotherapy in this group of patients.

Technical Approach: Patients with metastatic or residual adrenocortical carcinoma in whom further surgical removal of disease is not possible will be eligible. Prior radiotherapy or chemotherapy other than cis-platinum is allowed. Patients will be divided into good and poor risk categories with poor risk defined as the presence of one or more of the following criteria: (1) age $\geq$65 years, (2) poor tolerance to prior chemotherapy, and (3) extensive prior radiation therapy to over 30% of the bone marrow bearing areas.

Regimens: Good risk patients: cis-platinum, 100 mg/M^2 IV, repeated every three weeks, if recovery from toxicities occurs) plus O,P'-DDD, 1000 mg PO, three times a day. Poor risk patients: cis-platinum, 75 mg/M^2 IV, repeated every three weeks (if recovery from toxicities occurs, plus O,P'DDD, 1000 mg PO, four times a day, continuously. In the absence of a complete response, chemotherapy will be continued until progressive disease or unacceptable toxicity occurs. If complete response occurs, chemotherapy will be continued for 18 months or until progressive disease occurs. An adequate trial will be defined as one course of chemotherapy with both drugs followed by three weeks of observation.

Progress: No patients entered in FY 89. Two patients were entered at MAMC in FY 88. One patient developed persistent nausea, anorexia, and alteration of taste. As a result, cisplatin was stopped and the Mitotane dose was halved.

Group-wide: There have been no fatal toxicities in the 28 patients evaluated for toxicity. Anemia, thrombocytopenia, and uremia (1 patient each) are the Grade 4 toxicities reported.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/32 Status: On-going

Title: SWOG 8326/27: Evaluation of Combination Chemotherapy Using High Dose Ara-C in Adult Acute Leukemia and Chronic Granulocytic Leukemia in Blastic Crisis, Phase III

Start Date: 19 Feb 88 Est Completion Date: Feb 91

Dept/Svc: Medicine/Hematology Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

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LTC Lauren K. Colman, MC	MAJ Ruben D. Sierra, MC
MAJ Thomas M. Baker, MC	CPT Denis P. Bouvier, MC

Key Words: leukemia, chemotherapy, induction, consolidation

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Sep 89

Study Objective: To compare the effectiveness of three different drug combinations, using high dose Ara-C or high dose Ara-C in combination with m-AMSA or mitoxantrone for remission induction in relapsed adult leukemias including both acute non-lymphocytic leukemia, chronic granulocytic during accelerated or blastic phase, and untreated secondary acute leukemias, and to monitor the side effects of the above combination chemotherapy schedules.

Technical Approach: Patients will be randomized to ARM I: Ara-C, 3 gm/M^2, IV infusion every 12 hrs for 6 days; ARM II: Ara-C as in Arm I plus m-AMSA, 100 mg/M^2/day on days 7, 8, and 9; or ARM III: Ara-C as in Arm I plus mitoxantrone, 10 mg/M^2/day on days 7, 8, and 9. Bone marrow aspiration and biopsy will be performed on day 14, following induction therapy, with subsequent aspirations and biopsies performed every 7-10 days to determine when marrow recovery has occurred to start the next course of therapy. Patients with complete response will receive consolidation therapy. Consolidation therapy will consist of Arm I: Ara-C, 3 gm/M^2, IV infusion every 12 hrs for 3 days; ARM II: Ara-C as in Arm I plus m-AMSA, 100 mg/M^2/day on day 1; and ARM III: Ara-C as in Arm I plus mitoxantrone, 10 mg/M^2/day on day 1. Three courses of consolidation therapy will be given, administered every 28 days. A bone marrow aspiration and biopsy will be done prior to each consolidation course. No further treatment will be given after consolidation therapy. Pyridoxine will be given for 10 days during induction and 5 days during consolidation for control of neurotoxicity. Patients whose bone marrow remains A_3 at day 14, those who relapse after the attainment of a complete or partial remission, and those who develop potentially fatal nonmyelosuppressive toxicity will be taken off study.

Progress: No patients were entered at MAMC in FY 89. Two patients were entered at MAMC in FY 88 with no unexpected reactions.

Group-wide: Arm II was closed at the end of 1987 because of unacceptable toxicity.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 85/43 Status: Completed

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: LTC Howard Davidson, MC

Associate Investigators:

COL Irwin B. Dabe, MC
COL F.H. Stutz, MC
MAJ Thomas M. Baker, MC
MAJ Timothy O'Rourke, MC
MAJ Michael D. Stone, MC
CPT David Bryson, MC

Key Words: fludarabine phosphate, refractory, multiple myeloma

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jan 89

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: Closed to patient entry 1 Jan 89.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 86/53 Status: Completed

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: Sep 89

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 89 at MAMC. One patient was entered in FY 86 with no unexpected reactions. This patient died from disease in Oct 87.

Group-wide: This study was closed to patient entry 1 May 89. Preliminary findings indicate that toxicity is less on the carboplatin arm.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 86/07 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: MAJ Paul C. Sowray, MC**
Associate Investigators:
COL Irwin B. Dabe, MC MAJ Thomas M. Baker, MC
LTC Lauren K. Colman, 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: Sep 89

Study Objective: To compare the effects on remission duration and survival of two consolidation regimens: the L-10-M consolidation used in SWOG 8001 versus a regimen employing daunomycin, cytosine, arabinoside, 6-thioguanine and escalating methotrexate/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, adriamycin, methotrexate, cyclophosphamide, and adriamycin (36 days), followed by a 14 day rest period. On day 30, patients will have an Ommaya reservoir placed in the frontotemporal area of the skull. Patients failing to achieve an A_1 marrow status on induction therapy will go off study. Patients with complete remission will be randomized to one of the following consolidation regimens: ARM I (L-10-M) methotrexate and Ara-c, daily x 5 on days 1, 36, and 71; Ara-c and 6-thioguanine every 12 hr for 12 doses on days 15, 50, and 85; methotrexate days 15, 17, 57, and 59; vincristine and prednisone days 50 and 57; Lasparaginase beginning day 99, three times weekly for a total of 6 doses, and cyclophosphamide day 110 following last dose of Lasparaginase. Arm II: daunomycin days 1-3, Ara-C continuous infusion days 1-5, 6-thioguanine every 12 hr days 15, followed by a 21-28 day rest period. Methotrexate every 10 days from 28-98, L-asparaginase every 10 days 29-99. After a 2-week rest period, maintenance therapy will begin with vincristine, prednisone, adriamycin, 6-mercaptopurine, methotrexate (IT), methotrexate PO, dactinomycin, vincristine, prednisone, BCNU, cyclophosphamide, 6-mercaptopurine, and methotrexate (repeated every 21 wk for 36 mth or until relapse. An adequate trial will be the completion of remission induction.

Progress: No patients were entered at MAMC in FY 89. Four patients were entered in FY 86. Three have expired from their disease. No adverse effects reported at MAMC. Group-wide: Of 209 patients evaluated for induction toxicity, there have been 17 deaths due to infection, combined with hemorrhage, cerebral bleeding, and uremia in one case each. Of 73 patients evaluated in the consolidation phase, there have been no deaths.

*Replaced COL Dabe as PI, Sep 89.

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Howard Davidson, MC

Associate Investigators:

LTC Irwin B. Dabe, MC	MAJ David Dunning, MC
MAJ Thomas M. Baker, 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: Sep 89

Study Objective: To perform a Phase III randomized trial of intermediate dose intraperitoneal (IP) cis-platinum and intravenous (IV) cyclophosphamide vs intermediate dose IV cis-platinum and cyclophosphamide for optimal Stage III ovarian cancer; to evaluate the comparative toxicities of the two regimens; and to determine, in the setting of a prospective randomized trial, if the human tumor clonogenic assay with a wide range of drug concentration testing can accurately predict pathologic complete response to two-drug combination therapy in the setting of systemic and IP drug administration.

Technical Approach: Only patients with epithelial neoplasms will be eligible. Patients will be stratified by amount of residual disease and performance. They will be randomized to Arm I or Arm II. Arm I: IV cisplatin, 100 mg/m^2 plus IV cyclophosphamide, 600 mg/m^2 every 28 days for six courses. Arm II: IP cisplatin, 100 mg/m^2 plus IV cyclophosphamide, 600 mg/m^2, every 28 days for six courses. Patients with partial or no response will go off study. Those with clinical complete response will undergo second look laparotomy. Those with residual tumor at second look laparotomy will be taken off study and entered in an appropriate protocol. Those with pathologic complete response will be followed by observation only until evidence of progression of disease appears. All patients who receive any amount of chemotherapy will be evaluable for toxicity. Patients who receive at least two courses of therapy will be evaluable for response and survival.

Progress: No entries at MAMC in FY 89. One patient was entered in FY 87.

Group-wide: Abdominal cramping and pain are reported predominantly for patients on the IP arm. Leukopenia, granulocytopenia, and thrombocytopenia have been observed more frequently on the IV arm. Of 194 eligible patients, 4 had medical problems related to the IP arm, primarily due to adhesions from the catheter incision surgery.

Detail Summary Sheet

Date: 30 Sep 89 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: Sep 89

Study Objective: To compare the effectiveness of intravesical and percutaneous BCG immunotherapy given on a maintenance versus no maintenance schedule with respect to disease-free interval and rate of tumor recurrence in patients with transitional cell carcinoma of the bladder; to assess the toxicity of maintenance and no maintenance BCG immunotherapy; and to assess the association of intermediate strength PPD skin test reactivity with disease-free status in patients treated with BCG immunotherapy.

Technical Approach: Patients will be stratified according to prior chemotherapy, disease type, and PPD skin test conversion. One week following a standard transurethral resection, BCG, 120 mg lyophilized BCG organisms will be diluted in 50.5 cc of sterile, preservation-free saline. Fifty cc will be administered intravesically and 0.5 cc will be administered percutaneously. The BCG administration will be repeated weekly for a total of six weeks. Patients will then be randomized to the BCG maintenance or no maintenance arms. The BCG maintenance arm will consist of weekly intravesical and percutaneous BCG immunotherapy administrations repeated for three consecutive weeks at three months, six months, and every six months thereafter for a total treatment period of 36 months. Patient removal from the study will be determined by the type of tumor. Any patient with progression of disease, defined by an increase in tumor grade or stage beyond the highest previous grade or stage or an increase in the number or frequency or recurrences will be removed from the study.

Progress: The study was closed to patient entry 12/15/88. No patients were entered at MAMC in FY 89. A total of 11 subjects has been entered. One patient was taken off study due to severe urticarial reactions to BCG; another had severe hematuria attributed to BCG and was taken off study.

Group-wide: 313 patients had preliminary toxicity evaluations for BCG induction therapy. Two patients were coded as having treatment related deaths. One died of BCG induced systemic infection; the other died of liver disease possibly complicated by BCG induced disseminated intravascular coagulopathy.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 87/09 Status: Completed

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: LTC Howard Davidson, MC

Associate Investigators:

COL Irwin B. Dabe, MC
MAJ Thomas M. Baker, MC
MAJ Lauren K. Colman, MC
MAJ David Dunning, MC
MAJ Ruben Sierra, 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 glioblastoma 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 intra-cranial 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: The protocol was closed to patient entry 1 Nov 88 due to poor accrual and the inability to access the artery for the cisplatin infusion. There were no fatal toxicities in 17 evaluated patients. There were no complete responses on either regimen and only on partial response on each regimen.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 86/71 Status: Completed

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: 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: carcinoma, squamous cell, head & neck, chemotherapy

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Sep 89

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 who have received prior chemotherapy for recurrent disease or who have concomitant second primary cancer are not eligible. 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: The protocol was closed to patient entry 1 Mar 89. No patients entered at MAMC in FY 89. One patient was entered in FY 88 and one in FY 87, with no unusual toxicities reported. Both patients have died from their disease.

Group-wide: Of 222 patients evaluable for toxicity, there was one treatment-related death on the CDDP + 5-FU arm from myelosuppression and sepsis. Most Grade 4 toxicity has been hematologic.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/53 Status: On-going

Title: SWOG 8515: Evaluation of Menogaril (NSC 269148) in Non-Hodgkin's Lymphoma, Phase II

Start Date: 20 May 88 Est Completion Date: Apr 91

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: lymphoma, non-Hodgkin's, histology, menogaril

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Sep 89

Study Objective: To estimate the response rate and response duration for favorable and unfavorable histology Non-Hodgkin's lymphoma (NHL) treated with menogaril and to define the qualitative and quantitative toxicities of menogaril administered in a Phase II study.

Technical Approach: Patients will be stratified at initial registration by histology (favorable versus unfavorable).

Menogaril 160 mg/M^2 will be administered over 1 hour in 500 ml of 50% dextrose in water once every 28 days, provided the patient has a total absolute granulocyte count $\geq$2000 µl and a platelet count $\geq$100,000/ µl.

Treatment with menogaril will continue until disease progression. Patients with documented progression of disease or unacceptable toxicity will be removed from the study. All patients will be followed until death.

Doses will be modified in subsequent courses based on nadir counts. Patients experiencing granulocytopenia <1000/µl or thrombocytopenia <50,000/µl, following two dosage reductions will be taken off protocol treatment unless they have achieved a partial response, in which case one further dose reduction will be attempted.

Menogaril will be discontinued in the event of clinically detectable evidence of congestive heart failure. Patients who have received prior Adriamycin will undergo a follow-up MUGA scan prior to every third course of menogaril. The drug will be discontinued if the ejection fraction drops by more than 15% from baseline.

Progress: No patients entered at MAMC in FY 89. One patient was entered in this study in FY 88. Drug-induced phlebitis was reported in this patient.

Group-wide: Ten eligible patients have been registered on each strata of this study; accrual goal is 20 patients in each group.

Detail Summary Sheet

Date: 30 Sep 89 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: 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: non-Hodgkin's, CHOP, m-BACOD, ProMACE-CytaBOM, MACOP-B

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Sep 89

Study Objective: To compare in a randomized group-wide setting the complete response rate, response duration, and survival of patients with intermediate and high grade non-Hodgkin's lymphoma treated with one of four combination chemotherapy regimens: CHOP, m-BACOD, ProMACE-CytaBOM, or MACOP-B; and to compare the toxicities of each regimen in this patient population.

Technical Approach: Patients with prior chemotherapy or radiotherapy are ineligible. Arm I (CHOP every 3 weeks for 8 consecutive cycles): cyclophosphamide, doxorubicin, vincristine, and prednisone. Arm II (m-BACOD every 3 weeks x 10): cyclophosphamide, doxorubicin, vincristine, bleomycin, dexamethasone, methotrexate, and calcium leucovorin rescue after each MTX dose. Arm III (ProMACE-CytaBOM every 21 days, treated until complete remission plus 2 additional cycles): cyclophosphamide, doxorubicin, VP-16, prednisone, Ara-C, bleomycin, vincristine, methotrexate, calcium leucovorin rescue after each MTX dose, and trimethoprim-sulfamethoxazole. Arm IV (MACOP-B will be given over 12 weeks): methotrexate, calcium leucovorin rescue after each MTX bolus, doxorubicin, cyclophosphamide, vincristine, bleomycin, prednisone, and trimethoprim-sulfa. Patients with documented progressive disease may be taken off study at any time; however patients will preferably be restaged upon completion of the treatment program to assess response. Patients with less than a complete response at restaging will be taken off study. Patients whose clinical disease has disappeared and who appear to be in complete remission will undergo a complete laboratory and radiographic search for evidence of persistent lymphoma approximately one month after completion of therapy. If complete remission is confirmed, the patient will be observed with no further therapy.

Progress: No entries at MAMC.

Group-wide: Approximately 490 patients registered. The current accrual rate is 28 patients per month with a reasonable balance across treatment arms.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 87/96 Status: Completed

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: LTC Howard Davidson, MC

Associate Investigators:

COL Irwin B. Dabe, MC
LTC Lauren K. Colman, MC
MAJ Thomas M. Baker, MC
MAJ David Dunning, MC
MAJ Ruben Sierra, MC
CPT Denis Bouvier, MC

Key Words: cancer, bladder, advanced, MGBG

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Sep 89

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.

After 20 eligible patients have been entered, response data will be analyzed to determine if further investigation is warranted (Phase I). If further evaluation is warranted, 20 additional patients will be entered (Phase 2).

Progress: Data analysis determined that Phase 1 warranted advancement to Phase 2. The protocol was closed to patient entry 15 May 89 due to sufficient patient accrual. There were no entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/03 Status: On-going

Title: SWOG 8520: Cis-Diamminedichloroplatinum (II), Methotrexate and Bleomycin in the Treatment of Advanced Epidermoid Carcinoma of the Penis, Phase II

Start Date: 16 Oct 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
LTC Lauren M. Colman, MC
MAJ Thomas M. Baker, MC
MAJ David M. Dunning, MC
MAJ Ruben D. Sierra, MC
CPT Denis P. Bouvier, MC

Key Words: penis, carcinoma, epidermoid, cis-diamminedichloroplatinum (II), methotrexate, bleomycin

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Sep 89

Study Objective: To determine the response rate in patients with advanced epidermoid carcinoma of the penis treated with cis- platinum, methotrexate, and bleomycin and to evaluate the toxicity of this three-drug combination in this patient population.

Technical Approach: Cis-platinum, 75 mg/M^2, will be administered by IV infusion at 1 mg/min in normal saline (1 mg/cc) on day 1. Prior to, during, and after treatment with cis-platinum, the patient will be vigorously hydrated, intravenously and orally. Lasix, 40 mg IV bolus, will be given prior to cis-platinum. Patients will also receive methotrexate, 25 mg/M^2, IV bolus on days 1 and 8 and bleomycin, 10 units/M^2, IV bolus on days 1 and 8. Courses will be repeated every 21 days provided absolute granulocyte count is $\geq$1500/µl and platelet count is $\geq$100,000/µl.

Dosage modifications will be made for all three drugs following the initial and all subsequent cycles of chemotherapy, using standard Southwest Oncology Group chemotherapy toxicity criteria for any of the following toxicities: hematopoietic, renal, pulmonary, and neurotoxicity. Chemotherapy with bleomycin will be discontinued when a total cumulative dose of 200 units/M^2 has been reached.

Two cycles of chemotherapy will constitute an adequate trial. Patients with stable or responding disease will continue on treatment beyond two cycles until evidence of disease progression or unacceptable toxicity. Patients who have achieved a complete remission will discontinue all chemotherapy after six cycles. Patients who achieve a complete response will receive 6 courses of treatment.

Progress: No patients entered at MAMC.

Group-wide: Four eligible patients have been entered.

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Howard Davidson, MC

Associate Investigators:

COL Irwin B. Dabe, MC
LTC Lauren M. Colman, MC
MAJ Thomas M. Baker, MC
MAJ David Dunning, MC
MAJ Ruben Sierra, MC
CPT David R. Bryson, MC

Key Words: myeloma, refractory, glucocorticoid receptors

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Sep 89

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 months of treatment with 50 mg PO every other day, providing the toxicities remain acceptable and the patient remains responsive to therapy.

Progress: No patients entered at MAMC in FY 89. One patient was entered in FY 88, showed no response, and is now deceased.

Group-wide: Ninety-nine (99) patients have been accrued. There have been two instances of Grade 4 thrombocytopenia and two Grade 4 infections in 84 patients evaluated for toxicity.

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Howard Davidson, MC

Associate Investigators:

COL Irwin B. Dabe, MC
LTC Lauren M. Colman, MC
MAJ Thomas M. Baker, MC
MAJ David Dunning, MC
MAJ Ruben Sierra, 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: Sep 89

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 mins. Courses will be repeated at 4-week intervals until dose-limiting toxicity is reached or there is progression of disease.

Progress: No entries at MAMC.

Group-wide: The study was temporarily closed to patient entry on 15 Dec 87 to evaluate response and toxicity. Fifteen patients have been evaluated for toxicity. One patient had Grade 4 toxicities (leukopenia, thrombocytopenia, and granulocytopenia). Other toxicities include edema, mood swings, and tinnitus.

Of 15 patients evaluated for response, one had complete response after four months and one patient had a partial response lasting three months. The overall response rate is 14% with a median survival of 7.2 months.

Detail Summary Sheet

Date: 30 Sep 89 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 Howard Davidson, MC

Associate Investigators:
MAJ Thomas M. Baker, MC
COL Irwin B. Dabe, MC
MAJ David Dunning, MC
LTC Lauren K. Colman, 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: Sep 89

Study Objective: To estimate the response rate and survival of patients with limited small cell lung cancer when treated with concurrent chemo-radiotherapy followed by chemotherapy and late intensification with high dose cyclophosphamide and to assess the toxicity of this treatment program.

Technical Approach: Patients treated previously with chemo or radiotherapy are ineligible, except if radiation was given for localized, controlled skin cancer. Only patients with limited disease will be eligible. Patients will be taken off study for 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: This study was closed 1 May 88 due to sufficient patient accrual. Three patients were entered at MAMC, two of whom have died of disease.

Group-wide: This study was closed to patient entry 1 May 88; 56 eligible patients were entered. Myelosuppression was the main toxicity, with six patients dying from granulocytopenia, leukopenia, and/or infection. There were 29 complete responses and 13 partial responses in the first 47 patients evaluated (89%). The median survival was 10 months.

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Howard Davidson, MC

Associate Investigators:

COL Irwin B. Dabe, MC	MAJ Thomas M. Baker, 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: Sep 89

Study Objective: To test whether the addition of chemotherapy to surgery and radiotherapy prolongs disease-free survival and survival between the two study groups; to test whether the addition of chemotherapy to surgery and radiotherapy increases local control rates at the primary site and/or the cervical neck nodes; and to determine if the patterns of failure have been changed with the addition of chemotherapy.

Technical Approach: After surgery, patients will be randomized to either chemotherapy plus radiation therapy or radiation therapy alone. In the chemotherapy plus radiation therapy group, the chemotherapy will start 2-4 weeks after surgery and the radiotherapy will start approximately two weeks after completing chemotherapy. In the radiation therapy alone group, the radiation therapy will begin 2-4 weeks after surgery. Chemotherapy will be cis-platinum give day 1 and 5 FU given days 1-5 and repeated every 21 days for three courses. Patients who develop local or distant recurrence following therapy will be treated at the physician's discretion.

Progress: No entries at MAMC in FY 89. A total of three patients has been entered at MAMC. Lhermitte's syndrome occurred in one patient after radiation treatment.

Group-wide: Approximately 500 patients have been randomized. Of 284 patients evaluable for toxicity, no treatment-related deaths were reported. As expected, the chemotherapy and radiation arm had a higher incidence of patients with Grade $\geq$3 toxicities; 42% vs 15% on the radiation only arm. Most Grade 4 toxicities were hematologic.

Detail Summary Sheet

Date: 30 Sep 89 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: LTC Howard Davidson, 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
MAJ Thomas Baker, MC	CPT David Bryson, MC

Key Words: adenocarcinoma, colon, surgical, levamisole, 5-FU

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Sep 89

Study Objective: To assess the effectiveness of levamisole alone and levamisole plus 5-FU as surgical adjuvant regimens for resectable colon cancer; to compare each regimen to untreated controls to determine whether it yields improved survival and if it yields improved time to recurrence, with evaluations conducted independently in patients with Dukes stage B and Dukes stage C lesions.

Technical Approach: Patients with adenocarcinoma arising in the colon who have had a potentially curative section will be eligible. The patients with modified Dukes B_2 (serosal penetration) or B_3 (invasion of adjacent organs by direct extension) will be randomized to either follow-up without adjuvant therapy or adjuvant therapy with levamisole plus 5-FU. Patients with modified Dukes Stage C (involvement of regional lymph nodes) will be randomized to follow-up without adjuvant therapy, adjuvant therapy with levamisole alone, or adjuvant therapy with levamisole plus 5-FU.

Progress: No patients entered at MAMC in FY 89. Seven patients were entered in previous years with no unexpected toxicities.

Group-wide: This study was closed to patient entry 1 Oct 87. Of 755 patients evaluated for toxicity during the first course of chemotherapy, there were no Grade 4 or 5 toxicities on the levamisole alone arm. One patient on levamisole + 5-FU died due to leukopenia and 16 Duke's B and Duke's C patients on this regimen had Grade 4 toxicities during the first cycle, including leukopenia (11), granulocytopenia (4); stomatitis (2); thrombocytopenia (1) or combinations thereof. One patient died of anemia after completion of the first cycle of levamisole + 5-FU. For all cycles of treatment there were a large number of miscellaneous Grade 1, 2, or 3 toxicities. The investigators will continue to gather data on patient survival and disease free survival for analysis at a later date.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 87/22 Status: Completed

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 Thomas Baker, MC
MAJ Lauren K. Colman, MC
MAJ David Dunning, MC
MAJ Ruben Sierra, 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: Sep 89

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 by 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.

Group-wide: Accrual to this study has been rapid. Patient entry was closed 5/15/89. Of 129 eligible patients, there was one lethal toxicity (MVAC). Twenty-eight (28) percent of the patients treated with induction MVAC and 2% of those treated with cisplatin experienced life-threatening toxicities, primarily hematologic. Three patients treated with MVAC on crossover experienced life-threatening thrombocytopenia and/or leukopenia.

Detail Summary Sheet

Date: 30 Sep 89 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: MAJ Mark H. Kozakowski, MC**

Associate Investigators:	MAJ Thomas M. Baker, MC
COL Irwin B. Dabe, MC	MAJ David M. Dunning, MC
LTC Lauren K. Colman,MC	MAJ Ruben D. Sierra, MC
LTC Howard Davidson, 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: Sep 89

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 $\geq$4,000/mm, platelets $\geq$100,000/mm, creatinine $\leq$1.5 mg%, BUN $\leq$22 mg%, and/or creatinine clearance $\geq$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 in FY 89. One patient was entered in FY 88 and died of his disease 13 months later.

Group-wide: Approximately 70 entries; the required accrual is 112.

**Replaced COL Dabe as the PI, Sep 89.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 87/45 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: MAJ Paul C. Sowray, MC**

Associate Investigators:	COL Irwin B. Dabe, MC
LTC Lauren K. Colman, 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: Oct 88

Study Objective: To compare, among patients with acute nonlymphocytic leukemia, the rate of complete remission produced by induction regimens of either standard dose cytosine arabinoside and daunorubicin or high-dose cytosine arabinoside and daunorubicin; to compare the duration of complete remission and of disease-free survival among patients who receive one of the three combinations of induction and consolidation regimens listed below; to determine the comparative toxicities of these three programs, and to determine the feasibility of implementing a predetermined approach to supportive care for these patients in a multi-institutional cooperative group setting.

Technical Approach: Patients will be stratified according to age and institution. Induction therapy will consist of standard dose Ara-C plus daunorubicin (Arm I) or high dose Ara-C + daunorubicin (Arm II). Patients requiring a second cycle of induction will receive the same doses as cycle 1, following the recovery of hematologic toxicities. Consolidation chemotherapy will begin when bone marrow and blood counts have recovered or on day 28 after the last induction cycle. Patients initially randomized to Arm I will be randomized to Arm III (high dose, one cycle only) or Arm IV (standard dose, two cycles). Patients initially randomized to Arm II (high dose) will be assigned to Arm III. Following the completion of consolidation, no further therapy will be given and patients will be followed only. Supportive care will include a predetermined antibiotic regimen determined by the physician.

Progress: One patient entered at MAMC in FY 89 for a total of five entries. One patient on high dose Ara-C experienced adult respiratory distress syndrome (recorded toxicity) which was ultimately fatal. Two other patients died of their disease.

Group-wide: The accrual rate on this study is presently 15.5 patients per month, slightly below the predicted rate of 16.7, despite the fact that the study remains closed to patients $\geq$65.

**Replaced COL Dabe as PI, Sep 89.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 87/34 Status: Completed

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: LTC Howard Davidson, MC

Associate Investigators:

COL Irwin B. Dabe, MC
LTC Lauren K. Colman, MC
MAJ Thomas M. Baker, MC
MAJ David Dunning, MC
MAJ Ruben Sierra, MC
CPT David R. Bryson, MC

Key Words: small cell lung cancer, chemotherapy, CAV

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Sep 89

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) 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 brain irradiation beginning on day 1. For patients presenting with a solitary brain metastasis the dose will be 30 Gy in 10 fractions. 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: No entries at MAMC in FY 89. One patient was entered at MAMC in FY 87. This patient suffered marked leukopenia but recovered. Patient later died of disease.

Group-wide: 65 eligible patients have been entered. The major toxicity noted was myelosuppression; two patients with Grade 4 myelosuppression died of sepsis. There were two partial responses and 7 stable diseases in the first 57 patients evaluated. Median survival was two months.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/64 Status: On-going

Title: SWOG 8610: Prospective Randomized Clinical Trial of the Capillary Cloning System for Patients with Extensive Small Cell Lung Cancer, Phase III

Start Date: 16 Jan 89 Est Completion Date: May 92

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Mark H. Kozakowski, MC

Associate Investigators:
MAJ Everardo Cobos, MC
COL Irwin B. Dabe, MC
CPT Kenneth Bertram, MC
LTC Howard Davidson, MC
CPT Denis Bouvier, MC

Key Words: capillary cloning, randomization, VAC

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

Objective: To evaluate the ability of the capillary cloning system to improve upon patient response and survival when compared to a standard regimen and to assess whether cloning has a place in the clinical care of patients with extensive small cell lung cancer.

Technical Approach: Patients must be ≥18 years of age, have a SWOG performance status of 0-3, and have adequate marrow, hepatic, renal, and cardiac function. All patients must have been fully clinically staged and have histologic proof of small cell lung cancer with extensive disease, bidimensionally measurable or evaluable disease, tumor accessible by biopsy, thoracentesis, or paracentesis, etc, which can be submitted for *in vitro* drug sensitivity testing. Patients must not have had prior chemotherapy, immunotherapy, or radiation therapy except for CNS lesions which required emergency radiation therapy.

Patients will be stratified by performance status, percent of body weight loss in the three months prior to study entry, presence of CNS, marrow, or liver involvement, and number of metastatic sites. Patients will be randomized to receive either therapy with vincristine, Adriamycin, and Cytoxan or have their tumor sent for capillary cloning in order to define patient specific regimens. Patients with a complete response will receive chest and prophylactic cranial irradiation followed by 3 cycles of the previous chemotherapy, and then removed from treatment with monthly follow-ups. Patients with a partial response or stable disease will remain on treatment until disease progression.

Progress: No patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 89 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 Howard Davidson, MC

Associate Investigators:

COL Irwin B. Dabe, MC
LTC Lauren K. Colman, MC
MAJ Thomas M. Baker, MC
MAJ David M. Dunning, MC
MAJ Ruben D. Sierra, MC
CPT Denis P. Bouvier, MC

Key Words: sarcoma, soft tissue, bone, doxorubicin, decarbazine ifosfamide, mesna

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Sep 89

Study Objective: To determine if the addition of ifosfamide to doxorubicin and dacarbazine significantly changes the response rate, survival, and toxicity.

Technical Approach: Patients with histologically documented metastatic or unresectable sarcoma will be eligible. Metastatic osteogenic (OGS), Ewing's (ES), and rhabdomyosarcoma (RMS) will be assigned to Arm II (doxorubicin/DTIC plus ifosfamide) and will be analyzed separately. Kaposi's sarcoma and mesothelioma will be excluded. Patients will have had no prior chemotherapy for sarcomas and no prior doxorubicin. Patients will be stratified by stage, grade, and radiotherapy history. Patients will be randomized to receive either doxorubicin/DTIC or doxorubicin/DTIC + ifosfamide. Doxorubicin, 15 mg/m^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 maximum response or until disease progression. Patients with rapid disease progression will be removed from the study. Otherwise, there will be a minimum of two cycles of chemotherapy before removal.

Progress: Two patients were entered at MAMC in FY 89, one of whom died from the disease. One patient was entered in FY 87 and one in FY 88 (died of disease). Both patients had marked leukopenia with some neutropenic fever.

Group-wide: Of the 296 eligible patients, six treatment-related deaths have been documented. Arms 1 and 2 were closed to patient entry 1 May 89 due to sufficient accrual.

Detail Summary Sheet

Date: 30 Sep 89	Protocol No.: 89/45	Status: On-going

Title: SWOG 8621: Chemo-Hormonal Therapy of Postmenopausal Receptor-Positive Breast Cancer, Phase III

Start Date: 13 Mar 89	Est Completion Date: Mar 92
Dept/Svc: Medicine/Oncology	Facility: MAMC
Principal Investigator: LTC Howard Davidson	
Associate Investigators:	MAJ Mark Kozakowski, MC
COL Irwin B. Dabe, MC	CPT Kenneth Bertram, MC
MAJ Everardo Cobos, MC	CPT Denis Bouvier, MC
Key Words: chemotherapy, hormonal therapy, tamoxifen, DES	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $2316.00	Periodic Review: N/A

Objective: To compare initial combined chemo-hormonal therapy with initial hormonal therapy with respect to survival; to compare chemo-hormonal therapy using tamoxifen with that using DES with respect to survival; and to compare combined chemo-hormonal therapy with initial hormonal therapy with respect to response in patients with measurable disease.

Technical Approach: Postmenopausal females with recurrent or disseminated breast cancer, tumor positive for estrogen receptor or progesterone receptor, and adequate bone marrow and hepatic function will be eligible. Patients who have received prior hormonal therapy or chemotherapy will not be eligible. Prior adjuvant chemotherapy will be allowed if disseminated disease developed more than six months after completing adjuvant therapy, except for tamoxifen and DES. Patients with a history of deep vein thrombosis, cerebral embolus, stroke, congestive heart failure, or ischemic heart disease will not be eligible. No concurrent malignancy is allowed except for cured non-melanoma skin cancer, *in situ* cervical cancer, or other cancer from which the patient has been disease-free for five years.

Patients will be stratified by dominant disease (osseous vs soft tissue vs visceral) and disease status. Descriptive factors will be prior adjuvant therapy; presence or absence of ascites or pleural effusions; performance status; disease free interval; number of metastatic sites, and receptor status. Patients will be randomized to: Arm I (DES); Arm II (Tamoxifen); Arm III (DES + 5-FU + cyclophosphamide + methotrexate); or Arm IV (Tamoxifen + 5-FU + cyclophosphamide + methotrexate). Patients who respond (or have prolonged disease stabilization at six months and then relapse) to tamoxifen or DES will be treated with sequential secondary and tertiary hormonal therapy if they continue to have endocrine-receptor tumors. Patients with progressive disease or short term stable disease will go off study.

Progress: No patients have been entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 89 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: Sep 89

Study Objective: To compare the effectiveness in achieving remission of the three regimens; to determine if interferon alpha-2b prolongs remission duration and survival compared to no maintenance therapy for patients achieving remission; to determine if dexamethasone plus interferon alpha-2b will enable patients achieving only improvement with the chemotherapy induction to achieve remission, and to study various proposed prognostic factors in multiple myeloma.

Technical Approach: Agents to be used are Adriamycin (A), BCNU (B), cyclophosphamide (C), dexamethasone (D), melphalan, (M), prednisone (P), vincristine (V), and alpha-2b interferon. Patients previously untreated with chemotherapy with the diagnosis of multiple myeloma are eligible. Patients will be stratified as to tumor mass, prior radiation therapy, and risk category. Patients will be randomized to induction therapy as follows: Arm I- VMCP alternating with VBAP every 3 weeks; Arm II - VAD every 3 weeks; or Arm III - VMCPP alternating with VBAPP every 3 weeks. Induction therapy on arms I and III will be given for a minimum of 9 cycles and a maximum of 18 cycles. Arm II (VAD) induction therapy will be given for a minimum of 6 cycles and a maximum of 9 cycles. Arms I and III will require a minimum of 9 cycles of induction therapy and Arm II a minimum of 6 cycles before beginning maintenance therapy. 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 maintenance to alpha-b interferon or no maintenance. Evaluable patients failing to achieve 75% tumor regression will be ineligible for remission maintenance but will be registered on a non-randomized trial of dexamethasone plus alpha 2b interferon to determine if this therapy can convert the patient to a remission status.

Progress: No entries at MAMC. Group-wide: The current accrual rate is 15 patients/month; better than anticipated.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/33 Status: Completed

Title: SWOG 8626: Phase II Study of Recombinant DNA Gamma Interferon in Advanced Cancer of the Pancreas

Start Date: 19 Feb 88 Est Completion Date: Feb 91

Department/Service: Medicine/Oncology Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
COL Irwin B. Dabe, MC
MAJ Thomas M. Baker, MC
MAJ David Dunning, MC
MAJ Ruben Sierra, MC
Cpt Denis Bouvier, MC

Key Words: pancreas, cancer, recombinant DNA gamma interferon

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

Study Objective: To determine the clinical response rate of recombinant gamma interferon in pancreatic adenocarcinoma and to define the qualitative and quantitative toxicities of recombinant gamma interferon in a Phase II study.

Technical Approach: Patients must have pathologically verified measurable pancreatic adenocarcinoma, performance status of 0-2, adequate bone marrow, renal, and cardiac function. Patients without tumor involvement of the liver must have normal hepatocellular enzymes. Patients with tumor involvement of the liver must have a bilirubin less than two times the upper limit of normal and have SGOT/SGPT and alkaline phosphatase values less than five times the upper limit of normal. Patients may have had prior surgery and prior radiotherapy provided that no more than 25% of the bone marrow was irradiated, two weeks have elapsed since the last dose, and they have recovered from any toxicity. They may be receiving concomitant radiotherapy, provided that <10% of the bone marrow is irradiated and the irradiated lesion is not being followed for determination of response. They may not have had prior cytotoxic chemotherapy or biologic response modifiers. Patients must not have had a previous malignancy other than nonmelanomatous skin cancer or *in situ* cervical cancer. Patients will be stratified by prior radiotherapy and institution. Patients will be randomized to receive r-GIFN on either Arm I (IV bolus x 5 every other x 2) or Arm II (continuous infusion x 5). Patients on Arm I will receive a starting dose of 4.0×10^6 IU/M^2, Patients on Arm II will receive a starting dose of 0.25×10^6 IU/M^2. Courses of r-GIFN will be repeated at four week intervals as tolerated. Treatment with r-GIFN will continue until progression of disease.

Progress: No entries at MAMC.

Group-wide: Thirty-two patients were evaluated on this study. There were no responses on either arm. Both arms of the study have been permanently closed as gamma interferon appears inactive in pancreatic cancer.

Detail Summary Sheet

Date: 30 Sep 89 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
LTC Lauren K. Colman, MC
MAJ Thomas M. Baker, MC
MAJ David Dunning, MC
MAJ Ruben Sierra, 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: Sep 89

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 2 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. If a complete remission is achieved, 2 additional doses of dCF will be given, treatment will then be stopped and the patient observed at monthly intervals. If a complete or partial remission has not been achieved by 6 months, the patient will be crossed over to the 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: The accrual rate has been 12.7 patient/month, greater than anticipated. One patient in each arm was removed from treatment due to toxicity: allergic reaction to interferon and neurotoxicity with deoxycoformycin. Toxicities of both regimens have been fairly limited.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/58 Status: On-going

Title: SWOG 8692 (INT-0075): Therapy in Premenopausal Women with Advanced, ER Positive or PgR Positive Breast Cancer: Surgical Oophorectomy vs the LH-RH Analog, Zoladex: Phase III, Intergroup

Start Date: 19 May 89 Est Completion Date: Jun 94

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: LTC Howard Davidson

Associate Investigators:
COL Irwin B. Dabe, MC
MAJ Everardo Cobos, MC
MAJ Mark Kozakowski, MC
CPT Kenneth Bertram, MC
CPT Denis Bouvier, MC

Key Words: medical vs surgical castration, zoladex

Accumulative MEDCASE Cost: -0-

Est Accumulative OMA Cost: -0-

Periodic Review: N/A

Objective: To compare the response rate, the time to treatment failure, and survival of medical castration using Zoladex to surgical castration in premenopausal women with advanced, ER+ or PgR+ breast cancer; to assess the response rate to surgical castration in patients failing to respond to or relapsing on Zoladex and the response rate to Zoladex in patients failing to respond to or relapsing on surgical castration; to compare toxicities of medical castration and surgical castration; to assess the value of post-treatment hormone levels in predicting response to medical castration; and to asses the effect of long term Zoladex treatment on hormone levels in responding patients.

Technical Approach: Patients must have a performance status of 0-2. Patients with extensive liver metastases, lymphangitic lung metastases, or prior hormone therapy or chemotherapy for advanced disease will be ineligible. Prior adjuvant chemotherapy is allowed; adjuvant tamoxifen is allowed provided relapse occurred $\geq$ 6 months after completion of therapy. Patients will be stratified by disease status, dominant site of disease, performance status, and prior adjuvant tamoxifen (yes or no).

Patients will be randomized to receive either surgical oophorectomy or Zoladex, 3.6 mg subcutaneously every four weeks. Surgical castration patients clearly progressing after six weeks will be crossed over to Zoladex. Patients then developing progressive disease will be taken off study. Zoladex patients with clearly progressive disease after six weeks will cross over to surgical oophorectomy. Upon development of progressive disease, patients will be removed from the study.

Progress: No patients have been entered at MAMC.

Group-wide: Accrual is well below the projected 20 patients per arm per year. Hot flashes have been the most frequently reported toxicity in the 17 patients evaluated for toxicity. Other reported toxicities on Zoladex were flare reactions, mood swings, and fluid retention.

Detail Summary Sheet

Date: 30 Sep 89 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: MAJ Paul C. Sowray, MC**

Associate Investigators:	COL Irwin B. Dabe, MC
LTC Lauren K. Colman, 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: leukemia, hairy cell, splenectomized, pentostatin

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Sep 89

Study Objective: To compare the frequency of response between pentostatin and alpha-interferon treatment in patients with hairy cell leukemia who following splenectomy manifest active or progressive disease; to compare time to response, response duration, and toxicity of these two treatments; and to determine if pentostatin salvages nonresponders to alpha-interferon treatment and if alpha-interferon salvages nonresponders to pentostatin treatment.

Technical Approach: Patients will have had splenectomy at least 3 months prior to treatment, with no prior treatment with pentostatin or interferon. Patients will be randomized to either interferon or pentostatin.

Interferon ($2x10^6$ 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. Nonresponders 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: Approximate accrual is 70 subjects. No fatal toxicities have been reported.

**Replaced COL Dabe as PI, Sep 89.

Detail Summary Sheet

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

Title: SWOG 8697: (EST 3185, INT 0077), Phase III Combination Chemotherapy of Predominantly Hormone Insensitive Metastatic Breast Cancer: An Evaluation of CAF versus Rotation Regimens of CAF and TSAVBH Induction Therapy Followed by Observation or Maintenance Therapy with CMF(P)TH or CMFH Intergroup

Start Date: 17 Feb 89 Est Completion Date: Feb 92

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: LTC Howard Davidson

Associate Investigators:
COL Irwin B. Dabe, MC
MAJ Everardo Cobos, MC
MAJ Mark Kozakowski, MC
CPT Kenneth Bertram, MC
CPT Denis Bouvier, MC

Key words: chemotherapy, alternating, CAF, TsAVbH, CMF(P)TH

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

Objective: To investigate the induction efficiency and impact on time to treatment failure and survival of CAF* vs CAF-TsAVbH** used in a rotating schedule; to investigate the value of CMF(P)TH*** vs no maintenance treatment in duration of complete response and survival; and to evaluate on-study disease characteristics and patient discriminants with respect to prognostic use of the above objectives.

Technical Approach: All patients with ER negative tumors are eligible unless they have responded to prior hormone manipulation therapy. ER positive or ER unknown patients are eligible only if they have had prior therapeutic hormone manipulation and did not respond to this therapy. Patients must have a performance status of 0-3, adequate bone marrow, renal, and hepatic function, and a blood sugar $\leq$170 mg/dL. Patients will be stratified by ER status, prior adjuvant therapy (yes vs no); dominant metastatic site; disease free interval; and menopausal status.

Patients will be randomized to either CAF for six cycles or to CAF alternating with TsAVbH (three cycles of CAF alternating with three cycles of TsAVbH). Patients with a partial response or stable disease will be registered to receive CMFH**** and those with progressive disease will go off study. Patients with a complete response will be randomized to either CMF(P)TH or to observation. Cycles will be repeated every 29 days until relapse.

Progress: No patients have been entered at MAMC.

Group-wide: Approximately 100 patients entered.

*CAF - Cytoxan, Adriamycin, 5-FU
**TsAVbH - thiotepa, Adriamycin, vinblastine, halotestin
***CMF(P)TH - cyclophosphamide, methotrexate, 5-FU, prednisone, tamoxifen, halotestin
****CMFH - Cytoxan, methotrexate, 5-FU, halotestin

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/64 Status: On-going

Title: SWOG 8715: Evaluation of Amonafide in Advanced Sarcomas, Phase II

Start Date: 15 Jul 88 Est Completion Date: Jun 91

Dept/Svc: Medicine/Hematology Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators: COL Irwin B. Dabe, MC
CPT Denis P. Bouvier, MC

Key Words: sarcoma, advanced, amonafide, response, toxicity

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Sep 89

Study Objective: To evaluate the response rate of advanced sarcomas treated with amonafide and to assess the qualitative and quantitative toxicities of amonafide in a Phase II study.

Technical Approach: To be eligible, patients must have pathologically verified soft tissue sarcoma, at least one bidimensionally measurable site of disease, Karnofsky performance status of 2 or better, and an expected survival of at least eight weeks. Patients must not be pregnant. Mesothelioma, Kaposi's sarcoma, and osteogenic sarcoma will be ineligible for the study.

Patients will be treated with amonafide, 300 mg/M^2 IV on days 1-5, repeated every 21 days. Disease assessment will be every six weeks. Patients who require radiation therapy for new lesions or lesions increasing in size will be considered to have progressive disease and taken off study. Patients will continue treatment with amonafide until tumor progression; unacceptable toxicity, a delay in treatment of $\geq$3 weeks, or at the patients request for withdrawal. All patients will be followed until death.

Progress: No patients entered at MAMC. This study was temporarily closed to patient entry 15 Sep 88 while it is determined if the number of patients entered is sufficient for analysis.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/31 Status: On-going

Title: SWOG 8721: A Phase II Trial of Trimetrexate in the Treatment of Esophageal Cancer

Start Date: 17 Feb 89 Est Completion Date: Feb 92

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: LTC Howard Davidson

Associate Investigators:
MAJ Mark Kozakowski, MC
COL Irwin B. Dabe, MC
CPT Kenneth Bertram, MC
MAJ Everardo Cobos, MC
CPT Denis Bouvier, MC

Key Words: carcinoma, epidermoid, trimetrexate

Accumulative MEDCASE Cost: -0-

Est Accumulative OMA Cost: -0-

Periodic Review: N/A

Objective: To determine the response rate, response duration, and toxicity of trimetrexate given on a daily x 5 schedule every three weeks to patients with esophageal cancer.

Technical Approach: Patients must have a biopsy proven epidermoid carcinoma that is measurable. Patients may have had previous surgical therapy. If patients have had previous radiotherapy, they must have recovered from toxicities of radiotherapy, have demonstrated progressive disease with measurable disease outside of the previous radiation therapy port, and must have received radiotherapy to less than 25% of the bone marrow. Patients must have a performance status of 0-2 and adequate bone marrow, renal, and hepatic function. Patients may not be a candidate for potentially curative resection of tumor nor a candidate for potentially curative radiation therapy. They may not have received more than one prior combination chemotherapy and must not have ascites or pleural effusions.

Patients will receive trimetrexate, IV bolus daily for five days, every three weeks. Treatment with trimetrexate will continue until progression of disease.

Progress: No patients have been entered at MAMC.

Group-wide: Nine have patients have been registered. In the five patients who have been evaluated for toxicity, there were no Grade 4 or 5 toxicities. Most of the toxicities were hematologic with some mucositis and nausea/vomiting.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/75 Status: On-going

Title: SWOG 8723: Evaluation of Amonafide in Disseminated Malignant Melanoma, Phase II

Start Date: 16 Sep 88 Est Completion Date: Sep 91

Dept/Svc: Medicine/Hematology Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

LTC Irwin B. Dabe, MC MAJ Mark Kozakowski, MC

MAJ Everardo Cobos, MC CPT Denis Bouvier, MC

Key Words: melanoma, amonafide, response rate, toxicities

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review Sep 89

Study Objective: To evaluate the response rate of disseminated malignant melanoma treated with amonafide and to assess the qualitative and quantitative toxicities of amonafide administered in a Phase II study.

Technical Approach: An initial dose of amonafide, 300 mg/M ^{W}ill be administered by IV infusion over one hour daily for five days and repeated every 21 days. One course of therapy consists of one daily x 5 administration of amonafide. Measurable disease will be assessed at least every other course (every six weeks). Patients will continue treatment with amonafide until they fulfill one of the following criteria for removal from protocol treatment: (1) tumor progression at any time while on study; (2) unacceptable toxicity requiring discontinuation of chemotherapy; (3) patient withdrawal at his/her request; or (4) delay of treatment of $\geq$ three weeks.

Patients with no prior chemotherapy, stage IV disease, and pathologically verified malignant melanoma are eligible. Patients must have objectively measurable disease and a life expectancy of at least eight weeks. Pregnant patients are not eligible.

Progress: No patients entered at MAMC.

Group-wide: This study was temporarily closed to patient entry in Oct 87 to evaluate toxicity and response. The study was reactivated in Jul 89 because it was found on analysis that 30% of the patients registered on the study were ineligible for various reasons.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/69 Status: On-going

Title: SWOG 8734: A Phase II Trial of Low Dose Pala and High Dose 5-FU as a Short Term Infusion in the Treatment of Adenocarcinoma of the Stomach

Start Date: 19 Aug 88 Est Completion Date: Jun 91

Dept/Svc: Medicine/Hematology Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
COL Irwin B. Dabe, MC
CPT Denis P. Bouvier, MC

Key Words: adenocarcinoma, stomach, low dose Pala, high dose 5-FU

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Sep 89

Study Objective: To evaluate response to a new regimen consisting of a 24-hour infusion of high dose (effector) 5-FU and low dose (modulator) PALA in patients with advanced adenocarcinoma of the stomach and to assess the qualitative and quantitative toxicities of the regimen.

Technical Approach: To be eligible, patients must have a verified diagnosis of advanced gastric adenocarcinoma, objectively measurable lesions (excluding CNS metastases), central venous access placement prior to starting therapy, a Karnofsky performance status of 2 or better, and an expected survival of at least eight weeks. Patients must not have received prior chemotherapy and must not be pregnant.

An initial dose of PALA, 250 mg/M^2 IV over 15 minutes will be followed 24 hours later by 5-FU, 2,600 mg/M^2 IV over 24 hours. The PALA will remain constant. 5-FU will be monitored and dosage modifications made if necessary. One course of therapy will consist of eight weeks of administration of PALA and 5-FU, following which response evaluation will be made. Measurable disease will be assessed at least every course (every eight weeks). Patients failing to achieve a complete or partial remission or stable disease after one course of therapy will be removed from the study. Patients will remain on treatment until tumor progression at any time while on study; unacceptable toxicity requiring discontinuation of chemotherapy; or withdrawal by the patient at his/her request. All patients will be followed until death.

Progress: No entries at MAMC.

Group-wide: The study was temporarily closed to patient entry, 12/1/88, to evaluate toxicity and response. There were 26 eligible entries. Twenty patients have been evaluated for toxicity with no Grade 4 or 5 toxicities.

Detail Summary Sheet

Date: 30 Sep 89 | Protocol No.: 88/65 | Status: On-going

Title: SWOG 8736: Treatment of Localized Non-Hodgkin's Lymphoma: Comparison of Chemotherapy (CHOP) to Chemotherapy Plus Radiation therapy

Start Date: 15 Jul 88 | Est Completion Date: Jun 91

Dept/Svc: Medicine/Hematology | Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators: COL Irwin B. Dabe, MC
CPT Denis P. Bouvier, MC

Key Words: non-Hodgkin's lymphoma, chemotherapy (CHOP), radiation

Accumulative MEDCASE Cost: -0- | Est Accumulative OMA Cost: -0- | Periodic Review: Jul 89

Study Objective: To evaluate, in a cooperative group setting, the difference in survival, time to treatment failure, and toxicity of two curative approaches to the treatment of patients with localized, intermediate or high grade non-Hodgkin's lymphoma.

Technical Approach: All patients must have biopsy proven non-Hodgkin's lymphoma of intermediate or high grade histology except lymphoblastic lymphoma. Patients must have had all visible tumor removed (excisional biopsy) and must have clinically adequate liver and myocardial function to begin treatment at full doses. Patients with known central nervous system disease, previous cancer with a possibility for recurrence which might affect survival or prior chemo or radiotherapy will be ineligible. All patients will be stratified at the time of initial registration by the following: (1) age (<65 years vs ≥65 years); (2) Stage (I or I_e vs nonbulky II or II_e); (3) histology (diffuse large cell vs other); (4) location of disease (GI involved vs non-GI, abdominal vs non-GI, other); (5) all disease resected vs residual measurable disease. Patients will be randomized to CHOP* (Arm I) or to CHOP plus radiation therapy (Arm II). A complete course of chemotherapy on Arm I will consist of the administration of CHOP every 21 days for eight consecutive cycles unless progressive disease develops. A complete course of chemotherapy for Arm II will consist of the administration of CHOP every 21 days for three consecutive cycles unless progressive disease develops. Radiation therapy will begin immediately after the third cycle of CHOP. Radiation therapy dose, duration, and treatment volume will be determined jointly by the radiation oncologist and the medical oncologist. All patients will be followed at three month intervals until death.

*CHOP: Cyclophosphamide, 750 mg/M^2 IV, day 1.
Doxorubicin, 50 mg/M^2 IV, day 1.
Vincristine, 1.4 mg/M^2 IV, day 1
Prednisone, 100 mg/day po, days 1-5

Progress: Two patients were entered at MAMC, both in FY 89.

Group-wide: Approximately 40 patients have been entered with a good balance between the treatment arms.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/76 Status: On-going

Title: SWOG 8738: Treatment of Extensive Non-Small Cell Lung Cancer: Standard Dose Cisplatin versus High-Dose Cisplatin in Hypertonic Saline Alone versus High-Dose Cisplatin/Mitomycin-C, Phase III

Start Date: 16 Sep 88 Est Completion Date: Sep 91

Dept/Svc: Medicine/Hematology Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

LTC Irwin B. Dabe, MC CPT Kenneth Bertram, MC

MAJ Mark Kozakowski, MC CPT Denis Bouvier, MC

Key Words: non-small cell lung cancer, cisplatin, mitomycin-C

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jul 89

Study Objective: To compare standard dose cisplatin chemotherapy to high dose cisplatin in hypertonic saline alone to high dose cisplatin/mitomycin-C in a randomized study with stratification for known important prognostic factors with regard to response rate, response duration, and survival duration; and to compare the relative toxicities of these three chemotherapy regimens in patients with extensive non-small cell lung cancer.

Technical Approach: Patients will be randomized to one of the following:

Arm I: standard dose cisplatin (50 mg/M^2, IV) every four weeks for a maximum of eight cycles,

ARM II: high dose cisplatin alone (100 mg/M^2, IV) every four weeks for a maximum of four cycles,

ARM III: high dose cisplatin (100 mg/M^2 IV) plus mitomycin-C (8 mg/M^2 IV) given every four weeks for a maximum of four cycles.

All patients will have an initial assessment of response after two cycles and then reassessment after four cycles of therapy. Patients on Arm I who respond to treatment may receive continued therapy to a maximum of eight cycles. Upon progression of disease, unacceptable toxicity, or patient request, patients will be taken off treatment. All patients will be followed until death.

Progress: Three patients have been entered at MAMC, all in FY 89.

Group-wide: Accrual is running at about 50% of the expected rate.

Detail Summary Sheet

Date: 30 Sep 89	Protocol No.: 89/59	Status: On-going

Title: SWOG 8748: Alternating Induction Chemotherapy with Weekly Adriamycin and 5-Fluorouracil/Leucovorin Followed by Adriamycin and Cyclophosphamide: A Phase II Study in Poor Risk, Stage IV Breast Cancer

Start Date: 19 May 89	Est Completion Date: Jun 91
Dept/Svc: Medicine/Oncology	Facility: MAMC
Principal Investigator: LTC Howard Davidson	
Associate Investigators:	MAJ Mark Kozakowski, MC
COL Irwin B. Dabe, MC	CPT Kenneth Bertram, MC
MAJ Everardo Cobos, MC	CPT Denis Bouvier, MC
Key Words: breast cancer, chemotherapy, alternating	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $1320/patient	Periodic Review: N/A

Study Objective: To evaluate complete and partial response rates to the combination of alternating induction chemotherapy with weekly Adriamycin and 5-FU/leucovorin, followed by Adriamycin and cyclophosphamide in poor risk, Stage IV breast cancer; to assess toxicity from this combination; and to measure observed response, duration, and survival.

Technical Approach: Patients must have a histologic diagnosis of adenocarcinoma of the breast with biopsy or clinical evidence of bidimensionally measurable disseminated or recurrent disease. If bone metastases or pleural effusions are the only site of disease, patients are not eligible. Patients may not have brain or meningeal metastases. ER/PgR values may be of any combination with the following restrictions: ER-/PgR- or ER-/PgR unknown patients may have received no prior chemotherapy for disseminated disease; prior non-Adriamycin-containing adjuvant chemotherapy is permitted. Patients that are ER+/PgR+, ER-/PgR+, ER+/PgR-, ER+/PgR unknown or ER/PgR unknown are eligible if they have developed disease progression after receiving a non-Adriamycin based chemotherapy program for recurrent disease or within six months of completion of such a program as adjuvant therapy; and they must have either received and failed prior hormonal therapy or have visceral disease predictive for poor response to hormonal therapy. Prior treatment may include 5-FU (not 5-FU-CF) and cyclophosphamide. Prior Adriamycin is not allowed. Patients must have a performance status of 0-2; no history of congestive heart failure; adequate hepatic, renal and bone marrow function; and no history of other previous malignancy except primary squamous or basal cell carcinoma of the skin or cervical carcinoma *in situ* or Stage I. Adriamycin, 20 mg/M^2 will be given every other week for 12 weeks and then weekly. 5-FU, 600 mg/M^2, and calcium leucovorin, 500 mg/M^2, will be given every other week for six weeks, alternating with Adriamycin. Cyclophosphamide will be given daily starting with day 85.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 89	Protocol No.: 88/21	Status: On-going

Title: SWOG 8792 (EST 2886, INT 0079): Phase III Study of Alfa-nl (Wellferon) as Adjuvant Treatment for Resectable Renal Cell Carcinoma

Start Date: 15 Jan 88	Est Completion Date: Dec 90
Dept/Svc: Medicine/Hematology	Facility: MAMC
Principal Investigator: LTC Howard Davidson, MC	
Associate Investigators:	MAJ David M. Dunning, MC
COL Irwin B. Dabe, MC	MAJ Ruben D. Sierra, MC
MAJ Thomas M. Baker, MC	CPT Denis P. Bouvier, MC
Key Words: carcinoma, renal cell, Alfa-nl	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Sep 89

Study Objective: To assess in a controlled fashion the effectiveness of interferon alfa-nl (Wellferon) as a surgical adjuvant in patients with renal cell carcinoma. Study endpoints will be patient survival and time to recurrence.

Technical Approach: Patients must have histologic proof of adenocarcinoma of the kidney where complete resection of the primary tumor has been performed with neither gross nor microscopic evidence of residual disease. The primary kidney cancer must show at least one of the following indicators of poor prognosis: tumor invading perinephric fat; invasion of renal vein or vena cava; regional lymph node metastases, or contiguous metastases resected. Surgical margins must be free of tumor and radical nephrectomy and lymphadenectomy must have been performed. Performance status must be 0 or 1. Patients with prior or concurrent radiotherapy, chemotherapy, or systemic corticosteroid therapy are ineligible. Patients with impaired hepatic or renal function, angina, or active congestive heart failure, and seizure disorders as well as pregnant or lactating females are ineligible. Patients will be randomized to Wellferon or observation following definitive surgery. Adjuvant treatment will be started no later than 30 days after resection of the primary and regional nodes. Patients will be stratified according to modified TNM classification for renal tumors, tumor invasion of neighboring structures, and tumor involving regional nodes. Patients randomized to observation only will be followed at 3, 6, 9, 12, 18, and 24 months and every 6 months thereafter. Patients randomized to observation only will be taken off study on recurrence. Patients on the treatment arm will receive Wellferon as an intramuscular injection daily x 5 days every 3 weeks for a total of 12 cycles (nine months), unless recurrence of renal cell carcinoma is documented or intolerable toxicity occurs. These patients will be followed at 12, 18, and 24 months after entry and at six month intervals thereafter.

Progress: No patients entered at MAMC.

Group-wide: There have been no Grade 4 or 5 toxicities. Five patients randomized to the Wellferon arm experienced severe reaction (flu-like symptoms in 4 patients and granulocytopenia in one).

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/60 Status: On-going

Title: SWOG 8795 (INT-0094, EST-1888): Randomized Prospective Comparison of Bacillus Calmette-Guerin (BCG) and Mitomycin-C Therapy and Prophylaxis in Superficial Transitional Cell Carcinoma of the Bladder with DNA Flow Cytometric Analysis. Phase III

Start Date: 19 May 89 Est Completion Date: Jun 92

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Everardo Cobos, MC

Associate Investigators:

COL William D. Belville, MC	LTC John Vaccaro, MC
COL Irwin B. Dabe, MC	MAJ Mark Kozakowski, MC
COL Victor J. Kiesling, MC	CPT Kenneth Bertram, MC
LTC Howard Davidson	CPT Denis Bouvier, MC

Key Words: carcinoma, bladder, Calmette-Guerin, chemotherapy

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

Study Objective: To compare the efficacy of mitomycin-C to that of BCG in preventing recurrence of superficial Stage Ta and T1 transitional cell carcinoma of the bladder and to compare treatments with respect to differences in flow cytometry histogram findings of tumors at the time of recurrence.

Technical Approach: Patients must have a diagnosis of Stage Ta or T1 (Grades 1-4) transitional cell carcinoma of the bladder that has been completely resected. Concurrent unresectable carcinoma *in situ* (CIS) is allowed. Histologic confirmation of the disease must come from a transurethral resection done within 4 weeks prior to registration. A random biopsy done 1-4 weeks prior to registration is required. Patients must be judged to be at increased risk for tumor recurrence as demonstrated by 2 occurrences of tumor within 12 months prior to registration. Patients must not have received any prior systemic chemotherapy. Patients may have had treatment with any intravesical agent other than mitomycin-C or BCG; however, the treatment must not have been within 4 weeks prior to registration. Patients must not have received radiation therapy for treatment of bladder tumor within one year prior to registration. Patients must not have a history of another primary malignancy or CIS at any site other than the bladder. Patients must have adequate bone marrow reserve, adequate renal and liver function, and a performance status of 0-2. Patients will be stratified by CIS involvement: Stage Ta or T1 without concurrent CIS vs Stage Ta or T1 with concurrent CIS.

Patients will be randomized to BCG, 50 mg weekly x 6, then at wks 8 and 12 and then monthly for months 4-12 or mitomycin-C, 20 mg on the same schedule. Cystoscopy, cytology, biopsy, and flow cytometry will be done prestudy and at 3, 6, 9, and 12 months.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/66 Status: On-going

Title: SWOG 8796: Combination Chemotherapy for Advanced Hodgkin's Disease, Phase III Intergroup (INT 0074)

Start Date: 15 Jul 88 Est Completion Date: Jun 91

Dept/Svc: Medicine/Hematology Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators: COL Irwin B. Dabe, MC
CPT Denis P. Bouvier, MC

Key Words: Hodgkin's, advanced, chemotherapy, MOPP, ABVD

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Sep 89

Study Objective: To compare the effectiveness of the MOPP/ABV hybrid with sequential MOPP---->ABVD in patients with advanced or recurrent Hodgkin's disease and to determine which regimen is superior with respect to the following parameters: complete response rate, duration of complete response, freedom from progression, and survival.

Technical Approach: Patients must have histologic confirmation of Hodgkin's disease with no prior chemotherapy. Patients will be stratified according to age, prior radiotherapy, bulky disease, and performance status. They will then be randomized to MOPP repeated every 28 days for 6 cycles (Arm I) or to MOPP/ABV Hybrid repeated every 28 days for six cycles (Arm II). Patients on Arm I with a complete response will go on to ABVD repeated every 35 days for three cycles. Those with partial response will receive two MOPP cycles and then go on to ABVD for three cycles. Those with no change will go off study. Those patients on Arm II with complete response will receive two more cycles of MOPP/ABV. Those with partial response will continue MOPP/ABV to complete response or until a maximum of 12 cycles. Those with no change will be taken off study.

MOPP: Nitrogen mustard, 6 mg/M^2 IV, days 1 and 8
Vincristine, 1.4 mg/M^2 IV, days 1 and 8
Procarbazine, 100 mg/M^2 PO per day x 14 days
Prednisone 40 mg/M^2 PO per day x 14 days

ABVD: Adriamycin, 25 mg/M^2 IV, days 1 and 15
Bleomycin, 10 units/M^2 IV, days 1 and 15
Vinblastine, 6 mg/M^2 IV days 1 and 15
DTIC, 375 mg/M^2 IV, days 1 and 15

The MOPP/ABV hybrid consist of the MOPP regimen plus adriamycin, 35 mg/M^2 IV, day 8; bleomycin, 10 units/$M^2$2 IV day 8; and vinblastine, 6 mg/M^2 IV, day 8.

Progress: One patient entered at MAMC (FY 89).

Group-wide: This study was closed in Aug 89 due to sufficient patient accrual.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/65 Status: On-going

Title: SWOG 8812: Treatment of Limited Small Cell Lung Cancer with Concurrent Chemotherapy, Radiotherapy, With or Without GM-CSF, and Subsequent Randomization to Maintenance Interferon or No Maintenance

Start Date: 7 Jun 89 Est Completion Date: Jun 92

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Mark H. Kozakowski, MC

Associate Investigators:
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Key Words: small cell lung cancer, chemo/radiotherapy, interferon

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

Study Objective: To compare the days of neutropenia, the days of leukopenia, the incidence and severity of infections, the incidence and duration of fever, the days on antibiotics, and the days of hospitalization between patients receiving GM-CSF and those not receiving it; to evaluate the toxicities of GM-CSF; to evaluate the ability of rHuIFN α2a to prolong remission duration and survival; and to evaluate the toxicities of rHuIFN α2a.

Technical Approach: Patients must have histologically proven small cell carcinoma of the lung. Prior to treatment patients will be staged as to the extent of disease. Only patients with limited disease are eligible for this study. Patients must have evaluable or measurable disease, a pretreatment WBC >4,000 µl, absolute granulocyte count >1500 µl, platelet count >100,000/µl, serum creatinine of <2.0 mg%, creatinine clearance of >50 ml/min, and performance state of 0-2 by SWOG criteria. Pregnant patients or those with prior radiation therapy, chemotherapy, colony stimulating factors, or interferon are not eligible. Patients with malignant pericardial or pleural effusions, a past medical history of congestive heart failure, extensive pulmonary disease, poor pulmonary reserve, or a history of seizures are ineligible. Patients will be stratified at initial registration by institution and at second registration according to performance status (0-1 vs 2); sex; response (complete vs partial); and induction arm (GM-CSF vs no GM-CSF).

Patients will be randomized to receive induction chemotherapy (cis-platin + VP-16) and concurrent chest radiotherapy with or without GM-CSF. Consolidation chemotherapy will be as in induction but with no radiotherapy. Those patients achieving a complete remission will be randomized to receive or not receive maintenance therapy with recombinant alpha interferon. All patients who have achieved a complete response by week 33 will receive prophylactic cranial irradiation to the brain. Patients with stable disease, progression, or relapse at any point will be taken off study.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/80 Status: On-going

Title: SWOG 8814 (ECOG 4188, NCCTG 883051): Phase III Comparison of Adjuvant Chemoendocrine Therapy with CAF and Concurrent or Delayed Tamoxifen to Tamoxifen Alone in Postmenopausal Patients with Breast Cancer Having Involved Axillary Lymph Nodes and Positive Receptors

Start Date: 11 Sep 89 Est Completion Date: Sep 99

Dept/Svc: Medicine/Oncology Facility: MAMC

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Key Words: cancer, breast, chemotherapy, chemoendocrine

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $8692.00/yr	Periodic Review: N/A

Study Objective: To compare disease-free survival and overall survival of postmenopausal primary breast cancer patients with involved axillary nodes and positive estrogen and/or progesterone receptors treated with standard adjuvant therapy with long-term Tamoxifen or with chemoendocrine therapy with CAF, followed by long-term Tamoxifen or with concurrent chemoendocrine therapy with Tamoxifen and CAF and to compare the relative toxicity of the three therapies.

Technical Approach: Tumors must be pathologic stage T1, T2, or T3; N; MO (Stage II or selected Stage IIIA). Patients must have histologically proven adenocarcinoma of the breast with at least one positive lymph node (tumor and/or nodes must not be fixed). Patients must have undergone a radical, modified radical, or breast sparing procedure plus axillary dissection (level I or level II). Patients with bilateral breast cancer are ineligible. Estrogen and progesterone receptors must be assayed and one and/or the other must be positive by the institutional laboratory standards of $\geq$10 fmol/mg protein. Prestudy studies must reveal no evidence of metastatic disease. Prior hormonal or chemotherapy is not allowed and prior postmenopausal estrogen therapy is allowed but must be discontinued before registration. Stratification factors will include: involved nodes (1-3, >4); PgR+ (ER positive or negative) vs PgR- (ER positive); time from surgery to randomization ($\leq$6 vs >6 weeks).

Patients will be randomized to one of three treatment arms:

Arm I: Tamoxifen x 5 years
Arm II: Intermittent CAF x 6 courses followed by Tamoxifen x 5 years
Arm III: Intermittent CAF x 6 courses with concurrent tamoxifen x 5 years.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/21 Status: On-going

Title: SWOG 8899: A Prospectively Randomized Trial of Low-Dose Leucovorin Plus 5-FU or Observation Following Curative Resection in Selected Patients with Duke's B or C Colon Cancer

Start Date: 17 Feb 89 Est Completion Date: Feb 92

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: LTC Howard Davidson

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Key Words: colon, Duke's B/C, resection, chemo, observation

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $50.00	Periodic Review: N/A

Study Objective: To assess the effectiveness of 5-FU + high-dose Leucovorin as surgical adjuvant therapy for resectable colon cancer, when compared to surgery alone.

Technical Approach: Patients must have received a potentially curative surgery for colon cancer with neither gross nor microscopic evidence of residual disease following the complete resection. The resected specimen must pathologically verify a diagnosis of modified Duke's B-2, B-3, or C. The primary tumor must be above the peritoneal reflection. There must be no regional metastases that have not been resected enbloc with the primary lesion. Patients may not have had any prior chemotherapy nor exposure to 5-FU. Surgery must have taken place 21-30 days prior to registration. Patients must be maintaining oral nutrition and be ambulatory 50% of the day and have adequate bone marrow function. Patients may not have a concurrent second malignant disease nor any previous malignant tumor within three years.

Patients will be stratified by extent of invasion (limited to bowel wall vs into or through serosa vs perforation vs adherence to adjacent organs vs invasion of adjacent organs); extent of regional nodal metastases (none vs 0-4 vs >4); regional/mesenteric implants resected enbloc (yes/no); and obstruction (yes/no).

RANDOMIZE TO: (1) Observation

(2) Leucovorin 20 mg/m^2 + 5-FU 425 mg/m^2; days 1-5; repeat at 4 and 8 wks, then every 5 wks for a total of 6 courses

(3) Leucovorin 500 mg/m^2 + 5-FU 600 mg/m^2; Leucovorin by IV 2 hour infusion; 5-FU IV push beginning 1 hr after start of Leucovorin infusion; repeated weekly for 6 wks, followed by a 2-wk rest period; each 8-wk cycle (1 course) will be repeated for 4 courses.

Progress: Four patients at MAMC entered in FY 89.

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

F O R

P R O T O C O L S

UNIVERSITY OF WASHINGTON NEURO-ONCOLOGY GROUP

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/73 Status: On-going

Title: UWNG 86/01: Phase II Study of External Brain Irradiation and Hydroxyurea Followed by Procarbazine, CCNU, and Vincristine (PCV) for the Treatment of Primary Malignant Brain Tumors

Start Date: 19 Aug 88 Est Completion Date: Jul 91

Dept/Svc: Medicine/Hematology Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

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Key Words: brain, tumors, external irradiation, chemotherapy

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Sep 89

Study Objective: To evaluate radiation therapy plus hydroxyurea and PCV in terms of the following parameters: time to progression from start of therapy, response rates and stabilization rate, survival time from start of therapy, and quality of life and activity level (Karnofsky).

Technical Approach: Patients must have a primary intracranial malignant glioma. Most patients will have had some form of surgery. Treatment will begin within four weeks of the operation at which the current diagnosis was made or within four weeks of clinical diagnosis. No prior cytotoxic, chemotherapy, or radiation therapy will be permitted. Local field radiotherapy will be employed. Only one course of radiotherapy will be given. The total dose to the tumor will be 5940 cGy delivered in a period of 6-7 weeks. The tumor volume will include at least the enhanced portion of tumor based on CT scan and a 2-3 cm margin of normal tissue in all directions. Every other day during radiotherapy, beginning day 1, patients will receive hydroxyurea, 300 mg/M^2 every six hours. PCV treatment will begin within two weeks after radiotherapy. CCNU, 110 mg/M^2 po, will be given on day one of each course. Procarbazine, 60 mg/M^2 po will be given days 8-14. Vincristine, 1.4 mg/M^2, will be given IV push on days 8 and 29. Patients will be evaluated and courses given at six to eight week intervals in the absence of irreversible toxicity. Patients will remain on protocol until the completion of two full courses of PCV. If tumor progression is documented after the second course, the patient will be taken off protocol. If tumor progression is not demonstrated, PCV will be given for one year or a minimum of 6 courses (not to exceed 8 courses) and then stopped. All patients will be followed for survival. Patients who expire from tumor progression early in the course of therapy will be evaluable for analysis if one full course of PCV was administered.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 88/17 Status: On-going

Title: UWNG 87-01: Phase II Study of TPDCFH for Recurrent Malignant Brain Tumor

Start Date: 11 Dec 87 Est Completion Date: Sep 90

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: LTC Howard Davidson

Associate Investigators:

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Key Words: brain tumor, 6-thioguanine, procarbazine, dibromodulcitol, CCNU, 5-FU, hydroxyurea

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $100.00	Periodic Review: Oct 88

Study Objective: To determine whether TPDCFH chemotherapy for recurrent malignant glioma will increase time to progression and survival rate and to document the toxicity attendant on combined treatment.

Technical Approach: Patients will be eligible for this study if: they have received primary surgical treatment, radiotherapy, or adjuvant chemotherapy but no radiotherapy or chemotherapy for 8 weeks prior to entry; the tumor is a histopathologically confirmed recurrence of a malignant supratentorial glioma; liver and renal function are not seriously impaired (liver enzymes and serum creatinine within 1.5 x normal for laboratory; Karnofsky performance status is $\geq$60%. Recurrence will be signaled by worsening neurologic symptoms and signs measured by a neurologic examination. Enlargement of tumor volume as measured in contrast and noncontrast CT scans will serve as an additional criterion of recurrence. All patients will receive the following schedule:

0-66 hr: 6-thioguanine, 30 mg/sq.m., q. 6 hr p.o. x 12 doses
60-78 hrs: procarbazine, 50 mg/sq.m., q. 6 hr p.o. x 4 doses
60 hrs: dibromodulcitol, 400 mg/sq.m., p.o.
72 hrs: CCNU, 100 mg/sq.m., p.o.
Days 14 & 15: 5-FU, 1 g/sq.m. continuous infusion over 48 hrs
Day 15, hydroxyurea, 1 g/sq.m. p.o., 4 hours before the 5-FU infusion ends and at 4 hr intervals for a total of 3 doses

The cycle will be restarted on day 37-48, depending on toxicity level. In general WBC and platelets should increase to WBC >4000/cu mm and platelets >125,000/cu mm. Exceptions may be made to restart when WBC >3600/cu mm for patients with chronically depressed bone marrow.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/13 Status: On-going

Title: UWNG 88-01: Phase II Study of High Dose Methotrexate and Craniospinal Irradiation for the Treatment of Primary Lymphoma of the Central Nervous System

Start Date: 20 Jar 89 Est Completion Date: Nov 92

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: LTC Howard Davidson

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Key Words:

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $328.00	Periodic Review: N/A

Objective: To evaluate this regimen; the endpoints of analysis will be time to progression of disease from beginning of therapy; response rates and disease stabilization rates; survival time measured from the beginning of therapy; quality of life and activity level measured by Karnofsky performance status.

Technical Approach: Patients must have a non-Hodgkin's lymphoma of the central nervous system with adequate renal, bone marrow, and liver functions and a performance status of $\geq$70%. HIV antibody titer must be negative. No prior chemotherapy or radiotherapy is permitted.

Methotrexate, 4 g/m^2, will be administered over a four hour period. Calcium leucovorin, 25 mg, will be administered beginning 20 hours after completion of the methotrexate infusion and repeated for 8 doses parenterally on an every 6 hour basis following which an additional four doses will be administered every six hours by mouth. The methotrexate regimen will be administered every two weeks for three courses. Radiotherapy will begin two weeks after completion of methotrexate, and will consist of 5040 cGy to whole brain at 180 cGy/fraction (28 fractions) and 3060 cGy at 170 cGy/fraction (19 fractions) to spinal axis. Time to progression will be measured from the initiation of therapy until progression is documented. At that time the patient will be removed from the protocol and can be treated with other therapy as indicated. Patients will be followed until death.

Progress: No patients entered at MAMC.

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