Department of Clinical Investigation

Annual Research Progress Report

Fiscal Year **1990**

Madigan Army Medical Center
Tacoma, Washington 98431-5454

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ANNUAL PROGRESS REPORT

30 September 1990

DEPARTMENT OF CLINICAL INVESTIGATION

MADIGAN ARMY MEDICAL CENTER

TACOMA, WASHINGTON 98431-5454

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Department of Clinical Investigation
Madigan Army Medical Center
Tacoma, Washington 98431-5454

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13. ABSTRACT (Maximum 200 words)

This report covers all research protocols that were administratively or technically supported by the Department of Clinical Investigation, Madigan Army Medical Center, during FY 90. Included in the individual reports are title, investigators, funding, objective, technical approach, and progress for FY 90. 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.

14. SUBJECT TERMS

Research protocols, investigators, objectives, technical approach, progress, funding

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FISCAL YEAR 1990

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.

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 1990.

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.

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

UNIT SUMMARY FY 90

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	06	61C9A
C, Clinical Studies Service JONES, Robert E., M.D., LTC, MC	05	61C9B
C, Laboratory Animal & Surgery Svc MacMILLAN, James G., D.V.M., MAJ, VC	04	64C9B
C, Microbiology Svc van HAMONT, John E., Ph.D., CPT, MS	03	68A9B
C, Biochemistry Service (May - Sep 90) MOORE, Katherine H., Ph.D., CPT, MS	03	68C9C
C, Biological Research Svc HOOP, Rita C., M.S., CPT, MS	03	68C00
Biochemist PRICE, Gary H., LTC, MS	05	68C9B
NCOIC (Mar - Sep 90) SSG HANDY, Kevin	E6	92B3M4
NCOIC (Oct 89 - Mar 90 SGT SPAHN Shelley	E5	91T20
OR TECH (Oct 89 - Jun 90) SGT WILLIAMS, Gary L.	E5	91D20
Med Lab Spec (Oct 89 - Mar 90) SGT GONZALEZ/RESTO, Alexander	E5	92B10
Vet Animal Spec SGT HEATH, George	E5	91T20
Vet Animal Spec (Oct 89 - Mar 90) SPC WESTMORELAND, Jacalyn	E4	91T10

DESCRIPTION	RANK	MOS
Vet Animal Spec SPC WILLON, Thomas	E4	91T10
Med Tech (Oct 89 - Jan 90) KETTLER, Thomas M.	GS9	0644
Med Tech MATEJ, Louis A.	GS9	0644
Med Tech WRIGHT, James R.	GS9	0644
Computer Programmer Analyst (temp) PATIENCE, Troy H.	GS7	0334
Edit Asst/Steno WHITTEN, Nancy J.	GS6	1087
Sec/Steno HOUGH, Eugenia R.	GS5	0318
Maintenance Worker KAEO, Curtis	WG7	4749

FUNDING FY 90

MEDCASE Equipment	$132,678.00
CEEP	28,880.00
Civilian Salaries	179,704.00
Military Salaries	508,477.00
Consumable Supplies	96,234.00
Contractual Services	13,488.00
TDY	2,000.00
Rent	1,800.00
TOTAL	$962,456.00

GRANTS: AMOUNT: $140,000.00 Source: NIH

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

PRINCIPAL INVESTIGATOR: LTC Barbara S. Turner, AN

HSC #89222 MAMC #89028

3. Progress

During FY 90 there were 326 active protocols that received administrative and/or technical support during the year. Of these, 240 are presently ongoing; 2 are suspended, 62 were completed; and 22 were terminated.

There were 82 publications and 57 papers were presented at regional, national, or international meetings.

4. Fellowship/Residency Program Support

Fellowship/Residency programs using DCI: 18
Number of protocols: 159
Number fellows/residents holding protocols: 93

5. Other training programs using DCI:

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

Nurse Anesthetist Course protocols: 2

Active Duty Graduate Students protocols: 5

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

Commander

Madigan Army Medical Center
BG JOHN E. HUTTON, M.D., MC

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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 1990:

RENFER, Leonard G. CPT, MC	Digitally-Directed Transrectal Biopsy Using the Biopty Gun Versus Transrectal Needle Aspiration: A Comparison of Diagnostic Yield and Comfort

OTHER NOMINEES WERE:

DUNLOW, Susan G. CPT, MC	Microbiology of the Lower Genital Tract and Amniotic Fluid in Asymptomatic Preterm Patients with Intact Membranes and Moderate to Advanced Degrees of Cervical Effacement and Dilation
HERPOLSHEIMER, Arthur CPT, MC	Pulmonary Function of Pre-eclamptic Women Receiving Intravenous Magnesium Sulfate Seizure Prophylaxis
KAZRAGIS, Robert J. CPT, MC	Hepatitis B Vaccine (Recombivax) - Abbreviated Schedule Vaccination Trial
PLATT,McKay L. CPT, MC	Renal Viability After Suprarenal Inferior Venacaval Narrowing (Just How Much Can One Kidney Stand?)
VOCKROTH, John H. CPT, MC	Does Aluminum Absorption During Treatment with Sucralfate Affect Bone Metabolism?

PUBLICATIONS

FISCAL YEAR 1990

DEPARTMENT OF CLINICAL INVESTIGATION

Backous DD Farrow FA Friedl KE	Assessment of Pubertal Maturity in Boys Using Height and Grip Strength. J Adolescent Health Care 11(5): 1990
Friedl KE Hannan CJ Jones RE Plymate SR	High-Density Lipoprotein Cholesterol is Not Decreased If An Aromatizable Androgen Is Administered. Metabolism 39(1): 69-74, 1990
Jones RE	Ovarian Follicles in Reptile and Birds by S.S. Guraya (Book Review). Quarterly Review of Biology 65(0): 83, 1990
Lampe TH Plymate SR	Gonadotropin Response to Gonadotropin-Releasing Hormone (GNRH) in Men with Alzheimer's Disease. Clinical Research 38(1): 143, 1990
Lampe TH Veith RC Plymate SR Risse SC Kopeikin H Cubberley L Raskind MA	Pressor, Norepinephrine, and Pituitary Responses to Two TRH Doses in Alzheimer's Disease and Normal Older Men. Psychoneuroendocrinology 14(4): 311-20, 1989
Loop SM Plymate SR Ostenson RC Rosner W	The Role of Sex-Hormone Binding Globulin in the Growth of Human Prostate Carcinoma Cell Lines. Clinical Research 38(1): 147, 1990
Plymate SR Hoop RC Jones RE Matej LA	Regulation of Sex Hormone Binding Globulin (SHBG) Production by Growth Factors. Metabolism Clin Exp 39(9): 967-70, 1990
Plymate SR Namkung PC Matej LA Petra PH	Direct Effect of Plasma Sex Hormone Binding Globulin (SHBG) on the Metabolic Clearance Rate of 17 B-Estradiol in the Primate. J Steroid Biochemistry 36(4): 311-17, 1990
Strovas J	Height, Grip Strength Predict Injury Risk (based on two MAMC papers by Backous). Physician and Sportsmedicine 18(11): 24, 1990
van Hamont JE Wright JR	Analysis of Host-Reactive Hybridoma Clones Induced by Ureaplasma Urealyticum Antigens. Abstr Ann Meet Am Soc Microbio 90(0): 141, 1990

DEPARTMENT OF EMERGENCY MEDICINE

Gendron BP — Loxosceles reculsa Envenomation. Amer J Emergency Medicine 8(1): 51-54, 1990

Moore GP, Pace SA, Busby W — Comparison of Intraosseous, Intramuscular, and Intravenous Administration of Succinylcholine. Pediatr Emer Care 5(4): 209-210, 1989

DEPARTMENT OF FAMILY PRACTICE

Blount BW — Two Types of Metal Fume Fever: Mild vs Serious. Military Medicine 155(8): 372-77, 1990

Blount BW — Lightning Injuries. American Family Physician 42(2): 405-15, 1990

Gusberg SB, Lowman J, Gleming ID, Beahrs OH, Henley CE, Mixson WT, McGivney WT, Matchar DB, Mortenson LE, Hogan CM — Breakout 4: Health Professional Concerns in the Practice Setting. Cancer 65(10): 2413-14, 1990

Henley CE, Magelssen DJ — Faculty Development and Organizational Behavior. Academic Medicine 65(6): 406-09, 1990

Kugler JP, Connell FA, Henley CE — Lack of Difference in Neonatal Mortality Between Blacks and Whites Served by the Same Medical Care System. Journal of Family Practice 30(3): 281-288, 1990

Kugler JP, Connell FA, Henley CE — An Evaluation of Prenatal Care Utilization in a Military Health Care Setting. Military Medicine 155(1): 33-38, 1990

DEPARTMENT OF MEDICINE

Bouvier DP — Hypocalcemia and an Inappropriate Endocrine Response in Osteoblastic Metastatic Breast Cancer. Southern Medical Journal 82(12): 1574-76, 1989

Bouvier DP, Bell BK — Small Cell Carcinoma of the Pleura. Southern Medical Journal 82(11): 1437-1438, 1989

Bouvier DP
Fox CW
Frishberg DP
Kozakowski M
Cobos E

A Solitary Testicular Relapse of A Rhabdomyosarcoma in an Adult. Cancer 65(11): 2611-14, 1990

Cobos E
Gandara DR
Geier LJ
Kormani S

Post-Transfusion Purpura and Isoimmune Neonatal Thrombocytopenia in the Same Family. American Journal of Hematology 32(3): 235-36, 1989

Hobbs CJ
Plymate SR
Jones RE
Matej LA

Effect of Sex Hormone Binding Globulin (SHBG) on Testosterone Transport and Distribution. Clinical Research 38(1): 97, 1990

Koenig K
Lindberg J
Cushner H
Copley J

Effect of Citrate and pH on Aluminum Bioavailability. Kidney International 37(1): 305, 1990

Lyons MF
Pearce WA
Tsuchida AM

Meckel's Diverticulum: The Gastroenterologist's Bane of Abdominal Pain. Gastroenterology 98(5): A421, 1990

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Blakeslee DB
Andrade P

Nasal Polyps - A Manifestation of Allergy? Otolaryngology H&N Surg 101(6): 641-46, 1989

Radentz WH
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Congenital Common Blue Nevus. Archives of Dermatology 126(1): 124-25, 1990

Roth BJ
Crawford S

Fungal Infection with Non-Hodgkin's Lymphoma (letter). Chest 98(2): 512, 1990

Roth BJ
O'Meara TF
Cragun WH

The Serum Effusion Albumin Gradient in the Evaluation of Pleural Effusions. Chest 98(3): 546-49, 1990

Tsuchida AM
Lyons MF
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Walter MH

Endoscopic Balloon Dilation in Gastric Outlet Obstruction: 5 Year Experience on 25 Patients. Gastrointestinal Endoscopy 36(2): 188, 1990

Vockroth JH
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Tsuchida AM

Does Absorption of Aluminum During Treatment with Sucralfate Affect Bone Metabolism. Gastroenterology 98(5): 144, 1990

DEPARTMENT OF NURSING

Campbell LC
Weis FR

Comparison of Three Techniques on Time to Awakening, Time to Orientation, and Incidence of Nausea and Vomiting Using Alfentanil in Balanced Anesthesia in an Outpatient Surgical Setting. J Amer Assoc Nurse Anesthetist 58(3): 241-247, 1990

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Counselling Employees at Risk for HIV. AADHN Journal 37(10): 404, 1989

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Walker HJ
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Tuggle JM
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Young SB

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DEPARTMENT OF OB/GYN

Brady WK
Duff P
Read JA
Harlass FE

Reliability of Fetal Buttock Blood Sampling in Assessing the Acid-Base Balance of the Breech Fetus. Obstetrics and Gynecology 74(6): 886-88, 1989

Brady WK
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Plasma Fibronectin Concentrations During Normal Term Labor. Obstetrics and Gynecology 75(4): 619-21, 1990

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Aamodt LW

The Effect of Bacteriostatic Lubricant on Group B Streptococcal Cultures of the Female Genital Tract. Obstetrics and Gynecology 74(6): 848-50, 1989

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Dunlow SG, Duff P — Prevalence of Antibiotic Resistant Uropathogens in Obstetric Patients with Acute Pyelonephritis. Obstetrics and Gynecology 76(2): 241-44, 1990

Dunlow SG, Duff P — Microbiology of the Lower Genital Tract and Amniotic Fluid in Asymptomatic Preterm Patients with Intact Membranes and Moderate to Advanced Degrees of Cervical Effacement and Dilation. Amer Journal of Perinatology 7(3): 235-358, 1990

Harlass FE, Duff P — The Duration of Labor in Primiparas Undergoing Vaginal Birth After Cesarean Delivery. Obstetrics and Gynecology 75(1): 45-47, 1990

Harlass FE, Duff P, Herd M — The Evaluation of Urine pH in Screening for Asymptomatic Bacteriuria in Pregnancy. Military Medicine 155(2): 49-51, 1990

Kopelman JN, Miyazawa K — Biparietal Diameter Femur Length Ratio as Predictor of Trisomy-21. Amer J Obstetrics/Gynecology 162(5): 1346, 1990

Kopelman JN, Miyazawa K — Inadvertent 5-Fluorouracil Treatment in Early Pregnancy - A Report of 3 Cases. Reproductive Toxicology 4(3): 233-35, 1990

Lee RB, Burke TW, Park RC — Estrogen Replacement Therapy Following Treatment for Stage I Endometrial Carcinoma. Gynecologic Oncology 36(2): 189-91, 1990

DEPARTMENT OF PEDIATRICS

Albano EA, Pizzo EA, Kuhl J — Infections of the Immunocompromised Host with Cancer. IN Current Therapy in Pediatrics 20: 481-96, 1989; Eichenwald HF, Stroder J(eds) BC Becker, Inc.

Barker JA, McLean SD, Jordan GD, Krober MS, Rawlings JS — Primary Neonatal Herpes Simplex Virus Pneumonia. Ped Infectious Disease Journal 9(4): 285-89, 1990

Cohen ML Kelly PC Atkinson AW	Parent, Teacher, Child - A Trilateral Approach to Attention Deficit Disorder. Amer J Dis Child 143(10): 1229-1233, 1989
Hartman KR Mancojohnson M Rawlings JS Bower DJ Marlar RA	Homozygous Protein C Deficiency - Early Treatment with Warfarin. Amer J Ped Hematol y Oncology 11(4): 395-401, 1989
Kelly PC Atkinson AW	Attention Deficit Disorders and Depression - Reply. Pediatrics 84(4): 748-49, 1989
Moore DC	Body Image and Eating Behavior in Adolescent Boys.. Amer Journal Diseases Children 144(0): 475-79, 1990
Moore DC Ruvalcaba RH	Late Pubertal Gynecomastia Associated with Anabolic Androgen Therapy for Short Stature. Clinical Research 38(1): 173, 1990
Pierce JR Brennan M Campbell J McClurkan M Morgan JL Stracener CE	The Department of Military Medicine - A Graduate Medical Education Idea Whose Time Has Come.. Military Medicine 154(0): 536, 1989 1989
Stephan MJ	Autosomal Recessive Form of Mandibular Dysostosis. Amer Journal Medical Genetics 35(4): 493-95, 1990
Wardinsky TD Pagon RA Powell BR McGillivary B Stephan MJ Zonana J Moser A	Rhizomelic Chondrodysplasia Punctata and Survival Beyond One Year: A Review of the Literature and Five Case Reports. Clinical Genetics 38(2): 84-93, 1990
Weir MR Keniston RC Enriquez JI McNamee GA	Depression of Vitamin B6 Levels Due to Gentamicin. Veterinary & Human Toxicology 32(3): 235-38, 1990
Weir MR Keniston RC Enriquez JI McNamee GA	Depression of Vitamin B6 Levels Due to Theophylline. Annals of Allergy 65(1): 59-62, 1990

Weir MR
Smith DS

Stress Reaction of the Pars Interarticularis Leading to Spondylolysis - A Cause of Adolescent Low Back Pain. J Adolescent Health Care 10(6): 573-77, 1989

Weisman LE
Fischer GW
Marinelli P
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Pierce JR
Golden SM
Peck CC

Pharmacokinetics of Intravenous Immunoglobulin in Neonates. Vox Sanguinis 57(4): 243-48, 1989

DEPARTMENT OF PSYCHIATRY

Parkison SC
Kelly PC
Walker CE

Assessment and Treatment of Attention Deficit Hyperactivity Disorder. IN Innovations in Clinical Practice: A Source Book, PA Keller & Steven R. Heyman (eds) Volume 9, pp 87-105, 1990, Professional Resource Exchange, Sarasota, F

DEPARTMENT OF SURGERY

Beck RA

An Aid for Interosseous Wiring in Mandibular Fractures. Plastic & Reconstructive Surg 86(4): 803, 1990

Bowersox JC
Pearce WA
Carter PL

Acute Pouch Obstruction After Vertical Banded Gastroplasty. Gastrointestinal Endoscopy 36(2): 146-67, 1990

Burgess FW
Whitlock W
Davis MJ
Patane PS

Anesthetic Implications of Relapsing Polychondritis - A Case Report. Anesthesiology 73(3): 570-72, 1990

Dahl J
Wheeler B
Mukherjee D

Effect of Chlorhexidine Scrub on Postoperative Bacterial Counts. American Journal of Surgery 159(5): 486-88, 1990

Jones JC
Nyreen MR
Stowell V

Traumatic Diaphragmatic Hernia Presenting as A Chest Wall Mass. Chest 98(1): 248-49, 1990

Kaufmann CR

Pediatric Trauma - Getting Triage Right - Reply. JAMA 263(18): 2447, 1990

Kaufmann CR
Maier RV
Kaufman EJ
Rivara FP
Carrico CJ

Validity of Applying Adult Triss Analysis to Injured Children. J Trauma 30(7): 924, 1990

Kaufmann CR
Maier RV
Rivara FP
Carrico CJ

Evaluation of the Pediatric Trauma Score. JAMA 263(1): 69-72, 1990

Liening DA
Duncan NO
Blakeslee DB
Smith DB

Hypothyroidism Following Radiotherapy for Head and Neck Cancer. Otolaryngology H&N Surgery 103(1): 10-13, 1990

Mader TH
Taylor GR
Hunter N
Caputo M
Meehan RT

Intraocular Pressure, Retinal Vascular, and Visual Acuity Changes During 48 Hours of 10 Degree Head Down Tilt. Aviat Space Environ Med 61(9): 810-13, 1990

Mader TH
Wilson LA
Lubow M

Spontaneous Bleeding From a Normal-Appearing Iris: An Unusual Cause of Atypical Amaurosis Fugax. Annals of Emergency Medicine 19(9): 1066-68, 1990

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Cynerman A

An Automated Method of Quantifying Retinal Vascular Responses During Exposure to Novel Environmental Conditions. Ophthalmology 97(7): 875-81, 1990

Piatt JH

Multiple Subpial Transection in Treatment of Focal Epilepsy. J Neurosurgery 71(4): 629-30, 1989

Platt M
Kiesling V
Vaccaro JA

Eosinophilic Ureteritis Associated with Eosinophilic Cholangitis: A Case Report. Journal of Urology 144(1): 127-29, 1990

Vaccaro JA
Strand J
Kiesling VJ
Belville WD

Use of Resectoscope for Colon Cancer. Urologic Clin of North America 17(1): 63-66, 1990

Wilson WJ
Scranton PE

Combined Reconstruction of the Anterior Cruciate Ligament in Competitive Athletes. J Bone & Joint Surg, Amer Vol 7(5): 742-48, 1990

PRESENTATIONS

FISCAL YEAR 1990

DEPARTMENT OF CLINICAL INVESTIGATION

Friedl KE Dettori JR Hannan CJ Patience TH Plymate SR	Comparison of the Effects of High Dose Testosterone and Nandrolone to a Replacement Dose of Testosterone on Strength and Body Composition in Normal Men	VIII International Congress of Hormonal Steroids The Hague, NE 09/16/90
Hannan CJ Friedl KE Plymate SR	Effects of Testosterone on Apomorphine Induced Movements in the Rat	Workshop Conference on Androgen Therapy: Biologic and Clinical Consequences Marco Island, FL 01/17/90
Hannan CJ Kettler TM Dabe IB Clark TS	Delta Aminolevulinic Acid in Plasma by Free Amino Acid Analysis	14th International Symposium on Column Liquid Chromatography Boston, MA 05/20/90
Hoop RC Plymate SR Wiren KM	Transcriptional Regulation of Sex Hormone Binding Globulin (SHBG) Expression in a Human Hepatoma (HEP G2) Cell Line by Thyroxine (T4)	Society of Armed Forces Medical Laboratory Scientists Baltimore, MD 03/05/90
Hoop RC Wiren KM Plymate SR	Regulation of SHBG Gene Expression by Steroid and Peptide Hormones	VIII International Congress of Hormonal Steroids The Hague, NE 09/16/90
Lampe TH Plymate SR	Gonadotropin Response to Gonadotropin Releasing Hormone in Men with Alzheimer's Disease	Western Society for Clinical Investigation Carmel, CA 02/06/90
Loop SM Plymate SR Ostenson RC Rosner WA	The Role of Sex Hormone Binding Globulin in the Growth of Human Prostate Carcinoma Cell Lines	Western Society for Clinical Investigation Carmel, CA 02/06/90

Loop SM Plymate SR Ostenson RC Rosner WA	Sex Hormone Binding Globulin (SHBG) is a Growth Factor for Human Prostate Carcinoma in Vitro	Workshop Conference on Androgen Therapy: Biologic and Clinical Consequences Marco Island, FL 01/17/90
Nestler JE Powers LJ Matt DW Steingold KA Plymate SR Clore JN Blackard WG	Insulin Directly Suppresses Serum Sex Hormone Binding Globulin Levels in Obese Women with the Polycystic Ovary Syndrome	72nd Annual Meeting of the Endocrine Society Atlanta, GA 06/20/90
Plymate SR Jones RE McLachlan RI	Decreased Serum Inhibin Responses to Clomiphene in Infertile Men With a Varicocele	American Society of Andrology Columbia, SC 04/06/90
van Hamont JE Wright JR	Analysis of Host-Reactive Hybridoma Clones Induced by Ureaplasma urealyticum Antigens	1990 ASM Meeting Anaheim, CA 05/13/90
van Hamont JE Wright JR	Characterization of Human Sperm-Reactive Monoclonal Antibodies Induced by Ureaplasma urealyticum	Northwest Branch, American Society for Microbiology Moscow, ID 06/21/90
van Hamont JE Wright JR Patience TH	Quantitation of Ureaplasma urealyticum in Clinical Specimens by a Semi-automated Fifty Percent Color Change Unit (CCU50) Titration Employing Fractional Logarithmic Dilutions	Northwest Branch, American Society for Microbiology Moscow, ID 06/21/90
van Hamont JE Wright JR	Identification of Antiureaplasma Monoclonal Antibodies Which Fail to React with Homologous Immunizing Antigen	15th Ann Meeting, Society of Armed Forces Medical Laboratory Scientists Baltimore, MD 03/06/90

DEPARTMENT OF EMERGENCY MEDICINE

Burkle F Rice MM Madden	Ethical and Legal Considerations in Disaster Triage	World Association of Disaster and Emergency Medicine 12/31/89

Foutch R Magelssen MD MacMillan JG	The Esophageal Detector Device: A Rapid and Accurate Method for Assessing Tracheal Versus Esophageal Intubation in a Porcine Model	Society for Academic Emergency Medicine Minneapolis, MN 05/01/90
Foutch R Magelssen MD MacMillan JG	The Esophageal Detector Device: A Rapid and Accurate Method for Assessing Tracheal Versus Esophageal Intubation in a Porcine Model	Triservices Emergency Medicine Conference San Antonio, TX 03/01/90
Rice MM Burkle F	(Pact) 4 A New Concept in Teaching Disaster Medicine	World Association of Disaster and Emergency Medicine 12/31/89

DEPARTMENT OF MEDICINE

Anton B Langer S McCarty J	Biofeedback, Autogenic and Visualization Trining in the Treatment of Pediatric Migraine and Tension Headache	Association for Applied Psychophysiology and Biofeedback Washington, DC 03/24/90
Hobbs CJ Plymate SR Jones RE Matej LA	Effect of Sex Hormone Binding Globulin (SHBG) on Testosterone Transport and Distribution	American Federation of Clinical Research Carmel, CA 02/06/90
Hobbs CJ Plymate SR Matej LA	Effects of Sex Hormone Binding Globulin on Human Prostatic Carcinoma	VIII International Congress on Hormonal Steroids The Hague, NE 09/16/90
Hobbs CJ Plymate SR Jones RE Matej LA	The Role of Sex Hormone Binding Globulin and Albumin on Testosterone Transport Into Cerebrospinal Fluid	72nd Annual Meeting of The Endocrine Society Atlanta, GA 06/20/90
Jones RE Plymate SR Hobbs CJ	Influence of A23187 on Phospholipid Synthesis in Human Sperm.	American Society of Andrology Columbia, SC 04/06/90
Kazragis R Cooper RH	Hepatitis B Vaccine (Recombivax) - Abbreviated Schedule Vaccination Trial	Washington State Chapter of the American College of Physicians Seattle, WA 12/02/89

Lyons MF Pearce WA Tsuchida AM	Meckel's Diverticulum: The Gastroenterologist's Bane of Abdominal Pain	American Gastroenterological Association San Antonio, TX 05/13/90
Tsuchida AM	Fecal Occult Blood Testing	Family Practice/Emergency Medicine Conference Willingen, WG 02/01/90
Tsuchida AM	Abnormal LFT'S - Is It Viral Hepatitis or Not, Some Illustrative Case Problems	Family Practice/Emergency Medicine Conference Willingen, WG 02/01/90
Tsuchida AM Lyons MF Pearce WA Schlepp GE Walter MH	Endoscopic Balloon Dilation in Gastric Outlet Obstruction: 5 Year Experience on 25 Patients	Digestive Disease Week Annual Scientific Meeting San Antonio, TX 05/13/90
Vockroth JH Lyons MF Tsuchida AM	Does Absorption of Aluminum During Treatment with Sucralfate Affect Bone Metabolism?	American Gastroenterological Association San Antonio, TX 05/13/90

DEPARTMENT OF NURSING

Imbruglio LR	Developmental Evaluation of the NICU Graduate	Nursing Research Conference, Tripler Army Medical Center Honolulu, HI 10/04/89
Loan LA	Endogtracheal Suctioning in Newborns	Regional Nursing Research Conference Seattle, WA 03/03/90
Loan LA	The Effects of Head Rotation and Hyperoxygenation - Suction Sequences During Endotracheal Suctioning	Women's Health/ Perinatal Nursing Research Conference Seattle, WA 03/03/90
Smith PS	Physiological Effects of Positioning Premature Infants in Car Seats	Phyllis J. Verhonick Nursing Research Symposium Washington, DC 04/01/90

Sweat J	Quite Time for Post-op Patients	Phyllis J. Verhonick Nursing Research Symposium Washington, DC 04/01/90
Turner BS	Endotracheal Suctioning in Critically Ill Patients	National Teaching Institute, American Association of Critical Care Nurses San Francisco, CA 05/21/90
Turner BS	Endotracheal Suctioning in Newborns	National Conference of Neonatal Nurses San Francisco, CA 02/08/90
Turner BS	Hot Issues and Clinical Tips in Respiratory Care	National Conferences of Neonatal Nursing San Francisco, CA 02/07/90
Turner BS	Nursing Research: Practical Approaches and Pitfalls to Avoid	National Conference of Neonatal Nurses San Francisco, CA 02/07/90
VanderLaan JK Imbruglio LR	The Breast Feeding Experiences of Military Women	Women's Health/ Perinatal Nursing Research Conference Seattle, WA 03/03/90

DEPARTMENT OF OB/GYN

Christian SS Brady WK Read JA Kopelman JN	Vaginal Breech Delivery a Five Year Prospective Evaluation of a Protocol Using Computed Tomographic Pelvimetry	10th Annual Meeting of the Society of Perinatal Obstetricians Houston, TX 01/23/90
Herpolsheimer A Brady WK Yancey MK Pandian M Duff P	Pulmonary Function of Preeclamptic Women Receiving Intravenous Magnesium Sulfate Seizure Prophylaxis	38th Meeting of the American College of Obstetrics and Gynecologists San Francisco, CA 05/07/90
Herpolsheimer A Yancey MK Brady WK Jordan G Benson WL	Randomized Trial of Spontaneous Vaginal Delivery Versus Outlet Forceps Delivery in Term Pregnancies	Armed Forces Dist, American College of Obstetrics and Gynecologists 11/05/89

Yancey MK Hannan CJ Plymate SR Stone IK Friedl KE Wright JR	Effect on Serum Lipids and Lipoproteins of Continuous or Cyclic Medroxyprogesterone Acetate Treatment in Postmenopausal Women Treated with Conjugated Estrogens	45th Annual American Fertility Society Meeting 11/13/89
Yancey MK Hannan CJ Plymate SR Stone IK Friedl KE Wright JR	Effect on Serum Lipids and Lipoproteins of Continuous or Cyclic Medroxyprogesterone Acetate Treatment in Postmenopausal Women Treated with Conjugated Estrogens.	Arm For Dist of ACOG-NAACOG Washington, DC 11/05/89

PREVENTIVE MEDICINE SERVICE

Brandt C	Health Promotion and Disease Prevention Survey of Army Retirees	Health Promotion Meeting, US University of the Health Sciences 10/01/89

DEPARTMENT OF PEDIATRICS

Atkinson AW Knott MC Kelly PC et al	Receptive Language Processing and Attention Deficits-Impact of Methylphenidate	Annual Meeting of the Society of Behavioral Pediatrics Cambridge, MA 11/01/89
Moffitt D	Chronic Lung Disease in Childhood - The NICU Graduate	4th Annual Northwest Regional Neonatal Pediatric Respiratory Care Seminar Seattle, WA 02/16/90
Moore DC Johnson M	Adolescent Endocrinology	1990 Conference of the Northwest Society for Adolescent Medicine Victoria, BC 05/19/90
Moore DC Ruvalcaba R	Late Pubertal Gynecomastia Associated with Anabolic Androgen Therapy for Short Stature	Western Society for Pediatric Research Carmel, CA 02/06/90

Perkins TA	IRDS - The First Twenty-Four Hours	4th Annual Northwest Regional Neonatal Pediatric Respiratory Care Seminar Seattle, WA 02/16/90

DEPARTMENT OF SURGERY

Dahl J Wheeler B Mukherjee D	Effect of Chlorhexidine Scrub on Postoperative Bacterial Counts	76th Annual Meeting of the North Pacific Surgical Association Victoria, BC 11/10/89
Hetherington H	Primitive Neuroectodermal Tumors of the Head and Neck	Washington Chapter, American College of Surgeons 06/14/90
Kaufmann CR Maier RV Kaufman EJ Rivara FP Carrico CJ	Validity of Applying Adult Triss Analysis to Injured Children	50th Annual Meeting of the American Association for the Surgery of Trauma Tucson, AZ 09/06/90
Platt ML Vaccaro JA	Suprarenal Inferior Vena Cava Narrowing and Right Solitary Kidney Viability	Northwest Urological Association Meeting (won Resident's Award) Vancouver, BC 12/01/90
Vaccaro JA	PSA Values After Testosterone Stimulation	Northwest Urological Association Meeting Vancouver, BC 12/01/89
Vaccaro JA	PSA Values After Testosterone Stimulation	The Kimbrough Urological Seminar San Antonio, TX 12/01/89

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C = Completed S = Suspended

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DEPARTMENT OF CLINICAL INVESTIGATION

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/109 Status: On-going

Title: Characterization of Equine Inhibin: Sequence Analysis and Carbohydrate Composition

Start Date: 21 Sep 90 Est Completion Date: Oct 92

Department: Clinical Investigation Facility: MAMC

Principal Investigator: CPT Katherine H. Moore, MS

Associate Investigator: Kristine Wiren, Ph.D.

Key Words: equine inhibin, analysis, carbohydrate composition

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $8870.00 Periodic Review: N/A

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

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

Progress: The initial steps involved in the construction of a cDNA library to isolate the equine inhibin gene have been performed. mRNA has been extracted from equine ovary and testis and is in the process of being evaluated.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 83/84 Status: Completed

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 90

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: No additional subjects were entered in this study in FY 90. Approximately 260 subjects were studied.

The data support the concept that inhibin acts a negative feedback factor for FSH secretion. Further, the data suggest that serum inhibin is a measure of the relation of normal seminiferous tubule or Sertoli cell function to sperm production. The loss of these relationships in the two varicocele groups demonstrates that serum inhibin measurements can point to alterations in Sertoli cell function in a state of decreased sperm production.

A manuscript has been submitted for consideration for publication to the Journal of Clinical Endocrinology and Metabolism.

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

Annual Meeting of the American Society of Andrology, Columbia, SC, April 1990

Detail Summary Sheet

Date: 30 Sep 90 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: Sep 90

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: During FY 90, analysis of carbohydrate side chains following n-glucanase treatment of rabbit SHBG has been completed.

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

Detail Summary Sheet

Date: 30 Sep 90	Protocol No.: 88/20	Status: On-going
Title: Studies on the Production and Glycosylation of SHBG by Hep G2 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: Hep G2, ^{35}S methionine, SHBG, steroids, peptides		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $602.00	Periodic Review: Sep 90

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

Technical Approach: Hep G2 cells will be grown to confluence in 25 cm^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 Hep G2 library for the SHBG mRNA. When all data have been collected, differences in synthesis versus processing will be assessed between the various treatments using the ANOVA method.

Progress: Laboratory work has continued on this study during FY 90. Two papers have been published and an additional paper has been submitted for consideration for publication. A paper was presented at the 8th International Congress on Hormonal Steroids, The Hague, Netherlands, September 1990.

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

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

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 89/12 Status: Completed

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: Sep 90

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: 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. 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: The protocol has been completed. A paper was published in Psychoneuroendocrinology (Lampe, et al, Vol 14 (4), p 311, 1989,) and a paper was presented at the American Federation of Clinical Research (Western Society), Carmel, CA, February 1990.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 89/73 Status: Completed

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: Jun 90

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 to be 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 greater 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: The protocol was completed and a paper has been prepared for submission for presentation.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/76 Status: On-going

Title: Clinical and Molecular Investigations in Men With Decreased Spermatogenesis and a Varicocele

Start Date: 18 May 90 Est Completion Date: Apr 95

Department: Clinical Investigation Facility: MAMC

Principal Investigator: COL Stephen R. Plymate, MC

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

Key Words: spermatogenesis, varicocele,

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

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

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

Blood samples will be collected for Y-chromosome-specific DNA analysis from the following groups of men: 150-200 azoospermic and severly oligospermic males; 125-175 infertile men with a varicocele; 240-280 normal men; and 125-175 fertile men with a varicocele.

Progress: No patients entered. The study has not been implemented because the investigators are awaiting approval of an NIH grant proposal.

Detail Summary Sheet

Date: 30 Sep 90 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 90

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: Serovar VIII was shown to induce the production of antibodies which failed to react with the serovar VIII immunizing antigen but were specific for any one of a number of non-serovar VIII antigens. These data suggest that *Ureaplasma* could potentially exert a mitogenic effect on its host's immune system. Additionally, ELISA and Western blot Analysis of serovars III, V, and VIII indicated that ureaplasma-specified antigens can induce antibodies which specifically cross-react with either heterologous medium components, spermatozoa, human hepatocytes, mouse hepatocytes, or spleen tissue. Ureaplasmal antigens identified in this study could potentially induce an autoimmune response in a colonized host. Finally, a semiautomated fifty percent color change unit titration employing fractional logarithmic dilutions was developed and evaluated for the quantitation of *Ureaplasma* in clinical samples.

Papers reporting the findings of this study have been presented at four different national scientific meetings in 1990.

Detail Summary Sheet

Date: 30 Sep 90	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

Start Date: 15 Sep 89	Est Completion Date: Jul 90
Dept/Svc: Surgery/ General	Facility: MAMC
Principal Investigator:	CPT John E. van Hamont, MS (Jun 90)*
Associate Investigators:	COL Preston L. Carter, MC COL James L. Kelley, MC MAJ Ismail Jatoi, MC CPT Leonard N. Howard, MC
Key Words: breast cancer, phosphotyrosine, predictor	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $1150.00	Periodic Review: Sep 90

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

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

Progress: Procedures for peroxidase staining of phosphorylated tyrosine and C-Neu in paraffin-mounted tissue sections were established and evaluated using an A431 cell line exposed to recombinant-derived epidermal growth factor as a positive control. Paraffin sections from eight breast cancer patients have been obtained for immunohistochemical detection of the phosphotyrosine and C-Neu markers.

*Original PI: CPT Ismail Jatoi, MC

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

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DEPARTMENT OF DENTISTRY

Detail Summary Sheet

Date: 30 Sep 90 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 (Sep 89)*

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: pulpotomy, electrosurgical, formocresol, children

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $100.00	Periodic Review: Sep 90

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: No additional patients were entered in FY 90. A total of six patients has been entered. Patient treatment and data collection will continue in this joint project with the University of Washington.

PRESENTATION: American Academy of Pediatric Dentistry, May 1989.

* Dr. Allinder original PI

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/75 Status: Terminated

Title: Evaluation of the Three Fixation Techniques Commonly Used in Mandibular Advancement Surgery

Start Date: 18 May 90 Est Completion Date: May 95

Department: Dentistry Facility: MAMC

Principal Investigator: COL Douglas B. Boyd, DC

Associate Investigators: None

Key Words: mandibular surgery, advancement, fixation techniques

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

Study Objective: To test the hypothesis that there is a clinically significant difference in outcome between the three commonly used fixation techniques in the sagittal osteotomy for mandibular advancement and to establish a multicenter data base to store data generated from all orthognathic surgery patients at five major training institutions.

Technical Approach: Patients will be randomly assigned to one of three groups. The three groups will differ only in the type of osteosynthesis to be used at the time of surgery (wire and maxillomandibular fixation [MMF]; plate and limited MMF, or screw and no MMF). All patients will undergo a standardized preoperative work-up which will include history, physical exam, dental models, facial photographs, and radiographs. The patient history will include both demographic information and a general health history. Reasons for seeking treatment, length of previous orthodontic treatment, history of previous facial surgery or trauma, and preoperative symptoms such as pain, swelling, and joint clicking or locking will be included as well as a preoperative psychological assessment. Postoperative data collection immediately after surgery and at 2 and 12 months postsurgery will include a standardized questionnaire for subjective evaluation of postoperative complications and a physical exam to record infection, malunion, degree of lip paresthesia, occlusal changes, and TMJ pathology. Radiographs will be repeated at each follow-up and an MRI will be obtained pre- and postoperatively. Perioperative complications such as paresthesia and malunion will be evaluated and cephalographs will be evaluated to determine the stability associated with each technique as well as skeletal alterations. The condylar effects to be evaluated include changes in condylar position and morphology. Correlations between the type of fixation, the amount and direction of condylar displacement and subsequent development of morphologic joint changes will be investigated as well as the factors responsible for the development of postoperative TMJ dysfunction. All dependent variables will be evaluated with respect to the type of fixation employed so that factors can be identified which will help to determine which fixation techniques are best in which situations.

Progress: This protocol was terminated because the proposed NIH grant was not approved to fund the project.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 89/46 Status: Completed

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: Jun 90

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-conditicner 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: The project has been completed and a paper has been submitted for presentation. All point-of-use water conditioning systems tested caused a statistically significant reduction in fluoride ($p < .001$). Of particular note were reductions in fluoride concentration by the activated carbon filter (82%), the reverse osmosis system (84%), and the distillation unit (99%). These reductions are clinically significant and indicate that conditioning systems should be advised to have water tested and to consider fluoride supplementation to ensure adequate benefit from this caries prevention method.

Detail Summary Sheet

Date: 30 Sep 90 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 B. Boyd, DC
Key Words: genioplasty, evaluation, cephalometric, tissue changes
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Sep 90

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: Data collection has been completed and data analysis is in progress.

Detail Summary Sheet

Date: 30 Sep 90	Protocol No.: 90/44	Status: On-going

Title: Clinical Evaluation of Primary Dentition Wear and Temporomandibular Joint Dysfunction Signs

Start Date: 16 Mar 90	Est Completion Date: 1 Feb 91
Department: Dentistry	Facility: MAMC
Principal Investigator: Maj Curtis D. Goho, DC	
Associate Investigators: LTC Herschel L. Jones DC	
Key Words: temporomandibular joint dysfunction, dentition wear	

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

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

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

Progress: Ninety seven subjects have been entered and subject entry and examination are completed. Statistical analysis of data has been initiated.

Detail Summary Sheet

Date: 30 Sep 90 | Protocol No.: 90/45 | Status: On-going

Title: Prevalence of Abnormal Oral Findings and the Dental Needs in a Selected Patient Population with Cerebral Palsy

Start Date: 16 Mar 90 | Est Completion Date: Nov 90

Department: Dentistry | Facility: MAMC

Principal Investigator: MAJ Cynthia M. Guzman, DC

Associate Investigators: COL Gerald R. Aaron, DC

Key Words: cerebral palsy, dental needs

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $200.00	Periodic Review: N/A

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

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

Progress: Eighteen subjects have been examined and a parental questionnaire has been completed for each subject.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/32 Status: On-going

Title: An Assessment of Parental Desire to Accompany Their Child in the Dental Operatory

Start Date: 16 Feb 90 Est Completion Date: Feb 91

Department: Dentistry Facility: MAMC

Principal Investigator: LTC Herschel L. Jones, DC

Associate Investigators: COL Gerald R. Aaron, DC
LTC Paul E. Kittle, DC

Key Words: dental operatory, presence of parents,

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

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

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

Progress: Two patients have been entered in this study. Due to mission requirements, the protocol was placed on an inactive status by the investigators after these two patients. The project will be reactivated as of 9 Oct 90.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/68 Status: On-going

Title: Parental Recall of Informed Consent for Anesthesia Dental Procedures

Start Date: 19 Apr 90 Est Completion Date: Feb 91

Department: Dentistry Facility: MAMC

Principal Investigator: LTC Paul E. Kittle, DC

Associate Investigators: COL Gerald R. Aaron, DC
LTC Herschel L. Jones, DC

Key Words: consent, dental procedures, pediatrics, parents

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

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

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

Progress: No patients were enrolled in this study in FY 90 due to clinical delay and delays in processing the study. It is anticipated that patients will be enrolled beginning November 1990.

Detail Summary Sheet

Date: 30 Sep 90	Protocol No.: 90/46	Status: On-going

Title: The Fearful Pediatric Dental Patient's Response to Desensitization Techniques

Start Date: 16 Mar 90	Est Completion Date: Jan 91
Department: Dentistry	Facility: MAMC
Principal Investigator:	MAJ Adolfina M. Polk, DC
Associate Investigator:	LTC Paul E. Kittle, DC MAJ Steven C. Parkison, MS
Key Words: dentistry, fear, desensitization, pediatric	

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

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

Technical Approach: The study population will consist of 30, six to ten year old children who have had at least one unsuccessful dental appointment due to apprehensiveness/fear.

Group 1 will undergo a desensitization session consisting of filmed modeling (child visit to the dentist for a restorative procedure) and coping skills (breathing relaxation skills, pleasant imagery, calming self-talk).

Group 2 will undergo a desensitization technique involving filmed modeling, coping skills, and procedural and sensory information. These children will view the dental instruments used for a restorative procedure and a mock dental procedure using a doll/dentiform will be conducted.

Each session will be composed of a group of five children and will be conducted 1-2 days before the treatment appointment. The treating dentist will be unaware of the desensitization method that was used. The children will be videotaped at the restorative treatment appointment and multiple trained pediatric dental raters will view the videotape and submit a behavioral analysis grade for each child. A standardized, accepted clinical behavioral scale will be used to evaluate behavior categories and interrater reliability will be performed. Data will be analyzed by a non-parametric test of differences between groups, based on the behavioral scale.

Progress: Five children have been studied. A successful dental appointment was completed on four of the five children. The one failure was a severe behavioral management case.

Detail Summary Sheet

Date: 30 Sep 90	Protocol No.: 90/81	Status: On-going

Title: Determination of Optimum Dose and Schedule of Intravenous Dexamethasone for Prevention of Postsurgical Edema After Orthognathic Surgery

Start Date: 15 Jun 90	Est Completion Date: Jul 91
Department: Dentistry	Facility: MAMC
Principal Investigator:	MAJ Charles R. Weber, DC
Associate Investigators:	COL Douglas B. Boyd, DC
	CPT Michael C. Daines, MC
Key Words: edema, orthognathic surgery, dexamethasone	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $780.00	Periodic Review: N/A

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

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

Progress: Four patients have been entered in the study.

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

F O R

P R O T O C O L S

DEPARTMENT OF EMERGENCY MEDICINE

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/20 Status: On-going

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

Start Date: 19 Jan 90 Est Completion Date: May 90

Department: Emergency Medicine Facility: MAMC

Principal Investigator: CPT Jeffrey M. Cortazzo, MC

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

Key Words: COPD, magnesium sulfate, intravenous

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

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

Technical Approach: Subjects: 100 patients $\geq$ 45 years, with a $\geq$10 pack-year history of cigarette smoking, history of chronic outflow obstruction with FEV_1 $\leq$70% of predicted or $\leq$60% of FVC, and acute exacerbation of COPD with several days of worsening dyspnea associated with increased cough and sputum. A spirometry will be performed to document the FEV_1 and FVC. Patients with a definitive history of asthma, hypotension, renal failure, lobar or segmental consolidation, or treated with methylxanthines in the emergency room will be excluded.

Patients will have an IV heparin lock and complete blood count, serum theophylline and magnesium levels, and a chest x-ray will be done. They will then receive albuterol, 2.5 mg in 2 cc of normal saline, by nebulizer. The nebulizer will be repeated at 20 and 40 minutes. At the second nebulizer period, patients will be randomized to IV magnesium sulfate (0.5 mmol/min to equal 2 g total magnesium sulfate) or an IV placebo, given over 20 minutes. They will also receive methylprednisolone, 125 mg IVP, while receiving the second nebulizer treatment. Patients will be placed on cardiac and automatic blood pressure monitors, and deep tendon reflexes, respiratory rate, and spirometry will be assessed just prior to the second and third nebulizer treatments and at 60 minutes. Disposition and further treatment of the patients will be at the discretion of the treating physician. Patients who clear after one nebulized albuterol treatment will be excluded from data analysis.

FEV_1, PEF, respiratory rate, ED disposition (admission vs discharge), and subjective scores from a patient survey will be analyzed using ANOVA.

Progress: More than one third of the number of subjects planned for this study have been enrolled.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 89/75 Status: Completed
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: Sep 90

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: Pigs will be intubated in either the trachea or the esophagus, 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. 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. ANOVA will be used to evaluate both time and accuracy of the three methods among the various levels of expertise of the participants.

Progress: Conclusions: The EDD is more rapid than either $ETCO_2$ or clinical methods in determining endotracheal tube location in the porcine mode. Prior ventilation of the esophageal tube does not interfere with the accuracy of the EDD. A paper has been submitted for publication and an abstract was presented at two national scientific meetings.

Detail Summary Sheet

Date: 30 Sep 90	Protocol No.: 90/09	Status: Completed

Title: The Ability of Emergency Medicine Physicians to Determine the Severity of Patient Illness Over the Telephone

Start Date: 17 Nov 89	Est Completion Date: Nov 89
Department: Emergency Medicine	Facility: MAMC
Principal Investigator: CPT Kurt C. Kleinschmidt, MC	
Associate Investigator: LTC Matthew M. Rice, MC	
Key Words: illness, severity, telephone	

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

Study Objective: To determine how well emergency medicine residents can determine the severity of illness over the telephone of patients who call the emergency room for a consultation.

Technical Approach: Telephone consultations will be managed 24 hours a day by the second, third, and fourth year emergency medicine residents and attending physicians. Written consultations of all calls will be kept. Upon receipt of the telephone call, the administrative information will be recorded by the ward clerk. This will include the patients name, age, social security number, phone number, time of call, and chief complaint. A physician will then record a history, his recommendations to the patient, and the time spent on the call. Upon completion of the call, the physician will document on the record as to how urgently the patient needs to be evaluated by a physician by using three categories: (1) the patient should come to the emergency room at once; (2) the patient needs physician care but not immediately, or (3) the patient can be cared for at home using telephone recommendations. The progress of all patients in this study will be ascertained by a 1-7 day follow-up via the telephone, depending on the nature of the illness. If the patient has recovered by the time of the follow-up call, the evaluation will be complete. If the patient comes in for care during this period, the records of the visit will be evaluated. If the patient is still ill but has not come in for care, he will be asked to come in at that time. The urgency of the need for physician care at the time of the telephone consultation will be determined based on the information collected from the follow-up calls or the record reviews of those who did come in for care. Other information to be assessed will include a comparison of the sensitivity and specificity of physicians at different levels of training in evaluating a patient, an analysis of the frequency of the different chief complaints, and a determination of the amount of time spent on the telephone answering consultations.

Progress: Approximately 950 telephone consultations were tracked, with one-half having patient follow-up done. Multiple factors were tracked and Data Base IV was used as a file. Statistical work was done with the assistance of the the computer/statistics specialist at the Department of Clinical Investigation. The first draft of a paper has been written and critiqued by others. A re-write of the paper is in progress.

Detail Summary Sheet

Date: 30 Sep 90 | Protocol No.: 90/89 | Status: On-going

Title: Prehospital Intubation Assessment Methods

Start Date: 15 Jun 90 | Est Completion Date: Jun 91
Department: Emergency Medicine | Facility: MAMC
Principal Investigator: CPT Mark D. Magelssen, MC
MAJ Richard G. Foutch, MC
CPT Jeffrey E. Short
Key Words: intubation, esophageal detector device
Accumulative MEDCASE Cost: -0- | Est Accumulative OMA Cost: $830.00 | Periodic Review: N/A

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

Technical Approach: Patients, 18 years or older, who are nasally or endotracheally intubated in the prehospital or emergency department setting will be entered into the study, except for those with cricothyroidotomy or tracheostomy.

Physicians and paramedics will be briefed on the various methods of insuring recognition of esophageal intubation. These methods at MAMC include the Esophageal Detector Device (EDD), visualizing the tube passing through the vocal cords, listening over the lungs and epigastrium, moisture in the tube with exhalation, and continued evidence of adequate oxygenation of the patient. The physician or paramedic will assess the intubation tube placement, using all of the methods listed above. After Emergency Department personnel have taken over the care of the patient, the paramedic will complete a questionnaire that obtains data on the accuracy, ease of use, estimated time to use, and preference of methods as well as route (nasotracheal or orotracheal) and type of patient (medical or trauma).

Final determination of tube placement will be verified by the emergency medicine physician upon arrival to the Emergency Department.

Data will be entered into a spreadsheet with an ID number assigned to each data sheet. Differences will be isolated between the various methods. This will include: descriptive statistics on the data from the questionnaire, ANOVA for confidence in accuracy, and chi-square to isolate the best correlation in device placement.

Progress: This protocol is awaiting final approval of revisions required by the Institutional Review Board.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 88/62 Status: Completed

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: N/A

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 hour's 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 were enrolled in this study with evaluable data being collected on 24 of these subjects. There were slight differences in Nifedipine versus placebo, but these differences were not clinically significant. An unusual patient response to the placebo was a confounding factor for the study. Therefore, when the principal investigator completed his program and was reassigned, the study was not continued. A paper is being written for submission for publication.

Detail Summary Sheet

Date: 30 Sep 90 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 Lee E. Payne, MC (Jun 90)*
Associate Investigators: MAJ James I. Stubblefield, 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: Jun 90

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

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

Progress: Data collection was completed on 54 subjects. The data are now being analyzed.

* MAJ Stubblefield original PI

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/78 Status: On-going

Title: Oral Versus Intravenous Steroid: A Prospective Study in Acute Asthma, A Pilot Study

Start Date: 15 Jun 90 Est Completion Date: Dec 90

Department: Emergency Medicine Facility: MAMC

Principal Investigator: LCDR Richard S. Perren, MC

Associate Investigator: MAJ Kirin M. Russell, MC

Key Words: asthma, oral vs intravenous steroids

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

Study Objective: To compare the efficacy of oral prednisone and intravenous methylprednisolone in the treatment of adults with acute asthma exacerbation by comparing FEV_1, patient's subjective index, and physician evaluation of clinical course.

Technical Approach: The patient population will be 100 patients, ages 18-45 years of age, presenting to the Emergency Room with exacerbation of asthma, unrelieved by the usual home treatment. Each patient will be evaluated by the physician and tested with a portable spirometer. Oxygen saturations will be recorded per pulse oximetry. Arterial blood gases may be used in place of pulse oximetry if the clinical situation dictates. The patient will be asked to described symptoms as mild, moderate, or severe. Each patient will then be randomized in a double blind fashion to receive either IV methylprednisolone and oral grape Tang or oral prednisolone mixed with grape Tang and normal saline IV. All patients will receive oxygen and a beta-agonist as per emergency room protocol, three treatments, 20 minutes apart. Patients will be evaluated with spirometry to FEV_1 on arrival and every hour for three hours. Patients will be discharged or admitted as clinical circumstances warrant. Discharge steroid dosing will be left to the discretion of the treating physician. Follow-up evaluation will consist of repeat vital signs (every 30 minutes) physician examination (after initial treatment), patient symptom scale of 1-10 (every hour), and spirometry (every hour). Patients who are discharged will be contacted the following day for evaluation of subjective complaints and will be asked to rate themselves on the patient symptom scale. FEV_1 and FVC will be analyzed with analysis of variance with repeated measures. Analog scaled variables for physician exam and subjective index will be analyzed with appropriate nonparametric tests.

Progress: This study has not been implemented because it has not received final approval from the Human Use Committee.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 82/25 Status: On-going

Title: Emergency Room Proccdurc Training
Start Date: Feb 82 Est Completion Date: Feb 87
Department: Emergency Medicine Facility: MAMC
Principal Investigator: LTC Matthew M. Rice, MC (Jun 90)*
Associate Investigators: COL Frederick Burkle, MC
LTC Samuel T. Coleridge, MC
LTC Cloyd B. Gatrell, MC
MAJ Steven C. Dronen, MC
MAJ Stanley P. Liebenberg, VC
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: Jun 90

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 90.

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.

* MAJ Dronen original PI

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/16 Status: On-going

Title: Pediatric Intubation Training Utilizing the Ferret Model
Start Date: 20 Jan 90 Est Completion Date: Indefinite
Department: Emergency Medicine Facility: MAMC
Principal Investigator: LTC Matthew M. Rice, MC
Associate Investigators: LTC Cloyd B. Gatrell, MC
LTC Patrick C. Kelly, MC
Key Words: ferrets, intubation, pediatric life support course

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $400.00	Periodic Review: N/A

Study Objective: To enhance the clinical skills of health care providers in managing pediatric airways, specifically intubations. This protocol will be used to support the Pediatric Advanced Life Support Course. The participants in this course are members of the Army, the Air Force, the Navy, and the Public Health Service.

Technical Approach: Ferrets will be anesthetized and course participants will be given the opportunity to intubate a ferret employing a laryngoscope and endotracheal tube.

Administration and monitoring of anesthesia will be directly supervised or performed by the attending veterinarian. The veterinarian will be present at all times to assist, modify, or terminate the procedure.

Progress: Three training sessions were held utilizing this protocol in FY 90.

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 90 Protocol No.: 90/13 Status: Completed

Title: The Correlation of Physician Attitudes With Perceived Behavior and Actual Behavior With Respect to Health Promotion

Start Date: 15 Dec 89 Est Completion Date: Jan 90

Department: Family Practice Facility: MAMC

Principal Investigator: MAJ Benroe W. Blount, MC

Associate Investigators: MAJ Richard H. Bednarczyk, MC
MAJ Joan E. Eitzen, AN
MAJ Bruce M. LeClair, MC
CPT Michael L. Tuggy, MC

Key Words: attitudes, physician, health promotion

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

Study Objective: The purposes of the study are to: assess MAMC Family Practice physicians attitudes, self-perceived behavior, and actual behavior towards health promotion activities of their patients; to correlate attitudes with self-perceived behavior and each of these to actual behavior; to determine if there are differences in attitudes and behavior based on patient age or the training level of physicians; and to determine if there are predictors for which patients receive more health promotion activities from their family physician.

Technical Approach: Five second year residents and five Family Practice teaching staff will complete an attitude questionnaire and a self-perceived behavior questionnaire. Patient charts will then be audited to determine actual behavior. Patients will be divided into six age categories. From each study physician's patient panel, every fourth patient chart in each age category will be audited. The standard Medical Screening Checklist which is used for Quality Assurance will be used to audit the charts. Charts for children <13 years of age will be audited to determine health promotion by the physician for immunizations, fluoride, nutrition, growth chart, parenting skills, safety, hematocrit, blood pressure, development, and schoolwork. Those from 13-18 will be audited for these factors plus family history, smoking, alcohol, drugs, and contraception. Charts for patients $\geq$19 will be audited for these same items plus other medical screening items appropriate to age, such as testicular exam and breast self exam as well as glaucoma and hearing for elderly patients. Descriptive statistics and frequencies will be done as well as comparison of attitudes, self-perceived behavior and actual behavior and comparisons between age categories using Chi-square analysis. Patient predictors of health promotion activity will be obtained using frequency statistics and linear regression analysis.

Progress: Ten physicians participated in the study and 1200 patient records were audited. Data have been entered into the computer and analysis will be completed in the fall of 1990.

Detail Summary Sheet

Date: 30 Sep 90	Protocol No.: 90/67	Status: Completed

Title: The Content of Army Family Practice

Start Date: 20 Apr 90	Est Completion Date: 30 Jul 90
Department: Family Practice	Facility: MAMC
Principal Investigator: MAJ Benroe W. Blount, MC	
Associate Investigators: None	
Key Words: demographics, patient, physician, diagnosis	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $8.00	Periodic Review: N/A

Study Objective: To describe the content of Army Family Practice and the degree of similarities and differences in Army Family Practice among different geographic areas within the Army and to compare the content of Army Family Practice to that of civilian Family Practice in terms of patient demographics, physician demographics, diagnostic content, and procedural content in order to prepare effectively the Army Family Practice residents for successful practice in their future practices.

Technical Approach: Data on civilian Family Practice physicians will be obtained from publicly available aggregate data from the American Academy of Family Physicians. Data on civilian Family Practice content will be obtained from the data banks of the Department of Family Medicine at the University of Washington, which is publicly available from the U.S. Department of Health and Human Services. The data on Army Family Practice physicians will be obtained from the Office of the Surgeon General under the Freedom of Information Act. Data on the content of Army Family Practice will be obtained from the data set of the Ambulatory Care Data Base Study done by the Health Services Command, which included 70 clinical specialties at six Army medical facilities over a 21-month period. Data will be analyzed using the Statistical Package for the Social Sciences. The results will be presented as a description and comparison of Family Practice physicians, nonfederal to Army; a description and comparison of Family Practice patients, nonfederal to Army; a description of the diagnostic content of Army Family practice as to intra-Army site comparison and comparison to nonfederal Family Practice.

Progress: The project has been completed and a thesis presented as a requirement for a Master's degree at the University of Washington. The study revealed that neither nonfederal nor Army Family Practice was a homogeneous discipline. Both sectors have a large horizontal breadth in outpatient care. Environment does influence content and other major differences were noted in the specific frequency of diagnosis, patient age, and family physician characteristics. Even with these differences, there was an identifiable pattern of morbidity which Army Family Practice physicians enccuntered in outpatient practice. It is this pattern for which they are responsible and which could provide the core for the residency curriculum. As found in the nonfederal sector, Army Family Practice appears to accommodate itself to the community it serves.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 87/77 Status: Terminated

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: Jun 90

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 were unable to obtain funding elsewhere.

Detail Summary Sheet

Date: 30 Sep 90	Protocol No.: 90/43	Status: Completed

Title: The Efficacy of External Ankle Support Devices in Preventing Ankle Injuries Among Army Army Airborne Rangers

Start Date: 16 Mar 90	Est Completion Date: Mar 90
Department: Family Practice	Facility: MAMC
Principal Investigator: MAJ Wade A. Lillegard, MC	
Associate Investigator: CPT William C. Doukas, MC	
Key Words: ankle injuries, airborne, canvas & semi-rigid supports	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $98.00	Periodic Review: N/A

Study Objective: To evaluate the effectiveness of two different forms of external ankle support in preventing ankle injuries or decreasing their severity during military airborne insertions and/or the follow-on mission; to evaluate the comfort and practicality of these ankle supports in an elite Army unit during a routine training exercise; and to assess the effect of external ankle support devices on the incidence or severity of other lower extremity injuries, specifically knee, leg, and hip.

Technical Approach: Approximately 650 healthy, male soldiers from an Army Ranger regiment will be asked to participate during a routine training exercise. Prior to deployment, soldiers will be randomized into three groups. Group 1 will be issued a pair of lace-up canvas ankle supports, Group 2 will be issued a pair of semi-rigid plastic orthosis (air-stirrups), and Group 3 will be given no external support devices and will serve as the controls. Soldiers entering the study must wear the braces on each jump and will be encouraged to wear them on the follow-on mission. All injuries will be reported through the standard medical chain to the Battalion Surgeon who will evaluate, grade, and record all injuries and the type of brace worn. Soldiers will fill out a form which includes airborne experience, prior ankle injuries, number of jumps made on this exercise, type of brace worn, duration of wear, reasons for discontinuation, and injuries sustained. The StatView V1.1 Program will be used to analyze the results. To assure no significant difference between groups, ANOVA will be used to compare the means of height, weight, years in the Army, jump experience, and age. A chi-square test will be used to compare prevalence of prior ankle injuries among the three groups and injury rates will be compared using chi-square analysis with a 3x2 table.

Progress: Three hundred soldiers made two jumps each for a total of 600 jumps. Only two ankle injuries resulted (in the unbraced group). This low number of injuries was insufficient for statistical analysis.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/10 Status: Completed

Title: A Descriptive Study of Obstetrical and Perinatal Care With Emphasis on Several Factors Related to Morbidity and Other Outcomes - A Chart Review

Start Date: 17 Nov 89 Est Completion Date: Dec 89

Department: Family Practice Facility: MAMC

Principal Investigator: MAJ William F. Miser, MC

Associate Investigators:
MAJ B. Wayne Blount, MC
LTC Charles E. Henley, MC
CPT William L. Lang, MC
LTC Andrew M. Thompson, MC
LCDR Gerard D. Kennedy, MC, USN

Key Words: obstetric, perinatal care, morbidity

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $50.00	Periodic Review: N/A

Study Objective: There have been no studies to date looking at the full spectrum of obstetrical care from the first prenatal visit and continuing through the first three months after delivery. The objective of the study is to create a data base on obstetrical and perinatal care that can be used for teaching Family Practice residents. The detailed research objectives include: a descriptive study of single gestation pregnancies delivered at MAMC for a one year period; a gestational diabetes study; a screening of prenatal urine cultures; a nuchal cord study; a re-evaluation of birthweight curves; a study of anemia and hematocrits in pregnancy; a study of PAP smears at the initial OB visit; a study of circumcisions; a study on type of neonatal feeding; and studies to determine: if there is a difference in pregnancies and outcome for active duty soldiers, dependent wives, and unwed mothers; if patients who have had some form of uterine surgery have an increased risk of placental problems; the outcome of those patients that have first trimester bleeding and go on to deliver; the outcome of those that have a diagnosis of hyperemesis gravidarum during the first trimester of pregnancy; if amniocentesis increases the risk for other complications during pregnancy; if there is a month or time of year in which certain complications occur more frequently; the status of labor in women when admitted; if women women deliver more often during the night hours; the prevalence of sexually transmitted diseases which are detected during the initial OB visit; and the rate of infant admission during the first six months of life.

Technical Approach: Charts from approximately 3000 obstetrical patients with single gestation deliveries, as well as the charts of the infants, will be reviewed, with 193 specific pieces of information obtained.

Progress: The chart survey form that was created for use on this protocol has been adopted for use for data collection for teaching purposes by the Department of Family Practice at MAMC as well as at Tripler Army Medical Center and at Ft Bragg and Ft Belvoir.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/11 Status: Completed

Title: The Correlation of Personal Health Risk Appraisals and Attitudes Toward Health Promotion in Military Family Physicians

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

Department: Family Practice Facility: MAMC

Principal Investigator: MAJ William F. Miser, MC

Associate Investigators:
MAJ Wade A. Lillegard, MC
LTC Charles E. Henley, MC
CPT Hollandsworth, Ft Lee, VA
MAJ B. Wayne Blount, MC
LCDR Thomas A. Miller, MC

Key Words: health promotion, counselling, military physicians

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $20.00	Periodic Review: N/A

Study Objective: To describe the health risk profile of military family physicians; to determine if there is a difference between services and between types of practice (clinical, academic, administrative); to assess physicians' attitudes and practices on certain health promotion issues towards themselves and their patients; to correlate these attitudes and practices with their own health risk profile; and to determine perceived obstacles when counselling patients.

Technical Approach: Military family physicians attending the Uniformed Services Academy of Family Physicians Meeting, March 1990, will be asked to complete a questionnaire on their attitudes and practices regarding health promotion. They will also be asked to complete the U.S. Army Health Risk Appraisal Assessment Form. Blood cholesterol, blood pressure, skin fold thickness, height, weight, flexibility, and strength measurements will be performed using standard techniques. Data will be analyzed using the Statistical Package for Social Sciences. Means will be compared using ANOVA for independent samples and correlations will be done using Kendall's Tau. The Mann-Whitney U Test will be used to compare medians of the data involving the use of Likert scales.

Progress: Of 205 physicians recruited, 153 completed the survey. Over 38% were in the very good or excellent fitness category and none were in a poor fitness category. Nearly all (99%) agreed that health promotion is a major responsibility of the family physician, 86% felt that they practiced what they preached, and 78% felt that their own lifestyle could be used as a role model of health behavior. There were significant associations between the physicians' own health-related habits and their attitudes, practices, and perceived success in counselling patients on health promotion issues. The two common barriers mentioned toward health promotion were inability or unwillingness of patients to change their lifestyles and inadequate time to properly counsel patients on health risk behaviors. A thesis has been prepared as partial fulfillment of a Master's degree and the paper will also be submitted for publication.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 89/66 Status: Terminated

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: Sep 90

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: The investigators had planned to use ROTC cadets at Ft Lewis for summer training. 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.

The protocol was terminated in September 1990 due to the reassignment of the principal investigator and the inability to appoint a new principal investigator. No work was done on the protocol.

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

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DEPARTMENT OF MEDICINE

Detail Summary Sheet

Date: 30 Sep 90 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: Sep 90

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

Technical Approach: Allergists in the Army, Air Force, and Navy will participate in this multicenter study. Adult (≥21 years) subjects (n=200) requiring penicillin skin testing will be questioned for prior exposure to beta lactam antibiotics and will receive prick skin testing, followed by intradermal skin testing for each reagent to which there is no significant prick skin test reaction, to PPL, fresh pen G, penicilloate (MDM-A), penicilloate (TS-Sullivan), and penilloate (MDM-B), in the usual concentrations, as well as routine histamine and diluent controls. The two penicilloates and the penilloate are not commercially available and will be prepared in a single batch at FAMC. MDM-A and MDM-B will be prepared following Saxon's clarification of Levine's method. Penicilloate TS will be made by Sullivan's method. A blood sample will be drawn from subjects with positive skin test reactions and frozen for use in a future *in vitro* study of comparative potency of the testing reagents. It is hoped that at least 200 subjects without history of adverse penicillin reaction will be tested and that at least 30 skin test positive patients will complete the comparative potency phase of the study. The number of history-positive patients and the number of history-negative subjects in whom one or more skin test results are positive will be reported as a percentage of the total number of patients and subjects tested for each reagent. In the comparative potency evaluation, the 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: 75 patients have been entered at MAMC and a total of 169 from all participating institutions. One anaphylaxis reaction was reported at FAMC.

Detail Summary Sheet

Date: 30 Sep 90	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 90

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: One subject was entered in FY 90 for a total of four subjects. Preliminary data suggest that forced alkaline diuresis is safe and effective for ASA overdose, even when levels are greater than 100 mg/dl.

Detail Summary Sheet

Date: 30 Sep 90 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 (Aug 88)*

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 90

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

Eleven subjects were entered in FY 90, with data completion on four subjects.

* MAJ Nuovo original PI

Detail Summary Sheet

Date: 30 Sep 90 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: Sep 90

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: 47 additional subjects were enrolled in FY 90 for a total of 121 subjects. Data collection is complete on 115 of these subjects.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 89/27 Status: Completed

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: Sep 90

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: 18 subjects were entered in FY 90 for a total population of 63 subjects.

A manuscript has been accepted by Blood and an abstract has been submitted for presentation at the 1991 Annual Meeting of the American College of Physicians.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/59 Status: On-going

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

Start Date: 20 Apr 90 Est Completion Date: Apr 92

Department: Medicine/Cardiology Facility: MAMC

Principal Investigator: COL Roger F. Chamusco, MC

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

Key Words: coronary artery disease/chronic smokers

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $3525.00 Periodic Review: N/A

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

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

Progress: The investigators are awaiting the purchase of equipment to measure coronary sinus flow. The study will be implemented when it is received.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 89/04 Status: Terminated

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: MAJ Everardo Cobos, MC (Jun 90)*

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

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

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Jun 90

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 were entered. Responses were disappointing with nondurable partial response the best response. Toxicity was significant but not unexpected. The protocol was terminated due to lack of efficacy.

* CPT Bouvier original PI

Detail Summary Sheet

Date: 30 Sep 90 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: LTC Ronald H. Cooper, MC (Jun 90)*
Associate Investigator: CPT Robert J. Kazragis, MC
Key Words: hepatitis B, vaccine, conventional vs reduced dose
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $3785.00 Periodic Review: Jun 90

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: 16 patients were entered in FY 90 for a total of 76 subjects. The investigators will continue to draw serum samples until the 360 day samples on all patients are completed. Preliminary data at three months show percent seroconversion of 85.7%, 71.4%, and 80.0% for 10 mcg IM, 1 mcg ID, and 2 mcg ID, respectively, and mean anti-HBs titers of 135.0, 37.2, and 38.4, respectively.

An Abstract was presented at the Washington State/American College of Physicians Annual meeting in December 1989.

* CPT Kazragis original PI

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/80 Status: On-going

Title: Evaluation of Two Doses of SQ 32,756 (BV-araU) and Matching Placebo Capsules in the Treatment of Primary Varicella-Zoster Virus Infection (Chickenpox) in Immunocompetent Patients

Start Date: 15 Jun 90 Est Completion Date: Sep 91

Department: Medicine/Infectious Disease Facility: MAMC

Principal Investigator: COL Ronald H. Cooper, MC

Associate Investigator: LTC Rodney A. Michael, MC

Key Words: varicella zoster, SQ 32,756, dose evaluation

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

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

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

Progress: No patients have been entered. The investigators are awaiting approval of the study from Health Services Command.

Detail Summary Sheet

Date: 30 Sep 90 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 90

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: Six patients were entered in FY 89 for a total of 26 subjects. All toxicities were predictable. Early data indicate that this combined modality regimen appears to be effective in Stage III NSCLC and that ototoxicity is the limiting side effect.

An abstract has been accepted for presentation at the 1991 meeting of the American Society of Clinical Oncology

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

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 89/18 Status: Completed

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: Sep 90

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. 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: 158 subjects were entered in this study. Data analysis is in progress. Preliminary findings indicate that leukocyte esterase appears to be 92% sensitive and 57% specific in combined symptomatic/asymptomatic groups.

Detail Summary Sheet

Date: 30 Sep 90 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: Sep 90

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: Complete data have been obtained on 18 subjects for Part 1 of the study. No patients have been entered in Part 2.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 89/49 Status: Completed
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: Sep 90

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: This study demonstrates that in the rat a high affinity binding protein such as SHBG can decrease plasma clearance and CSF appearance of ^{3}H-T, and the final CSF concentration of steroid is, in part, dependent on the "free" plasma fraction, regardless of type of plasma binding proteins present.

An abstract of this work was presented at the 1990 meeting of the Western Section of the American Federation for Clinical Research and at the 1990 meeting of the Endocrine Society.

Detail Summary Sheet

Date: 30 Sep 90 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: Sep 90

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 tolbutamide modified intravenous glucose tolerance test will be performed at the end of each two week placebo period and at the end of each six week treatment period. Each individual will serve as both control and subject. Data will be analyzed using the Statview II program for the Macintosh computer system.

Progress: Two subjects were entered in this study in FY 90 for a total of 25 subjects. Twelve subjects completed the entire protocol. Anthropometric measurements, SMA-20, CBC, steroid hormones, lipids, and glucose tolerance data have been collected on all subjects throughout the study and results have been entered into a computerized database. Insulin assays have been performed. The MINMOD IVGTT analysis program has been purchased to characterize the IVGTT data.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 88/49 Status: Terminated

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 (Sep 89)*

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 90

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 ≥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 were entered. Upon re-evaluation, it was determined that, in light of revisions required by the FDA, the study could not be performed.

* CPT Horan original PI

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 89/51 Status: Terminated

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 Investigator: LTC W. Hal Cragun, MC

Key Words: cefpodoxime proxetil, cefaclor, randomized, blinded

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $150.00 Periodic Review: Sep 90

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 were entered. The protocol was terminated due to the difficulty in obtaining subjects.

Detail Summary Sheet

Date: 30 Sep 90	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: Sep 90

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: Eight patients were enrolled in FY 90 for a total of 17 subjects. Light reflection rheography and duplex scanning have been performed on each patient with no adverse reactions.

Detail Summary Sheet

Date: 30 Sep 90 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 Cost: -0- MEDCASE Est Accumulative OMA Cost: $785.00 Periodic Review: Sep 90

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: No further work has been done on this protocol. 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 90 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 siz , functional relationship, hepatic/mitochondrial forms

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: 708.00	Periodic Review: Sep 90

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

Technical Approach: Human sperm will be collected and prepared. Ligase will be protected with 5 mM p-aminobenzamidine and extracted with 1.0% Triton X-100. The crude preparation will be delipidated by serial washings with n-butanol, acetone, and ether. The final pellet will be dried under nitrogen and reconstituted in 10 mM phosphate buffer. Affinity chromatography with Blue Sepharose CL-6B will be the principle purification step. Ligase will be eluted from the column with palmitoyl CoA dissolved in phosphate buffer. Fractions will be collected, read at 280 nm to determine the presence of protein, and assayed for ligase activity.

It is possible that several proteins which require nucleotides will be retained on the column; the eluate obtained by adding a palmitoyl CoA solution should contain those enzymes which possess a relatively high affinity for acyl CoA. Ligase acyl CoA:L-glycerol -3-phosphate transferase, palmitoyl carnitine O-acyl transferase and palmitoyl CoA deacylase would fall into the latter category. Ligase differs from the other acyl CoA dependent enzymes by virtue of an approximate 50-100 fold lesser affinity for palmitoyl CoA and an absolute requirement for ATP. By using a concentration gradient of palmitoyl CoA and/or an ATP elution step, these properties should facilitate purification of ligase.

Classical purification procedures for ligase are extremely complicated and involve multiple intermediate steps. On the other hand, affinity chromatography of a related enzyme using a related matrix yielded a 14-fold increase in specific activity with a single pass over the column. Purity and sizing of ligase will be accomplished by isoelectric focusing, polyacrylamide gel electrophoresis, and size exclusion chromatography (either HPLC or Sephadex G200). Protein will be determined with a BioRad kit and ligase specific activity will be calculated after each purification step.

Progress: The investigators are currently trying to isolate sperm plasma membranes.

Detail Summary Sheet

Date: 30 Sep 90 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: Sep 90

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: No further work was done on this study in FY 90. Previous work has demonstrated that fresh human spermatozoa can incorporate palmitic and docosahexaenoic acid into exogenous and endogenous lysophosphatides. Presented at the 1988 Meeting, Amer Soc Andrology (Jones, Plymate: J Androl 9:41, 1988). Publication: Journal of Andrology 10:346-50, 1989.

Detail Summary Sheet

Date: 30 Sep 90 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: Sep 90

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 currently are attempting to isolate sperm plasma membranes.

Detail Summary Sheet

Date: 30 Sep 90 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 90

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: The investigators conclude that short term incubation of human sperm with A23187 appears to suppress 22:6 incorporation into phosphatidylethanolamine and does not influence phosphatidylcholine synthesis.

Presentation: American Society of Andrology 1990 (J Androl 11: P49, 1990).

Detail Summary Sheet

Date: 30 Sep 90 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 90

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: One patient was entered in FY 90. Tissue samples are pending analysis. Further accrual of patients has been hampered by a reduction in the number of VBG procedures.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/38 Status: On-going

Title: Detailed Studies Into Membrane Lipid Synthesis in Human Sperm

Start Date: 16 Feb 90 Est Completion Date: Feb 99

Dept/Svc: Medicine/Endocrinology Facility: MAMC

Principal Investigator: LTC Robert E. Jones, MC

Associate Investigators: COL Stephen R. Plymate, MC
CPT Brenda K. Bell, MC

Key Words: sperm, membrane lipid synthesis, pathways

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $3494.00	Periodic Review: N/A

Study Objective: To elucidate the biochemical pathways for membrane lipid synthesis (excluding cholesterol) present in freshly ejaculated human spermatozoa from donors of proven fertility.

Technical Approach: Sperm will be washed and the sample diluted to achieve a concentration of $2x10^8$ sperm/ml. The incubation buffer, optimized for fatty acid activation, will consist of 380 mM TRIS [pH 8.4], 20 mM ATP, 20 mM $MgCl_2$, 0.1 mM coenzyme A (CoASH), 5 mM dithiothreitol, and 10-50 µM fatty acid, either ^{3}H-9,10-16:0, ^{14}C-1-16;0, or ^{14}C-1-22;6. The reaction will be initiated by the addition of 10^7 sperm. Blank incubations will be performed in the absence of CoASH or the specific starting substrate to investigate the metabolic mechanisms of lipid turnover. Methylation of phosphatidylethanolamine (PE) will be measured by incubating ^{3}H-methyl-S-adenosylmethionine (SAM) with diacyl PE or a ^{14}C-labeled fatty acid, ^{3}H-SAM and 1-acyl-2-lyso PE. Another pathway for plasmalogen or ether lipid synthesis in nongerminal tissues will be assessed by incubating sperm with ^{14}C-22:6, 1-palmitoyl-32-lyso PI (phosphatidylinositol) or -PC (phosphatidylcholine) and ^{3}H-1-hexadecanol in the aforementioned buffer. Alternatively, ^{3}H-hexadecanol, ^{14}C-22:6, unlabeled 16:0 will be coincubated with dihydroxyacetone phosphate (DHAP). The reaction will be terminated after 1 hour and lipids will be extracted and dried. Incorporation of labeled fatty acids into sphingomyelin (SM) will be determined by detection of the fatty acyl radiolabel in the SM region of the thin layer chromatography (TLC) plates. After resolubilization in chloroform and methanol, lipids will be separated on LK5 TLC plates. Standards will be run on each plate and spots corresponding to standards will be scraped and counted. Plasmalogen formation will be assessed by performing mild acid hydrolysis on the extracted phospholipids prior to TLC or before rechromatography and determining DPM's in the fatty aldehyde and lysophospholipid regions. The presence of ether lipids will be determined by their resistance to alkaline and enzymatic hydrolysis prior to TLC. Mono and diacyl phospholipid synthesis will be assessed by free fatty acid release from SM and by using phospholipases A_2 (PLA_2) and B (PLB).

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

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/57 Status: On-going

Title: Synthesis of Phospholipids in Spermatozoa From the Laboratory Rat *(Rattus norvegicus)*: A Pilot Study

Start Date: 20 Apr 90 Est Completion Date: May 90

Department: Medicine/Endocrine Facility: MAMC

Principal Investigator: LTC Robert E. Jones, MC

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

Key Words: sperm membrane phospholipids, animal model

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $320.00	Periodic Review: N/A

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

Technical Approach: Mature, sexually rested male rats will be euthanized and both testes and epididymes will be removed. Testicular sperm will be harvested and epididymal sperm will be flushed from the lumen with normal saline. Sperm will be washed in an isotonic buffer and resuspended at a concentration of 200 million/ml. Long chain fatty acid: CoA ligase will be measured with 3H-16:0 and 14C-22:6 as substrates. Phospholipid synthesis from labeled free fatty acids and either lyso-phosphatidylcholine or lyso-phosphatidylethanolamine will be determined using thin layer chromatography to separate phospholipid classes.

Ligase activity will be calculated as nmoles fatty acyl CoA formed/min/mg protein. Phospholipid synthesis will be expressed as nmoles fatty acid incorporated/hr/10 million sperm. Descriptive statistics will be used in the analysis.

Progress: Epididymal spermatozoa from three rats were isolated and washed. The spermatozoa were incubated with labelled palmitic acid or docosahexaenoic acid in the presence of lysophosphatides. There was no incorporation of fatty acids into phospholipids; therefore, rats do not appear to be an appropriate model for study unless unique optima for phospholipid synthesis are present in rats.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/77 Status: On-going

Title: Accuracy of Four Hour and Six Hour Urine Urea Nitrogen Measurements in Patients Receiving Nutritional Support

Start Date: 18 May 90 Est Completion Date: Dec 90

Department: Medicine/Internal Facility: MAMC

Principal Investigator: CPT Lynn M. Keenan, MC

Associate Investigator: MAJ Richard H. Snyder, MC

Key Words: urine urea nitrogen measurements, nutritional balance

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $118.00	Periodic Review: N/A

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

Technical Approach: Thirty medical or surgical patients with or without Foley catheters, receiving total parenteral or enteral nutrition will be studied. The following information will be obtained from the patient's chart: diagnosis, baseline albumin, pre-albumin, total lymphocyte count, electrolytes, magnesium, phosphorus, and calcium. On day one of the study, a four hour urine specimen will be obtained between 0800 and 1200 hours. Patients will then have a six hour urine specimen obtained from 1200 to 1800 hours. On day two of the study, a 24 hour urine collection will be begun for urine urea nitrogen and creatinine. Specimens will then be processed for determination of urea nitrogen, and the 24-hour specimens will be processed for creatinine. Values for urine urea nitrogen will then be placed into the following formulas to determine positive or negative nitrogen balance:

Nitrogen balance = intake nitrogen - output nitrogen

Output nitrogen = UUNmg/100 cc x urine vol + 100 + 20% of UUN + 2 gm/day.

The values for 4 and 6 hour urine samples will be extrapolated to fit into the formula. Urine and serum creatine will be obtained to calculate creatinine clearance. The Student's t-test will be utilized to review the data obtained.

Progress: Thirty patients have been entered with the results of only eight patients being usable due to the fact that some of the lab slips were inadvertently discarded before being recorded in the study files.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/98 Status: On-going

Title: Does Laparoscopy Add to the Diagnosis of Nonfocal Liver Disease

Start Date: 17 Aug 90 Est Completion Date: Apr 92

Department: Medicine/Internal Facility: MAMC

Principal Investigator: CPT Robert J. Lodato, MC

Associate Investigators: MAJ Michael F. Lyons, MC
MAJ Gregory E. Schlepp, MC
MAJ Amy M. Tsuchida, MC

Key Words: liver disease, laparoscopy, pinch & core biopsy

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

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

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

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

Detail Summary Sheet

Date: 30 Sep 90 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: Sep 90

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 90. 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 90 Protocol No.: 89/53 Status: Terminated

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: May 90

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: This study was terminated due to apparent clinical failure of treatment with itraconazole.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/62 Status: On-going

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

Start Date: 20 Apr 90 Est Completion Date: Oct 91

Department: Medicine/Internal Facility: MAMC

Principal Investigator: CPT Timothy R. Murray, MC

Associate Investigators:

COL Roger F. Chamusco, MC	MAJ Doreen Saltiel, MC
COL Klaus Jade, MC	MAJ Anthony R. Truxal, MC
LTC Howard M. Cushner, MC	CPT William T. Brown, MC
MAJ Duane J. Jeffers, MC	CPT Donna Mercado, MC
MAJ Alice Mascette, MC	CPT James W. Norys, MC

Key Words: embolism/cholesterol/left heart catheterization

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $3400.00	Periodic Review: N/A

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

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

Progress: 25 patients have been entered.

Detail Summary Sheet

Date: 30 Sep 90	Protocol No.: 90/69	Status: Completed

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

Start Date: 20 Apr 90 Est Completion Date: Dec 90

Department: Medicine/Internal Facility: MAMC

Principal Investigator: CPT Sheri E. Nottestad, MC

Associate Investigators: MAJ Everardo Cobos, MC
MAJ Alice M. Mascette, MC
MAJ Galynn E. Schilhab, MC

Key Words: heparin, inhibition, nitroglycerin

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

Study Objective: To determine if the previously reported inhibition of heparin effect by I.V. nitroglycerin is dose related.

Technical Approach: Data will be collected on 100 patients, ages 35-85, admitted to the Coronary Care Unit for presumed unstable angina or acute myocardial infarction and treated with I.V. nitroglycerin and I.V. heparin. Patients will be managed in the usual fashion by the primary physicians with PTT values obtained after institution of heparin and adjustments in heparin dose made as determined by the primary physician. When the PTT value is first obtained in the range from 55-90, the dose of heparin and the dose of nitroglycerin will be recorded. To insure that both medications are at steady state when PTT values are measured, phlebotomy for PTT will be made at least one hour after a dose change in nitroglycerin and at least six hour after a dose change in heparin. For analysis of data, patients will be divided into two groups based on the dose of I.V. nitroglycerin; 5-20 mcg or >100 mcg. Patients whose nitroglycerin dose fits neither group will be excluded from analysis. The mean heparin dose will be calculated for both groups and the statistical significance determined. In addition, the effect of age, weight, severity of angina, and degree of congestive heart failure will also be evaluated. The mean dose of heparin for the two groups will be compared using an unpaired t-test. ANOVA will be used to determine the significance of age, weight, severity of angina, and degree of congestive heart failure.

Progress: Data were collected on 130 patients. Statistical analysis is in progress. Preliminary data indicate no dose relationship between I.V. nitroglycerin and I.V. heparin.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/99 Status: On-going

Title: Comparison of the Serum Effusion Albumin Gradient to Traditional Criteria for Transudates in Patients with Pleural Effusions Secondary to Congestive Heart Failure

Start Date: 17 Aug 90 Est Completion Date: Sep 91

Department: Medicine/Pulmonary Facility: MAMC

Principal Investigator: CPT Bernard J. Roth, MC

Associate Investigator: LTC William H. Cragun, MC

Key Words: heart failure, serum effusion, transudates, exudates

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $635.00	Periodic Review: N/A

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

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

Progress: The protocol is awaiting final approval of revisions required by the Institutional Review Board and has not been implemented.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/36 Status: On-going

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

Start Date: 16 Feb 90 Est Completion Date: Dec 91

Dept/Svc: Medicine/Cardiology Facility: MAMC

Principal Investigator: MAJ Doreen Saltiel, MC

Associate Investigators:	LTC George Rebecca, EAMC
COL Roger F. Chamusco, MC, MAMC	LTC Dale Wortham, MC, WRAMC
COL Richard A. Davis, MC, FAMC	MAJ Thomas Martyak, MC, WBAMC
COL Joseph A. Paris, MC, LAMC	MAJ Alice Mascette, MC, MAMC
LTC Cloyd B. Gatrell, MC, MAMC	CPT Sheri Nottestad, MC, MAMC

Key Words: myocardial infarction, rt-PA, 3-hour vs 90-minute

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $15,000.00	Periodic Review: N/A

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

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

Progress: Approximately ten patients have entered the study.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 87/59 Status: Terminated

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 Gregory E. Schlepp, MC (Nov 89)*

Associate Investigators:
MAJ Marshall E. McCabe, MC
LTC Thomas F. O'Meara, MC
MAJ Amy M. Tsuchida, 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: Sep 90

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. The study was terminated due to an alternative protocol for treatment of duodenal ulcers.

* MAJ Schlepp was the original PI in Mar 87 and left in May 88. He returned to MAMC in Nov 89. MAJ Amy Tsuchida was the interim PI.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/35 Status: On-going

Title: Home Intravenous Antibiotic and Heparin Therapy in a Military Setting

Start Date: 16 Feb 90 Est Completion Date: Feb 91

Dept/Svc: Medicine/Internal Medicine Facility: MAMC

Principal Investigator: CPT Philip S. Schwartz, MC (Jun 90)*

Associate Investigators: MAJ Richard H. Snyder, MC
CPT Anne E. Vockroth, MC

Key Words: IV therapy, home setting, family member or patient

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

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

Technical Approach: Approximately 30, medically stable patients ≥ 18 years will be enrolled. Eligible patients will be those requiring >10 days total antibiotic therapy (minimum 5 days of home care) and patients requiring 7-14 days of heparin therapy secondary to deep venous thrombosis.

Before patients are released from the hospital, the patient and a family member will be given instruction in maintaining the access device, drug mixture and storage, infusion technique, therapy monitoring, and trouble shooting of potential side effects of the therapy. If proficiency and compliance can not be documented after an appropriate period of instruction, the patient will be taken off study.

A home health nurse will be present for the first dose of medication. Thereafter, the medication will be given by the patient or the trained family member. The home health nurse will make periodic home visits to check on the patient's progress (at least every three days). Samples for laboratory analysis will be drawn by the home health nurse as recommended for the drug each individual patient is receiving.

The paired t-test will be used to compare actual cost to hospital cost and safety will be described using frequencies.

Progress: Approximately 10 subjects have been entered in the study.

* Dr. Vockroth, original PI.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/07 Status: On-going

Title: Treatment of Thrombocytopenia, Hemolytic Anemia, or Neutropenia with Ascorbic Acid

Start Date: 17 Nov 89 Est Completion Date: Oct 91

Dept/Svc: Medicine/Hematology Facility: MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ Patrick L. Gomez, MC
LTC Howard Davidson, MC
MAJ Mark H. Kozakowski, MC
MAJ Kenneth A. Bertram, MC
CPT Denis P. Bouvier, MC
MAJ Everardo Cobos, MC
CPT Robert Sheffler, MC

Key Words: thrombocytopenia, hemolytic anemia, neutropenia

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $585.00 Periodic Review: N/A

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

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

Progress: Two patients have been entered in the study. It has been difficult to find patients with immune neutropenia and immune hemolytic anemia refractory to standard therapy. The presentation of these patients tends to be sporadic.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/82 Status: On-going

Title: A Pilot Study of Carboplatin and Daily Oral Etoposide in the Treatment of Advanced Non-small Cell Lung Cancer

Start Date: 15 Jun 90 Est Completion Date: Jun 93

Department: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ Everardo Cobos, MC
LTC Howard Davidson, MC
MAJ Patrick L. Gomez, MC
MAJ Kenneth Bertram, MC
MAJ Robert L. Sheffler, MC

Key Words: lung cancer, non-small cell, carboplatin, etoposide

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $3000/yr Periodic Review: N/A

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

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

Progress: Two patients have been entered with no adverse effects.

Detail Summary Sheet

Date: 30 Sep 90 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 90

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 90. Three of the eight subjects have evidence of primary hypothyroidism on the basis of the TRH testing. One subject had an elevated baseline TSH but normal response to TRH. Those found to be hypothyroid have been treated with thyroid hormones. Follow-up TRH testing has been incomplete. Urinary T_4, T_3 assay development has not been accomplished. Preliminary results indicate a higher incidence of hypothyroidism associated with the nephrotic syndrome than previously reported.

Detail Summary Sheet

Date: 30 Sep 90	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 90

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 90. In previous years, four patients have been entered. Patient recruitment has been slow due to the rarity of patients with primary adrenal insufficiency.

Detail Summary Sheet

Date: 30 Sep 90 | 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 Stanley Allison, MC
COL Francis G. LaPianan, MC
COL Leonard Wartofsky, MC
LTC Robert E. Jones, 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 90

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: One patient was entered in this study in FY 90 for a total of two entries at MAMC. Ten subjects have been entered Army-wide.

This study is nearly complete with the data being analyzed. Recruitment of suitable patients has been unexpectedly slow, apparently due to a decline in severe Graves' ophthalmopathy nation wide. A manuscript is being prepared for submission for publication.

Detail Summary Sheet

Date: 30 Sep 90 | Protocol No.: 87/35 | Status: Completed

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: COL Gary T. Treece, MC (Jun 90)*

Associate Investigator: LTC Stanley S. Levsky, DC

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: Jun 90

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: Two patients were entered in FY 90 for a total of 64 subject enrollments.

Coincident with the PCS of an important coinvestigator and the accumulation of a sufficient number of subjects, the protocol is deemed complete. In at least one subject previously undiagnosed, diabetes mellitus was detected by determining gingival blood glucose. Whole blood glucose will now be determined from stored samples. Following the completion of these determinations, statistical analyses will be performed to determine the correlations between gingival blood glucose and plasma and whole blood glucose simultaneously obtained.

* LTC Levsky original PI.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 88/34 Status: Completed

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 90

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. The protocol was closed by Pharmacia due to sufficient accrual of patients.

**Original PI

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/19 Status: On-going

Title: A Comparison of Ranitidine 300 mg HS, Ranitidine 300 mg BID, Ranitidine 300 mg TID, and Ranitidine 300 MG QID in the Treatment of Duodenal Ulcer Disease

Start Date: 16 Jan 90 Est Completion Date: Jan 92

Dept/Svc: Medicine/Gastroenterology Facility: MAMC

Principal Investigator: MAJ Amy M. Tsuchida, MC

Associate Investigators: MAJ Michael F. Lyons, MC
MAJ Gregory E. Schlepp, MC

Key Words: duodenal ulcer disease, Ranitidine

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

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

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

Progress: Two patients have been enrolled in the study with healing at 4 weeks of treatment with no complications.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 89/54 Status: Completed

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: May 90

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: Ten subjects were entered. Results showed an increase in 24 hour aluminum excretion from 6.3 to 187.8 mcg/24 hours and a decrease in phosphate excretion form 1094.2 to 798.2 mg/24 hours. All other parameters measured did not change significantly, indicating that there was no significant change in bone metabolism after 3 days of treatment with sucralfate.

An abstract has been submitted for presentation and a paper was submitted for consideration for the Steger Research Award.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/105 Status: On-going

Title: Efficacy of Oral Versus Intravenous Estrogens for the Control of Uremic Bleeding

Start Date: 21 Sep 90 Projected Completion Date: Jan 91

Department: Medicine/Interr Facility: MAMC

Principal Investigator: C i S. Willadsen, MC

Associate Investigators: I c l M. Cushner, MC
·do Cobos, MC
'er L. Cadiz, MC
L. Mercado, MC

Key Words: uremic bleedir ns, oral, intravenous

Accumulative MEDCASE ulative Periodic Review:

Cost: -0- $2500.00 N/A

Study Objective: To deter al estrogens are as effective as IV estrogens in corre mal bleeding times in uremic patients.

Technical Approach: The e s of oral estrogens for the control of uremic bleedin mpared to intravenous estrogens by measuring the bl in affected patients. The sample will include 20 n tients with a bleeding time greater than 8 minutes a ronic renal failure or end-stage renal disease on dia uremia (creatinine clearance of <25 cc/min and platele on <2 weeks prior to enrollment). Collected data wil istory of bleeding, age, sex, and type of renal disease. times will be compared via an unpaired T test.

Progress: This protocol v ly approved and has not been implemented.

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 90	Protocol No.: 90/12	Status: On-going

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

Start Date: 13 Nov 89	Est Completion Date: Dec 89
Department: Nursing	Facility: MAMC
Principal Investigator:	MAJ Patricia J. Chessher, AN
Associate Investigator:	LTC Vicky M. Sheldon, AN
Key Words:	health promotion, patients, acute care nurses

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

Study Objective: To describe the predisposing, enabling, and reinforcing factors perceived by staff nurses as affecting their use of health promotion; to determine under what conditions staff nurses consider health promotion activities for a patient can be effective, and to determine the extent to which staff nurses consider it is their responsibility to promote their patients' health.

Technical Approach: Approximately 60 staff nurses from the Acute Care Nursing Section will be enrolled. A study packet containing a cover letter and a questionnaire will be distributed to each subject. A follow-up postcard will be sent to each subject at three weeks to urge individuals to return the questionnaire, if they have not done so. The questionnaire will consist of two parts. Section one addresses knowledge, attitudes, and perceptions of the effectiveness of health promotion as well as the amount of time available to teach health promotion to patients and the time spent in teaching health promotion. Section two is a demographic data form.

Descriptive statistics, central tendency, distribution and range will be used for data analysis. Correlations and associations between measures and self-reported behavior will be done. Demographic data will be used to describe the characteristics of the sample.

Progress: Analysis of data is in progress.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/70 Status: Completed

Title: A Study of Cultural and Perinatal Factors that Affect Postpartum Outcomes for Asian Women and Their Families

Start Date: 20 Apr 90 Est Completion Date: Apr 92

Department: Nursing Facility: MAMC

Principal Investigator: COL Donna J. DeVore, AN

Associate Investigator: Maura G. Egan, Ph.D.

Key Words: postpartum outcome, Korean, culture, perinatal factors

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

Study Objective: To determine the factors that contribute to positive postpartum outcomes for Korean women by investigating the delivery of culturally appropriate nursing care for immigrant Korean women from their perspective and that of the nursing staff involved with their care during the course of maternity through postpartum care.

Technical Approach: Thirty Asian women, not more than 3 months postpartum, >18 years of age will be studied as well as LPN and RN nursing staff. The study will use a descriptive, correlational design to examine the retrospective birth experience, as well as postpartum and family outcomes for two groups of Asian women and their families (MAMC Korean patients and Vietnamese women from Virginia Mason Hospital in Seattle). The study will include data collection from the nursing staff at the two medical centers where the women have delivered. The patient subjects will be interviewed by the researcher and/or bilingual field assistants to collect demographic data, data on the perinatal and postpartum experience, perceived support for culturally appropriate care, and perceived family adaptation to the birth experience. In addition, the Family APGAR (Smilkstein, 1982) will be translated and administered to the subjects. The OB nursing staff from all shifts on the appropriate units will be asked to complete a survey questionnaire to collect data on both subjective and objective appraisal of their knowledge of culturally appropriate care. Content analysis and descriptive statistics will be used to analyze the data. Chi square, correlations, and t-tests will be used, where appropriate, to determine relationships between variables and within and between the staff and cross-cultural patient samples.

Progress: Thirty Asian women and 23 nurses were entered in the study. The nurses expressed a need for more information about how to care for culturally diverse patients and expressed concern and conflict over the dilemma of trying to help acculturate the Asian patients and teach western practices viz a viz trying to support the patients in their health beliefs and practices. Data have been analyzed using only descriptive statistics and the data from the patients at Virginia Mason have not been compared to that of the MAMC patients because of insufficient sample size at Virginia Mason.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/05 Status: Completed

Title: The Effects of Lumbar Support on the Incidence of Adult Post-Spinal Anesthesia Headache

Start Date: 17 Nov 89 Est Completion Date: Dec 89

Department: Nursing Facility: MAMC

Principal Investigator: MAJ Kenneth I Hartz, AN

Associate Investigators: COL Michael R. Moon, MC
COL Sidna P. Wimmer, MS
Janet A. Marvin, MN
Susan L. Woods, MN

Key Words: spinal anesthesia, headache, lumbar support

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $140.00	Periodic Review: N/A

Study Objective: To determine it the use of lumbar support during surgery is associated with a reduced incidence of adult post-spinal anesthesia headache.

Technical Approach: Approximately 60 patients for whom a spinal anesthetic is the technique of choice and who are in the supine or low lithotomy position will be studied. A preoperative questionnaire obtaining information on headache history, back pain, and state of anxiety will be completed by the anesthesia care provider. Patients will be randomly assigned to either have a foam rubber lumbar support used during surgery or to a control group with no lumbar support. Pressure on the spine will be monitored by use of a bladder from a blood pressure cuff attached to a mercury manometer via pressure tubing. Intraoperative and post-operative questionnaires will also be filled out by the anesthesia care provider to obtain information pertinent to the study. The patient will be asked to complete a post-operative questionnaire regarding the recovery period, the amount of back pain, and the number and intensity of headaches after surgery.

Descriptive statistics and the Chi square test will be used for data analysis. Statistical comparisons will be made on the basis of the presence or absence of a post-spinal anesthetic headache, using the Chi-square test. The relationship of other variables to the incidence of headache such as age, gender, hydrational status, history of chronic headaches, time of ambulation after surgery, anxiety level, and position during surgery will be examined. Other variables will include type of spinal needle, amount of trauma in placing the needle, and amount of pressure applied by the lumbar support. The data obtained in this study will also be compared to that reported in the literature.

Progress: Eleven subjects received lumbar support and 17 were in the control group. Among those who reported back pain, the intensity of the back pain was significantly higher in those in the nonsupport group. No other significant differences were found. A thesis has been completed as a requirement of an advanced degree in nursing at the University of Washington.

Detail Summary Sheet

Date: 30 Sep 90	Protocol No.: 90/33	Status: Completed

Title: Differences in Levels of Knowledge About Anesthesia Nursing Between Entry Level Nursing Students and Senior Nursing Students

Start Date: 16 Feb 90	Est Completion Date: Feb 93
Department: Nursing	Facility: MAMC
Principal Investigator:	CPT Jeffrey L Jerde, AN
Associate Investigators:	CPT Daniel K. DeVelde, AN CPT John L. Hawkins, AN CPT Daniel D. Smith, AN CPT Shirley A. Spirk, AN LT Werner H. Beckerhoff, R.N., USPHS
Key Words: nursing roles, student knowledge, questionnaire	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $5.00
	Periodic Review: N/A

Study Objective: To determine the level of knowledge that entry level and senior level nursing students possess concerning nurse anesthesia.

Technical Approach: Questionnaires will be sent to 2000 nursing students in either their first year of nursing studies or in their last year of nursing studies. The source of subjects will be the National League of Nursing approved Baccalaureate Schools of Nursing. Part I of the questionnaire will obtain demographic data. Part II of the questionnaire will elicit information regarding knowledge of the different extended nursing roles, using the Likert Scale.

An individual item analysis will be performed utilizing frequency distribution. The questions from the Likert Scale will be scored and totaled. The Student's t Test will be utilized to determine if a statistically significant difference exists between entry level and senior level nursing students based on the Likert scores. The Pearson's r test will be utilized to determine if any relationships exist within the groups based on the Likert scores and the demographic data. A probability of $P < 0.05$ will be utilized for the inferential statistics.

Progress: The study has been completed and a paper has been submitted for consideration for publication.

Data analysis supports the hypothesis that there is a statistically significant increase in the knowledge levels of the senior level nursing students. It is unclear, however, whether or not this knowledge increase is a direct result of the information provided to the students by their program of nursing education.

Detail Summary Sheet

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

Title: An Exploration of the Effect of Aging and Exercise on Maximal Oxygen Intake in Women Between the Ages of 22 to 50 Years

Start Date: 20 Jul 90	Est Completion Date: Aug 90
Department: Nursing	Facility: MAMC
Principal Investigator: MAJ Laurie A. McNabb, AN	
Associate Investigator: LTC Barbara S. Turner, AN	
Key Words: exercise, aging, women	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $45.00	Periodic Review: N/A

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

Technical Approach: Active duty Army Nurse Corps female officers will be studied; 25 between the ages of 22 and 31, and 25 between the ages of 32 and 50. The subjects will complete a two-mile run and will be timed. Estimates of maximal oxygen consumption will be calculated from the two-mile run times.

The subjects will also be asked to complete a questionnaire which will elicit information on the type and the amount of exercise the subjects regularly perform.

Predicted values of maximal oxygen intake as determined by the two-mile run time and the age will be compared between the two age groups by using the Student's t test. Relationships of age and physical activity status will be examined and plotted by using simple linear regression analysis.

Progress: Forty-three women were entered in the study and data analysis is in progress.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/06 Status: On-going

Title: Assessing Parental Stress in the NICU

Start Date: 17 Nov 89	Est Completion Date: Dec 89	
Department: Nursing	Facility: MAMC	
Principal Investigator:	2LT Carla Nye, USAR	
Associate Investigator:	LTC Lorna Imbruglio	
Key Words: stress, NICU, parental		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A

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

Technical Approach: Fifty mother-father dyads will be studied. The charge nurse will determine if the parents are emotionally stable enough to be asked to take part in the study. Parents will be asked to fill out the Parental Stressor Scale: Neonatal Intensive Care Unit and a parent background information form. Parents will complete the forms separately. Demographic data will be obtained from the infant's chart. The investigator will attempt to determine the sources of parental stress in the NICU; if the mothers' overall perceptions of stress differ from the fathers'; if single mothers' perceptions of overall stress differ from those of married mothers; if the experience of previously having an infant in an NICU is related to overall perception of stress; if there is a relationship between gestational age of the infant and the parent's overall perceptions of stress; if there is a relationship between the severity of the infant's medical complications and the parent's perception of stress; and if there is a relationship between the years of schooling the parent has completed and the perceptions of stress in the Staff Behaviors and Communication dimension.

The Statistical Package for the Social Sciences will be used to analyze the data. T-tests will be used to assess the differences between mothers and fathers, single mothers and married mothers, and previous experience with the NICU versus no previous experience. Relationships between parent and infant characteristics and overall stress scores will be answered using correlative statistics.

Progress: Thirty-two mothers and 26 fathers of 32 infants have completed the study.

Detail Summary Sheet

Date: 30 Sep 90	Protocol No.: 90/97	Status: On-going

Title: Descriptive Study of the Sleep Patterns of the Mechanically Ventilated Premature Infant Before, During, and After Endotracheal Suctioning

Start Date: 17 Aug 90	Est Completion Date: Sep 90
Department: Nursing	Facility: MAMC
Principal Investigator: MAJ Arleen E. Roots, AN	
Associate Investigators: NICU Staff, MAMC	
Key Words: premature infants, sleep patterns, ventilated	

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

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

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

Progress: This study is awaiting final approval of revisions as required by the Institutional Review Board and has not been implemented.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 89/11 Status: Completed
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: Jul 90

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 additional subjects were entered in FY 90 for a total of 30 subjects. Papers have been presented at four different regional/national scientific meetings.

**Funded by an NIH grant.

Detail Summary Sheet

Date: 30 Sep 90 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: Jul 90

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: Grant funding has been received. Equipment and supplies are being procured, data collectors trained, and software programmed for data collection. Subject entry should begin in November 1990.

**Funded by an NIH grant.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/72 Status: On-going

Title: Piglet Tracheal Epithelial Injury and Regeneration Following Endotracheal Suctioning

Start Date: 18 May 90 Est Completion Date: May 93

Department: Nursing Facility: MAMC

Principal Investigator: LTC Barbara S. Turner, AN

Associate Investigators: LTC Thomas E. Wiswell, MC
MAJ James G. MacMillan, VC

Key Words: endotracheal suctioning, animal model

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

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

Technical Approach: Control animals (14) will be sedated and then euthanized (two at a time) acutely on days 3, 7, 10, 14, 17, and 21 and the trachea harvested. Sham piglets (14) will be sedated, intubated, and ventilated for 6 hours, without suctioning taking place. They will be euthanized at time periods as above and the trachea harvested. Group 1 (35) and Group II (35) piglets will be intubated and ventilated. After the piglets have been stabilized on the ventilator each will receive either PEEP (Group 1) or ZEEP (Group II) once every 60 minutes for the six hours of mechanical ventilation. The piglets in Groups 1 and 2 will be euthanized in groups of 5, acutely and at 3, 7, 10, 14 and 21 days post-suctioning and the trachea harvested. At the time of necropsy, the location of the tip of the endotracheal tube will be marked by placing a ligature in the tracheal wall. The heart and lungs will be removed en bloc and grossly examined. The trachea and mainstem bronchi will be dissected free and sectioned into 13 cross sections for examination, including scanning electron microscopy and light microscopy.

Descriptive and inferential statistics will be used to determine the total epithelial cell count, goblet cell count, and ciliated cell count from each section. The ratio of ciliated cell to goblet cells will be calculated for all cross sections to determine the tracheal epithelial response to injury. Changes in the cell counts over time will be analyzed. Corrected predicted total epithelial cell counts will be determined, using the control piglets as a standard, correcting for tracheal diameter.

PROGRESS: This has not be implemented because the investigators are awaiting a decision on grant approval from the NIH.

Detail Summary Sheet

Date: 30 Sep 89 Protocol No.: 89/79 Status: Completed

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: 43 women responded to the questionnaire for a return rate of 49%. Military women who gave birth during the inclusive dates initiated breast feeding at rates virtually identical to all women delivering at the same hospital. The actual duration of breast feeding was shorter than anticipated in the majority of these women. The women found work schedule and responsibilities to be a major determinant in their decision to stop breast feeding. The majority responded that they would breast feed another child and would continue to breast feed after returning to work. A thesis has been submitted as a partial fulfillment for a Master of Nursing degree at the University of Washington.

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

F O R

P R O T O C O L S

DEPARTMENT OF OB/GYN

Detail Summary Sheet

Date: 30 Sep 90 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: Sep 90

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 20 patients were entered in FY 90 for a total of 60 patients entered.

Detail Summary Sheet

Date: 30 Sep 90 | 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 90

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: Forty-eight patients were entered in FY 90 for a total of 99 subjects.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 87/115 Status: Completed

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 90

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: Thirty-five patients were entered in FY 90 for a total of 157 subjects. Six minor vaginal rashes have been reported. The data are being analyzed by the Upjohn Company.

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

Detail Summary Sheet

Date: 30 Sep 90	Protocol No.: 90/74	Status: On-going

Title: Documentation of Ureteral Function via Intraoperative Ultrasound

Start Date: 18 May 90	Est Completion Date: Jul 90
Department: OB/GYN	Facility: MAMC
Principal Investigator:	CPT John B. Browning, MC (Jul 90)*
	LTC Gordon O. Downey, MC
	CPT Kevin C. Turner, MC
Key Words: ureteral function, during surgery, ultrasound	

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

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

Technical Approach: Subjects - 10, age range - 18-75 years

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

The preoperative and intraoperative ultrasound will be compared using descriptive statistics.

Progress: No patients have been entered in this study due to the unexpected reassignment of Dr. Turner, the original principal investigator.

* CPT Turner, original principal investigator

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/83 Status: On-going

Title: Ultrasound Compared to Intravenous Pyelography in Demonstrating Ureteral Function Into the Bladder

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

Department: OB/GYN Facility: MAMC

Principal Investigator: CPT John B. Browning, MC

Associate Investigators: LTC Gordon O. Downey, MC
LTC John A. Vaccaro, MC
CPT Richard W. Knight, MC
CPT Kevin C. Turner, MC

Key Words: ureteral function, ultrasound, IV pyelography

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

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

Technical Approach: Number of subjects = 100
Age range - 18-75

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

Progress: No patients have been entered as the protocol has not received final approval from the Institutional Review Board.

Detail Summary Sheet

Date: 30 Sep 90 | Protocol No.: 86/40 | Status: Completed

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 (Aug 88)*

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: Sep 90

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

Technical Approach: This study will be done as part of a group study under the direction of MAJ Enrique Hernandez, MC, Tripler Army Medical Center.

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: Four patients were entered in this study in previous years at MAMC.

The accrual goal has been met and all data collected. The investigators at Tripler Army Medical Center are in the process of writing a manuscript.

* Dr. Lee, original PI

Detail Summary Sheet

Date: 30 Sep 90	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 (Aug 88)*
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: Sep 90

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 at MAMC.

* COL Lee original PI.

Detail Summary Sheet

Date: 30 Sep 90	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: Sep 90

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

Technical Approach: With the animal in the supine position, a 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: Four training labs utilizing this protocol were held in FY 90.

Detail Summary Sheet

Date: 30 Sep 90	Protocol No.: 90/03	Status: Completed

Title: Comparison of Absorbable Staples versus Standard Suture Closure of Vaginal Vaults During Abdominal Hysterectomies in Goats *(Capra hircus)*

Start Date: 20 Oct 89	Est Completion Date: Jan 90
Department: OB/GYN	Facility: MAMC
Principal Investigator:	CPT Susan G. Dunlow, MC
Associate Investigators:	COL James L. Kelley, MC
	LTC Gordon O. Downey, MC
	CPT John E. van Hamont, MS
Key Words: hysterectomy, vaginal vault, absorbable staples	
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $2400.00
	Periodic Review: N/A

Study Objective: To compare a standard vaginal closure technique (interrupted 2.0 vicryl sutures) during abdominal hysterectomies with the newer absorbable staples as to development of infection along the vaginal cuff, adhesion formation to surrounding organs, and histopathologic evidence of necrosis and repair.

Technical Approach: After determination of the appropriate amount of *E. coli* in three goats, a known inoculum of *E. coli* will be placed into the vagina of 20 goats. Ten goats will have the vaginal vault closed in the standard fashion and 10 goats will have the vaginal vault closed with absorbable staples. Otherwise, the hysterectomies will be performed identically. An absorbable, monofilament suture will be used to close the peritoneum and fascia in a running, bulk closure, and staples will be used on the skin. Cultures will be obtained from the peritoneal cavity. One week later, the animals will be re-explored and cultures will be obtained from the peritoneal cavity, the abdominal side of the vaginal cuff, and the vaginal side of the vaginal cuff, after excision of the top of the vagina. If an infection is present in the abdominal incision at re-exploration, appropriate cultures and tissue samples will also be obtained. The amount of adhesions between the vaginal cuff and the adjacent organs will be noted. All cultures will be specifically cultured for *E. coli* on plates containing spectinomycin and nalidixic acid *(E. coli* will be resistant to both of these agents) in order to determine the amount of original inoculum present without contamination from other organisms present in the goat. The vaginal tissue obtained at re-exploration will be evaluated by: (1) permanent sections will be obtained for histopathology and compared for amount of necrosis, inflammatory cells, fibrin deposits, and presence of fibroblasts; (2) homogenized tissue extract for total bacterial count per gram of tissue will be prepared; and (3) permanent tissue sections previously stained with an H&E stain will be exposed to type specific antisera in order to identify these organisms in the tissue sections and facilitate identification of the presence of inflammatory cells in the tissue.

Progress: The animal surgeries were completed on 15 Jun 90. Data are being analyzed and a manuscript is being prepared for submission for publication.

Detail Summary Sheet

Date: 30 Sep 90 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: Sep 90

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: 112 subjects were entered in this study in FY 90 for a total of 365 subjects. No new results have been found with increased numbers as compared to preliminary findings reported in the previous year; i.e., 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 90 Protocol No.: 89/26 Status: Completed

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 functio.

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $4.36	Periodic Review: Apr 90

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: Ten subjects were entered. The results demonstrated a significant decrease in pulmonary function in term pre-eclamptic patients receiving magnesium sulfate seizure prophylaxis. Furthermore, the data suggest that the observed decrease in respiratory function of pre-eclamptic women in labor receiving magnesium sulfate prophylaxis is due to a generalized respiratory muscle weakness.

A paper has been submitted to the American Academy of Gynecology for consideration for presentation.

Detail Summary Sheet

Date: 30 Sep 90 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 Jerome N. Kopelman, MC (Aug 90)*
Associate Investigators:
COL Patrick Duff, MC MAJ Glenn Jordan, MC
MAJ W. Kim Brady, MC MAJ Douglas A. Milligan, MC
Key Words: Unasyn, Augmentin, tocolytic therapy, 7 days vs term
Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $5960.00 Periodic Review: Aug 90

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

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

Revision (Aug 90): The IV antibiotics arm of this study was dropped due to an inability to obtain a suitable placebo.

Progress: No patients entered due to difficulties in obtaining a suitable placebo.

* MAJ Milligan original PI.

Detail Summary Sheet

Date: 30 Sep 90 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 Jerome N. Kopelman, MC (Aug 90)*

Associate Investigators: COL Patrick Duff, MC
MAJ W. Kim Brady, MC
MAJ Glenn Jordan, MC
MAJ Douglas A. Milligan, MC

Key Words: PPROM, Unasyn, Augmentin

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $3574.00 Periodic Review: Aug 90

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. The investigators are still awaiting the arrival of a suitable placebo.

* MAJ Milligan original PI

Detail Summary Sheet

Date: 30 Sep 90	Protocol No.: 90/34	Status: On-going

Title: Cordocentesis in an Animal Model

Start Date: 16 Feb 90	Est Completion Date: Dec 90
Department: OB/GYN	Facility: MAMC
Principal Investigator:	MAJ Jerome N. Kopelman, MC (Aug 90)*
Associate Investigators:	COL John A. Read, MC
	MAJ Douglas A. Milligan, MC
Key Words: animal model,	goat, cordocentesis
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-
	Periodic Review: Aug 90

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

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

Progress: One animal has been scanned. The investigators have been unable to visualize cords well. They plan to attempt new scans with a different machine.

* Dr. Milligan original PI

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/106 Status: On-going

Title: Evaluation of Efficacy of Twelve Hour Urine Collections in the Diagnosis of Pre-Eclampsia

Start Date: 21 Sep 90 Est Completion Date: Dec 90

Department: OB/GYN Facility: MAMC

Principal Investigator: CPT Wilma I. Larsen, MC

Associate Investigators: MAJ Jerome N. Kopelman, MC
CPT Montgomery E. Thorne, MC

Key Words: pre-eclampsia, urine, 12-hour

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $230.00	Periodic Review: N/A

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

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

Progress: This study is awaiting final approval from the Institutional Review Board.

Detail Summary Sheet

Date: 30 Sep 90 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: Sep 90

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: Twenty-eight patients were entered in this study in FY 90 for a total of 200 entries. No adverse reactions to the medications have been reported.

Randomization and patient entry have been completed with data collection continuing.

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

Detail Summary Sheet

Date: 30 Sep 90	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: Sep 90

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 90 for a total of 26 entries.

**Replaced Dr. Sargeant as PI, Jul 88

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 88/54 Status Terminated

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: Jun 90

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. The human use portion of the study was terminated in July 90 due a lack of time to complete the study and the reassignment of the principal investigator.

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

Detail Summary Sheet

Date: 30 Sep 90 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 William J. Polzin, MC (May 90)*

Associate Investigators:	MAJ Mark J. Kozakowski, MC
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: May 90

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

Technical Approach: Approximately 1500 pregnant females between 18 and 35 years of age without known coagulopathy will be studied. Before entry a physical exam, including detailed obstetric history and thromboembolic disease history; prothrombin (PT) and partial thromboplastin time (PTT); and anticardiolipin antibody (ACA) will be done. Subjects with a prolonged PTT will undergo evaluation to include 1:1 mixing study and platelet neutralization procedure; Russell viper venom test if 1:1 mixing study is consistent with the lupus anticoagulant. Subjects who have a normal PTT will be followed for the remainder of the pregnancy and have a PTT and ACA drawn at the time of delivery. If the PTT is prolonged, the 1:1 mixing study and platelet neutralization procedure will be repeated and then performed again at the time of delivery. If a fetal death or spontaneous abortion occurs, anticardiolipin antibody will be done. A prolonged PTT and a correctable platelet neutralization procedure at any stage will constitute the presence of the lupus anticoagulant. The frequency of the lupus anticoagulant in pregnancy will be calculated as well as the frequency of spontaneous abortion when the lupus anticoagulant is present.

Revision - May 90: This revisions changed the population to include all pregnant women and added an objective to determine the number of patients who convert during the gestation period. The written consent form was waived by the IRB since the blood would be drawn for patient care and this protocol would fit the category of a health care delivery study.

Progress: Approximately 1500 patients have been studied.

* MAJ Kozakowski original PI

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/37 Status: On-going

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

Start Date: 16 Feb 90 Est Completion Date: Jan 91

Department: OB/GYN Facility: MAMC

Principal Investigator: MAJ William J. Polzin, MC

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

Key Words: IUGR, antiphospholipid antibody, lupus anticoagulant

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $399.00	Periodic Review: N/A

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

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

Progress: Approximately 40 patients have been entered in this study. Approximately 30% of the patients thus far are positive for anticardiolipid antibody and none have been positive for lupus anticoagulant. This is a significant difference.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/73 Status: On-going

Title: The Prevalence of Positive Urine Toxicology Screens in a Military Obstetric Population

Start Date: 18 May 90 Est Completion Date: Jul 90

Department: OB/GYN Facility: MAMC

Principal Investigator: MAJ WilliamJ. Polzin, MC

Associate Investigators: COL John A. Read, MC
LTC Michael L. Smith, MS (AFIP)
MAJ W. Kim Brady, MC
MAJ Jerome N. Kopelman, MC

Key Words: toxicology screens, urine, military OB population

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $2200.00 Periodic Review: N/A

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

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

Progress: All samples have been collected and shipped to AFIP for analysis.

Detail Summary Sheet

Date: 30 Sep 90 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 Montgomery E. Thorne, MC (Jul 90)*
Associate Investigators: LTC Charles E. Henley, MC
MAJ W. Kim Brady, MC
CPT Michael J. Murray, 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: Sep 90

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: No additional subjects were entered in FY 90. Antepartum GBS screening cultures have been obtained on all subjects and are being reviewed.

* Dr. Murray original PI

Detail Summary Sheet

Date: 30 Sep 90 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: Sep 90

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: Two patients were entered in FY 90. All subjects have had ultrasound and laboratory studies completed. Data are currently being analyzed.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 89/25 Status: Terminated

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: Jun 90

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: No patients were entered in FY 90. The number of man-hours required for this study was exorbitant and scheduling with Radiology was very difficult. Therefore, the protocol was terminated upon the reassignment of Dr. Turner.

Of the 12 patients studied in previous years, no significant pelvimetry findings were found that would correlate with a successful vaginal delivery.

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 90	Protocol No.: 90/48	Status: On-going

Title: The Token Test for Children in Identifying and Following Treatment Efficacy in Attention Deficit Hyperactivity Disorder

Start Date: 16 Mar 90	Est Completion Date: Mar 91
Department: Pediatrics	Facility: MAMC
Principal Investigator: MAJ Edward J. Coll, MC	
Associate Investigator: LTC Patrick C. Kelly, MC	
Key Words: attention deficit hyperactivity, Token Test	

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

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

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

Progress: Sixteen ADHD subjects and sixteen control subjects have been entered. A paper has been submitted for presentation at the Uniformed Services competition.

Initial data indicate that children with ADHD demonstrate deficiencies in receptive language and that a subgroup of these children show an improvement in receptive language measures while on methylphenidate. However, the subtle nature of these findings is not well demonstrated by the TTC. The investigators suspect that an expansion of the TTC items would improve its sensitivity in evaluating children with ADHD.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 87/50 Status: Completed

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: Sep 90

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 64 additional patients in FY 90 for a total of 117 entries. Comparison of measles antibody response after MMR for well-controlled infants versus infants with URI showed significantly more vaccine failures (no detectable measles antibody in covalent serum) for babies with colds.

A paper has been submitted for publication and an abstract has been submitted for presentation at the Pediatric Triservice Meeting, 1991.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 87/51 Status: Completed

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: Sep 90

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. Forty-six (46) patients were entered in FY 90 for a total of 195 entries. Bacteriologic failures were more common in children given once daily penicillin for streptococcal pharyngitis. The children given penicillin either two or four times daily had comparable outcomes.

A paper has been submitted for publication and an abstract has been submitted for presentation at the Pediatric Triservice Meeting, 1991.

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

Detail Summary Sheet

Date: 30 Sep 90 | Protocol No.: 88/25 | Status: Terminated

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: Sep 90

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 $\geq$39.5° C of unknown origin and WBC $\geq$15,000. Children with a temperature $\geq$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. Subjects will have a urinalysis, urine cultures, and chest x-rays. Patients will be randomized to receive oral Augmentin in divided doses or ceftriaxone in a single IM injection each 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. 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: Four additional patients were entered at MAMC in FY 90 for a total of 12 entries. The investigators on this multicenter study were unable to accrue sufficient subjects to produce useful information.

Detail Summary Sheet

Date: 30 Sep 90 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: Sep 90

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: Gentamicin toxicity was not produced in rabbits given 10 or 40 mg/kg/day for five days. Additional rabbits will be studied with gentamicin dosing extended to 10 days.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/22 Status: Terminated

Title: A Treatment IND for Retrovir Brand Zidovudine (AZT) Therapy of Pediatric Patients with HIV Disease

Start Date: 19 Jan 90 Est Completion Date: Indefinite

Department: Pediatrics Facility: MAMC

Principal Investigator: COL Marvin S. Krober, MC

Associate Investigators: None

Key Words: HIV, Retrovir, ages 3 months to 12 years, treatment

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

Study Objective: To facilitate use of Retrovir in HIV-infected children, 3 months to 12 years of age, who are either symptomatic or have less than 400 CD4 + lymphocytes and to monitor adverse events attributable to Retrovir.

Technical Approach: This is a multicenter, open-label, uncontrolled treatment protocol. Retrovir will be given orally at an initial dosage of 180 mg/M^2 every six hours. Dose will be recalculated every two months. Hematologic tests will be performed every 2 weeks during the first 2 months of therapy and thereafter every 2 to 4 weeks depending on drug tolerance and severity of disease. Children who develop hematologic abnormalities will have the dose reduced by approximately 30%. Therapy will be resumed at the original dose level if the child's hematologic status returns to baseline and remains stable for at least one month after dose reduction. Children who develop progressive bone marrow suppression will have therapy temporarily discontinued until hematologic parameters stabilize. After temporary discontinuation of the drug and stabilization of the hematologic parameters, children will resume dosing at a reduced level. If hematologic parameters remain stable for one month at the reduced dose, the original dose level will be resumed. Due to anticipated problems in patient follow-up, calculation of rates of adverse events and performance of survival analysis will not be appropriate in this context. Data will be evaluated only for signals of serious adverse events not seen in the clinical trials program and for increased frequency of known adverse events.

Progress: This protocol was terminated when the drug received FDA approval. One patient was entered and has been treated for six months. It is too early to determine any results of the study.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/71 Status: On-going

Title: Pyridoxine as Specific Therapy and Prophylaxis in the Treatment of Theophylline-Induced Seizures in Mouse and Rabbit Models

Start Date: 18 May 90 Est Completion Date: May 91

Department: Pediatrics Facility: MAMC

Principal Investigator: COL Marvin S. Krober, MC (Aug 90)**

Associate Investigators: COL Michael R. Weir, MC
LTC Patrick C. Kelly, MC
LTC Joseph P. McCarty, MC
CPT Gregory M. Glenn, MC

Key Words: seizures, theophylline-induced, therapy, prophylaxis

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $420.00 Periodic Review: N/A

Study Objective: To investigate the therapeutic efficacy of pyridoxine in seizures secondary to theophylline overdose in rodent models.

Technical Approach: Part I Inbred male mice will be divided into a control group of 10 mice (250 mg/kg aminophylline, 75% expected to seize) and a pretreatment group. The pretreatment group will be subdivided into four groups of 10 mice and given 25, 50, 100, and 250 mg/kg of IP pyridoxine, respectively. A third group will be given 250 mg/kg of IP aminophylline and then pyridoxine at the onset of seizure, and subdivided into four groups of 10 mice, given 25, 50 100, and 250 mg/kg, respectively. Time to seizure and mortality rate will be observed. In this fashion, it is anticipated that a dose-response range can be established based on human models.

Part II: After a successful dose-response range has been established in Part I, initial EEG trials with external electrodes will be attempted on conscious untreated rabbits. If reliable EEG results can not be obtained in this manner, then the rabbits will be anesthetized and stainless steel screw electrodes will be placed overlying the dura in both centroparietal areas with a reference electrode placed in the frontal sinus. Bipolar recording of EEG activity will be recorded on a Grass recorder and EKG and respirations will also be monitored using the Grass recorder.

Six New Zealand white rabbits will be anesthetized and given 115 mg/kg of IV aminophylline over 50 minutes with an expected seizure rate of 80% with a mean time to seizure of 108 minutes. The first group of 3 animals will be pretreated with the same mg/kg dose of pyridoxine as found to be effective in Part I. The second group of 3 animals will be given a mg/kg dose of pyridoxine as found to be effective in Part I at the onset of seizures. If apnea occurs, assisted ventilation will be given for a maximum of 10 minutes to minimize the mortality secondary to apnea alone. Time to seizure,

**CPT Glenn, original principal investigator

duration of seizure and mortality rates will be noted. Pre and post aminophylline PLP levels will be determined as well as PLP, theophylline, and standard chemistries at the onset of seizure. Once seizures are controlled with the pyridoxine, PLP and theophylline levels will again be determined. These findings will be correlated with EEG findings.

Revision I (20 Jul 90): Initial findings (using mice) indicated that pyridoxine may have an effect in preventing theophylline seizures. The investigators then did a pilot study in an attempt to maximize the therapeutic effect by providing 500 mg/kg pyridoxine, after 250 mg/kg theophylline and noted a significant delay in time to seizure. The protocol was revised to allow the investigators to serially inject 250 mg/kg of pyridoxine at 5, 15, and 50 minutes after the theophylline dose in order to provide pyridoxine levels over the time frame of seizures in the control group and to achieve an experimental number, balanced by sex. In previous experimental groups, female mice appeared to predominate in the seizure group. Therefore, 20 additional control females will be studied in order to alleviate any effect due to sex. If results are promising, the investigator will then commence with Part II of the protocol, using larger animals.

Revision II (17 Aug 90): A revision was approved to add a study of the use of propranolol in place of pyridoxine in the acute model with the 30 mice given theophylline as before. Instead of a large single dose of pyridoxine, a large single dose of propranolol will be given. Several doses will be given in order to find a dose-range. Also a chronic model using 30 mice will be studied. Animals will be given half the acute dose of theophylline daily for five days. Half of the animals will be given the mg equivalent dose of pyridoxine while the remainder will be given isovolemic saline.

Revision III (21 Sep 90): The studies showed that EEG changes caused by aminophylline could be reversed with acute pyridoxine, followed by a 230 mg/kg/50 min pyridoxine infusion. The animals developed theophylline levels of 192 µg/ml immediately and fell to 99 µg/ml at 3-4 hours and were asymptomatic when returned to their cages. Six of 6 animals died shortly thereafter, raising the question of whether prolonged infusion of pyridoxine until blood levels fell to therapeutic ranges in 3 half-lifes would result in saving the subject. Therefore, the protocol was amended to study 6 rabbits with prolonged pyridoxine infusion (approximately 12 hours).

Progress: Mice studies showed decreased mortality in animals given pyridoxine to prevent theophylline-induced seizures. Initial rabbit studies (Part II) showed reversal of abnormal EEG when given pyridoxine. See Revision 1 (above) for further information on results of mice studies. See Revision III for results of Revision II. Revision III has not been implemented.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/92 Status: On-going

Title: Core Project: Evaluation of Diagnostic Assays for Human Immunodeficiency Virus (HIV) in Children with Evidence of HIV Exposure or HIV Illnesses

Start Date: 20 Jul 90 Est Completion Date: Sep 91

Department: Pediatrics Facility: MAMC

Principal Investigator: COL Marvin S. Krober, MC

Associate Investigators: COL James S. Rawlings, MC
MAJ Joanna Beachy, MC
MAJ Thomas A. Perkins, MC

Key Words: HIV, assays, detection, correlation

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

Study Objective: To analyze laboratory assays for detection of HIV infection in children and to correlate the results with the clinical status of the child.

Technical Approach: This will be a multicenter study funded by Walter Reed Army Medical Center. The plan of this protocol is to evaluate the usefulness of new assays as they are developed, using blood from HIV-infected or high risk children. Blood will be sent to the laboratory for standard HIV testing using those tests that are most developed. Surplus will be utilized for less well developed assays or stored for future analysis. Results from the tests will be compared to conventional assays used to diagnose adult HIV infection, such as ELISA, western blot, and culture, to determine their usefulness in children. These specimens will also be used to develop improvements and new methods for HIV testing in children.

This analysis will be done in 120 - 150 individuals at three month intervals to determine if changes in these tests correlate with changes in the patient's clinical or immunological status. Most of the data generated in this protocol will be qualitative and will be correlated to quantitative clinical data using Spearman's Rank Correlation. Logistic regression will be used for correlating the numerical data to noncontinuous clinical measures. Analysis of data from different clinical groups (patients who remain asymptomatic versus those who develop AIDS) will be compared using two-way ANOVA to determine significant differences between clinical groups.

Progress: No patients have been entered in this study to date.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/93 Status: On-going

Title: Epidemiology of HIV in Pediatric and Perinatal Patients: A Natural History Study

Start Date: 20 Jul 90 Est Completion Date: Jul 93

Department: Pediatrics Facility: MAMC

Principal Investigator: COL Marvin S. Krober, MC

Associate Investigators: COL James S. Rawlings, MC
MAJ Joanna Beachy, MC
MAJ Thomas A. Perkins, MC

Key Words: HIV, computer data base, evaluate, long-term Follow-up

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

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

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

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

Detail Summary Sheet

Date: 30 Sep 90	Protocol No.: 90/107	Status: On-going

Title: Perinatal HIV Infection: Epidemiology and Natural History

Start Date: 21 Sep 90	Est Completion Date: Apr 95
Department: Pediatrics	Facility: MAMC
Principal Investigator:	COL Marvin S. Krober, MC
Associate Investigators:	COL James S. Rawlings, MC MAJ Joanna Beachy, MC MAJ W. Kim Brady, MC MAJ Thomas A. Perkins, MC
Key Words: HIV, perinatal, epidemiology, natural history	

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

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

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

Subjects will be divided into two subsets: (1) HIV+ mother and HIV+ infant and (2) HIV+ mother and HIV- infant. Descriptive statistics will be used to describe the entire sample and prevalence comparisons will be made for the two major subsets. Analytic methods may involve both univariate and multivariate techniques.

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

Detail Summary Sheet

Date: 30 Sep 90	Protocol No.: 90/108	Status: On-going

Title: Role of Anticonvulsants in Theophylline Toxicity

Start Date: 21 Sep 90	Est Completion Date: Sep 91	
Department: Pediatrics	Facility: MAMC	
Principal Investigator:	COL Marvin S. Krober, MC	
Associate Investigators:	COL Michael R. Weir, MC	
	LTC Patrick C. Kelly, MC	
	LTC Joseph P. McCarty, MC	
Key Words: anticonvulsants, theophylline toxicity		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: 916.00	Periodic Review: N/A

Study Objective: To test whether conventional anticonvulsants have any effect on the EEG in theophylline toxicity.

Technical Approach: Each rabbit will receive 115 mg/kg aminophylline intravenously, followed within 30 minutes by either valium (0.2 mg/kg), phenobarbital (20 mg/kg), or phenytoin (12 mg/kg), with six animals receiving each anticonvulsant. The remaining six animals will receive aminophylline as above, followed by pyridoxine 45 mg/kg IV push and then 230 mg/kg/hour for a one hour infusion. EEG tracings will be obtained at 15 minute intervals for three hours. The rabbits will then be observed for a period of three days. Results will be of a descriptive nature with mean $\pm$ standard deviation being the primary statistic.

Progress: This is a new study which will be implemented when the animals become available.

Detail Summary Sheet

Date: 30 Sep 90 | 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: Sep 90

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: Eighteen additional patients were entered in FY 90 for a total of 55 subjects.

A poster presentation, utilizing data from this study, was presented at the 1990 meeting of the Association for Applied Psychophysiology and Biofeedback.

**Replaced Dr. McClintock, Oct 88.

Detail Summary Sheet

Date: 30 Sep 90 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 90

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: 43 additional patients were entered in FY 90 for a total enrollment of 178 patients.

Data collection is continuing. Preliminary analysis has yielded a table of normal thyroid dimension + two standard deviations for each sex and age, 12-18 years.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 88/18 Status: Completed

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: Sep 90

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: No subjects were entered in this study in FY 90; 126 subjects were enrolled in previous years.

A significant proportion of preteen girls is 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.

A manuscript is in progress.

PRESENTATION: Triservices Pediatric Meeting, March 1989.

Detail Summary Sheet

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

Title: A Phase III Open Protocol for a Multicenter Study for the Treatment of Central Precocious Puberty with D-Trp^{6}-Des-Gly^{10}-N-ethylamide-LHRH, A Long-Acting Analog of Luteinizing Hormone Releasing Factor (Deslorelin)

Start Date: 20 Jul 90 Est Completion Date: Dec 95

Department: Pediatrics Facility: MAMC

Principal Investigator: COL Dan C. Moore, MC

Associate Investigators: None

Key Words: precocious puberty, Deslorelin

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

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

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

Progress: This protocol has just received approval from Health Service Command. No subjects have been entered.

Detail Summary Sheet

Date: 30 Sep 90 | Protocol No.: 90/79 | Status: On-going

Title: Use of Metoclopramide with Chloral Hydrate for Sedation

Start Date: 15 Jun 90 | Est Completion Date: Jan 91
Department: Pediatrics | Facility: MAMC
Principal Investigator: CPT George D. Patrin, MC
Associate Investigator: LTC Joseph P. McCarty, MC
Key Words: sedation, children, chloral hydrate, metoclopramide
Accumulative MEDCASE Cost: -0- | Est Accumulative OMA Cost: $42.06 | Periodic Review: N/A

Study Objective: To demonstrate a more complete and reliable sedative effect with chloral hydrate, utilizing less drug, by adding metoclopramide to the preprocedure regimen.

Technical Approach: Approximately 100 children, age range 6 months to 12 years, requiring sedation for CT, MRI, or EEG, will be studied. One hour prior to the exam time, the subjects will be given 50 mg/kg of chloral hydrate po along with either 0.4 mg/kg (maximum 5 mg) Reglan or placebo, in a randomized fashion. If not asleep within 45 minutes, they will get an additional 25 mg/kg of chloral hydrate. Questionnaires will be completed immediately after the procedure by the parent and by the technician detailing the time of onset of sedation, its completeness, and any failed events or untoward effects. Placebo will be compared to Reglan regarding dose of chloral hydrate needed, effect on onset of action, duration, and completeness in terms of allowing the test procedure to be done.

Progress: No patients have been entered because the placebo has not been available. The placebo has now been received and patient entry is ready to commence.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/52 Status: Terminated

Title: EXOSURF Pediatric Sterile Powder Treatment IND Protocol, EXO-501

Start Date: 16 Mar 90 Est Completion Date: Mar 91

Department: Pediatrics Facility: MAMC

Principal Investigator: MAJ Thomas A. Perkins, MC

Associate Investigator: COL James S. Rawlings, MC

Key Words: respiratory distress syndrome, artificial surfactant

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

Study Objective: To study the efficacy of artificial surfactant (EXOSURF Pediatric) treatment in Group 1: prophylactic treatment of premature infants with birthweights of 700-1100 grams who are at great risk of developing Respiratory Distress Syndrome (RDS); Group 2: rescue treatment of infants 700-1350 grams birth weight who have developed RDS; and Group 3: rescue treatment of infants >1350 grams birth weight who have developed RDS.

Technical Approach: This treatment is offered nationwide to 500 medical centers until final FDA approval of EXOSURF Pediatric for general use. The use of EXOSURF Pediatric will be restricted to infants who require intubation and mechanical ventilation for their medical condition. EXOSURF will be carefully administered into the infant's lung through an endotracheal tube with a special side-port adaptor. Group 1 (as described above) will have a single prophylactic 5 cc/kg dose administered within 30 minutes of birth; Group 2 will be administered two 5 cc/kg rescue doses, twelve hours apart, with the first dose being administered at 2-24 hours after birth; Group 3 will be administered two 5 cc/kg rescue doses, twelve hours apart, with the first dose being administered at 2-24 hours after birth. Patients will be assessed at 72 hours and followed until 28 days of life, hospital discharge, or death, whichever comes first.

Progress: No patients were entered at MAMC. The protocol was terminated in August 1990 due to FDA approval of the agent.

Detail Summary Sheet

Date: 30 Sep 90 | Protocol No.: 90/58 | Status: On-going

Title: Neonatal Emergency Procedure Training in the Rabbit Model

Start Date: 20 Apr 90 | Est Completion Date: Indefinite
Department: Pediatrics | Facility: MAMC
Principal Investigator: MAJ Thomas A. Perkins, MC
Associate Investigators: LTC Matthew M. Rice, MC
Key Words: training, neonatal emergency, rabbit model
Accumulative MEDCASE Cost: -0- | Est Accumulative OMA Cost: $864/yr | Periodic Review: N/A

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

Technical Approach: This training is designed for junior housestaff who are inexperienced in the management and emergency care of sick infants. Demonstration by a staff neonatologist of the various procedures to be learned will be performed before any hands on attempts by the interns and residents. The animal lab will allow the student to observe and practice to proficiency those life-saving skills necessary in the management and stabilization of the neonatal patient.

Telazol, 15 mg/kg, and xylazine, 5 mg/kg IM, will be administered to induce and maintain anesthesia. Additional anesthesia will be administered in increments as needed. The rabbits will be intubated with a 2-3 mm i.d. endotracheal tube and ventilation will be maintained as necessary with 100% oxygen. Tracheal intubation, venous cutdown, needle thoracocentesis, and chest tube insertion will be performed by each intern or resident in attendance.

Progress: Twenty-two (22) physicians were trained in FY 90.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 88/07 Status: Terminated

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 90

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 90. Twenty patients were entered in FY 88. The investigators terminated the protocol due to the inability to solve logistical problems.

Detail Summary Sheet

Date: 30 Sep 90 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: Jun 90

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

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

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

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

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

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

F O R

P R O T O C O L S

PREVENTIVE MEDICINE SERVICE

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/14 Status: Suspended

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

Start Date: 19 Jan 90 Est Completion Date: Jun 91

Service: Preventive Medicine Facility: MAMC

Principal Investigator: MAJ Margot R. Krauss, MC (Jun 90)*

Project Director: MAJ John G. McNeil, MC, WRAIR

Key Words: HIV infection, seroconversion, controls, AD personnel

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

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

Technical Approach: The multicenter study will be conducted using a case-control design. A case will be defined on the basis of seroconversion to antibody to HIV using ELISA with duplicate Western Blot confirmation. There will be one control for each male subject and three controls for each female subject. Controls will be selected at random from the group of all uninfected active duty personnel at the same installations where cases seroconvert and will be matched for age (± 2 yrs), gender, ethnicity, rank (junior enlisted, senior enlisted, officer), and length of service. Controls must have tested negative on or after the date their matched case seroconverted. Subjects and controls will be interviewed by trained interviewers from collaborating civilian health agencies who are blinded to the HIV antibody status of study participants. The interview will be conducted from an HIV Seroconversion Risk Factor Study form which is divided into the following sections: demographic information, medical history, risk factors for drug use, risk factors for sexual history, and risk factors for other risks. The investigators anticipate that 160 to 230 incident cases will be eligible for recruitment each year and feel that the majority of these cases can be recruited.

In any multi-risk factor study such as this, the problem of chance statistical associations being made between exposure and outcome exists if repeated statistical testing is performed. For this reason, methods of analysis beyond statistical will be employed. These methods will include calculation of measures of effect (e.g., matched odds ratios and confidence intervals) for various risk behaviors as well as matched multivariate (e.g., proportional hazards, conditional logistic regression) analyses.

Progress: Four patients and seven controls were entered in the study. The protocol was suspended as of 30 Sep 90 due to a lack of funding.

* MAJ McNeil 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

DEPARTMENT OF PSYCHIATRY

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/95 Status: Completed

Title: An Investigation of the Relationship Between Patients' Self-Report of Memory Functioning and Performance on Empirical Measures of Memory

Start Date: 17 Aug 90 Est Completion Date: Oct 90

Department: Clinical Psychology Facility: MAMC

Principal Investigator: CPT Fred H. Brown, MS

Associate Investigators: LTC Kenneth A. Zych, MC
Carl Dodrill, Ph.D.
Alberta Klaus-Hagen, M.S.

Key Words: memory problems, functioning, performance, self-report

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $25.00 Periodic Review: N/A

Study Objective: To empirically describe the relationship between patients' self-report of memory problems and performance on standardized measures of memory functioning.

Technical Approach: A minimum of 40 adult patients will be tested. All subjects will receive a detailed clinical interview prior to the administration of any tests. All subjects will then be administered the Memory Functioning Questionnaire (MFQ), a 64 item self-report measure of memory functioning, prior to any psychometrics being administered. The psychometrician will be blinded to the subjects' responses to the MFQ. The subjects will then be administered a full battery of neuropsychological tests, to include memory measures and personality instruments. The instruments of interest to this study are the MFQ, the Wechsler Memory Scale-Russell Revision (WMSR), a standardized test of verbal and visual memory, and the Rey Auditory Verbal Learning Test (RAVLT), a standardized test of verbal memory. The subjects' scores on the MFQ will be compared to the scores they obtain on the WMSR and the RAVLT. In addition, an item analysis of the MFQ will be conducted to study the reliability and validity of this instrument. Data will be analyzed using appropriate nonparametric statistics.

Progress: The study has been completed, with 62 subjects entered. Self-report of memory is not related to memory test performance, except in subjects acknowledging psychological difficulties. A paper has been submitted for publication.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 89/32 Status: Completed

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: Jun 90

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. No further patients were entered due to the departure of the investigators.

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 90 Protocol No.: 90/49 Status: On-going

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

Start Date: 16 Mar 90 Est Completion Date: Mar 91

Department: Clinical Psychology Facility: MAMC

Principal Investigator: Alberta Klaus-Hagen, M.S. (Jul 90)

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

Key Words: neuropsychological data base, military population

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $200.00 Periodic Review: N/A

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

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

Progress: The study has not been implemented due to the departure of Dr. Clark and the appointment of a new principal investigator.

*Original principal investigator

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/50 Status: On-going

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

Start Date: 16 Mar 90 Est Completion Date: Mar 91

Department: Clinical Psychology Facility: MAMC

Principal Investigator: Alberta Klaus-Hagen, M.S. (Jul 90)

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

Key Words: cognitive deficits, Luria-Nebraska Neuropsychological Battery, sensitivity

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $25.00	Periodic Review: N/A

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

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

Progress: Data has been collected on 46 subjects.

* Original PI

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 89/69 Status: Terminated

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: Jan 90

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: No patients were entered. The drug has been approved by the FDA.

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

F O R

P R O T O C O L S

DEPARTMENT OF SURGERY

Detail Summary Sheet

Date: 30 Sep 90 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: Sep 90

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: Six training sessions, involving 24 physicians, were conducted in FY 90.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 89/24 Status: Completed

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: Sep 90

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: The project was completed with 50 subjects who fulfilled the study requirements. No predictive value of SACE level was noted for HIV positive subjects. Group statistics showed no differences for HIV positive and HIV negative subjects.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/01 Status: Terminated

Title: Free Dermal Fat Grafts in Expanded Tissue Recipient Pockets in the Pig

Start Date: 20 Oct 89 Est Completion Date: Apr 90

Dept/Svc: Surg/Otolaryngology Facility: MAMC

Principal Investigator: CPT Richard A. Beck, MC

Associate Investigators: MAJ Newton O. Duncan, MC

Key Words: grafts, dermal, expanded tissue

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $2700.00 Periodic Review: N/A

Study Objective: To determine if free dermal fat grafts have improved survival and predictable rates of resorption after implantation in expanded tissue pockets in the pig model and to determine the histologic characteristics of the capsule which forms around expanded/nonexpanded silicone prostheses and the free dermal fat grafts at specified intervals following transplantation.

Technical Approach: Under general anesthesia, a 12 cm incision will be made in the flank perpendicular to the dorsum, midway between the fore and hind limbs, and a 10 x 12 cm rectangular pocket will be elevated in the subcutaneous plane. The procedure will be repeated on the contralateral flank, creating 4 subcutaneous pockets. Each pocket will be assigned to one of three groups. Group I - a 250 ml rectangular tissue expander will be placed with the injection port located dorsally and sequentially inflated. Saline (40 Ml) will be injected percutaneously at the time of initial placement. The tissue expander will be inflated to maximum capacity over a period of 5 weeks by percutaneously adding 42 ml of saline at weekly intervals. Group II - the tissue expander will be placed as in Group I and filled with enough saline to eliminate dead space and the potential for hematoma/seroma formation. Group III - no expander will be placed. Six weeks after the initial procedure the tissue expanders will be removed and a biopsy of the capsule will be taken from random recipient pockets in Groups I and II. Then a thin split skin graft will be taken from the skin overlying the forelimb and the hindlimb. The 3 groups will be further divided into Groups A and B. Dermal fat grafts (taken from the skin overlying the forelimb and the hindlimb) containing the exposed dermis and the attached underlying fat will be placed in the recipient pockets of Group A (small graft) and Group B (large graft) Dermal fat grafts will be placed in the same subcutaneous plane previously elevated in Group III animals, while Groups I and II will have the grafts placed within the capsule surrounding the prosthesis. Grafts will be removed at intervals of 2, 4, and 8 weeks, their bulk will be measured and they will be subjected to detailed histological examination. Student's t-test will be used to compare weight at grafting, weight at sacrifice, and percent fat survival.

Progress: Due to the length of the approval process plus the renovation of the Laboratory Animal Surgery suite, the principal investigator did not have the time available to complete this project.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/17 Status: Completed

Title: Cardiovascular Effects of Pseudoephedrine in Medically Controlled Hypertensive Patients

Start Date: 16 Jan 90 Est Completion Date: Jan 91

Dept/Svc: Surgery/Otolaryngology Facility: MAMC

Principal Investigator: CPT Richard A. Beck, MC

Associate Investigators: COL W. Pierre Andrade, MC
LTC Howard M. Cushner, MC
CPT Sharon M. Seguin, MC

Key Words:

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $4,180.00	Periodic Review: N/A

Study Objective: To determine if 120 mg of controlled-release pseudoephedrine, taken in a BID dosing schedule by patients with medically controlled hypertension, will produce clinically significant cardiovascular changes.

Technical Approach: Thirty (30) patients with medically controlled hypertension with stable blood pressure and no known secondary causes of hypertension will be studied. Patients will be enrolled in a double-blind, crossover study and randomly assigned to receive either 120 mg of pseudoephedrine or a placebo on a BID schedule for 15 doses. On day 1, baseline blood pressure and pulse will be obtained and the the first dose of medication will be taken under the supervision of an investigator. Blood pressure and pulse will then be taken every 60 minutes for the next four hours. All blood pressure measurements will be taken from the same arm and in a sitting position. Patients will be allowed to engage in sedate activities between measurements. On days 3, 4, and 8, at the same time each day, the patient will have blood pressure and pulse measured as described above and will fill out a symptom questionnaire. After a minimum of 48 hours on medication, a serum sample for pseudoephedrine level will be drawn between 4 and 9 hours after the last dose of medication. On days 9-14, the patients will take no study medication in order to allow a washout interval. The patient will then be crossed over to the other medication for an eight day interval. Initial dose and monitoring procedures will be identical to those previously described. The changes in pulse and systolic and diastolic blood pressure will be assessed by analysis of variance of repeated measurements. A one-tailed test may be used since there is no pharmacologic basis to expect that pseudoephedrine would lower blood pressure on a short term basis.

Progress: This project was completed with 25 subjects who fulfilled the study requirements. No clinically significant cardiovascular effects were identified as a result of pseudoephedrine administration.

A manuscript has been submitted to The Laryngoscope and a paper has been selected for presentation at one regional and one national scientific meeting.

Detail Summary Sheet

Date: 30 Sep 90	Protocol No.: 90/18	Status: On-going

Title: A Prospective Comparison of Arthroscopic vs Open Anterior Cruciate Ligament Reconstructions Utilizing the Central One Third of the Patellar Tendon

Start Date: 16 Jan 90	Est Completion Date: Jan 91
Dept/Svc: Surgery/Orthopedics	Facility: MAMC
Principal Investigator: CPT Scott E. Cameron, MC	
Associate Investigator: MAJ William J. Wilson, MC	
Key Words: ACL reconstruction, open vs arthroscopic method	

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

Study Objective: To compare arthroscopic and open anterior cruciate ligament reconstructions utilizing the central one third of the patellar tendon.

Technical Approach: Fifty (50) patients will be entered in this prospective, double-blind study. Patients will be randomized to ACL reconstruction utilizing either the open or the arthroscopic method. Open reconstructions will be performed as described by Lambert (Clin Ortho 172:85, 1983), with the exception that the central one third of the patellar tendon will be used as a free graft as opposed to a vascularized graft. The arthroscopic procedure varies from the open procedure in that the graft is passed without formal arthrotomy and generally a notchplasty is a more limited procedure. The notch is not widened unless the graft is physically impinged by the femur. Although open excision of the fat pad is not performed, often a portion of the fat pad is removed with the shaver.

Central one third patellar tendon ACL reconstructions will be studied; acute vs chronic, with or without meniscal pathology. Patients scheduled for arthroscopic reconstructions that have to be converted to open procedures will be excluded as well as those who are restricted in weight bearing secondary to osteochondral defects that have been drilled or secondary to meniscal repairs. The methods will be compared as to operating time; tourniquet time; pain medicine required during the first three post-operative days; incidence of infrapatellar contracture syndrome; range of motion at 1, 3, and 6 months post-surgery; isokinetic (Cybex) muscle (quadriceps and hamstring) testing at six months; Lachmans, pivot shift, anterior drawer test; KT 1000 measurements at six months; and possibly a subjective patient evaluation at the six month mark. Standard descriptive statistics will be used for all collected variables. In addition, comparisons between the two procedures will be performed on range of motion, Cybex measurements, and atrophy using the Student's t test, and the Mann Whitney non-parametric test will be used to compare pain.

Progress: Fifty patients have been entered in the study and patient entry is completed.

Detail Summary Sheet

Date: 30 Sep 90 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: COL Preston L. Carter, MC (Sep 90)*

Associate Investigators: MAJ Stephen B. Smith, MC
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 90

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-two additional patients were entered in this study in FY 90 for a total of 50 entries. Patient entry is complete with chart review at defined periods in progress.

* MAJ Smith original PI
**Funded by a joint VA/DoD grant.

Detail Summary Sheet

Date: 30 Sep 90 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: Sep 90

Study Objective: To become proficient in intraocular lens implantation and to gain investigator status with FDA requirements, in order to provide a new technique in ophthalmic surgical care for our patients.

Technical Approach:

1. Obtain appropriate instruments to accomplish the procedure.

2. Obtain research investigator status with companies that have FDA approval to supply the lenses.

3. Implant lenses in 10 rabbits as a training experience for surgical nurses and assistants in this procedure.

4. Implant lenses in appropriately selected patients in order to provide visual rehabilitation.

5. To eventually establish this as a routine procedure in the military medical armamentarium of ophthalmic care.

Progress: Approximately 250 IOL's were implanted in FY 90. One patient had to have the lens removed because it rubbed the cornea; however, the cornea was not damaged.

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 90 Protocol No.: 88/40 Status: Completed

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 Craig J. Christenson, MC (Nov 89)*

Associate Investigators: MAJ Richard O. Jones, MS
CPT Ernest L. Mollohan, MS

Key Words: periosteum, stripping/nonstripping, x-rays

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Aug 90

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 abductovalgus, 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: Sixty three patients (68 feet) were entered in the study. Three patients had to be deleted from the study due to inadequate follow-up leaving 65 first metatarsal osteotomies that were studied.

No statistical difference was found between the two procedures. Although statistical significance was not demonstrated, the authors believe that the increased rates of displacement of the osteotomy site and delayed unions in the non-stripped group infers a potential source of postoperative complications. Further studies with a higher number of patients may be necessary to demonstrate significance.

A manuscript has been accepted for publication by The Journal of Foot Surgery.

* CPT Mollohan original PI

Detail Summary Sheet

Date: 30 Sep 90 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 90

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: Three training sessions were held in FY 90. Three residents were trained and are now able to complete an end-to-end arterial anastomosis on the rat model in 3-4 hours, depending on the individual's surgical skills.

**MAJ Cosio replaced LTC Wheeler as the principal investigator in Sep 89.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/104 Status: On-going

Title: Evaluation of the Effectiveness of the U.S. Army's Hearing Conservation Program: An Epidemiologic (Prevalence) Study

Start Date: 21 Sep 90 Est Completion Date: Nov 90

Department: Surgery/Audiology Facility: MAMC

Principal Investigator: MAJ Richard W. Danielson, MC

Associate Investigators: Thomas Kremenski, R.N., B.S.N.

Key Words: hearing conservation, U.S. Army

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $335.00	Periodic Review: N/A

Study Objective: To determine and accurately describe the distribution and magnitude of hearing loss that pervades the population of combat arms branch soldiers stationed at Ft Lewis, Washington.

Technical Approach: The effectiveness of the U.S. Army Hearing Conservation Program will be assessed by comparing data collected prior to 1990 to data collected before the introduction of this program. Data includes age, rank, branch of service (determined via an individual's MOS), audiometric data (i.e., hearing threshold levels), and hearing profile. Data will be stratified by age and rank within each branch. The prevalence of each hearing profile category within each branch will be determined. The mean hearing threshold levels for each test frequency and within each branch will be calculated. The prevalence of hearing profiles and the means of the hearing threshold levels will be compared across each branch and these measures will also be compared with the findings reported in the study by Walden, et al, (1975), Tech Rep IAO 4745, WRAMC, US Army Audiology and Speech Center, Washington, DC.

Progress: Audiometric records have been acquired from the Ft Lewis Hearing Evaluation Automated Registry and transferred to the computer system at the Department of Clinical Investigation.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/08 Status: On-going

Title: Radical Retropubic Prostatectomy and Orchiectomy for Stage C Carcinoma of the Prostate

Start Date: 17 Nov 89 Est Completion Date: Nov 94

Dept/Svc: Surgery/Urology Facility: MAMC

Principal Investigator: MAJ Rodney Davis, MC

Associate Investigators: LTC John A. Vaccaro, MC
MAJ Ian M. Thompson, MC

Key Words: prostatic carcinoma, orchiectomy, Lupron

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $1800.00	Periodic Review: N/A

Study Objective: To determine the efficacy of combined hormonal and surgical therapy for carcinoma of the prostate.

Technical Approach: This study will be done in collaboration with Brooke Army Medical Center, using approximately 30 patients. Patients with histologically proven adenocarcinoma of the prostate and evidence of Stage C disease will be eligible. Staging will be done by prostatic acid phosphatase, bone scan, IVP, and cystoscopy (normal and no evidence of extraprostatic spread). Initial evaluation of eligible patients will include CT scan of the pelvis, transrectal ultrasound, BUN/creatinine/SGOT/LDG/alkaline phosphatase, urinalysis, urine culture, CBC with platelet count, physical exam, rectal exam, serum testosterone, and PSA. Histologic evaluation of the prostate biopsy will include Gleason's grade. Patients will be placed on either Lupron therapy, one injection/day for two months, or they will undergo bilateral simple orchiectomy. The initial evaluations will be repeated at the end of the two month treatment period. Patients will then undergo staging pelvic lymphadenectomy. If palpably enlarged lymph nodes are noted, frozen section diagnosis will be obtained. If frozen section confirms nodal positive disease, no further therapy will be provided and patients will be removed from the study. If frozen sections at the time of staging lymphadenectomy are negative of if nodes are palpably normal, patients will undergo radical retropubic prostatectomy. The following data will be recorded during hospitalization: duration of hospitalization, intraoperative and postoperative complications, number of blood units transfused, duration of catheterization, nodal status, seminal vesicle status, and capsular status. Patients will be followed at 3, 6, 9, and 12 months with rectal exam, prostatic acid phosphatase, creatinine, BUN, and bone scan. Follow-ups will then continue once yearly, indefinitely. As survival statistics for Stage C carcinoma of the prostate are readily available and reproducible, the study will not be controlled. Available survival statistics for untreated Stage C carcinoma of the prostate will be compared with study patients using the methodology of Kaplan and Meier (J Amer Stat Ass 53:1958).

Progress: One patient has been entered in this study.

Detail Summary Sheet

Date: 30 Sep 90 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: LTC William E. Eggebroten, MC (Nov 89)*
Associate Investigators: COL Stanley C. Harris, MC
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 90

Study Objective: To provide training to general surgery, emergency medicine, and family practice residents and, specifically, to teach proper management of the initial one hour following major trauma.

Technical Approach: During a laboratory session involving goat surgery, each student in the group will be directly involved in a hands-on performance of a venous cutdown, a cricothyroidotomy, a tube thoracostomy, peritoneal lavage, and pericardiocentesis. This course will be conducted 3-4 times/year at MAMC.

Progress: Two ATLS courses were presented with approximately 48 physicians receiving training.

* COL Harris original PI

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/96 Status: On-going

Title: Craniofacial Onlay Bone Augmentation with a Xenogeneic Osteoinductive Implant in a Rabbit Model

Start Date: 17 Aug 90 Est Completion Date: Apr 91

Department: Surgery/Otolaryngology Facility: MAMC

Principal Investigator: CPT Hugh E. Hetherington, MC

Associate Investigators: COL Jeffrey O. Hollinger, DC
MAJ Michael R. Morris, MC

Key Words: osteoinductive implant, craniofacial onlay,

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $3500.00 Periodic Review: N/A

Study Objective: To assess the potential use of a biodegradable xenogeneic osteoinductive implant as a craniofacial onlay and compare this with allogeneic demineralized membranous bone implants and autogenous membranous bone onlay grafts. Survival, maintenance of implanted volume and shape, and the extent of bony replacement will be assessed.

Technical Approach: The study will consist of three parts; the production of the demineralized bone and osteoinductive implants, the placement of both implant types and autogenous membranous bone onlay grafts subperiosteally on the rabbits' snouts; and gross and histomorphometric analysis of the specimens after euthanasia. The implants will be manufactured by Dr. Hollinger as the US Army Institute of Dental Research and will be surgically implanted in the rabbit model. After 20 weeks, the animals will be euthanized and the implants harvested with the attached underlying bones, followed by gross and histomorphometric analysis. Two rabbits will be used for technique development. Twelve rabbits will be used and the relative positions of the graft and implants will be rotated so that they occupy each of the three possible positions in four rabbits per position. Analysis of variance and multiple variance tests will be used to determine the percent of change in volume between the three methods. Analysis of variance test will be used to compare the trabecular volume at 20 weeks between the three methods.

Progress: Development is proceeding on the osteoinductive implants with implantation in the rabbits expected to proceed within a few weeks.

Detail Summary Sheet

Date: 30 Sep 90 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 90

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: Subject entry is complete with 36 subjects entered. Collection of follow-up data is in progress.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/04 Status: Terminated

Title: Monitoring the Middle Latency Response in Combination with Digital Filtering as a Means For Obtaining Auditory Thresholds in Infants

Start Date: 20 Oct 89 Est Completion Date: Mar 90

Dept/Svc: Surgery/Audiology Facility: MAMC

Principal Investigator: Lynne Johnson, B.A.

Associate Investigator: MAJ Richard W. Danielson, MS

Key Words: auditory thresholds, infants, middle latency response

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $263.00 Periodic Review: Aug 90

Study Objective: To obtain normative auditory threshold values from infants using Middle Latency Response (MLR) evoked potential testing and to determine which parameters of digital filtering will allow optimum identification of MLR thresholds without artifacts generated by analog filtering.

Technical Approach: Ten male and 10 female infants, aged birth to six months, will be studied. Only full term infants with normal delivery, Apgar score ≥ 7, no family history of hearing impairment, no perinatal infection, and no anatomic malformations involving the head or neck will be eligible. Infants will be tested with tympanometry prior to behavioral and MLR testing. The infant's binaural hearing will be screened in a sound field using Behavioral Observation Audiometry. The level of infants' responses to narrow band noise and speech will be documented. A speech awareness threshold will be gathered via live voice presentation of nonsense syllables and the child's name. Responses to frequency modulated narrow band noise will be documented. Live voice presentations will be peaked on the audiometer VU meter. The child will be seated in the test booth directly between two speakers and an observer will be seated facing the infant to report subtle responses to sound, such as eye-widening, quieting, eyeshift, or beginning headturn. Infants passing this screening will be tested with the MLR. Tone pips (500 and 3000 Hz) will be delivered through earphones to obtain information regarding low and high frequency hearing. Bracketing of different intensities will occur with presentations directly at estimated auditory threshold and 20 db above and below this level. Responses will be recorded on the side of the head, ipsilateral to the stimulation. Wide band 1-2000 Hz EEG activity will be gathered with a Nicolet Pathfinder evoked potential response unit on a computer disk for later filtering with the Nicolet digital analysis program. A variety of different filter settings will be utilized to determine which setting provides for optimal observation of the MLR waveforms. Analysis of variance for repeated measures will be used for statistical analysis.

Progress: The project was terminated following numerous unsuccessful attempts to find the correct instrumentation needed to complete the study. No subjects were entered. Attempts to find the correct test parameters were done, using the principal investigator and audiology staff volunteers.

Detail Summary Sheet

Date: 30 Sep 90	Protocol No.: 90/02	Status: Completed

TITLE: Tissue Expansion of the Facial Nerve in an Animal Model

Start Date: 20 Oct 89	Est Completion Date: Feb 90
Dept/Svc: Surg/Otolaryngology	Facility: MAMC
Principal Investigator: CPT David J. Malis, MC	
Associate Investigator: MAJ John McGath, MC	
Key Words: tissue expanders, facial nerve, axono-neurotemesis	

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $2000.00	Periodic Review: N/A

Study Objective: To determine the feasibility of tissue expanders for expansion of peripheral branches of the facial nerve (cranial nerve VII) without inducing axono- or neurotemesis.

Technical Approach: An incision will be made on the dorsal buccal region of the face parallel to the anticipated course of the dorsal buccal branch of the facial nerve. ENMG (Electroneuromyographic) readings will be taken to establish baseline amplitude and latency readings for the nerve and its innervated muscle. A 5 cm segment of nerve will be mobilized and the tissue expander placed deep to the mobilized nerve with the nerve situated in the expander's groove. The distance between the proximal and distal reference points will be measured. The injector port will be placed subcutaneously in the region of the supra-orbital scalp, with repeat ENMG readings taken. The unexpanded side of the face will serve as the control. The animals will then be randomly assigned to groups. Group 1 (pressure dependent): Prior to each intervention, nerve conduction latency will be reassessed. If the latency is >20% of baseline, no expansion will take place. If nerve latency is >20% of baseline on 5 consecutive intervention days, the facial nerves and tissue expanders will be retrieved and analyzed. If no latency deficits are demonstrable, intraluminal (IL) expander pressure will be measured, and the expander will be injected with a normal saline solution sufficient to raise the expander's IL pressure to 40 mm Hg. ENMG readings will be taken and the volume injected noted. This procedure will be repeated every other day for 90 days. Group 2 (ENMG dependent): The same as Group 1 except that a normal saline solution sufficient to cause an increase in latency by 20% will be injected and then volume will be removed from the expander to the point at which latency began to increase. At 90 days, pressure and ENMG data will be collected, the nerve and the associated tissue expander will be retrieved, and the fluid volume within the expanders will be aspirated and noted and the distance between the proximal and distal reference points will be measured. Specimens and tissue expanders will be histologically evaluated. Nerve specimens will be evaluated for axon count, organization, and perineural atrophy. Mean length between the whole experimental group, its sub-sets, and control nerves will be compared. Mean latency and amplitude values, rate of infusion, total volume infused, and histologic characteristics will be descriptively analyzed.

Progress: Ten pigs were studied. A manuscript is in preparation.

Detail Summary Sheet

Date: 30 Sep 90	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: Sep 90

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 90 Protocol No.: 90/60 Status: On-going

Title: Clinical Evaluation of PS Medical Lumbar Access Catheter (IDE #G890156- PS Medical)

Start Date: 20 Apr 90 Est Completion Date: Apr 91

Department: Surgery/Neurosurgery Facility: MAMC

Principal Investigator: LTC William J. Morris, MC

Associate Investigators: None

Key Words: morphine delivery/short term/lumbar access device

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $1000.00	Periodic Review: N/A

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

Technical Approach: Approximately 100 patients will be studied in this multi-institution protocol. Patient eligibility will be based on pain of cancerous origin or therapies associated with cancer; conventional pain management methods have been unsatisfactory; previous opioid experience; infection free; and life expectancy at least 1 month. Pregnant patients will be excluded.

The LAC is designed to provide short term access to either the lumbar epidural space or the lumbar subarachnoid space for morphine sulfate delivery and will also provide a means for sampling cerebrospinal fluid. The use of this device also allows the investigator to evaluate a patient's ability to withstand infusion therapy. The specific lumbar access location will be determined by the investigator based on the individual patient's condition and pain management requirements. The surgical technique for placement of the LAC is similar to that used for other lumbar catheters and is not investigational in nature. The catheter will be left in place for a period of 7 days for the delivery of a preservative-free morphine sulfate. To avoid the introduction of unnecessary variables, only Duramorph will be used. The initial dosage and delivery route will be determined for each patient by the investigator, based on the patient's daily narcotic experience prior to device placement. The decision to increase or decrease the dosage throughout the investigation will be the responsibility of the investigator. A morphine administration log will be maintained on a daily basis to monitor morphine in-take. A satisfactory device performance assessment will be determined by the absence of the following characteristics: kinked catheter; broken catheter; catheter occlusion; catheter migration; leakage of fluid into surrounding tissues; leakage of fluid from connector, filter or injection site; or filter occlusion.

Progress: The study has not been implemented because final HSC approval has not been obtained.

Detail Summary Sheet

Date: 30 Sep 90	Protocol No.: 90/61	Status: On-going
Title: Clinical Evaluation of PS Medical Lumbar Access Device (IDE #G880264 - PS Medical)		
Start Date: 20 Apr 90	Est Completion Date: Apr 91	
Department: Surgery/Neurosurgery	Facility: MAMC	
Principal Investigator: LTC William J. Morris, MC		
Associate Investigators: None		
Key Words: morphine delivery/chronic pain/lumbar access device		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $1000.00	Periodic Review: N/A

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

Technical Approach: Approximately 100 patients will be studied in this multi-institution protocol. Patient eligibility will be based on pain of cancerous origin or therapies associated with cancer; conventional pain management methods have been unsatisfactory; previous opioid experience; tolerance to bolus injection of morphine sulfate in lumbar subarachnoid or lumbar epidural space; infection free; life expectancy at least 1 month; and tissue surrounding port implantation site sufficient to accommodate port size. Pregnant patients will be excluded.

The LAD is designed to provide percutaneous access to either the lumbar epidural space or the lumbar subarachnoid space for morphine sulfate delivery to manage a patient's cancer pain and will also provide a means for sampling cerebrospinal fluid. The specific lumbar access location will be determined by the investigator based on the individual patient's condition and pain management requirements. The surgical technique for placement of the LAD is similar to that used for other lumbar catheters and is not investigational in nature. To avoid the introduction of unnecessary variables, only Duramorph will be used. The initial dosage and delivery route will be determined for each patient by the investigator, based on the patient's daily narcotic experience prior to device placement and preoperative epidural or subarachnoid morphine bolus assessment. The decision to increase or decrease the dosage throughout the investigation will be the responsibility of the investigator. A morphine administration log will be maintained on a daily basis to monitor morphine in-take. A follow-up report will be completed at 1 week, 2 weeks, and 1 month following device implantation. Subsequent follow-ups will be performed on a monthly basis up to 12 months. A satisfactory device performance assessment will be determined by the absence of the following characteristics: kinked catheter; broken catheter; catheter/port occlusion; device-caused necrosis/tissue erosion; component migration; catheter/port junction disconnect, and leakage of fluid into surrounding tissues.

Progress: The study has not been implemented because final HSC approval has not been obtained.

Detail Summary Sheet

Date: 30 Sep 90	Protocol No.: 90/51	Status: Suspended

Title: Sonolith 3000 Clinical Study for Gallbladder Stones (For Use Alone or in Combination with Actigall Therapy)

Start Date: 16 Mar 90	Est Completion Date: Nov 90
Department: Surgery	Facility: MAMC
Principal Investigator:	MAJ Michael J. O'Reilly, MC
Associate Investigators:	LTC William E.Eggebroten, MC MAJ Christopher R.Kaufmann, MC
Key Words: gallbladder, lithotripsy	

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

Study Objective: To determine if extracorporeal shockwave lithotripsy (ESWL) is a safe and effective means for elimination of gallstones, with or without adjuvant Actigall therapy.

Technical Approach: This study is being conducted in over 30 sites, utilizing approximately 600 patients. Subjects will be 18-100 yrs old, anesthesia class I, II, or III, functioning gallbladder, 1-3 gallstones, largest stone <30 mm, total stone aggregate <46mm, and radiolucent stones <20% calcium. Patients will have pretreatment laboratory and screening evaluations to to determine patency of the cystic duct, functionality of the gallbladder, and verification of stone burden. Treatment A will consist of ESWL with subsequent evaluation of need for Actigall therapy. Treatment B will consist of Actigall therapy for a minimum of 10 days followed by ESWL treatment followed immediately with continued Actigall therapy. In both treatments, each patient will be evaluated at 7-45 days post-ESWL for fragmentation success and the need for a possible second ESWL treatment. Patients with gallstone fragments >5 mm will be administered a second ESWL treatment, provided liver function tests are <2.5 times the upper limit of normal, there is no evidence of edema of the gallbladder wall, and the gallbladder is functioning. In Treatment A, Actigall will be administered if two ESWL treatments do not result in fragments <5 mm or the gallbladder is not clearing fragments <5 mm. Any patient with a clear gallbladder for 3 months will be considered a success and Actigall therapy will be discontinued at that time. Patients will be evaluated immediately post-treatment, at hospital discharge, and at 1, 3, and 6 month intervals after the last ESWL treatment. Any patient that continues to have symptoms will be taken off study and followed to investigate potential remaining effects of ESWL on future outcome. Demographic and baseline characteristics will be evaluated for comparability to determine the validity of combining data for pooled analysis. Analysis will include evaluation of patient symptoms, stone size, number of stones, presence/absence of fragmentation, and gallbladder clearing of remaining fragments.

Progress: This study has been suspended because the lithotriptor which this study was to utilize and which was to be purchased by the Urology Service for clinical use, has not been purchased. Purchase of the lithotriptor will probably be delayed until the Urology Service moves into the new hospital building in 1991.

Detail Summary Sheet

Date: 30 Sep 90 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: Sep 90

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: The procedural phase of this study has been completed. Thirty-six rabbits were used. Data analysis is in progress.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 89/29 Status: Completed

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: May 90

Study Objective: To determine the degree of suprarenal inferior vena caval (SR-IVC) narrowing that will allow for right renal survivability.

Technical Approach: Narrowing of the SR-IVC will be accomplished on 15 pigs 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 0 for the control group. Serum creatinine will be drawn every other day postoperatively to assess renal function. Renal vein and inferior vena caval thrombosis will be assessed four weeks postoperatively.

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. This information will be used as a pilot study to develop a protocol to study tracheal trauma and regeneration.

Progress: Results from the study of 12 pigs determined that a rise in IVC pressure >30 cm of water after supra-renal IVC ligation is predictive of subsequent thrombosis and renal demise. This study was clinically significant for the patient with a left tumor invading the vena cava in that the desperate surgeon might consider leaving the right kidney in place if IVC pressures remain <30 cm H_2O after temporary IVC occlusion.

A paper was presented to the Kimbrough Urologic Society and won an Honorable Mention. The paper won the Resident's Competition at the Northwest Urologic Society Meeting.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 88/56 Status: Terminated

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 90

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: One patient was entered in the study in FY 90 for a total of 14 subjects. The protocol was terminated because the investigators were unable to obtain enough eligible patients to complete the study. There was also a problem with patient compliance with the study design.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/94 Status: On-going

Title: The Effect of 5α-Reductase Inhibitor on Dihydrotestosterone Levels Within Prostate Tumors Implanted In Athymic Nude Mice

Start Date: 20 Jul 90 Est Completion Date: Dec 90

Department: Surgery/Urology Facility: MAMC

Principal Investigator: CPT Leonard G. Renfer, MC

Associate Investigator: COL Stephen R. Plymate, MC

Key Words: prostate tumor, 5α-reductase inhibitor

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: $1100.00 Periodic Review: N/A

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

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

Progress: This is a new study which is awaiting final approval from the Institutional Review Board.

Detail Summary Sheet

Date: 30 Sep 90	Protocol No.: 90/15	Status: On-going

Title: Investigation of Cryotreatment on the Epiphysis of Growing Rabbit Bones

Start Date: 19 Jan 90	Est Completion Date: Jan 91
Dept/Svc: Surgery/Orthopedics	Facility: MAMC
Principal Investigator:	CPT James S. St. Louis, MC
Associate Investigators:	COL D. Scott Smith, MC COL Roberto Barja, MC, DDEAMC MAJ Michael Tidwell, MC, DDEAMC CPT Harvey Montigo, MC, DDEAMC
Key Words: cryotreatment, epiphysis, bones, growth	

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

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

Technical Approach: Number or rabbits studied: 15

The lateral aspect of the distal femur of the right leg will be exposed and the CT-73 cryosurgical system will be applied with a microprobe to freeze the area. The left rear leg will be operated in the same manner, except the cryoprobe will not be applied. After a six week period for bone growth, the animals will be euthanized. A pathologist will then determine the gross effect on growth plates and any deformities present on the right versus the left femur. Microscopic specimens of the cryotreated epiphyses will be examined to evaluate remaining potential growth of microvascular structures and uniformity of cryological effects. Data will be evaluated using a paired t test between right and left sides to compare the legs at an alpha level of .05.

Progress: This study has not yet begun due to the renovation of the Laboratory Animal Facility.

Detail Summary Sheet

Date: 30 Sep 90 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 90

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.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 86/86 Status: Completed

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: LTC John A. Vaccaro, MC (Nov 89)*

Associate Investigators: COL William D. Belville, MC
COL Irwin B. Dabe, MC

Key Words: prostate, carcinoma, RU 23908, leuprolide

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Mar 90

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 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. All subjects at MAMC have now completed the study.

* COL Belville original PI

Detail Summary Sheet

Date: 30 Sep 90 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. Vaccar 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 90

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: Two additional subjects were enrolled in the study in FY 90 for a total of nine entries.

The protocol has been approved at WRAMC and will be conducted as a joint study in order to accrue sufficient subjects.

***Replaced Dr. Kiesling as the PI, Sep 89
**Replaced Dr. Evans as the PI, Dec 87

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 89/03 Status: Terminated

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: LTC John A. Vaccaro, MC (Nov 89)*

Associate Investigators: COL William D. Belville, MC
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 study was terminated due to constraints in the number of personnel assigned to the Urology Clinic.

* COL Belville original PI

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 89/42 Status: Completed

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: LTC John A. Vaccaro, MC (Nov 89)*

Associate Investigators: COL William D. Belville, MC
LTC Rodney Michael, MC

Key Words: cefpodoxime proxetil, cefaclor, UTI, safety, efficacy

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

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 were entered in this study. All patients have completed the study. The study has been closed by Besselaar Associates due to sufficient accrual of patients.

* COL Belville original PI

Detail Summary Sheet

Date: 30 Sep 90	Protocol No.: 89/68	Status: Completed

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: Sep 90

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: All of the 48 specimens were analyzed. There was no rise in prostate specific antigen.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/21 Status: On-going

Title: Provocative Androgen Testing in Patients at High Risk for Persistent Carcinoma After Radical Prostatectomy

Start Date: 19 Jan 90 Est Completion Date: Jan 92

Dept/Svc: Surgery/Urology Facility: MAMC

Principal Investigator: LTC John A. Vaccaro, MC

Associate Investigator: MAJ Rodney Davis, MC

Key Words: androgen testing, carcinoma, prostatectomy

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

Study Objective: To develop a test to identify those patients, with PSA (prostate-specific antigen) within normal limits after radical prostatectomy, who have persistent disease.

Technical Approach: This study will be done in conjunction with the University of Washington. Approximately 30 males, ages 40-75 will be studied. To be eligible, patients must be fully recovered from radical prostatectomy performed at least 3 months previously, have a serum PSA $\leq$0.4 ng/ml, and have had no additional therapy. Patients will be high risk for persistent disease, i.e., Stage B tumor confined to the capsule but with Gleason combined grade higher than 8; pathological stage C1 (capsular perforation); C2 (positive surgical margins); C3 (positive seminal vesicles); or D1a (microscopic lymph node involvement). The patient will undergo clinical restaging, including digital rectal exam, abdominal pelvic CT scan, bone scan, cystoscopy, and transrectal biopsy of the urethral vesicle anastomosis. Patients without evidence of persistent disease will then be given 100-300 mg of testosterone enanthate every week for 8 weeks. PSA levels will be determined each week. Should the patient's PSA level become >0.4 ng/ml, the patient will be immediately restaged (while on testosterone stimulation) and then the stimulation will be stopped and the PSA and testosterone values observed until testosterone nadir (approximately one month). If PSA levels rise further (>0.3 ng/ml) at any time during this withdrawal, treatment will be immediately started. If PSA stabilizes or falls during testosterone withdrawal and a lesion was demonstrated, the patient will be restaged. If no lesion is found during testosterone stimulation, the patient will also be restaged prior to treatment. Treatment will consist of either pelvic or prostatic bed radiation or hormone ablation therapy either by orchiectomy, LH-RH agonists, or diethylstilbestrol (3 mg/day), according to patient preference and established medical criteria. Patients without PSA elevation during the 8 week period will also be restaged at the end of testosterone stimulation but thereafter will be followed (without further treatment) by PSA and testosterone levels monthly for six months and every 3 months thereafter. Bone scans will be determined every 6 months for a year.

Progress: No patients have been entered in this study due to the difficulty in finding patients that are eligible and agree to participate.

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 90 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: Jun 90

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 90. One patient is still 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 90 | 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: Jun 90

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 90. 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 90 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: Jun 90

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 regimen. Patients with M1 marrow after the first regimen of induction or M1 or M2A marrow at any time after completion of induction will have a bone marrow transplant if a suitable donor is available and the patient/family wishes to pursue this course of action. At the end of induction, patients with remission and no donor will be entered in a consolidation phase which will consist of 2 cycles of high-dose Ara-C and L-asparaginase, followed by two cycles of 6thioguanine, vincristine, ara-C 5-azacytidine, and cyclophosphamide, and then one cycle of VP 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 Week 8 of the study.

Progress: No patients entered in FY 90. One patient previously entered has completed therapy and is being followed.

**Replaced Dr. Hartman as PI, Aug 88
*Original PI

Detail Summary Sheet

Date: 30 Sep 90 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: Jun 90

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 90 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: Jun 90

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. No patients were entered in FY 90. One patient was entered in the study in Aug 89.

Detail Summary Sheet

Date: 30 Sep 90 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: Jun 90

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: No patients entered in FY 90. One patient was entered in this study in FY 89 and died of the disease.

Detail Summary Sheet

Date: 30 Sep 90 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: Jun 90

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 90 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: Jun 90

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 VP-16, 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 90 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: Jun 90

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 90	Protocol No.: 90/100	Status: On-going
Title: CCG 1881: Treatment of Newly Diagnosed Acute Lymphoblastic Leukemia in Children Aged 2-9 Years Inclusive, with White Blood Count <10,000/UL, Phase III		
Start Date: 17 Aug 90	Est Completion Date: Indefinite	
Department: Pediatrics	Facility: MAMC	
Principal Investigator: Edythe Albano, M.D., DAC		
Associate Investigators: None		
Key Words: leukemia, lymphoblastic, chemotherapy		
Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: N/A

Study Objective: To assess the contribution of delayed intensification to event-free survival, disease-free survival, and overall survival rates in good prognosis patients with acute lymphoblastic leukemia (ALL) as well as to assess the toxicity of delayed intensification; to refine the current CCSG definition of what constitutes good prognosis ALL; to select out a group of less favorable good prognosis patients based upon blast cytogenetics at diagnosis and upon poor treatment response as assessed on the day 14 bone marrow; to assess event-free survival, disease-free survival, and overall survival for these less favorable patients after treating them with the addition of delayed intensification therapy to standard CCG "good prognosis" therapy; to assess the feasibility of collecting blast cell immunophenotypic and cytogenetic data in the context of a large cooperative group study; and to evaluate the prognostic significance of platelet counts $<100,000/mm^3$ and those $\geq 100,000/mm^3$ at diagnosis in girls with good prognosis ALL.

Technical Approach: Patients will be induced with vincristine, prednisone, and L-asparaginase. CNS prophylaxis will be carried out using 6 doses of IT methotrexate during induction and consolidation, followed by maintenance doses every 12 weeks. Consolidation will consist of daily 6-mercaptopurine coupled with a 2-week taper of oral prednisone. Consolidation will be followed by an 8-week interim maintenance phase during which 2 pulses of vincristine and prednisone given at 4-week intervals will be administered along with daily 6-mercaptopurine and weekly methotrexate. At week 16, patients will be randomized to receive (Regimen B) or not receive (Regimen A) delayed intensification (a 4-week reinduction using vincristine adriamycin, L-asparaginase, and dexamethasone and a 3-week reconsolidation utilizing cyclophosphamide, cytosine arabinoside, 6-thioguanine and IT methotrexate). Maintenance therapy for both regimens will consist of monthly pulses of vincristine and prednisone, along with daily oral 6 mercaptopurine, weekly oral methotrexate, and IT methotrexate every 12 weeks. The duration of maintenance therapy will be two years for girls and three years for boys. Patients with unfavorable blast cell cytogenetics at diagnosis and patients with an m_3 day 14 bone marrow response will be nonrandomly assigned to delayed intensification.

PROGRESS: One patient has been entered on this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/101 Status: On-going

Title: CCG 1882: Treatment of Newly Diagnosed Acute Lymphoblastic Leukemia in Children with a Poor Prognosis, Excluding Infants and Patients with Lymphoma-Leukemia or FAB L3 Blasts, Phase III

Start Date: 17 Aug 90 Est Completion Date: May 95

Department: Pediatrics Facility: MAMC

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

Associate Investigators: None

Key Words: leukemia, ALL, children, chemotherapy

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

Study Objective: To show that the Berlin Frankfurt Munster (BFM) regimen without cranial radiation plus intensive intrathecal (IT) methotrexate will produce an approximate 80% event free survival in children with high risk acute lymphocytic leukemia (ALL) who have M1/M2 marrow response on day 7 of BFM induction; to improve event free survival in children with high risk ALL showing an M3 response on Day 7 of BFM therapy by intensifying standard BFM by (a) addition of non-myelosuppressive chemotherapy to consolidation, reconsolidation courses (vincristine, L-asparaginase), (b) addition of a second reinduction/reconsolidation course; (c) replacement of interim maintenance (oral 6-MP, oral methotrexate) with Capizzi I (vincristine, escalating parenteral methotrexate, L-asparaginase) intensification, (d) addition of a second Capizzi I intensification course following the first reinduction/reconsolidation course, (e) escalating 6-MP and methotrexate dosage during maintenance to maintain an absolute neutrophil count between 750-1500; to study further the impact of day 7 marrow status on outcome in children with high-risk ALL; and to obtain information concerning cytogenetic abnormalities and immunophenotype distribution in children with high-risk ALL.

Technical Approach: All patients entered on this study will be given BFM induction. A day 7 marrow will be performed and patients will be classified as either good responders (M1/M2) or poor responders (M3). Patients who are good responders and subsequently show an M1 marrow on day 29 will be randomized to receive either standard BFM (cranial RT and IT methotrexate) or BFM with only IT methotrexate as CNS prophylaxis. Patients who are poor responders and subsequently show an M1 marrow on day 28 will be nonrandomly assigned to an augmented BFM program which includes a second reinduction/reconsolidation course, additional vincristine and L-asparaginase during consolidation and reconsolidation, and two courses of Capizzi methotrexate in place of interim maintenance in an effort to improve disease free survival. Patients >10 years of age will be included on this high risk trial since CCG 105 showed that these patients had a worse outcome than younger patients, regardless of treatment regimen. Patients with lymphoma syndrome and/or FAB L3 morphology will be excluded.

Progress: No patients have been entered on this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/102 Status: On-going

Title: CCG 1883: Treatment of Newly Diagnosed Acute Lymphoblastic Leukemia in Infants Less Than 12 Months of Age, Phase III

Start Date: 17 Aug 90 Est Completion Date: Dec 93

Department: Pediatrics Facility: MAMC

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

Associate Investigators: None

Key Words: ALL, infants, chemotherapy

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

Study Objective: To prevent leukemic relapse and improve event free survival of infants <12 months with acute lymphoblastic leukemia (ALL) using intensive induction and consolidation therapy, followed by an intensification phase consisting of a reinduction, reconsolidation; to determine prospectively the prognostic significance and biologic implications of lymphoblast surface membrane immunophenotype and karyotypic analysis with respect to the treatment utilized in this study; to investigate the impact on duration of event-free survival of the addition of aggressive cytoreductive chemotherapy administered immediately following remission induction and again during intensification; to continue to investigate the efficacy of intensive intrathecal (IT) chemotherapy and very high-dose, protracted, systemic infusions of methotrexate in addition to high-dose Ara-C as CNS prophylaxis in an effort to mitigate the potential neurotoxicity of conventional CNS prophylaxis incorporating whole brain radiotherapy in children of this age group; to include and standardize vigorous supportive care measures; to prospectively evaluate the effect of ALL and its treatment on development outcome and to identify children who may be at risk for later learning difficulties which may be responsive to early intervention efforts.

Technical Approach: Patients <12 months with newly diagnosed ALL will have immunophenotypic analysis, as well as karyotypic analysis of pretreatment bone marrow samples. All patients will receive intensive induction therapy consisting of vincristine, daunomycin, prednisone, L-asparaginase, and IT chemotherapy. Following remission induction, patients will receive consolidation therapy consisting of high-dose cytosine arabinoside with L-asparaginase, followed by 3 very high-dose, protracted (24 hr) systemic infusions of methotrexate with high-dose citrovorum factor rescue alternating weekly with IT cytosine arabinoside and cyclophosphamide. Consolidation therapy will be followed by an interim maintenance therapy consisting of IV methotrexate and L-asparaginase (Capizzi I) and IT chemotherapy. Following this, intensification therapy consisting of reinduction with vincristine, daunomycin, L-asparaginase, and reconsolidation therapy with high-dose cytosine arabinoside, very high-dose systemic methotrexate, and cyclophosphamide will be administered. Maintenance therapy will consist of oral 6-mercaptopurine and methotrexate with periodic vincristine and prednisone pulses, as well as IT chemotherapy.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/103 Status: On-going

Title: CCG 1884: A Comparison of Idarubicin to Daunomycin in A Multi-Drug Treatment of ALL in Marrow Relapse

Start Date: 21 Sep 90 Est Completion Date: Indefinite

Department: Pediatrics Facility: MAMC

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

Associate Investigators: None

Key Words: cancer, ALL, daunomycin, idarubicin

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $15,000.00	Periodic Review: N/A

Study Objective: To compare the efficacy and toxicities of Idarubicin (IDR) and Daunomycin (DNM) when used in combination with vincristine (V), prednisone (P), and L-asparaginase (L) to induce second marrow remission in children with acute lymphoblastic leukemia (ALL) who have experienced a first marrow relapse while on therapy or within one year of discontinuing therapy.

Technical Approach: A four-drug induction program with VPL and anthracycline will be used. In order to compare toxicity and efficacy, all patients will be randomized to receive either IDR or DNM. A rescue reinduction (Capizzi II) will be given to patients who do not enter remission with the four drugs, but these patients will not be evaluable for the maintenance vs bone marrow transplant question. All patients who achieve remission on VPL-IDR or VPL-DNM will be consolidated with two cycles of Capizzi I. This will also provide a brief period to arrange for bone marrow transplant for those patients with a histocompatible sibling who will be treated on CCG-1006. Patients who do not have a suitable donor will remain on this study and receive maintenance therapy with Capizzi I and intermittent reinduction pulses of high-dose Ara-C and anthracycline. The anthracycline will be the same one used in induction and will be used in this phase either until a total cumulative lifetime anthracycline dose reaches 550 mg/m^2 (calculating each 12.5 mg/m^2 of IDR as 45 mg/m^2 of DNM equivalent) or until cardiotoxicity occurs (whichever occurs first). It is recommended that patients going to bone marrow transplant not receive more than 450 mg/m^2 total prior lifetime dose of anthracycline. Maintenance therapy will be continued for 2 1/2 years if the patient remains disease free.

Progress: No patients have been entered on this study at MAMC.

Detail Summary Sheet

Date: 30 Sep 90 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: Jun 90

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 90 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: Jun 90

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

GYNECOLOGY ONCOLOGY GROUP PROTOCOLS

Detail Summary Sheet

Date: 30 Sep 90 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: Nov 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 90. Protocols 26D, 26O, and 26Z were closed to patient accrual in FY 90 due to sufficient numbers of patients.

Detail Summary Sheet

Date: 30 Sep 90 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 89

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 90. Three patients were entered in previous years.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 83/18 Status: Terminated

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 89

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 90. One patient was entered at MAMC in FY 87.

The study was classified as terminated because the GOG is no longer collecting data on the patients on this protocol.

Detail Summary Sheet

Date: 30 Sep 90 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 89

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 90 at MAMC. In previous years three patients had been entered. All died of their disease.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 82/30 Status: Terminated

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 89

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 90. One patient entered at MAMC during FY 84 with no response to AZQ; death by cancer of cervix.

This study was classified as terminated because the GOG is no longer collecting data on these patients.

Detail Summary Sheet

Date: 30 Sep 90 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 89

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 90. One patient was entered in FY 85 and died from squamous cell carcinoma of the cervix.

Detail Summary Sheet

Date: 30 Sep 90 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: Nov 89

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 90. Two patients were entered in previous years and died of the disease.

Detail Summary Sheet

Date: 30 Sep 90 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: Nov 89

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 90 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: Nov 89

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 90 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: Nov 89

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 90 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: Nov 89

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 90 Protocol No.: 88/59 Status: Completed

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: Nov 89

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 90. One patient entered at MAMC in FY 88 and died of disease.

Detail Summary Sheet

Date: 30 Sep 90 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: Nov 89

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 90 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: Nov 89

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 90 Protocol No.: 90/23 Status: On-going

Title: GOG 26 GG: A Phase II Trial of Fazarabine (ARA-AC, 1-BETA-D-Arabinofuranosyl-5-Azacytosine, NSC 281272, IND 29722C) in Patients With Advanced/Recurrent Cervical Cancer

Start Date: 19 Jan 90 Est Completion Date: Indefinite

Department: OB/GYN Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

Associate Investigators: None

Key Words: cervical cancer, advanced, resistant, Fazarabine

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

Study Objective: To screen for activity of new agents or drug combinations in patients with advanced malignancies. Its intent is to determine tne efficacy of chemotherapeutic agents in patients whose advanced malignancies have been resistant to high priority methods of treatment.

Technical Approach: To be eligible, patients must have histologically confirmed, advanced, recurrent, persistent, metastatic, or local gynecologic cancer with documented disease progression; lesions that are measurable and can be followed for tumor response; abdominal, pelvic, or other masses which can be defined in at least two dimensions by palpation or by x-ray; a GOG performance Grade 0, 1, or 2 (Karnofsky scale 30-100); free of clinically significant infection; off previous chemotherapy for at least 3 weeks; recovered from effects of recent surgery, radiotherapy, or chemotherapy; passed the nadir blood counts from previous therapy, and a granulocyte count $\geq 1500/mm^3$, platelet count $\geq 100,000/mm^3$, BUN ≤ 25 mg%, creatinine ≤ 1.5 mg%, bilirubin ≤ 1.1 mg, and SGOT ≤ 5 IU.

Fazarabine will be administered at a dose of 40 mg/M^2/day for five days. Cycles of therapy will be repeated every 28 days.

Patients with a response or stable disease will continue therapy until progression of disease is documented or adverse effects prohibit further therapy. Patients with progressive disease will have Fazarabine discontinued. Patients will be monitored for adverse effects and dose levels modified as necessary.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/24 Status: On-going

Title: GOG 26HH: A Phase II Trial of 5-Fluorouracil and Leucovorin in Advanced Metastatic or Recurrent Pelvic Malignancies

Start Date: 19 Jan 90 Est Completion Date: Indefinite

Department: OB/GYN Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

Associate Investigators: None

Key Words: cervical cancer, advanced, resistant, Fazarabine

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

Study Objective: To screen for activity of new agents or drug combinations in patients with advanced malignancies. Its intent is to determine the efficacy of chemotherapeutic agents in patients whose advanced malignancies have been resistant to high priority methods of treatment.

Technical Approach: 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, and SGOT ≤ 5 IU.

Leucovorin will be given in a dose of 20 mg/M^2 daily for 5 days and repeated at 4 and 8 weeks and thereafter every 5 weeks.

5-FU will be infused in a dose of 425 mg/M^2 daily for 5 days immediately after the Leucovorin has been given and will be repeated at 4 and 8 weeks and thereafter every 5 weeks.

An adequate trial will be one course of treatment and living four weeks for additional tumor assessment provided death is not due to tumor progression. All patients entered on study will be evaluable for toxicity. Patients will remain on study and continue receiving the drugs until disease progression or until toxicity prevents further treatment.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 90 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 89

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 90. In previous years, eight patients were entered on the protocol. Five patients are still being followed.

Detail Summary Sheet

Date: 30 Sep 90 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: Nov 89

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 90. Six patients have been entered in previous years, with three of them still being followed.

Detail Summary Sheet

Date: 30 Sep 90 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 89

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 90. Two patients were entered at MAMC in previous years and one is still being followed. The protocol is closed to patient entry.

Detail Summary Sheet

Date: 30 Sep 90 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: Nov 89

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 90. Six patients were entered in previous years. Three patients died of the disease and three are currently being followed on this protocol. The study has been closed to patient entry.

Detail Summary Sheet

Date: 30 Sep 90 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 89

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 90. 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 90 Protocol No.: 82/36 Status: Terminated

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: Nov 89

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 90. In previous years four subjects were entered.

This protocol is classified as terminated because the GOG is no longer collecting data on these patients.

Detail Summary Sheet

Date: 30 Sep 90 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: Nov 89

Study Objective: To evaluate the role of adjunctive extrafascial hysterectomy in the treatment of suboptimal Stage IB carcinoma of the cervix, the survival and patterns of failure in bulky IB cervix cancer, and the prognostic value of pretreatment endometrial sampling in suboptimal Stage IB carcinoma of the cervix; and to study the toxicity of a combined radiation and surgical therapeutic program.

Technical Approach: Eligible patients: patients with primary, untreated, histologically confirmed invasive carcinoma of the uterine cervix, FIGO Stage IB, as confirmed by cervical biopsy and endometrial sampling.

Regimen I: Following recovery from radiation therapy, patients will undergo para-aortic and common iliac nodal sampling, abdominal washings, and intra-abdominal exploration.

Regimen II: Following recovery from radiation therapy, patients will undergo para-aortic and common iliac nodal sampling, abdominal washings, and intra-abdominal exploration plus total extrafascial hysterectomy.

All patients will be followed for five years. Patients found to have more extensive disease (i.e., positive para-aortic nodes, intra-abdominal metastasis) will be treated at the discretion of the physician and will be followed for five years.

Progress: No patients entered at MAMC in FY 90. One patient entered at MAMC in FY 86 and has been lost to follow-up.

Detail Summary Sheet

Date: 30 Sep 90 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: Nov 89

Study Objective: To evaluate the biologic behavior of ovarian tumors of low malignant potential; to evaluate the effectiveness of chemotherapy against this disease (initially, a Phase II study of melphalan); and to evaluate the response rate to cisplatin in melphalan failures.

Technical Approach: Patients without prior chemotherapy or radiotherapy who have had adequate surgical staging will be eligible. Patients with no grossly visible residual disease will receive no treatment and be followed for 5 years if there is no subsequent disease. If there is no grossly visible clinically apparent residual for 12 months, the patients will have second look surgery and then proceed to melphalan treatment (5 days every four weeks) or follow-up (complete response). With progression after melphalan, patients will proceed to third look and cis-platin treatment (once every three weeks for eight weeks) or follow-up. If there is no evidence of response after three courses of cis-platin, the treatment will be discontinued. Patients who have progression during the first 12 months will be treated as above except they will proceed directly to melphalan treatment without second look surgery. Follow-up will be for a minimum of five years with clinical examination every three months for the first two years, then every six months thereafter.

Progress: One new patient entered in FY 90 for a total of seven subjects.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 84/26 Status: Completed

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: Nov 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 90 Protocol No.: 84/27 Status: Completed

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: Nov 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 90 Protocol No.: 87/11 Status: Completed

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: Nov 89

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 in 76H in FY 89 (lost to follow-up); one patient was entered in 76G in FY 87 (progressive disease, taken off study); and one patient was entered in 76J in FY 88 (died of disease). All sections of this study have been closed to patient entry.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 89/06 Status: Completed

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: Nov 89

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 was entered in this study in FY 89 and has been lost to follow-up. The study was closed to patient entry in August 1989.

Detail Summary Sheet

Date: 30 Sep 90 | Protocol No. 88/52 | Status: Completed

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: Nov 89

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 90. One patient was entered in the study at MAMC in FY 87 and died of the disease.

Detail Summary Sheet

Date: 30 Sep 90 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: Nov 89

Study Objective: To evaluate the effect of adjuvant vinblastine, bleomycin, and cisplatin (VBP) chemotherapy in patients with endodermal sinus tumor and choriocarcinoma of the ovary (pure and mixed) after removal of all gross tumor; to evaluate the role of serum markers, especially alpha fetoprotein and HCG, in predicting recurrence; to evaluate the role of reassessment laparotomy in determining response, detecting early relapse, and planning further therapy; and to compare the biologic behavior of pure endodermal sinus tumors with mixed germ cell tumors containing endodermal sinus elements. Per addendum of Jan 87: to evaluate the acute and chronic toxicity of this chemotherapy on gonadal and reproductive function.

Technical Approach: Patients with totally resected Stage I choriocarcinoma, endodermal sinus tumor, or embryonal carcinoma of the ovary with negative peritoneal washings, normal (or falling at a rate that does not suggest residual disease) serum AFP and beta-HCG levels, and adequate bone marrow, renal, and hepatic function will be studied. Stages II and III will also be eligible if all gross tumor is resected. After recovery from surgery, patients will receive 3 cycles of VBP therapy. Patients who show evidence of progression while on VBP therapy will be candidates for GOG Protocol 26. Patients completing three cycles of treatment clinically free of disease will undergo reassessment laparotomy. Patients with recurrent disease at reassessment laparotomy will be candidates for GOG Protocol 26. To be evaluable a patient will receive at least one week of chemotherapy and live another two weeks. Each patient will remain on study until adverse effects prohibit further therapy or until evidence of progression is noted.

**Per addendum of Jan 86: the title has been changed as shown above; vinblastine has been replaced by VP-16; Grade 3 immature teratoma has been added for entry and evaluation.

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 86/08 Status: Completed

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, medroxyprogesterone acetate

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

Study Objective: To determine the relative efficacy of two dose schedules of oral medroxyprogesterone acetate (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.

Detail Summary Sheet

Date: 30 Sep 90	Protocol No.: 85/90	Status: Completed

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: Nov 89

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 90 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: Nov 89

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: Two patients were entered at MAMC in FY 90.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 86/14 Status: Completed

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: Nov 89

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. All sections of this study have been closed by GOG.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 87/27 Status: Completed

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 89

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. Closed to patient entry.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 87/101 Status: Completed

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: Nov 89

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. Closed to patient entry.

Detail Summary Sheet

Date: 30 Sep 90 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: Nov 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 - 2 years
Other sarcomas - 6 years

Progress: No entries at MAMC.

Detail Summary Sheet

Date: 30 Sep 90 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: Nov 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. 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 90	Protocol No.: 87/103	Status: Completed

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: Nov 89

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 90 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: Nov 89

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 90 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: Nov 89

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 90 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: Nov 89

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 90 at MAMC. One patient was entered in FY 88 and is still being followed.

Detail Summary Sheet

Date: 30 Sep 90 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: Nov 89

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 90 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: Nov 89

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 90. Two patients were entered in FY 88. Both died of the disease.

Detail Summary Sheet

Date: 30 Sep 90 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 89

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: No patients entered in FY 90. 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 90 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: Nov 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: No patients entered at MAMC in FY 90. One patient was entered in FY 89 and died of the disease. One patient was entered in FY 87.

Detail Summary Sheet

Date: 30 Sep 90 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: Nov 89

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 90. Two patients were entered FY 87. Both are still being followed.

Detail Summary Sheet

Date: 30 Sep 90 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: Nov 89

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 90 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: Nov 89

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 90 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: Nov 89

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.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 89/07 Status: Completed

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: Nov 89

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 antiemetic 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 90 Protocol No.: 90/25 Status: On-going

Title: GOG 102E: Intraperitoneal Administration of Cisplatin (NSC #119875) and Etoposide (VP-16) (NSC #141540) in Patients with Residual Ovarian Carcinoma

Start Date: 19 Jan 90 Est Completion Date: Indefinite

Department: OB/GYN Facility: MAMC

Principal Investigator: LTC Gordon O. Downey, MC

Associate Investigators: None

Key Words: cancer, ovarian, cisplatin, etoposide

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

Study Objective: To determine the activity of Cisplatin and Etoposide when used by the intraperitoneal route in patients who have persistent minimal residual disease epithelial ovarian malignancies after standard therapy, and to evaluate further the toxicity of this combination of drugs.

Technical Approach: Eligible patients: those with primary histologically documented epithelial carcinoma of the ovary; partial or incomplete responses to combination chemotherapy or minimal residual disease ($\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; and bilirubin and SGOT $\geq$ two times normal. A special eligibility requirement for this protocol is that patients have creatinine $\leq$ 1.5 mg%.

Cisplatin, 100 mg/m^2, and Etoposide, 200 mg/m^2, will be given intraperitoneally and repeated at four week intervals or as soon thereafter as toxicity has resolved. If more than six weeks pass from the time of the last treatment and toxicity has not resolved, the patient will go off study. Dosage of medications will be modified if required by toxicity. Appropriate antiemetics, hydration, and Mannitol diuresis will be administered.

Treatment will continue for a total of six cycles in responding patients or in patients with nonevaluable disease. Patients with progressive disease will go off study. Following the completion of six cycles of therapy, patients with nonevaluable disease and those in a clinically-defined complete remission will undergo an exploratory laparotomy to further define the status of disease and the nature of the response. If the patient is found to be in a surgically-defined complete response, the patient will be followed without further treatment. If residual disease is present, the patient will go off study to receive alternative treatment.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 90 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: Nov 89

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 90 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: Nov 89

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 90 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: Nov 89

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 90 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: Nov 89

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 90 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: Nov 89

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 90 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: Nov 89

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 90 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: Nov 89

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.

Detail Summary Sheet

Date: 30 Sep 90	Protocol No.: 90/26	Status: On-going

Title: GOG 8907: DNA Content of Hydatidiform Moles as a Predictor of Persistent Gestational Trophoblastic Neoplasia

Start Date: 19 Jan 90	Est Completion Date: Indefinite
Department: OB/GYN	Facility: MAMC
Principal Investigator: LTC Gordon O. Downey, MC	
Associate Investigators: None	
Key Words: cancer, neoplasia, trophoblastic, DNA content	

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

Study Objective: To determine: if aneuploidy identifies a subset of high-risk hydatidiform moles; if ploidy status has sufficient predictive value to justify prophylactic chemotherapy of certain molar pregnancies; if proliferative activity, as estimated from cell cycle distribution, has any prognostic value; the number of paraffin blocks that constitutes an appropriate sampling of a molar pregnancy in order to establish presence of aneuploid cell lines; and if ploidy or proliferative index, as measured on either the mole or subsequent biopsy material, can predict the pattern of postmolar gestational trophoblastic neoplasia to be either metastatic or nonmetastatic and the response to various treatment regimens; and to assess persistence of ploidy status by comparing ploidy of molar tissue with ploidy status of subsequent tissue samples obtained after development of postmolar gestational trophoblastic disease.

Technical Approach: Flow cytometry will be used to measure ploidy and proliferative rate on archival tissues on patients identified as having complete hydatidiform mole pregnancies. These patients have previously been identified by entry on GOG Protocol #55. Results of lab measurements on tissue will be compared to clinical characteristics of post molar course, treatment received, if any, and response to such treatment. The incidence of aneuploidy in tissue samples from staging work-up in those patients who have developed persistent gestational trophoblastic neoplasia will be assessed. Information regarding cell cycle kinetics and growth fraction will be used to correlate tumor responses to treatment regimens in consideration of cell cycle phase specificity for various agents.

Progress: Blocks are being submitted to GOG for analysis.

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: Nov 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 90 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: Jun 90

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 90 for a total of two subjects.

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

F O R

P R O T O C O L S

PUGET SOUND ONCOLOGY CONSORTIUM

Detail Summary Sheet

Date: 30 Sep 90 | 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: Nov 89

Study Objective: To examine the effect of intraperitoneal therapy on disease free survival in patients with no disease or minimal residual disease following second-look surgery and to document the complication rate associated with the use of intraperitoneal chromic phosphate or chemotherapy in patients previously treated with systemic chemotherapy.

Technical Approach: Following standard induction chemotherapy, patients with Stage IIb, IIc, or III epithelial carcinoma of the ovary will have second-look laparotomy in the standard fashion. The second look procedure will include resection of any remaining female genital organs. If the patient has no evidence of gross persistent disease greater than 1.0 cm at the time of second look, a Tenckhoff catheter will be inserted.

If the pathologic findings from the second look procedure show no evidence of persistent tumor, the patient will receive 15 millicuries of intraperitoneal P-32 in 1000-1500 ml of normal saline, with appropriate rotation of position to assure proper distribution of the P-32.

If the patient has positive disease within the peritoneal cavity, she will receive chemotherapy with cisplatin (100 mg/m^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 90. 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 90 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: Oct 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 90 at MAMC. One patient was entered in FY 84 at MAMC on the observation arm and expired from the disease in FY 86.

Group-wide: 208 patients entered. There have been two treatment related deaths; one due to congestive heart failure which was probably due to arteriosclerotic disease but Adriamycin cardiotoxicity could not be excluded, and one due to mitomycin-C associated hemolytic uremic syndrome with thrombocytopenia.

Detail Summary Sheet

Date: 30 Sep 90 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: Oct 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 90. Twelve patients were entered in previous years. Two patients have died of their disease, five were taken off study, and five are being followed. The study was closed to patient entry in 1987.

Detail Summary Sheet

Date: 30 Sep 90 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: Oct 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: No new patients entered at MAMC in FY 90; 35 subjects have been entered in this study at MAMC. Seven of these patients are still being followed.

Groupwide: 288 eligible patients have been entered. Toxicities have been similar for both arms. No fatal toxicities have been reported.

Detail Summary Sheet

Date: 30 Sep 90 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:

COL William D. Belville, MC
COL Irwin B. Dabe, MC
COL Friedrich H. Stutz, MC
MAJ Thomas M. Baker, MC
MAJ Alfred H. Chan, MC
MAJ Timothy J. O'Rourke, MC
MAJ Michael D. Stone, MC

Key Words: cancer, bladder, BCG immunotherapy, adriamycin

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Oct 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. All three have been taken off study and are being followed.

Detail Summary Sheet

Date: 30 Sep 90 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
COL Irwin B. Dabe, MC
COL Donald Kull, MC
COL Friedrich H. Stutz, MC
MAJ Thomas M. Baker, MC
MAJ Alfred H. Chan, MC
MAJ Timothy J. O'Rourke, MC
MAJ Michael D. Stone, MC

Key Words: cancer, bladder, irradiation, cystectomy

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Oct 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 90. One patient was entered during FY 84 and was randomized to cystectomy alone, tolerated the procedure well, and is being followed. This study was closed to patient entry November 1989.

Detail Summary Sheet

Date: 30 Sep 90 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: Oct 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 90. Six patients were entered in previous years; four patients have expired from the disease.

Detail Summary Sheet

Date: 30 Sep 90 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
MAJ Thomas M. Baker, MC
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: Oct 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 90. Eleven patients have been entered at MAMC in previous years. The protocol was closed to patient entry in May 88, but data collection has not been completed.

Preliminary group-wide data indicate that this has proven to be a positive study; the CMFP arm has shown superior disease free survival.

Detail Summary Sheet

Date: 30 Sep 90 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
COL Friedrich H. Stutz, MC
MAJ Thomas M. Baker, MC
MAJ Timothy O'Rourke, MC
MAJ Michael Stone, MC
CPT David Bryson, MC

Key Words: Toxicity, patterns, prophylaxis

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Oct 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 90. Three patients were entered at MAMC in previous years. Two of the patients have expired of the disease and one patient is still in follow-up at MAMC. The study was closed to patient entry in March 1988.

Group-wide data show that none of the regimens has been highly toxic. A significant difference has been shown among the four arms. A difference has been noted in favor of the two arms not receiving prophylactic cranial irradiation.

Detail Summary Sheet

Date: 30 Sep 90 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:
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COL Irwin B. Dabe, MC
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COL Friedrich H. Stutz, MC
MAJ Michael D. Stone, MC

Key Words: cancer, breast, ER+, metastatic, chemotherapy

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Oct 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 90. One patient entered at MAMC in FY 86 has died of the disease.

Group-wide: 233 eligible patients have been entered. There has been one treatment related death on the combination arm from bacteremia secondary to leukopenia. Seventeen of 61 patients had toxicities of Grade 3 or greater, compared to 8 of 63 on aminoglutethimide and 3 of 69 on megestrol.

Detail Summary Sheet

Date: 30 Sep 90 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:
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MAJ Thomas Baker, MC
MAJ Timothy J. O'Rourke, 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: Oct 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 90. Three have been entered in previous years. Two the these patients have died of progressive breast cancer.

Group-wide: 537 patients were entered in this study. There was one fatal toxicity due to acute respiratory distress syndrome. The study was closed to patient entry 15 June 1990.

The quality of life component of this study was discontinued in January 1989 because of poor compliance in completing questionnaires.

Detail Summary Sheet

Date: 30 Sep 90 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 89

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 90. Two patients were entered at MAMC in FY 88. One patient died of the disease and one patient developed persistent nausea, anorexia, and alteration of taste. As a result, cisplatin was stopped and the Mitotane dose was halved.

The study was closed to patient entry in July 1989.

Detail Summary Sheet

Date: 30 Sep 90 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:

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: leukemia, chemotherapy, induction, consolidation

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Oct 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 90. Two patients were entered at MAMC in FY 88 with no unexpected reactions. Both have died of the disease.

Group-wide: Arm II was closed at the end of 1987 because of unacceptable toxicity.

Detail Summary Sheet

Date: 30 Sep 90 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:

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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: Oct 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; L-asparaginase beginning day 99, three times weekly for a total of 6 doses, and cyclophosphamide day 110 following last dose of L-asparaginase. Arm II: daunomycin days 1-3, Ara-C continuous infusion days 1-5, 6-thioguanine every 12 hr days 15, followed by a 21-28 day rest period. Methotrexate every 10 days from 28-98, L-asparaginase every 10 days 29-99. After a 2-week rest period, maintenance therapy will begin with vincristine, prednisone, adriamycin, 6-mercaptopurine, methotrexate (IT), methotrexate PO, dactinomycin, vincristine, prednisone, BCNU, cyclophosphamide, 6-mercaptopurine, and methotrexate (repeated every 21 wk for 36 mth or until relapse. An adequate trial will be the completion of remission induction.

Progress: One patient was entered at MAMC in FY 90 for a total of six subjects. Five patients were entered in previous years, all of which have expired from their disease. No adverse effects reported at MAMC.

*Replaced COL Dabe as PI, Sep 89.

Detail Summary Sheet

Date: 30 Sep 90 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
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MAJ Lauren K. Colman, MC
MAJ David Dunning, MC
MAJ Ruben Sierra, 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: Oct 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 90. One patient was entered in FY 87.

Group-wide: 363 eligible patients have been entered. There have been no fatal toxicities reported. Granulocytopenia has been the predominant toxicity reported on both arms.

Detail Summary Sheet

Date: 30 Sep 90 | 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: Oct 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 90. A total of 10 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.

Detail Summary Sheet

Date: 30 Sep 90 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
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MAJ Thomas M. Baker, MC
MAJ David M. Dunning, MC
MAJ Ruben D. Sierra, 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: Oct 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 90. One patient was entered in this study in FY 88 and has expired from the disease. Drug-induced phlebitis was reported in this patient.

Group-wide: Forty-four eligible patients have been registered on this protocol. There have been no fatal toxicities.

Detail Summary Sheet

Date: 0 Sep 90 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
LTC Lauren K. Colman, MC
MAJ Thomas M. Baker, MC
MAJ David Dunning, MC
MAJ Michael D. Stone, 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: Oct 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: 735 eligible patients have been entered. There is a reasonable balance across treatment arms by stratification factors and by the type of institution.

Detail Summary Sheet

Date: 30 Sep 90 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:

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LTC Lauren M. Colman, MC	MAJ Ruben D. Sierra, MC
MAJ Thomas M. Baker, 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: Oct 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: Nineteen eligible patients have been entered. Six patients have experienced toxicities of Grade 3 or worse (33%).

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 87/44 Status: Completed

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: Oct 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 ≤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 90. One patient was entered in FY 88, showed no response, and is now deceased. Protocol was closed to patient entry 1 Jan 90.

Group-wide: 119 eligible patients were accrued. There have been two instances of Grade 4 thrombocytopenia, two Grade 4 infections, and one instance of Grade 4 malaise in 118 patients evaluated for toxicity.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 87/10 Status: Completed

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:

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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: Oct 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. This study was closed to patient entry 15 Feb 90.

Detail Summary Sheet

Date: 30 Sep 90 | 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: Oct 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.

Detail Summary Sheet

Date: 30 Sep 90 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: Oct 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 90. A total of three patients has been entered at MAMC. One patient is still being followed. The study was closed to patient entry 1 Feb 90.

Detail Summary Sheet

Date: 30 Sep 90 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
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Key Words: adenocarcinoma, colon, surgical, levamisole, 5-FU

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: -0-	Periodic Review: Oct 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 90. Seven patients were entered in previous years with no unexpected toxicities. This study was closed to patient entry in October 1987.

Detail Summary Sheet

Date: 30 Sep 90 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: Oct 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: One entry at MAMC in FY 90; one patient was entered in FY 88 and died of his disease 13 months later.

Group-wide: 91 eligible patients have been entered.

**Replaced COL Dabe as the PI, Sep 89.

Detail Summary Sheet

Date: 30 Sep 90 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 89

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: No patients entered at MAMC in FY 90. Five patients have been entered; four have expired from the disease and one is off study.

Group-wide: 570 eligible patients have been entered. The accrual goal is 600 patients.

**Replaced COL Dabe as PI, Sep 89.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 89/64 Status: Completed

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: Oct 89

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. The protocol was closed to patient entry 1 Jan 90.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 87/110 Status: On-going

Title: SWOG 8616: Intergroup Phase III Randomized Study of Doxorubicin and Dacarbazine 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, dacarbazine ifosfamide, mesna

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Oct 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: No patients were entered at MAMC in FY 90. 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 393 eligible patients, eight treatment-related deaths have been documented. All were associated with Grade 4 myelosuppression. Arms 1 and 2 were closed to patient entry 1 May 89 due to sufficient accrual.

Detail Summary Sheet

Date: 30 Sep 90 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: Oct 89

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.

Groupwide: 40 eligible patients have been entered. The tamoxifen arm was closed 1 Jul 90.

Detail Summary Sheet

Date: 30 Sep 90 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
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: myeloma, multiple, VMCP, VBAP, VAD, VMCPP, VBAPP, alpha-2b interferon, dexamethasone

Accumulative MEDCASE Cost: -0- Est Accumulative OMA Cost: -0- Periodic Review: Oct 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. 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: 458 patients have been entered. Two patients on the VAD arm died of leukopenia and one died of gastrointestinal bleeding.

Detail Summary Sheet

Date: 30 Sep 90 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: Oct 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: 325 patients have been entered. There have been no fatal nonhematological toxicities (histological toxicity evaluation is incomplete). In general, flu-like symptoms are more common with IFN, while infections and nausea/vomiting/anorexia are more common with DCF.

Detail Summary Sheet

Date: 30 Sep 90 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:
MAJ Mark Kozakowski, MC
COL Irwin B. Dabe, MC
CPT Kenneth Bertram, MC
MAJ Everardo Cobos, MC
CPT Denis Bouvier, MC

Key Words: medical vs surgical castration, zoladex

Accumulative MEDCASE Cost: -0-

Est Accumulative OMA Cost: -0-

Periodic Review: Oct 89

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: 62 eligible patients have been entered, with slow accrual being a problem. There have been no Grade 4 toxicities.

Detail Summary Sheet

Date: 30 Sep 90 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. Feray, 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: Oct 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 86 subjects. No fatal toxicities have been reported.

**Replaced COL Dabe as PI, Sep 89.

Detail Summary Sheet

Date: 30 Sep 90 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:
MAJ Mark Kozakowski, MC
COL Irwin B. Dabe, MC
CPT Kenneth Bertram, MC
MAJ Everardo Cobos, 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: Oct 89

Objective: To investigate the induction efficiency and impact on time to treatment failure and survival of CAF* vs CAF-TsAVbH** used in a rotating schedule; to investigate the value of CMF(P)TH*** vs no maintenance treatment in duration of complete response and survival; and to evaluate on-study disease characteristics and patient discriminants with respect to prognostic use of the above objectives.

Technical Approach: All patients with ER negative tumors are eligible unless they have responded to prior hormone manipulation therapy. ER positive or ER unknown patients are eligible only if they have had prior therapeutic hormone manipulation and did not respond to this therapy. Patients must have a performance status of 0-3, adequate bone marrow, renal, and hepatic function, and a blood sugar ≤170 mg/dL. Patients will be stratified by ER status, prior adjuvant therapy (yes vs no); dominant metastatic site; disease free interval; and menopausal status. Patients will be randomized to either CAF for six cycles or to CAF alternating with TsAVbH (three cycles of CAF alternating with three cycles of TsAVbH). Patients with a partial response or stable disease will be registered to receive CMFH**** and those with progressive disease will go off study. Patients with a complete response will be randomized to either CMF(P)TH or to observation. Cycles will be repeated every 29 days until relapse.

Progress: No patients have been entered at MAMC.

Group-wide: 265 patients entered, with one treatment-related death (cardiac arrest 302 days after entry into the alternating therapy arm).

*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 90 Protocol No.: 90/39 Status: On-going

Title: SWOG 8710: Trial of Cystectomy Alone Versus Neoadjuvant M-VAC + Cystectomy in Patients with Locally Advanced Bladder Cancer (INT-0080/EST-1877 CALGB-8891)

Start Date: 16 Feb 90 Est Completion Date: Mar 92

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: LTC John A. Vaccaro, MC

Associate Investigators:

LTC Howard Davidson, MC	MAJ Mark H. Kozakowski, MC
MAJ Kenneth A. Bertram, MC	MAJ Robert L. Sheffler, MC
MAJ Everardo Cobos, MC	MAJ Paul C. Sowray, MC
MAJ Patrick L. Gomez, MC	CPT Denis P. Bouvier, MC

Key Words: bladder cancer, cystectomy, cystectomy + M-VAC

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

Study Objective: In patients with locally advanced bladder cancer: to compare the survival of those treated with cystectomy alone to those treated with M-VAC, followed by cystectomy in a randomized phase III neoadjuvant trial and to quantify the tumor down-staging effect on neoadjuvant M-VAC.

TECHNICAL APPROACH: Patients must have a histologically proven diagnosis of T_2-T_{4a}, N_0, M_0 transitional cell carcinoma of the bladder with or without squamous differentiation and with normal organ function documented by careful pretreatment staging, including a pathologic assessment of tumor grade and depth of invasion, within 6 weeks prior to protocol entry. Patients will be randomized to either radical cystectomy (Arm I) or to M-VAC (methotrexate, vinblastine, adriamycin, cisplatin) plus radical cystectomy (Arm 2). Patients will be stratified according to age (>65 years old vs $\leq$65 years old) and stage: T_2 vs T_3, T_{4a}. Patients will be followed every three months for the first year after cystectomy, every six months the second year, and yearly thereafter. Arm II patients will be removed from the study if unacceptable toxicity develops or if there is documented disease progression. Arm I and Arm II patients will be removed from the study if tumor recurs. The primary endpoint for comparison of treatment arms will be survival. The secondary endpoint is to evaluate changes in clinical staging parameters in Arm II patients and, specifically, whether down-staging to pCR, documented from cystectomy specimens, carries any positive survival prognosis in Arm II.

Progress: No patients entered at MAMC.

Groupwide: 93 eligible patients entered. The accrual rate continues to be a significant problem since it is below the target accrual rate of 6.2 patients per month. In the past six months the accrual rate has dropped to 2.7 patients per month.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 88/64 Status: Completed

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: Oct 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.

The study was temporarily closed to patient entry 15 Sep 88 and then was permanently closed when it was determined that the number of patients entered was sufficient for analysis.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/84 Status: On-going

Title: SWOG SWOG 8719: Evaluations of Didemnin B or Ifosfamide/Mesna in Endocrine Resistant Prostate Cancer and of Ifosfamide/Mesna in Patients Without Prior Endocrine Manipulation, Phase II

Start Date: 15 Jun 90 Est Completion Date: May 92

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Everardo Cobos, MC

Associate Investigators:	MAJ Mark H. Kozakowski, MC
LTC Howard Davidson, MC	MAJ Robert L. Sheffler, MC
MAJ Kenneth A. Bertram, MC	MAJ Paul C. Sowray, MC
MAJ Patrick L. Gomez, MC	CPT Denis P. Bouvier, MC

Key Words: cancer, prostate, endocrine resistant, chemotherapy

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

Study Objective: To evaluate the likelihood of response for each regimen in order to assess whether either treatment should be advanced to further studies; to evaluate the qualitative and quantitative toxicities of the regimens; and to explore the response rate, toxicity, and time to progression of patients with no prior or concomitant endocrine treatment who are treated with Ifosfamide/Mesna for measurable Stage D_2 prostatic cancer.

Technical Approach: Patients must have a histologically confirmed diagnosis of adenocarcinoma of the prostate and advanced (Stage D_2) disease with objective evidence of progression following prior endocrine treatment. Newly diagnosed Stage D_2 patients without prior endocrine manipulation will be placed directly on Arm II.

Patients will be randomized to ei' er Arm I (Didemnin B, IV, once every 28 days) or to Arm II (If ide and Mesna, IV, days 1-5, every 21 days). After two cour treatment, patients will be evaluated, and will continue o me arm until progression of disease.

Progress: No patients have b d at MAMC.

Groupwide: Thirty-eight pati been entered group-wide.

Detail Summary Sheet

Date: 30 Sep 90 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:
COL Irwin B. Dabe, MC
MAJ Everardo Cobos, MC
MAJ Mark Kozakowski, MC
CPT Kenneth Bertram, MC
CPT Denis Bouvier, MC

Key Words: carcinoma, epidermoid, trimetrexate

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

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: 18 eligible patients have been registered. One patient died due to acute aspiration; both the cancer and the toxicity were felt to contribute to his death. Grade 4 toxicity was reported in eight patients, all hematologic.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 88/75 Status: Completed

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 Oct 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 closed to patient entry 1 Jun 90. Twenty eligible patients were entered. Four patients (25%) had Grade 4 hematologic toxicity and one (10%) had a Grade 4 pulmonary embolism.

All eligible patients have been evaluated for response and there were no responses. Amonafide does not appear to be active in metastatic melanoma when administered at this dose and schedule. There is no evidence to suggest that amonafide should be studied further in this disease site.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 88/69 Status: Completed

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: Oct 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 closed 1 Jan 90 due to sufficient accrual of patients.

Detail Summary Sheet

Date: 30 Sep 90 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: Oct 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: One patient was entered in FY 90 for a total of three subjects.

Group-wide: 153 eligible patients have been entered with a good balance between the treatment arms. Grades 3 and 4 granulocytopenia or leukopenia have been common.

Detail Summary Sheet

Date: 30 Sep 90 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: Oct 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: Two patients were entered at MAMC in FY 90 for a total of five subjects; two have died of the disease.

Group-wide: 316 eligible patients have been entered. The study was closed to patient entry 1 Jun 90 based on a formal interim analysis which rejected the hypothesis that the survival of patients on the high dose cisplatin arm was 25% better than that of patients on the standard dose arm. There were two fatal toxicities on high dose cisplatin alone and one fatal toxicity on high dose cisplatin plus mitomycin-C.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 89/59 Status: Completed

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:
COL Irwin B. Dabe, MC
MAJ Everardo Cobos, MC
MAJ Mark Kozakowski, MC
CPT Kenneth Bertram, MC
CPT Denis Bouvier, MC

Key Words: breast cancer, chemotherapy, alternating

Accumulative MEDCASE Cost: -0-

Est Accumulative OMA Cost: $1320/patient

Periodic Review: Oct 89

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. 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. The study was closed to patient entry 1 Mar 90 due to sufficient patient accrual. The observed complete response rate was only 10% and new data indicate that low-dose continuous infusion 5-FU has a "salvage" response rate in metastatic breast cancer in the same range as that seen for 5-FU/CF, with the additional factor that the continuous approach is associated with almost no myelosuppression.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/63 Status: On-going

Title: SWOG 8789: A Randomized Study of Etoposide + Cisplatin and Etoposide + Carboplatin (CBDCA) in the Management of Good Risk Patients with Advanced Germ Cell Tumors

Start Date: 20 Apr 90 Est Completion Date: Apr 93

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ Patrick L. Gomez, MC
LTC Howard Davidson, MC
MAJ Mark H. Kozakowski, MC
MAJ Kenneth A. Bertram, MC
MAJ Robert L. Sheffler, MC
MAJ Everardo Cobos, MC
CPT Denis P. Bouvier, MC

Key Words: testis/germ cell/etoposide/cisplatin/carboplatin

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

Study Objective: To determine in a randomized trial the differences in response, toxicity, time to relapse, and survival between two active chemotherapy regimens; etoposide + cisplatinum and etoposide + carboplatin, for good risk patients with germ cell tumors.

Technical Approach: Patients with active advanced Stage II or Stage III testicular nonseminomatous germ cell tumor with a probability of complete response of >0.5 will be eligible. Patients will be randomized to Treatment Arm A (carboplatin + etoposide, given every 28 days for four cycles) or Treatment Arm B (cisplatin + etoposide every 21 days for four cycles). Following completion of chemotherapy, a complete assessment of all sites of disease will be performed. Following completion of four cycles of chemotherapy and radiographic and marker assessment, surgical resection of all residual masses will be done if deemed necessary by the principal investigator. If no residual malignant tumor or only mature teratoma is completely resected at surgery, no further therapy will be administered. If residual malignant tumor is found but is completely excised, then two more cycles of treatment will be administered. If residual malignant tumor is found but is unresectable, then the patient will receive additional therapy with standard GCT regimens or other therapy as may be indicated at the discretion of the treating physician.

Progress: One patient was entered at MAMC in FY 90.

Groupwide: 228 patients have been accrued; Grade 4 toxicities include leukopenia and thrombocytopenia.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/53 Status: On-going

Title: SWOG 8791 (INT-0087): Adjuvant Trial of Soft Tissue Sarcomas, Phase III

Start Date: 16 Mar 90 Est Completion Date: Dec 92

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:	MAJ Patrick L. Gomez, MC
LTC Howard Davidson, MC	MAJ Mark H. Kozakowski, MC
MAJ Kenneth A. Bertram, MC	MAJ Robert L. Sheffler, MC
MAJ Everardo Cobos, MC	CPT Denis P. Bouvier, MC

Key Words: sarcomas, surgery, adjuvant chemotherapy

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $12,000.00	Periodic Review: N/A

Study Objective: To assess whether adjunctive chemotherapy with Adriamycin, DTIC, and Ifosfamide/Mesna can improve the survival and disease-free survival of selected patients with soft tissue sarcomas and to establish a repository of frozen sarcoma tissues to be used for ancillary genetic and flow cytometric analysis.

Technical Approach: As a consequence of of several studies which show conflicting results as to further treatment after surgery and radiation for local control of the disease, most clinicians advise these patients to either undergo no further therapy or to enter on clinical trials such as this. Since the completion of the aforementioned trials, Ifosfamide has been demonstrated to be an extremely active agent in advanced soft tissue sarcoma. Therefore, it would seem logical to combine this new effective agent with the best alternative old regimen which consists of DTIC and Adriamycin. This combination stands the best chance of showing improvement in survival if used in the adjuvant setting. In this study, patients will receive local treatment and then be randomized to either standard therapy (which is observation) or to combination chemotherapy with Adriamycin, DTIC, Ifosfamide, and Mesna, to be given by continuous infusion in the hospital over 4 days once every 21 days for a total of 6 courses.

Progress: No patients entered at MAMC.

Groupwide: Two patients have been entered.

Detail Summary Sheet

Date: 30 Sep 90 | 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:
COL Irwin B. Dabe, MC
MAJ Thomas M. Baker, MC
MAJ David M. Dunning, MC
MAJ Ruben D. Sierra, MC
CPT Denis P. Bouvier, MC

Key Words: carcinoma, renal cell, Alfa-nl

Accumulative MEDCASE Cost: -0- | Est Accumulative OMA Cost: -0- | Periodic Review: Oct 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: 171 patients have been entered. There have been no Grade 5 toxicities. One patient experienced a Grade 4 neurologic reaction, two experienced extreme fatigue and became bedridden, and one experienced Grade 4 neutropenia.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/40 Status: On-going

Title: SWOG 8793 (EST-3886): Randomized Phase III Evaluation of Hormonal Therapy versus Observation in Patients with Stage D_1 Adenocarcinoma of the Prostate Following Pelvic Lymphadenectomy and Radical Prostatectomy

Start Date: 16 Feb 90 Est Completion Date: Feb 92

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: LTC John A. Vaccaro, MC

Associate Investigators:

LTC Howard Davidson, MC	MAJ Mark H. Kozakowski, MC
MAJ Kenneth A. Bertram, MC	MAJ Robert L. Sheffler, MC
MAJ Everardo Cobos, MC	MAJ Paul C. Sowray, MC
MAJ Patrick L. Gomez, MC	CPT Denis P. Bouvier, MC

Key Words: prostate, adenocarcinoma, cystectomy, hormonal therapy

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

Study Objective: To determine the time to progression and survival in patients with histologically confirmed Stage D_1 adenocarcinoma of the prostate, following radical prostatectomy and pelvic lymphadenectomy, treated with no immediate hormonal therapy compared to those treated immediately with hormonal therapy; to determine the effect of early hormone therapy on local control of D_1 prostate cancer; to determine whether the effects of hormonal manipulation on progression or patterns of failure are modified by tumor grade, prior TUR, number and grade of involved nodes; to determine if an initially elevated acid phosphatase level predicts a poor response to therapy; to determine whether pretreatment hypogonadism is predictive of a poor response to hormonal therapy; and to evaluate the role of the prostate specific antigen in assessing response, progression, and survival.

Technical Approach: Patients must have undergone a radical prostatectomy within 12 weeks prior to randomization and must have no evidence of disease. Patients with a history of previous hormonal, radiation, systemic or intravesical chemotherapy, a history of other neoplasms in the past 5 years, and those previously treated for prostate cancer (except for prostatectomy and/or pelvic lymph node dissection) are ineligible.

Patients will be randomized to hormonal therapy (Zoladex or orchiectomy) or to observation. The treating physician, after consultation with the patient, will determine if the patient receives Zoladex or orchiectomy therapy. Patients randomized to observation, who subsequently progress systemically, will have hormonal management instituted within 6 weeks of systemic progression. Patients randomized to hormonal therapy or who are later put on hormonal therapy will be taken off study if disease progression occurs.

Progress: No patients entered at MAMC.

Groupwide: 46 patients have been entered. Mild renal toxicity, hot flashes, and neurologic toxicity were common.

Detail Summary Sheet

Date: 30 Sep 90 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: Oct 89

Study Objective: To compare the efficacy of mitomycin-C to that of BCG in preventing recurrence of superficial Stage Ta and T1 transitional cell carcinoma of the bladder and to compare treatments with respect to differences in flow cytometry histogram findings of tumors at the time of recurrence.

Technical Approach: Patients must have a diagnosis of Stage Ta or T1 (Grades 1-4) transitional cell carcinoma of the bladder that has been completely resected. Concurrent unresectable carcinoma *in situ* (CIS) is allowed. Histologic confirmation of the disease must come from a transurethral resection done within 4 weeks prior to registration. A random biopsy done 1-4 weeks prior to registration is required. Patients must be judged to be at increased risk for tumor recurrence as demonstrated by 2 occurrences of tumor within 12 months prior to registration. Patients must not have received any prior systemic chemotherapy. Patients may have had treatment with any intravesical agent other than mitomycin-C or BCG; however, the treatment must not have been within 4 weeks prior to registration. Patients must not have received radiation therapy for treatment of bladder tumor within one year prior to registration. Patients must not have a history of another primary malignancy or CIS at any site other than the bladder. Patients must have adequate bone marrow reserve, adequate renal and liver function, and a performance status of 0-2. Patients will be stratified by CIS involvement: Stage Ta or T1 without concurrent CIS vs Stage Ta or T1 with concurrent CIS.

Patients will be randomized to BCG, 50 mg weekly x 6, then at wks 8 and 12 and then monthly for months 4-12 or mitomycin-C, 20 mg on the same schedule. Cystoscopy, cytology, biopsy, and flow cytometry will be done prestudy at 3, 6, 9, and 12 months.

Progress: No patients entered at MAMC. Groupwide, 190 eligible patients have been entered with no Grade 4 toxicity or treatment-related deaths.

Detail Summary Sheet

Date: 30 Sep 90 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: Oct 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) is in the follow-up stage.

Group-wide: This study was closed in Aug 89 due to sufficient patient accrual.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/85 Status: Completed

Title: SWOG 8802: Evaluation of Echinomycin in Renal Cell Carcinoma, Phase II

Start Date: 15 Jun 90 Est Completion Date: Jul 93

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Everardo Cobos, MC

Associate Investigators:	MAJ Mark H. Kozakowski, MC
LTC Howard Davidson, MC	MAJ Robert L. Sheffler, MC
MAJ Kenneth A. Bertram, MC	MAJ Paul C. Sowray, MC
MAJ Patrick L. Gomez, MC	CPT Denis P. Bouvier, MC

Key Words: carcinoma, renal cell, echinomycin

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

Study Objective: To evaluate the likelihood of response in order to assess whether echinomycin should be advanced to further studies and to evaluate the qualitative and quantitative toxicities of echinomycin administered in a Phase II study.

Technical Approach: All patients must have histologically proven bidimensionally measurable renal cell carcinoma which is either metastatic or recurrent. Patients with CNS metastases are eligible if there is measurable disease outside the CNS and if the patients have received radiotherapy to these lesions prior to registration. Patients may have received prior hormonal therapy. Patients must not have received more than one prior biologic regimen. Patients may have had prior surgery or radiotherapy. Patients must not have received prior cytotoxic chemotherapy.

Echinomycin will be given intravenously once every 28 days with disease assessment at day 49. Complete and partial responders and those with stable disease will continue to be treated every 28 days until disease progression.

Progress: No patients were entered on this study at MAMC.

The study was closed in July 1990 due to sufficient patient accrual. Group-wide, 28 patients were evaluated for toxicity with adverse drug reaction reports filed on six patients: two had anaphylaxis, one had highly elevated transaminase levels, one had hypercalcemia, one had hypertension, dizziness/vertigo, fever without infection, facial flushing, and shortness of breath, and the sixth stopped breathing for two minutes. Data are being analyzed for response rates.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/64 Status: On-going

Title: SWOG 8809: A Phase III Study of Alpha-Interferon Consolidation Following Intensive Chemotherapy with ProMACE-MOPP (Day 1-8) in Patients with Low Grade Malignant Lymphomas

Start Date: 20 Apr 90 Est Completion Date: Apr 94

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:	MAJ Patrick L. Gomez, MC
LTC Howard Davidson, MC	MAJ Mark H. Kozakowski, MC
MAJ Kenneth A. Bertram, MC	MAJ Robert L. Sheffler, MC
MAJ Everardo Cobos, MC	CPT Denis P. Bouvier, MC

Key Words: lymphoma, alpha-interferon consolidation

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

Study Objective: To compare the disease-free survival of patients with low grade malignant lymphoma who receive alpha-interferon consolidation therapy after intensive induction with chemotherapy, with or without radiation therapy, to those who receive induction therapy alone; to determine the complete response rate, response duration, and survival of low grade lymphoma patients treated with ProMACE-MOPP; and to compare the toxicities of induction and induction plus consolidation therapy in this patient population.

Technical Approach: Patients must have biopsy proven, measurable, Stage III or IV non-Hodgkin's lymphoma of low grade histologies. Patients will receive 6 cycles of induction chemotherapy (ProMACE-MOPP, days 1-8) unless progressive disease develops during this treatment. At the completion of induction therapy, patients will be restaged to assess response. Patients whose clinical disease has disappeared and who appear to be in complete remission will undergo a complete radiographic and laboratory evaluation for evidence of persistent lymphoma approximately one month after completion of chemotherapy. If no evidence of disease is found these patients will be randomized to Alpha IFN or observation. Patients in partial response and whose bone marrow remains positive after 6 cycles of induction chemotherapy will receive 2 additional cycles of chemotherapy and then be reevaluated. If the bone marrow remains involved or the patient has less than a partial response after a total of 8 cycles, the patient will be removed from further protocol therapy. If after 8 cycles, the bone marrow is negative and the patient is in partial response, the patient will receive radiotherapy. Complete responders after induction chemotherapy; complete responders after induction chemotherapy plus radiation therapy; and partial responders after chemotherapy plus radiation therapy will be randomized to consolidation alpha interferon or observation, approximately one month after completion of therapy.

Progress: One patient was entered in this study at MAMC in Apr 90. Groupwide, 161 eligible patients have been entered. Eighty-five patients have been evaluated for toxicity of ProMACE-MOPP chemotherapy. Two fatal toxicities have been reported and Grade 4 toxicity was common.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/54 Status: On-going

Title: SWOG 8810: Six Courses of 5-Fluorouracil and Cisplatinum with Correlation of Clinical and Cellular DNA Parameters in Patients with Advanced, Untreated, and Unresectable Squamous Cell Carcinoma of the Head and Neck, Phase II, Pilot Study

Start Date: 16 Mar 90 Est Completion Date: Mar 93

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Patrick L. Gomez, MC

Associate Investigators:

LTC Howard Davidson, MC	MAJ Michael R. Morris, MC
MAJ Kenneth A. Bertram, MC	MAJ Robert L. Sheffler, MC
MAJ Everardo Cobos, MC	MAJ Paul C. Sowray, MC
MAJ Mark H. Kozakowski, MC	CPT Denis P. Bouvier, MC

Key Words: head & neck, carcinoma, squamous cell, chemotherapy

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $8200.00	Periodic Review: N/A

Study Objective: To evaluate, following three and six courses of treatment, the likelihood of increased numbers of patients achieving complete response rates when given three additional courses of the same regimen; to evaluate the qualitative and quantitative toxicities of 5-fluorouracil and cisplatinum following three and six courses of treatment; and to evaluate by serial biopsy and flow cytometry the correlation of the cellular DNA parameters of degree of aneuploidy (DNA index) and proliferative activity (SPF) with the patients clinical characteristics, tumor morphology, cytotoxic response, disease free interval, and survival.

Technical Approach: Patients must have a histologically confirmed diagnosis of advanced unresectable squamous cell carcinoma of the head and neck, Stage IV, and not be eligible for SWOG protocol of higher priority. Nasopharyngeal primary tumor will be excluded. Biopsy specimens for flow cytometry will be taken before treatment. Patients will be treated with three courses of 5-FU and cisplatinum combination chemotherapy. Patients achieving a partial response or complete response will continue for an additional three courses of therapy. Patients who have no response after three courses will be taken off study and a biopsy will be taken for flow cytometry. Patients will have a triple endoscopy and re-biopsy of the primary site and lymph nodes for flow cytometry analysis within four weeks of completion of treatment following the full six courses of therapy or at any time that disease recurs. All patients will be followed until death.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 90 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:
MAJ Everardo Cobos, MC
COL Irwin B. Dabe, MC
CPT Kenneth Bertram, MC
LTC Howard Davidson
CPT Denis Bouvier, MC

Key Words: small cell lung cancer, chemo/radiotherapy, interferon

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

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; and induction arm. Patients will be randomized to receive induction chemotherapy (cis-platinum + VP-16) and concurrent chest radiotherapy with or without GM-CSF. Consolidation chemotherapy will be as in induction but with no radiotherapy. Those patients achieving a complete remission will be randomized to receive or not receive maintenance therapy with recombinant alpha interferon. All patients who have achieved a complete response by week 33 will receive prophylactic cranial irradiation to the brain. Patients with stable disease, progression, or relapse at any point will be taken off study.

Progress: No patients entered at MAMC. Groupwide: 102 eligible patients have been entered. This study was temporarily closed in November 1989 due to excessive toxicity and reopened in December 1989 with reduced doses of CDDP and VP-16.

Detail Summary Sheet

Date: 30 Sep 90 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

Principal Investigator: LTC Howard Davidson

Associate Investigators:	MAJ Paul C. Sowray, MC
MAJ Everardo Cobos, MC	CPT Kenneth Bertram, MC
MAJ Patrick L. Gomez, MC	CPT Denis Bouvier, MC
MAJ Mark Kozakowski, MC	CPT Robert Sheffler, MC

Key Words: cancer, breast, chemotherapy, chemoendocrine

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $8692.00/yr	Periodic Review: Oct 89

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: Three patients were entered at MAMC, all in FY 90.

Groupwide: 217 eligible patients have been entered; 24 patients have had Grade 4 myelosuppression.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/41 Status: On-going

Title: SWOG 8828: A Phase II Trial of Carboplatin (CBDCA) in Relapsed or Refractory Acute Myeloid Leukemia

Start Date: 16 Feb 90 Est Completion Date: Feb 92

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ Patrick L. Gomez, MC
LTC Howard Davidson, MC
MAJ Mark H. Kozakowski, MC
MAJ Kenneth A. Bertram, MC
MAJ Robert L. Sheffler, MC
MAJ Everardo Cobos, MC
CPT Denis P. Bouvier, MC

Key Words: AML, carboplatin, induction, consolidation

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

Study Objective: To evaluate the complete remission rate of carboplatin (CBDCA) in patients with relapsed or refractory acute myeloid leukemia (AML); to assess the qualitative and quantitative toxicities of these patients; and to identify the pattern of treatment failure by the criteria of Preisler.

Technical Approach: Patients must have a bone marrow aspiration and biopsy demonstrating AML with FAB subtype M1-M7. Patients must be in relapse or must have had a treatment failure of Preisler type 1 or 2 on the most recent induction attempt. Patients must have received only one prior remission induction regimen for AML. Patients with prior CML or myelodysplastic syndrome or those who have received prior radiotherapy or chemotherapy for non-AML conditions are ineligible.

Induction: Carboplatin, 300 mg/M^2/day continuous intravenous infusion daily for 5 days.

Second induction course: If the bone marrow on Day 21 shows >10% blasts and cellularity $\geq$30%, patients will be treated with carboplatin 300 mg/M^2/day continuous intravenous infusion daily for 5 days beginning Day 22.

Patients who do not achieve a remission after two induction courses will be removed from protocol treatment.

Consolidation: If A-1 marrow is achieved: carboplatin 210 mg/M^2/day continuous intravenous infusion daily for 5 days. Patients will receive only one consolidation course.

There will be no maintenance treatment.

Patients will be removed from the protocol at any time unacceptable toxicity occurs.

Progress: No patients entered at MAMC. Groupwide, 7 eligible patients have been entered. One patient died of renal failure after five days of treatment.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/27 Status: On-going

Title: SWOG 8851 (EST 5811, INT-0101): Phase III Comparison of Combination Chemotherapy (CAF) and Chemohormonal Therapy (CAF + Zoladex or CAF + Zoladex + Tamoxifen) in Premenopausal Women with Axillary Node-Positive, Receptor-Positive Breast Cancer--Intergroup

Start Date: 19 Jan 90 Est Completion Date: Dec 99

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

MAJ Kenneth A. Bertram, MC
MAJ Everardo Cobos, MC
MAJ Patrick L. Gomez, MC
MAJ Mark H. Kozakowski, MC
MAJ Robert L. Sheffler, MC
MAJ Paul C. Sowray, MC
CPT Denis P. Bouvier, MC

Key Words: cancer, breast cancer, chemotherapy, chemohormonal

Accumulative MEDCASE Cost: -0-

Est Accumulative OMA Cost: $8200.00

Periodic Review: N/A

Study Objective: To compare the recurrence rates, disease-free intervals, relative toxicities, and hormone-receptor-positive survival for premenopausal women with axillary lymph node-positive breast cancer given adjuvant therapy with combination chemotherapy using cyclophosphamide, doxorubicin, and 5-FU (CAF) alone or CAF followed by Zoladex, or CAF followed by Zoladex plus Tamoxifen; and to assess the effect of CAF, CAF plus Zoladex, and CAF plus Zoladex and Tamoxifen on hormone levels (LH, FSH, and estradiol) in these patients.

Technical Approach: Patients will be nonpregnant females who have undergone excision of the primary breast tumor mass, proven histologically to be invasive breast adenocarcinoma and must have one or more pathologically involved axillary nodes. Patients who undergo total mastectomy may receive post-operative radiotherapy at the discretion of the investigator. Patients who have had prior hormonal therapy or chemotherapy for breast cancer are ineligible. Patients will be randomized to CAF alone for six cycles or to CAF for 6 cycles followed by monthly Zoladex for 5 years, or to CAF for 6 cycles followed by daily Tamoxifen and monthly Zoladex for 5 years.

Adjuvant therapy will be instituted as soon as possible after mastectomy or lumpectomy. The interval between definitive surgery and initiation of adjuvant chemotherapy will not be >12 weeks. When planned, radiation therapy may be administered prior to or after (within 4 weeks of) completion of 6 cycles of adjuvant chemotherapy.

Progress: One patient was entered in this study in August 1990.

Groupwide: 215 patients have been entered.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/47 Status: On-going

Title: SWOG 8854: Prognostic Value of Cytometry Measurements on Breast Cancer DNA From Postmenopausal Patients with Involved Nodes and Receptor Positive Tumors: A Companion Protocol to SWOG 8814

Start Date: 16 Mar 90 Est Completion Date: Mar 98

Department: Medicine Facility: MAMC

Principal Investigator: LTC Howard Davidson

Associate Investigator: None

Key Words: breast cancer, cytometry, DNA

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

Study Objective: To determine if ploidy analysis of breast cancer by routine clinical flow cytometry (CFM) technique can predict response to therapy and survival of patients registered to SWOG 8814 and to determine if ploidy analysis by image processing technique more accurately predicts patient response to therapy and survival than ploidy analysis by flow cytometry.

Technical Approach: Two paraffin blocks, one representing the highest grade region of the primary tumor, the second representing the highest grade regional metastasis in a positive lymph node, will be used. From each of these blocks, two to five sections will be cut and a nuclear suspension prepared. From each suspension, a cytospin preparation will be prepared and stained with Dif-Quik to ensure that the cells present in the H & E slide are represented adequately in the nuclear preparation. A second cytospin preparation will be prepared for staining by the Feulgen technique for image processing DNA analysis. The remainder of the nuclear preparation will be stained with propidium iodide following RNase digestion for FCM DNA analysis. Cox regression modeling will be used to explore the prognostic value of ploidy status as determined by FCM and by image processing, in conjunction with the covariates tumor size, age, ER and PgR levels, and number of nodes.

Progress: No patients entered at MAMC.

Groupwide: 66 patients entered.

Detail Summary Sheet

Date: 30 Sep 90	Protocol No.: 90/28	Status: On-going

Title: SWOG 8857: Alternating Cisplatin/VP-16 with Continuous CAV and Consolidation Chemotherapy for Extensive Small Cell Lung Cancer with PCI for Complete Responders

Start Date: 19 Jan 90	Est Completion Date: Nov 92
Dept/Svc: Medicine/Oncology	Facility: MAMC
Principal Investigator: MAJ Mark H. Kozakowski, MC	
Associate Investigators:	MAJ Patrick L. Gomez, MC
LTC Howard Davidson, MC	MAJ Robert L. Sheffler, MC
MAJ Kenneth A. Bertram, MC	MAJ Paul C. Sowray, MC
MAJ Everardo Cobos, MC	CPT Denis P. Bouvier, MC
Key Words: cancer, small cell lung, chemotherapy	

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

Study Objective: To assess response rate, especially rate of complete response (CR), and toxicity of a dose-intensive approach to induction chemotherapy in which cisplatin/VP-16 is alternated with cyclophosphamide, adriamycin, and vincristine; consolidation therapy will be given to responders with one cycle of each induction regimen, coupled with prophylactic brain irradiation in CR patients; and to measure survival in patients so treated.

Technical Approach: All patients must have extensive disease (Stage 4 by the international staging system).

Regimen A: Cisplatin - 50 mg/m^2 days 1 and 8 (IV)
VP-16 - 50 mg/m^2/day for 14 days (PO)

Regimen B: Cytoxan - 60 mg/m^2/day for 21 days (PO)
Adriamycin - 20 mg/m^2/week for 3 weeks (IV)
Vincristine - 2 mg on day 1 of cycle (IV)

Patients will be entered on Regimen A, followed by a two week rest period. They will then be entered on Regimen B, which will be followed by a one week rest period. Regimen A will be repeated at weeks 9 and 24. Regimen B will be repeated at weeks 13 and 28. Patients will be restaged after completion of the second cycle of Regimen B (week 17). Patients who have a clinical CR by week 17 at restaging will be administered prophylactic whole brain irradiation on week 24. For patients presenting with brain metastases, radiation will be given on day 1 rather than beginning at day 162 (week 24). Patients with progression of disease or unacceptable toxicity will be removed from the study. All patients will be followed until death.

Progress: Two patients were entered in FY 90 at MAMC.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/55 Status: On-going

Title: SWOG 8892 (EST-2388, RTOG-8817, INT-0099): A Study of Radiotherapy With or Without Concurrent Cisplatin in Patients With Nasopharyngeal Cancer, Phase III

Start Date: 16 Mar 90 Est Completion Date: Mar 93

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Patrick L. Gomez, MC

Associate Investigators:

LTC Howard Davidson, MC	MAJ Michael R. Morris, MC
MAJ Kenneth A. Bertram, MC	MAJ Robert L. Sheffler, MC
MAJ Everardo Cobos, MC	MAJ Paul C. Sowray, MC
MAJ Mark H. Kozakowski, MC	CPT Denis P. Bouvier, MC

Key Words: nasopharyngeal cancer, radiotherapy, w/wo cisplatin

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $3900.00	Periodic Review: N/A

Study Objective: To compare radiotherapy with radiotherapy and concurrent cisplatin, followed by three courses of 5-FU + cisplatin for complete response rate, time to treatment failure, overall survival, pattern of recurrence, and qualitative and quantitative toxicities.

Technical Approach: To be eligible, patients must have histologically proven nasopharyngeal carcinoma (excluding adenocarcinoma), Stage III or IV with no evidence of distant metastatic disease, and must not be eligible for higher priority SWOG studies. Patients will be randomized as follows:

Arm I: *radiation therapy alone for approximately 7 weeks*
Arm II: 3 courses of cisplatin (days 1, 22, and 43) concurrent with radiotherapy followed by three courses of 5-FU + cisplatin.

Measurable disease must be assessed at least every eight weeks the first year of follow-up. Patients will be seen in follow-up every two months the second year, every three months the third year, and every four months thereafter. A tumor biopsy for flow cytometry will be obtained if tumor recurs.

Progress: No patients entered at MAMC.

Groupwide: Accrual to this study has been poor. Eight patients have been registered. One patient on the combination arm has been evaluated for toxicity. This patient had Grade 4 stomatitis.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/86 Status: On-going

Title: SWOG 8894 (INT-0105, EST-2889): A Comparison of Bilateral Orchiectomy with or without Flutamide for the Treatment of Patients with Histologically Confirmed Stage D_2 Prostate Cancer

Start Date: 15 Jun 90 Est Completion Date: Apr 93

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

LTC John A. Vaccaro, MC	MAJ Mark H. Kozakowski, MC
MAJ Kenneth A. Bertram, MC	MAJ Robert L. Sheffler, MC
MAJ Everardo Cobos, MC	MAJ Paul C. Sowray, MC
MAJ Patrick L. Gomez, MC	CPT Denis P. Bouvier, MC

Key Words: prostate cancer, orchiectomy, Flutamide

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

Study Objective: To compare survival, progression free survival, and qualitative and quantitative toxicities between patients with orchiectomy alone and patients with orchiectomy plus Flutamide.

Technical Approach: Patients must have a histologically proven diagnosis of pathologic stage D_2 adenocarcinoma of the prostate with evidence of metastatic disease. Patients must not have had prior hormonal therapy, chemotherapy, or biological response modifiers. Patients will be randomized to bilateral orchiectomy plus placebo po three times a day day with meals or to bilateral orchiectomy plus Flutamide po three times a day with meals. Upon disease progression, patient treatment will be unblinded. Patients treated with Flutamide will be taken off protocol. Patients treated with placebo will be offered flutamide given according to the protocol guidelines until the next evidence of progression at which time they will be taken off study.

Progress: One patient has been entered at MAMC.

Group-wide, the study has accrued rapidly with an average of 31 patients per month.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/29 Status: On-going

Title: SWOG 8897 (EST-2188, CALGB-8897, INT -0101): Phase III Comparison of Adjuvant Chemotherapy With or Without Endocrine Therapy in High-Risk, Node Negative Breast Cancer Patients, and a Natural History Follow-up Study in Low-Risk, Node Negative Patients (Intergroup)

Start Date: 19 Jan 90 Est Completion Date: Jan 93

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:	MAJ Mark H. Kozakowski, MC
MAJ Kenneth A. Bertram, MC	MAJ Robert L. Sheffler, MC
MAJ Everardo Cobos, MC	MAJ Paul C. Sowray, MC
MAJ Patrick L. Gomez, MC	CPT Denis P. Bouvier, MC

Key Words: chemotherapy (CMF, CAF), endocrine therapy, radiation

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $5000.00	Periodic Review: N/A

Study Objective: To compare disease-free survival and overall survival of high risk primary breast cancer patients with negative axillary lymph nodes treated with standard adjuvant chemotherapy for 6 cycles; either CMF (cyclophosphamide, methotrexate, 5-FU) or CAF (cyclophosphamide, adriamycin, 5-FU); to assess the value of the addition of tamoxifen for five years compared to no tamoxifen in these patients; to compare the toxicity of the therapies; to assess the prognostic significance of DNA flow cytometry in patients with small, occult invasive breast cancer treated by local therapy only; and to evaluate the disease-free survival and survival of low risk invasive breast cancer patients determined by receptor status, tumor size, and % S phase treated by local therapy only.

Technical Approach: Patients must have undergone a radical, modified radical, or breast sparing procedure plus level 1 and 2 axillary lymph node dissection. Patients with bilateral breast cancer, prior hormonal or chemotherapy, or previous or concurrent malignancy are ineligible. Low risk patients will be followed but will not receive adjuvant therapy. High risk patients will be randomized to: (1) CMF x 6 cycles; (2) CAF x 6 cycles; (3) CMF x 6 cycles followed by tamoxifen; or (4) CAF x 6 cycles followed by tamoxifen. Patients will start adjuvant chemotherapy within 12 weeks of definitive surgery. Patients who have had a breast sparing procedure and axillary dissection will receive radiation therapy, either before or after CMF or CAF (at the discretion of the treating physician). Radiotherapy and tamoxifen may be given together. Patients will be removed from the study for unacceptable toxicity, development of local/regional or metastatic disease; or noncancer related illnesses that prevent continuation of therapy or regular follow-up. Patients will be followed until death.

Progress: Three patients were entered on this study in FY 90.

Groupwide: 873 patients have been entered. Grade 4 toxicities include granulocytopenia and nausea on the CMF arms; granulocytopenia, leukopenia, vomiting, and stomatitis on the CAF arms.

Detail Summary Sheet

Date: 30 Sep 90 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

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: colon, Duke's B/C, resection, chemo, observation

Accumulative MEDCASE Cost: -0-

Est Accumulative OMA Cost: $50.00

Periodic Review: Oct 89

Study Objective: To assess the effectiveness of 5-FU + high-dose Leucovorin as surgical adjuvant therapy for resectable colon cancer, when compared to surgery alone.

Technical Approach: Patients must have received a potentially curative surgery for colon cancer with neither gross nor microscopic evidence of residual disease following the complete resection. The resected specimen must pathologically verify a diagnosis of modified Duke's B-2, B-3, or C. The primary tumor must be above the peritoneal reflection. Patients may not have had any prior chemotherapy nor exposure to 5-FU. Patients must be maintaining oral nutrition and be ambulatory 50% of the day and have adequate bone marrow function. Patients may not have a concurrent second malignant disease nor any previous malignant tumor within three years. Patients will be stratified by extent of invasion (limited to bowel wall vs into or through serosa vs perforation vs adherence to adjacent organs vs invasion of adjacent organs); extent of regional nodal metastases (none vs 0-4 vs >4); regional/mesenteric implants resected enbloc (yes/no); and obstruction (yes/no).

RANDOMIZE TO: (1) Observation
(2) Leucovorin 20 mg/m^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.

Revision (Jan 90): Observation arm closed (due to positive results seen in SWOG 8591); two new arms added (5-FU + levamisole & 5-FU + low dose leucovorin + levamisole.

Progress: Five patients entered at MAMC in FY 90 for a total of nine subjects. One patient has died of the disease.

Groupwide: 471 subjects accrued with no unexpected toxicities.

Detail Summary Sheet

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

Title: SWOG 8905: Phase II/III Study of Fluorouracil and Its Modulation in Advanced Colorectal Cancer

Start Date: 19 Jan 90 Est Completion Date: Jun 92

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:	MAJ Mark H. Kozakowski, MC
MAJ Kenneth A. Bertram, MC	MAJ Robert L. Sheffler, MC
MAJ Everardo Cobos, MC	MAJ Paul C. Sowray, MC
MAJ Patrick L. Gomez, MC	CPT Denis P. Bouvier, MC

Key Words: cancer, colorectal, fluorouracil

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $20,780.00	Periodic Review: N/A

Study Objective: To determine and compare response rates and toxicities of 5-fluorouracil given by different schedules and/or with biochemical modulators to patients with advanced colorectal cancer and to compare patient survival on the different 5-FU regimens.

Technical Approach: All patients must have disseminated or recurrent colorectal cancer. Patients will be randomized to one of seven regimens:

- Arm I: 5-FU, IV push x 5 days every 5 weeks
- Arm II: Low dose Leucovorin, IV push x 5 days followed by 5-FU IV push x 5 days every 4 weeks x 2, then every 5 weeks
- Arm III: High dose Leucovorin IV, Days 1, 8, 15, 22, 29, 36 followed by 5-FU (same days) every 8 weeks
- Arm IV: 5-FU continuous infusion, days 1-28, every 5 weeks
- Arm V: 5-FU continuous infusion, days 1-18 preceded by Leucovorin IV push, days 1, 8, 15, 22 every 5 weeks
- Arm VI: 5-FU alone, 24 hour infusion, days 1, 8, 15, 22, every 4 weeks
- Arm VII: PALA IV, days 1, 8, 15, 22 followed by 5-FU, 24 hour infusion, days 2, 9, 16, 23, every 4 weeks

Patients will be continued on study until progression of disease or unacceptable toxicity. Patients will be followed to death.

Progress: No patients entered in this study at MAMC.

Groupwide: 157 eligible patients entered. Ninety-eight patients have been evaluated for toxicity with the toxicity profile as expected for 5-FU containing regimens.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/65 Status: On-going

Title: SWOG 8906: Evaluation of Merbarone in Hepatoma, Phase II Study

Start Date: 20 Apr 90 Est Completion Date: Apr 93

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:
MAJ Kenneth A. Bertram, MC
MAJ Everardo Cobos, MC
MAJ Patrick L. Gomez, MC
MAJ Mark H. Kozakowski, MC
MAJ Robert L. Sheffler, MC
MAJ Paul C. Sowray, MC
CPT Denis P. Bouvier, MC

Key Words: hepatoma, merbarone

Accumulative MEDCASE Cost: -0-

Est Accumulative OMA Cost: -0-

Periodic Review: N/A

Study Objective: To evaluate the response rate and response duration of hepatomas treated with merbarone, given as a five day continuous intravenous infusion, every 21 days, and to evaluate the qualitative and quantitative toxicities of merbarone administered on this schedule.

Technical Approach: All patients must have a histologically proven diagnosis of hepatoma. Patients will receive treatment as stated above. While the patient is receiving merbarone, objective disease status will be assessed every six weeks. Patients will continue treatment with merbarone until progression of disease or unacceptable toxicity requiring discontinuation of chemotherapy. Patients will be followed until death.

Progress: No patients entered at MAMC.

Groupwide: 4 subjects have been accrued. Twenty patients will be accrued. If at least one response is seen, an additional 15 patients will be accrued.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/87 Status: On-going

Title: SWOG 8910: Evaluation of Low Dose Continuous 5-Fluorouracil (5-FU) and Weekly Cisplatinum (CDDP) in Advanced Adenocarcinoma of the Stomach

Start Date: 15 Jun 90 Est Completion Date: Jun 93

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Everardo Cobos, MC

Associate Investigators:

LTC Howard Davidson, MC
MAJ Robert L. Sheffler, MC
MAJ Kenneth A. Bertram, MC
MAJ Paul C. Sowray, MC
MAJ Patrick L. Gomez, MC
CPT Denis P. Bouvier, MC

Key Words: stomach, adenocarcinoma, 5-FU, cisplatinum

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

Study Objective: To evaluate response to low dose continuous 5-FU and weekly cisplatinum in patients with advanced adenocarcinoma of the stomach and to assess the qualitative and quantitative toxicities of this regimen.

Technical Approach: Patients must have a histologically confirmed diagnosis of advanced gastric adenocarcinoma which is objectively measurable. Patients may not have CNS metastases. Patients may not have had prior chemotherapy but may have received prior immunotherapy. Patients who have had prior surgery and radiotherapy are eligible as long as they have recovered from associated toxicities and complications. Patients will be classified by performance status: 0-1 vs 2. Patients will be given a continuous infusion of 5-FU daily plus cisplatinum weekly for 8 weeks, then every other week. At eight weeks, patients with complete or partial response or stable disease will continue treatment until disease progression. Patients with disease progression at eight weeks will go off study.

Twenty patients will be accrued. If three, four, or five responses are seen, an additional 15 patients will be accrued.

Progress: No patients have been entered at MAMC.

Group-wide: 16 patients have been entered on the study. It is still too early for assessment of response or toxicity.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/110 Status: On-going

Title: SWOG 8915: A Phase II Study of 6-Thioguanine Administered as 120 Hour Continuous Infusion for Refractory or Recurrent Small Cell Carcinoma

Start Date: 20 Apr 90 Est Completion Date: Apr 93

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Patrick L. Gomez, MC

Associate Investigators:
MAJ Mark H. Kozakowski, MC
LTC Howard Davidson, MC
MAJ Robert L. Sheffler, MC
MAJ Kenneth A. Bertram, MC
MAJ Paul C. Sowray, MC
MAJ Everardo Cobos, MC
CPT Denis P. Bouvier, MC

Key Words: cancer, small cell carcinoma, 6-thioguanine

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

Study Objective: To assess the response rate of 6-thioguanine and the qualitative and quantitative toxicities of this drug administered as a 120 hour continuous infusion in patients with refractory (progression while on treatment) or recurrent small cell lung cancer.

Technical Approach: Patients must have recurrent or refractory small cell lung cancer after treatment with one first line combination chemotherapy regimen. Patients must not have received more than one prior treatment regimen. Limited disease patients must have also failed prior radiotherapy. All patients must have measurable disease. Patients must have adequate renal and hepatic function and a SWOG performance status of 0-2. Patients will be classified by performance status: 0-1 vs 2. A course of 6-thioguanine will consist of a 120 hour infusion followed by a rest period of four weeks. Patients will be treated with 35 mg/M^2/day on days 1-5, every 35 days. Patients may not receive concurrent hormonal, biologic, or cytotoxic therapy or concurrent palliative radiation therapy to the measurable lesions being followed for response. Treatment will continue until progression of disease. The accrual rate is anticipated to be 24 patients per year. Thus the study should be completed in about 15 months from activation.

Progress: No patients entered at MAMC.

Groupwide: eight subjects had been registered as of 30 Jun 90. Four patients have been evaluated for toxicity; one patient had Grade 3 nausea.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/66 Status: On-going

Title: SWOG 8916: Evaluation of Merbarone in Pancreatic Adenocarcinoma, A Phase II Study

Start Date: 20 Apr 90 Est Completion Date: Apr 93

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:	MAJ Patrick L. Gomez, MC
LTC Howard Davidson, MC	MAJ Mark H. Kozakowski, MC
MAJ Kenneth A. Bertram, MC	MAJ Robert L. Sheffler, MC
MAJ Everardo Cobos, MC	CPT Denis P. Bouvier, MC

Key Words: pancreas, adenocarcinoma, merbarone

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

Study Objective: To evaluate the response rate and response duration in pancreatic adenocarcinoma treated with merbarone given as a five day continuous intravenous infusion, every 21 days and to evaluate the qualitative and quantitative toxicities of merbarone administered on this schedule.

Technical Approach: Patients must have a pathologically verified diagnosis of adenocarcinoma of the exocrine pancreas that is advanced, recurrent, or progressive, and not amenable to surgery or radiotherapy.

Merbarone will be given 1000 mg/M^2 IV continuous infusion days 1-5, every 21 days. While the patient is receiving merbarone, objective disease status will be assessed every six weeks. Patients will continue treatment with merbarone until progression of disease or unacceptable toxicity. All patients will be followed to death.

Progress: No patients have been entered at MAMC.

Groupwide: 14 patients have been registered. It is still too early for assessment of response or toxicity.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/111 Status: On-going

Title: SWOG 8921: Phase II Trials of Cyclophosphamide/IL-2, DTIC/IL-2, and DTIC/Cisplatinum/Tamoxifen in Stage IV Melanoma

Start Date: 21 Sep 90 Est Completion Date: Sep 93

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ Patrick L. Gomez, MC
LTC Howard Davidson, MC
MAJ Mark H. Kozakowski, MC
MAJ Kenneth A. Bertram, MC
MAJ Robert L. Sheffler, MC
MAJ Everardo Cobos, MC
CPT Denis P. Bouvier, MC

Key Words: cancer, melanoma, chemotherapy

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

Study Objective: To evaluate the response rates and assess the qualitative and quantitative toxicities associated with each of the three regimens: cyclophosphamide (CTX) and IL-2; dacarbazine (DTIC) and IL-2; and DTIC, cisplatin (CDDP), and tamoxifen (TAM).

Technical Approach: Patients must have histologically proven Stage IV malignant melanoma which is measurable. Patients must not have symptomatic pleural effusions or ascites. Patients must have had no prior chemotherapy or IL-2 therapy for Stage IV disease. Patients may have received other prior immunotherapy for Stage IV disease, adjuvant therapy for melanoma (not including IL-2, DTIC, or cisplatin), or prior surgery and/or radiation therapy provided 21 days have elapsed since the completion of treatment and they have recovered from all side effects. Patients who have received prior adjuvant therapy that included IL-2, DTIC, or cisplatin are eligible provided relapse did not occur while the patient was on treatment and at least six months have elapsed since the end of treatment. Patients will be stratified by sites of active disease (skin and/or lymph nodes only versus any other sites), performance status, and prior treatment for disseminated disease.

The treatment regimens are not designed to be compared in a randomized fashion but rather as three simultaneously evaluable treatment regimens. Arm I utilizes cyclophosphamide and IL-2 given every three weeks until maximum response. Arm II utilizes DTIC and IL-2 given every four weeks. Both Arms I and II are using IL-2 in a fashion designed to minimize toxicity and allow the drugs to be given as an outpatient. Arm III utilizes DTIC and cisplatinum, given every three weeks in conjunction with tamoxifen, given daily. Treatment on Arms II and III is given until disease progression.

Progress: No patients entered at MAMC.

Groupwide: 18 patients have been registered. It is too early for evaluation of response and toxicity.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/88 Status: On-going

Title: SWOG 8923: "Neo-FAC" for Poor Prognosis Stage IV Breast Cancer, A Phase II Pilot Study

Start Date: 15 Jun 90 Est Completion Date: Apr 93

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:	MAJ Patrick L. Gomez, MC
LTC Howard Davidson, MC	MAJ Mark H. Kozakowski, MC
MAJ Kenneth A. Bertram, MC	MAJ Robert L. Sheffler, MC
MAJ Everardo Cobos, MC	CPT Denis P. Bouvier, MC

Key Words: breast cancer, Neo-FAC

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

Study Objective: To assess complete response and toxicity of a dose-intensive approach to treatment of metastatic breast cancer with a combination of daily oral Cytoxan, weekly Adriamycin, and 5-FU by continuous infusion on a low-dose continuous basis, followed by weekly Methotrexate; and to measure time to treatment failure and survival in patients so treated.

Technical Approach: Patients must have histologically confirmed diagnosis of breast cancer with recurrent or metastatic disease with at least one measurable or evaluable site. Patients may have had no prior chemotherapy for disseminated or recurrent breast cancer. Prior adjuvant chemotherapy is permitted, if it was completed.

Patients will be stratified according to ER+ vs ER- vs ER unknown; Pgr+ vs PgR- vs PgR unknown; prior adjuvant chemotherapy; prior hormonal therapy, performance status, and brain metastases.

Patients will be treated with 5-FU given on a continuous basis via an ambulatory pump through a permanently placed central venous catheter. In addition, patients will receive Adriamycin once a week, Cytoxan pills daily, and Prednisone pills daily for seven weeks. If more than 25 weekly doses of Adriamycin are needed, the Adriamycin will be changed to weekly Methotrexate. Once the patient progresses, this chemotherapy regimen will be discontinued and an alternate treatment plan determined by the primary physician.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/31 Status: On-going

Title: SWOG 8926: Evaluation of Low Dose Continuous Infusion 5-Fluorouracil in Patients With Advanced and Recurrent Renal Cell Carcinoma

Start Date: 19 Jan 90 Est Completion Date: Jan 93

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
MAJ Patrick L. Gomez, MC
LTC Howard Davidson, MC
MAJ Mark H. Kozakowski, MC
MAJ Kenneth A. Bertram, MC
MAJ Robert L. Sheffler, MC
MAJ Everardo Cobos, MC
CPT Denis P. Bouvier, MC

Key Words: toxicity, disease response, renal cell, 5-FU

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

Study Objective: To evaluate the likelihood of response in order to assess whether low dose continuous infusion 5-FU should be advanced to further studies and to assess the qualitative and quantitative toxicities.

Technical Approach: Patients not eligible for higher priority SWOG studies with histologically proven renal cell carcinoma, which is advanced and/or recurrent, are eligible for this study. Patients may not have received prior cytotoxic chemotherapeutic regimens. No prior malignancy is allowed except for adequately treated basal cell skin cancer or other cancer for which the patient has been disease-free for five years.

Patients will receive 5-FU, 300 mg/M^2/day, IV by continuous infusion via a semi-permanent infusion device. Patients will also receive pyridoxine, 150 mg PO daily. Patients will be examined and graded weekly for subjective/objective evidence of developing toxicities according to the SWOG toxicity criteria. Patients will be assessed every four weeks for disease response. Patients with a complete or partial response or stable disease will continue on treatment for six months. Patients with progressive disease or unacceptable toxicity will be taken off study. Patients who develop an intercurrent illness which would affect assessments of clinical status to a significant degree or require discontinuation of the drug will also be taken off study. If there is tumor progression at any time following the six months of treatment and response, therapy may be reinstituted.

Progress: No patients entered at MAMC.

Groupwide: 40 subjects have been accrued. Thirty-one patients have been evaluated for toxicity. There was one fatal toxicity due to aspiration of gastric contents. This patient also had lymphopenia. Thirty-nine percent (39%) have had some GI toxicities and 39% have had some hematologic toxicity.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/112 Status: On-going

Title: SWOG 8931 (EST-3189) (INT-0108): Phase III Comparison of Cyclophosphamide, Doxorubicin, and 5-Fluorouracil (CAF) and a 16-Week Multi-Drug Regimen as Adjuvant Therapy for Patients with Hormone Receptor Negative, Node-positive Breast Cancer

Start Date: 21 Sep 90 Est Completion Date: Sep 93

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:	MAJ Patrick L. Gomez, MC
LTC Howard Davidson, MC	MAJ Mark H. Kozakowski, MC
MAJ Kenneth A. Bertram, MC	MAJ Robert L. Sheffler, MC
MAJ Everardo Cobos, MC	CPT Denis P. Bouvier, MC

Key Words: cancer, breast cancer, adjuvant chemotherapy

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

Study Objective: To compare disease-free and overall survival and toxicities in node positive receptor-negative breast cancer patients receiving adjuvant CAF or a 16-week multidrug chemotherapy regimen.

Technical Approach: Patients must be female and must have undergone excision of the primary breast tumor mass, proven histologically to be invasive breast adenocarcinoma, and must have one or more pathologically involved axillary nodes. Prior malignancies are limited to a curatively treated basal or squamous cell carcinoma of the skin, carcinoma *in situ* of the cervix, or other cancer if the patient has been disease-free $\geq$ five years. Patients who have had prior hormonal therapy or chemotherapy for breast cancer are ineligible.

Patients will be stratified by the number of positive axillary nodes, menopausal status, and pathologic size of the primary tumor at the largest dimension. Patients will be randomized to CAF (cyclophosphamide, doxorubicin, and 5-FU), given every 28 days for six cycles or a 16-week multidrug regimen: cyclophosphamide, doxorubicin, vincristine, methotrexate, 5-FU (600 mg/M^2), and leucovorin, given weeks 1, 3, 5, 7, 9, 11, 13, and 15, with 5-FU, 300 mg/M^2, given on alternate weeks.

Progress: No patients entered at MAMC.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/42 Status: On-going

Title: SWOG 8943: Evaluation of Merbarone in Advanced Soft Tissue Sarcomas, Phase II

Start Date: 16 Feb 90 Est Completion Date: Feb 91

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: MAJ Paul C. Sowray, MC

Associate Investigators:
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MAJ Mark H. Kozakowski, MC
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CPT Denis P. Bouvier, MC

Key Words: cancer, soft tissue sarcomas, merbarone

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

Study Objective: To assess the response rate of advanced soft tissue sarcomas treated with Merbarone and to evaluate the qualitative and quantitative toxicities of Merbarone administered in a Phase II Study.

Technical Approach: Patients must have histologic diagnosis of unresectable or metastatic soft tissue sarcoma. Ineligible histologies include Kaposi's sarcoma, Ewing's sarcoma, lymphoma, and extraskeletal chondrosarcoma. Patients must not have received more than one prior biologic or chemotherapy regimen and must have been off previous chemotherapy or radiation therapy for at least 4 weeks.

Patients will be stratified by performance status (0-1 vs 2); prior chemotherapy regimens (0 vs 1); prior biologic regimens (0 vs 1); and prior radiotherapy (yes vs no).

Patients will be treated with Merbarone, 1000 mg/M^2, IV, continuous infusion on days 1-5, repeated every 21 days, with disease assessment every 6 weeks. Patients with complete response, partial response, or stable disease will continue this treatment until progression of disease or unacceptable toxicity occur.

Progress: No patients entered at MAMC.

Groupwide: 16 eligible patients have been registered. Toxicity has been mild to moderate in the three patients evaluated for toxicity.

Detail Summary Sheet

Date: 30 Sep 90 Protocol No.: 90/56 Status: On-going

Title: SWOG 8997 (ECOG 3887): Phase III Chemotherapy of Disseminated Advanced Stage Testicular Cancer With Cisplatin Plus Etoposide With Either Bleomycin or Ifosfamide

Start Date: 16 Mar 90 Est Completion Date: Mar 93

Dept/Svc: Medicine/Oncology Facility: MAMC

Principal Investigator: LTC Howard Davidson, MC

Associate Investigators:

LTC John A. Vaccaro, MC	MAJ Mark H. Kozakowski, MC
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MAJ Everardo Cobos, MC	MAJ Paul C. Sowray, MC
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Key Words: testes, cancer, chemotherapy

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $12,862.00	Periodic Review: N/A

Study Objective: To determine the objective response rate and duration of remission of BEP compared to VIP combination chemotherapy; to determine the toxicity of VIP compared to BEP combination chemotherapy; to confirm the efficacy and toxicity of intravenous Mesna as a urothelial protective agent.

Technical Approach: Patients must have a histologic diagnosis of advanced disseminated germ cell tumor and no prior chemotherapy or radiation therapy. Patients will be randomized to VIP (cisplatin, ifosfamide, mesna, and etoposide) to BEP (cisplatin, etoposide, and bleomycin). The regimen will be repeated every three weeks for four cycles. Bleomycin will be omitted for postsurgery chemotherapy in BEP patients. Patients in complete remission at the end of four courses of therapy will receive no further treatment. If there is radiographic or serologic evidence of persistent disease and residual tumor is surgically resectable, surgery will be performed. Patients who have complete or near complete resection of residual radiographic abnormalities with the pathologic finding of fibrosis/necrosis and those who have complete resection of mature or immature teratoma will receive no further treatment. Patients who have complete resection of residual disease which histologically shows viable carcinoma will receive two more courses of the original induction therapy. If residual tumor is deemed unresectable, patients will be followed monthly until disease progression with no further therapy. If relapse occurs in complete or partial responders less than 4 weeks after day 1 of the last course of induction therapy, the patient will be taken off study.

Progress: No patients entered at MAMC.

Groupwide: 120 subjects have been registered. The accrual goal is 300 patients. It is too early to make any statements regarding response or survival. Fifty-one percent (51%) of 39 patients analyzed experienced life-threatening or lethal toxicities. This includes three lethal reactions and 17 life-threatening toxicities, primarily leukopenia.

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

F O R

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UNIVERSITY OF WASHINGTON NEURO-ONCOLOGY GROUP

Detail Summary Sheet

Date: 30 Sep 90 | 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

Associate Investigators:

COL Irwin B. Dabe, MC
CPT Denis P. Bouvier, MC
MAJ Joseph H. Piatt, Jr., MC
Robert Goodkin, M.D., DAC

Key Words: brain, tumors, external irradiation, chemotherapy

Accumulative MEDCASE Cost: -0- | Est Accumulative OMA Cost: -0- | Periodic Review: Oct 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 90 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:

COL Irwin B. Dabe, MC	MAJ Joseph H. Piatt, MC
COL Michael Potter, MC	MAJ Ruben Sierra, MC
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MAJ David Dunning, MC	Frederic Helmer, M.D.

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 89

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 90	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 Jan 89	Est Completion Date: Nov 92
Dept/Svc: Medicine/Oncology	Facility: MAMC
Principal Investigator: LTC Howard Davidson	
Associate Investigators:	MAJ Joseph Piatt, MC
COL Irwin B. Dabe, MC	MAJ Frank Zimba, MC
MAJ Kenneth Bertram, MC	CPT Denis Bouvier, MC
MAJ Everardo Cobos, MC	Edythe Albano, M.D.
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Key Words: cancer, lymphoma, CNS, methotrexate, irradiation

Accumulative MEDCASE Cost: -0-	Est Accumulative OMA Cost: $328.00	Periodic Review: Oct 89

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: One patient entered at MAMC in FY 88; none in FY 90.

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