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ANNUAL RESEARCH PROGRESS REPORT, FISCAL YEAR 1981,(U)
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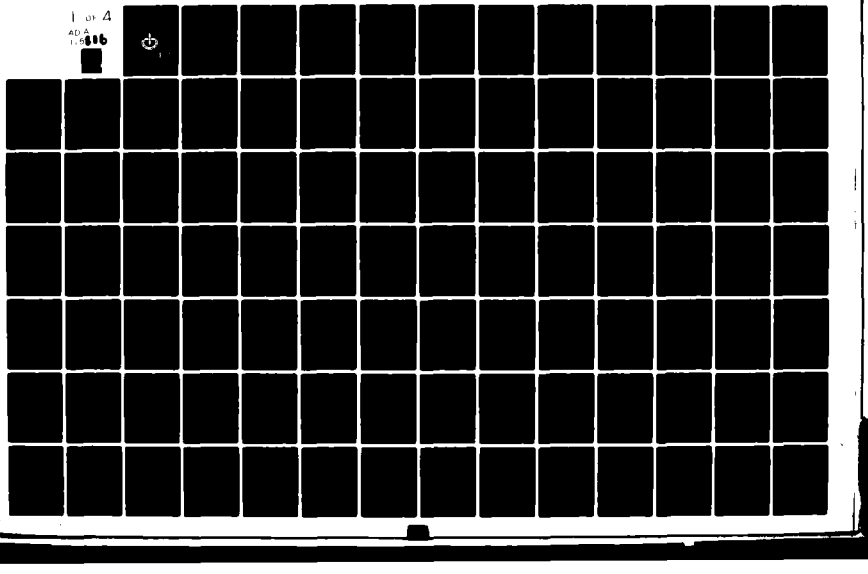

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DEPARTMENT
OF
CLINICAL INVESTIGATION

ANNUAL RESEARCH PROGRESS REPORT

FISCAL YEAR 1981

MADIGAN ARMY MEDICAL CENTER
TACOMA, WASHINGTON 98431

REPORTS CONTROL SYMBOL MED-300

ANNUAL PROGRESS REPORT

30 September 1981

DEPARTMENT OF CLINICAL INVESTIGATION

MADIGAN ARMY MEDICAL CENTER

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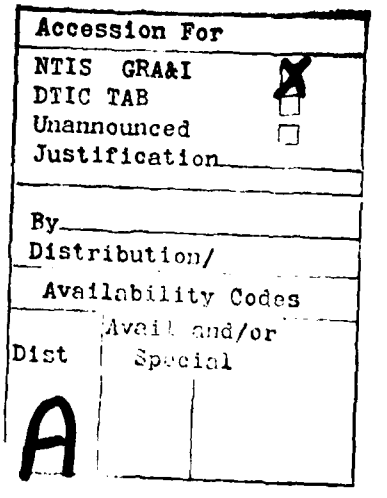

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SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

REPORT DOCUMENTATION PAGE		READ INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER MED-300	2. GOVT ACCESSION NO.	3. RECIPIENT'S CATALOG NUMBER
4. TITLE (and Subtitle) ANNUAL RESEARCH PROGRESS REPORT (U)		5. TYPE OF REPORT & PERIOD COVERED Annual FY 81 6. PERFORMING ORG. REPORT NUMBER
7. AUTHOR(s) Bruce L. Fariss, M.D., COL, MC		8. CONTRACT OR GRANT NUMBER(s)
9. PERFORMING ORGANIZATION NAME AND ADDRESS Department of Clinical Investigation Madigan Army Medical Center Tacoma, Washington 98431		10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS
11. CONTROLLING OFFICE NAME AND ADDRESS Commander Madigan Army Medical Center Tacoma, Washington 98431		12. REPORT DATE 1 October 1981 13. NUMBER OF PAGES 331
14. MONITORING AGENCY NAME & ADDRESS(if different from Controlling Office) US Army Health Services Command Department of the Army ATTN: HSPA-I Fort Sam Houston, Texas 78234		15. SECURITY CLASS. (of this report) Unclassified 15a. DECLASSIFICATION/DOWNGRADING SCHEDULE
16. DISTRIBUTION STATEMENT (of this Report) Approved for public release: distribution unlimited.		
17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report) N/A		
18. SUPPLEMENTARY NOTES The findings in this report are not to be construed as an official Department of the Army position unless so designated by other authorized documents.		
19. KEY WORDS (Continue on reverse side if necessary and identify by block number) Unit summary; research protocols (objective, method, progress, status); publications; presentations.		
20. ABSTRACT (Continue on reverse side if necessary and identify by block number) ~~Subject~~ This report identifies those individuals who are conducting investigative protocols at Madigan Army Medical Center. An abstract of each protocol giving abbreviated technical objectives, methods, and progress is presented.		

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

FOREWORD

The Department of Clinical Investigation has been given a greater role in the training of professionals. There has been an increasing number of training protocols, which in themselves will not result in publications, but hopefully will stir the imagination of some of the participants. As quoted from Cortisone, Memoirs of a Hormone Humter* by Edward C. Kendall, "Imagination is a phenomenon that is the basis of creative genius. It is an essential ingredient of progres, and yet it can lead to the generation of hope and expectation that have no substance in fact. Experience can develop the power to control one's imagination, but it is difficult to contemplate in a detached and impersonal manner the approach of a moment that could determine the direction and pattern of the remaining days of one's scientific career."

It is the responsibility of the Department of Clinical Investigation to fan the flame of imagination, to be supportive of investigators, to offer encouragement when things are not always what they would seem to be, and to assist investigators in their creative genius, resulting hopefully in acceptance by their peers in the form of a publication or presentation.

The staff at Department of Clinical Investigation offer their heart-felt appreciation to those investigators who have diligently sought to complement their data with more and more information which enables them to have an acceptable publication. It is only through presenting-investigators that the Department of Clinical Investigation can exist. The Department attempts to offer a service in the form of a research environment for the professional staff of the hospital. It is apropos to end this forward with the hope of wisdom and a quote by Cowper as quoted in The Great Physician, A Short Life of Sir William Osler** by Edith Gittings Reid, "Knowledge and Wisdom, far from being one, have ofttimes no connection. Knowledge dwells in heads replete with thoughts of other men; Wisdom in minds attentive to their own. Knowledge is proud that he has learned so much, Wisdom is humble that he knows no more."

Bruce L. Fariss

BRUCE L. FARISS, M.D.
COL, MC
Chief, Department of Clinical Investigation

*Charles Scribner's Sons, New York, 1971, p 125
**Oxford University Press, New York, 1931, p 42

UNIT SUMMARY FY 81

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, FARISS, Bruce L., MC	06	61C9A	
C, Clin Studies Svc PLYMATE, Stephen R., MC	05	61C9B	
C, Surg & Animal Care Svc LIEBENBERG, Stanley P.	04	64C9B	
C, Microbiology Svc CRUMRINE, Martin H., MSC	04	68A9C	PCS Jul 81
C, Physiology Svc JACOB, Willis H., MSC	04	68J9C	
C, Biochemistry Svc LITTLE, James S.	03	68C9C	
NCOIC HAYES, James E.	E6	91T30	
Med Lab Spec ORTIZ, Abigail	E3	92B10	
OR Tech PAGE, Lawrence	E4	91D10	
Vet Animal Spec GIALDINI, Gwen T.	E4	91T10	
Vet Animal Spec BEMIS, Joseph L.	E2	91T10	
Vet Animal Spec FEROCE, David L.	E4	91S10	
Vet Animal Spec Vacant			

DESCRIPTION	RANK	MOS
Med Tech GARRISON, Mina	GS9	0644
Med Tech GRAVES, James	GS9	0644
Med Tech MATEJ, Louis	GS9	0644
Edit Asst/Steno WHITTEN, Nancy J.	GS6	1087
Sec/Steno SMITH, Peggy J.	GS4	0318
Maintenance Worker MALLOUF, Jerry	WG7	4749

	FUNDING
MEDCASE Equipment	$130,085.00
Capital Equipment	20,000.00
Personnel Services (Civilian salaries)	118,154.00
Consumable Supplies	81,000.00
Contractual Services	2,000.00
TOTAL	351,239.00

3. Progress

During FY 81 there were 252 active protocols. Of these, 164 are presently ongoing; 71 were completed; and 17 terminated. In addition, administrative work has been done on 11 protocols that are pending approval at MAMC, making a total of 263 protocols that received support (administrative or technical) during the year.

There were 30 publications, 16 papers are in press, and 18 papers have been submitted and are in the process of review by the publisher. There were 27 presentations at regional, national or international meetings.

4. Committee Members

Commander
Madigan Army Medical Center
BG Guthrie L. Turner, Jr., M.D., MC

CLINICAL INVESTIGATION COMMITTEE

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ACKNOWLEDGEMENTS

I would like to take this opportunity to thank those investigators who replied to our requests promptly and, even though it is tempting, I will not castigate those investigators who were slow and at times delinquent in responding to our requests. I thank Nancy Whitten for the effort which is obvious in the complilation of this publication which is ever-increasing in size.

PUBLICATIONS - FY 1981

DEPARTMENT OF CLINICAL INVESTIGATION

Publications:

Fariss, B.L., Fenner, D.K., Plymate, S.R., Brannen, G.E., Jacob, W.H., and Thomason, A.M.: Seminal Characteristics in the Presence of a Varicocele Compared to Expectant Fathers and Pre-Vasectomy Individuals. Fertil Steril 35: 325-27, 81.

Froelich, C.J., Plymate, S.R., Searles, R.P., and Davis, L.E.: Simultaneous Occurence of Depressed Cell Mediated Immunity and Two Postulated Cell Mediated Disorders: Guillain-Barre' Syndrome and Lipoid Nephrosis. Ann Int Med 94(4): 485, 1981.

Jennings, P.B., Whitten, N.J., and Sleeman, H.K.: The Diagnosis and Treatment of Shock in the Critical Care Patient. In Veterinary Critical Care; Sattler, F.P., Knowles, R.P., and Whittick, W.G., (ed), Lea and Febiger, Philadelphia, 1981, pp 486-524.

Karp, L.E., Williamson, R.A., Moore, D.E., Shy, K.K., Plymate, S.R., and Smith W.D.: The Sperm Penetration Assay: A Useful Test in Assessing Male Infertility. Obstet Gynecol 57(5):620-23, 1981.

Little, J.S., Rill, W.L., Hawley, H.P., and Liu, C.T.: Effect of Streptococcus pneumonia Infection in Rats on Hepatic Water Content, Electrolyte Concentration, and Chemical Composition. Amer J Vet Res 42(8):1328-31, 1981.

Plymate, S.R., Przasnyski, E.J., Bassett, M.L., and Fariss, B.L.: Mechanism of Antiandrogen Effects of Cimetidine. Clin Res 28:721A, 1980.

IBID; Clin Res 29:84A, 1981.

Plymate, S.R., Fariss, B.L., Bassett, M.L., and Matej, L.A.: Obesity and Its Role in Polycystic Ovary Syndrome. JCEM 52:1246-48, 1981.

Plymate, S.R., Fariss, B.L., Smith, M.L., Jacob, W.H., and Matej, L.A.: Seminal Fluid Androgen Binding Protein. Andrologia 13(4):308-13, 1981.

Plymate, S.R., Paulsen, C.A., and Smith, M.L.: The Value of Sex Hormone Binding Globulin in Clinical Medicine. The Ligand Review 3:7-11, 1981.

Smith, M.L., Luqman, W.A., and Fariss, B.L.: Size Heterogeneity of Immunoreactive Prolactin in Stored Semen and Seminal Plasma. Arch Andrology 7: 259-262, 1981.

Ward, G.S., Crumrine, M.H., Mattloch, J.R.: Inflammatory Exostosis and Abscessation in a Rabbit Associated with Fusobacterium nucleatum. Lab Anim Sci 31:280-81, 1981.

PUBLICATIONS FY 81 - Department of Clinical Investigation (Cont)

Ward, G.S.: What's Your Diagnosis? Spare Parts. Lab Animal 10(1):13-14, 1981.

Ward, G.S.: What's Your Diagnosis? Tied Up Tubes. Lab Animal 10(3)17-18, 1981.

Accepted for Publication:

Wang, C., Plymate, S.R., Nieschlag, E., and Paulsen, C.A.: Salivary Testosterone in Men: Further Evidence of a Direct Correlation with Free Serum Testosterone. Accepted by JCEM September 1980.

Ward, G.S. and Byland, R.R.: Concentrations of Halothane in 17 Veterinary Operating or Treatment Rooms During Normal Operations. Accepted by JAVMA, April 1981.

Ward, G.S. and Byland, R.R.: Concentrations of Methoxyflurane and Nitrous Oxide in Veterinary Operating Rooms. Accepted by JAVMA, July 1981.

Submitted for Publication: Department of Clinical Investigation

Fariss, B.L. and Smith, M.L.: The Effect of Total Pancreatectomy, Pancreatic Duct Ligation, and the Administration of Alloxan on Serum Zinc Levels in Sheep. Submitted to Proc Soc Exp Biol Med.

Little, J.S.: Effect of Streptococcus pneumoniae Infection on the Synthesis of Rat Liver Plasma Membranes. Submitted to Proc Soc Exp Bio Med.

Little, J.S., Kishimoto, R.A., and Canonico, P.G.: Intracellular Fate of Phase I Coxiella burnetii in Guinea Pig Peritoneal Macrophages. Submitted to J Infec Immun.

Ward, G.S., Walker, H.L., and Page, L.E.: Catheterization for Direct Blood Pressure Monitoring in the Unanesthetized Rat. Submitted to Lab Animal Science.

Ward, G.S. and Hayes, J.E.: Morphine Addiction in the Pig-Tailed Macaque (Macaca nemestrina). Submitted to Lab Animal Science.

Ward, G.S., Guiry, C.C., Alexander, L.L.: Tetracycline-Induced Anaphylactic Shock in a Dog. Submitted to JAVMA.

DENTAL ACTIVITY

Publications:

Harrison, J.W. and Hand, R.E.: The Effect of Dilution and Organic Matter on the Antibacterial Property of 5.25% Sodium Hypochlorite. J Endodontics 7(3):128-32, 1981.

DEPARTMENT OF EMERGENCY MEDICINE

Publication:

Pryor, G.J., Kilpatrick, W.R., and Opp, D. E.: Local Anesthesia in Minor Lacerations: Topical TAC vs Lidocaine Infiltration. Ann Emer Med 9:568-71, 1980.

Submitted for Publication:

Dice, W.H., Ward, G.S., Kelley, J., and Kilpatrick, W.R.: Lack of Pulmonary Toxicity. Submitted to Ann Emer Med .

DEPARTMENT OF MEDICINE

Publications:

Chadband, R.B., Reed, J.W., and Fariss, B.L.: HDL-Cholesterol and Glucose Tolerance Tests in Young Male Survivors of Myocardial Infarctions. (Abstract) Abstracts of the 63rd Annual Endocrine Society Meeting, #1151, p 370.

Clayton, W.L., Gibbons, R.B., Randolph, K.A., and Bulley, W.A.: Synovial Fluid Analysis Following Meniscectomy, A Prospective Study. Arth Rheum 24(7):951-53, 1981.

Luqman, W.A. and Smith, M.L.: The Effect of Freezing and Storage on Seminal Immunoreactive Prolactin. J Endocrinol Invest 4:433, 1980.

Accepted for Publication:

Biesbroeck, R.C., Albers, J.J., Wahl, P.W., Weinberg, C.R., Bassett, M.L., and Bierman, E.L: Abnormal Composition of High Density Lipoproteins in Non-Insulin Dependent Diabetics. Accepted by Diabetes, September 1981.

Covelli, H.D., Beekman, J., and Weled, B.: Efficacy of Continuous Positive Airway Pressure Administered by Face Mask. Accepted by Chest, August 1981.

Submitted for Publication:

McClain, J.B., Knight, C.G., and Kubiak, K.: Post-Operative Enterococcal Endophthalmitis. Submitted to Arch Ophthalmol.

DEPARTMENT OF NURSING

Accepted for publication:

Glor, B.A. and Barko, W.: Sociotechnical Systems Using an Industrial Tested Technology to Design Quality Assurance Standards in Health Care Systems. Accepted by Mil Med, August 1981.

DEPARTM6NT OF OB/GYN

Accepted for publication:

Lee, R.B. and Park, R.C.: Bladder Dysfunction Following Radical Abdominal Hysterectomy. Accepted by Gynecol Oncol, March 1981.

Lee, R.B., Neglia, W., and Park, R.C.: Cervical Carcinoma in Pregnancy. Accepted by Obstet Gynecol, Feb 81.

DEPARTMENT OF PATHOLOGY

Publication:

Oberhofer, T.R.: Characteristics and Biotypes of Pasteurella multocida Isolated from Humans. J Clin Microbiol 13:566-71, 1981.

Accepted for Publication

Oberhofer, T.R.: Characteristics of Human Isolates of Unidentified Fluorescent Pseudomonads (UFP) Capable of Growth at 42°C. Accepted by J Clin Microb, July 1981.

Oberhofer, T.R. and Towle, D.W.: Evaluation of the Rapid Penicillinase Paper Strip Text for Detection of Beta-Lactamase. Accepted by J Clin Microbiol, September 1981.

Submitted for Publication:

Oberhofer, T.R. and Back, A.E.: Isolation and Cultivation of Haemophilus ducreyi Recovered from Human Sources. Submitted to J Clin Microbiol.

DEPARTMENT OF PEDIATRICS

Publications:

Marinelli, P.V.: Mean Airway Pressure Calculations - Further Comments (Leter to the Editor). J Pediatrics 99(1):168-69,1981.

Marinelli, P.V., Ortiz, A., and Alden, E.R.: Acquired Eventration of the Diaphragm: A Complication of Chest Tube Placement in Neonatal Pneumothorax. Pediatrics 67:552-54, 1981.

Marinelli, P.V., Pettett, G., and Alden, E.R.: Manual Artificial Ventilation in the Newborn. J Amer Osteo Assn 80:104, 1981.

Mease, A.D., Burgess, D.P., and Thomas, P.J.: Irreversible Neutrophil Aggregation, A Mechanism of Decreased Newborn Neutrophil Chemotactic Response. Amer J Pathol 104:98-102, 1981.

Publications: Department of Pediatrics (Cont)

Yeatman, G.W. and Van Dang,V.: Cao Gio (Coin Rubbing): Vietnamese Attitudes Toward Health Care. JAMA 244:2748-49, 1981.

Yeatman, G.W.: Paternal Separation and the Military Dependent Child. Mil Med 146, May 81.

Yeatman, G.W.: Twenty-four Hour Telephone Triage: An Expedient to Ambulatory Child Care. Mil Med 146(4):249-53, 1981.

Accepted for Publication:

Yeatman, G.W. and Moore, D.C.: Chromosomal Abnormalities in Adolescents - Detection and Intervention. In Chronic Disorders in Adolescents, M.S. Smith, (ed), PSG Publishing Company.

Submited for Publication:

Marinelli, P.V., Pettett, G., and Alden, E.R.: Manual Artificial Ventilation in the Newborn: An Analysis of Equipment, Technique, and Application. Submitted to Pediatrics.

Pettett, P.G., Wiswell, T.E., and Rawlings, J.S.: Serum Erythropoietin Activity in Neonatal Polycythemia. Submitted to J Pediatrics.

Stephan, M., Ponzi, J., Smith, D., and Alden, E.R.: Scalp Vertex Aplasia Cutis and Its Origin. Submitted to Pediatrics.

Wickham, L.K., Marinelli, P.V., Knudson, R.P., and Alden, E.R.: Peripheral Artery Catheterization: A Review. Submitted to Amer J Dis Child.

PHYSICAL MEDICINE & REHABILITATION SERVICE

ACCEPTED FOR PUBLICATION

Gatens, P.F. and Saeed, M.A.: Combat Boot Palsy. Accepted by Mil Med, July 1981.

Saeed, M.A. and Gatens, P.F.: Accessory Nerve Palsy, A Hazard of Lymph Node Biopsy. Accepted by Mil Med, June 1981.

Saeed, M.A. and Kraft, G.H.: Bilateral Suprascapular Neuropathy. Accepted by Orthopaedic Review, June 1981.

Saeed, M.A. and Gatens, P.F.: Compound Nerve Action Potential of the Medial and Lateral Plantar Nerves Through the Tarsal Tunnel. Accepted by Arch Phy Med Rehab, June 1981.

Saeed, M.A., Gatens, P.F., and Singh, S.: Differential Diagnosis of Winging of the Scapula. Accepted by Amer Family Physician, April 1981.

Submitted for Publication: Physical Medicine & Rehabilitation Service

Gatens, P.F. and Saeed, M.A.: Abnormalities in the Paraspinals - Sometimes the Only EMG Abnormality in the Evaluation of Nerve Root Syndromes. Submitted to Arch Phy Med Rehab.

Gatens, P.F. and Saeed, M.A.: Electromyographic Findings in the Intrinsic Muscles of Normal Feet. Submitted to Arch Phy Med Rehab.

Saeed, M.A. and Gatens, P.F.: Anterior Interosseous Nerve Syndrome - Unusual Etiologies. Submitted to Arch Phy Med Rehab.

Saeed, M.A., Dresner, M.L., and Gatens, P.F.: Electromyography fo the Bulbocavernosus Muscle in the Evaluation of Neurogenic Bladder. Submited to J Urology.

Saeed, M.A., Dresner, M.L., and Singh, S.: The Bulbocavernosus Reflex in Impotence. Submitted to Arch Phy Med Rehab.

DEPARTMENT OF PSYCHIATRY

Publication:

Parker, R.A. and Youngren, J.N. : The Fort Lewis Smoking Control Clinic: A Major Follow-up Study. Mil Med 146:38-41, 1981.

DEPARTMENT OF OB/GYN

Publication:

Smythe, A.R. and Sakakini, J.: Maternal Metabolic Alterations Secondary to Terbutaline Therapy for Premature Labor. Obstet Gynecol 57(5):566-70,1981.

DEPARTMENT OF SURGERY

Publication:

Hays, L.L.: The Frey Syndrome. News Bulletin, Amer Acad Otolaryngol Head-and Neck Surg. 20 Sep 81.

PRESENTATIONS - FY 1981

DEPARTMENT OF CLINICAL INVESTIGATION

Little, J.S.: Binding of Insulin to Hepatic Nuclei Isolated from Streptococcus pneumoniae Infected Rats and Subsequent Effect on RNA Synthesis. HSC Annual Clinical Invstigation Conference, Sep 81, San Antonio, TX

Plymate, S.R.: Bimodal Effects of Opiates in LH Secretion in the Primate. HSC Annual Clinical Investigation Conference, Sep 81, San Antonio, TX.

Plymate, S.R., Fariss, B.L., Dresner, M.L., Garrison, M.J., and Matej, L.A.: The Incidence of Testicular Dysfunction in Impotence. Second Annual Meeting of the Society of Military Endocrinologists, 17 June, 1981, Cincinatti, OH.

Plymate, S.R., Fariss, B.L., Matej, L.A., and Bassett, M.L.: Effects of Obesity on Sex Steroid Binding Globulin in Polycystic Ovarian Disease. Pacific Coast Fertility Society, 17 Oct 80, Scottscdale, AZ. Abstract: Fertil Steril 34: 299, Sep 80.

Plymate, S.R., Przasnyski, E.J., Bassett, M.L., and Fariss, B.L.: Mechanism of Antiandrogen Effects of Cimetidine. Western Society for Clinical Research, Feb 81, Carmel, CA. Abstract: Clin Res 28(4):721A, Oct 80 and Clin Res 29(1): 84A, Feb 81.

Plymate, S.R., Ward, G.S., Fariss, B.L., Matej, L.A., and Garrison, M.J.: Mechanisms of Prolactin Regulation of Testicular Function. The Endocrine Society Meeting, 17 June 1981. Abstract: Abstracts of Endocrine Society Meeting, #56, p 96.

Ward, G.S. and Jacob, W.H.: Effects of Naloxone on Hypotension in the Pig-Tailed Monkey. HSC Annaul Clinical Investigation Conference, Sep 81, San Antonio, TX.

Ward, G.S., Fariss, B.L., Liebenberg, S.P., and Hayes, J.E.: Elevation of Blood Sugar Associated with Stress of Handling in the Rabbit. HSC Annual Clinical Investigation Conference, Sep 81, San Antonio, TX.

DEPARTMENT OF EMERGENCY MEDICINE

Dice, W.M.: Kerosene Ingestion. Univ Assoc Emergency Medicine Ann Meeting, Apr 81, San Antonio, TX.

Dice, W.M., Kerosine Ingestion. Amer Coll Emerg Phys, Sep 81, New Orleans, LA.

DEPARTMENT OF FAMILY PRACTICE

Madlon-Kay, D.J., McClain, J.B.L., and Crumrine, M.H.: Gonorrhea Screening in Women: When Is It Cost Effective? American Academy of Family Practice, Sep 81, Las Vegas, NV, Outstanding Exhibit.

DEPARTMENT OF MEDICINE

Chadband, R.B. Reed, J.W., and Fariss, B.L.: HDL-Cholesterol and Glucose Tolerance Tests in Young Male Survivors of Myocardial Infarctions. Second Annual Meeting of the Military Endocrinologists Meeting, 17 June, 1981, Cincinatti, OH. Abstract: Abstracts of Military Endocrinologists Meeting, 1981, p 4.

Clayton, W.K., Gibbons, R.B., Randolph, K.A., and Bulley, W.A.: Synovial Fluid Following Meniscectomy - A Prospective Study. Present Concepts in Internal Medicine Conference sponsored by ACP, Letterman Army Medical Center, Oct 80.

Pangaro, L.N., Little, J.S., Fariss, B.L., and Burman, K.D.: Binding of L-Thyroxine (T_4) and L-Triiodothyronine (T_3) to Purified Rat Liver Plasma Membranes: Changes in Hyperthyroidism and Fasting. American Thyroid Association, 18 Sep 81, Minneapolis, MN, p T-17 of abstracts.

DEPARTMENT OF PEDIATRICS

Alden, E.R.: Children in the ER - Whose? Triservices Pediatric Meeting, Mar 81, San Antonio, TX.

Alden, E.R., Bascom, J., and Walsh, M.: Children in the ER - Whose Patients? American Academy of Pediatrics, Oct 80, Detroit, MI, Abstract #S-24.

Byrne, M., Guller, B., and Alden, E.R.: Electrocardiographic Abnormalities in Critically Ill Children Without Heart Disease. American Academy of Pediatrics, Military Section, Detroit, MI, Oct 80.

Marinelli, P.B.: Artificial Ventilation of the Newborn. 25th Annual Osteopathic Research Meeting, Mar 81, Chicago, IL.

Marinelli, P.V., Pettett, P.G., and Alden, E.R.: Manual Ventilation of the Newborn. An Analysis of Equipment and Technique. 16th Annual Uniformed Services Pediatric Seminar, March 1981, San Antonio, TX.

Marinelli, P.V., Pettett, P.G., and Alden, E.R.: Manual Artificial Ventilation of the Newborn. American Academy Pediatrics Perinatal Seminar, District VIII, June 1981, Cour d'Alene, ID.

Presentations: Department of Pediatrics (Cont)

Marinelli, P.V.,, Pettett, P.G., Alden, E.R., Wickham, L., and Ward, G.S.: The Effect of Steroid Dose on Pulmonary Function of Multiple Gestation Premature Lambs. 16th Annual Uniformed Services Pediatric Seminar, Mar 81, San Antonio, TX.

Pettett, P.G. and Marinelli, P.V.: The Effect of Sampling Site on the White Blood Cell Count in Neonates. Aspen Military Perinatal Seminar, July 1981, Aspen, CO.

Yeatman, G.W. and Sujansky, E.: Thumb Adduction Deformity in X-Linked Mental Retardation Without Hydrocephalus. American Academy of Pediatrics, Military Section, Oct 80, Detroit, MI.

DEPARTMENT OF SURGERY

Camp, R.A.: Repair of Post-Traumatic Hyperextensionnn of the Metacarpophalangeal Joint of the Thumb. 44th Annual Meeting of the Western Orthopedic Association, Oct 80, Honolulu, HI.

Camp, R.A. and Callahan, M.J.: Ball and Socket Interphalangeal Joint Arthrodesis. Western Orthopedic Association, Oct 80, Honolulu, HI.

Wells, J., Gernon, W.H., Ward, G.S., Davis, R.K., and Hays, L.L.: Otosurgical Model in the Guinea Pig (Cavis porcellus)., American Academy of Otolaryngology-Head and Neck Surgery, Sep 81, New Orleans, La.

Hays, L.L., Novack, A.J., and Worsham, J.C.: The Frey Syndrome, A Simple Effective Treatment. American Academy of Otolaryngology Meeting, Sep 81, New Orleans, LA.

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OFFICE OF THE 9TH DIVISION SURGEON

DEPARTMENT OF EMERGENCY MEDICINE

DEPARTMENT OF FAMILY PRACTICE

DEPARTMENT OF MEDICINE

DEPARTMENT OF NURSING

DEPARTMENT OF OB/GYN

DEPARTMENT OF PATHOLOGY

DEPARTMENT OF PEDIATRICS

PHYSICAL MEDICINE AND REHABILITATION SERVICE

PREVENTIVE MEDICINE ACTIVITY

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DEPARTMENT OF SURGERY

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PEDIATRIC ONCOLOGY BRANCH PROTOCOLS

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

F O R

P R O T O C O L S

DEPARTMENT OF CLINICAL INVESTIGATION

TITLE: Renal Glycosuria: Evaluation of Renal Function, Carbohydrate Metabolism and Possible Development of Diabetes Mellitus

PRINCIPAL INVESTIGATOR: COL Bruce L. Fariss, MC

PROFESSIONAL ASSISTANT: None

WORK UNIT NO: 69/01

TECHNICAL OBJECTIVE

To study patients with renal glycosuria in an attempt to further classify these patients. More importantly, we shall attempt to distinguish those patients who may develop diabetes mellitus by studying responses to oral glucose and intravenous glucose and tolbutamide with measurement of blood and urine glucose and insulin levels. The patients will be reevaluated at yearly intervals up to five years to determine the incidence of diabetes mellitus.

METHOD

Forty patients who are found to have flat or normal oral glucose tolerance tests with renal glycosuria shall be evaluated.

Day 1: History, physical examination, routine CBC, chest x-ray, STS, regular hospital diet (300 gm CHO).

Day 2: Twenty-four hour urine for Na, K, CO_2, Cl_2, Ca, P, SGOT, alkaline phosphatase, BUN, creatinine, uric acid and serum electrophoresis. Urinary pH measured at each voiding.

Day 3: Oral glucose tolerance blood and urine glucose and plasma insulin levels.

Day 4: Intravenous glucose tolerance test (25 gm), blood and urine glucose and plasma insulin.

Day 5: Infusion of glucose, intravenous to calculate the splay (renal tubular reabsorption as a function of lead presented to the tubule). Inulin and endogenous creatinine clearances to be done in conjunction with the glucose infusion.

Day 6: Day of rest.

Renal Glycosuria - Fariss

Day 7: Tolbutamide tolerance test (1.0 gm I.V.) specimens for glucose and insulin at 0, 2, 15, 30, 45, 60, 90, 120, 150, and 180 minutes.

Days 8, 9, and 10: NH/Cl loading p.o. with measurement of hydrogen secretory capacity, net acidification and ammonia production each day.

PROGRESS

(80 10 - 81 09) At the conclusion of 12 years, ten of the original 40 patients can be located. During the first five years of this evaluation, two individuals developed diabetes mellitus. Insulin response in approximately 1/4 of the individuals is markedly elevated. There was no correlation of responses within the group.

STATUS: (C)

TITLE: The Effects of Chronic Hyperglycemia on Pregnancies and Fetuses in Sheep During Gestation

PRINCIPAL INVESTIGATOR: COL Bruce L. Fariss, MC

PROFESSIONAL ASSISTANTS: LTC Paul B. Jennings, VC
LTC George S. Ward, VC

WORK UNIT NO: 74/06

TECHNICAL OBJECTIVE

The objectives of this project are to determine the effect of hyperglycemia upon pregnancies as manifested by frequency of abortions and hydramnios and possible developmental abnormalities of the fetuses.

METHOD

The study will be composed of three groups of pregnant ewes with as close proximity of the date of conception as possible. All groups will be given food and water ad lib.

1. The control group will be comprised of six animals with no treatment.

2. Group #2 will be composed of seven animals which have undergone subtotal pancreatectomy. The diabetes mellitus produced surgically will be managed by the injection of intermediate acting insulin such as NPH. Blood sugars will be monitored frequently as indicated clinically.

3. The third group will be composed of seven animals which have indwelling catheters for infusion of hypertonic sugar solutions with a lambda infusion system. The systems are portable, weighing less than 3 lbs and can be strapped to the backs of the animals without difficulty. Blood sugars will be monitored at frequent intervals with an attempt to keep blood sugars between 200 and 300 mg/100 ml of blood at all times.

The course of the pregnancies will be observed for each group of animals. Blood sugars for each group will be determined at frequent intervals during the gestation. At delivery the neonate will be examined pathologically for evidence of pulmonary, liver, pancreatic, kidney, and possible developmental abnormalities.

The Effects of Chronic Hyperglycemia - Fariss

PROGRESS

(80 10 - 81 09) It has been observed that total pancreatectomy in sheep does not produce diabetes mellitus. However, intravenous glucose does show an abnormal utilization.

As a side line, serum zinc levels have been studied and found to be increased in animals following total pancreatectomy or ligation of the pancreatic duct in contrast to normal animals.

STATUS: (O)

TITLE: Adrenal Hyperplasia in Pacific Salmon

PRINCIPAL INVESTIGATOR: COL Bruce L. Fariss, MC

PROFESSIONAL ASSISTANTS: LTC Stephen Plymate, MC

WORK UNIT NO: 80/01

TECHNICAL OBJECTIVE

To determine if the administration of a salt-retaining hormone, desoxycorticosterone, will prevent adrenal gland hyperplasia in the Pacific salmon and to determine if the Pacific salmon can spawn and survive.

METHOD

It is proposed that a total of 20 Pacific salmon be captured while in salt water. These fish are to be sexually mature and will be retained in holding pens. Half of the fish will be treated with desoxycorticosterone in oil, intramuscularly. Blood samples will be obtained from the fish for the measurement of plasma hydroxycorticosteroid, desoxycorticosterone, and aldosterone. Following the administration of the desoxycorticosterone, all of the fish (treated and controls) will be placed in a holding tank until spawning occurs. Following spawning, the fish will be returned to the holding pen in the salt water for follow-up observations of survival.

PROGRESS

(80 10 - 81 09) A comparison of adrenal functions is being made between the Pacific salmon and trout. ACTH stimulation tests are being employed.

STATUS: (O)

TITLE: Evaluation of the Cyclic Nature of Human Semen Content

PRINCIPAL INVESTIGATOR: MAJ Willis H. Jacob, MSC

PROFESSIONAL ASSISTANTS: CPT Michael L. Smith, MSC
Robert Modarelli, M.D., LTC, MC (Ret)

WORK UNIT NO: 78/34

TECHNICAL OBJECTIVE

To determine semen quality by measuring sperm count, sperm motility, sperm morphology, and various constituents of seminal fluid. These findings will then be analyzed for cyclic patterns.

METHOD

1. Test Subjects: Twenty to thirty healthy volunteers will be selected from the 9th Infantry Division or the 62nd Medical Group. Selection will be based on physical examination and medical history. Individuals will be excluded from the project for any of the following reasons: evidence of active venereal disease; a history of testicular varicocele; currently using the sauna on a regular basis; currently taking any medication; any adverse finding during the physical examination. Volunteers will abstain from the use of alcohol and other drugs throughout the semen collection phase of the project. Volunteers will abstain from sexual intercourse for a period beginning 48 hours before collection of the first semen sample and extending throughout the sample collection period.

2. Semen Collection and Analysis: Semen samples will be collected daily for a period of 20 to 25 days. Samples will be collected during a specified 30-minute period each day. The semen, obtained through masturbation, will be ejaculated directly into plastic containers which are free of trace metals. The samples will be allowed to liquefy for one hour at room temperature (240°C). The liquefied samples will be measured for volume and color, and then will be divided into two portions. One portion will be assayed immediately for viscosity, sperm count, sperm motility, and sperm morphology. The other portion of the samples will be centrifuged and the sperm-free seminal fluid will be retained for assay of seminal fluid constituents to include prostaglandins, gonadotropins, trace metals, and carbohydrates.

Evaluation of the Cyclic Nature of Human Semen Content - Jacob

PROGRESS

(78 04 - 81 09) Twelve healthy young men obtained daily semen specimens for 20 days. There were wide variations in sperm density, semen volume, and total count in each subject. Percentage of oval forms was the most stable semen factor. Significant positive correlations were found between sperm density and total counts in ten subjects and between total count and semen volume in eight subjects. However, when all specimens from all subjects were combined there were significant positive correlations between sperm density and total count, total count and semen volume, and total count and percentage of oval forms. There was a significant negative correlation between sperm density and the semen volume. No cyclic, or regular, pattern could be detected in any of the subjects.

The investigators plan further experiments when a new population can be obtained.

STATUS: (O)

PRESENTATION: Jacob, W.H., Smith, M.L., Plymate, S.R., and Cricco, C.F.: Daily Variations in Human Semen Quality. Pacific Coast Fertility Society Meeting, October 1979.

TITLE: Correlation of the Effects of Semen Sperm Count and Prostaglandin Content on Fertility in Human Males

PRINCIPAL INVESTIGATOR: MAJ Willis H. Jacob, MSC

PROFESSIONAL ASSISTANTS: CPT Michael L. Smith, MSC
MAJ Jeffrey S. Rakoff, MC
Robert Modarelli, M.D., LTC, MC (Ret)

WORK UNIT NO: 78/45

TECHNICAL OBJECTIVE

To compare the semen quality of men of known fertility to that of men who are apparently infertile. The parameters of semen quality will be sperm count, sperm motility, sperm morphology, sperm viability, seminal prostaglandins, seminal fructose, seminal zinc, seminal gonadotropins. and gonadal steroids. Seminal prostaglandin content will be compared with each of these parameters.

METHOD

Semen specimens will be collected from 20-25 volunteers of known fertility and from 20-25 volunteers with apparent infertility. Following a urological evaluation, each volunteer will be asked to provide three semen specimens. Each volunteer will provide a semen specimen following a 48-hour period of abstinence from sexual activity. Subsequent samples, obtained at the end of a 48-hour abstinence period, will be given at one-week intervals for a two-week period. Each volunteer will ejaculate directly into a plastic container which is free of trace metals. The specimens will be analyzed for volume, color, sperm count, sperm motility, sperm morphology, prostaglandins E, prostaglandins F, and various other seminal fluid components such as fructose, zinc, gonadotropins, and gonadal steroids.

PROGRESS

(78 06 - 81 09) Efforts are being made to obtain a significant number of subjects to complete this study. Also, the efficacy of HPLC in assaying the prostaglandins is being evaluated.

STATUS: (O)

PUBLICATION: Fariss, B.L., Fenner, D.K., Plymate, S.R., Brannen, G.E., Jacob, W.H., and Thomason, A.M.: Seminal Characteristics in the Presence of a Varicocele Compared to Expectant Fathers and Pre-Vasectomy Individuals. Fertil Steril 35:325-27, 1981.

TITLE: Effects of Exogenous Iodine on the $^{I}123$ Uptake of Patients with Hyperthyroidism and an Elevated $^{I}123$ Uptake

PRINCIPAL INVESTIGATOR: LTC Stephen R. Plymate, MC

PROFESSIONAL ASSISTANTS: COL Stanton Brown, MC
COL Bruce L. Fariss, MC
LTC K. David McCowen, MC
MAJ Martin L. Bassett, MC
MAJ Robert Chadband, MC

WORK UNIT NO: 80/12

OBJECTIVE

To determine if exogenous iodine can be a cuase of depressed iodine uptake in patients with classic, that is high, iodine uptake type hyperthyroidism.

METHOD

Ten patients with hyperthyroidism as documented by elevated T^4, T^3RIA, and FTI levels with $^{I}123$ uptakes above the upper limit of normal (25% at 24 hours) will have total serum iodine and 24 hour urinary iodine measurements performed. When these samples are collected, the patients will be given 500 µgm of iodine a day as SSKI for 10 days and the $^{I}123$ uptakes, serum T^4, T^3RIA, and free thyroxin index measurements and the 24 hour urinary iodine measurements will be repeated. SSKI has been used for short term treatment of patients with hyperthyroidism, and the use of this drug in treatment of these patients would therefore not be experimental. The administration of SSKI will delay definitive treatment of the hyperthyroidism for at least 10 days if the patient requests surgery. If $^{I}131$ treatment is requested, there will be a delay of definitive treatment of three weeks. During this time, propranolol will be used for symptomatic control. The Student's t Test will be used for data analysis.

PROGRESS

(80 01 - 81 09) This protocol was terminated due to the small number of patients that was available and to time constraints upon the investigators due to the departure of two of the co-investigators.

STATUS: (T)

TITLE: Evaluation of Phosphate Deprivation on Renal Calcium Metabolism in Patients with Idiopathic Hypercalciuria and Calcium Nephrolithiasis

PRINCIPAL INVESTIGATOR: LTC Stephen R. Plymate, MC

PROFESSIONAL ASSISTANTS: LTC William D. Belville, MC
LTC Timothy F. McNamara, MC
CPT Jeannie Gallo, SP
1LT Joye Bucklin, SP, USAR
David Baylink, MD

WORK UNIT NO: 80/20

TECHNICAL OBJECTIVE

To evaluate the effects of phosphate depletion on renal tubular calcium conservation.

METHOD

Male patients with the diagnosis of idiopathic hypercalciuria on at least two occasions with no secondary disease causing hypercalciuria will be asked to collect six consecutive 24 hour urines in 2 portions: (1) urine excretion after the first morning void and throughout the day and evening; and (2) the first morning void completing the 24 hour period, and blood samples will be drawn fasting. After the first day of collection, the subjects will be placed on a diet containing 190 mg phosphate/day for 5 days. Assays to be performed on serum samples include total serum calcium, ionized serum calcium, serum inorganic phosphate, serum magnesium, serum creatinine, serum CO2, serum chloride, phosphokinase, serum 24,25 dihydroxycholecalciferol, 1,25 dihydroxycholecalciferol, immunoreactive parathyroid, and immunoreactive calcitonin. The assays performed on 24 hour urine samples will include calcium, phosphate, creatinine magnesium, pH, and cyclic AMP. The phosphate content of the diet will be determined by ashing. Those subjects on medication for hypercalciuria will discontinue it for at least 3 weeks prior to the study. Control subjects will be age-matched male volunteers without a prior history or relative with a history of idiopathic hypercalciuria or renal stones.

PROGRESS

(80 02 - 81 09) This protocol was terminated due to the PCS of the investigators and the inability of the investigators to coordinate the project (done in conjucntion with American Lake Veteran's Hospital) due to time and location restrictions.

STATUS: (T)

TITLE: Effects of Testosterone and Estrogen Administration on Endorphin and Enkephalin Release in the Human Female

PRINCIPAL INVESTIGATOR: LTC Stephen R. Plymate, MC

PROFESSIONAL ASSISTANTS: COL Bruce L. Fariss, MC
CPT Allan F. Avbel, MC

WORK UNIT NO: 80/69

OBJECTIVE

To determine if women with polycystic ovary disease syndrome have an abnormal or dichotomous response in the release of endorphin and enkephalin and if this response is mediated by the gonadal steroids.

METHOD

Five women with normal weight and normal ovulation, as determined by basal body temperature, histories, and/or progesterone levels during the luteal phase of the menstrual cycle, will be given 25 mg of testosterone proprionate IM in the early follicular phase of the cycle (within the first three days after cessation of menstruation) and will again be given testosterone proprionate, 25 mg IM, during the mid-luteal phase which will be counted as days 21 to 23 following the onset of menstruation. Three blood samples will be drawn 15 minutes apart on the day before and the day after administration of the testosterone proprionate. Samples will be assayed for LH, FSH, progesterone, testosterone, β-lipotropin, and β-endorphin. Data analysis will be by Student's t test.

PROGRESS

(80 09 - 81 09) This study has been completed and an abstract is being prepared for submission to the Endocrine Society.

STATUS: (C)

TITLE: Mechanism of HCG in Spermatogenesis During Testosterone Suppression

PRINCIPAL INVESTIGATOR: LTC Stephen R. Plymate, MC

PROFESSIONAL ASSISTANTS: COL Bruce Fariss, MC
LTC George Ward, VC
Mina Garrison, MT
Louis Matej, MT

WORK UNIT NO: 80/70

OBJECTIVE

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

METHOD

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

PROGRESS

(80 07 - 81 09) The study has demonstrated that T and HCG are additive in depressing testicular steroidogenesis and seminiferous tubule function. More studies are planned.

STATUS: (O)

PRESENTATION: Mechanisms of Prolactin Regulation of Testicular Function; Endocrine Society Meeting, 17 Jun 81. Abstract #56, p.96.

TITLE: Effect of Obesity on the Sex Steroid Binding Globulin (SSBG) Response to Estrogen in the Post-Menopausal Female

PRINCIPAL INVESTIGATOR: LTC Stephen R. Plymate, MC

PROFESSIONAL ASSISTANTS: COL Bruce L. Fariss, MC
LTC Richard Belts, MC
Edna Backup, M.D., DAC
Cynthia Quashie, R.N., DAC
Lavell Aloisio, R.N., DAC
Mina Garrison, M.T., DAC
Louis Matej, M.T., DAC

WORK UNIT NO: 81/27

TECHNICAL OBJECTIVE

It has been demonstrated that the obese female has a low SSBG, seemingly independent of her androgen or estrogen status. The purpose of this study is to determine if the reason for the low SSBG is a decreased production of the protein in response to estrogen.

METHOD

Twenty obese females (>140% IBW) and twenty normal weight females (>80% and <120% IBW) who are being placed on estrogen in the OB/GYN Clinic for post-menopausal symptoms will be studied. Prior to estrogen therapy the patients will have had LH/FSH, TSH, prolactin, estradiol, estrone, testosterone, and SSBG levels drawn. Four weeks after being placed on estrogen, the studies will be repeated. Statistics will be determined by Student's t test and linear regression analysis.

PROGRESS

(80 12 - 81 09) The technical portion of the project is completed and a manuscript has been started. Approximately 30 patients were studied.

STATUS: (C)

TITLE: Hormonal Determinants of Impotence

PRINCIPAL INVESTIGATOR: LTC Stephen R. Plymate, MC

PROFESSIONAL ASSISTANTS: COL Bruce L. Fariss, MC
Mina Garrison, M.T.
Louis Matej, M.T.

WORK UNIT NO: 81/28

TECHNICAL OBJECTIVE

To determine the frequency of gonadal disorders in impotent men.

METHOD

One hundred males will be studied in succession who present for impotence and subsequently have testosterone levels drawn. This biases the study since the physician has determined that the patient needs a testosterone level. However, if a high incidence of testosterone deficiency it to be found, it would be suspected that this would be the group in which the high incidence would be found. Blood samples will be analyzed for lack of LH/FSH, testosterone, and estradiol. Results will be subjected to analysis of variants, Student's t test, and linear regression analysis.

PROGRESS

(80 12 - 81 09) Fifty men presenting consecutively for impotence were studied. Primary and secondary gonadal failure was found as a cause of impotence in 12% of the patients. The changes in testosterone levels were associated with higher prolactin levels in the younger patients and higher SHBG levels in the older subjects.

STATUS: (C)

PRESENTATION: Second Annual Military Endocrinologists Meeting, 17 June 1981, Cincinatti, OH.

TITLE: Use of Sex Steroid Binding Globulin as a Predictor of Response to Endocrine Therapy in Breast Carcinoma

PRINCIPAL INVESTIGATOR: LTC Stephen R. Plymate, MC

PROFESSIONAL ASSISTANTS: COL Friedrich H. Stutz, MC
COL Dick R. Smith, MC
MAJ Lauren Colman, MC
MAJ Allan Avbel, MC
Louis Matej, M.T., DAC

WORK UNIT NO: 81/39

TECHNICAL OBJECTIVE

To determine if measurement of sex steroid binding globulin (SSBG), which when elevated indicates increased estrogen effect in a person, will be helpful in determining response from hormonal manipulations in breast carcinoma. Estrogen receptors in breast carcinoma are reliable in predicting a positive response to estrongen therapy 50% of the time. Even with the addition of progesterone receptors this prediction of response approaches only 65% and once the tumor has been removed, if there are further metastatic lesions, the ability to perform the receptor assay is no longer possible.

METHOD

Patients who come to surgery for breast cancer will have a serum measured for SSBG and the tumor measured for estrogen receptors. These two measurements will be compared to subsequent response of estrogen therapy. Patients, post-surgery, in whom the tumor is not available but are being subjected to endocrine manipulative therapy (anti-estrogen, Tamoxifen or diethylstilbestrol) or ablative endocrine therapy will also have SSBG levels drawn and measured. Patients will then be followed to determine the response to therapy and its relation to SSBG. Initially, 20 patients in each category will be studied.

PROGRESS

(81 02 - 81 09) The technical portion of the project has been completed with 80 patients studied. The data are now being evaluated and an abstract in being written.

STATUS: (C)

TITLE: Testosterone and HCG Effects on Testicular Steroidogenesis

PRINCIPAL INVESTIGATOR: LTC Stephen R. Plymate, MC

PROFESSIONAL ASSISTANTS: COL Bruce L. Fariss, MC
MAJ Stanely Liebenberg, VC
MAJ Allan Avbel, MC
SSG James Hayes
Louis Matej, B.S.

WORK UNIT NO: 81/92

TECHNICAL OBJECTIVE

To determine the mechanism of inhibition of intertesticular testosterone production by HCG and testosterone.

METHOD

Six groups of adult male Wistar rats >250 gm will have baseline serum drawn for LH, FSH, and testosterone. All animals will be kept on a 14 hour light, 10 hour dark cycle. Group A will receive sesame oil twice weekly for 12 weeks. Group B will receive 150 µgm/100 gm BW testosterone enanthate twice weekly for 12 weeks. Group C will receive 150 µgm/100 gm BW testosterone enanthate twice weekly for six weeks and the same regimen plus 18 U HCG QD for an additional six weeks. Group D will receive 300 µgm/100 gm BW testosterone enanthate for six weeks and the same regimen plus 18 U HCG QD for an additional six weeks. Group E will receive 150 µgm testosterone enanthate/100 gm BW plus 18 U HCG twice weekly for six weeks, and the same regimen plus the addition of Teslac 5 µgm daily for six more weeks. Group F will receive 150 µgm testosterone enanthate/100 gm BW twice weekly for six weeks and then 18 U HCG daily plus 10 mg Teslac twice a day for six weeks. After the 12 weeks, blood will again be drawn, the animals sacrificed, the testes and epididymis removed, weighed, and frozen. Intratesticular DHT, E_2, and ABP will be measured in the testicle and androgen binding protein measured in the epididymus. Histology will be performed to include mean seminiferous tubule diameters.

PROGRESS

(81 07 - 81 09) Animals have been acquired and the investigators have begun the administration of the agents.

STATUS: (O)

TITLE: The Effect of Opiates on the Release of Gonadotropins in the *Macaca nemestrina*

PRINCIPAL INVESTIGATOR: LTC Stephen R. Plymate, MC

PROFESSIONAL ASSISTANT: MAJ Stanley P. Liebenberg, VC

WORK UNIT NO: 81/93

TECHNICAL OBJECTIVE

To further study the effects of endorphins on the hypothalamic-pituitary gonadal axis of the *Macaca nemestrina* monkey. Opiate compounds have been shown to release LH from the glands of humans. It is well known that the morphine addicted human can become hypogonadotropic.

METHOD

Six female *Macaca nemestrina* monkeys will be addicted to morphine. When they become amenorrheic with maintenance of their weight by appropriate food supplement and have not lost significant body weight, gonadotropins will be drawn every 10 min for 1 hr and 20 min. Next, a bolus of naloxone will be given and samples drawn for 120 min. The animals will be continued on morphine and 2 weeks later given a bolus of LH releasing hormone with samples for gonadotropins drawn every 10 min for 120 min. The animals will then be withdrawn from the morphine and again a bolus of naloxone will be administered during the luteal phase of the menstrual cycle with serum samples drawn every 10 min for 120 min before and after administration of naloxone. Samples will be assayed for progesterone to determine the point of time in the menstrual cycle and menstrual cycle timing will be determined by watching sex skin swelling. LH will be measured by Leydig cell bioassay. Data will be analyzed by appropriate T test and linear regression.

PROGRESS

(81 07 - 81 09) The investigators are now in the process of addicting the animals.

STATUS: (O)

PRESENTATION: Bimodal Effects of Opiates in LH Secretion in the Primate. HSC Annual Clinical Investigation Conference, Sep 81, San Antonio, TX.

TITLE: Development of Teaching Models for Microvascular Anastomosis, Microneural Reconstruction and Tissue Reimplantation

PRINCIPAL INVESTIGATOR: LTC George S. Ward, VC

PROFESSIONAL ASSISTANT: None

WORK UNIT NO: 78/11

TECHNICAL OBJECTIVE

To develop teaching models for instruction and perfection of residents or staff in the field of microsurgery.

METHOD

Different species of laboratory animals and anatomical areas will be evaluated to determine which offer the least technical difficulties. Those models which are most successful will then be perfected for end to end and end to side arterial anastomosis. If interest and demand continue, models for microneural reconstruction and tissue reimplantation will also be developed. Various steps will be documented with photography. Contrast radiography will be used to demonstrate vascular patency.

The models developed under this protocol will be used to familiarize residents or other personnel with microsurgical techniques or to refresh staff proficiency prior to clinical application.

PROGRESS

(77 12 - 81 09) The investigator continued to develop new techniques and to refine old ones during the year. With the approval of new protocols from different departments within the hospital for teaching microsurgery techniques to both staff and residents, this protocol has met its objective.

STATUS: (C)

Development of Teaching Models for Microvascular Anastomosis, Microneural Reconstruction, and Tissue Reimplantation - Ward

PRESENTATION:

Wells, J.R., Ward, G.S., Eckland, D., Jackson, S., and Hays, L.L.: Opportunities in Microvascular Anastomosis: A Self-Instructional Method. Annual Meeting of the American Academy of Otolaryngology, 28 Sep - 2 Oct 80, Anaheim, California. Scientific Exhibit #SE-27.

ABSTRACT:

IBID, Otolaryngology, Head and Neck Surgery 88:214, 1980.

TITLE: Level of Anesthetic Gases in Local Veterinary Operating Rooms

PRINCIPAL INVESTIGATOR: LTC George S. Ward, VC

PROFESSIONAL ASSISTANTS: CPT Michael L. Smith, MSC
CPT Robert R. Byland, MSC

WORK UNIT NO: 79/11

TECHNICAL OBJECTIVE

To determine the level of exposure to anesthetic gases by operating room personnel in local veterinary hospitals and to evaluate the efficacy of waste anesthetic gas scavenging systems in use.

METHOD

Levles of halothane or metophane during scheduled operations under normal conditions will be monitored. If a scavenging system is present, levels will be monitored during its usage and after it is discontinued to determine effectiveness. A Milan Infrared Portable General Purpose Gas Analyzer will be used. If levels of anesthetic gases are consistently too low to be accurately determined by the Milan Gas Analyzer, gas chromatography will be utilized.

PROGRESS

(78 11 - 81 09) The surgery rooms of 14 private veterinary practices were monitored during surgery under routine working conditions to determine methoxyflurane (MOF) concentrations. Four of the fourteen rooms exceeded the maximum recommended concentration of 2 ppm. The average time spent in surgery was 2 hours. Nitrous oxide concentrations were determined in four veterinary surgery rooms. The average N_2O concentration for three rooms without waste anesthetic gas scavenging was 138 ppm. Contration of N_2O in the waste anesthetic gas scavenged surgery room was 14 ppm which was below the maximum recommended concentration of 25 ppm. Fourteen surgeries and three treatment rooms were monitored for ambient levels of halothane. Ten of the 17 rooms reached levels exceeding the NIOSH recommended maximum of 2 ppm. Rooms with scavenging devices averaged 1.4 ppm whereas unscavenged averaged 5.2 ppm. It is recommended that veterinary facilities monitor their operating rooms and install scavenging equipment to obtain the least waste anesthetic gas exposure possible.

Two articles have been written from the data obatined on this protocol and have been accepted for publication by the Journal of the American Veterinary Medical Association.

STATUS: (C)

TITLE: Xyladrol Evaluation in the Primate (*Macaca nemestrina*)

PRINCIPAL INVESTIGATOR: LTC George S. Ward, VC

PROFESSIONAL ASSISTANTS: LTC Stephen R. Plymate, MC

WORK UNIT NO: 79/93

TECHNICAL OBJECTIVE

To determine if Xyladrol, an investigative veterinary pre-anesthetic/anesthetic agent, is potentially addictive, utilizing a morphine addicted pig-tailed macaque as a test animal, and to determine if any toxicity is evidenced at a continuous clinical usage rate.

METHOD

Phase 1: One monkey will be addicted to morphine and spontaneous withdrawal signs will be noted. Decreasing alleviating doses may be administered as necessary. This phase will allow observing personnel to become familiar with the ten signs of the morphine abstinence syndrome and determination of the dosage of morphine for addiction in the *Macaca nemestrina*. During this phase, a chart will be constructed to grade the degree of withdrawal symptoms.

Phase 2: Six monkeys will be addicted to morphine by the rapid addiction method at a level determined in Phase 1. The maintenance level will probably approach 12-15 mg/kg, which will be given in divided intramuscular doses BID. Substitution for morphine will then be attempted with three test substances. Xyladrol (the formulation utilized throughout this study will be 15 mg xylazine and 5 mg etoxadrol per milliliter) will be administered at the following levels: 0.025; 0.05; 0.1; 0.2; and 0.4 ml/kg. Codeine will be administered in two trials each at: 3, 6, and 12 mg/kg. Saline will be the placebo treatment. Morphine antagonistic effect will also be determined. Three test substances will be used; Xyladrol and saline at the same doses as above, and Levallorphan tartrate (Lorfan-Roche) at 0.05; 0.1 and 0.3 mg/kg. A scoring card or chart will be kept on each monkey for each trial. At least one day on normal morphine maintenance will separate each trial. Menstrual cycles will be monitored and levels of estrogen, FSH, and LH will be determined weekly. LH-RH will be administered at various stages of addiction. The morphine substitution and antagonistic study is required to satisfy FDA suggestions for data to be submitted by development companies. Following the study, addicted monkeys will be gradually weaned by decreasing doses of morphine.

Xyladrol Evaluation in the Primate - Ward

Phase 3: Six different monkeys will be given a clinical dosage of Xyladrol for a period of 21 consecutive days. Clinical signs and evidence of neurological changes or addiction will be noted. Serum chemistries will be done at days 0,2,4,6,13, and 21. Complete blood counts will be done on days 0,4,13,18, and 21. Urinalysis will be done on days 0,7,14, and 21. Ophthalmologic examinations will be done on days 0,7,14, and 21. Body weights will be recorded weekly. Menstrual cycles will be monitored and serum estrogen, FSH, and LH will be determined weekly. If changes are noted in any parameters, these will be followed every 14 dyas for 2-3 months or return to normalcy in 3 monkeys. The other 3 monkeys will continue Xyladrol treatment at increasing doses similar to the rapid morphine addiction schedule to determine if addiction develops. Complete histopathology will be performed on any animal that might expire.

PROGRESS

(79 09 - 81 09) This protocol has been completed. The following conclusions pertain to the *Macaca nemestrina* as it was the only animal utilized. (1) There is no substitution effect, i.e., withdrawal signs are not abolished when Xyladrol is administered to a morphine dependent monkey after 48 hours of abstinence; (2) Xyladrol does not antagonize morphine. No withdrawal symptoms result when it is administered to a morphine addicted moneky; (3) clinical chemistries are not affected by 21 daily injections of 0.15 ml/kg Xyladrol; (4) There was a 25% decrease in the number of leukocytes with a slight shift to the left after 21 daily Xyladrol injections; (5) no eye lesions were produced as a result of 21 daily Xyladrol injections; (6) the intraocular pressure is less under Xyladrol anesthesia than under ketamine anesthesia; and (7) no withdrawal symptoms were observed in 3 pig tailed macaques after 39 days of Xyladrol administration.

STATUS: (C)

TITLE: Serum Glucose Levels in Restrained vs Non-Restrained Rabbits

PRINCIPAL INVESTIGATOR: LTC George S. Ward, VC

PROFESSIONAL ASSISTANTS: COL Bruce L. Fariss, MC
SSG James Hayes, USA

WORK UNIT NO: 81/14

TECHNICAL OBJECTIVE

To compare serum glucose levels in rabbits at hourly intervals under normal bleeding (stressful) conditions with serum glucose levels in blood obtained by cage bleeding (non-stressful) conditions.

METHOD

Ten New Zealand White rabbits will be anesthetized and a catheter placed in an external jugular vein. Two days later the rabbits will be placed in restraint boxes, the ears irritated to dilate blood vessels, and 4 consecutive hourly blood samples taken. A period of two weeks rest will be given during which the rabbits are handled daily to reduce fear of handling. The rabbits will then be anesthetized and a catheter placed in the contralateral external jugular. Two days later 4 consecutive hourly blood samples will be drawn while the rabbits remain in their cages unrestrained. The samples will be analyzed for levels of glucose, cortisol, and norepinepherine. The differences between the restrained and non-restrained values will be compared by the paired T-text method of statistical analysis.

PROGRESS

(80 11 - 81 09) The process of obtaining blood from rabbits has been observed to cause elevation of blood sugar. This elevation correlates with elevation of the catecholamine levels. Cortisol does not correlate to the blood sugar levels.

The principal investigator will be changed to COL Bruce Fariss due to the PCS of LTC Ward.

STATUS: (O)

PRESENTATION: Ward, G.S., Fariss, B.L., Liebenberg, S.P., and Hayes, J.: Elevation of Blood Sugar Associated with Stress of Handling in the Rabbit. HSC Annual Clinical Investigation Conference, San Antonio, TX, Sep 81.

TITLE: Cervical Esophageal Reconstruction Utilizing a Free Jejunal Graft

PRINCIPAL INVESTIGATOR: LTC George S. Ward, VC

PROFESSIONAL ASSISTANTS: LTC Terence L. Babcock, MC
CPT Wallace E. Taylor, MC
CPT Harry L. Walker, VC
CPT James R. Wells, MC

WORK UNIT NO: 81/38

TECHNICAL OBJECTIVE

To perfect a technique for surgical replacement of damaged cervical esophagus.

METHOD

Six random source conditioned dogs weighing a minimum of 20 kg will be used. Preparation will include NOP 24 hours before surgery, mineral oil, chloromycetin and neomycin per os 12 hours before surgery wtih chloromycetin continuing for 6 days post op. Anesthesia will be induced by IV pentothal and maintained by halothane-oxygen. A standard surgical prep will be followed by sterile procedures as follows: a section of jejunum 20% longer than the resected portion of esophagus will be removed by one surgical team and an intestinal anastomosis performed. The other surgical team will resect a 6 cm segment of cervical esophagus and prepare recipient artery and vein for anastomosis. The jejunal graft will be interposed in the cervical esophagus in an isoperistaltic position. Post operative feeding will be IV for 2 days then by pharyngostomy tube using blended dog food. Evaluation will include esophagoscopy, esophagogram, and histology of anastomosis site at sacrifice.

PROGRESS

(81 01 - 81 06) This protocol had to be terminated due to the departure of the principal investigator and two of the assistants.

STATUS: (T)

TITLE: Effect of Naloxone on Hypovolemic Hypotension in the Pig-Tailed Monkey

PRINCIPAL INVESTIGATOR: LTC George S. Ward, VC

PROFESSIONAL ASSISTANTS: MAJ John B. McClain, MC
MAJ Willis H. Jacob, MSC
CPT Harry L. Walker, VC

WORK UNIT NO: 81/58

TECHNICAL OBJECTIVE

To determine if naloxone, an opiate antagonist with no agonist activity, will reverse endotoxin induced hypotension and hypovolemic hypotension in other species as has been demonstrated in the rat model. The effectiveness of this agent in the dose ranges where it has been used in humans with no ill effects will also be studied.

METHOD

Six monkeys will be given 20 mg of ketamine hydrochloride and then administered halothane via a mask. When a surgical plane of anesthesia is reached, intracaths will be inserted in the femoral artery and vein and systolic, diastolic, and mean blood pressures and electrocardiogram will be recorded simultaneously. Halothane anesthesia will be stopped and when the blood pressure reaches a stable maximum, hypovolemia will be induced by withdrawing blood into heparinized syringes over at least a 20 minute period until a mean of approximately 35-40 mm Hg is reached. This mean will be maintained for a minimum of 20 minutes and then the test solution, either 2 mg/kg naloxone prepared in 2 cc of sterile water or 2 cc saline alone, will be administered. The amount of volume administered will be predrawn to negate volume effect. The blood pressure will be followed for one hour or until stability is reached. If drastic blood pressure decreases occur or death seems imminent, blood readministration will be immediate. After blood pressure measurements have been completed, the blood will be readministered and the catheters removed. Each monkey will serve as its own saline control in a random manner with the trials being at least 30 days apart. Blood pressure data will be analyzed for significance with the Student's t test to compare values post-saline treatment with values post-naloxone administration.

PROGRESS

(81 03 - 81 09) Six monkeys have been studied. The results are inconclusive at this time. More tests will be performed.

STATUS: (O)

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

F O R

P R O T O C O L S

OFFICE OF THE 9TH DIVISION SURGEON

TITLE: Hydrogen Breath Analysis After First Feedings in Infants in Intensive Care Nursery

PRINCIPAL INVESTIGATOR: LTC Charles Mitchell, MC

PROFESSIONAL ASSISTANTS: CPT Richard Meidell, MC
CPT James Little, MSC

WORK UNIT NO: 81/107

TEHCNICAL OBJECTIVES

To determine if there is malabsorption in infants in the intensive care nursery after first feedings and if there is predictive value of impending necrotizing enterocolitis in those infants who have malabsorption.

METHOD

A minimum of 20 patients will be studied before and after one of the initial feedings of formula. Expired air will be obtained at 0, 2, and 4 hours. In infants mechanically ventilated, the air may be obtained via a one-way volume. Non-ventilated infants will have sampling obtained from a catheter nasal apparatus connected to a syringe. Breath hydrogen will be measured by gas chromatograph equipped with a reduction gas detector.

PROGRESS

(81 08 - 81 09) This protocol was approved in August. Personnel and equipment are being assembled and coordinated. The technical portion is exptected to start within a few weeks.

STATUS: (O)

TITLE: Hydrogen Breath Analysis in Normal Newborns

PRINCIPAL INVESTIGATOR: LTC Charles Mitchell, MC

PROFESSIONAL ASSISTANTS: CPT Richard Meidell, MC
CPT James S. Little, MSC

WORK UNIT NO: 81/108

TECHNICAL OBJECTIVE

To determine if normal newborns malabsorb any of their formula feedings.

METHOD

A minimum of 30 patients will have samples taken of expired air. This will be done using a painless catheter apparatus in one anterior nares. The samples will be taken before the first feeding, at 2 hours and 4 hours. Breath hydrogen will be measured by gas chromatograph equipped with a reduction gas detector.

PROGRESS

(81 08 - 81 09) This protocol was approved in August. Personnel and equipment are being assembled and coordinated. The technical portion is expected to start within a few weeks.

STATUS: (O)

TITLE: Hydrogen Breath Analysis in Children with Chronic Non-Specific Diarrhea

PRINCIPAL INVESTIGATOR: LTC Charles Mitchell, MC

PROFESSIONAL ASSISTANTS: MAJ Marsha Van Wagner, ANC
CPT James S. Little, MSC

WORK UNIT NO: 81/109

TECHNICAL OBJECTIVE

To determine if ingestion of various carbohydrates is related to the chronic non-specific diarrhea syndrome; the hypothesis being that malabsorbed carbohydrates act osmotically to increase the fluid content of stools and that malabsorbed molecules are fermented by clonic bacteria producing hydrogen; therefore, hydrogen detected in the breath of previously fasting patients implicates malabsorption and subsequent diarrhea.

METHOD

Subject will be tested, fasting, on three different mornings. First test - cereal given without milk, using water as the fluid; second test - lactose as 20% solution; third test - sucrose. After the feeding the breath will be sampled at 0, 60, and 120 minutes. The breath will be sampled by a large catheter inserted into the anterior nares, a finger pressed against the opposite nares. A smaller tube will be inserted into the larger and attached to a syringe. At mid-expiration, a few ml will be aspirated to a total of approximately 20 ml and insufflated into a vacuum test tube. Breath hydrogen will be measured by gas chromatograph equipped with a reduction gas detector.

PROGRESS

(81 08 - 81 09) This protocol was approved in August. Personnel and equipment are being assembled and coordinated. The technical portion is expected to start within a few weeks.

STATUS: (O)

TITLE: The Prevalence of Cardiovascular Risk Factors in Physically Fit Soldiers

PRINCIPAL INVESTIGATOR: CPT Victoria S. Rains, MC

PROFESSIONAL ASSISTANTS: LTC Stephen R. Plymate, MC
MAJ John M. Harris, Jr., MC
CPT James S. Little, MSC
Mina Garrison, B.S.

WORK UNIT NO: 81/32

TECHNICAL OBJECTIVE

To determine the prevalence of cardiovascular risk factors in young, physically fit service members during usual duty and under severe combat training.

METHOD

The study population will be drawn from a brigade of infantry soldiers who will be evaluated for risk factors prior to a winter field exercise, during the second week of the exercise, and following their return from this exercise. Risk factors to be studied include: HDL cholesterol, total cholesterol, testosterone-estradiol binding globulin, and testosterone-estradiol. The sex steroids are to be studied because of the demonstrated effects of combat training on serum androgens. It has also been shown that serum androgens directly affect the levels of HDL cholesterol. Each subject will answer a questionnaire relating to cardiovascular risk factors. If statistical significance is not obtained on the 100 soldiers tested, a larger number of men will be analyzed.

PROGRESS

(80 12 - 81 09) One hundred patients have been evaluated. The data are now being analyzed.

STATUS: (C)

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

TITLE: Effects of Alcohol on the Hepatotoxic Properties of an Acute Acetaminophen Overdose

PRINCIPAL INVESTIGATOR: CPT Doreen M. Dargon, MC

PROFESSIONAL ASSISTANTS: LTC George S. Ward, VC
CPT James S. Little, MSC

WORK UNIT NO: 81/30

TECHNICAL OBJECTIVES

To evaluate the effects of acute and chronic alcohol on the hepatotoxicity of acetaminophen; to ascertain specific risks or benefits from acute and chronic alcohol ingestion with a concomitant acetaminophen overdose and determine whether mortality varies; and to determine whether glutathione deficiency is the cause of increased or decreased hepatotoxicity when acetaminophen is acutely ingested in the setting of chronic alcohol usage.

METHOD

Phase 1: Phase 1 will be concerned with acute alcohol ingestion. Forty male rats will be divided into 4 groups of equal weight and fed a normal diet and water *ad libitum*. The first group will be a control; the second group will be force fed one predetermined LD50 dose of acetaminophen; the third group will be force fed one dose of alcohol to achieve a serum level of approximately 200 µg/ml; and the fourth group will receive both acetaminophen and alcohol. Rats will be weighed prior to the study and at sacrifice. Liver function tests will be performed to determine baseline values and at 12 hour intervals up to and including 36 hours post ingestion. Rats will be sacrificed at 36 hrs after ingestion and liver weights will be determined and liver sections prepared for light microscopy. A portion will also be fixed in glutaraldehyde for electronmicroscopy if light microscopy proves inadequte. Data will be compared to determine if acute alcohol ingestion alters the hepatotoxic effects of an acute acetaminophen overdose.

Phase 2 - chronic alcohol ingestion. Forty male rats will be used. Group 1 will be force fed alcohol daily for 3 weeks to achieve serum alcohol levels of 200 µg/ml. This will correspond to approximately 40% of their caloric intake per day. The other 60% will be obtained from a normal rat diet. Group 2 will be treated the same as Group 1 plus given a single LD50 dose of acetaminophen after the 3 weeks of alcohol ingestion. Group 3 will be treated the same as Group 2 plus treatment with diethyl maleate to deplete glutathione. Group 4 will be treated with diethyl maleate to deplete glutathione and then force fed an LD50 dose of acetaminophen.

Effects of Alcohol on the Hepatotoxic Properties of an Acute Acetaminophen Overdose - Dargon

Liver function tests will be performed on all rats prior to the experiment to determine baseline values, at 3 weeks after the initiaion of the experiment to determine the effects of alcohol or glutathione depletion, and at 12 hour intervals after the LD50 dose of acetaminophen, up to 36 hours at which time all rats will be sacrificed. Liver weights will be determined and liver sections prepared for light microscopy and electronmicroscopy. Electronmicroscopy will be performed only if no changes are observed with the light microscope. Data will be compared to determine the effects of chronic alcohol ingestion, acetaminophen, and glutathione depletion.

PROGRESS

(80 12 - 81 09) Serum enzyme measurements for SGOT, SGPT, alkaline phosphatase, and 5'nucleodase were performed on approximately 30 animals on several different occasions. Prolonged treatment with ethanol had no significant effect on any of the liver function enzymes measured.

Approximately 30 rats in whom alcoholism had been induced and approximately 30 rats in a control group were given acetaminophen in varying doses. Preliminary results suggest that the ethanol treated animals were not any more susceptible than the controls and, in fact, may be less susceptible.

Further experiments will be done in an effort to validate these preliminary findings.

STATUS: (O)

TITLE: Evaluation of Peak Expiratory Flow Rates as an Early Predictor of Admission for Patients with Acute Bronchospasm

PRINCIPAL INVESTIGATOR: CPT Braxton H. DeGarmo, MC

PROFESSIONAL ASSISTANTS: MAJ William R. Kilpatrick, MC
LTC Henry Covelli, MC

WORK UNIT NO: 81/41

TECHNICAL OBJECTIVE

To evaluate peak expiratory flow rate (PEFR) as an early predictor of admission for patients with pulmonary disease who present in acute bronchospasm.

METHOD

Phase I: The hand-held Wright Peak Flow Meter to be utilized will be compared with similar computerized spirometric parameters in order to assess its sensitivity in measuring changes in airways disease. This will be done by randomly testing PEFR in 30 patients scheduled for routine spirometry. The highest of 3 PEFR measurements in each patient will then be correlated to the computerized $FEV_{1.0}$, PEFR, MMEF, and other spirometric values. The highest three values will be used throughout the study because the test is effort related. The patient's best effort will correlate better with the actual severity of his/her disease.

Phase II: Each patient in three different groups will be treated by a physician in the ER according to the SOP. The RN will administer medications and the PEFR test and the physician will have no knowledge of results during treatment and disposition of the patient. Group I (10-15 years of age) will undergo PEFR testing upon admission to the ER, 15 minutes after the first dose of epinephrine, and prior to discharge from the ER, whether admitted or released to go home. Group II (age 15-40, otherwise healthy) will undergo PEFR upon admission, 15 minutes after first dose of epinephrine, after bronchosol therapy, and prior to release from the ER. Group III (age >40, cardiac disease, hypertension, severe COPD) will undergo PEFR testing upon admission to ER, after bronchosol therapy, one hour after starting IV aminophylline, and prior to release from ER. All patients will be contacted 12-24 hours after release from ER for a subjective follow-up of their condition. If the patient was admitted, the physician will be asked for his reasons for admission.

PROGRESS

(81 02 - 81 09) Phase I is near completion.

STATUS: (O)

TITLE: Hydrocarbon Induced Changes in Lung Tissue After GI Absorption

PRINCIPAL INVESTIGATOR: CPT William H. Dice, MC

PROFESSIONAL ASSISTANTS: LTC James Kelley, MC
MAJ William Kilpatrick, MC
MAJ George Ward, VC
1LT Joseph High, MSC

WORK UNIT NO: 80/75

TECHNICAL OBJECTIVE

To determine if pulmonary damage can result from gastrointestinal absorption of hydrocarbons.

METHOD

Esophageal transection and placement of a gastrostomy will be performed on 12 healthy dogs. Control radiographs will be taken before surgery. After allowing for an adequate period for recovery of GI function, evidenced by a return to normal bowel movements, an LD_{50} dose of kerosene will be instilled in all gastrostomies. At 24 hr post installation, one half of the animals will be sacrificed following radiologic exam of the lungs. The other one half will have radiographs at 24, 48, and 72 hr. Sacrifice will occur after 72 hr radiographs have been obtained. Autopsies will be performed, and the tissue perserved for light microscopic examination of the brain, major organs, and gastrointestinal tract.

PROGRESS

(80 09 - 81 09) Gastrostomies and cervical esophageal transections with a proximal esophageal fistula were performed on 11 dogs. Following a return to normal bowel function each animal was given 20 cc/kg of a commercial grade kerosene by gastrostomy tube. No clinical complications or radiologic or histologic evidence of pulmonary changes due to kerosene were found. The lack of pulmonary pathologic changes following keosene ingestion in dogs protected from aspiration suggests that the treatment for kerosene poisoning should be confined to supportive measures. Induction of emesis is contraindicated in the management of hydrocarbon ingestion.

STATUS: (C)

PRESENTATION: Dice, W.H., Ward, G.S., Kelley, J., and Kilpatrick, W.R.: Lack of Pulmonary Toxicity Following Gastrointestinal Absorption of Kerosene. Univ Assoc for Emerg Med Ann Meeting, San Antonio, TX, Apr 81.

IBID: Amer Coll Emerg Phy, New Orleans, LA, Sep 81.

TITLE: Emergency Room Procedure Training

PRINCIPAL INVESTIGATOR: MAJ Wilson R. Kilpatrick, MC

PROFESSIONAL ASSISTANTS: LTC George S. Ward, VC
MAJ Robert D. Smith, MC

WORK UNIT NO: 80/04

TECHNICAL OBJECTIVE

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

METHOD

After a lecture with visual demonstration of the procedures, in an initial session each resident will be assigned a large anesthetized dog. Under staff supervision the following procedures will be performed: venous cutdown; peritoneal lavage; cricothyreotomy; tracheostomy; chest tube insertion; lateral thoracotomy; cross clamping aorta; and cardiac wound repair. Six months after the initial session, the residents will repeat the procedures and will be timed for each procedure to simulate emergency conditions and to evaluate how effective the initial training has been.

PROGRESS

(80 10 - 81 09) Six Emergency Medicine residents and five staff members have been trained in techniques of multiple emergency procedures during the past year.

Due to the departure of MAJ Kilpatrick and LTC Ward, CPT Steven C. Dronen, MC, will assume the duties of principal investigator and MAJ Stanley Liebenberg, will act as the veterinary assistant, for the forthcoming year.

STATUS: (O)

TITLE: Severity of Illness in After-Hours E.R. Visits: The Physician's Assessment versus the Patient's

PRINCIPAL INVESTIGATOR: CPT Robert E. Stuart, MC

PROFESSIONAL ASSISTANT: CPT Joseph Divita, MC

WORK UNIT NO: 80/59

TECHNICAL OBJECTIVE

To compare the patient's estimation of the urgency/severity of his medical problem with the physician's assessment in after-hours emergency visits and to gather information about what kind of services after-hours patients expect.

METHOD

Patients presenting between 1700 and 0800 weekdays and on a 24-hour basis on weekends will be included for a period of two weeks. At the time of the patient's visit, the physician will place a code number on the chart as follows: (1) true emergency; (2) acute or chronic severe illness; (3) acute minor illness; (4) chronic minor illness; and (5) no illness found. The patient will be asked to complete a questionnaire at the time he presents for treatment as to his opinion of his illness as categorized above and if he thought he was presenting to the ER or an after-hours walk-in clinic. Later, a telephone survey of patients will be done by an assistnat who does not have access to the code, asking patients to categorize their opinion of their illness after seeing the physician.

PROGRESS

(80 07 - 81 09) Data collection is completed. The data are being analyzed. When this is completed, a paper will be written for submission for publication.

STATUS: (O)

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 FAMILY PRACTICE

TITLE: Cost-Effectiveness of Gonorrhea Screening in Women

PRINCIPAL INVESTIGATOR: CPT Diane J. Madlon-Kay, MC

PROFESSIONAL ASSISTANTS: MAJ John B. McClain, MC
MAJ Martin Crumrine, MSC

WORK UNIT NO: 81/31

TECHNICAL OBJECTIVES

To determine the prevalence of asymptomatic gonorrhea in the female population in the Family Practice Clinic at MAMC; to make a "decision tree" type of analysis of the costs of screening and treating gonorrhea as compared to the cost of undetected gonorrhea in women; to define a population of women in the Family Practice Clinic for which gonorrhea prevalence is sufficiently high to warrant screening.

METHOD

Women presenting to the Family Practice Clinic for PAP smears will be cultured for gonorrhea on transgrow medium. Patient's age, race, marital status, gravidity, parity, birth control method, and symptoms will be recorded. Data from the literature show that a prevalence rate of 13% or greater is necessary for screening of asymptomatic women to be cost-effective. A subpopulation with a sufficiently high prevalence to justify screening will be sought, using a chi-square analysis of the data obtained from the patients.

PROGRESS

(80 12 - 81 09) The cost-effectiveness of gonorrhea screening in women was analyzed. A positive culture rate of 13% or greater was determined by decision analysis techniques to be necessary for screening to be cost-effective. A prospective study demonstrated that gonorrhea screening in the MAMC Family Practice Clinic is not cost-effective.

STATUS: (C)

PRESENTATION: Gonorrhea Screening in Women: When is it Cost Effective? American Academy of Family Physicians, Las Vegas, NV, September 1981. AWARD for outstanding exhibit.

TITLE: Diamine Oxidase Levels and Asthma in Pregnancy

PRINCIPAL INVESTIGATOR: CPT Diane J. Madlon-Kay, MC

PROFESSIONAL ASSISTANTS: MAJ Rebecca Sullivan, MC
CPT James Little, MSC

WORK UNIT NO: 81/73

TECHNICAL OBJECTIVE

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

METHOD

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

PROGRESS

(81-04 - 81-09) Eight pregnant asthmatics have been entered in this project. They are having monthly spirometry and blood drawn for diamine oxidase levels. The blood is being frozen while the assay is being developed.

STATUS: (O)

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

F O R

P R O T O C O L S

DEPARTMENT OF MEDICINE

TITLE: Comparison of Captropril and Propranolol with Added Hydrochlorothiazide, If Necessary, in the Treatment of Moderate Essential Hypertension

PRINCIPAL INVESTIGATOR: MAJ Lawrence Agodoa, MC

PROFESSIONAL ASSISTANTS: LTC Robert V. Hollison, Jr., MC
Ralph E. Cutler, M.D.
Martin Burke, M.D.

WORK UNIT NO: 80/73

TECHNICAL OBJECTIVE

To evaluate and compare the antihypertensive activity and possible adverse effects of captopril to those occurring with conventional propranolol treatment.

METHOD

This study is being done in conjunction with Harborview Hospital, Seattle, WA. Approximately 20 adult patients with mild to moderate hypertension, ages 20-75, will be studied. The following patients will be excluded: pregnant women, nursing mothers, potential child bearers who are not practicing contraception, mycoardial infarction within one month, severe kidney failure and bronchial asthma or severe obstructive lung disease. The study will be divided into three periods. Period A: Patients will discontinue any prior antihypertensive drugs and be given a placebo for approximately two weeks to allow the investigators to see how severe the hypertension is prior to initiating the comparative drug study. At the end of this period patients with a diastolic blood pressure >100 and <120 mm HG will be assigned by random choice to either captopril or propranolol treatment groups. Period B: Patients receiving propranolol will have brief physical examination at 3, 4, 6, and 8 weeks. Blood and urine will be obtained at weeks 2 and 6. Patients receiving captopril will have a physical examination weekly for 12 weeks at which time blood will be obtained for blood counts. Alterations in either drug doses may be made during any clinic visit and hydrochlorothiazide may be added if necessary to control blood pressure. Period C: The dose of medication established in Period B will be continued for 8 weeks. Propranolol patients will be seen at weeks 2, 4, and 8 . Blood and urine tests will be repeated at the end of the study period. Captopril patients will continue weekly visits for 4 weeks and then every 2 weeks for the remainder of the period. Blood and urine tests will be repeated at the end of this study period.

Comparison of Captropril and Propranolol - MAJ Lawrence Agodoa

PROGRESS

(80 10 - 81 09) This protocol was inactive for several months due to the departure of the principal investigator and complications in getting an IND number. However, the drug has now been approved for this use by the FDA and the Upjohn Company has requested that the investigators begin the collection of data.

STATUS: (O)

TITLE: The Relationship of Improving Diabetic Control by Home Monitoring of Blood Glucose to Hemoglobin A_{IC} Measurements and Leukocyte Chemotaxis, Phagocytosis, and Intracellular Killing in Diabetic Patients

PRINCIPAL INVESTIGATOR: CPT Allan Avbel, MC

PROFESSIONAL ASSISTANTS: LTC David McCowen, MC
MAJ Martin Crumrine, MSC
MAJ Martin Bassett, MC

WORK UNIT NO: 79/55

TECHNICAL OBJECTIVE

To demonstrate that chemotaxis, phagocytosis, and intracellular killing by polymorphonuclear leukocytes in diabetic patients can be normalized and maintained by optimum control of blood glucose levels.

METHOD

Fifteen patients with poor blood glucose control who have had no previous insulin therapy or are poorly controlled on their present regimen and are non-acidotic will be asked to participate. Fifteen healthy volunteers, age matched, without diabetes, cancer, current infection, recent surgery, or having taken any medications for two weeks will be selected to act as controls for the leukocyte function studies.

Blood glucose will be monitored by home use of an Ames "Eyetone" meter and Dextrostix measurements (6 times/day) until stable and then maintaining tight control by weekly measurement of hemoglobin A_{IC}. Insulin dosage will be adjusted using twice daily dosages of regular and NPH insulin to closely approximate fasting blood sugars between 80 and 120 mg%.

When the patients are hospitalized for control of their diabetes, they will be instructed in the use of the Dextrostix and the Eyetone meter and in the recording of blood sugar, urine sugar and acetone, caloric intake, and activity, along with instruction in insulin use, diet, etc. A regimen of regular and NPH insulin in the mornings and evenings will be used. Upon return to the home, approximately one week will be needed to "fine tune" the control and stabilize the insulin dosage. Thereafter, when a patient begins to slip from control, he/she will be reissued the home monitoring kit for various periods of time to maintain control.

The Relationship of Improving Diabetic Control - Avbel

Leukocyte Function Tests: Whole heparinized blood will be drawn at the beginning of hospitalization, between 2 and 4 weeks after control, and again 2-4 months after control is achieved, and evaluated along with appropriate control samples.

Hemoglobin A_{1C}: Hemoglobin A_{1C} will be checked at the beginning of hospitalization and then weekly during the study with concomitant fasting blood sugars and fasting urine sugar and acetone values to check against the patient's chart of home obtained values and to monitor the overall control over a period of approximately 4-6 months.

PROGRESS

(78 12 - 81 09) A hemoglobin A_{1C} assay technique was completed and tested. However, chemotaxis, phagocytosis, and killing assays were not perfected. Due to the departure of all the investigators, this protocol had to be terminated.

STATUS: (T)

TITLE: In vivo Uptake of $^{131}I^-$ by Semen and Other Body Fluids

PRINCIPAL INVESTIGATOR: CPT Allan Avbel, MC

PROFESSIONAL ASSTS: COL Bruce Fariss, MC
COL S. Brown, MC
MAJ Willis Jacob, MSC
James Graves, DAC
CPT Michael Smith, MSC

WORK UNIT NO: 80/44

TECHNICAL OBJECTIVE

To investigate the in vivo uptake of $^{131}I^-$ by human semen and to compare this to the uptake in other body fluids. Also, the effects of this $^{131}I^-$ on spermatogenesis will be investigated.

METHOD

Twelve hyperthyroid men and 6 men with thyroid cancer receiving $^{131}I^-$ for partial or complete thyroid ablation will be selected for study. Semen, blood, saliva, perspiration, and a 24-hour urine will be collected from these patients at various intervals following dosing. The first patient will be used to determine these intervals. This patient will give samples at 1,3,6,14 and 80 day(s) post-dosing then the intervals will be adjusted for the other patients to obtain a reasonable activity-time plot for each type of body fluid. Semen will be collected by having the patients masturbate and ejaculate into a polypropylene specimen container. After liquefaction, one ml will be counted in a gamma scintillation counter and a routine semen analysis will be done. 5cc of blood will be drawn into an EDTA tube: $^{131}I^-$ activity will be determined in one ml of whole blood and one ml of plasma. Saliva will be collected by having the patient chew wax, then expectorate into a polypropylene container. $^{131}I^-$ activity will be determined in one ml. Sweat will be collected utilizing pilocarpine for stimulation. 24 hour urine will be collected in 3L plastic bottles. $^{131}I^-$ activity in 2 ml will be determined. After data is collected the distribution of $^{131}I^-$ in body fluids at various periods after oral dosings will be assessed and an activity time plot will be constructed for each patient. Changes in semen analysis will also be determined. The sperm will be separated from the seminal plasma with differential radioactive counts being performed in an attempt to learn whether the iodide is bound to the sperm.

In Vivo Uptake of $^{131}I^-$ by Semen and Other Body Fluids - Smith

PROGRESS

(80 05 - 81 09) A literature review and most of the method protocols have been completed. Due to the departure of the principal investigator and time restrictions placed on the new principal investigator, no patients have been entered on this study. Collection of subjects is to begin shortly.

STATUS: (O)

TITLE: The Effects of a Chronic Hyperthyroid State on Testicular Steroidogenesis in the Rat

PRINCIPAL INVESTIGATOR: CPT Allan Avbel, MC

PROFESSIONAL ASSISTANTS: COL Bruce Fariss, MC
LTC Stephen Plymate, MC
Mina Garrison, B.S., DAC

WORK UNIT NO: 81/110

TECHNICAL OBJECTIVE

To elucidate the relative contribution of intratesticular E_2 levels on sex hormone production in the hyperthyroid rat and the effect of a natural circulating absence of SSBG (as is seen in the rat) on sex hormone equilibrium in the hyperthyroid state.

METHOD

Forty control rats will be injected with saline as a placebo, daily. Forty experimental rats will be injected with a daily dose of 30 µgm of thyroxine. Ten animals from each group will be sacrificed at 1, 2, 4, and 8 weeks into the study and serum samples taken and analyzed for FSH, LH, T, DHT, and E_2 levels. Testicular samples will be analyzed for T, DHT, E_2 and SSBG.

PROGRESS

(81 08 - 81 09) This protocol has been open only a short time. Rats are now being bred in sufficient quantities to meet the needs of the protocol.

STATUS: (O)

TITLE: Cis-Platinum, 5-FU Chemotherapy of Advanced Head and Neck Squamous Cell Carcinoma

PRINCIPAL INVESTIGATOR: CPT Thomas M. Baker, MC

PROFESSIONAL ASSISTANTS: COL Donald Kull, MC
COL Friedrich H. Stutz, MC
LTC Dennis M. Lanier, MC

WORK UNIT NO: 81/106

TECHNICAL OBJECTIVES

To determine response rates of patients with previously untreated Stage III and IV squamous cell CA of head and neck as well as response rates of similar patients who have had prior treatment and have local or systemic recurrence; to determine survival of previously untreated patients receiving preoperative or preradiotherapy chemotherapy and compare this survival to that of previously treated similar patients at MAMC or from the literature; to determine type and severity of adverse effects of the chemotherapy.

METHOD

Patients who meet the criteria as listed in the protocol will receive cis-platinum, 80 mg/M^2, given with hydration and manitol diuresis, followed by 5-FU, 1000 mg/M^2 by IV infusion, for 4 consecutive days. A second course is repeated in 3 weeks. After 2 courses, patients that have not had prior treatment should then be re-evaluated by radiotherapy and surgery for further therapy. In patients who have recurrent or metastatic disease, treatment is given every 3-4 weeks for as long as the tumor is controlled and the patient tolerates the side effects reasonably well.

PROGRESS

(81 08 - 81 09) Four patients have begun therapy, three having had prior treatment and one having had no prior therapy. Patients have been on therapy only for a short while and no results are available.

STATUS: (O)

TITLE: Serum High Density Lipoprotein Concentrations in Non Insulin-Dependent Diabetes Mellitus

PRINCIPAL INVESTIGATOR: MAJ Martin L. Bassett, MC

PROFESSIONAL ASSTS: Robert Biesbroeck, M.D., Univ of Washington
COL Bruce Fariss, MC
LTC K. David McCowen, MC
MAJ Wijdan Luqman, MC
MAJ Robert Chadband, MC

WORK UNIT NO: 80/09

TECHNICAL OBJECTIVE

The purpose of this joint protocol with the University of Washington is to evaluate HDL levels in stable, untreated, non-insulin dependent adult diabetics. This study will provide important baseline data on HDL concentrations in this diabetic population. Hemoglobin $A1_c$ levels will also be determined and compared with the baseline HDL levels. Hemoglobin $A1_c$ is presently thought to reflect the chronic state of overall control of blood glucose values in the diabetic. It will be of significant interest to compare the $HA1_c$ levels with the HDL value to assess the effect of the degree of hyperglycemia on HDL cholesterol. These substances will also be compared to triglycerides, cholesterol, blood sugar, insulin, and other lipoproteins.

METHOD

Approximately 50 adult type II diabetic patients on no oral hypoglycemic medication will be stuied. The patients will be asked to come to the Endocrine Clinic after an overnight fast on two different mornings approximately 60 days apart. They will have 30 cc of blood drawn, give a urine specimen, and complete a questionnaire designed to assess the patient's diabetic stability. Blood analyses will be done by the University of Washington under Dr. Biesbroeck's direction.

PROGRESS

(80 01 - 81 09) Study has been completed and a paper has been accepted for publication. In the insulin dependent group, triglycerides were inversely related to HDL cholesterol and positive to HDL trigylcerides. There was no relationship between total triglycerides and lipoprotein A_1. If adjustment is made for factors that may affect HDL cholesterol levels and for lipoprotein A_1, a highly significant inverse correlation between HDL cholesterol and HDL triglycerides emerged. Abnormal HDL composition is characteristic of untreated non-insulin dependent diabetes only in part relating to increased plasma triglyceride levels.

STATUS: (C)

TITLE: The Acute Effects of Water Loading and Deprivation on ADH Levels on Two Patients with Essential Hypernatremia

PRINCIPAL INVESTIGATOR: MAJ Martin L. Bassett, MC

PROFESSIONAL ASSTS: CPT Robert Chadband, MC
LTC Stephen R. Plymate, MC
COL Bruce L. Fariss, MC
LTC K. David McCowen, MC

WORK UNIT NO: 80/10

TECHNICAL OBEJCTIVE

To determine the response of plasma ADH to water loading and water deprivation in two patients with essential hypernatremia.

METHOD

Two patients will be admitted to the hospital for a two day stay.

Day 1 - Water load: After an overnight (12 hr) fast without fluids, each patient will have an indwelling IV catheter inserted with D_5W solution running. Blood samples will be removed, after flushing the catheter, every hour (15-20 cc's) to measure plasma ADH, serum Na^+, plasma osmolality, and serum glucose. Approximately 4-5 hours and up to 100 cc's of blood will be needed for this phase. During the test, oral water will be given at a dosage of 20 cc/kg of body weight and supplemental D_5W added to lower the serum Na^+ to approximately 145 mEq/dl. The theoretical consideration of cerebral edema will be watched for with vital signs, mental status checks, and observation every 30 min at a minimum. Urine osmolality will be checked hourly and urine volume and body weight recorded.

Day 2 - Water deprivation: After a normal breakfast and fluid ad lib during the previous night, no fluids will be given for approximately 8 hours. The indwelling IV line will be in place from the previous day. Baseline blood samples will be drawn for the same measurements as on Day 1 through the flushed IV line until urine osmolality changes less than 30 mg/hr or until 3% of body weight is lost. At that point, 5 units of aqueous vasopressin (ADH) will be given IM and the same samples obtained one hour later. Urine osmolality and body weight will be measured hourly. This test will take approximately 8 hours and 200 cc's of blood to complete. As on Day 1, patients will be monitored every 30 minutes.

The Acute Effects of Water Loading and Deprivation - Bassett

Osmolalities, serum sodiums, and vasopressins will be compared during the water loading and water deprivation studies. Patterns will be evaluated, if present, and comparisons made with accepted normal values.

PROGRESS

(80 01 - 81 09) Plasma ADH samples were collected on only one patient. The other patient was lost to the study because of a change in residence. In the one patient studied, the vasopressin levels changed with water deprivation but not of a magnitude to be measurable.

STATUS: (C)

TITLE: Prophylactic Alternate Day Corticosteroid Therapy Following Irradiation for Lung Carcinoma

PRINCIPAL INVESTIGATOR: COL J. Waylon Black, MC

PROFESSIONAL ASSISTANTS: COL Donald Kull, MC
LTC Jerome F. Beekman, MC

WORK UNIT NO: 81/91

TECHNICAL OBJECTIVE

To evaluate the effectiveness of alternate day corticosteroids in preventing radiation pneumonitis and pulmonary fibrosis with their associated loss in lung function due to chest irradiation for lung carcinoma.

METHOD

Patients receiving chemotherapy will be excluded from the study. Forty to fifty patients selected for irradiation therapy will be assigned in a double blind random fashion by the Pharmacy to receive either 60 mg of prednisone qod or a placebo qod for one year. The placebo will contain all except the active ingredient of the prednisone tablet. PFT's, CXR, and clinical exam will be performed prior to treatment at 3, 6, and 12 months. This evaluation will add only an additional PFT to what is now routine follow-up. The data will be analyzed using the objective and subjective evaluation of patients after the placebo code is broken.

PROGRESS

(81 07 - 81 09) An IND number had to be obtained on this protocol due to the use of the drug, delaying the start of the protocol. The protocol is now awaiting approval from OTSG.

STATUS: (O)

TITLE: Compliance and Efficacy in Administration of Oral Cephalosporins in an Outpatient Setting

PRINCIPAL INVESTIGATOR: CPT Hyrum Blackburn, MC

PROFESSIONAL ASST: MAJ John McClain, MC
CPT Arden L. Ashton, MC

WORK UNIT NO: 80/35

TECHNICAL OBJECTIVE

To compare two different administration schedules of cephalosporins in the treatment of urinary and skin and skin structure infections.

METHOD

Patients reporting to the Outpatient Clinic will be randomized into group A, who will receive Cefadroxil, 1000 mg po qd for 7 days, and group B, who will receive Cephapirin, 250 mg po qid for 7 days. An additional two day supply of pills will be given as extra pills. The patients will have a clinical follow-up at 10 days when pill count will be done and evaluation of the underlying infection is made. Efficacy will be analyzed by chi square. Compliance will be analyzed by considering all patients who forgot to take one or more pills during therapy by chi square. A second analysis will correlate number of pills omitted with chance of treatment failure. One hundred patients will be treated in each group.

PROGRESS

(80 03 - 80 09) To date, 65 patients have been evaluated for the study. Because of the design of the study, a fraction of those patients have been entered presumptively before culture results are back based on clinical findings. Only 16 of 65 patients turned out to have urinary infections as defined by greater than 100,000 bacteria/ml of urine. This is too low and the protocol design is being redone. The failure rate in both groups seems to be the same.

Due to the departure of CPT Ashton, CPT Blackburn will assume the responsibilities as principal investigator on this protocol.

(80 10 - 81 09) This protocol could not be continued further due to the departure of the investigators.

(C)

TITLE: Determination of Factors with a Negative Predictive Value of Blood Cultures on a General Medicine Service

PRINCIPAL INVESTIGATOR: CPT David S. Brantley, MC

PROFESSIONAL ASSISTANT: MAJ John B. McClain, MC

WORK UNIT NO: 81/15

TECHNICAL OBJECTIVE

To define factors present in a clinical situation with a negative predictive value determining blood culture positivity.

METHOD

Approximately 200 patients with an oral temperature >100.4^{o}F, an oral temperature <97.5^{o}F, or a temperature increase >2^{o}F over a 6-hour period will have two sets of blood cultures drawn in paris after a Betadine skin prep. Needles will be switched when transferring blood to the culture bottles. Staph epi., P. acne, and diphtheroids will not be considered pathogens unless more than two consecutive sets are positive. Data will be analyzed by regression analysis methods for factors affecting blood culture positivity.

PROGRESS

(80 11 - 81 09) This project was terminated due to the inability to accrue sufficient data to analyze. This difficulty primarily secondary to ward services not complying with protocol and therefore generating insufficient data.

STATUS: (T)

TITLE: Isolation and Identification of Cell Wall Deficient Bacteria from Crohn's Disease Patients

PRINCIPAL INVESTIGATOR: CPT Floyd V. Burton, MC

PROFESSIONAL ASSISTANTS: MAJ Martin H. Crumrine, MSC
MAJ Henry J. Zielinski, MC

WORK UNIT NO: 81/29

TECHNICAL OBJECTIVE

An attempt will be made to isolate cell wall deficient organisms from a filtrate derived from inflamed bowel tissue of Crohn's disease patients.

METHOD

Specimens of diseased tissue from Crohn's Disease patients, normal tissue from control patients, and disease tissue from positive control patients (ulcerative colitis) will be aseptically washed in Columbia Broth supplemented with 10% sucrose after the removal of fecal material. One half the speimen will be aseptically minced in Columbia Broth with 10% sucrose and the other half in Tryptic Soy Broth supplement with 10% sucrose and then centrifuged at 500 RPM for 3 min and filtered through 0.45 microfilters, with these 2 filtrates used as the cultured material. Three plates each of chocolate agar and tryptic soy agar will be inoculated with 0.1 cc of each filtrate, incubated aerobically at 35°C, and checked for growth every other day. Three tubes of each of the following will be inoculated with one cc of each filtrate for 48 hours: Columbia broth, tryptic soy broth, and brain heart infusion broth each supplemented with 10% sucrose and 20% gamma-globulin free horse serum and the same media supplemented with 5% sucrose and 20% gamma-globulin-free horse serum. Gram stain will be done on the 3rd and 5th days, then every other day until day 12, and then every third day until day 30. When growth is detected, a diphasic medium of supplemental mycoplasma agar and broth will be used to stabilize the cell wall deficient bacteria. After 1-2 weeks incubation, the organism will be subcultured to thioglycolate and chocolate media to complete the reversion process. Conventional tests will be performed for identification when the reversion process is complete.

PROGRESS

(80 12 - 81 06) No patients with Crohn's disease were avialable. Two patients were entered as controls. No cell wall deficient organisms were isolated from either patients' bowel specimen. The study was terminated due to the PCS of the investigators.

STATUS: (T)

TITLE: The Clinical Evaluation of Naloxone (NARCAN) as a Diagnostic Agent in the Differential Diagnosis of Hyperprolactinemia.

PRINCIPAL INVESTIGATOR: MAJ Robert Chadband, MC

PROFESSIONAL ASSISTANTS: COL Bruce Fariss, MC
LTC Stephen Plymate, MC

WORK UNIT NO: 80/15

TECHNICAL OBJECTIVE

To determine if, by comparing the results of the prolactin response to bromocryptine and Narcan, a separation can be made between pituitary hypersecretors and hypothalamic hyperstimulators.

METHOD

To be eligible, patients must have had two prolactins >20 ng/ml by RIA. Twenty-five patients will be evaluated. One week after the standard evaluation for hyperprolactinemia, baseline prolactins will be drawn and then at 5, 30, 60, and 120 minutes. Narcan, 0.8 mg IV, will then be given thru heparin lock. Phlebotomy of 10cc will again be done at 0, 15, 30, 60, 90, 120, 150, and 180 minutes. 5cc will be spun and sent for prolactin analysis. The following week, patients will be given 2.5 mg bromocryptine PO and phlebotomy will again be performed as before. After completion of these tests, patients will be treated in accordance with standard medical care for the suspected cause of hyperprolactinemia. Patients will be followed on a monthly basis for at least 6 months. After collection of the raw data, results will be analyzed using Student's t Test and linear regression analysis.

PROGRESS

(80 02 - 81 09) Due to the lengthy approval procedures associated with this protocol and the immenent departure of the principal investigator when it was approved, no patients were entered on this protocol at MAMC. MAJ Chadband will transfer this protocol to DDEAMC as soon as possible.

STATUS: (O)

TITLE: Comparison of Ipecac and Gastric Lavage in Removal of Stomach Contents in the Treatment of Toxic Ingestion

PRINCIPAL INVESTIGATOR: MAJ Robert Chadband, MC

PROFESSIONAL ASSTS: COL Bruce L. Fariss, MC
LTC James Bascom, MC
COL Joel Sim, MC

WORK UNIT NO: 80/16

TECHNICAL OBJECTIVE

To study the comparative benefit of emesis and gastric lavage in the treatment of acute toxic ingestion.

METHOD

Twenty-five patients will be admitted in sequence with toxic ingestion of solid materials (pills). The patients to be studied will be between 18-40 years old who have no recognized contraindications to Ipecac/emesis (allergy, corrosives, petroleum products, decreased sensorium, or absent gag reflex). 15 cc of Ipecac will be given PO. Emesis will be continued until clear (the standard endpoint of therapy). Patients will be placed on their left side and an Ewald tube will be placed PO and the stomach contents lavaged with normal saline with 250-500 cc minimum. Gross observation will be made on aspirate for food or pill particles.

PROGRESS

(80 02 - 81 06) Insufficient data was collected before the PCS of the principal investigator and the protocol has been terminated.

STATUS: (T)

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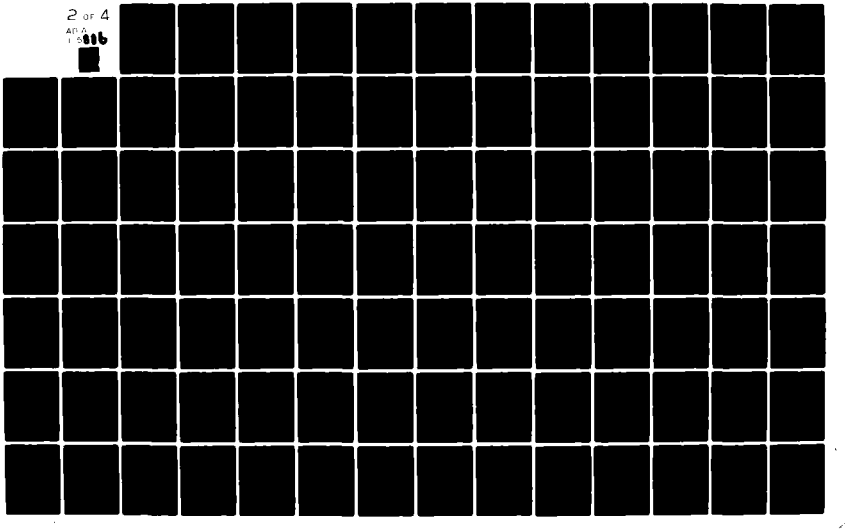

TITLE: To Determine if Tolinase (Tolazamide) Exerts Clinically Detectable β Adrenergic Stimulatory Effects in AODM Patients without Known ASCAD

PRINCIPAL INVESTIGATOR: MAJ Robert Chadband, MC

PROFESSIONAL ASSTS: COL Bruce Fariss, MC
COL Theodore Steudel, MC

WORK UNIT NO: 80/17

TECHNICAL OBJECTIVE

To determine which patients may or may not be suitable for the use of oral hypoglycemic agents and to determine if there is a possible risk of β stimulatory effects on AODM patients without known ASCAD.

METHOD

Ten patients, who have no allergy to the medication and no known symptomatic ischemic cardiac disease by history, physical, or baseline ECG and who would normally be considered as candidates for oral agents will initially receive 250 mg Tolinase while continuing on appropriate diabetic diet. All patients will have a baseline ECG followed by Holter monitor and graded Bruce Treadmill Test (BTM). Patients developing ischemic symptoms on BTM will be withdrawn and treated appropriately. Initial fasting and 2hPP glucoses will be done and records of urine reductions will be recorded. Tolinase dosage will be increased at one week intervals as necessary to obtain a 2hPP glucose <250 mg% and followed for a total of 3 months with fasting and 2hPP glucoses to the maximal dose of 750 mg/day. Blood levels of oral agents will be drawn after one week on stabalizing dose and before BTM. Patients will be withdrawn from the study with decompensation, DKA, or ischemic coronary symptoms.

Ten patients who are age matched AODM, sex matched, and on diet therapy will be used as controls.

All patients will be asked to record any palpitation or cardiac symptoms and will be followed at one month intervals as outpatients.

PROGRESS

(80 02 - 81 09) No patients have been entered into this study to date. The protocol is to be transferreed to DDEAMC since MAJ Chadband is now stationed there.

STATUS: (O)

TITLE: Treatment of Rheumatoid Arthritis with Oral Zinc Sulphate

PRINCIPAL INVESTIGATOR: COL Sidney Cloud, MC

PROFESSIONAL ASSISTANTS: COL Robert B. Gibbons, MC
MAJ Michael D. Herring, MC

WORK UNIT NO: 79/12

TECHNICAL OBJECTIVE

To determine whether changes in serum zinc levels and/or serum histidine levels will correlate with improvements of arthritic symptoms or with occurrence of side effects in patients with rheumatoid arthritis taking oral zinc sulfate.

METHOD

Patients with rheumatoid arthritis who have been taking oral zinc sulfate will be studied at monthly intervals with evaluation of disease activity accomplished by patient assessment and measurement of grip strength, enumeration of joints with active disease and by sedimentation rate. Blood for zinc and histidine will be drawn at monthly intervals. These subjects will be followed long-term and the investigators will continue to correlate activity of disease with zinc and histidine levels. Statistical analysis of data will compare zinc and histidine with the recorded variables of the disease.

PROGRESS

(79 02 - 81 09) Comparison of the serum levels of zinc and histadine with the clinical course of disease showed no correlation with the status of disease and levels of serum zinc. The anticipated correlation between serum levels of zinc and the use of oral histadine was not found. This study shows no benefit in the control of rheumatoid arthritis by the addition of either zinc or histadine plus zinc to the treatment program.

STATUS: (C)

TITLE: Distribution of Gold Used to Treat Rats with Adjuvant Arthritis

PRINCIPAL INVESTIGATOR: COL R. Sidney Cloud, MC

PROFESSIONAL ASSISTANTS: MAJ George S. Ward, VC

WORK UNIT NO: 79/13

TECHNICAL OBJECTIVE

To determine the distribution of gold salts injected in rats with adjuvant arthritis and to correlate distribution with effect on the arthritis.

METHOD

Adult male rats will be given gold by injection or by mouth. Disseminated arthritis will be produced by the injection of Freund's adjuvant. The animals will be sacrificed at 4, 8, 12, and 16 days and tissue surveyed for gold concentration. Clinically, the degree of arthritis will be compared in the control versus the treated animals.

PROGRESS

(78 11 - 81 09) Rats injected with Freund's adjuvant demonstrated a localized inflammatory reaction and a systemic arthritis. The use of gold salts given IM reduced the amount of both local and systemic arthritis to a statistically significant degree only with high-dose gold. The low-dose gold-treated animals had as much arthritis as the control group. Determinations of tissue levels of gold have not been completed.

STATUS: (O)

TITLE: Study of the Effect of d-Penicillamine and Chloroquine on Antigen and Mitogen-Induced Human Lymphocyte Proliferation

PRINCIPAL INVESTIGATOR: COL R. Sidney Cloud, MC

PROFESSIONAL ASST: MAJ Martin Crumrine, MSC

WORK UNIT NO: 80/43

TECHNICAL OBJECTIVE

To determine if d-penicillamine and/or chloroquine inhibit lymphocyte transformation induced by antigens and mitogens in treatment.

METHOD

Human peripheral blood mononuclear cells (PBM) from 10 normal volunteers will be stimulated in tissue culture by the addition of concanavalin A (Con A), pokeweed mitogen (PWM), phytohemagglutinin (PHA) and streptokinase-streptodornase (SKSD). The culture will be done in triplicate in microtiter plate.

Initially the effect of d-penicillamine (d-Pen) and chloroquine (AM) added to the cultures piror to stimulation will be studied. The amount of DNA synthesis will be measured by incorporation of tritiated thymidine (3HT). The time of optimum effect will be established by assaying 3HT uptake daily from the second through the sixth day. The length of culture producing optimum inhibition will be used in the remaining investigation.

The effect of varying concentration of d-Pen and AM will be studied against optimal and suboptimal concentrations of Con A and PHA.

The effect of adding d-Pen and AM at different times in the cycle of stimulation will be done with the agents added at time of stimulation and at 1, 2, 4, and 48 hours post stimulation. To determine whether the lymphocytes are injured so they can not be stimulated, PBM will be cultured with Con A for 24 hours and then washed to remove Con A. These cells will then be cultured for 48 hours with and without the inhibiting

drugs. Another way to study this effect will be to culture PBM with the inhibiting agents for 5 days, wash the cells, and continue culture for 48 hours in fresh media with the mitogens and with or without fresh autologous monocytes. Additional studies on the role of monocytes will be done by reducing the number of monocytes in the cultures.

Cell death will be evaluated by trypan blue exclusion and cell counts. Possible formation of suppressor cells will be evaluated by adding preincubated monocytes to stimulated cultures containing normal monocytes.

Data will be analyzed using the paried t test and chi^2 analysis to compare stimulated to non-stimulated values and the response of treated vs untreated controls.

PROGRESS

(80 05 - 81 09) The technical portion of this study has been completed and data are being analyzed.

STATUS: (O)

TITLE: Study of the Effects of Drug Treatment in Rheumatoid Arthritis: I. The Effect of *in vivo* Gold Injection on Mononuclear Cell Stimulation *in vitro*.

PRINCIPAL INVESTIGATOR: COL R. Sidney Cloud, MC

PROFESSIONAL ASST: MAJ Martin Crumrine

WORK UNIT NO: 80/46

TECHNICAL OBJECTIVE

To determine if gold acts *in vivo* to inhibit mononuclear cell function as measured by response to mitogens *in vitro*. The relationships of frequency of injection and dose will be correlated with effect on lymphoblastic transformation by mitogens.

METHOD

Twenty patients receiving gold injections for RA will be studied. Controls will be 20 patients with RA not receiving gold, antimalarials, penicillamine, or immunosuppressive drugs. Patients will be grouped for analysis according to frequency of gold injections and dose of gold injected.

Venous blood will be collected just prior to injection of gold and 24-48 hours after (a minimum of two and a maximum of three times with each patient). Clinical data to include duration of disease, laboratory data on disease, activity in ESR, latex fixation for RF, ANA, and estimation of benefit of therapy by the patient and by the physician will be correlated with the results. Patient controls will have two samples of blood drawn approximately one month apart.

PBM will be separated from the blood by standard ficoll separation techniques and cultured in triplicate in microtiter plates. Phytohemaglutinin, pokeweed mitogen, concanavalin A or streptokinase/streptodornase will be used to stimulate the cells. Incorporation of tritiated thymidine into DNA of pheripheral blood mononuclear cells (PBM) on the third day of culture will be measured in stimulated and non-stimulated cells. Gold levels in the PBM will be measured by atomic absorption. Student's t test and chi square analysis will be performed on the data to compare the study and control populations.

PROGRESS

(80 06 - 81 09) This study has been completed. In 17 patients with active rheumatoid arthritis under current therapy of IM gold, there was no difference in lymphocyte transformation by mitogens in relation to time intervals between injections.

STATUS: (C)

drugs. Another way to study this effect will be to culture PBM with the inhibiting agents for 5 days, wash the cells, and continue culture for 48 hours in fresh media with the mitogens and with or without fresh autologous monocytes. Additional studies on the role of monocytes will be done by reducing the number of monocytes in the cultures.

Cell death will be evaluated by trypan blue exclusion and cell counts. Possible formation of suppressor cells will be evaluated by adding preincubated monocytes to stimulated cultures containing normal monocytes.

Data will be analyzed using the paried t test and chi^2 analysis to compare stimulated to non-stimulated values and the response of treated vs untreated controls.

PROGRESS

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PRINCIPAL INVESTIGATOR: COL R. Sidney Cloud, MC

PROFESSIONAL ASST: MAJ Martin Crumrine

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PBM will be separated from the blood by standard ficoll separation techniques and cultured in triplicate in microtiter plates. Phytohemaglutinin, pokeweed mitogen, concanavalin A or streptokinase/streptodornase will be used to stimulate the cells. Incorporation of tritiated thymidine into DNA of pheripheral blood mononuclear cells (PBM) on the third day of culture will be measured in stimulated and non-stimulated cells. Gold levels in the PBM will be measured by atomic absorption. Student's t test and chi square analysis will be performed on the data to compare the study and control populations.

PROGRESS

(80 06 - 81 09) This study has been completed. In 17 patients with active rheumatoid arthritis under current therapy of IM gold, there was no difference in lymphocyte transformation by mitogens in relation to time intervals between injections.

STATUS: (C)

TITLE: Effect of Gold on Skin Transplant Rejection in Rats

PRINCIPAL INVESTIGATOR: COL R. Sidney Cloud, MC

PROFESSIONAL ASSISTANTS: COL Thomas Coppin, MC
LTC George S. Ward, VC
MAJ Martin Crumrine, MSC

WORK UNIT NO: 81/60

TECHNICAL OBJECTIVE

To determine if gold will modify the skin graft rejection reaction in rats.

METHOD

Thirty Holtzman strain and 30 Wistar strain rats will be used. Each strain will be divided into 3 groups of 10. Each group will receive weekly injections of 10 mg/kg gold (myochrysine), saline, or thiomalate (the vehicle in myochrysine). Twenty-four hours after the fourth injection, each rat will have a skin transplant from a rat of the opposing strain and an autograft reversed 180°. Skin transplants will be clinically evaluated biweekly. On the 21st day after skin transplantation, the rats will be anesthetized and blood harvested from the heart using sterile techniques. The rats will than be killed and transplantation sites harvested for histopathology. The presence of humoral antibodies will be evaluated by either compliment fixation or hemagglutination inhibition.

PROGRESS

(81 03 - 81 09) There was no difference in the histologic changes seen between homografts and heterografts with or without gold treatment. This indicates that factors other than homograft rejection were responsible for the histological changes seen. These factors will have to be isolated and corrected before the effect of gold on grafting can be documented.

STATUS: (O)

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

PRINCIPAL INVESTIGATOR: LTC Henry D. Covelli, MC

PROFESSIONAL ASSTS: LTC Jerome Beekman, MC
LTC Donald Kull, MC
MAJ Barry Weled, MC

WORK UNIT NO: 79/77

TECHNICAL OBJECTIVE

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

METHOD

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

PROGRESS

(80 10 - 31 09) Eight patients were studied on this protocol during FY 81 and routine data have been collected. More patients are required before the study can be completed.

STATUS: (O)

TITLE: Conjunctival Biopsy in the Diagnosis of Sarcoidosis

PRINCIPAL INVESTIGATOR: LTC Henry D. Covelli, MC

PROFESSIONAL ASSISTANTS: COL Stanley Sollie, MC
LTC Stanley Allison, MC
MAJ Jerome Beekman, MC
MAJ Bruce Bellin, MC
MAJ Leslie P. Fox, MC
MAJ Barry Weled, MC
CPT Myron Whitehead, MC

WORK UNIT NO: 79/85

TECHNICAL OBJECTIVE

To evaluate the usefulness of conjunctival biopsy as a primary means of diagnosing sarcoidosis.

METHOD

Patients with a tentative diagnosis of sarcoidosis based on accepted clinical, radiologic, and biochemical criteria will have baseline evaluations to include chest x-ray, PPD and anergy battery, angiotension converting enzyme level, erythrocyte sedimentation rate, arterial blood gases, and pulmonary function tests to assess disease activity. These patients will undergo slit lamp examination. Patients with conjunctival follicles will have those follicles biopsed and those with normal appearing conjunctiva will have random biopsies. Tissue will be examined histologically for noncaseating epithelioid granulomata with hematoxylin and eosin stain. If granulomata are observed, the specimen will be examined utilizing polarized light microscopy and stained and examined for acid fast bacilli and fungi. If no granulomata are observed, no further examination will be done. Patients will then be evaluated with transbronchial lung biopsy. If the diagnosis is not established by this method, further invasive diagnostic procedures will not be done unless deemed necessary for the management of the patient. Data on the field from transbronchial biopsy will be compared to that from conjunctival biopsy. In addition, disease activity as manifest by serum ACE level will be correlated with biopsy positivity.

Conjunctival Biopsy in the Diagnosis of Sarcoidosis - Covelli

PROGRESS

(80 10 - 81 09) At present, 20 patients have entered the study. However, at least 30 patients are needed to complete the study. Data gathering has become more difficult since this technique has become a standard of care.

STATUS: (O)

TITLE: 5-Azacytadine in Acute Leukemia

PRINCIPAL INVESTIGATOR: LTC Irwin Dabe, MC

PROFESSIONAL ASSTS: COL Friedrich Stutz, MC
MAJ Lauren Colman, MC

WORK UNIT NO: 80/19

TECHNICAL OBJECTIVE

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

METHOD

5 Azacytidine will be given in a dose of 300 mg/M^2/day for 5 days in three or four divided doses each day. Courses will be repeated every three weeks unless there is earlier evidence of recovery from myelotoxicity. If bone marrow cellularity is less than 20% at three weeks from the last course, chemotherapy will be with-held until marrow cellularity exceeds 20%. Dosages for the next course will then be reduced by one third. If there is no improvement in the bone marrow after the initial course, the drug dosage for the second course will be increased by one third.

PROGRESS

(80 06 - 80 09) Two patients have been treated on this study:

a. One had myelomonocytic leukemia and had been previously treated on several regimens with only a brief response to DNR/Ara-C. She received two cycles of AZA achieving a minimal response to the first (decrease in marrow blast % from 80-35) and very little response to the second (45% blasts in the marrow six weeks later). She died of uncontrolled leukemia. The only toxicity was nausea and vomiting.

b. The other had myelomonocytic leukemia and after no response to Ara-C/BTG and DNR/Ara-C was given two cycles of AZA, achieving a good partial response after the first cycle. She died of uncontrolled CNS leukemia during marrow aplasia from the second dose.

(80 10 - 81-09) No patients were entered on this study during FY 81.

STATUS: (O)

TITLE: m-AMSA in Acute Leukemia

PRINCIPAL INVESTIGATOR: LTC Irwin B. Dabe, MC

PROFESSIONAL ASSISTANTS: COL F.H. Stutz, MC
MAJ Lauren K. Colman, MC

WORK UNIT NO: 81/54

TECHNICAL OBJECTIVES

The purpose of this study is to examine the efficacy of m-AMSA in patients with acute leukemia refractory to conventional therapy.

METHOD

Patients will receive m-AMSA 90 mg/M^2 per day by continuous IV infusion for 5 days. One half of the daily dose (45 mg/M^2) will be dissolved in 1000 ml of D5W and infused over a 12 hour period. If there has been no reduction in the marrow leukemic infiltrate by day 17 following the second course of m-AMSA, patients will be taken off study. If leukemic infiltrate is reduced by each of the first two courses, a third and additional courses may be given according to the above guidelines as long as there is progressive improvement short of CR. Patients who demonstrate significant reduction in leukemia infiltrate short of remission will also be retreated at the above dose level. Patients achieving a CR will go on to receive consolidation and maintenance therapy when the granulocyte count is >1500/MM^3 and platelets are >100,000/MM^3 .

PROGRESS

(81 03 - 81 09) This protocol has not received final approval from HSC and no patients have been registered at MAMC.

STATUS: (O)

TITLE: Clinical Correlates of the Abnormal Oral Cholecystogram

PRINCIPAL INVESTIGATOR: CPT David M. Dunning, MC

PROFESSIONAL ASSISTANTS: MAJ John M. Harris, Jr., MC
Herbert F. Cowgill, M.D.

WORK UNIT NO: 81/48

TECHNICAL OBJECTIVE

To analyze the symptoms and past medical history of those patients who will receive oral cholecystography in a prospective manner and attempt to develop a decision rule which will allow physicians to accurately determine which patients will have an abnormal oral cholecystogram.

METHOD

All persons scheduled to receive an oral cholecystogram in the outpatient Radiology Department will be asked to fill-out a questionnaire. Data collection will then be analyzed and correlated with roentgenographic findings. Using collected data, an attempt will be made to develop a decision rule which would allow a physician to more accurately determine which are most likely to have an abnormal cholecystogram based on clincal history. Results will also be tabulated on patients not completing the questionnaire to permit evaluation of selective bias. A minimum of 25 patients will be studied.

PROGRESS

(81 03 - 81 09) This has been temporarily suspended while the principal investigator is TDY. Upon his return, the study will resume.

STATUS: (O)

TITLE: Coronary Arteriography in the Army

PRINCIPAL INVESTIGATOR: MAJ John M. Harris, Jr., MC

PROFESSIONAL ASST: COL John Hill, MC

WORK UNIT NO: 80/60

TECHNICAL OBJECTIVE

To explore the use of coronary arteriography in Army Medicine, to evaluate certain technical aspects of the procedure, and to better define the nature of coronary artery disease in the active duty population.

METHOD

The proposed study will encompass all Army medical centers performing coronary arteriography. The proposed collection form will be distributed to the other medical centers for comments, then there will be completion of a procedure manual and trial of data collection at MAMC. After final revision of collection form, if necessary, initiation of data collection will begin at each medical center. A computer program for screening and initial display of data will be developed. At the completion of the first year of data collection the data will be anlayzed for a report to the Association of Army Cardiology.

The study will be a prospective survey of current practices. All patients who undergo left heart catheterization will be included. Baseline data will be collected on all patients who undergo cardiac angiography.

PROGRESS

(80 10 - 81 09) All Data has been collected. Participants have been asked to review their data before final submission for analysis. When all participants have forwarded their information, all data will be analyzed and a paper will be written.

STATUS: (O)

TITLE: Comparison of Two Post-Myocardial Infarction Protocols in an Outpatient Setting

PRINCIPAL INVESTIGATOR: COL John C. Hill, MC

PROFESSIONAL ASSISTANT: CPT Sandra F. Yaney, ANC, USAR

WORK UNIT NO: 81/112

TECHNICAL OBJECTIVE

To determine the effects of an existing outpatient cardiac rehabilitation program at MAMC on weight change, smoking patterns, and unscheduled patient presentations to health facilities for angina or its correlates in persons two to eight months post-myocardial infarction.

METHOD

The Cardiac Care Unit Admission Book will be reviewed and patients between 30 and 65 years of age who meet the other criteria as listed in the protocol, will be asked to participate in an outpatient exercise program. Those who are unable or unwilling to attend the sessions will serve as the control group. Four months after the initiation of the program, the total number of unscheduled emergency room/clinic visits for angina or its correlates will be tabulated for both groups. Weights, recorded at routine follow-ups will be totalled for each group and compared as both a total and relative quantity, based on New York Life Insurance Standardized Weight Tables. Smoking behavior change will be evaluated and the two groups compared. All results will be analyzed for statistical significance and the implications of the study discussed.

PROGRESS

(81-08 - 81 09) This is a new protocol and patient collection is in progress.

STATUS: (O)

TITLE: Intracoronary Thrombolysis with Streptokinase in the Hyperacute Phase of Myocardial Infarction (Western Washington Randomized Trial)

PRINCIPAL INVESTIGATOR: COL John C. Hill, MC

PROFESSIONAL ASSISTANTS: COL W. Theodore Steudel, MC
LTC John W. Kirk, MC
MAJ Roger F. Chamusco, MC

WORK UNIT NO: 81/114

TECHNICAL OBJECTIVE

To determine the efficacy of intracoronary thrombolysis in the therapy of acute transmural myocardial infarction.

METHOD

This will be a randomized community-wide therapeutic trial. To qualify, patients must be <75 years of age and in reasonably good health and functional state prior to the acute event. Patients found, on arteriography and ventriculography, to have thrombosis of the coronary artery supplying the ischemic region of myocardium will enter the randomized trial. Control patients will be maintained on IV heparin and then coumadin for the remainder of their hospitalization. Patients randomized to Streptokinase will receive 4,000 units/min into the thrombosed vessel for a period of up to 60 min. Arteriography of the thrombosed vessel will be done every 15 min or when clot lysis is suspected. Following thrombolysis or after 60 min of Streptokinase infusion, the patient will undergo repeat left ventriculography and then monitored on IV heparin for four days and on coumadin until hospital discharge. Treatment and control groups will undergo identical evaluation including serial enzymes and electrocardiograms and early (12-48 hr) and follow-up isotope ventriculograms (12-16 days). Follow-up tomographic thallium imaging for the quantification of infarct size will be at 25-35 days following study.

PROTOCOL

(81 08 - 81 09) This protocol is awaiting approval from the HSRRB.

STATUS: (O)

TITLE: Theophylline Induced Seizure: Increased Susceptibility with Prior Episode?

PRINCIPAL INVESTIGATOR: CPT Arthur R. Knodel, MC

PROFESSIONAL ASSISTANTS: LTC Henry D. Covelli, MC
LTC Jerome F. Beekman, MC
LTC Georgio Turella, MC
MAJ Stanley P. Liebenberg, VC
CPT James S. Little, MSC

WORK UNIT NO: 81/96

TECHNICAL OBJECTIVE

To evaluate whether the seizure threshold for theophylline is altered by a prior theophylline induced seizure.

METHOD

Ten beagle dogs will be used and will have continuous EEG monitoring. An arterial line will be used to draw serum theophylline levels while a venous line will serve for the infusion. A baseline EEG will be obtained and the animal will then be given a theophylline bolus, a linear decreasing concentration of theophylline, and a continuous infusion of theophylline. This will result in an immediately achieved steady state level of serum theophylline. Five, fifteen, and thirty minutes after the bolus serum theophylline determinations will be made to assure a steady state level. Every one-half hour the dosage of theophylline will be increased to achieve a 10 mg/mm increment of theophylline. This will be continued until an EEG documented seizure occurs. One week later the study will be repeated on the same dogs to determine if their threshold has been altered by the prior theophylline induced seizure.

PROGRESS

(81 07 - 81 09) Most details of theophylline dosage and EEG monitoring have been worked out. Investigators thus far have been unable to complete the theophylline infusion. The dogs do not tolerate the paralysis induced by neuromuscular blockade. This has been discussed with Dr. John Holaday at WRAIR and Dr. Frank C. Torttela at Temple University. Investigators are hopefull that this problem will be solved.

STATUS: (O)

TITLE: Reversal of Endotoxin Produced Hypotension in the Rat

PRINCIPAL INVESTIGATOR: MAJ John B. McClain, MC

PROFESSIONAL ASSTS: MAJ Martin Crumrine, MSC
LTC George S. Ward, VC

WORK UNIT NO: 80/13

TECHNICAL OBJECTIVE

It has been demonstrated in the rat model that naloxone, an opiate antagonist with no agonist activity, will reverse endotoxin induced hypotension and hypovolemic hypotension. This is a new and unexpected observation. The hemodynamic role of endorphin receptors is totally undefined. If these phenomena are reproducible and transferable across species lines then naloxone may prove useful in the therapy of hypotensive states in humans. The investigators will also study the effectiveness of this agent in the dose ranges where it has been used in humans with no ill effects.

METHOD

All studies will be conducted in conscious rats with chronically indwelling arterial and venous catheters. Two days prior to administration of the endotoxin, the animals will be anesthetized with phenobarb (50 mg/kg) and the carotid artery and jugular vein will be cannulated and the catheters brought out subcutaneously from the site of implantation. Arterial catheters will be connected to a transducer graph system. The venous catheter will be used for injections. On the day of experimentation, endotoxin (12 mg/kg) is given IV followed by 0.3 ml of saline flush to insure that the drug has infused. Naloxone will be given as an IV bolus to the following groups of 10 rats each: Group A - Endotoxin only; Group B - 10 mg/kg at 15 min; Group C - 10 mg/kg at 30 min; Group D - 10 mg/kg at 60 min; and Group E - 2 mg/kg at 30 min. Parameters which will be measured are: survival at the end of 30, 60, 90, and 120 minute post-endotoxin periods. Pulse and blood pressure throughout the experimental period. Survival data will be analyzed using the chi square method. Blood pressure data will be analyzed for significance with the Student's t test to compare values at a common interval from endotoxin administration.

Reversal of Endotoxin Produced Hypotension in the Rat - McClain

PROGRESS

(80 01 - 81 09) The investigators duplicated the hemorrhagic model of Holaday et al in an attempt to add to inferential data concerning endogenous opiates and shock. Administration of morphine resulted in prompt sustained rise in mean arterial pressure. Saline administration showed a small change which is probably due to volume administration. The differences of blood pressure were not significant at base line or at time 0 but were different at P less than .0001 for every point thereafter. The two groups were not significantly different in weight or amount of blood removed. At 14 hours, there were two deaths in the control group and none in the morphine group. We noticed an unusual event in some of the experimental animals. About one in four of the animals while having blood withdrawn during maintenance of hypotension would become very agitated. Their blood pressure would return to normal ranges within 1-2 minutes and could not be lowered by further withdrawal of blood. The rats lost consciousness with MAP of around 100 mm Hg. Their blood pressure came down only during their agonal period. Since these animals did not fit our hypotensive criterion they were not included in the study. The unusual pressor response which occurred in some of the animals spontaneously has been seen by other investigators. It may represent a native pressor reflex which the administration of morphine simply hastens.

STATUS: (C)

TITLE: Susceptibility of Anaerobic Bacteria to Vancomycin

PRINCIPAL INVESTIGATOR: MAJ John McClain, MC

PROFESSIONAL ASSISTANTS: MAJ Martin Crumrine, MSC
MAJ Shannon Harrison, MC
Andrew Back, DAC

WORK UNIT NO: 80/34

TECHNICAL OBJECTIVE

To define in a quantitative manner using broth, agar, and disk methods the susceptibility of anaerobic genera to vancomycin in concentrations normally achieved in the therapy of human patients.

METHOD

Anaerobic isolates will be re-identified according to accepted methods of anaerobic identification. Organisms will be handled in gas-pak's and a glove box. Anaerobic organisms will have susceptibilities performed using brogh and agar dilution techniques and disc susceptibility techniques. The glove box is to be made by the Instrumentation Department at WRAIR.

PROGRESS

(80 03 - 81 09) Forty organisms were tested. Generally, the Gram positive cocci and positive rods were susceptible to vancomycin. Bacteroides were uniformly resistant as expected.

STATUS: (C)

TITLE: Experimentally Induced Respiratory Distress Secondary to a High Carbohydrate Load Provided Parenterally

PRINICPAL INVESTIGATOR: LTC Michael S. Olsen, MC

PROFESSIONAL ASSISTANTS: LTC Henry D. Covelli, MC
LTC Jerome F. Beekman, MC
MAJ Stanley Liebenberg, VC

WORK UNIT NO: 81/95

TECHNICAL OBJECTIVE

To provide an experimental model to measure the potential detrimental effects of the high carbohydrate loads currently found in most TPN solutions.

METHOD

Increased CO_2 production will be experimentally induced in an anesthetized laboratory animal by providing the bulk of the animal's nutritional support as parenteral carbohydrate. In the lipogenic state, the deeply anesthetized animal should be unable to increase its minute ventilation in reponse to the larger CO_2 load.

After equilibration on a ventilator so that pH and arterial blood gases are normal and stable and respiratory quotient is less than one, the animal (dog) will be provided nutrition parenterally. The CHO calories will be increased gradually until the animal enters the lipogenic state. The CHO intake will be stabilized at the lipogenic level for at least 24 hr. The CHO intake will then be reduced until the animal is once again in a near fasting state. Arterial blood gases, VO_2, VCO_2, and VE will be measured at regular intervals while the animal is on the ventilator.

PROGRESS

(80 07 - 80 09) Supplies are being collected and equipment and personnel have been scheduled to support this protocol. The actual technical portion will begin in approximately two weeks.

STATUS: (O)

TITLE: Rat Liver Membrane Binding of Thyroid Hormones

PRINCIPAL INVESTIGATOR: MAJ Louis Pangaro, MC

PROFESSIONAL ASSISTANTS: CPT James Little, MSC
MAJ Hans De Ruyter, MC
LTC Kenneth Burman, MC
COL Bruce Fariss, MC

WORK UNIT NO: 81/16

TECHNICAL OBJECTIVES

To determine if there are specific receptors on plasma membranes which will bind active thyroid hormones; to determine whether this binding is affected by various stresses and pathologic states and by various chemical agents which are of clinical and laboratory interest.

METHOD

Preparation of purified rat liver membranes, membrane and subcellular characterization, and radioreceptor assay methods as outlined in the protocol. The 10 male Sprague-Dawley rats used as control animals for T_3 and T_4 displacement analysis fed ad lib, fasted overnight (6 with daily intraperitoneal saline). The experimental groups will be: 6 female rats; 6 male rats fed ad lib (not specifically fasted); 6 male rats fasted four days (water ad lib); 10 male rats made hyperthyroid by daily intraperitoneal injection of T_4; 10 male rats made hypothyroid by thyroidectomy (with daily injections q.i.d. saline). Control animal liver membranes are compared to membranes with *in vitro* addition of aniline naphtalene, ipodate, iopanoic acid, tyropanoate, propranolol, propylthiouracil, methimazole, and amiodarong. Thyronine analogue displacement curves are compared with the addition of T_4; T_3; reverse T_3 ($3'3'5'T_3$); Tetrac; triae; D-T_4; D-T_3; $3'5'T_2$; $3,5T_2$; $3,3'T_2$; 3-T_1; $3'T_1$; T_0.KI.

PROGRESS

(80 11 - 81 09) Preliminary results show there is saturable, high affinity binding of T_4 and T_3 to purified rat liver plasma membranes; hyperthyroidism decreased MBC for T_4; fasting increased MBC for T_3; and iopanoic acid interfered with binding, ipodate did not. Plasma membrane binding shows different characteristics from nuclear binding. Its role in thyroid action remains to be clarified. Further experiments will be performed to try to clarify this role and to validate the preliminary results.

STATUS: (O)

Rat Liver Membrane Binding of Thyroid Hormones - Pangaro

PRESENTATION: Pangaro, L.N., Little, J.S., Fariss, B.L., and Burman, K.D.: Binding of L-Thyroxine (T_4) and L-Triiodothyronine (T_3) to Purified Rat Liver Plasma Membranes: Changes in Hyperthyroidism and Fasting. Amer Thyroid Assoc, 57th Meeting, Minneapolis, MN, 18 Sep 81, Abstract # T-17.

TITLE: Daunomycin Therapy in Acute Leukemia (Phase II)

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANT: None

WORK UNIT NO: 78/04

TECHNICAL OBJECTIVE

This is not a research study, but rather a treatment protocol involving an experimental drug. The objective is to continue the use of daunomycin in combination with other conventional chemotherapeutic agents for the treatment of leukemia as an extension of Phase I of the protocol, but with a different regimen of drugs.

METHOD

Daunomycin in combination with cytosine arabinoside, 6-thioguanine, vincristine, and prednisone will be given for seven days as remission induction treatment. A bone marrow sample will be obtained in 2-4 weeks; if evidence of the leukemia persists, a second induction course will be given. If leukemia cells are visibly absent, one to two additional courses will be given as consolidation therapy in an attempt to eliminate any residual leukemic cells. At that point, maintenance therapy will be provided. Dosage and duration of therapy are outlined in paragraph 6.0 of the protocol.

PROGRESS

(79 10 - 81 09) Two patients have been treated:

1. Patient had a T-cell leukemia and was given one cycle as consolidation of complete remission achieved by vincristine and prednisone. He was transferred to another hospital within days afterward, so the ultimate outcome is not known, though he had little in the way of immediate side effects.

2. This patient had a smouldering myelomonocytic leukemia with a prior partial response to Ara-C/btg but rapid relapse. His marrow was cleared of blasts (severe hypoplasia), but he died of aspergillosis prior to marrow recovery.

The protocol is now considered completed as daunomycin has been approved for general use.

STATUS: (C)

TITLE: I. Determination of the Effects of Chemotherapy and of Malignancy on the Nutritional Status of the Patient; II. Hyperalimentation of Nutritionally Depleted Patients to Improve Their Survival and Response to Chemotherapy

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: Suresh B. Katakkar, M.D.
LTC Joel W. Black, MC
LTC Charlene P. Holt, MC
MAJ John J. Pelosi, MSC
CPT Jeannie Gallo, SP
Mary J. Oboy, R.N., DAC
Marleen Black, R.N.

WORK UNIT NO: 79/65

TECHNICAL OBJECTIVE

It has been known that chemotherapeutic drugs by causing nausea, vomiting, and anorexia do interfere with nutrition of cancer patients; however, so does the progressive malignancy. The objective is to measure objectively tumor responses or non-response and the side effects of chemotherapy and do objective measurements of nutritional status of the patients and attempt to delineate what role both chemotherapy and progressive malignancy play in causing nutritional imbalance.

Once inbalance is documented, the investigators plan to hyperaliment these patients and determine the effects on their nutritional status, tolerance of chemotherapy, and objective tumor response.

METHOD

1. All newly diagnosed cancer patients (approximately 50) will have an assessment of nutritional status as a baseline; including cell mediated immunity.

2. Patients will be classified as having adjuvant chemotherapy or chemotherapy for metastatic disease.

3. Nutritional assessment will be done every 4 weeks and cell mediated immunity will be determined every 12 weeks, unless abnormal at the beginning, on those patients who are on chemotherapy.

4. The side effects at chemotherapy will be graded according to SWOG criteria.

5. The objective response to tumor will be measured every 4 weeks if the objective tumor measurement is by special procedures such as liver or bone scan, in which case they will be done every 12 weeks.

6. If the patient is nutritionally depleted and unable to take oral feeding, then only will he be hospitalized for parenteral feeding or enteral tube feeding. Hyperalimentation will be done for a period of 10-15 days. However, such an aggressive step will be taken only if the underlying malignancy has reasonable chance of response to thearpy and meaningful life is judged to be left by the investigators.

PROGRESS

(79 03 - 81 09) Nutritional assessment was done to determine the effect of chemotherapy and the tumor upon the nutritional status of 14 outpatients with breast, lung, or colo-rectal cancer. Two assessments were completed, one before the first course of chemothearpy and the other after 3 to 4 months of therapy. Interpretation of the nutritional data was confounded by the effect of the chemotherapy on WBC, lymphocytes, and skin testing results. This fact was considered in interpreting the data and nutritional status and resulted in the standard and modified assessments. It is the opinion of the investigators that the modified nutritional assessment more accurately reflects the nutritional status for the patients (both standard and modified assessments were done). The overall nutritional status for these patients, as viewed by the modified nutritional assessment, showed that 7 of the 14 patients showed an improvement in nutritional status from the first to the second assessment. Four of the 14 showed declines in nutritional status and three of the patients showed no significant change. Type of cancer seemed to have no significance in the study. From this small study, it was impossible to predict which group of patients would show an improvement or a decline in nutritional status, and the study reinforces the idea that each patient should be evaluated separately in that the critical point in treatment may be different for each patient. A larger study of this area is suggested.

Part II of this study was not done.

STATUS: (C)

TITLE: Dietary Fat and Its Relation to Recurrence of Breast Cancer

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC K. David McCowen, MC
LTC Stephen R. Plymate, MC
Suresh B. Katakkar, M.D.
MAJ Martin L. Bassett, MC
1LT Ellen Bracy, SP

WORK UNIT NO: 79/66

TECHNICAL OBJECTIVE

To determine the role of the dietary fat through prolactin-estrogen balance for the recurrence of the breast cancer both in pre and postmenopausal patients.

METHOD

The plan is to investigate the role of dietary fat by obtaining the normal dietary patterns in high risk group and breast cancer patients (approximately 40). A diet history will be taken and a blood sample obtained to determine serum prolactin, estradiol, serum cholesterol, and triglyceride levels. These patients will be closely followed in the Oncology Clinic and an attempt will be made to correlate the fat content, prolactin-estrogen ratio, and the recurrence of breast cancer with the disease-free interval.

PROGRESS

(80 10 - 81 09) Due to the departure of the original principal investigator plus the departure of three of the co-investigators, time restrictions required that this protocol be terminated after four patients had been entered.

STATUS: (T)

TITLE: Case Control Questionnaire for Patients with Large Bowel Cancer and Their Relatives Without It.

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANT: Suresh B. Katakkar, M.D., DAC

WORK UNIT NO: 79/78

TECHNICAL OBJECTIVE

To identify and confirm factors associated with large bowel cancer. Controls are siblings of patients with large bowel cancer in order to eliminate most hereditary and cultural factors.

METHOD

All colo-rectal cancer patients at Madigan who are, in the opinion of the physician, willing and able to complete a questionnaire and have a sibling who is willing and able to do the same will be asked to complete a questionnaire including questions regarding life style, diet, family history, medical history, and the Srole Anomie Scale. Phase I will be a pilot study to include 30-50 matched pairs. After evaluation of the pilot study, Phase II will be initiated to include 500+ matched pairs of patients. There will be an annual follow-up of patients and analysis of response. Long-term follow-up is planned to determine if risk factors correlate with actual colo-rectal cancer incidence.

PROGRESS

(79 10 - 80 09) Six patients were entered by MAMC and 18 by other institutions for the pilot study. Since then the protocol has been revised and submitted for NCI funding as a SWOG study. If funding is forthcoming, the revised protocol will be submitted for approval.

(80 10 - 81 09) The follow-up study was not funded by NCI. Plans for submission to Fred Hutchinson Cancer Research Center, Seattle, WA, are under consideration.

STATUS: (O)

TITLE: High Dose Oral Provera for ER+ and ER Unknown Metastatic Breast Cancer in Post-menopausal Women

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: MAJ Lauren K. Colman, MC
CPT Thomas M. Baker, MC

WORK UNIT NO: 81/101

TECHNICAL OBJECTIVE

To determine whether or not Provera administered orally in a dose of 800 mg per day can cause regression of recurrent breast cancer occurring in the post-menopausal woman.

METHOD

Patients with histologically proven breast cancer who are at least one year post-menopausal with extensive breast cancer are eligible for this protocol. Patients with estrogen receptor positive tumor are eligible as well as those where the estrogen receptor status is unknown. Patients must have measurable disease and will have a careful preoperative evaluation and follow-up. Treatment will consist of 800 mg of oral Provera per day taken in divided doses. Treatment will continue for as long as the tumor remains stable or regresses. Unacceptable toxicity or patient refusal of treatment will be reasons for removal from the study.

PROGRESS

(81 07 - 81 09) This protocol is awating approval before implementation.

STATUS: (O)

TITLE: The Effect of Nephrosis on Treated Hypothyroidism

PRINCIPAL INVESTIGATOR: LTC Gary L. Treece, MC

PROFESSIONAL ASSISTANTS: COL Bruce L. Fariss, MC
COL Stanton Brown, MC
LTC Stephen R. Plymate, MC
MAJ Lawrence Agodoa, MC
MAJ Louis N. Pangaro, MC
MAJ David Turnbull, MSC

WORK UNIT NO: 81/56

TECHNICAL 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?

METHOD

Patients to be studied are: normals; normal treated with L-thyroxine for one month; sujects with hyperthyroidism; with hypothyroidism, primary untreated; with hypothyroidism treated for one month with L-thyroxine; with the nephrotic syndrome; subjects with the nephrotic syndrome treated for one month with L-thyroxine. A 24-hour urine for volume, creatinine, total protein, urine protein, electrophoresis, T_4, and T_3 will be completed, and the following day, after an overnight fast, blood 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). Thyrotrophin releasing hormone test will then be performed, fasting, 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. Exceptions to the protocol include the following: (a) urine protein electrophoresis will not be performed on urine with a total protein of <150 mg for 24 hours; (b) patients with known cardiovascular disease or age >50 years will be excluded from the treated groups; and (c) 24-hour urines will be obtained prior to or at least 72 hours after the TRH test.

PROGRESS

(81 03 - 81 09) Three patients with the nephrotic syndrome have been studied in an untreated state. One of these patients has been found to be hypothyroid and is being further evaluated. Additional patients are being sought and blood and urine is being stored. Work will soon begin on the establishment of the urinary T_4 and T_3 assays.

STATUS: (O)

TITLE: In vitro Identification of Tumor Associated Antigens

PRINCIPAL INVESTIGATOR: COL Clarence M. Virtue, MC

PROFESSIONAL ASSISTANT: MAJ Martin H. Crumrine, MSC

WORK UNIT NO: 75/14

TECHNICAL OBJECTIVE

The purpose of this investigation is to identify, using an in vitro technique, the tumor associated antigens of breast carcinoma.

METHOD

Phase I: Ten C_3H-strain mice with implanted murine breast carcinoma will be obtained, and, after tumor growth has progressed beyond palpable stage, the mice will be sacrificed, and tumor tissue removed. Tissue treatment as listed in protocol.

Phase II: Tumor tissue obtained from the Department of Pathology (either from autopsy or surgical specimen) and non-tumor tissue from the same subject will be emulsified and treated in a similar manner as the mouse tumor tissue outlined in Phase I.

Phase III: Once the specific tumor associated antigens from mouse breast carcinoma are separated (Phase I), the antigens will be pooled and held at $-80^{\circ}C$. Forty C_3H-strain mice with implanted murine breast carcinoma will be obtained. Ten of these mice will be separated and have no further procedures. Twenty other mice will undergo resection of the tumor mass, and ten will subsequently receive an injection of the specific murine tumor associated antigens (obtained in Phase I) combined with Fruend adjuvant, followed by a booster injection with tumor associated antigen without tumor resection. The mice will then be observed and compared.

PROGRESS

(80 10 - 81 09) In a previous year, murine mammary tumor tissue extraction has been subjected to molecular separation in Sephadex G200 column. Concentrated separation segments have been given to subject mice before tumor load given and mice were observed for tumor growth.

This protocol had to be cancelled this fiscal year, due to the departure of all of the investigators.

STATUS: (T)

TITLE: Immunotherapy of Murine Mammary Carcinoma

PRINCIPAL INVESTIGATOR: COL Clarence M. Virtue, MC

PROFESSIONAL ASSISTANTS: LTC Joel W. Black, MC
MAJ George S. Ward, VC

WORK UNIT NO: 77/77

TECHNICAL OBJECTIVE

Immunotherapy has as yet made only a minimal contribution to the treatment of malignant disease, due in large measure to the lack of pure tumor associated antigen. If tumor associated antigen were obtained in pure form and administered with Levamisol so as to enhance the anti-tumor immune response, after surgery and chemotherapy had reduced tumor load, results might be markedly improved. The purpose of this protocol is to explore that possibility, using mammary tumor-bearing mice.

METHOD

Murine mammary tumors from tumor-bearing mice will be excised, the tumor tissue homogenized in saline and freeze-thawed, and the supernatant concentrated by dialysis against dry silica gel and passed through G-200 sephadex column for separation. The separate fractions so obtained will then be concentrated and small aliquots of each fraction will be tested for tumor antigen by skin testing on the mice whose tumors have been excised. Fractions identified as having tumor associated antigens will then be processed by quantitative electrophoresis to separate the individual proteins. These individual fractions will be concentrated and the fraction containing tumor antigen will be identified by skin testing on tumor-excised mice. After identification of specific tumor antigen fractions, more will be separated from additional tumor and used to treat various groups of mice as outlined in the protocol. All groups of mice will be compared for length of survival.

PROGRESS

(80 10 - 81 09) In a previous year, C_3H mice were divided into control and treatment groups with various treatment groups receiving Cytoxan and tumor vaccine prepared by Sephadex G-200 column separation. Mice were given a mammary tumor load and observed.

This study had to be cancelled during fiscal year 1981 due to the departure of the investigators.

STATUS: (T)

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

TITLE: A Comparison of the Bain's Anesthesia Circuit to the Circle Absorber System in Relation to Changes in Oxygen Measurements

PRINCIPAL INVESTIGATOR: CPT Craig E. Anderson, ANC

PROFESSIONAL ASSISTANTS: LTC Michael R. Moon, MC
MAJ Leo A. Le Bel, ANC

WORK UNIT NO: 81/49

TECHNICAL OBJECTIVE

To compare the merits of two breathing circuits, the Bain's Circuit and the semi-closed circle absorber, in improving post-operative pO_2 as measured by ear oximetry.

METHOD

Approximately 16 patients scheduled for elective surgery requiring general endotracheal anesthesia will be randomized to two groups utilizing the last two digits of the SSAN for randomization. One group will be anesthetized using the Bain's Circuit and the other group will be anesthetized using a circle system. Data will be collected twice on each patient with the use of the ear oximeter. Preoperative pO_2 will be measured the night before surgery for both groups. Postoperative pO_2 will be measured within 90 minutes post-completion of surgery and there will be at least 6 hours between the pre and post-operative measurements. F Test will be used to analyze data for significant differences.

PROGRESS

(81 03 - 81 09) Thirty patients were studied in each group. Utilizing an F test, it was determined that the variances of the two groups were not significantly different; therefore, the investigators conclude that the Bains' Circuit and the Circle CO_2 absorber circuit are no different in terms of their lasting effects on the human pulmonary system as measured by sO_2.

The principal investigator is in the process of preparing a paper from the data.

STATUS: (O)

TITLE: A Research Proposal to Study the Effects of Pretreatment with Gallamine, Pancuronium, and Curare on the Action of Succinylcholine

PRINCIPAL INVESTIGATOR: MAJ Leslie D. Collar, ANC

PROFESSIONAL ASSISTANTS: LTC Michael R. Moon, MC
MAJ Leo A. Le Bel, ANC

WORK UNIT NO: 81/50

TECHNICAL OBJECTIVE

To determine the optimum combination of dosages and/or combinations of drugs that minimize the chance of complications while at the same time providing the fastest time to onset of optimal intubation conditions.

METHOD

The sample population who meet the criteria for the study as stated in the protocol will be divided into four groups of at least 10 subjects by randomization. Group I will be the control group. Each subject will be given a routine premedication. After preoxygenation and from the induction of anesthesia until total paralysis for intubation is achieved, the patient will continue to be ventilated with 100 % oxygen via face mask. During the induction, members of Group I will receive a paralyzing dose of succinylcholine chloride, injected into a free flowing IV line via a T-piece connected directly at the catheter site. The time of injection will be noted and a stop watch started. At periodic intervals, muscle relaxation will be assessed using a nerve stimulator with the amplitude control knob set at maximum. The ulnar nerve will be stimulated at the ulnar groove for observation of flexion of the fingers and adduction of the thumb. When no response is elicited, the stop watch will be stopped and time recorded. The same procedures will be followed for groups 2, 3, and 4, with one exception. In addition to the succinylcholine, groups 2, 3, and 4 will receive a pretreatment dose of gallamine, pancuronium, and d-tubocurarine, respectively.

PROGRESS

(81 03 - 81 09) A total of 20 patients were investigated, 5/group. An effort was made to determine which group more closely approximated the control group. No appreciable difference was found in time from administration of succinylcholine to abolishment of muscle twitch. MAJ Collar is in the process of writing the study up in final form.

STATUS: (O)

TITLE: Effect of Hemoglobin Concentration on Depth of Anesthesia Using Enflurane

PRINCIPAL INVESTIGATOR: CPT Steven P. Kelsch, ANC

PROFESSIONAL ASSISTANTS: LTC Michael R. Moon, MC
MAJ Leo A. LeBel, ANC

WORK UNIT NO: 81/51

TECHNICAL OBJECTIVE

To determine if, when using Enflurane inhalation anesthesia, hemoglobin concentration influences the depth of anesthetic level as measured by changes in pulse rate and blood pressure.

METHOD

Subjects (minumum of 25) in ASA category I and non-obese who are admitted for elective orthopedic procedure on an upper or lower extremity will be studied. Premedication: demoral, vistaril, atropine, dose appropriate to age, hieght, and weight. Preoperative measurements: hemoglobin level and preinduction pulse and blood pressure base line. Induction with sodium pentothal and inbutation following curare and anectine. Maintenance with N_2O, O_2, Enflurane. Record Enflurane concentration required to maintain pulse and blood pressure within 20% of base line for 75% of procedure.

PROGRESS

(81 03 - 81 09) The data collection is complete on a total of 25 subjects. The data is presently being statistically analyzed.

STATUS: (O)

TITLE: Mothers as Assessors of Their Childrens' Temperatures Without Using Thermometers

PRINCIPAL INVESTIGATOR: MAJ Kathleen Mauro, ANC

PROFESSIONAL ASSISTANT: MAJ Marcia Van Wagner, ANC

WORK UNIT NO: 81/40

TECHNICAL OBJECTIVE

To determine the validity of mothers' perception as assessors of their childrens' temperature without using thermometers. The ability of mothers to accurately assess their childrens' temperature will be analyzed in relation to certain background data.

METHOD

Children who are acutely stressed or in need of immediate medical attention will not be asked to participate in the study. For the purpose of this study, fever will be defined as oral temperature of 100° or higher. Approximately 50 subjects will be studied whose mother states that the child has had a fever in the past 24 hours, who are 3-12 years, and who are able to tolerate an oral temperature assessment. Mothers will be interviewed and asked for background information such as age, educational level, and race. The mother will then be asked to touch her child (place will not be specified) and estimate the child's temperature. Descriptive statistics will be used to analyze data. Background characteristics of the mothers will be examined separately in relation to the accuracy of the assessment of the temperature and analyzed using Chi square statistical procedures.

PROGRESS

(81 02 - 81 09) The study demonstrated that 76% of the mothers were accurate assessors of the temperature of their child. Mothers with afebrile children were slightly more accurate (80% vs 70%). Correct assessment was not related to maternal age, education, number of children, race, thermometer use within 24 hours, or the child's actual temperature. Accuracy was significantly related to the child's sex. Mothers assessing daughters were significantly more accurate ($p=0.10$).

STATUS: (C)

TITLE: The Effects of Anesthetic Waste Gases on Army Nurse Corps Anesthetists

PRINCIPAL INVESTIGATOR: CPT Mary L. Muench, ANC

PROFESSIONAL ASSISTANTS: LTC Michael R. Moon, MC
MAJ Leo A. LeBel, ANC

WORK UNIT NO: 81/52

TECHNICAL OBJECTIVE

To determine the incidence rate of spontaneous abortion and congenital abnormalities experienced by Army Nurse Corps anesthetists and their spouses.

METHOD

Approximately 200 active duty ANC anesthetists will be surveyed to determine basic biographical data, pregnancy history of the past three years, and specific data concerning the working environment. The incidence rates for spontaneous abortions and congenital abnormalities will be tallied and p values computed to determine the significance of differences between male and female respondents. Data for the entire study group will be compared for significant differences with similar data from other existing studies.

PROGRESS

(81 03 - 81 09) Questionnaires have been returned with a good response rate and responses have been tabulated. Investigator is now in the process of statistically analyzing the data and will summarize the study in a paper.

STATUS: (O)

TITLE: The Effects of Laryngoscopy with Intubation at Variable Time Periods After Lidocaine Spray on Blood Pressure and Heart Rate

PRINCIPAL INVESTIGATOR: CPT Candace L. Plumlee, ANC

PROFESSIONAL ASSISTANTS: LTC Michael R. Moon, MC
MAJ Leo A. LeBel, ANC

WORK UNIT NO: 81/53

TECHNICAL OBJECTIVE

To evaluate the cardiovascular effects of intubation at a time interval of thirty seconds and sixty seconds post spray of four percent lidocaine.

METHOD

Patients (10/group) scheduled for elective surgery requiring general anesthesia, ASA classification I without regular medication consumption will be premedicated on a mg/kg basis with identical medications and appropriate IV fluids. A rapid induction technique will be utilized: curare 3 mg IV, 5 L O_2 via face mask for 3-5 minutes, thiopental 4 mg/kg IV without test dose followed immediately with succinylcholine IV 1.5 mg IV. Post induction sequence dependent upon group assignment: Group I - laryngoscopy with lidocaine 4% intratracheal spray 3 mg/kg followed immediately with tracheal intubation; Group II - laryngoscopy with spray followed by 30 seconds of mask ventilation with 100% O_2 then second laryngoscopy with intubation; Group III - laryngoscopy with spray followed by ventilation for 60 seconds then second laryngoscopy with intubation. Data collection will be systolic/diastolic BP and heart rate. Time of readings will be as follows: (1) original reading with patient awake in the OR prior to administration of any IV medication; (2) just prior to laryngoscopy with intubation; (3) 30 seconds, one minute, and 90 seconds post intubation. Analysis of variance will be used to analyze data.

PROGRESS

(80 03 - 80 09) At the present time data has been collected on fifteen subjects.

STATUS: (O)

TITLE: MATERNAL STRESS EFFECTS ON FETAL ACTIVITY

PRINCIPAL INVESTIGATOR: LTC Aida L. Rivera, ANC

PROFESSIONAL ASSISTANTS: COL Joseph Sakakini, MC
MAJ Raymond Parker, MSC

WORK UNIT NO: 79/84

TECHNICAL OBJECTIVE

To determine the effects of maternal anxiety and emotional stress on fetal activity during the last month of gestation.

METHOD

Subjects: 200 normatensive, married, primagravida women in the last month of gestation; age 19-30 years; weight gain <25 pounds. The subjects will be given the Taylor Manifest Anxiety Scale. The 30 patients with the highest scores and the 30 patients with the lowest scores will be tested by a 20 minute fetal monitoring tracing in order to determine the existence of any significant differences in fetal activity. Subjects will be followed to delivery and all data obtained from mothers who deliver abnormal fetuses will be deleted from the study. Factors other than stress (smoking, alcohol) will be identified and will be considered when tabulating results. This will be a double blind study and test scores will be ranked in a frequency distribution in order to pick the 30 highest and the 30 lowest scores. If ties scores are present, the needed scores will be drawn at random. The Split Plot Factorial Analysis of Variances - 2.3 will be used for computation of data.

PROGRESS

(79 07 - 81 09) 172 pregnant, primipara, healthy women during the second or third trimester of pregnancy were studied. No significant correlation was found between maternal manifest anxiety and the dependent variables, nor were there any significant differences between different levels of anxiety and the dependent variables. The level of anxiety was assessed controlling for the use of tobacco, alcohol, and caffeinated substances. It was observed that drinking mothers who scored low on anxiety had infants with higher Apgar five scores than drinking mothers who scored high on anxiety. A significant weight difference was found between the infants of non-caffeine users who scored high and low on anxiety. Caffeine alone was also found related to Apgar one scores; the infants of caffeine users had lower scores than the infants of the non-users.

Maternal Stress Effects of Fetal Activity - Rivera

To test fetal activity, 22 women from the original sample who scored high or low on anxiety were submitted to a fetal activity test; their level of stress was also measured. Anxiety and stress were then related to fetal activity and fetal Apgar scores. The data demonstrated that low anxiety favors fetal activity. These fetuses also responded to their movement with more frequent increase in fetal heart rate than the fetuses of mothers who scored high on anxiety. The findings also suggest that some amount of stress could be conducive to a reactive fetus, a sign interpreted by the OB practitioner as an indicator of fetal wellbeing. However, in this instance, a reactive fetus was found not to indicate fetal wellbeing since reactive and non-reactive fetuses had no differences in Apgar scores and number of complications at birth.

LTC Rivera presented a thesis from this protocol to the Pacific Lutheran University as partial fulfillment of the requirements for a degree in Master of Arts in Social Sciences-Human Relations.

STATUS: (C)

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

TITLE: Life Stress, Social Supports, and Personality Factors in Human Male Infertility: Attitudes and Experiences of Men Wishing to Become Fathers

PRINCIPAL INVESTIGATOR: LTC Richard Belts, MC

PROFESSIONAL ASSISTANTS: COL Martin Dresner, MC
MAJ Willis Jacob, MSC
MAJ Raymond Parker, MSC
L. Neal Teng, Ph.D. (Candidate)
Stanley Sue, Ph.D.

WORK UNIT NO: 81/76

TECHNICAL OBJECTIVE

To avoid methodological problems of previous research while attempting the first double-blind investigation of how levels of external or intrapsychic stress, social supports, and individual personality characteristics relate to human male infertility.

METHOD

All new male patients seen in the Inferility Clinic will be eligible to participate. There will be an experimental group and a control group made up of expectant fathers. The experimental group will be divided into (1) patients with a medically identifiable cause of infertility; (2) idiopathic infertiles; and (3) patients with no abnormal findings based on the serial semen analyses. All subjects will complete a brief general information form providing personal background and demographic data. Psychometric parameters will be measured by a 47 item Life Experiences Survey (high stress) the 117-item Hassles Scale (low stress), the Minnesota Multiphasic Personality Inventory, and a 20-item revision of the Perceived Social Supports Scale. Physiological measures in determining fertility will include at least two but preferably three standard semen analyses assessing sperm count, motility, volume, and morphology. A urologic examination in addition to the standard medical procedures will be done if this has not been previously performed. All psychometric testing will be done before the results of the semen analyses or urologic exam are known to either the physician or the patient.

PROGRESS

(81 04 - 81 09) This protocol was terminated due to the difficulty of gathering a large enough population for statistical purposes.

STATUS: (T)

TITLE: Antepartum Fetal Heart Rate Monitoring and Subsequent Fetal Outcome at Delivery

PRINCIPAL INVESTIGATOR: LTC Edward E. Dashow, MC

PROFESSIONAL ASSISTANTS: COL Joseph Sakakini, MC
LTC Roger A. Spencer, MC

WORK UNIT NO: 81/37

TECHNICAL OBJECTIVES

To review all pregnancies where antepartum monitoring was used and assess the following: (1) the outcomes of various abnormal tracings; (2) the results of this institution relative to those of other large institutions such that our methods and outcomes may be compared; (3) to review our data for a yet unpublished semmingly ominous deceleration pattern represented by spontaneous deceleration without apparent stimulus.

METHOD

All charts containing antepartum heart rate tracings for the past two years will be reviewed for the following: (1) changes which commonly denote fetal jeopardy; (2) spontaneous decelerations not precipitated by contractions; (3) comparison purposes with other large institutions; and (4) interesting cases which would then be placed in a teaching file.

PROGRESS

(81 01 - 81 09) Two thousand charts have been reviewed with 16 charts being positive. All positives have been associated with fetal jeopardy.

STATUS: (O)

TITLE: Management of Premature Rupture of Membranes in Patients at 34-40 Weeks Gestation

PRINCIPAL INVESTIGATOR: LTC Edward E. Dashow, MC

PROFESSIONAL ASSISTANTS: COL Joseph Sakakini, MC
MAJ Alexander R. Smythe, MC

WORK UNIT NO: 81/55

TECHNICAL OBJECTIVES

(1) To ascertain whether a decreased Caesarean section rate will result with conservative management in the patient with rupture of membranes and an "unripe" cervix at 34-40 weeks gestation; and (2) To judge whether a decreased infection rate will result with conservative management in the above patient group as opposed to those where labor is medically initiated immediately in spite of the unprepared cervix.

METHOD

Following initial evaluation, patients who are ≥34 weeks gestation will be placed in three groups. Group A (Bishop's inducibility score >7) will be induced and/or augmented as expeditiously as possible and evaluated per usual obstetrical guidelines. Group B (Bishop's score <7 and odd terminal SSN digit) will be placed under observation using standard obstetrical monitoring and treated according to the progress of each patient. Group C (Bishop's score <7 and even terminal SSN digit) will be induced or augmented as soon as possible following admission to the labor and delivery unit.

PROGRESS

(81 03 - 81 09) Eight patients have entered each arm of the study. Thus far, conservative management and early inducement have shown equal results with no ill effects from the initial management.

STATUS: (O)

TITLE: Gynecological Oncology Procedure Training

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANTS: LTC Richard Belts, MC
LTC George Ward, MC

WORK UNIT NO: 81/42

TECHNICAL OBJECTIVES

To provide training to OB-GYN residents in the technical aspects of various types of abdominal resections and anastomoses, to include training in the use of stapling instruments.

METHOD

Each resident participating will be provided with a large anesthetized dog. Under staff supervision, the following procedures will be accomplished on each animal:

1. exploratory laparotomy
2. resection and end to end anastomosis of small bowel
3. resection and end to side anastomosis of small bowel to colon
4. side to side anastomosis using the GIA stapler
5. end to end bowel anastomosis using the EEA stapler.

At the completion of each session, the animal will be sacrificed.

PROGRESS

(81 02 - 81 09) This protocol has not been implemented. It will begin when the new operating room is completed and the training schedule is changed.

STATUS: (O)

TITLE: Effects of Pure HCG, Progesterone, HPL, Estradiol 17-B, and Estriol on Migration Inhibition Factor in Vitro.

PRINCIPAL INVESTIGATOR: CPT Arthur S. Maslow, MC

PROFESSIONAL ASSISTANT: LTC Stephen R. Plymate, MC

WORK UNIT NO: 81/94

TECHNICAL OBJECTIVE

The fetal allograft enjoys an immune competence which prevents its rejection by the maternal host. The mechanism of this competence is unknown at this time. The object of this project is to determine what effect(s) various concentrations of the hormones noted above have on migration inhibition factor, one of the potent soluble factors produced by lymphocytes during the immune reaction.

METHOD

Blood will be obtained from five pregnant patients in the first trimester. Lymphocyte stimulation assay (comparing PHA and pokeweed) will be run parallel with M.I.F. assay to test effects of various concentrations of the individual hormones tested on M.I.F. If inhibitory effects are noted, assays will then be attempted of the hormones used in conjunction with one another (i.e., HCG and progesterone). Guinea pigs will be injected with a substance to produce monocytes in the abdominal cavity. They will then be sacrificed and the monocytes will be harvested and used in a study to determine beta HCG on migration inhibition factor. The guinea pig monocytes will be used because they are produced in abundance and are easily harvested as opposed to human monocytes. The experiment is designed to test the function of migration inhibition factor produced by human lymphocytes and the effect of migration inhibition factor on the monocytes (in this case guinea pig monocytes).

PROGRESS

(81 07 - 81 09) Equipment and supplies have now be assembled. The investigators are now in the process of developing an outline for the conduct of the various aspect of the study.

STATUS: (O)

TITLE: Management of Intractable Postpartum Hemorrhage by the Use of 15-Methyl Prostaglandin F2 Alpha-Tromethamine Salt

PRINCIPAL INVESTIGATOR: COL Jospeh Sakakini, MC

PROFESSIONAL ASSISTANT: LTC Edward E. Dashow, MC

WORK UNIT NO: 81/36

TECHNICAL OBJECTIVE

To study the effects of 15-methyl prostaglandin F2 Alpha-THAM given IM to individuals having postpartum hemorrhage secondary to uterine atony that have been treated with all other conventional methods.

METHOD

This drug will only be utilized after the conservative management has failed and the patient is then considered for a surgical procedure to stop the severe postpartum hemorrhage and only if the use of the drug is not contraindicated by asthma, hypersensitivity to the drug, active cardiac, pulmonary, renal, or hepatic disease, or a history of these conditions or anemia, jaundice, or epilepsy. At the time of the infusion, the IV infusion of oxytocin will be discontinued. The IV fluids will be continued and no further methergine will be given. Vital signs will be monitored and recorded every 15 min and continued for two hours after the final injection. Hemoglobin and hematocrit will be checked at 24 and 48 hours after the last injection. The volume of blood loss after delivery and the amount of blood loss after the initial injection will be estimated and recorded. The degree of contraction of the uterus will be determined by palpation before the injection and one-half hour after each injection. The rate of hemorrhage will be estimated one-half hour after each injection and recorded as either increased, unchanged, or stopped. The presence of lacerations of the genital tract and retained placental fragments will be ruled out prior to entrance in the study.

PROGRESS

(81 01 - 81 09) Thus far the above treatment has been used once without success. This was secondary to a grossly infected uterus. The investigators are continuing to scan for further subjects.

Due to the departure of COL Sakakini, LTC Edward Dashow will become the principal investigator.

STATUS: (O)

TITLE: Fetal Heart Rate Response and Maternal Uterine Contraction Response to Amniocentesis in Pregnancy

PRINCIPAL INVESTIGATOR: Alexander R. Smythe, MAJ, MC

PROFESSIONAL ASSISTANT: Edward Blackmon, CPT, MC

WORK UNIT NO: 80/08

TECHNICAL OBJECTIVE

To quantitate the fetal heart rate response and uterine contraction response to amniocentesis at various gestational ages during pregnancy.

METHOD

Pregnant patients who undergo diagnostic amniocentesis for L/S ratio for reasons such as repeat cesarean section, medical of elective induction of labor for reasons such as diabetes hypertension, or Rh disease, or for premature labor and a premature fetus will be included in this study.

The patient will be placed on an external fetal clorometric monitor for fetal activity determination for 30 minutes prior to amniocentesis. A realtime ultrasound will be performed to assess the bipartietal diameter and placental localization and amount of amnionic fluid present. An amniocentesis will be performed in the usual fashion and fetal heart rate response and uterine contraction pattern response will be assessed for 30 minutes after amniocentesis.

The measured parameters will be analyzed for indications of fetal stress or fetal well-being at the time of the performance of the amniocentesis. Comparison will be made with fetal parameters and uterine contractions for the baseline during the amniocentesis.

PROGRESS

(80 01 - 81 09) This project has been compelted. There was no increase in uterine irritability secondary to amniocentesis. The fetal heart rate response to amniocentesis is an indicator of fetal wellbeing.

A paper has been accepted for presentation at the Armed Forces Section of the American College of OB/GYN in October 1981.

STATUS: (C)

TITLE: Impact of Fetal Monitoring on the Premature Infant

PRINCIPAL INVESTIGATOR: MAJ Alexander Smythe, MC

PROFESSIONAL ASSTS: COL Joseph Sakakini, MC
D. A. Luthy, M.D.
E. B. Larson, M.D.
K. K. Shy, M.D.
G. VanBelle, M.D.

WORK UNIT NO: 80/48

TECHNICAL OBJECTIVE

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

METHOD

Follow-up will be performed on infants who have had fetal monitoring. Those fetuses which have had electronic fetal monitoring and fetal scalp blood sampling done will be followed and compare to randomized traditional auscultation fetal heart rate. Comparisons of fetal outcome and wellbeing will be made. A comparison will be made of infants <1100 gm and >1100 gm. Infants will be followed and evaluated for evidence of retardation, cerebral palsy, and hearling loss at 6 months, 1 year, 1½ years, and 2 years.

PROGRESS

(80 06 - 81 09) This project has not begun due to changes required in the protocol by both HSC and the IRB at the University of Washington. However, all revisions have been made and approved, organizational difficulties have been resolved, and funding has been resolved so the protocol will commence within the next few weeks.

STATUS: (O)

TITLE: Ritodrine Hydrochloride Applications to Fetal Distress

PRINCIPAL INVESTIGATOR: LTC Roger A. Spencer, MC

PROFESSIONAL ASSISTANTS: COL Joseph Sakakini, MC
LTC Edward Dashow, MC

WORK UNIT NO: 81/17

TECHNICAL OBJECTIVE

To determine if ritodrine hydrochloride in arresting labor will interrupt fetal distress, reduce fetal acidosis, and result in healthier infants with less requirement for neonatal intensive care with consequent reduced hospital costs.

METHOD

Phase I (pilot study): Subjects will be patients in whom fetal monitoring indicates fetal distress and a decision is made to perform cesarean section. Subjects will receive 250 micrograms per minute ritodrine hydrochloride IV or sterile saline in equal volume in a random double-blind method. No attempt will be amde to delay cesarean section. If after this infusion, labor has stopped and fetal distress is no longer in evidence, the patient will be observed for 30 minutes, after which cesarean section will be performed. If fetal distress reoccurs, cesarean section or the best treatment for the patient will be performed immediately. At cesarean section, umbilical artery and vein pH will be measured from a sample obtained immediately after passing the infant to the pediatrician in attendance. Apgar scores at 1, 5, and 10 minutes and duration of intensive care will be recorded. At the end of Phase I the code will be broken and the groups compared according to parameters of Apgar score, umbilical artery and vein pH, duration of neonatal intensive care, and hospital costs. Phase II: If the study group shows no harmful effects compared to the control group, 70 additional patients will be studied and further analyzed.

PROGRESS

(80 11 - 81 09) Notification of approval was received in March 1981. Two patients have been entered in the protocol. Another 2½ years is anticipated to collect enough patients (30) for statistical significance.

Due to the departure of LTC Spencer, the principal investigator, effective 1 Oct 81, is LTC Edward Dashow.

STATUS: (O)

DETAIL SHEETS

FOR

PROTOCOLS

DEPARTMENT OF PATHOLOGY

TITLE: The Effect of In Vivo Vitamin B6 Supplementation on In Vitro Lymphocyte Transformation

PRINCIPAL INVESTIGATOR: MAJ Richard Keniston, MC

PROFESSIONAL ASSISTANTS: CPT Michael Smith, MSC
Louis Matej, M.T., DAC

WORK UNIT NO: 79/21

TECHNICAL OBJECTIVE

To demonstrate that optimum human lymphocyte transformation in vitro requires in vivo vitamin B6 (as pyridoxal phosphate, PLP). PLP is required for the biosynthesis of the polyamines, which are required for optimal DNA synthesis by nitrogen-stimulated T-lymphocytes. Most human beings are far from being saturated with PLP, and, therefore, their immune function might benefit from vitamin B6 supplementation.

METHOD

Normal volunteers: Ten male and ten female volunteers will follow the schedule below. All lymphocyte transformations (LT) will be done by the ^{3}H-thymidine uptake method without mitogen, using phytohemagglutinin and concanavalin A. Vitamin B6 assays will be completed on serum by an enzymatic method. Total blood drawn for both procedures will be 20 ml/drawing.

Schedule:
- 0 wks - L.T., B6 assay, begin multivitamins, p.o. 2 mg B6, q.d.
- 4 wks - L.T., B6 assay, begin B6 vitamins p.o., 50 mg q.d.
- 6 wks - L.T., B6 assay
- 12 wks - L.T., B6 assay, end B6 supplementation
- 14 wks - L.T., B6 assay
- 20 wks - L.T., B6 assay, end multivitamin supplementation
- 24 wks - L.T., B6 assay

The magnitude of mitogen stimulation will be compared in steps 1-7. These will also be correlated with serum B6 levels.

Chronically ill volunteers: Chronically ill patients with apparent immune deficiency will be identified. B6 levels will be determined and the immune dificient patients will be given B6 supplementation. A condensed form of the schedule above will be followed. Any improvement in the patient's in vitro and in vivo immune response will be noted. In vitro response will be measured by lymphocyte transformation and in vivo response by clinical signs.

The Effect of In Vivo Vitamin B6 Supplementation on In Vitro Lymphocyte Transformation - Keniston

PROGRESS

(80 10 - 81 09) Work continues on this project. To date, the data show that dietary vitamin B6 supplementation markedly stimulates the (methyl-^{3}H)thymidine uptake of PPHA stimulated normal human lymphocytes. Evidence has been presented that a critical role of vitamin B6 in human lymphocyte activation is the generation of putrescine and polyamines, which are required for optimal macromolecular synthesis. Interestingly, the observed degree of stimulation of HDA synthesis (2 to 3-fold) was similar to that seen with megadoses of vitamin C. A paper was written but was not accepted due to the small number of subjects in the study.

Currently, a paper is being prepared entitled "Hypoalbumin with Vitamin B6 Deficiency and Mortality". From April to July 1981, all patients who had SMAC albumins at MAMC (11,099) were followed and the results correlated with one-month mortality. A highly significant inverse correlation was found. PLP levels were found to correlate with albumin levels. From this, an equation relating mortality to PLP levels was derived. It is thus possible to predict mortality with a high degree of accuracy if either the albumin level or PLP level is known. A hypothesis relating PLP deficiency to impaired macromolecular synthesis is presented.

Studies are also being done on a project relating PLP to aminoglycoside toxicity. Preliminary results show that PLP reverses the antimicrobial effect of gentamycin in vitro for a few usually highly susceptible bacteria. Also, PLP readily forms covalent complexes with aminoglycoside antibiotics at neutral pH in organic solutions, suggesting that aminoglycosides may deplete PLP in man. Hypotheses as to how B6 deficiency results in improved immune function and susceptibility to infection by PLP synthesizing organisms are also being developed.

STATUS: (O)

PULBICATION: Keniston, R.C.: Polyamine-Pyridoxal 5'-Phosphate Interaction: Effects of pH and Phosphate Concentration on Schiff's Base Formation. Physiol Chem Phys 11:465-70, 1979.

PRESENTATION: Role of Vitamin B6 and Putrescine in Human Lymphocyte Activation: Beneficial Effect of Dietary Vitamin B6 Supplements. Joint Meeting, British Columbia Society of Clinical Chemists and American Association for Clinical Chemists (NW Section), 20-22 Sep 79, Harrison Hot Sptings, BC.

TITLE: The Role of Bacterial and Chlamydial Agents in Acute Epididymitis and the Effect of Antibiotic Therapy

PRINCIPAL INVESTIGATOR: LTC John K. Podgore, MC

PROFESSIONAL ASSISTANTS: CPT Robert U. Finnerty, MC
COL Alfred S. Buck, MC

WORK UNIT NO: 78/20

TECHNICAL OBJECTIVE

To determine what role certain infectious agents (*Mycoplasma*, *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and aerobic colliform bacteria) play in the etiology and pathogenesis of acute epididymitis; and to compare two commonly used forms of therapy for treatment of epididymitis.

METHOD

Study population: All males seen with the diagnosis of acute epididymitis who are hospitalized at Madigan Army Medical Center and who have had no antibiotic therapy in the month preceding the current episode of epididymitis.

Controls: A group of age and race-matched controls will be selected from Ft Lewis military personnel undergoing routine physical examinations.

Two urethral swabs will be obtained using calcium alginate swabs; the first for culture of *N. gonorrhoeae* and Gram stain; the second for culture of *C. trachomatis* and *U. urealyticum*.

Urine specimens: The first 10 cc of voided urine and a midstream urine will be obtained. The sediment of the first voided urine and midstream urine will be examined for number of WBC per high-powered field and bacteria. Both urine specimens will be cultured quantitatively for coliforms.

Blood specimens: 10 cc will be obtained by venipuncture for serology for *C. trachomatis*.

Similar urine and blood specimens will be obtained from the controls.

When surgery is clinically indicated to rule out torsion of the testicle, direct cultures of epididymal fluid will be

obtained at scrotal exploratory surgery. Radionucleatide scrotal scans will be done on all patients within 48 hours to rule out testicular torsion.

Treatment: All patients will be placed at bed rest with scrotal elevation until afebrile and pain has subsided.

If no coliforms are seen on the initial unspun urine and the midstream urine culture shows less than 10^3 coliforms per ml, the patient will be randomly treated with 100 mg doxycycline b.i.d. for 10 days or with 500 mg ampicillin q.i.d. for 10 days. If the patient's medical records or history indicate possible allergy to either of these agents, the alternate safe agent will be administered.

If coliforms are seen on the initial unspun urine or grown from any specimen with colony counts greater than 10^3/ml, patients will be treated individually according to results of urine cultures and antibiotic sensitivity patterns. Patients will be instructed not to have intercourse for at least 14 days after initiation of treatment.

Follow-up: All patients will be reexamined at 3, 7, 14 days, and 6 weeks after initiation of therapy. The presence of scrotal erythema, edema, and tenderness will be noted and recorded by standard protocol. Repeat cultures will be performed at 7 and 14 days and 6 weeks for *C. trachomatis*, *U. urealyticum*, and any other pathogen initially recovered. Ten cc of convalescent blood will be obtained for serologic testing at 14 days and 6 weeks.

PROGRESS

(77 12 - 81 09) The progress on this protocol has been pending during the last half of the fiscal year while another collaborator was sought in the Urology Service. As soon as a new co-investigator is available from the Urology Service, more patients will be entered. Preliminary results have been tabulated and were presented at the American Public Health Association Meeting in November 1980.

STATUS: (O)

TITLE: The Effect of Antibiotic Therapy in the Last Trimester of Pregnancy Upon the Incidence of Neonatal Conjunctivitis and Pneumonia Due to *Chlamydia trachomatis*.

PRINCIPAL INVESTIGATOR: LTC John K. Podgore, MC

PROFESSIONAL ASSISTANTS: COL Errol Alden, MC
LTC Richard Belts, MC
Catherine Yokan, M.D., DAC

WORK UNIT NO: 78/38

TECHNICAL OBJECTIVE

To determine the effect of treatment with erythromycin, 500 q.i.d. for 14 days, administered orally to pregnant women during the last trimester of pregnancy with cervical *Chlamydia trachomatis* colonization. The incidence of subsequent neonatal colonization and conjunctival and pulmonary infection will be noted in treatment and control infants over a one-year interval after delivery.

Addendum: The effect of erythromycin therapy on the vaginal and neonatal carriage of this organism will be simultaneously studied.

METHOD

Cervical specimens will be obtained on sterile cotton swabs during the routine 32-week pelvic examination.

Serum specimens will be obtained from a portion of blood routinely drawn for rubella antibody screening. The microimmunofluorescent serology for chlamydia will be done according to standard methods.

Conjunctival and nasopharyngeal specimens will be obtained during the nursery discharge examination and at the 4 week, 2 month, and 6 month examinations.

Serum specimens will be obtained from the study children at 6 and 12 months for the microimmunofluorescent serology titer for chlamydia.

Conjunctival specimens will be obtained from all study infants that present with acute conjunctivitis for Giemsa stains, bacterial and chlamydial cultures.

The Effect of Antibiotic Therapy in the Last Trimester of Pregnancy - Podgore

Nasopharyngeal specimens will be obtained for Gram stain, bacterial, and chlamydial culture in all study infants presenting with pneumonia during the first year of life.

All patients with positive chlamydial cultures will be assigned randomly into the treatment and non-treatment groups. The treatment group will receive 500 mg erythromycin q.i.d. for 14 days.

Culture of the vaginal vault and rectum for Group B streptococci prior to and following therapy with erythromycin will be done.

PROGRESS

(78 06 - 81 09) Erythromycin administered to women in the third trimester of pregnancy and their spouses was effective in eradicating *Chlamydia trachomatis* and preventing neonatal infection.

STATUS: (C)

PRESENTATION: Podgore, J.K., Belts, R., Alden, E., and Alexander, E.R.: Effectiveness of Maternal Third Trimester Erythromycin in Prevention of Infant *Chlamydia trachomatis* Infection. 20th Interscience Conference on Antimicrobial Agents and Chemotherapy, sponsored by American Society for Microbiology, 22-24 September 1980, Abstract #524.

PRESENTATION: Uniformed Services Pediatric Meeting, San Antonio, Texas, April 1981.

AWARD: Margelith Award for Excellence in Clinical Research

TITLE: A Double-Blind Controlled Study Comparing Erythromycin and Amoxicillin Treatment During the Last Trimester of Pregnancy in Prevention of Infant *Chlamydia trachomatis* Infection

PRINCIPAL INVESTIGATOR: LTC John K. Podgore, MC

PROFESSIONAL ASSISTANT: LTC Richard Belts, MC

WORK UNIT NO: 80/72

TECHNICAL OBEJCTIVE

To determine if erythromycin or amoxicillin administered orally to women in the third trimester of pregnancy and doxycycline administered to their spouses will result in the elimination of *C. trachomatis* from cervical and urethral sites as well as prevent colonization and infection in their infants.

METHOD

The subjects will be pregnant women who have *C. trachomatis* isolated from their cervical culture at the routine 32-week gestation exam and their spouses. The women will receive either 250 mg erythromycin q.i.d for 14 days of amoxicillin, 500 mg q.i.d. for 14 days. The spouses will receive doxycycline 100 mg twice a day for 14 days. Upon agreement to participate in the study, a repeat cervical culture will be obtained and the spouse will have an anterior urethral culture for *C. trachomatis*. Other necessary specimens will be obtained. All study infants will have conjunctival and nasopharyngeal specimens obtained at the 2-week, 1, 3, and 6 month examinations. Serum and tear specimens will be obtained at 6 months for microimmunofluorescent antibody titre. Conjunctival specimens will be obtained for Giemsa stain and bacterial and *C. trachomatis* culture in all study infants that present with acute conjunctivitis during the first 6 months. A posterior nasopharyngeal specimen and viral cultures will be obtained from all study children presenting with pneumonia in the first 6 months and serum at the time and 2-3 weeks later for antibody titres. Repeat cervical cultures will be obtained at the time of the 6-week post-partum exam and all patients with *C. trachomatis* will be treated with an effective antibiotic to eliminate the infection and followed-up with cultures. Follow-up urethral cultures will be obtained one week post-therapy from male subjects.

PROGRESS

(80 11 - 81 09) This project was begun in April 1981 when final approval was received from the HSRRB. Data collection is in progress. It is estimated that it will take 9-12 more months to collect enough patients.

STATUS: (O)

TITLE: The Role of Rotavirus in Acute Winter Diarrhea of Egyptian Children

PRINCIPAL INVESTIGATOR: LTC John K. Podgore, MC

PROFESSIONAL ASSISTANT: MAJ Martin Crumrine, MSC

WORK UNIT NO: 81/74

TECHNICAL OBJECTIVE

To determine if rotavirus can be detected in the stool specimens of children treated at the Elshatby University Hospital Oral Rehydration Center, Alexandria, Egypt, for acute diarrhea and dehydration in the month of January 1981.

METHOD

During the principal investigator's TDY to this institution, 50 Egyptian children presenting with acute diarrhea and dehydration were evaluated and treated by the medical staff in the routine manner. Stools that were obtained for routine bacterial and parasitic examinations were saved at the investigator's request. Also during this period, stool specimens were saved from 15 children hospitalized for various reasons except diarrhea. The stool specimens were suspended in normal saline and frozen at -5° to -10° C for three months. The patient specimens and 15 control specimens will be coded to eliminate any evidence of the source. The Rotavirus Elisa Assay Kit will be utilized to test all samples in duplicate, blindly.

PROGRESS

(81 04 - 81 09) The specimens have been processed and the data is being analyzed. The resulting information will be used to serve as a pilot for a large scale diarrhea project at the Naval Medical Research Unit #3 in Cairo, Egypt.

STATUS: (C)

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

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

PRINCIPAL INVESTIGATOR: COL Errol R. Alden, MC

PROFESSIONAL ASSISTANTS: LTC Paul B. Jennings, VC
LTC Ronald W. Brenz, MC
LTC Gary Pettett, MC

WORK UNIT NO: 74/19

TECHNICAL OBJECTIVE

To teach infant resuscitation procedures to nurses, nurse clinicians, OB-GYN residents, and other nonpediatric physicians who may be called upon to treat pediatric emergencies. Many physicians and paramedics have never had the training opportunity to attempt intubation of an awake living creature. The kitten, immobilized with ketamine hydrochloride, gives the student the opportunity to visualize vocal cords, precipitate laryngospasm, and learn the difficulties associated with emergency intubation.

METHOD

Weaned kittens, weighing 0.5 to 1.0 kg will be used in these teaching sessions. Ketamine hydrochloride (22 mg/kg) plus atropine sulfate (0.04 mg/kg) will be administered intramuscularly to each kitten. Intubation will be performed with the kittens on their backs, using a pediatric laryngoscope, and sizes 8-14 French endotracheal tubes. Kittens may be used for several consecutive weekly sessions until they grow too large to be utilized. The procedure is not harmful to the kittens.

PROGRESS

(80 10 - 81 09) A teaching model for pediatric intubation, utilizing ketamine-sedated kittens, has been provided for physicians and ancillary medical personnel at Madigan. A dosage of 22 mg/kg of ketamine, administered IM to weaned kittens, produces some sedation but maintains laryngeal reflexes comparable to the awake human neonate. Practice sessions with this living model continue to fulfill a needed requirement for medical personnel who may be called upon in pediatric emergencies. Due to the PCS of COL Alden, the principal investigator will be changed to LTC Gary Pettett

STATUS: (O)

A Teaching Model for Pediatric Intubation Utilizing Ketamine-Sedated Kittens - Alden

PUBLICATION: Jennings, P.B., Alden, E.R., and Brenz, R.W.: A Teaching Model for Pediatric Intubation Utilizing Ketamine-Sedated Kittens. Pediatrics 53:283-84, 1974.

EXHIBIT: Alden, E.R. and Jennings, P.B.: Animal Models for Neonatal Resuscitation.

a. Annual Meeting of the American Academy of Pediatrics, Chicago, IL, Oct 1976.
Gold Award for Outstanding Exhibit for Teaching Value.

b. Annual Meeting of the American Medical Association, San Francisco, CA, Jun 1977.
Certificate of Merit

c. American Veterinary Association
Atalnta, GA, Jul 1977.

d. Annual Meeting of the Association of Military Surgeons, Washington, DC, Nov 1977.

TITLE: Comparison of Incidence of Asymmetrical Tonic Neck Reflex (ATNR), Tonic Labyrinthine Reflex (TLR), and Neurological Soft Signs in Categories I, II, and III with Category IV Active Duty Soldiers

PRINCIPAL INVESTIGATOR: COL Richard M. Graven, MC

PROFESSIONAL ASSISTNATS: LTC Barbara Bascom, MC
MAJ Jane K. Sweeney, SP
MAJ Willis Jacob, MSC

WORK UNIT NO: 81/78

TECHNICAL OBJECTIVE

To determine whether there is an increased incidence of primitive reflexes and neurological soft signs among category IV active duty soldiers.

METHOD

One hundred or more active duty soldiers will be evaluated for the presence of ATNR, TLR, and neurological soft signs. Following the collection of data, the soldiers' category classifications will be obtained. The data will then be analyzed regarding the occurrence of each primitive reflex and number of soft signs in the category I, II, and III soldiers as compared to the category IV soldiers. Conclusions will then be drawn regarding the value of these tests as screening tools in the population studied.

PROGRESS

(81 05 - 81 09) Currently data is still being collected. Individuals have been tested from all categories of active duty soldiers with positive findings in all categories. It has not been determined at this point if there are significantly more positives in category IV soldiers.

STATUS: (O)

TITLE: Evaluation of New Technique for Bone Marrow Biopsy

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANTS: COL Jack Frost, DC
LTC Irwin Dabe, MC
LTC Arthur Krakow, DC
MAJ George Ward, VC
MAJ Rehka Dhru, MC
MAJ Alan Mease, MC

WORK UNIT NO: 80/68

TECHNICAL OBJECTIVE

To develop instrumentation and technique for rapid bone marrow biopsy in children using high speed dental drill and a comparison of standard technique with Jamishidi & Illinois needle vs dental drill technique in animal system for: a. accuracy of histology; b. technical feasibility; c. pain decrease; and d. speed of procedure.

METHOD

Animal model: biopsy - iliac creast one side with classic technique and opposite side with new dental drill; cross-check smears for distortion and accuracy of sampling. To achieve different patient size simulation, 3 groups of animals will be used with at least 3 animals in each group. Animals used will be sheep, large dogs, and small dogs. Animals will be anesthetized with a general anesthetic. The reviewer of the slides will have no prior knowledge of which procedure was used to obtain the samples. If samples prove to be of good quality, a follow-up protocol will be prepared for human application.

PROGRESS

(80 08 - 81 09) Instrumentation was explored, but no suitable instrumentation was found before the protocol had to be terminated due to the departure of the principal investigator and the majority of the professional assistants.

STATUS: (T)

TITLE: Self-Inflating vs Flow-Inflating Resuscitation Bags: A Comparison and Development of A Teaching Model

PRINCIPAL INVESTIGATOR: MAJ Philip V. Marinelli, MC

PROFESSIONAL ASSISTANTS: COL Errol R. Alden, MC
MAJ Amil Ortiz, MC
MAJ Lawrence Wickham, MC

WORK UNIT NO: 80/06

TECHNICAL OBJECTIVES

(1) To evaluate respiratory parameters (i.e., tidal volume, PIP, PEEP) of three main types of manual resuscitation bags; (2) To determine respiratory frequency most commonly employed (stated vs actual); (3) To assess the "feel" of bagging, i.e, the clinical determination of lung complicance; (4) To underscore the need for continuous airway pressure monitoring; (5) To develop an experimental model for teaching and reenforcement of proper ventilatory techniques in newborn resuscitation to medical and paramedical personnel.

METHOD

Fifty physicians and 30 nurses at Madigan will be asked to test the bags. Another 300 physicians will be solicited for participation at the Uniformed Services Meeting. A Bourns Infant Lung Simulator and the Hewlett Packard Respiratory Integrator will be monitored while using the bags. Respiratory frequency, tidal volumes, PIP, and PEEP will be recorded and graphically displayed. The volunteers will be asked for their subjective evaluations of the parameters. A comparison of these subjective parameters will be made to the recorded findings.

PROGRESS

(80 01 - 81 06) Forty-eight participants (pediatricians, obstetricians, and NICU nursing staff) were studied. Each participant was tested with a self-inflating bag and a flow-infalting bag. CONCLUSIONS: Current newborn resuscitation practices are characterized by use of the self-inflating bag, the reliance on clinical skills to determine optimum airway pressure, and inconsistent and inefficent oxygen administration. The disregard of recommended newborn resuscitation guidelines is attributed to the marked variation in an individual's skill in the application of newborn MAV, rather than lack of knowledge. The technique of newborn manual artificial ventilation is an important therapeutic modality. The safe and effective application of newborn MAV mandates the need for intensive education and training of delivery room attendants, and periodic reevaluation of techniques and equipment.

Self-Inflating vs Flow-Inflating Resuscitation Bags: A Comparison and Development of A Teaching Model - Marinelli

STATUS: (C)

PUBLICATION: Marinelli, P.V. Mean Airway Pressure Calculations-Further Comments. J Pediatrics 99(1): 168-69, 1981.

TITLE: A Pediatric Military Survey of Newborn Resuscitation

PRINCIPAL INVESTIGATOR: MAJ Philip V. Marinelli, MC

PROFESSIONAL ASSISTANTS: COL Errol R. Alden, MC
MAJ Amil Ortiz, MC
MAJ Lawrence Wickham, MC

WORK UNIT NO: 80/07

TECHNICAL OBJECTIVES

To document and critically evaluate how newborn resuscitative measures are presently performed at military facilities throughout the world with specific attention to bag preference and methods of monitoring airway pressure, and to determine if there is a difference in management between MEDDACS and MEDCENS.

METHOD

A questionnaire with 15 questions will be mailed to all military pediatricians and nurse practitioners. The replies will be statistically analyzed to determine the type of resuscitation bag most commonly used and how airway pressure is monitored. This information can be related to institution size, branch of service and time of training.

PROGRESS

(80 01 - 81 09) Questionnaries were mailed to 483 pediatric practitioners associated with the Uniformed Health Services stationed in the continental US, Europe, and the far east. The format consisted of 16 multiple choice questions concerning resuscitation equipment, methodology, and individual as well as institutional biographical data. All responses were anonymous. A response rate of 71.2% was obtained. More than two-thirds of the pediatric practitioners had received their training within the past five years and almost one-third were involved in newborn resuscitation on a weekly or more frequent basis. This population overwhelmingly preferred the self-inflating bag (71%) and relied on clinical skill and judgment (80%) to monitor airway pressure. A paper has been submitted for publication that gives the results in greater detail. Also, this project was combined with MAMC project #80/06 (Self-Inflating vs Flow-Inflating Resuscitation Bags) and the progress section to #80/06 gives the results of the combined study.

STATUS: (C)

A Pediatric Military Survey of Newborn Resuscitation - Marinelli

PUBLICATION: Marinelli, P., Pettett, G., and Alden, E.: Manual Artificial Ventilation in the Newborn. J Amer Osteo Assn 80:104, 1981

PRESENTATION: Marinelli, P.V., Pettett, P.G., and Alden, E.R.: Manual Ventilation of the New born. An Analysis of Equipment and Technique. 16th Annual Uniformed Services Seminar, San Antonio, TX, March 1981.

PRESENTATION: Marinelli, P.V.: Artificial Ventilation of the Newborn. 25th Annual Osteopathic Research Meeting, Chicago, IL, March 1981.

PRESENTATION: Marinelli, P.V., Pettett, G., and Alden, E.R.: Manual Artificial Ventilation of the Newborn. Amer Acad Pediatrics Perinatal Seminar, District VIII Cour d'Alene, ID, June 1981.

TITLE: Prevalence of Thyroid Dysfunction in Juvenile Onset Diabetic Children and Its Relationship to Immunotype

PRINCIPAL INVESTIGATOR: MAJ Dan C. Moore, MC

PROFESSIONAL ASSISTANT: None

WORK UNIT NO: 81/88

TECHNICAL OBJECTIVE

To define the percentage of juvenile onset diabetic children who have thyroid dysfunction as assessed by measurement of thyroid antibodies, T_4, T_3RU, and TSH response to TRH infusion. HLA typing will be done and a correlation made between those patients with evidence of thyroid autoimmunity and dysfunction and their immunotype to see if a subgroup of patients with juvenile onset diabetes can be identified by HLA typing who will be at risk for development of thyroid dysfunction in later life.

METHOD

Twenty-five patients, 18 years of age or less, will have a TRH test which will consist of three blood samples taken as follows:

a. Baseline - for TSH T_4, T_3U, thyroid antibodies, HLA type and hemoglobin A_1C.
b. Injuction of TRH, 7 µg/kg IV
c. 30 minutes - blood sample for TSH
d. 60 minuets - blood sample for TSH

Measurement of TSH, T_4, T_3U, thyroid antibodies, HLA type and hemoglobin A_1C are accepted tests in the management of the diabetic. The TRH test is a standard test to evaluate thyroid function.

PROGRESS

(81 07 - 81 09) Patient selection has begun. This protocol has only been open for one and a half months.

STATUS: (O)

TITLE: The Association of Adolescent High Blood Pressure to Maternal Toxemia

PRINCIPAL INVESTIGATOR: MAJ Dan C. Moore, MC

PROFESSIONAL ASSISTANTS: Jeanette Welker, R.N.
Roger Meyer, M.D., MPH

WORK UNIT NO: 81/89

TECHNICAL OBJECTIVE

To determine the association of adolescent high blood pressure to the mother's report of toxemia in pregnancy. The presence/absence of toxemia will be assessed by use of a questionnaire. Other factors known to affect adolescent blood pressure will be controlled for.

METHOD

The population will be adolescents between the ages of 12-18 years who receive blood pressure readings as part of routine care and whose blood pressure after three readings is in the 90th percentile of those tested. Fifty adolescents will be studied along with a control of 50 age, sex, and Quetelet index-matched adolescents with normal blood pressure. The mothers of both groups will be asked to fill out a questionnaire to include family history of hypertension, pregnancy and delivery history, and information as to the diet and lifestyle of the adolescent. A random selection of 10 mothers in each group will have their medical records checked for validation of the information received through the interview questions. The interviewer will have no information of the blood pressure of the adolescent; therefore the study will be blind.

PROGRESS

(81 07 - 81 09) Subject selection has begun. This protocol has only been open for one and a half months.

STATUS: (O)

TITLE: Somatomedin-C and Gonadal Hormones in Precocious Sexual Development and in Relation to Medroxyprogesterone Treatment

PRINCIPAL INVESTIGATOR: MAJ Dan C. Moore, MC

PROFESSIONAL ASSISTANTS: LTC Stephen R. Plymate, MC
Vincent C, Kelley, M.D.

WORK UNIT NO: 81/113

TECHNICAL OBJECTIVE

To define the abnormalities of pituitary, adrenal, and gonadal function in patients with precocious sexual development in order to discern whether certain laboratory determinations correlate with clinical stages of sexual precocity and can be predictive of subsequent course; discern whether any of these same parameters can be used to predict response to medroxyprogesterone therapy; and assess the relative effect of medroxyprogesterone in suppressing somatomedin-C and sex steroids of gonadal vs adrenal origin.

METHOD

Thirty patients with precocious sexual development (males under 9 years and females under 8 years) will be given a physical examination rating of pubertal status according to the system of Tanner. Plasma LH, FSH, E_1, E_2, T, DHEAS, bone age films, and skull films will be done. Blood samples will be drawn for somatomedin-C, somatomedin bioassay, Δ_4 androstenedione and SHBG. Once a diagnosis is made, patients will be followed at 3 month intervals according to standard procedure. Those patients in whom it is clinically indicated will be placed on medroxyprogesterone therapy (100-200 mg IM every 2 weeks). Those patients placed on medroxyprogesterone will have initial blood tests repeated at 3 and 6 months to assess effect of therapy.

PROGRESS

(81 09 - 81 09) This protocol has just received Committee approval. The investigators are now starting to collect subjects.

STATUS: (O)

TITLE: Tension Pneumothorax - A Teaching Model

PRINCIPAL INVESTIGATOR: LTC Gary Pettett, MC

PROFESSIONAL ASSISTANTS: COL Errol Alden, MC
LTC George S. Ward, VC

WORK UNIT NO: 76/29

TECHNICAL OBJECTIVE

To provide training in diagnostic and surgical skills in the treatment of tension pneumothorax and to provide ongoing teaching sessions.

METHOD

New Zealand white rabbits weighing 700-2500 grams are anesthetized initially with an intramuscualr injection of ketamine hydrochloride and promazine hydrochloride. Five minutes after injection, the chest wall is shaved and prepared for surgery. EKG leads are placed on the rabbit and the heart rate and QRS voltage monitored on an oscilloscope. Surgical procedure as outlined in protocol. During the training session, the pathophysiology of TPT is discussed with each student. The entire training session can be accomplished in less than two hours for a group of 3 to 5 people.

PROGRESS

(80 10 - 81 09) A tension pneumothorax induced in a small rabbit is an excellent teaching model for the treatment of tension pneumothorax in the small human neonate. The rabbit model is inexpensive, readily available, and recreates the clinical condition of a tension pneumothorax in an educational environment. This continues to be a valuable teaching model with sessions held on a regular basis for pediatric personnel, ICU students, interns, and residents.

PUBLICATION: Henderson, R., Alden, E., Jennings, P.B., and Hofmann, J.R.: Tension Pneumothorax - A Teaching Model. Pediatrics 58:861-62, 1976.

PRESENTATION: (Exhibit) Jennings, P.B., Alden, E.R., and Henderson, R.W.: Teaching Models for Neonatal Resuscitation. Annual Meeting of the Association of Military Surgeons of the United States, Nov 1977, Washington, DC.

STATUS: (C)

TITLE: Standardization of a Screening Instrument for Developmental Soft Signs in Normal Children

PRINCIPAL INVESTIGATOR: LTC Carl A. Plonsky, MC

PROFESSIONAL ASSISTANT: CPT Heather Smith, MC

WORK UNIT NO: 79/16

TECHNICAL OBJECTIVE

To devise and standardize a screening examination for neuro-developmental soft signs. Standardization will be done on a large number of normal children. The examination will then be given to a number of children with known minimal brain dysfunction and the results compared.

METHOD

A soft signs screening examination, method manual, and score sheet have been devised. The screening examination will be individually administered to 100 normal children, grades kindergarten through third grade. Thirty children will be tested by more than one examiner on the same day as a test for inter-examiner reliability, and 30 children will be re-tested one week later as a test of test-retest reliability. The age at which each of the developmental signs is found to be absent in 90% of this normal population will be calculated and tabulated. A sample of children with known MBD will be given the examination and the results compared to those of the normal population. After the pilot study is completed, the test instrument will be evaluated and refined and given to the entire on-post school population, kindergarten through third grade.

PROGRESS

(79 09 - 81 09) Comparison shows that the group of soft signs, when taken together as a total score, support the concept of measurement of neurodevelopment maturation in the school age child. The soft sign examination performed on children with minimal brain dysfunction is statistically significantly different from scores obtained in the control subjects. These findings are supportive of the conclusion that minimal brain dysfunction is a neuromaturational delay. An article for publication is in the process of being written.

Standardization of a Screening Instrument for Developmental Soft Signs in Normal Children - Plonsky

STATUS: (C)

PRESENTATION: Plonsky, C and Smith, H.: The Soft Neurological Signs in School-Age Children. Presented to American Academy of Pediatrics, 15 Oct 79, San Francisco, CA.

TITLE: Comparison of Capillary (Heelstick) and Central (Venous) Total White Blood Cell Counts and Differentials in Normal Newborn Infants

PRINCIPAL INVESTIGATOR: CPT Bruce E. Willham, MC

PROFESSIONAL ASSISTANTS: COL Errol R. Alden, MC
MAJ Amil Ortiz, MC
MAJ Lawrence Wickham, MC
CPT Michael Byrne, MC

WORK UNIT NO: 79/82

TECHNICAL OBJECTIVE

To determine if a statistically significant difference exists between total white blood cell counts and differentials in blood samples obtained from normal healthy newborns during the first 24 hours after birth by heelstick and by venous sampling from peripheral veins. This will define the "normal" standards and provide a basis for evaluation of "sick" newborns.

METHOD

Simultaneous blood samples by heelstick and by venipuncture will be taken and standard methods will be used to determine total WBC and differentials. Whenever possible the sampling will coincide with and compliment sampling performed for routine purposes. Data will be analyzed using the paried t statistic to determine if the peripheral WBC differ from the central WBC. Also, regression analysis of the data will be performed to evaluate associations of central and peripheral counts.

PROGRESS

(79 07 - 81 09) Alternate samples of capillary and venous blood were obtained on 32 healthy term infants. Significant differences were evident between heelstick and venous WBC and ANC. The mean difference of ABC between sampling sites was 27.9% of the venous sample. Capillary PCV was greater than in venous specimens. Increased I/T ratios were consistently obtained from venous specimens. In 87.5% of the patients, the higher WBC values were consistently obtained from the site with a higher PCV. It is apparent that the WBC, ANC, and ABC vary widely with respect to sampling site. Caution in interpretation of this laboratory test is advised until laboratory evaluations are standardized for each vascular compartment.

STATUS: (C)

PRESENTATION: Aspen Perinatal Conference, Aspen, CO, July 1981.

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

F O R

P R O T O C O L S

PHYSICAL MEDICINE AND REHABILITATION SERVICE

TITLE: Comparison of Five Physical Medicine Treatment Approaches for Shoulder Bursitis, Tendonitis, and Lateral Epicondylitis of the Elbow

PRINCIPAL INVESTIGATOR: MAJ Mohammad A. Saeed, MC

PROFESSIONAL ASSISTANTS: MAJ Ronald J. Franklin, AMSC
1LT John S. Halle, AMSC
2LT Barry L Karalfa, AMSC

WORK UNIT NO: 80/41

TECHNICAL OBJECTIVE

In an effort to obtain better symptomatic patient relief, the Physical Medicine Service at Madigan has designed five distinct treatment protocols for the subject disorders. The purpose of this study is to quantify the effectiveness of these treatment procedures.

METHOD

One hundred patients clinically identified as having either shoulder bursitis or tendonitis of the shoulder or elbow will be randomly assigned to one of five treatment categories: (1) ultrasound with coupling agent; (2) ultrasound with hydrocortisone coupling agent; (3) TENS with coupling agent; (4) TENS with hydorcortisone coupling agent; and (5) injection with lidocaine and hydrocortisone. All of these treatment programs also include identical home exercise regimes and ice treatment. Prior to treatment, each patient's pain will be assessed by the McGill pain questionnaire. Following a five day treatment period, each patient will again assess his pain by repeating the questionnaire. The data will be analyzed by the Matched Student's t Test and a Two-Way Analysis of Variance.

PROGRESS

(80 10 - 81 09) Data has been collected on approximately 90 patients. A preliminary statistical analysis is being undertaken to compare the five treatment approaches and to determine if further collection is deemed necessary and worthwhile.

STATUS: (C)

TITLE: Sensory Medial and Lateral Plantar Nerve Latencies Through Tarsal Tunnel in Normal Adult Subjects

PRINCIPAL INVESTIGATOR: MAJ Mohammad A. Saeed, MC

PROFESSIONAL ASSISTANT: None

WORK UNIT NO: 81/13

TECHNICAL OBJECTIVE

To present a standardized and reproducible technique to determine sensory latency of medial and lateral plantar nerves across the tarsal tunnel by standard EMG equipment without electronic averager.

METHOD

Forty to fifty normal adult subjects with no history or clinical evidence of any disorder which would affect the peripheral nervous system will be included in the study. As additional screening, sural nerve conduction will be performed on each subject and anyone found to have an abnormal value will be excluded. Using an electronic thermometer, temperature will be taken over the tarsal tunnel, and on the medial and lateral sole of the foot. Right or left foot will be examined randomly. Tests will be performed using a TECA TE4 electromyogram with paper recording. Rectangular pulses of 0.5-0.1 m/sec will be used with a supramaximal stimulus intensity ranging up to 300 volts. Pick up bipolar surface electrode will be placed on the posterior tibial nerve proximal to flexor retinaculum. Orthodromic evoked responses will be recorded when medial plantar nerve is stimulated at a distance of 10, 14, and 18 cm and at the great toe. Lateral plantar nerve will be stimulated a 14 and 18 cm and the little toe. Ground electrode will be placed over the dorsum of the foot. Four stimulation points for the medial plantar and three for the lateral plantar nerve will be used in order to determine the best location for obtaining a consistent and reproducible evoked response. Distal latencies of the medical and lateral plantar nerves will be measured and recorded on the EMG paper. The data will be subjected to mean standard deviation.

PROGRESS

(80 11 - 81 09) Forty-one subjects ranging in age from 20 to 76 years with a temperature range of 26-32.5°C were tested. Orthodromic latencies for the medial plantar nerve for distances of 10, 14, and 18 cm and the great toe were 2.4±SD 0.15, 3.2±SD 0.26, 4.0±SD 0.22, and 5.0±SD 0.38, respectively. Lateral plantar nerve latencies for 14 and 18 cm segments were 3.2±SD 0.25 and 3.0±SD 0.27, respectively. These standard values should allow more accurate

assessment of tarsal tunnel syndrome and peripheral neuropathies since the orthodromic method involves a mixed motor and sensory nerve action potential and should be more sensitive to early changes than a pure motor nerve action potential.

STATUS: (C)

DETAIL SHEETS

FOR

PROTOCOLS

PREVENTIVE MEDICINE ACTIVITY

TITLE: Estimation of Exposures of Premature Infants to Ionizing Radiation, Primarily From X-Ray Sources.

PRINCIPAL INVESTIGATOR: 1LT John H. Pickering, MSC

PROFESSIONAL ASSISTANT: SFC Joseph H. Smith

WORK UNIT NO: 80/49

TECHNICAL OBJECTIVE

To evaluate whole body exposures to premature infants and relate the estimates to threshold damage of various tissue and/or organs.

METHOD

The investigators will survey the x-ray source used for these infants and determine the skin entrance exposure with the techniques used by the x-ray department. A sheet will be attached to the beds of the infants and the x-ray technician will indicate the number of exposures taken of a particular infant. Film badges will be placed with the infants on a random basis to estimate scatter radiation from adjacently exposed patients.

PROGRESS

(80 10 - 81 09) The start of this project was delayed due to personnel shortages. The principal investigator was then transferred so the project was terminated.

STATUS: (T)

TITLE: The Effects of Low Exposure Levels to Anesthetic Gases in Operating Rooms at MAMC

PRINCIPAL INVESTIGATOR: CPT Gary L. Shrum, MSC

PROFESSIONAL ASSISTANTS: LTC John Heggers, MSC
LTC George S. Ward, VC
CPT Michael Smith, MSC
CPT Robert R. Byland, MSC

WORK UNIT NO: 77/72

TECHNICAL OBJECTIVE

To evaluate the levels of anesthetic gas the anesthesiologist and operating room personnel receive with the present type of gas delivery, recovery, and disposal systems used at this center.

METHOD

1. Coordinate with OR supervisor and anesthetist as to the length of time various operations take and the gases used; (2) Schedule 12 operations to test for gases; (3) Use previous ventilation survey results for room volume and air turnover rate to predict gas concentrations; (4) determine prior to any operation the effect of opening and closing of OR doors has on the air flow; (5) Set up the Miran I.R. unit and calibrate; (6) Using the 10-foot sampling hose, collect samples during the operation around gas delivery systems, the anesthesiologist, and OR personnel's breathing zones every 15 minutes and record on a strip chart; (7) analysis of collected data.

PROGRESS

(77 10 - 81 10) Three series of measurements were initially made. However, due to the departure of the original principal investigator and the professional assistants, the new principal was unable to obtain personnel and provide the time required to continue this protocol; therefore, it has been terminated.

STATUS: (T)

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

TITLE: The Neuropsychological Correlates of Hyperthyroidism and Its Treatment

PRINCIPAL INVESTIGATOR: MAJ Lloyd I. Cripe, MSC

PROFESSIONAL ASSISTANTS: LTC Gary Treece, MC
MAJ Louis Pangaro, MC
MAJ Raymond Parker, MC

WORK UNIT NO: 81/75

TECHNICAL OBJECTIVE

To determine the neuropsychological correlates of hyperthyroidism and the effects of treatment.

METHOD

Approximately 30 subjects presenting with a diagnosis of spontaneous hyperthyroidism, whose management and treatment have been decided by the primary physician, will be entered in the study. Phase I will include the administration of the entire Halstead-Reitan Neuropsychological Test Battery during the physician's initial diagnostic work-up. Phase II - Patients will be randomly assigned to receive either propranolol, 40 mg q.i.d. or a placebo. After 7-10 days of drug therapy patients will again be given the Halstead Reitan Battery and blood levels will be checked. Phase III - the test battery will be administered for the third time after the patient has been euthyroid for one month as determined by TFT. Thirty controls without psychiatric, neurological, or thyroid disease will be matched with the experimental group for age, sex, intelligence, and education. They will be administered the Halstead-Reitan Battery on the same schedule as the experimental group. Thyroid status would be determined at each testing by blood levels for hormones. Hoteling's Multiple T-tests for multivariant data will be utilized to make comparisons between the groups for the three testings. Correlations with test measures and blood levels will also be made.

PROGRESS

(81 04 - 81 09) The investigators are in the process of training a volunteer to help administer the tests and collect the data.

STATUS: (O)

TITLE: Parental Discrimination in the First 2 Weeks of Life

PRINCIPAL INVESTIGATOR: MAJ Robert C, Hulsebus, MSC

PROFESSIONAL ASSISTANT: None

WORK UNIT NO: 81/99

TECHNICAL OBJECTIVE

To determine the earliest age at which young infants can discriminate their parents on the basis of listening to their voices. This research is designed to extend findings gained in earlier research by this author.

METHOD

Comparisons will be conducted during the first 2 weeks after birth. Mothers of the infants and a female stranger will be compared and fathers and a male stranger will be compared. For the comparison the adults will wait until the infant begins and maintains a frequent, mild fussing pattern. For half the infants, the parent will then speak first and for the other half the adult stranger will speak first. Each adult speaking will stand behind the infant's head out of the infant's sight, and no one will be within the infant's field of vision. A prepared one-minute talk will be given by the adult and the infant's fussing during the talk will be recorded. After a rest period, the infant will hear the second adult speaking from the script and this will also be recorded. Analysis of the crying patterns will be conducted by means of a multichannel event recorder and more than one scorer. A criterion pause of 5 seconds will be utilized. The tapes will be analyzed to observe if this five second pause occurs more frequently in response to the parent or to the stranger. Each test group will consist of 25 subjects.

PROGRESS

(81 07 - 81 09) The actual technical portion of the study has just begun with the testing of the first subject.

STATUS: (O)

TITLE: Psychological Variables Related to Childbirth and Early Infant Development

PRINCIAPL INVESTIGATOR: MAJ Anthony C. Zold, MSC

PROFESSIONAL ASSISTANTS: CPT Richard H. Rubes, MSC
CPT (USAR) Maren Stavig, ANC

WORK UNIT NO: 81/59

TECHNICAL OBJECTIVE

To study selected psychological and behavioral variables during pregnancy which may affect ease of delivery, medical complications, and early growth and development of the infant. Specifically, the independent variables to be investigated are: (1) maternal expectations of delivery and of the infant; (2) mother's perception of the husband's emotional support; (3) orgasmic history of the mother; (4) participation in various childbirth preparation programs; and (5) significant depression during pregnancy.

METHOD

Obtain interview and depression scale data from volunteers at 30-36 weeks gestation. After the birth, recontact mother for a brief followup interview to obtain mother's subjective rating of the delivery and the infant. Conduct record search for selected variables: length of labor, presence of complications, status of newborn, and the bonding rating between mother and child. At the 2-month well-baby followup visit request mother to repeat the Zung Self-Rating Depression Scale and do a record search on the development of the infant. Data analysis will include descriptive statistics, correlation, and contingency table analysis.

PROGRESS

(81 03 - 81 09) Interviews and testing of over 200 patients have been completed. Interviews after delivery have been completed on over 100 patients. Review of all inpatient medical records is in progress. Followup at Well-Baby Clinic is scheduled for January through May 1982.

STATUS: (O)

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

TITLE: Study of Delayed/Nonunion in Jones Fracture

PRINCIPAL INVESTIGATOR: COL Virginia M. Badger, MC

PROFESSIONAL ASSISTANT: MAJ Stanely P. Liebenberg, VC

WORK UNIT NO: 81/98

TECHNICAL OBJECTIVE

To study the rate of healing of an experimentally produced fracture of the 5th metatarsal diaphysis (the Jones fracture) if: the lesion is left untreated; the lesion is stabilized by internal fixation; or the sress is removed across the fracture site by sectioning of the peroneus brevis tendon.

METHOD

Ten adult rabbits will be utilized for the study (20 feet - hind feet only). After anesthetization with rompum and ketamine, a transverse fracture at the proximal diaphysis of the 5th metatarsal will be created by direct visualization. Six feet with metatarsal lesions will be left without internal fixation; eight metatarsals will be fixed by insertion of "K" wires for internal fixation; and eight will be left without fixation but will have a section of the peroneus brevis tendon at the tuberosity. The feet will be x-rayed weekly until the lesions are healed. The lesions will be studied pathologically at intervals depending on rate of radiographic healing.

PROGRESS

(81 07 - 81 09) Operative lesions have been completed with sacrifice of animals. Histological studies are pending.

STATUS: (O)

TITLE: A System for Data Storage and Retrieval Using a Microcomputer: Carcinoma of Prostate Patients, Madigan Army Medical Center

PRINCIPAL INVESTIGATOR: COL Alfred S. Buck, MC

PROFESSIONAL ASSISTANTS: LTC William D. Belville, MC
LTC Martin L. Dresner, MC
MAJ Willis H. Jacob, MSC
MAJ Roger H. Schoenfeld, MC
CPT Carl F. Cricco, MC
CPT Robert U. Finnerty, MC

WORK UNIT NO: 80/36

TECHNICAL OBJECTIVE

To test the concept of a microcomputer-based system for storage and processing of patient records.

METHOD

The population selected for this study are all patients with carcinoma of the porstate seen at Madigan. A systems analyst will review the data and develop a program which will be designed to permit the following: (1) open file on patient; (2) update data in the file; (3) retrieve the complete file; (4) retrieve a single category of data (variable) from the file of one or more patients; and (5) retrieve a single category of data (variable) from two or more groups of patients and perform the required statistics for comparisons between the groups. The system will be evaluated after it has been operational for six months. If the program is found to be workable, it will be turned over to the Automation Management Office for implementation.

PROGRESS

(80 10 - 81 09) A software computer program is to be available within two months. The next step should be the purchase of an appropriate computer terminal with the advice of the Automated Management Office.

STATUS: (O)

TITLE: General Surgery Procedure Training

PRINCIPAL INVESTIGATOR: LTC Preston L. Carter, MC

PROFESSIONAL ASSISTANTS: LTC Dick R. Smith, MC
CPT Harry L. Walker, VC

WORK UNIT NO: 81/26

TECHNICAL OBJECTIVE

To provide training to General Surgery residents in the technical aspects of various types of abdominal resection and anastomosis, to include training in the use of stapling instruments.

METHOD

Each resident will be provided with a large anesthetized dog. Under staff supervision, the following procedures will be accomplished on each animal:

1. Exploratory laparotomy
2. Resection and end to end anastomosis of small bowel
3. Resection and end to side anastomosis of small bowel to colon
4. Side to side anastomosis using the GIA stapler
5. Gastric transection using the TA 90 stapler
6. End to end bowel anastomosis using the EEA stapler
7. Mass closure of abdominal laparotomy wound

At the completion of each session, the animal will be sacrificed and residents will assist in cleaning the surgical suite and in the care of instruments.

PROGRESS

(80 12 - 81 09) The procedures outlined in the protocol were carried out successfully; residents involved in the protocol were introduced to the capabilities of the Department of Clinical Investigation Lab at Madigan. As a sequela to this protocol, a training protocol for interns, residents, and other surgeons, using the canine model, has been established at Madigan (#81/90).

STATUS: (C)

TITLE: End to Side Distal Gastrectomy in Dogs

PRINCIPAL INVESTIGATOR: LTC Preston L. Carter, MC

PROFESSIONAL ASSISTANTS: CPT Bruce A. Snyder, MC
MAJ Stanley P. Liebenberg, VC

WORK UNIT NO: 81/77

TECHNICAL OBJECTIVE

To assess the safety and validity of the end to side distal gastrectomy, hypothesizing that this method might provide the functional advantage of the Bilroth I gastrectomy, while avoiding the hazard of performing an end to end anastomosis in the face of scarring of the duodenal bulb.

METHOD

Ten dogs are porposed for the initial trial. Large dogs will be subjected to distal gastretcomy and end to side gastroduodenal reconstruction with oversewing of the end of the duodenal stump. The surgery will be performed in a sterile manner with broad spectrum antibiotic coverage. Postoperatively, the dogs will be fed IV for several days and then progressed to oral intake of normal dog ration. Approximately 30 days later, surviving dogs will be reexplored and the gastroduodenal anastomosis resected and inspected for healing and patency. The dogs will be sacrificed at the end of the reexploration and concomitant general surgical procedures included in the general surgery training protocol will be carried out also prior to sacrifice.

PROGRESS

(81 05 - 81 09) Three of the test dogs have successfully undergone the procedure. Two of the animals were subsequently sacrificed in accordance with the protocol. The third is recovering from the initial procedure. There have been no problems with the design or technical surgical aspects of the protocol.

STATUS: (O)

TITLE: General Surgery Resident/Surgical Intern Training Protocol for Technical Skills in Surgery

PRINCIPAL INVESTIGATOR: LTC Preston L. Carter, MC

PROFESSIONAL ASSISTANTS: LTC Dick R. Smith, MC
MAJ Stanley P. Liebenberg, VC

WORK UNIT NO: 81/90

TECHNICAL OBJECTIVE

This is a formal program to expose junior surgical residents and surgical interns to certain basic technical skills in surgery, with emphasis on skills needed in the clinical practice of General Surgery, and, secondarily, to familiarize the resident and intern personnel with the capabilities and potentials of the Department of Clinical Investigation at Madigan.

METHOD

This is a continuation of a similar previous protocol and is in conjunction with the end to side gastrectomy protocol. Dogs which have survived the end to side gastrectomy will be sacrificed after reexploration. Prior to sacrifice, the house officer participating on that day will perform one or more of the following procedures on the still anesthetized dog: end to end anastomosis of the small bowel; splenectomy; gastrostomy; EEA stapled anastomosis; nephrectomy; end to side portocaval shunt; and suture of cardiac laceration. After these procedures, the animal will be sacrificed (before it is allowed to awaken) and the stomach/duodenal area removed for further gross and microscopic study in the end to side gastrectomy protocol.

PROGRESS

(81 07 - 81 09) This protocol in conjunction with the end to side distal gastrectomy protocol is ongoing at the present time. It is providing the desired technical exposure to junior surgical residents and interns and will be continued as planned through the completion of the aforementioned protocol.

STATUS: (O)

TITLE: Early Definitive Treatment of Pilonidal Abscess vs Delayed Definitive Treatment. A Prospective Randomized Study.

PRINCIPAL INVESTIGATOR: LTC Preston Carter, MC

PROFESSIONAL ASSISTANTS: LTC James F. Bascom, MC
CPT Robert B. Freeman, MC
CPT Edward Pullen, MC

WORK UNIT NO: 81/104

TECHNICAL OBJECTIVE

Conventional treatment of pilonidal abscess has consisted of incision and drainage over a point of fluctuance lateral to the midline, followed at a variable interval by definitive excision of the midline tracts. A proposed alternative method is to perform the incision and drainage in the midline with excision of the midline tracts in the process. The objective of this study is to study the two methods to see if there is any advantage in terms of minimizing the patient morbidity of one method over the other.

METHOD

Patients who have had previous surgical treatment of pilonidal disease and minors will be excluded. Patients will be randomized to one of the two treatment methods outlined above and will be followed until complete healing has occurred. Hospitilization time, if any; loss of time from work; healing time; and complications related to either treatment method will be studied. A minimum of ten patients per group will be studied.

PROGRESS

(81 08 - 81 09) The investigators are awaiting suitable patients for clinical randomization. Based on past frequency of this condition at Madigan, completion should take about 9 months.

STATUS: (O)

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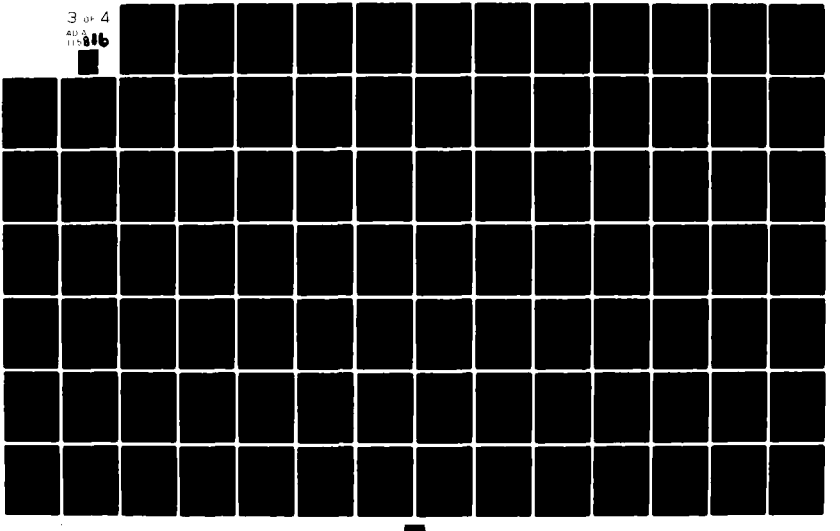

TITLE: Bulbocavernosus Reflex and Conduction Velocity of Dorsal Penile Nerve in Normal Men

PRINCIPAL INVESTIGATOR: COL Martin L. Dresner, MC

PROFESSIONAL ASSISTANT: MAJ Mohammad A. Saeed, MC

WORK UNIT NO: 80/67

TECHNICAL OBJECTIVE

To determine the normal values of the bulbocavernosus reflex arc as transmitted through the dorsal penile nerve as an indicator of peripheral neuropathy. Peripheral neuropathy is one of the causes of organic impotence.

METHOD

Approximately 25 men will be studied with electrophysiological testing of the bulbocavernosus reflex to determine reflex latency and conduction velocity of the dorsal penile nerve. Subjects will have no history or clinical evidence of any disorder which would affect the peripheral nervous system and sural nerve conduction will be tested to rule out subclinical pheripheral neuropathy. A monopolar teflon coated needle electrode will be placed in either the right or left bulbocavernosus muscle and the dorsal penile nerve will be stimulated with bipolar stimulator electrode at the base of the penis and the glans penis using TECA TE4 electromyogram. These stilumi will be delivered with a frequency of 1/second and a pulse duration of 0.5 msec. At least five identical responses will be recorded. Motor unit action potential of bulbocavernosus muscles, recruitment pattern in bulbocavernosus muscles, reflex latency, wave form, and dorsal penile nerve conduction velocity will be evaluated.

PROGRESS

(80 10 - 81 09) Of the 55 patients studied, the bulbocavernosus reflex was abnormal in 11 patients when the stimulation was done at the base of the penis. The number of abnormal reflex studies increased to 15 patients when the stimulation was done at the glans penis. The range of the bulbocavernosus reflex was from 25 msec to 100 msec. More patients will be studied.

STATUS: (O)

PRESENTATION: Singh, S., Dresner, M., and Saeed, M.: Bulbocavernosus Reflex in Men with Impotence. Amer Assoc of Electromyography & Electrodiagnosis, 26 Sep 80.

TITLE: An Evaluation of the Safety and Efficacy of Cyanoacrylate Ester in Ossicular Reconstruction and Nerve Graft Anastomosis in the Guinea Pig Middle Ear

PRINCIPAL INVESTIGATOR: COL William H. Gernon, MC

PROFESSIONAL ASSISTANT: CPT Roy Kim Davis, MC

WORK UNIT NO: 77/88

TECHNICAL OBJECTIVE

To determine the safety and efficacy of cyanoacrylate ester in the middle ear; specifically, for ossicular reconstruction for histological changes in the oval window area and in the facial nerve. In addition, the use of this compound in tympanoplasty would be a natural extension of this project. The intended purpose of this study is to open the door for the use of cyanoacrylate ester in human surgery, initially on an experimental basis.

METHOD

The investigators propose to use Histoacryl and Crazy Glue to do interpositions (incus) on a test group of guinea pigs as well as place glue on the facial nerve, perhaps to do facial nerve anastomoses, and to place the glue in the oval window area. Approximately 39 animals would be utilized. At 3, 6, and 12 months, 12 experimental animals and one control animal would be sacrificed. Histological temporal bone studies would then be conducted at AFIP.

PROGRESS

(80 10 - 81 09) Sixteen animals have been studied and sacrificed. The skulls and temporal bones are being processed at the ENT Section of the AFIP. When these results are known further studies may be needed. From preliminary results, a paper has been submitted for publication.

STATUS: (O)

PRESENTATION: Wells, J., Gernon, W.H., Ward, G.S., Davis, R.K., and Hays, L.L.: Otosurgical Model in the Guinea Pig (Cavis porcellus). Amer Acad Otolaryn-Head and Neck Surg, New Orleans, LA, September 1981.

TITLE: Teaching Program for Practical Microsurgery

PRINCIPAL INVESTIGATOR: LTC Thomas G. Griffith, MC

PROFESSIONAL ASSISTANTS: COL Leonard L. Hays, MC
LTC David Ekland, MC
MAJ Stanley Jackson, MC
LTC George S. Ward, VC
MAJ Robert Kenevan, MC

WORK UNIT NO: 77/92

TECHNICAL OBJECTIVE

To establish a formal training program at Madigan Army Medical Center in clinical microsurgery.

METHOD

The teaching program will be established at the Department of Clinical Investigation, and a room will be set aside for the project where equipment for the microsurgery can be housed. A schedule of two afternoons per week will be set aside for teaching sessions. Animal model preparations (cadaver and live) will be developed by the verterinary surgical consultant with the support of the clinical teaching staff. Sessions will begin with lectures, followed by practical exercises in anatomy and step-by-step instruction in the surgical techniques.

PROGRESS

(80 10 - 81 09) This continues to be a valid program for teaching microsurgical techniques for microvascular and peripheral microneurologic surgery. Residents are learning ene to end, end to side and interposition vein grafting of 1 mm vessels. Epineural and grouped fascisular peripheral nerve repair are taught. Free cutaneous transfer is performed using the inferior epigastric abdomen flap on rats.

STATUS: (O)

TITLE: Medical Treatment of the Frey Syndrome

PRINCIPAL INVESTIGATOR: COL Leonard L. Hays, MC

PROFESSIONAL ASSISTANT: Alvin J. Novack, M.D.
University of Washington

WORK UNIT NO: 76/06

TECHNICAL OBJECTIVE

1. To study objectively the true incidence of the Frey syndrome in post-parotidectomy patients by means of the Minor Starch Iodine Test.

2. To determine the effect of, and patient satisfaction with, medical management comparing on a double blind basis topical use of a placebo, varying concentrations of scopolamine hydrobromide, and the newer anticholinergic agent, glycopyrrolate.

3. To investigate the value and practicality of iontophoresis of the above agents to increase the duration of satisfactory control of sweating.

4. To compare the topical use of a patient's most effective antiperspirant on the involved facial skin with the result from the topical use of the most effective agent in the double blind series for that patient.

METHOD

Phase I - Double-blind treatment with ¼%, 1%, and 3% scopolamine hydrobromide cream, 0.1% glycopyrrolate, and a placebo; comparison by the patient as to effectiveness; and retreatment after drug dosage adjustment if the patient fails to respond.

Phase II - Utilize iontophoretic introduction of the best anticholinergic agent to a group of volunteers with significant sweating symptoms and to a group who are medical failures and compare action and duration of action with iontophoretic introduction using tap water, Ringer's lactate, or saline.

Phase III - Patients who fail medical treatment or have become dissatisfied with the the medical treatment and have significant symptoms confirmed on minor starch-iodine testing will be offered surgery such as flap elevation or tympanic neurectomy.

Medical Treatment of the Frey Syndrome - Hays

PROGRESS

(79 10 - 81 10) Initially, the investigators examined 129 patients who had undergone parotidectomy between 1960 and 1970. Sixty per cent of the sample - an incidence consistent with that reported elsewhere - attested to experiencing gustatory sweating and flushing during mastication. Of 78 symptomatic patients, 37 (47%) sought treatment. Nineteen elected to use only an anti-perspirant and 16 agreed to the use of topical glycopyrrolate. Later 6 more patients joined this group. Among these 22 patients, topical glycopyrrolate produced satisfactory control of symptoms in 21 (95%). Scopolamine elicited a variable response in concentrations ranging from 0.1% to 3%. Owing to its more numerous side effects and greater potential toxicity, scopolamine has been excluded from investigation for the last four years. Further work is planned to see what dosage is best on the patients who have a borderline satisfactory response to date.

STATUS: (O)

PUBLICATION: Hays, L.L.: The Frey Syndrome: A Review and Double Blind Evaluation of the Topical Use of a New Anti-chloinergic Agent. Laryngoscope 88:1796-1824, 1978.

PUBLICATION: Hays, L.L.: The Frey Syndrome. News Bulletin, The American Acad Otolaryngology-Head and Neck Surgery, 20 Sep 81.

PRESENTATION: Hays, L.L., Novack, A.J., and Morsham, J.C.: The Frey Syndrome, A Simple Effective Treatment. American Academy of Otolaryngology Meeting, New Orleans, LA, Sep 81.

TITLE: Microvascular Study on Dogs. A Study Project for Reconstruction Using Omental Free Grafts

PRINCIPAL INVESTIGATOR: LTC Dennis Lanier, MC

PROFESSIONAL ASSISTANTS: LTC Preston Carter, MC
LTC David Ekland, MC (USAR)
MAJ Stanley Liebenberg, MC

WORK UNIT NO: 81/111

TECHNICAL OBJECTIVES

(1) to develop a study protocol for microvascular surgery on dogs using omentum as free grafts to peripheral vessels. (2) to direct application to clinical situation in head and neck surgery in ENT. (3) To maintain technical expertise in microsurgery.

METHOD

After general anesthesia is given to the dog, a section of omentum complete with vascular pedicle will be harvested from the abdomen. A defect created on the neck of the same dog will be filled by the omentum and a vascular anastomosis performed to the thyroid artery. A split thickness skin graft will immediately be removed from the animal and placed over the omentum for epithelial coverage. By monitoring the fate of the split thickness skin graft, the viability of the omental graft could be ascertained. No biopsy will be necessary as the fate of the graft would be visibly apparent.

PROGRESS

(81 08 - 81 09) Preliminary work has begun to improve microsurgery techniques on single animal (guinea pig). The reconstruction using omental free grafts will begin in the near future.

STATUS: (O)

TITLE: Tourniquet Hemostasis - A Clinical Study

PRINCIAPL INVESTIGATOR: CPT Hubert S. Reid, MC

PROFESSIONAL ASSISTANTS: COL Richard A. Camp, MC
MAJ Willis H. Jacob, MSC
CPT James Little, MSC

WORK UNIT NO: 81/57

TECHNICAL OBJECTIVE

To determine if reduced tourniquet pressures will give adequate hemostasis for extremity surgery.

MEHTOD

Randomly selected patients undergoing elective surgery on extremities will be used for the study. The tourniquet will be applied and the pressure required to occlude arterial flow will be determined by Doppler stethoscope. A pressure 50 mm Hg higher than this will be used for the procdure and elevated if required. The operating surgeon will determine the adequacy of hemostasis. Basic data will be gathered on each patient for correlation: height, weight, age, medical history, thigh circumference, and tourniquet size.

PROGRESS

(81 03 - 81 09) A method was described for objectively determining tourniquet settings by means of cessation of peripheral arterial blood flow as determined by Doppler stethoscope. These tourniquet settings were significantly lower than those suggested in textbooks and in the literature without compromising effective tourniquet hemostasis. Lowered tourniquet pressures reduce the risk of injury due to local tourniquet effects.

An abstract has been accepted for presentation at the Western Orthopaedic Society in October 1981. This abstract will also be presented at the Annual Meeting of the Society of Military Orthopaedic Surgeons in November 1981. A manuscript is in preparation.

STATUS: (C)

TITLE: The Effect of Dimethyl Sulfoxide on the Uptake of Cisplatin From the Urinary Bladder of the Dog

PRINCIPAL INVESTIGATOR: MAJ Roger Schoenfeld, MC

PROFESSIONAL ASSISTANTS: LTC William Belville, MC
MAJ Eduardo S. Blum MC
MAJ Carl F. Cricco, MC
LTC Samuel J. Insalaco, MC
MAJ Willis H. Jacob, MSC
LTC George S. Ward, VC

WORK UNIT NO: 79/57

NOTE: Thio-TEPA was the original drug to be utilized in this study. Being unable to develop a successful thio-TEPA assay, cisplatin was used in the study due to the ease of measurement by atomic absorption spectrometry and because its medium-sized molecular weight avoids excessive absorption. The original protocol is listed below.

TEHCNICAL OBJECTIVE

Thio-TEPA has been used in the management of various types of neoplasias for almost two decades. However, its use in the managment of urinary bladder carcinoma has had mixed results. In addition, the cytotoxic effects of thio-TEPA on the hematopoietic tissues are a severe side effect in its use. The objective of this study is to determine if intravesicular thio-TEPA can be more effectively transported through the urinary bladder wall using DMSO as a carrier.

METHOD

Ten dogs will be divided into groups I and II (4 dogs each) and Group III (2 dogs). The test solution (50 ml) will be instilled into the urinary baldder of each animal and maintained there for one hour. The test solutions are: Group I - 45 mg thio-TEPA in 50% DMSO; Group II - 45 mg thio-TEPA in an isotonic salt solution; and Group III - 50% DMSO in an isotonic salt solution. The Group III animals are to verify that DMSO does not interfere with thio-TEPA identification.

Blood samples will be obtained from the caudal vena cava and the external jugular vein immediately before instillation of the test solution and at 5, 10, 20, 40, and 60 min after instillation. One blood sample will be taken from a small vein on the bladder surface at 15 min and the test solution will be withdrawn from the bladder at 60 minutes.

Two dogs from Groups I and II will be studied for toxicity following a complete treatment regime, consisting of four weekly treatments as described above. These animals will have bone marrow, liver, kidney, and spleen biopsies before the first treatment. One week following the last treatment, the dogs will be sacrificed and tissue sections of the same

organs plus the urinary bladder and lens will be taken. These tissues will be examined histopathologically for evidence of toxic changes. Complete blood counts will also be performed at weekly intervals.

The remaining two dogs in Groups I and II will have a section of urinary bladder removed following the test solution instillation. This tissue section will be divided and one part homogenized and extracted for thio-TEPA analysis and the other section evaluated histopathologically.

The withdrawn test solution, blood samples, and bladder tissue extracts will be analyzed by spectrophotometry to determine levels of thio-TEPA. The results will be compared to determine effectiveness of DMSO in increasing absorption of thio-TEPA.

PROGRESS

(79 10 - 80 09) Progress on this protocol has been hampered by the difficulty in developing a suitable assay for Thio-TEPA. Initial efforts to develop a spectrophotometric assay for Thio-TEPA failed because of the low sensitivity of the assay. Subsequent attempts to use a gas chromatographic procedure also failed. Thio-TEPA has been set aside until a high pressure liquid chromatograph becomes available. 5-fluorouracil is now being investigated and progress is being made in developing a gas chromatographic assay for this agent. Cis-Platinum will be studied after the series using 5-fluorouracil has been completed.

Due to the departure of CPT Cricco, CPT Robert Finnerty, MC, has assumed the duties as principal investigator of the project.

(80 09 - 81 09) Due to the early departure of CPT Finnerty, MAJ Roger Schoenfeld took over this protocol. Cisplatin was the drug used under his direction. Two dogs received DMSO and one dog served as a control receiving cisplatin only. This pilot study was encouraging. The results suggest that DMSO is useful by transporting cisplatin into the muscle layer of the canine bladder. With an acceptable assay, serum levels of cisplatin can be monitored and dosages can be adjusted to avoid untoward side effects. A larger series is planned to solidify and extend these observations. The clinical applicability shows promise. The investigators plan to test DMSO with other drugs also.

STATUS: (O)

TITLE: Lid Magnets for Correction of Orbicularis Palsy

PRINCIPAL INVESTIGATOR: COL Stanley C. Sollie, MC

PROFESSIONAL ASSISTANTS: MAJ Kurt Guelzow, MC
MAJ Frederick A. Mausolf, MC

WORK UNIT NO: 75/27

TECHNICAL OBJECTIVE

To study the effects of the insertion of lid magnets on the tarsal plates of the lids involved in seventh nerve palsy.

METHOD

Patients with seventh nerve palsy will be evaluated, and, if the palsy persists longer than six months without showing improvement and if the eye is affected by the lack of lid closures, these patients will be considered for the surgery. The surgery consists of implanting lid magnets, supplied through Wolfgang D. Muhlbauer, Department of Plastic and Reconstructive Surgery, Klinikum rechts der Isar of the Technical University, Munich, Germany. A skin incision is made in the upper and lower lid and the magnets are sutured to the tarsus. The skin incision in then closed.

PROGRESS

(80 10 - 81 09) No additional lid magnets were implanted in the past two fiscal years. All of the patients in the study who are in the area have remained free of complications. However, the results have been only fair. Therefore, the investigators have no future plans to use these magnets again.

STATUS: (C)

TITLE: Implantation of Intraocular Lenses

PRINCIPAL INVESTIGATOR: COL Stanley C. Sollie, MC

PROFESSIONAL ASSISTANTS: LTC Stanley C. Allison, MC
LTC Christopher G. Knight, MC
MAJ Bruce D. Bellin, MC
CPT Lawrence E. Hannon, MC
LTC John C. Goodin, MC

WORK UNIT NO: 79/64

TECHNICAL OBJECTIVE

To become proficient in intraocular lens implantation and to gain investigator status with FDA requirements, thereby providing a new technique in ophthalmic surgical care for our patients.

METHOD

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

(80 10 - 81 09) Intraocular lenses are being implanted in a high percentage of routine cataract extractions. The success rate and incidence of complications continue to be acceptable. The investigators plan to continue this operation with slight alterations as the state of the art and the skill levels of the investigators improve.

STATUS: (O)

TITLE: Use of Brainstem Evoked Response (B.S.E.R.) in Identification of Learning Disabilities

PRINCIPAL INVESTIGATOR: CPT Wallace E. Taylor, MC

PROFESSIONAL ASSISTANTS: MAJ Carl F. Loovis, MSC
MAJ A. W. Atkinson, MC
Mary W. Loovis, M.S.
Susan Boyce, M.S.

WORK UNIT NO: 81/97

TECHNICAL OBJECTIVE

To determine if significant differences exist in auditory evoked response between children with auditory processing problems and normal children randomly selected.

METHOD

Ten randomly selected 8 and 9-year old Caucasian males will be subjected to puretone and speech audiometry, tympanometry, and B.S.E.R. audiometry. Ten Caucasian males, 8 and 9-year olds, suspected of having auditory-related learning disabilities by review of school achievement testing will be given the sections of the Illinois Test of Psycholinguistic Abilities, subserving audition, and auditory processing. Those children scoring less thatn 25th percentile in at least one subtest will be given the same battery of audiologic tests as the control group. The choice of Caucasian males was made on the basis of evidence which suggests that B.S.E.R. potentials differ from sex to sex, race to race, and with age. By limiting the make-up of the the group, these differences will be eliminated. Questionnaires will also be answered by parents involving history of potential risk. Statistical analysis will be by t-test. If difference exists, but are not statistically significant, additional number of children will be studied.

PROGRESS

(81 07 - 81 09) Supplies and personnel are being accumulated and coordinated. Patient selection will begin with the advent of the school year.

STATUS: (O)

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

TITLE: SWOG 7433, Non-Hodgkin's Lymphomas (Stage I, I_E, II and II_E). A Phase III Study

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC
PROFESSIONAL ASSISTANT: LTC H. Irving Pierce, MC
WORK UNIT NO: 77/53

TECHNICAL OBJECTIVE

To compare the remission rate, remission duration and survival in patients with non-Hodgkin's lymphoma, pathologic stages I, I_E, II and II_E treated with extended field radiotherapy (supradiaphragmatic mantle or abdominal field) alone or with extended field radiotherapy plus combination chemotherapy (Cytoxan, Hydroxyl-daunorubicin(adriamycin), Oncovin (vincristine), and prednisone).

METHOD

Patients newly diagnosed (no type of prior therapy) with non-Hodgkin's lymphoma except mycosis fungoides and diffuse lymphocytic well differentiated lymphoma will be thoroughly evaluated for extent of disease and then randomized to either radiation therapy or radiation therapy plus chemotherapy. If the patient does not achieve a complete remission after completion of his treatment course, he will be removed from the study. Those achieving complete remission will be followed for two years or until relapse.

PROGRESS

(77 08 - 80 09) One patient was entered during FY 80 but was ineligible because of bone marrow involvement found at a later date; patient is alive and in remission. One patient was treated from May 1978 to November 1978; in complete remission on last follow-up in September 1980.

(80 10 - 81 09) No new patients were registered. Investigators continue to follow the patient registered in May 1978 who is still in complete remission.

STATUS: (O)

TITLE: SWOG 7510, Intensive Adjuvant Chemotherapy with or without Oral BCG Immunotherapy for Patients with Locally Advanced Adenocarcinoma of the Large Bowel

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC
PROFESSIONAL ASSISTANT: LTC H. Irving Pierce, MC
WORK UNIT NO: 77/18

TECHNICAL OBJECTIVE

To determine the efficacy of adjuvant chemotherapy with the highly effective combination of Methyl CCNU (MeCCNU) and 5-Fluorouracil (5-FU) and to determine whether this is added to by immunotherapy with oral Bacillus Calmette-Guerin (BCG) on the disease-free interval and survival of patients with Duke C large bowel adenocarcinoma.

METHOD

Patients will be randomly assigned to either of the two following regimens:

Chemotherapy alone - Methyl CCNU, given orally on day 1, plus intravenous 5-Fluorouracil, given intravenously weekly for three doses would constitute one course. Courses would begin every eight weeks.

Chemotherapy plus immunotherapy - Chemotherapy as described above plus immunotherapy in the form of oral BCG given every two weeks.

PROGRESS

(76 12 - 80 09) Eleven (11) patients are now on study and they are currently being followed for possible recurrence. The range of treatment varies from 48 months to 4 months. As of 1 Oct 80, no patients have shown evidence of recurrence.

(80 10 - 81 09) One of the above patients was lost to follow-up. The ten others are still being followed and all were evaluated in 1981. Nine of the ten are in complete remission 1½ to 5 years from registration. One patient had a tooth abscess and developed two CNS lesions. No tumor or abscess was found on craniotomy. The investigators can not determine at this point if this is a recurrence.

STATUS: (O)

TITLE: SWOG 7521, Adjuvant Melanoma Protocol

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC
PROFESSIONAL ASSISTANT: LTC H. Irving Pierce, MC
WORK UNIT NO: 77/38

TECHNICAL OBJECTIVE

1. To determine the efficacy of BCNU, hydroxyurea, and imidazole carboxamide (BHD) in preventing the recurrence of disease and prolonging the survival of patients with primary malignant melanoma who have received definitive surgical treatment for their primary lesions, have no evidence of residual disease, but in whom by the clinical and pathological characteristics of the primary lesion can be predicted to have a high incidence of recurrence. 2. To determine the efficacy of combination chemotherapy (BHD) with and without BCG in preventing the development of metastases and prolonging the disease-free interval and survival of patients with recurrent malignant melanoma which has been surgically excised ("minimal residual disease"). 3. To determine the immunocompetence of patients with malignant melanoma and any correlation with prognosis. 4. To determine the influence of chemotherapy and chemoimmunotherapy upon the immunocompetence of these patients with malignant melanoma.

METHOD

Patients who have a histologically confirmed diagnosis of malignant melanoma and have not been previously treated with chemotherapy or radiation therapy and meet the other criteria as outlined in the protocol shall be entered in the study. Patients will be classified as follows for randomization: Class I - localized disease; Class II - regional and solitary distant metastatic disease. Patients with Class I disease will be randomized between BHD and no treatment. Patients with Class II disease will be randomized to either BHD or BHD + BCG. Patients will be treated for one year or until recurrent disease develops. Patients randomized to no treatment will be followed in a similar fashion. After one year of treatment patients are to remain on study and be followed on no treatment.

SWOG 7521 - Stutz

PROGRESS

(80 10 - 81 07) No patients were entered on this protocol during FY 81 at MAMC. Previously one patient was randomized to the no treatment arm with recurrence after 11 months. A second patient received one course of treatment and refused further therapy because of side effects.

STATUS: (C)

TITLE: SWOG 7622, Combined Modality for Mycosis Fungoides -- Stage I (Phase II)

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC
PROFESSIONAL ASSISTANTS: LTC H. Irving Pierce, MC
WORK UNIT NO: 77/60 LTC D.E.Gehle, MC

TECHNICAL OBJECTIVE

1. To compare the effectiveness of combined electron beam therapy and adjuvant chemotherapy vs electron beam therapy alone for patients with Stage I mycosis fungoides to determine the time to recurrence and to determine the percentage of recurrence.
2. To determine the effectiveness of adjuvant chemotherapy and survival patterns of such patients.
3. To determine the value of staging laparotomy in the management of mycosis fungoides.

METHOD

Patients who have two or more skin biopsies read as mycosis fungoides by a pathology panel and who meet other criteria as listed in the protocol will be randomized to receive electron beam therapy alone or electron beam therapy and adjuvant chemotherapy. Electron beam total body irradiation will be given via the Stanford Technique to a dose of 3000-5000 rads/40-60 days. Following the completion of electron beam therapy a rest period of four weeks is completed before chemotherapy is started. Chemotherapy will consist of: Cytoxan, 450 mg/M^2 IV on day 1 only; adriamycin, 30 mg/M^2 on day 1 only; vincristine, 1.4 mg/M^2 on day 1; prednisone, 100 mg orally for 5 days; and bleomycin, 2 units/M^2 IV 30" after vincristine on day 1. A total of 8 cycles at 3-week intervals will be delivered. Patients will be followed indefinitely or to a point of relapse.

PROGRESS

(77 03 - 81 09) No patients have been registered on this protocol.

STATUS: (C)

TITLE: SWOG 7632, Combined Modality Protocol for Recurrent Breast Cancer, Phase III

PRINCIPAL INVESTIGATOR: CCL Friedrich H. Stutz, MC
PROFESSIONAL ASSISTANT: LTC H. Irving Pierce, MC
WORK UNIT NO: 77/63

TECHNICAL OBJECTIVE

1. To establish the survival of breast cancer patients when treating the first recurrence with a coordinated hormonal chemotherapeutic approach.

2. To determine the efficacy of a response to the antiestrogen Tamoxifen in predicting response to ablative surgery.

3. To correlate hormonal manipulations with estrogen and progestrone receptors where possible.

METHOD

First recurrence patients who have been surgically and/or radiotherapeutically treated with the intent of cure of their primary disease and who meet other criteria as outlined in the protocol will be divided into two groups. Group I (no prior castration) will receive Tamoxifen, 10 mg BID, followed by castration plus Tamoxifen. Responding patients will subsequently undergo adrenalectomy or hypophysectomy; nonresponding patients will receive chemotherapy. Group II (prior castration) will start on Tamoxifen. Responding patients will after relapse go directly to adrenalectomy or hypophysectomy; nonresponding patients will go directly to chemotherapy. Surgical guidelines and chemotherapy as outlined in protocol.

PROGRESS

(77 08 - 81 09) One patient has been previously reported who had remission and died 5 months later. One patient was treated for 18 months and taken off protocol due to other complications. A third patient was entered on the protocol one month ago and it is too early for evaluation.

STATUS: (O)

TITLE: SWOG 7703, Radiation Therapy in Combination with BCNU, Dimethyl Triazeno Imidazole Carboxamide (DTIC) or Procarbazine in Patients with Malignant Gliomas of the Brain. Phase III

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC
PROFESSIONAL ASSISTANT: LTC H. Irving Pierce, MC
WORK UNIT NO: 77/74

TECHNICAL OBJECTIVE

To compare the effectiveness of radiation therapy plus BCNU, radiation therapy plus DTIC, and radiation therapy plus procarbazine for remission induction, duration of remission, and survival in patients with malignant gliomas of the brain.

METHOD

Patients with histologically confirmed primary central nervous tumors of the following histologic types will be entered on the study: astrocytoma, grades 3 and 4 (glioblastoma multiforme). Other criteria: surgery with histologic diagnosis within the prior four weeks and no prior chemotherapy of any type with the exception of corticosteroids. Patients will be randomly allocated to one of the three programs: (1) radiation therapy plus BCNU; (2) radiation therapy plus procarbazine; (3) radiation therapy plus DTIC (dosage as outlined in the protocol). Since survival time is an important end point of this study, each investigator will be required to follow each patient until death and to report the death.

PROGRESS

(77 09 - 80 09) One patient was entered on the study in January 1981 and transferred to Portland, Oregon, two months later without continuing treatment.

STATUS: (C)

TITLE: SWOG 7713/14, Chemoimmunotherapy in Non-Hodgkin's Lymphoma CHOP vs CHOP + Levamisole vs CHOP + Levamisole + BCG for Remission Induction Therapy: Levamisole vs No Maintenance after Remission Induction

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC
PROFESSIONAL ASSISTANT: LTC H. Irving Pierce, MC

WORK UNIT NO: 78/02

TECHNICAL OBJECTIVE

1. To compare the effectiveness, in terms of rate of response of two chemoimmunotherapy regimens (CHOP + levamisole vs CHOP + levamisole + BCG) against CHOP for remission induction in previously untreated patients with non-Hodgkin's lymphoma.
2. For patients proven to be in complete remission after induction, to compare the duration of documented complete response obtained by continued maintenance immunotherapy with levamisole vs no maintenance therapy.
3. For patients with imparied cardiac function (not eligible for treatment with adriamycin), with mycosis fungoides, or with only a partial response to 11 courses of treatment with CHOP-levamisole + BCG, to estimate the complete response rate obtained by continued chemoimmunotherapy with COP + levamisole.
4. To estimate the CNS relapse rate in patients with diffuse lymphomas when CNS prophylaxis with intrathecal cytosine arabinoside is used.
5. To continue to evaluate the impact of systematic restaging of patients judged to be in complete remission and the value of expert hematopathology review of diagnostic material from all cases.
6. To establish baseline and serial data on immunologic status in both chemoimmunotherapy groups.

METHOD

Patients with a diagnosis of non-Hodgkin's lymphoma established by biopsy with no prior chemotherapy are eligible. Patients with chronic lymphocytic leukemia are ineligible. Patients with preexisting cardiac diasease or mycosis fungoides are ineligible for the CHOP programs, but will be treated with COP + levamisole. Patients will be stratified according to nodular or diffuse histologies, adequate or imparied bone marrow reserves, presence or absence of bone marrow involvement, and performance status. Initial drug doses are based on bone marrow reserve. Treatment plans as outlined in the protocol.

SWOG 7713/14 - Stutz

PROGRESS

(77 12 - 80 09) One patient was registered in FY 81 and treated with good partial remission as of the end of the fiscal year. One patient previously reported with complete remission is still disease free after two years. One patient previously reported with progressive disease during treatment has expired.

STATUS: (O)

TITLE: SWOG 7725, Continuous 5-Drug Induction with Intermittent CMPF vs CMPF + Levamisole for Maintenance in Patients with Estrogen Receptor Negative Breast Cancer, Phase III.

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC
PROFESSIONAL ASSISTANT: LTC H. Irving Pierce, MC
WORK UNIT NO: 78/16

TECHNICAL OBJECTIVE

To determine the respective effects of levamisole on the duration of response and survival of patients with advanced breast cancer concurrently treated with maintenance chemotherapy after a successful remission induction trial of continuous Cooper regimen; and to accumulate data on immunologic variables under the conditions of chemotherapy alone and combined chemotherapy and immunotherapy with levamisole of advanced breast cancer.

METHOD

Patient Eligibility: only patients proven to be estrogen receptor negative are eligible. Patients must have a life expectancy of 2 months and measurable lesions and no previous chemotherapy other than adjuvant chemotherapy. Patients coming off additive hormonal therapy and antiestrogens must have been off therapy for 6 weeks and have increasing disease. If the 6 week observation period off hormones appears to be excessively risky, the patient may be entered provided that 3 weeks have elapsed since last day of hormonal therapy and disease is rapidly progressive. Prior surgical ablative endocrine therapy must have taken place 3 weeks prior to entry if the disease is rapidly progressive and 10 weeks if slowly progressive. Patients with previous cancer immunotherapy or who had relapsed while receiving multiple durg adjuvant chemotherapy are ineligible. Concomitant therapy with mithramycin is not allowed, and concomitant therapy with corticosteroids (other than prednisone) is allowed only in adrenalectomized or hypophysectomized patients.

Treatment: All patients will undergo a remission induction trial with continuous Cooper regimen in the following fashion:

SWOG 7725 - Stutz

Vincristine	0.625 mg/M^2	IV once a week for 8 weeks
5-Fluorouracil	300 mg/M^2	IV " " "
Methotrexate	15 mg/M^2	IV " " "
Cyclophosphamide	60 mg/M^2	PO daily for 8 weeks
Prednisone	30 mg/M^2	PO daily for 2 weeks, reduce
	to 20 mg/M^2	PO for next 2 weeks, reduce
	to 10 mg/M^2	until day 49, then taper to nothing by day 56

Patients with increasing disease after 6 weekly induction cycles will go off study. After achievement of remission or stable status, the patients will be randomly allocated to the following treatment arms:

Army I - Maintenance "Intermittent Cooper Regimen"

5-Fluorouracil	180 mg/M^2	PO daily x 5 days, q 28 days
Methotrexate	4 mg/M^2	PO " " " "
Cyclophosphamide	120 mg/M^2	PO " " " "
Prednisone	40 mg/M^2	PO " " " "

Arm II - *Intermittent Cooper + levamisole*

The same as Arm 1 plus levamisole 100 mg/M^2 daily in 3 divided doses on days 4-6, 11-13, and 18-20 of each cycle.

As with all studies, dose modifications will be made when necessary.

PROGRESS

(78 02 - 81 07) Seven patients were entered in the study with partial or complete response from two to twelve months and later expired.

STATUS: (C)

TITLE: SWOG 7727/28, Combination Chemoimmunotherapy Utilizing BCNU, Hydroxyurea, and DTIC (BHD) with Levamisole versus DTIC Plus Actinomycin-D in the Treatment of Patients with Disseminated Malignant Melanoma, Phase III.

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC
PROFESSIONAL ASSISTANT: LTC H. Irving Pierce, MC
WORK UNIT NO: 78/12

TECHNICAL OBJECTIVE

To determine remission induction rates, remission duration, survival, and toxicity in patients with disseminated malignant melanoma treated with BHD (BCNU, hydroxyurea, DTIC), BHD plus levamisole, and intermittent single high dose DTIC plus actinomycin D in a prospective, randomized clinical study.

METHOD

Patient Eligibility: histologically proven disseminated malignant melanoma with no previous treatment with any of the agents involved; measurable disease and estimated survival of at least two months; adequate renal and hepatic function; BUN >25 mg% or creatinine >1.5 mg% and bilirubin >2.5 mg%; hepatic or renal metastases are eligible provided organ function is adequate; recovery from the toxic effects of prior therapy and completion of RT to bone marrow bearing areas at least two weeks prior to entry.

Brain metastasis treatment: decadron 8-12 mg/day x 3 PO then tapered at the discretion of the investigator; day 3 begin total irradiation, 4000 rads over 2 week period; chemotherapy or chemoimmunotherapy will begin on the second week of radiotherapy.

Hepatic metastasis treatment: hepatic artery cannulation via femoral artery or brachial artery route. DTIC 200 mg/M^2/day over 24 hr infusion in 1000 ml of D_5W x 5 days; after 5-7 days patient will begin either chemotherapy or chemoimmunotherapy.

Patients will be stratified according to performance status and age. Treatment arms: I. (a) BHD - normal marrow (b) imparired marrow; II. (a) BHD + levamisole - normal marrow (b) impaired marrow; and III. (a) actinomycin D + high dose DTIC - normal marrow (b) imparied marrow.

If patients on BHD + levamisole or actinomycin D + DTIC have no response in the 2 initial courses, they will be crossed over. Patients not responding to BHD alone will be taken off study after an adequate trial. Dosages, courses of treatment, and

SWOG 7727/28 - Stutz

Patients not responding to BHD alone will be taken off study after an adequate trial. Dosages, courses of treatment, and modifications are given in detail in the protocol.

PROGRESS

(78 02 - 81 09) Four patients were registered. Three had severe progressive disease, relapsed, and expired. One patient has been on study since June 1981 with stable disease and symptomatic improvement at present.

STATUS: (O)

SWOG 7765 - Adriamycin and Single Dose DTIC in Soft Tissue and Bone Sarcomas, Phase II

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: Suresh B. Katakkar, M.D., DAC
LTC Irwin Dabe, MC

WORK UNIT NO: 80/21

TECHNICAL OBJECTIVE

To determine the effectiveness and tolerance of adriamycin and single dose DTIC in patients with metastatic sarcomas who have failed on higher priority treatment protocols.

METHOD

Patients who have failed on higher priority treatment and who have not previously received adriamycin and DTIC and who have adequate bone marrow reserve will have 60 mg/M^2 administered IV at 21 day intervals followed by 750 mg/M^2 DTIC infused over a 45 minutes period. Inadequate bone marrow reserve patients: the same procedure with adriamycin administered at a dose of 40 mg/M^2 and DTIC at a dose of 500 mg/M^2.

PROGRESS

(80 06 - 81 09) No patients have been registered on the protocol.

STATUS: (C)

TITLE: SWOG 7804, Adjuvant Chemotherapy with 5-Fluorouracil, Adriamycin, and Mitomycin-C (FAM) vs Surgery Alone for Patients with Locally Advanced Gastric Adenocarcinoma

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC
PROFESSIONAL ASSISTANTS: LTC H. Irving Pierce, MC
WORK UNIT NO: 78/42 Suresh B. Katakkar, M.D., DAC

TECHNICAL OBJECTIVE

To determine the efficacy of adjuvant chemotherapy with FAM on the disease-free interval and survival of patients with TNM stage-groups IB, IC, II and III gastric adenocarcinoma compared to potentially curative surgery alone.

METHOD

Patient Eligibility: patients must have TNM stage-group IB, IC, II or III gastric adenocarcinoma and no microscopic or gross residual postoperatively; no prior chemo- or radiotherapy; no medical contraindications to chemotherapy with FAM; serum bilirubin <2.0 mg/100 ml; SGOT and SGPT less than three times the upper limit of normal values; creatinine clearance >75 cc/min; BUN ≤25 mg%; serum creatinine ≤1.5 mg%; WBC >4,000; and platelets >100,000.

Treatment: After surgery, patients will be randomized to either Treatment 1 (no further therapy) of 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

(78-07 - 81-09) No patients entered on this study.

STATUS: (O)

TITLE: SWOG 7806, Cis-Diamminodichloroplatinum (II) in the Treatment of Refractory Epidermoid Carcinoma of the Esophagus, Phase II.

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC
PROFESSIONAL ASSISTANTS: LTC H. Irving Pierce, MC
Suresh B. Katakkar, M.D., DAC
WORK UNIT NO: 78/35

TECHNICAL OBJECTIVE

To determine the response rate and survival, with some degree of precision, utilizing cis-diamminodichloroplatinum II (CACP) in the treatment of patients with squamous cell carcinoma of the esophagus which is growing despite more standard therapy.

METHOD

Patient Eligibility: Patient must have biopsy confirmed diagnosis of epidermoid carcinoma of the esophagus. Adenocarcinoma of the esophagus is not eligible. Patient must have an absolute granulocyte count of $\geq$2,000 and a platelet count of $\geq$150,000 and must be past the present nadir resulting from any prior therapy. Patient must have a BUN of no higher than 20 mg% and a serum creatinine no higher than 1.4 mg% or creatinine clearance in excess of 75 cc/minute. Two functioning kidneys and an unobstructed urinary tract are required.

Treatment: CACP 50 mg/M^2 IV infusion over an 1-4 hour interval, days 1 & 8 of each 28 day course. Prior to every dose, the patient must receive at least 1,000 cc of fluids above usual intake (also on the evening before administration).

As long as there is evidence of tumor regression or disease stability at an acceptable level without unacceptable toxicity the CACP will be continued indefinitely. Although 30 days on therapy will constitute an adequate tiral, an attempt will be made to give each patient two complete courses if the clinical status is acceptable.

PROGRESS

(78-09 - 81-09) No patients entered on the study.

STATUS: (C)

TITLE: SWOG 7808, Combination Modality Treatment for Stages III and IV Hodgkin's Disease, MOPP #6

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC
PROFESSIONAL ASSISTANTS: LTC H. Irving Pierce, MC
WORK UNIT NO: 78/47 Suresh B. Katakkar, M.D., DAC

TECHNICAL 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.

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.

METHOD

Patient Eligibility: Patients must have histologic diagnosis of Hodgkin's disease classified by the Lukes and Butler System; no prior chemotherapy; 15 years of age or older. Patients with a history of congestive heart failure, valvular heart disease, or serious obstructive or restrictive pulmonay disease will be excluded.

Treatment: All patients except those with prior radiotherapy must receive radiation therapy consultation before chemotherapy is started.

Treatment 1: Normal marrow patients will receive 6 cycles of MOP-BAP

Treatment 2: Imparied bone marrow patients will receive 6 cycles of MOP-BAP with dose modifications.

Complete remission (CR) patients will be randomized between Treatment 3 (no treatment) and Treatment 4 (levamisole). Partial remission (PR) patients without prior radiation therapy or residual bone marrow involvement will receive Treatment 6 (radiation therapy). PR patients with prior radiation therapy 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). CR patients without prior radiation therapy will receive Treatment 5 (radiation therapy for CR). Doses for chemotherapy and radiotherapy can be found in para 5.0 of the protocol.

SWOG 7808 - Stutz

PROGRESS

(78 09 - 79 09) One patient was treated for 7+ months with excellent partial response. He was taken off the protocol because he chose to continue chemotherapy rather than go to radiotherapy as required by the protocol.

(79 09 81 09) Five patients were treated during this period with complete resmission as of 30 Sep 81.

STATUS: (O)

TITLE: SWOG 7811 - Brain Metastases Protocol, Phase III

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC
PROFESSIONAL ASSISTANTS: LTC H. Irving Pierce, MC
WORK UNIT NO: 79/03 Suresh B. Katakkar, M.D., DAC

TECHNICAL OBJECTIVE

To determine the effectiveness of combined radiation therapy and metronidazole (Flagyl) in the treatment of patients with brain metastases from primary malignancies outside the central nervous system, compared with radiation therapy alone, as determined by objective response (brain and/or CAT scan) and/or increase in functional neurologic level and duration of response.

To determine the toxicity of multiple dose administration of metronidazole and radiation therapy.

METHOD

Patients will have had no prior radiation to the brain. Patients with brain metastases will be treated with whole brain irradiation therapy. A second group will be treated with whole brain irradiation therapy plus metronidazole.

PROGRESS

(79 03 - 81 09) One patient has been treated. After one course of metronidazole, patient refused further treatment because of nausea and vomitting; patient later expired.

STATUS: (O)

TITLE: Treatment of Advanced Germ Cell Neoplasms of the Testis: Remission Induction with Vinblastine, Bleomycin, with Low-Dose or High-Dose Cis-Platinum; Surgical Removal of all Residual Tumor Following Remission Induction; Maintenance Therapy with CTX, Actinomycin-D, Adriamycin and Vinblastine, Phases II-III. SWOG 7817.

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC
PROFESSIONAL ASSISTANT LTC H. Irving Pierce, MC
WORK UNIT NO: 79/04 Suresh B. Katakkar, M.D., DAC

TECHNICAL OBJECTIVE

To determine in a randomized fashion the effectiveness of cis-platinum given in the conventional low-dose schedule daily x 5 days vs high-dose intermittent treatment in remission induction of disseminated testicular cancer, when combined with vinblastine and bleomycin.

To determine the survival of patients who achieve a partial remission and are rendered disease-free by surgical removal of residual disease and maintained on the same chemotherapy as patients who achieved complete remission status on chemotherapy alone.

To determine the effectiveness of cyclophosphamide, actinomycin-D, adriamycin, and vinblastine, in the maintenance of remission status.

To document the nature and extent of the hematologic and non-hematologic side effects of the various drug combinations.

METHOD

Patients with carcinoma of the testis will be treated randomly with cis-platinum utilizing the low dose schedule vs the high dose intermittent treatment when combined with vinblastine and bleomycin. These patients will then be maintained on cyclophosphamide, actinomycin-D, adriamycin, and vinblastine.

PROGRESS

(79-11 - 81-09) No patients have been entered on this protocol.

STATUS: (C)

TITLE: SWOG 7823/24/25/26 - ROAP-AdOAP in Acute Leukemia, Phase III

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC
PROFESSIONAL ASSISTANTS: LTC H. Irving Pierce, MC
Suresh B. Katakkar, M.D., DAC
WORK UNIT NO: 79/02

TECHNICAL OBJECTIVE

To compare the efficacy of the 4-drug combination chemotherapy regimen, ROAP (Rubidazone, Vincristine, Arabinosyl Cytosine, and Prednisone) to AdOAP (the same combination using Adriamycin in place of Rubidazone) in adult acute leukemia, as determined by remission duration and survival.

To determine the comparative toxicity of these regimens.

To determine whether late intensification therapy at 9 months after complete remission will improve long-term, disease free survival.

To determine whether immunotherapy using Levamisole for 6 months after 12 months of complete remission on chemotherapy improves disease-free survival.

To determine the effects of intrathecal Ara-C on the incidence of CNS leukemia.

To determine reproducibility of the FAB/histologic classification and correlation to response to therapy in 200 consecutive cases of acute leukemia.

To study the effects of intensive supportive care in the management of acute leukemia.

METHOD

For remission induction Group A will receive ROAP and Group B will receive AdOAP. When leukemic cells are no longer visible in the bone marrow consolidation therapy will begin with one-half the patients receiving only chemotherapy consisting of the same drugs , but in reduced dosage. The other one-half will receive the same drugs with the addition of cytosine arabinoside in the spinal fluid at weekly intervals for 8 weeks. If a complete remission persists, maintenance therapy will be given consisting of vincristine, cytosine arabinoside, and prednisone for 5 days at monthly intervals for 9 months. One half of these patients will then receive late intensification

therapy consisting of a combination of vincristine, prednisone, and methotrexate, and 6-mercaptopurine for 5 days. The other one-half will receive 3 additional months of maintenance therapy, at which time all patients will be randomized into one group receiving no further treatment and another group receiving levamisole for 2 days of each week for 6 months.

PROGRESS

(79 04 - 80 09) Four patients were registered on this protocol.

(1) brief complete response - patient later died.

(2) complete response for 7 months; then relapse and death.

(3) complete response with one course; transferred to BAMC.

(4) partial response with two courses; expired after CNS relapse.

(80 10 - 81 09) One patient was registered during FY 81 and remains in complete remission.

STATYSL (0)

TITLE: Combined Modality Therapy for Breast Carcinoma, Phase III - SWOG 7827

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: Suresh B. Katakkar, M.D., MC
LTC Irwin B. Dabe, MC

WORK UNIT NO: 79/96

TECHNICAL OBJECTIVES

To compare the disease-free interval and recurrence rates in:

estrogen receptor positive premenopausal patients with Stage II disease using combination chemotherapy alone vs combination chemotherapy and oophorectomy;

estorgen receptor positive postmenopausal patients with Stage II disease using combination chemotherapy plus tamoxifen vs tamoxifen alone vs combination chemotherapy alone;

estrogen receptor negative patients with Stage II disease using one vs two years of combination chemotherapy;

To compare the effect of these various adjunctive therapy programs upon survival patterns and to correlate the estrogen receptor status with disease-free interval and survival.

METHOD

Patients with a histologically proven diagnosis of breast cancer (Stage II or Stage III) with 1 or more pathologically involved axillary nodes will receive one of the following treatments:

(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.

Any patient undergoing segmental mastectomy (lumpectomy) will receive 6 wks of radiation therapy in addition to the treatment they are randomized to receive.

*C - cyclophosphamide; M - methotrexate; F - 5-fluorouracil; V - vincristine; P - prednisone

SWOG 7827 - Stutz

PROGRESS

(80 02 - 81 09) Six patients have been registered at MAMC on this protocol. There have been six complete remissions and two partial remissions with patients doing well at this date.

STATUS: (O)

TITLE: SWOG 7828 - Combined Modality Therapy for Extensive Small-Cell Carcinoma of the Lung.

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANT: Suresh B. Katakkar, M.D., MC

WORK UNIT NO: 79/91

TECHNICAL OBJECTIVES

To compare the efficacy of two non-cross-resistant regimens (cell-cycle specific vs cell-cycle-non-specific) during induction.

To determine whether administration of a second non-cross-resistant regiment in consolidation can convert stable disease or partial response to a better quality of response.

To determine the effect of intentional, early alternation of non-cross-resistant regimens on the complete response rate.

To determine whether reinduction at 24 and 52 weeks has a favorable effect on response duration and survival.

To determine whether administration of intrathecal methotrexate at reinduction can affect the incidence of non-brain CNS relapse.

METHOD

Patients with extensive small-cell carcinoma of the lung as confirmed by a pathologist will receive the following treatments:

INDUCTION: (6 weeks) Treatment 1: Regimen A - VMV*
Treatment 2: Regimen B - VAC*
Treatment 3: Regimen C - VMV-VAC

*VMV - Vincristine, methotrexate, VP-16
*VAC - Vincristine, adriamycin, cyclophosphamide

CONSOLIDATION: (6 weeks): Original Regimen A - CR (complete responders) receive M/VP-16; PR (partial responders) or SD (stable disease) receive AC
Original Regimen B - CR receive AC PR and SD receive M/VP-16
Original Regimen C - CR, PR, and SD receive M/VP-16 for 3 weeks and AC for second three weeks

MAINTENANCE: Prophylactic WBR plus maintenance chemotherapy with Cytoxan and VP-16 for 3 courses (28 day intervals).

SWOG 7828 - Stutz

At 24 weeks all patients undergo a second randomization to receive reinduction therapy or continue with maintenance chemotherapy only. All those who receive reinduction therapy will receive the original treatment plus intrathecal methotrexate. Patients randomized to receive no reinduction therapy will continue to receive cyclophosphamide and VP-16.

At 52 weeks CR's will receive no further therapy. PR's and SD's will continue to receive cyclophosphamide and VP-16 every 28 days for a total of 2 years on therapy or until progressive disease develops.

PROGRESS

(79 12 - 80 09) Two patients were registered.

(1) complete response for 3 months followed by CNS recurrence and death.

(2) partial response for three weeks followed by early death.

(80 10 - 81 09) No patients were entered at MAMC during this period.

STATUS: (C)

SWOG 7841 - Phase II-III Comparison of FAM + Vincristine vs Chlorozotocin in the Treatment of Advanced Gastric Adenocarcinoma

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: Suresh B. Katakkar, M.D., MC
LTC Irwin Dabe, MC

WORK UNIT NO: 80/22

TECHNICAL OBJECTIVES

To determine the effectiveness (as determined by response rate and survival) of 5-FU + mitomycin-C + adriamycin and vincristine (V-FAM) in the treatment of advanced, previously untreated gastric adenocarcinoma.

To determine the efficacy as determined by response rate and survival of chlorozotocin in the treatment of previously untreated gastric adenocarcinoma.

To compare the relative effectiveness of the two treatments.

To determine by crossover, after relapse or failure on V-FAM or chlorozotocin, the effectiveness as determined by response rate and survival of the alternate treatment in advanced gastric adenocarcinoma with prior therapy.

To determine the toxicities of such treatments.

METHOD

Patients with histologically proven gastric adenocarcinoma, Stage IV in extent will be randomized to the following treatments:

Treatment 1: V-FAM -one course equals 8 weeks
Treatment 2: Chlorozotocin - one course equals 6 weeks

Patients with response or stable disease should be treated again after the appropriate interval on the same treatment regimen. Patients failing to respond or relapsing after response to their treatment arm will receive the alternative treatment.

PROGRESS

(80 02 - 81 09) One patient has been treated for 10 months with stable disease.

STATUS: (O)

TITLE: SWOG-7860 - MGBG Open Groupwide to Refractory Lymphomas

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
LTC Archie W. Brown, MC

WORK UNIT NO: 81/61

TECHNICAL OBJECTIVES

To determine response rate and remission duration with primary weekly intravenous therapy using MGBG in patients with advanced esophageal, breast, pancreatic, colorectal, and head and neck carcinoma and lymphoma; to define the qualitative and quantitative toxicity of this regimen.

METHOD

Patients with histologically confirmed diagnoses of lymphomas with progressive disease resistant to standard therapy are eligible for treatment with MGBG. Patients must have measurable disease and meet other criteria as outlined in the protocol. These patients will receive MGBG, 600 mg/M^2, by infusion in D5W or normal saline on a single arm. No randomization will take place; however, patients will be stratified according to type of lymphoma. The treatment continues for as long as the tumor responds, i.e., remains stable or shrinks. Treatment will be discontinued if the patient experiences intolerable toxicity or refuses further treatment.

PROGRESS

(81 03 - 81 09) No patients were registered on this protocol at MAMC.

STATUS: (O)

TITLE: SWOG 7912 - Gallium Nitrate in Patients with Malignant Lymphoma - Hodgkin's and Non-Hodgkin's, Phase II

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin Dabe, MC
Suresh B. Katakkar, M.D., DAC

WORK UNIT NO: 80/02

TECHNICAL OBJECTIVE

To determine the efficacy, as measured by response rate, of gallium nitrate in patients with malignant lymphoma, both Hodgkin's and non-Hodgkin's types, in patients who have received prior therapy and are not eligible for higher priority studies; and to determine the nature and degree of toxicity of this drug.

METHOD

Patients will receive 2 liters of fluid over their normal intake within 12 hours prior to gallium nitrate administration. Just prior to administration 500 cc of normal saline will be infused over 2 hours. Patients will be treated at a dose of 700 mg/M given as a 30 min IV infusion in 200 ml of normal saline and repeated every two weeks. In the event that myelosuppression persists at day 14, bi-weekly WBC and platelet counts are to be determined and subsequent courses of gallium nitrate are to be given only when there is bone marrow recovery. Patient eligibility, response, and dosage modifications as listed in the protocol.

PROCRESS

(80 04 - 81 09) No patients were registered on this protocol.

STATUS: (C)

TITLE: SWOG 7916 - Phase II Evaluation of Gallium Nitrate in Metastatic Urological Malignancies: Testicular, Bladder, Prostate, and Kidney

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: MAJ Irwin Dabe, MC
Suresh B. Katakkar, M.D., DAC

WORK UNIT NO: 80/23

TECHNICAL OBJECTIVE

To determine the efficacy of gallium nitrate as determined by response and survival in patients with metastatic urological malignancies which include: testicular, bladder, prostate, and kidney; who have failed on higher priority treatment.

METHOD

Patients are eligible who are not candidates for studies of higher priority and who have histologically proven incurable advanced metastatic testicular carcinoma, bladder carcinoma, prostate or kidney carcinoma. Patients should not have had more than two previous types of combination or single agent chemotherapy trials.

All patients will be treated at a dose of 700 mg/m^2 given as a 30 minute IV infusion in 200 ml of normal saline. Course will be repeated every two weeks if blood counts, and liver and renal functions permit. An adequate trial will consist of two courses of therapy.

PROGRESS

(80 06 - 81 09) No patients have been registered on this protocol. Study is now only open to bladder patients.

STATUS: (O)

TITLE: SWOG 7917 - Gallium Nitrate in Previously Treated Patients with Metastatic Breast Cancer, Phase II.

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin Dabe, MC
Suresh B. Katakkar, M.D., DAC

WORK UNIT NO: 80/24

TECHNICAL OBJECTIVES

To determine the efficacy of gallium nitrate in metastatic carcinoma of the breast who have failed standard therapy; and to determine if an initially positive gallium scan predicts response.

METHOD

Patients who have histologic proof of breast cancer, currently Stage IV in extent, will be eligible. After hydration, patients will receive 700 mg/M^2 gallium nitrate in 250 cc normal saline over 30 minutes. Therapy will be repeated every 2 weeks if BUN, creatinine, WBC, and platelets are satisfactory. An adequate trial will consist of 2 courses of therapy (4 weeks). Patients will remain on protocol until complete remission unless unsatisfactory stable disease or increasing disease is noted after 2 courses of therapy or moderate or severe renal toxicity or clinical hearing loss occurs.

PROGRESS

(80 06 - 81 09) No patients were registered on this protocol.

STATUS: (C)

TITLE: SWOG 7918 - Evaluation of m-AMSA in Lymphoma-Hodgkin's and Non-Hodgkin's

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin Dabe, MC
Suresh B. Katakkar, M.D., DAC

WORK UNIT NO: 79/98

TECHNICAL OBJECTIVES

To determine the antitumor activity of AMSA used in a single dose schedule in patients with Hodgkin's and non-Hodgkin's lymphoma as determined by response rate and duration of response, who have failed on higher priority treatment protocols; and to determine the nature and degree of toxicity of this drug.

METHOD

Patients with advanced Hodgkin's or non-Hodgkin's lymphoma who have failed on prior therapy, will be given m-AMSA IV in a dose of 120mg/M^2 for good risk patients and 90 mg/M^2 for poor risk patients, and adjusted doses for patients with abnormal liver function. Treatment will be given every 3-4 weeks if blood counts and liver functions permit. Two courses are considered an adequate trial.

PROGRESS

(80 02 - 81 09) No patients have been registered on this protocol.

STATUS: (C)

TITLE: SWOG 7920 - m-AMSA in Hepatocellular Carcinoma, Gallbladder Carcinoma, and Bile Duct Carcinoma, Phase II

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin Dabe, MC
Suresh B. Katakkar, M.D., DAC

WORK UNIT NO: 79/99

TECHNICAL OBJECTIVE

To determine the efficacy of m-AMSA at a dose of 120 mg/M^2 IV every three weeks in producing regressions or remission in patients with hepatocellular, bile duct, and gallbladder carcinoma.

METHOD

Patients with histologically confirmed hepatocellular, gallbladder, or bile duct carcinoma beyond hope of surgical cure are eligible. Good risk patients will receive 120 mg/M^2 in 500 cc of Dextrose and water over one hour. Poor risk will receive 90 mg/M^2 and abnormal liver function patients will receive 60 mg/M^2. Courses will be repeated every 3-4 weeks if WBC is greater than 3500 and platelet count is greater than 100,000 and liver functions have returned to baseline. An adequate trial will be defined as two courses of therapy. Patients will remain on therapy as long as they respond.

PROGRESS

(80 02 - 80 09) Two patients were registered: (1) had progression on treatment and was taken off study after one month; and (2) had progression on treatment and was taken off study after one month, expired 4 months later.

(80 10 - 81 09) No new patients were entered during this time period.

STATUS: (O)

TITLE: SWOG 7921 - Phase II Evaluation of MGBG in Metastatic Carcinoma of the Breast

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin Dabe, MC
Suresh B. Katakker, M.D., DAC

WORK UNIT NO: 79/100

TECHNICAL OBJECTIVES

To determine response rate and remission duration with weekly intravenous therapy using MGBG in patients with carcinoma of the breast who have failed on higher priority treatment protocols.

METHOD

Patients must not be eligible for SWOG studies of a higher priority and must have histologically proven incurable metastatic carcinoma of the breast. MGBG will be given in an initial dose of 600 mg/M^2 IV in D_5W or normal saline over no less than 30 minutes. The drug will be given on a weekly schedule providing the WBC is greater than 3000, platelet count is greater than 100,000, and the patient has recovered from any encountered stomatitis. An adequate trial will consist of 3 courses of treatment. Patients will continue on treatment as long as they respond and tolerate toxicity.

PROGRESS

(80 02 - 81 09) No patients were registered on this protocol.

STATUS: (C)

TITLE: SWOG 7923 - Gallium Nitrate in Metastatic Squamous Cell CA and/or Local Recurrence Squamous Cell CA of the Head and Neck.

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin Dabe, MC
Suresh B. Katakkar, M.D., DAC

WORK UNIT NO: 80/25

TECHNICAL OBJECTIVES

To determine the efficacy as determined by response rate of gallium nitrate in patients with metastatic squamous cell carcinoma and/or local recurrent squamous cell carcinoma of the head and neck who have failed on higher priority treatment protocols; and to determine if gallium scan results may be predictive of anti-tumor effect.

METHOD

Patients who have histologically confirmed incurable, advanced metastatic squamous cell carcinoma or local recurrent squamous cell carcinoma of the head and neck are eligible. Patients after hydration will receive 700 mg/M^2 gallium nitrate in 250 cc normal saline over 30 minutes. This course will be repeated every 2 weeks if BUN, creatinine, WBC, and platelets are satisfactory. An adequate trial will consist of 2 course of thearpy (4 weeks). Patients will be treated until either complete remission of increasing disease is noted.

PROGRESS

(80 05 - 81 09) No patients were registered on this protocol.

STATUS: (C)

TITLE: SWOG 7924 - Multimodal Therapy for Limited Small Cell Carcinoma of the Lung, Phase III.

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin Dabe, MC
Suresh B. Katakkar, M.D., DAC

WORK UNIT NO: 80/26

TECHNICAL OBJECTIVES

To determine the efficacy of sequentially alternating mutually noncross-resistant, multidrug regimens in remission induction and intensification therapy in patients with limited small cell lung carcinoma; to determine the value of chest radiotherapy added to intensive systemic chemotherapy in reducing chest recurrences and in improve of survival; to determine the relative efficacy and toxicity of low-dose, extensive chest radiation when used in close chronologic sequence with systemic multiagent chemotherapeutic regimens; to determine whether radiotherapy ports should be set according to tumor size prior to or after induction chemotherapy; and to determine the value of combined systemic chemotherapy and radiotherapy in the control of bulky chest disease.

METHOD

Patients with histologically or cytologically confirmed small cell carcinoma of the lung are eligible. Patients will be treated for 8 weeks with combination chemotherapy of methotrexate, vincristine, VP-16, adriamycin, and cyclophosphamide. Following the completion of induction chemotherapy, patients will be treated as follows: Complete remission: patients will be randomized to receive either chest and whole brain radiotherapy followed by chemotherapy or whole brain radiotherapy alone followed by chemotherapy. Partial remission or stabilized disease: patients will be randomized to receive either extended field and whole brain radiotherapy followed by chemotherapy or involved field and whole brain radiotherapy followed by chemotherapy. Patients with progressive disease after induction chemotherapy will go off study.

PROGRESS

(80 02 - 81 09) Six patients have been registered on this protocol. with three complete responses, one partial response, and in two patients they have not been treated long enough for evaluation.

STATUS: (O)

TITLE: SWOG 7927/28 - Chemotherapy for Multiple Myeloma, Phase III

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin Dabe, MC
Suresh B. Katakkar, M.D., DAC

WORK UNIT NO: 80/27

TECHNICAL OBJECTIVES

To compare the effectiveness of four different drug combinations for remission induction in previously untreated patients with multiple myeloma; and, for patients with a 75% tumor reduction, to evaluate the role of 12 months of chemotherapy maintenance with vincristine, cyclophosphamide, and prednisone vs these drugs plus levamisole, when compared with previous experiences.

METHOD

Patients previously untreated with chemotherapy (except prednisone) with a diagnosis of multiple myeloma, Stage I, II, or III, will be eligible for the study. Patients will receive remission induction treatment with one of the following: (1) vincristine, melphalan, cyclophosphamide, and prednisone (VMCP) for 3 courses followed by vincristine, BCNU, adriamycin, and prendisone (VBAP) for 3 courses, every 3 weeks; (2) VMCP for 3 courses followed by VBAP for 3 courses every 3 weeks plus levamisole; (3) vincristine, cyclophosphamide, and prednisone (VCP) every 3 weeks; or (4) VCP every 3 weeks plus levamisole. Treatment will continue on all regimens for a minimum of 6 months, until a 75% tumor reduction has occurred, but no longer than 18 months in the absence of remission. Patients who are responsive to remission induction with Treatments 1 or 3 will receive maintenance treatment with VCP. Patients responsive to induction therapy with Treatments 2 or 4 will receive maintenance tretment with VCP plus levamisole. Treatment cycles are repeated at 21 day intervals for 12 months provided the absolute granulocyte count is at least 1,000 and the platelets count is at least 80,000.

PROGRESS

(80 02 - 81 09) Two patients have been registered. (1) there was no response after nine months and the patient was taken off the protocol. (2) Too early for evaluation.

STATUS: (O)

TITLE: SWOG 7931 - Evaluation of AMSA in Metastatic or Advanced Adenocarcinoma of the Stomach and Pancreas, Phase II.

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin Dabe, MC
Suresh B. Katakkar, M.D., DAC

WORK UNIT NO: 80/28

TECHNICAL OBJECTIVES

To determine the antitumor activity of AMSA as determined by response rate and duration of response used in a single dose schedule in patients with metastatic adenocarcinomas of the stomach and pancreas who have failed on higher priority treatment protocols; and to determine the nature and degree of toxicity of this drug.

METHOD

Patients who are ineligible for SWOG studies of higher priority who have histologically proven, incurable, advanced metastatic adenocarcinoma of the stomach or pancreas are eligible. Good risk patients will receive AMSA in a single dose schedule: 120 mg/M^2 dissolved in 500 ml of D/W and infused IV over no less than one hour. Poor risk patients will start at a dose of 90 mg/M^2. After bone marrow and liver function recovery, repeat courses of AMSA will be given at 21 day intervals. Patients will be removed from the study if increasing disease is noted after 2 courses of therapy.

PROGRESS

(80 06 - 80 09) Two patients were registered on this protocol: (1) was registered but never treated due to sudden complications, expired July 1980; (2) received one course of mAMSA in August 1980 without response, expired 16 days later of her cancer.

(80 10 - 81 09) No new patients were registered during FY 81.

STATUS: (C)

TITLE: SWOG 7934 - Evaluation of AMSA in Metastatic Squamous Carcinoma of the Head and Neck

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin Dabe, MC
Suresh B. Katakkar, M.D., DAC

WORK UNIT NO: 80/29

TECHNICAL OBJECTIVES

To determine the antitumor activity, response rate and duration of response in patients with metastatic squamous cell carcinoma of the head and neck who have failed on higher priority treatment protocols; and to determine the nature and degree of toxicity of this drug.

METHOD

Patients who are not eligible for SWOG studies of higher priority with histologically proven incurable metastatic or locally advanced squamous cell carcinoma of the head and neck are eligible for this study. Good risk patients will receive AMSA in a 3 day schedule of 40 $mg/M^2/d$ x 3 IV. AMSA will be dissolved in 500 ml of D/W and infused IV over no less than one hour. Poor risk patients will start at a dose of 30 $mg/M^3/d$. Upon adequate bone marrow and liver function recovery, repeat courses will be given at 21 day intervals. An adequate trial will be defined as 2 courses of therapy.

PROGRESS

(80 06 - 81 09) No patients were registered on this protocol.

STATUS: (C)

TITLE: SWOG 7935 - Chemotherapy of Functioning and Non-Functioning Islet Cell CA with Chlorozotocin, Phase II.

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin Dabe, MC
Suresh B. Katakkar, M.D., DAC

WORK UNIT NO: 80/30

TECHNICAL OBJECTIVES

To study the response of functioning and non-functioning islet cell carcinoma to chlorozotocin and to obtain pathology materials for review on all patients entered into this study.

METHOD

Patients who have a biopsy-proven diagnosis of islet cell carcinoma not amenable to further surgical therapy with a life expectancy of at least six weeks are eligible. Patients treated with streptozotocin will be analyzed separately. All patients will receive chlorozotocin at six week intervals - good risk at 200 mg/M^2 IV bolus or rapid infusion and poor risk at 100 mg/M^2. Subsequent courses of treatment will be repeated every six weeks assuming hematologic recovery as manifested by a WBC greater than 4000 and platelets greater than 100,000, and a normal BUN and creatinine value. An adequate trial is one course of therapy. Therapy will be continued in the presence of stable disease or in the presence of a response until increasing disease is apparent.

PROGRESS

(80 06 - 81 09) No patients were registered on this protocol.

STATUS: (C)

TITLE: SWOG 7937 - Evaluation of m-AMSA in Metastatic Carcinoma of the GU Tract Except Renal Carcinoma, Phase II.

PRINCIPAL INVESTIGATOR: COL Freidrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin Dabe, MC
Suresh B. Katakkar, M.D., DAC

WORK UNIT NO: 80/31

TECHNICAL OBJECTIVES

To determine the antitumor activity of m-AMSA in patients with metastatic carcinoma of the genito-urinary tract as determined by response rate, duration of response, and survival, who have failed on higher priority treatment protocols; and to determine the nature and degree of toxicity of this drug.

METHOD

Patients with histologically confirmed incurable metastatic carcinoma as follows are eligible: renal pelvis transitional cell carcinoma, bladder transitional cell carcinoma; prostatic adenocarcinoma; all other malignancies (except renal) may be entered by specific cell-type and will be evaluated separately. Good risk patients will receive AMSA in a single dose of 120 mg/M^2 dissolved in 500 ml of D/W infused IV over no less than one hour every 21 days. Poor risks will receive 90 mg/M^2. If bilirubin is greater than 2 mg%, the initial dose will be 75 mg/M^2. An adequate trial is defined as two courses of therapy. Subsequent courses of AMSA are to be given only when there is full bone marrow recovery. Patients will remain on the protocol as long as they respond or until they experience intolerable toxicity.

PROGRESS

(80 02 - 81 09) No patients were registered on this protocol.

STATUS: (O)

TITLE: SWOG 7940/41/43 - Evaluation of 5-FU vs A Phase II Drug in Metastatic Adenocarcinoma of the Large Bowel, Phase II-III.

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
Suresh B. Katakkar, M.D., DAC

WORK UNIT NO: 80/65

TECHNICAL OBJECTIVES

To determine the relative activity of a Phase II Drug (MGBG or gallium nitrate) in previously untreated patients with disseminated colon and rectal cancer; to compare the survival of patients with disseminated colon cancer receiveing MGBG or gallium nitrate as first therapy to the survival of patients receiving a fluorinated pyrimidine, 5-FU therapy first; and to determine the effect of previously administered MGBG or gallium nitrate on the response rate seen with 5-FU in patients with disseminated colon and rectal cancer.

METHOD

Patients must have biopsy proven adenocarcinoma arising from the colon or rectum to be eligible. Patients will be randomized in to Arm I (chemotherapy with 5-FU) or Arm II (chemotherapy with either MGBG or gallium nitrate). Arm I will receive 5-FU by IV bolus injection days 1-5, repeated every four weeks. Arm II will receive either MGBG every week to be given as an IV infusion in D5W or NS over no less than 30 minutes into a freely running IV or gallium nitrate given as a 30 minute IV infusion in 200 ml of normal saline, repeated every two weeks. Upon response/relapse or disease progression, patients will be crossed-over to the opposite treatment arm providing they meet eligibility criteria.

PROGRESS

(80 07 - 81 09) No patients were registered on this protocol at MAMC. Terminated due to lack of patients group-wide.

STATUS: (T)

TITLE: SWOG-7940/44 - Evaluation of 5-FU vs a Phase II Drug in Metastatic Adenocarcinoma of the Large Bowel, Phase II, Utilizing Dihydroxyanthracenedione (DHAD) as the Phase II Drug

PRINCIPAL INVESTIGATOR: COL Friedrich P. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin D. Babe, MC
LTC Archie W. Brown, MC

WORK UNIT NO: 81/62

TECHNICAL OBJECTIVES

To determine the relative activity of a Phase II drug (DHAD) in previously untreated patients with disseminated colon and rectal cancer; to compare the survival of patients with disseminated colon cancer receiving a Phase II agent (DHAD) as first therapy to the survival of patients receiving a fluorinated pyrimidine, 5-FU therapy first; to determine the effect of a previously administered Phase II drug (DHAD) on the response rate seen with 5-FU in patients with disseminated colon and rectal cancer.

METHOD

This protocol is a continuation of the 79/40 series where the standard drug, 5-FU, is compared with new phase II drugs for metastatic adenocarcinoma of the large bowel not amenable to surgical extirpation. Patients with extensive adenocarcinoma of the colon or rectum who have clinically measurable disease and have had no previous chemotherapy are eligible for the study. These patients must meet other criteria as outlined in the protocol. Treatment consists of randomization between two arms: Arm I - 5-FU and Arm II - DHAD. Treatment is randomly assigned If there is relapse after a response or if there is no response a cross-over will take place. Patients receiving 5-FU first will then receive DHAD and vice versa. Treatment will continue on the respective agent for as long as the patient is responding to the current treatment (tumor remains stable or decreases in size). Treatment will be discontinued if the patient experiences intolerable side effects or refuses further treatment.

PROGRESS

(81 03 - 81 09) One patient has been registered. Disease was stable for three months and then there was progression. Patient is alive with disease two months post-treatment.

STATUS: (O)

TITLE: SWOG 7958 - Evaluation of m-AMSA in Metastatic or Recurrent Epithelial Carcinomas of the Female Genital Tract, Phase II.

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
Suresh B. Katakkar, M.D., DAC

WORK UNIT NO: 80/37

TECHNICAL OBJECTIVES

To determine the antitumor activity of AMSA in patients with metastatic or recurrent epithelial carcinomas of the ovary, endometrium, cervix, vagina, or vulva who have failed on higher priority treatment protocols; and to determine the nature and degree of toxicity of AMSA in patients treated by the split-course three-day schedule.

METHOD

Patients are eligible who have a histologically proven diagnosis of incurable advanced metastatic or recurrent epithelial carcinoma of the ovary, endometrium, cervix, vagina, or vulva. The patients will be divided into two treatment groups: good risk patients and poor risk patients. All patients will be treated by a split dose, 3-day schedule. Dose for good risk: 40 mg/M^2/day, IV, for three days. Dose for poor risk: 30 mg/M^2/day, IV, for three days. Total daily dose will be dissolved in 250-500 ml of D/W and given IV over one hour. Repeat courses of AMSA will be given at 21 day intervals. In the event that myelosuppression persists at day 21, biweekly WBC and platelet counts will be done and subsequent courses of AMSA will be given only when there is bone marrow recovery.

PROGRESS

(80 05 - 81 09) One patient has been registered on the protocol. After six months of therapy he at present has a good partial response.

STATUS: (O)

TITLE: SWOG 7959 - Evaluation of MGBG in Metastatic Renal Carcinoma

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin Dabe, MC
Suresh B. Katakkar, M.D., DAC

WORK UNIT NO: 80/38

TECHNICAL OBJECTIVES

To determine the response-rate and remission duration with weekly intravenous therapy using MGBG in patients with metastatic renal carcinoma; and to define the qualitative and quantitative toxicity of this regimen.

METHOD

Patients with a histologically proven diagnosis of incurable, advanced metastatic renal cell carcinoma will be eligible. MGBG will be given at a dose of 600 mg/m^2 as an IV infusion in D5W or NS over no less than 30 minutes into a freely running IV. The drug will be given on a weekly schedule providing the WBC is greater than $3,000/mm^3$ and the platelet count is greater than $100,000/mm^3$ (or have returned to baseline if the initial values are lower than this) and the patient has recovered from any encountered stomatitis, muscle weakness or drug induced pain. An adequate trial will consist of three courses of treatment.

PROGRESS

(80 07 - 81 09) No patients were registered on this study.

STATUS: (C)

TITLE: SWOG-7963 - Trial of m-AMSA in Myeloma Cancer, Phase II

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
MAJ Lauren K. Colman, MC

WORK UNIT NO: 81/82

TECHNICAL OBJECTIVES

To determine the efficacy of m-AMSA at a dose of 120 mg/M^2 IV every 3 weeks in producing regressions or remission in metastatic myeloma cancer, which is resistant to standard chemotherapy; to determine the effect of m-AMSA on survival of patients with metastatic myeloma cancer which is resistant to standard chemotherapy; to correlate in vitro m-AMSA sensitivities in the tumor stem cell colony drug system and in vivo m-AMSA activity in patients with metastatic myeloma cancer, which is resistant to standard chemotherapy.

METHOD

Patients with histologically confirmed multiple myeloma with measurable disease refractory to standard treatment are eligible for the study. Patients must meet other criteria as outlined in the protocol. Patients will be stratified as good risk or poor risk as well as those with abnormal liver function tests. Treatment consists of one arm only and will vary according to stratification and will be given every 3-4 weeks for as long as the disease remains stable or regresses and the patient tolerates the medications satisfactorily.

PROGRESS

(81 05 - 81 09) No patients were registered on this protocol at MAMC.

STATUS: (O)

TITLE: SWOG 7965 - Chemotherapy or Chemotherapy and Immunotherapy Following Initial Surgery and/or Radiotherapy for Treatment of Early Squamous Cell Cancer of the Head and Neck

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin Dabe, MC
Suresh B. Katakkar, M.D., DAC

WORK UNIT NO: 80/32

TECHNICAL OBJECTIVE

To determine if the disease-free interval and survival of patients in high risk categories of squamous head and neck cancer can be improved by adjuvant methotrexate after initial surgery, radiotherapy or both have resulted in no clinically evident disease.

METHOD

Patients with histologically confirmed squamous cell carcinoma of the head and neck who have been rendered clinically disease free by surgery or radiotherapy with the following stages and sites are eligible: Pharynx Stage I-IV (MO); supraglottic and glottic larynx Stage II and IV and subglottic larynx Stage I-IV (MO); oral cavity Stage II-IV (MO); and nasal cavity/paranasal sinus Stage I-IV (MO). These patients will be randomized to receive either no treatment or MTX at a dose of 12 mg/M^2 IM daily for 3 days every 21 days for one year or until relpase or inability to tolerate drug because of toxicity.

PROGRESS

(80 04 - 81 09) No patients were registered on this protocol.

STATUS: (O)

TITLE: SWOG 7980 - Study of Cis-Diammine Dichloroplatinum (DDP) for Recurrent Gliomas, Phase II.

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin Dabe, MC
Suresh B. Katakkar, M.D., DAC

WORK UNIT NO: 80/39

TECHNICAL OBJECTIVES

To determine the efficacy of the chemotherapeutic agent DDP in the treatment of gliomas recurrent after prior therapy with irradiation (plus or minus chemotherapy); and to determine the duration of response and survival of patients receiving this therapy.

METHOD

Patients with gliomas (Grade I-IV) who have recurred following cranial irradiation will be eligible. The starting dose for all patients will be 35 mg/M^2/day given IV on 3 consecutive days. The next course of chemotherapy will be initiated in 3-4 weeks as long as blood counts have recovered and the serum creatinine, BUN, and creatinine clearance measurements are satisfactory. A minimum of 2 courses of therapy will be considered an adequate trial to evaluate efficay and toxicity. A course is defined as a treatment plus a 3 week observation period.

PROGRESS

(80 07 - 81 09) No patients were registered on this study.

STATUS: (O)

TITLE: SWOG 7982 - Chlorozotocin in the Treatment of Advanced Sarcomas, Phase II.

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin Dabe, MC
Suresh B. Katakkar, M.D., MC

WORK UNIT NO: 80/40

TECHNICAL OBJECTIVES

To determine if chlorozotocin in a dose of 120 mg/M^2 has significant activity in sarcomas by determination of response rate and duration; and to describe toxicities of chlorozotocin not yet defined.

METHOD

Patients with a biopsy-proven diagnosis of soft-tissue or bone sarcoma are eligible for the study. Patients will begin treatment on chlorozotocin at 120 mg/M^2 IV bolus every six weeks. An adequate trial will consist of one course of treatment (6 weeks). Subsequent courses will be given in those patients achieving a tumor response or stable disease provided WBC and platelet counts are satisfactory.

PROGRESS

(80 05 - 81 09) No patients were entered on this study.

STATUS: (C)

TITLE: SWOG-7984 - The Treatment of Chronic Stage CML with Pulse, Intermittent Busulfan Therapy with or without Oral Vitamin-A, Phase III

PRINCIPAL INVESTIGATOR: LTC Irwin B. Dabe, MC

PROFESSIONAL ASSISTANTS: COL F. H. Stutz, MC
MAJ Lauren K. Colman, MC

WORK UNIT NO: 81/80

TECHNICAL OBJECTIVES

To determine the efficacy of standard pulse, intermittent busulfan therapy plus oral vitamin A in prolonging the chronic phase of CML, and hence in prolonging survival.

METHOD

Patients with a diagnosis of chronic stage CML for one year or less with no prior therapy are eligible. Patients will be stratified into those who had a splenectomy and those who did not. Randomization will be to busulfan alone or busulfan plus oral vitamin A. Stratification is also by age, <20 or >20 years. Treatment will continue for as long as the patient responds to the treatment and does not have unacceptable toxicity.

PROGRESS

(81 05 - 81 09) No patients were registered on this protocol at MAMC.

STATUS: (O)

TITLE: SWOG 7985 - Combined Modality Treatment for ER- Breast Cancer, Phase III

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
Surech B. Katakkar, M.D., DAC

WORK UNIT NO: 80/66

TECHNICAL OBJECTIVES

To compare disease-free interval and survival among control group Stage I (and Stage II node negative) breast cancer patients whose tumors are determined to be ER- at the time of mastectomy, versus Stage I (and Stage II node negative) ER- patients treated with adjuvant cyclophosphamide, methotrexate, 5-FU, and vincristine (CMFV)for 6 months; and to document recurrence patterns among untreated patients with Stage I breast cancer whose tumors are determined to be ER- at the time of mastectomy.

METHOD

Patients must have undergone a radical, modified radical or total mastectomy, or segmental mastectomy with axillary node dissection for potentially curable, histologically proven breast carcinoma, whose axillary nodes are negative for tumor and whose estrogen receptor assay on the primary tumor is less than 10 fetamoles/mg cytosol protein in order to be eligible for study (Stage I or II, node negative). Patients with bilateral malignancies are ineligible. Patients will be stratified by tumor size, type of mastectomy, and menopausal status. They will be randomized to Arm I to receive no fruther treatment until relapse or Arm II to receive combination chemotherapy with CMFV for 6 months on a 21 day cycle if WBC's and platelets are satisfactory. Patients who receive a segmental mastectomy must receive post-operative radiation therapy which satisfies the radiation therapy guidelines in this protocol. Chemotherapy must be started by 28 days post-segmental mastectomy even though the patient will still be receiving radiation therapy.

PROGRESS

(80 07 - 81 09) Patient registered and is in complete remission after 9 months.

STATUS: (O)

TITLE: SWOG 7990 - Intergroup Testicular Study

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin Dabe, MC
Suresh B. Katakkar, M.D., DAC

WORK UNIT NO: 80/33

TECHNICAL OBJECTIVES

(1) To compare the disease-free survival and overall survival for surgery alone (with chemotherapy for relapsers) vs surgery plus early adjuvant chemotherapy in patients with resectable Stage II testicular cancer. (2) To register and follow patients with non-seminoma, non-choriocarcinoma Stage I testicular cancer to define prognostic variables which may predict recurrence in this stage group. (3) To define the difference in disease-free rates and patterns of recurrence, based upon histologic subtypes and extent of disease on initial presentation. (4) To evaluate the role of marker substances such as HCG, alpha-fetoprotein, and lactic dehydrogenase in the early detection and management of recurrences in patients with Stage I and Stage II testicular carcinoma. (5) To evaluate the accuracy of lymphangiograms, CAT scans, and ultrasound studies for staging of retroperitoneal nodal involvement.

METHOD

Patients with histologically confirmed carcinoma (not pure seminoma or choriocarcinoma) of the testis Stage I (limited to testis and adjacent structures) or Stage II (extends beyond the testis but not beyond the regional draining lymph node region) who have had an orchiectomy will be eligible. Patients will undergo bipedal lymphangiogram with the intent of retroperitoneal node dissection. Serum markers may be obtained and studied prior to orchiectomy and must be obtained prior to lymphadenectomy and one and two weeks after. If at two weeks any marker is positive but falling, markers should be repeated at 3-4 weeks and the 4-week value must be normal or serial determinations must be declining with time at a rate predicted by the known serum half-life of the marker. Entry will be at 2-4 weeks postoperatively. Stage I patients will be followed routinely and tumor markers should be negative 4 weeks postop. Stage II unresectable patients are not eligible. Stage II resectable patients will be treated

in two treatment groups. Group I: no adjuvant chemotherapy with monthly followup until recurrence. Group II: adjuvant chemotherapy with vinblastine, bleomycin, and cis-platinum. Stages I and II who were originally randomized to the follow-up group and Stage II relapsing after chemotherapy will be further treated with vinblastine, bleomycin, and cis-platinum. Patients in complete or partial remission or showing improvement after relapse induction will receive maintenance treatment with vinblastine, repeated every 4 weeks until complete remissions have received 104 weeks of therapy and partial remissions and improvements may continue indefinitely. All other patients will go off study.

PROGRESS

(80 04 - 81 09) No patients were registered on this protocol.

STATUS: (O)

TITLE: SWOG 8003 - Evaluation of MGBG in Non-Oat Cell CA of the Lung Phase II

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
LTC Archie W. Brown, MC

WORK UNIT NO: 81/01

TECHNICAL OBJECTIVES

To determine the response-rate and remission duration with weekly intravenous therapy using MGBG in patients with non-oat cell carcinoma of the lung who have failed on higher priority treatment protocols and to define the qualitative and quantitative toxicity of this regimen.

METHOD

Patients with histologically proven, incurable, advanced metastatic, non-oat-cell carcinoma of the lung are eligible. Patients who have prior chemo- or radiotherapy are eligible provided 4 weeks have elapsed since therapy and the nadirs of leukopenia and thrombocytopenia are surpassed with evidence of hematologic recovery. Patients will be stratified by prior chemotherapy (yes or no). Patients will receive adequate pretreatment evaluations and follow-up. An initial dose of 600 mg/M^2 will be given as an IV infusion in D5W over no less than 30 minutes into a freely running IV line. The drug is to be given on a weekly schedule provided the WBC is $\geq$3000/mm^3 and platelets are $\geq$100,000/mm^3 and the patient has recovered from any encountered stomatitis. An adequate trial will consist of three courses of treatment.

PROGRESS

(80 10 - 81 09) No MAMC patients were registered on this protocol.

STATUS: (C)

TITLE: SWOG 8004 - Evaluation of DHAD in Soft Tissue and Bone Sarcomas Phase II

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
LTC Archie W. Brown, MC

WORK UNIT NO: 81/02

TECHNICAL OBJECTIVES

To determine the efficacy, by response-rate, of dihydroxyanthracenedione (DHAD) in patients with soft tissue and bone sarcomas who have failed on higher priority treatment protocols and to determine the nature and degree of toxicity of this drug used in a single dose every-three-week schedule.

METHOD

All patients with extensive, incurable soft tissue or bone sarcoma who have become resistant to standard chemotherapy will be treated with DHAD provided they have clearly measurable lesions. Other reasons for stopping the treatment are patient refusal and intolerable side effects. This will be a one-armed study in that all patients will receive the same treatment; 12 mg/M^2 IV infusion in 100 cc D5W over 30 minutes, repeated every 3 weeks. An adequate trial will consist of two 3-weeks courses of treatment. Duration of response will be measured from the achievement of response to the first sign of relapse.

PROGRESS

(80 10 - 81 09) No patients were entered into this protocol as MAMC.

STATUS: (C)

TITLE: SWOG-8005 - Evaluation of DHAD in Refractory Malignant Lymphomas, Phase II

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
LTC Archie W. Brown, MC

WORK UNIT NO: 81/63

TECHNICAL OBJECTIVES

To determine response rate and response duration of patients with refractory malignant lymphomas, both Hodgkin's disease and non-Hodgkin's lymphoma treated with anthracenedione used in a single dose every-three-week schedule; to define the qualitative and quantitative toxicities of anthracenedione administered in a Phase II study.

METHOD

All Patients with malignant lymphoma resistant to standard therapy, who have measurable disease, are eligible for this study. Patients must meet other criteria as outlined in the protocol. For patients who have received prior chemotherapy or radiotherapy, four weeks must have elapsed since the end of therapy and bone marrow recovery must be documented. Patients will be stratified by type of lymphoma and then treated with DHAD, initially 12 mg/M^2 infused in D5W over 30 minutes, in a one-armed trial without randomization. Patients will be treated for as long as the tumor responds or remains stable. Patients will be taken off study if intolerable side effects occur or the patient refuses further treatment.

PROGRESS

(81 03 - 81 09) No patients were registered on this protocol at MAMC.

STATUS: (O)

TITLE: SWOG-8008 - Evaluation of Dihydroxyanthracenedione (DHAD) in Refractory Breast Cancer, Phase II

PRINCIPAL INVESTIGATOR: CCL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
LTC Archie W. Brown, MC

WORK UNIT NO: 81/03

TECHNICAL OBJECTIVES

To determine the response-rate and remission duration of refractory breast cancer in patients treated with anthracenedione used in a single dose every-three-week schedule and to define the qualitative and quantitative toxicities of anthracenedione administered in a Phase II study.

METHOD

All patients with a histopathologically confirmed diagnosis of breast cancer who have measurable disease and whose disease has become refractory to standard chemotherapy will be treated with DHAD. These patients will also meet other criteria. Patients will receive 12 mg/M^2 (good risk) or 10 mg/M^2 (poor risk) in 100 cc D5W IV infusion over 30 minutes, repeated every 3 weeks. Treatment is continued for as long as the tumor is stable or regressing. Reasons for discontinuation of treatment include patients refusal and intolerable side effects.

PROGRESS

(80 10 - 81 09) No patients have been registered on this protocol at MAMC.

STATUS: (O)

TITLE: SWOG-8009 - Evaluation of Dihydroxyanthracenedione (DHAD) in Patients with Refractory Small Cell Lung Cancer, Phase II

PRINCIPAL INVESTIGATOR: CCL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
LTC Archie W. Brown, MC

WORK UNIT NO: 81/04

TECHNICAL OBJECTIVES

To determine the response-rate and remission duration of refractory small cell lung cancer in patients treated with anthracenedione used in a single dose every-three-week schedule and to define the qualitative and quantitative toxicities of anthracenedione administered in a Phase II study.

METHOD

All patients with histopathologically proven small cell carcinoma of the lung with measurable disease who have become refractory to standard chemotherapy will be treated for as long as the tumor remains unchanged or regresses. Reasons for discontinuation of chemotherapy are patient refusal and intolerable toxicity. This is a one-armed treatment; 12 mg/M^2 IV infusion in 100 cc D5W over 30 minutes, repeated every 3 weeks.

PROGRESS

(80 10 - 81 09) No patients have been registered on this protocol at MAMC.

STATUS: (O)

TITLE: SWOG-8010 - Evaluation of Dihydroxyanthracenedione (DHAD) in Advanced Prostate Cancer, Phase II.

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
LTC Archie W. Brown, MC

WORK UNIT NO: 81/05

TECHNICAL OBJECTIVES

To determine the response-rate and remission duration in patients with prostate cancer treated with dihydroxyanthracenedione used in a single dose every-three-week schedule and to define the qualitative and quantitative toxicities of dihydroxyanthracenedione administered in a Phase II study.

METHOD

All patients with pathologically verified histologic diagnosis of prostate cancer who have failed standard chemotherapy and have measurable disease will be treated with DHAD for as long as the tumor regresses or remains stable. If the tumor progresses, the patient refuses further treatment, or toxicities become untolerable, the patient will be removed from the protocol. Treatment will be 10 mg/M^2 IV infusion in 100 cc D5W (poor risk) or 12 mg/M^2 (good risk), repeated every 3 weeks. Patients will be stratified by prior chemotherapy.

PROGRESS

(81 10 - 81 09) No patients have been entered on this protocol at MAMC.

STATUS: (O)

TITLE: SWCG-8011 - Evaluation of Dihydroxyanthracenedione (DHAD) in Patients with Advanced Renal Cell Carcinoma, Phase II

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
LTC Archie W. Brown, MC

WORK UNIT NO: 81/06

TECHNICAL OBJECTIVES

To determine the response-rate and duration of response in patients with advanced renal cell carcinoma treated with dihydroxyanthracenedione used in a single dose every-three-week schedule and to define the qualitative and quantitative toxicities of dihydroxyanthracenedione administered in a Phase II study.

METHOD

All patients with advanced renal cell carcinoma with clearly measurable lesions will be given DHAD for as long as the tumor remains stable or regresses. DHAD will be continued for as long as the patient accepts treatment and has no intolerable side effects. Treatment will be given as a 12 mg/M^2 IV infusion in 100 cc D5W over 30 minutes, repeated every 3 weeks.

PROGRESS

(80 10 - 81 04) No patients were entered on the protocol at MAMC.

STATUS: (C)

TITLE: SWOG 8012 - Treatment for Advanced Adenocarcinoma and Large Cell Carcinoma of the Lung: FOMi vs. CAP vs. FOMi/CAP, Phase III

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
LTC Archie W. Brown, MC

WORK UNIT NO: 81/21

TECHNICAL OBJECTIVES

To evaluate by pairwise comparison the response-rate, duration of response, and survival of three regimes, FOMi, CAP, and FOMi/CAP, in patients with advanced (TMN Stage III M_1) adenocarcinoma and large cell undifferentiated carcinoma of the lung; to evaluate the degree of non-cross resistance of FOMi in CAP failures and of CAP on FOMi failures; to compare the toxicities and side effects of FOMi and CAP.

METHOD

Patients with histologically confirmed diagnosis of adenocarcinoma of the lung or large cell undifferentiated carcinoma of the lung will be eligible for this protocol. Alveolar cell carcinoma patients will also be eligible but will be treated under the FOMi arm only. Patients with metastatic disease (TNM Stage III M_1) are eligible. This excludes patients who have metastases only to ipsilateral hilar nodes (N_1) and/or mediastinal nodes (N_2). Patients whose disease can be encompassed within a single radiation port are not eligible. Prior chemotherpy patients are ineligible, however prior radiation therapy is acceptable as long as the patient has measurable disease outside the radiation field. Patients with brain metastases are eligible and can receive concomitant radiation to the brain. Patients will be stratified prior to randomization by cell type, performance status, presence or absence of bone metastasis. Randomization is to Arm I (FOMi) and Arm 2 (CAP) and an alternating regimen (Arm 3) utilizing FOMi and CAP as described in the protocol. If the patients on Arm 3 (alternating FOMi/CAP) relapse on FOMi, CAP will be continued and FOMi discontinued. If there is a relapse on CAP, FOMi will be continued as a single arm. Patients will be treated for as long as the disease remains stable or regresses. Other reasons for discontinuation of the protocol are patient refusal or intolerable side effects.

PROGRESS

(80 12 - 81 09) Three patients treated. (1) received one dose, expired one month later with progression of disease (subadequate trial). (2) Received treatment for 3 months before progression of

disease and death three months after progression recommenced.
(3) Patients treated for 2 months with no change before progression began.

STATUS: (O)

TITLE: SWOG-8015 - Evaluation of Two Combination Chemotherapy Programs, Adriamycin and Cis-Platinum (AP) versus Adriamycin, Cis-Platinum plus VP 16-213 (VAP), in the Treatment of Extensive Squamous Cell Carcinoma of the Lung, Phase III.

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
LTC Archie W. Brown, MC

WORK UNIT NO: 81/22

TECHNICAL OBJECTIVES

To determine the activity, in terms of response-rate, remission duration, and survival in patients with extensive squamous cell (epidermoid) carcinoma of the lung, for two combination chemotherapy programs; Adriamycin and Cis-platinum (AP) versus VP 16-213, Adriamycin and Cis-platinum (VAP); to evaluate the relative toxicities of these respective regimens; to assess the feasibility and reliance of applying "measurable versus evaluable" criteria of tumor regression in determing therapeutical response; to correlate tumor grade with response and survival.

METHOD

Patients with extensive squamous cell (epidermoid) lung cancer which has spread beyond the hemithorax and ipsilateral scalene, supraclavicular and mediastinal lymph nodes, equivalent with TNM Stage III class M_1 or with any T or N other than mediastinal, supraclavicular scalene node involvement, or patients with evidence of disease beyond the confines of a single radiation therapy port are eligible for the treatment. Patients who have initially be treated with radiation but have failed and have a measurable lesion are eligible as well. Patients with prior chemo or immunotherapy are not eligible. Patients must have pathologic proof of squamous cell carcinoma of the lung and a measurable lesion. Patient must meet other criteria as well as outlined in the protocol. Patients will be stratified to good risk and poor risk patients. They will be randomized to treatment with adriamycin/platinum or VP 16/adriamycin/platinum and followed on treatment for as long as disease remains stable or regresses on treatment. Reasons for removal from the protocol are patient refusal and intolerable side effects.

PROGRESS

(80 12 - 81 09) No patients from MAMC have been entered on the protocol.

(STATUS: (O)

TITLE: SWOG-8020 - Adriamycin + VP-16 vs Adriamycin Alone in Advanced Adenocarcinoma of the Breast, Phase II.

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
LTC Archie W. Brown, MC

WORK UNIT NO: 81/23

TECHNICAL OBJECTIVES

To determine the efficacy of the Adriamycin and VP-16 combination in the treatment of previously treated patients with disseminated breast cancer, as determined by response-rate, compared with Adriamycin alone; and to determine the length of the remission on VP-16 maintenance after an Adriamycin/VP-16 regimen.

METHOD

Patients with histologically proven breast cancer, stage 4, with measurable lesions who have previously become resistant to CMFVP will be eligible. They will be stratified by ER receptor status, ER positive, ER negative, or ER unknown. Patients with current congestive heart failure or prior adriamycin treatment are not eligible. Prior radiation, hormonal, or chemotherapy may be permitted; however, four weeks must have elapsed since prior hormonal therapy and two weeks since radiation or chemotherapy was administered. Patients must have recovered from previous treatment toxicities with evidence of hematologic recovery. These will be stratified into good and poor risk patients and randomized between adriamycin plus VP 16 (Arm 1) and adriamycin alone (Arm 2). Treatment will be given for as long as the disease remains stable or regresses and for as long as the patient tolerates the chemotherapy.

PROGRESS

(80 12 - 81 09) Two patients treated:

1. Partial response for two months with death one month after relapse.
2. Patient refused treatment after one dose and expired three months later.

STATUS: (O)

TITLE: SWOG-8025 - Combination Chemotherapy for Chronic Lymphocytic Leukemia, Phase II

PRINCIPAL INVESTIGATOR: LTC Irwin B. Dabe, MC

PROFESSIONAL ASSISTANTS: COL F. H. Stutz, MC
MAJ Lauren K. Colman, MC

WORK UNIT NO: 81/81

TECHNICAL OBJECTIVES

To determine the response rate and duration of remission in patients with CLL treated with combination chemotherapy consisting of prednisone, vincristine, cytosine arabinoside, Cytoxan, and adriamycin. To be eligible for treatment, patients must have evidence of marrow failure (Rai Stage 3 or 4) or rapidly progressive disease; to correlate parameters obtained in the clinical, pathological, and immunological staging with response to treatment; to determine the effect of stopping chemotherapy after patients have achieved a complete remission plus 2 consolidation courses, in order to define a cured or stabilized fraction of patients.

METHOD

Patients with chronic lymphocytic leukemia fulfilling the criteria as outlined by the Rai classification of CLL (all stages) are eligible for this protocol. Patients who have been treated previously with a single alkylating agent are eligible but will be analyzed separately. Patients may not have received prior adriamycin or Ara-C, however; patients previously treated with radiation therapy alone are eligible, and these patients will also be analyzed separately. The protocol consists of Arm I which is applicable to Rai Classification, stages 1 and 2,which is registration only (no treatment) with careful documention of the progression of the disease; and Arm II, Ria Classification 3-4, consisting of chemotherapy with a combination of prednisone, Oncovin, Ara-C, cyclophosphamide, and hydroxyduanorubicin (adriamycin). Treatment will continue for as long as the patient responds on Arm II. Patients on Arm I at the time of progression to stage 3 or 4 will be eligible for treatment on the same combination chemothearpy regimen. Patients will be followed indefinitely or until death.

PROGRESS

(81 05 - 81 09) No patients were registered on this protocol at MAMC.

STATUS: (O)

TITLE: SWOG-8027 - The Natural History of Pathological Stage T_{1-2} N_0 M_0 ER+ Breast Cancer, Phase III

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe
LTC Archie W. Brown, MC

WORK UNIT NO: 81/64

TECHNICAL OBJECTIVES

To document recurrence rates, patterns of recurrence, and survival among patients with Stage I or Stage II node negative (T_{1-2} N_0 M_0) breast cancer whose tumors are determined to be estrogen receptor positive at the time of surgery.

METHOD

Patients having undergone radical, modified radical, or adequate local excision with node dissection for histologically proven breast carcinoma whose axillary nodes are negative for tumor and whose estrogen receptor status is positivie are eligible. Patients undergoing local adequate exicision with axillary node sampling as primary treatment must receive radiation therapy beginning 14-20 days post-operatively as outlined in the protocol. Only patients with pathologic Stage T_{1-2} N_0M_0 with a primary tumor of $\leq$5 cm are eligible. The primary tumor must be movable in relationship to the anterior chest wall and may not be involved with extensive skin ulcerations. This protocol involves no randomization or treatment. It consists only of follow-up and documentation of natural history. Patients will be stratified by primary tumor size, <2 cm vs 2 to 5 cm, and by menopausal status. Patients will be followed until relapse or for 10 years, whichever comes sooner.

PROGRESS

(81 03 - 81 09) Four patients have been registered. One patient has been followed for five months and three patients have been followed for one month.

STATUS: (O)

TITLE: SWOG-8028 - Evaluation of DHAD in Gynecologic Cancers, Phase II

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Roger B. Lee, MC
LTC Irwin B. Dabe, MC

WORK UNIT NO: 81/65

TECHNICAL OBJECTIVES

To determine the response rate and remission duration in patients with gynecologic tumors treated with DHAD used in a single dose every-three-week schedule; to define the qualitative and quantitative toxicities of DHAD as administered in this Phase II study.

METHOD

Patients with a histologically confirmed diagnosis of epithelial ovarian, endometrial, or squamous cervical carcinoma with extensive disease and measurable lesions are eligible. Patients must meet other criteria as outlined in the protocol. Patients wtih congestive heart failure or previous adriamycin treatment are not eligible. These patients will be stratified by good risk and poor risk as defined in the protocol and treated on a one-armed study with DHAD with some variation of the dose depending on whether the patient is good risk or poor risk. Treatment will continue for as long as the tumor remains stable or decreases in size. Treatment will be discontinued for patient refusal of further treatment or intolerable side effects.

PROGRESS

(81 03 - 81 09) One patient registered; received one dose only with progression of disease and death two months after registration.

STATUS: (C)

TITLE: SWOG-8030 - Evaluation of DHAD in Advanced Squamous Cell Carcinoma of the Head and Neck, Phase II.

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
LTC Archie W. Brown, MC

WORK UNIT NO: 81/46

TECHNICAL OBJECTIVES

To determine the response-rate and remission duration in patients with advanced squamous cell carcinoma of the head and neck treated with DHAD used in a single dose every-three-week schedule; to define further the qualitative and quantitative toxicities of DHAD.

METHOD

Patients with histologically confirmed diagnosis of squamous cell carcinoma of the neck or adenoid cystic carcinoma of the head and neck with measurable disease are eligible if they have become resistant to standard chemotherapy. Only patients with advanced disease not ammenable to surgery or radiation are eligible. All patients must have measurable disease and have recovered from toxicities of previous therapies. Patients will be stratified according to prior chemotherapy or no prior chemotherapy and then will be treated with DHAD without randomization (12 mg/M^2 IV infusion in 100 cc D5W over 30 minutes, repeated every three weeks). Treatment will continue for as long as the tumor remains stable or shrinks. Treatment will be discontinued if the tumor progresses, if intolerable side effects occur, or if the patient refuses further treatment.

PROGRESS

(81 02 - 81 09) No patients at MAMC were registered on this protocol.

STATUS: (O)

TITLE: SWOG-8031 - Evaluation of DHAD in Refractory Multiple Myeloma, Phase II

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
MAJ Lauren K. Colman, MC

WORK UNIT NO: 81/83

TECHNICAL OBJECTIVES

To determine the response rate and response duration of patients with refractory multiple myeloma treated with dihydroxyanthracenedione (DHAD) used in a single does every-three-week schedule; to define the qualitative and quantitative toxicities of DHAD administered in a Phase II study.

METHOD

Patients with multiple myeloma refractory to standard treatment or protocols of higher priority are eligible for this protocol. Patients must have clearly measurable myeloma protein levels to be eligible. These patients must also meet other criteria as outlined in the protocol. Stratification will be done according to response to prior treatment and prior treatment with adriamycin. Initial dose is 9 mg/M^2 given as an IV infusion in 100 cc of D5W over 30 minutes and repeated every 3 weeks. Treatment continues for as long as tumor remains stable or is improving. Patient refusal of further treatment and intolerable toxicity will cause discontinuation of the patient on the protocol.

PROGRESS

(81 05 - 81 09) No patients were registered on this protocol at MAMC.

STATUS: (O)

TITLE: SWOG-8032 - Evaluation of DHAD in Acute Leukemia, Phase II

PRINCIPAL INVESTIGATOR: LTC Irwin B. Dabe, MC

PROFESSIONAL ASSISTANTS: COL Friedrich H. Stutz, MC
LTC Archie W. Brown, MC

WORK UNIT NO: 81/47

TECHNICAL OBJECTIVES

To determine the efficacy of dihydroxyanthracenedione (DHAD) in patients with adult acute leukemia, who have failed on higher priority treatment protocols, as determined by response-rate and remission duration; to determine the nature and degree of toxicity of this drug used in a single-dose every-three-week schedule.

METHOD

Patients with a bone marrow diagnosis of acute leukemia in relapse after standard treatment or treatment with SWOG studies of higher priority are eligible. Careful monitoring of cardiac status is required, and patients who had prior adriamycin exceeding 400 mg/M^2 are ineligible. This is a one-armed study without randomization and patients will receive DHAD 14 mg/M^2 every three weeks for as long as the patient does not have progression and tolerates the treatment.

PROGRESS

(81 02 - 81 09) No patients were registered on this protocol at MAMC.

STATUS: (O)

TITLE: SWOG-8038 - Vinblastine in Advanced Ovarian Cancer, Phase II

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin R. Dabe, MC
LTC Roger B. Lee, MC

WORK UNIT NO: 81/72

TECHNICAL OBJECTIVES

To determine the response rate and remission duration with intravenous therapy using Velban as a continuous infusion in patients with advanced ovarian cancer; to define further the qualitative and quantitative toxicity of the continuous infusion of Velban.

METHOD

This is a Phase II study using vinblastine infusion. Patients with extensive epithelial ovarian tumors with measurable disease are eligible. Patients must meet other criteria as outlined in the protocol. The Velban will be administered as a continuous 5-day infusion once every three weeks. This will be continued as long as the tumor remains stable or shrinks. Treatment will be discontinued for patient refusal of further treatment or intolerable toxicity. Patients will be stratified according to bilirubin, SGOT and alkaline phosphotase status.

PROGRESS

(81 04 - 81 09) No patients have been registered on this protocol at MAMC.

STATUS: (O)

TITLE: SWOG-8040 - Evaluation of Combination Chemotherapy (FAM-S) vs. a Phase II Drug in Pancreatic Adenocarcinoma, Phase II

PRINCIPAL INVESTIGATOR: CCL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
MAJ Lauren K. Colman, MC

WORK UNIT NO: 81/84

TECHNICAL OBJECTIVES

To determine the response rate and survival in patients with advanced pancreatic adenocarcinoma treated with 5-FU, Adriamycin, Mitomycin-C, and Streptozotocin (FAM-S); to determine further the toxicity of the FAM-S regimen; to determine the activity of a Phase II drug in previously untreated patients with advanced adenocarcinoma of the pancreas by determination of response rate and duration of response and survival; to determine further the toxicity of each Phase II agent.

METHOD

Patients with histologically confirmed adenocarcinoma of the exocrine pancreas with distant metastasis (liver, peritoneum) and those with localized disease not amenable to curative surgery or radiotherapy are eligible. All patients must have objectively measurable disease and have not received any prior chemotherapy or radiation therapy. Patients must also meet other criteria as outlined in the protocol. Patients will be stratified according to biopsy only performed vs palliative bypass procedures and performance status. Subsequently, the patients will be randomized to either a combination chemotherapy regimen consisting of 5-FU, adriamycin, mitomycin, and streptozotocin or a Phase II agent which will be changed periodically when sufficient patients are accumulated on one arm. If the patient fails or has a response and subsequently has increasing disease, a cross-over is recommended. Patients on FAM-S will cross over to the Phase II agent and vice versa. Chemotherapy will continue for as long as the disease remains stable or the tumor is shrinking. Progressive disease, patient refusal of further treatment, or intolerable side effects are criteria for discontinuation of the protocol.

PROGRESS

(81 05 - 81 09) No patients were registered on this protocol at MAMC.

STATUS: (O)

TITLE: SWOG-8042 - Evaluation of MGBG in Pancreatic Adenocarcinoma, Phase II

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
MAJ Lauren K. Colman

WORK UNIT NO. 81/85

TECHNICAL OBJECTIVES

To determine the response rate and its duration in patients with advanced adenocarcinoma of the pancreas treated with MGBG; to determine the qualitative and quantitative toxicities of MGBG when given on this schedule.

METHOD

This protocol is an adjunct to SWOG 8040. In this protocol, MGBG is the Phase II agent set forth in the master protocol; therefore the methods of the protocol will be the same as for SWOG 80/40.

PROGRESS

(81 05 - 81 09) No patients have been registered on this protocol at MAMC.

STATUS: (O)

TITLE: SWOG-8043, Evaluation of DHAD in Pancreatic Adenocarcinoma, Phase II

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
MAJ Lauren K. Colman, MC

WORK UNIT NO: 81/86

TECHNICAL OBJECTIVES

To determine the antitumor activity of DHAD, as determined by response rate and duration of response, used in a single dose schedule every three weeks in patients with advanced adenocarcinoma of the pancreas; to determine additional information concerning the nature and degree of toxicity of this drug.

METHOD

This protocol is an adjunct to SWOG 8040. In this protocol, MGBG is the Phase II Agent set forth in the master protocol; therefore, the methods of the protocol will be the same as for SWOG 80/40.

PROGRESS

(81 05 - 81 09) No patients have been registered on this protocol at MAMC.

STATUS: (O)

TITLE: SWOG-8092 - Use of Human Tumor Cloning System to Select Chemotherapy for Patients with Ovarian Cancer Refractory to Primary Therapy

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Iriwn B. Dabe, MC
LTC Roger B. Iee, MC

WORK UNIT NO: 81/87

TECHNICAL OBJECTIVES

To utilize the human tumor cloning assay to select single agent chemotherapy for patients with epithelial-type ovarian cancer, refractory to standard therapy; to determine if the human tumor cloning system can be utilized to select the therapy of individual patients in a cooperative group setting.

METHOD

Patients with a pathologic diagnosis of epithelial-type ovarian cancer in pleural or peritoneal fluid or with solid tumor are eligible to have specimens sent to tumor cloning laboratories . These specimens will be cultured and incubated with antineoplastic agents to determine their sensitivity to these chemotherapeutic agents. In ovarian cancer resistant to standard tretment, treatment recommendations will be made. All these patients should have measureable disease. Other tumor specimens will be tested; however, no treatment recommendations will be made in these instances, especially when the patient was previously untreated with chemotherapy. This is an ancillary study and involves treatment only in patients with epithelial type ovarian cancer. This treatment continues for as long as the patient responds, tolerates the treatment, and continues to accept the investigational treatment.

PROGRESS

(81 05 - 81 09) Two patients have been registered on this protocol. Neither of the two specimens grew in culture.

STATUS: (O)

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

TITLE: GOG #20: A Randomized Comparison of Adriamycin Versus No Further Therapy in Patients with Uterine Sarcomas, Stage I & II (Phase III Study)

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 81/100

TECHNICAL OBJECTIVES

To determine if adjuvant chemotherapy will improve the cure rate in uterine sarcoma Stages I & II.

METHOD

Patients with histologically proven sarcomas of the uterine corpus with no known gross residual disease following surgery will be eligible. Patients who are not medically operable and who receive only radiotherapy are ineligible. Patients who have not had radiotherapy and who are randomized to no chemothearpy will have radiotherapy at that point unless recurrent disease occurs. Patients with impaired hepatic function will be eligible but if randomized to adriamycin will receive a dose reduction. Patients with prior radiotherapy will receive adriamycin once every three for eight cycles, to be started one to four weeks postoperatively or post-radiation therapy. They will then be followed every 3 months for 2 years, every 6 months for 3 more years, and yearly up to 10 years from entry. Those with no prior radiotherapy will receive no treatment, but will be assessed every 6 weeks for 6 months. After that, they will be assessed every 3 months for 2 years, every 6 months for an additional 3 years, and then yearly up to 10 years from entry.

PROGRESS

(81 07 - 81 09) No patients have been registered on this protocol at MAMC.

Group wide there were 120 entries of which 81 were evaluable. The 81 entries fall into 4 cell type categories, early and advanced disease categories, and 4 modes of therapy. Such numerous classifications of patients do not presently permit a meaningful analysis of any sub-category.

The treatment portion of this protocol is completed and all subjects are in follow-up; therefore the protocol is considered completed.

STATUS: (C)

TITLE: GOG #24: Treatment of Women with Cervical Cancer Stages IIB, IIIB, and IVA Confined to the Pelvis and/or Para-aortic Nodes with Radiotherapy versus Radiotherapy plus Immunotherapy (Intravenous C-parvum), Phase III

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 81/11

TECHNICAL OBJECTIVES

To assess the therapeutic effectiveness of immunotherapy (intravenous C-parvum) used concomitantly with radiation in patients with advanced carcinoma of uterine cervix.

METHOD

Patients with primary, previously untreated histologically confirmed invasive carcinoma of the uterine cervix, clinically Stage II-B, Stage III-B, or Stage IV-A (confined to the pelvis or para-aortic nodes) will be eligible. Clinical Stage I-B patients found at surgery to have disease extending to the pelvic sidewall will also be eligible. The following types of histologically confirmed cervical malignancy are eligible: squamous carcinoma, mixed squamous and adenocarcinoma, adenocarcinoma, and adenosquamous carcinoma. Patients previously treated with pelvic irradiation will be ineligible. Patients will undergo pelvic examination under anesthesia followed immediately by exploratory laparotomy. Patients will be stratified by stage of disease and status of para-aortic nodes and randomly assinged to receive one of the following treatment regimens. Regimen I - radiotherapy alone to begin no sooner than two weeks and no longer than 6 weeks following surgery for a maximum of 10 weeks with quarterly follow-up for 3 years and 6 months thereafter. Regimen II: radiotherapy for a maximum of 10 weeks plus C. parvum every 2 weeks during radiotherapy, then every 4 weeks for 1 year total from start. Follow-up same as for Regimen I.

PROGRESS

(80 11 - 81 09) No entries at MAMC.

Group-wide, preliminary results show no difference between the two arms.

This protocol has been replaced by GOG #52.

STATUS: (C)

TITLE: GOG #25: A Randomized Comparison of Melphalan Alone Versus Melphalan Therapy Plus Immunotherapy (Corynebacterium parvum) in the Treatment of Women with Stage III (Optimal) Epithelial Carcinoma of the Ovary (Phase III)

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 81/34

TECHNICAL OBJECTIVES

To evaluate the relative effectiveness of melphalan or melphalan plus immunotherapy (Corynebacterium parvum) as adjunctive therapy to at least laparatomy and debulking of as much tumor as is prudent, and total abdominal hysterectomy, bilateral salpingoophorectomy and omentectomy, when technically feasible, in Stage III optimal epithelial tumors of the ovary in a randomized prospective study. Optimal is defined as residual tumor mass no greater than 3 cm at surgery.

METHOD

Patients who have undergone laparotomy in optimal category 3 with proven primary Stage III epithelial cancer of the ovary who have undergone tumor-reductive surgery will be included in this study. Patients with prior chemotherapy or pelvic/abdominal irradiation will be ineligible. Patients will be randomized no later than 8 weeks after surgery. Regimen A: melphalan alone, 7 mg/M^2/day x 5 days, PO every 4 weeks. After three courses responders continue for 10 courses or 18 months whichever comes first and non-responders go off study. Follow-up will be quarterly for 2 years. Regimen B: Melphalan as above plus C. parvum, 4 mg/M^2 IV day 7 following chemotherapy. Responders continue chemotherapy for 10 courses or 18 months whichever comes first. Follow-up every 6 months for 3 years. Non-responders will go off study.

PROGRESS

(81 01 - 81 09) No entries at MAMC.

Group-wide there have been 202 evaluable cases. There is no significant difference when the duration of progression-free interval and survival are compared by therapy.

STATUS: (C)

TITLE: GOG #26-L: A Phase II Trial of Tamoxifen in Patients with Advanced Endometrial Adenocarcinoma

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 81/66

TECHNICAL OBJECTIVES

To determine the efficacy of Tamoxifen in patients whose advanced malignancies have been resistant to higher priority methods of treatments in a Phase II study.

METHOD

Eligible patients are those who have histologically confirmed advanced recurrent persistent metastatic or local endometrial carcinoma with documented disease progression. Patients will receive tamoxifen 10 mg PO b.i.d for a minimum of 8 weeks or until progression or adverse effects prohibit further therapy. Patients with stable disease after 8 weeks will receive 20 mg PO b.i.d. Patients with a response after 8 weeks will continue therapy at 10 mg PO b.i.d until progression of disease or adverse effects prohibit further therapy. If a tumor flare is suspected instead of progression, treatment will be continued for a total of 8 weeks and the patient reevaluated at that time.

PROGRESS

(81 03 - 81 09) No entries at MAMC.

Group-wide there have been 13 entries. The pathology review is pending. No analysis is avaible.

STATUS: (O)

TITLE: GOG #31: A Randomized Comparison of Local Excision Versus Cryosurgery in Patients with Limited Grade 1, 2 or 3 Cervical Intraepithelial Neoplasia

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 81/07

TECHNICAL OBJECTIVES

To evaluate and compare the immediate and long-term effectiveness of outpatient cryotherapy and outpatient local excision in the treatment of limited cervical epithelial neoplasia (CIN), grades 1, 2 and 3 in a randomized prospective study.

METHOD

To be eligible, patients must have a tissue diagnosis of cervical intraepithelial neoplasia. The lesions must be completely delineated through the culposcope and must involve only one quadrant of the portio. Only patients with histologic diagnosis with CIN 1 (mild dysplasia), CIN 2 (moderate dysplasia), and CIN 3 (severe dysplasia, carcinoma in situ) will be eligible. Patients will be randomly assigned by GOG headquarters to be treated with either cryosurgery or surgical excision. Details of each treatment can be found in the protocol. Treatments will be done on an outpatient basis. Follow-up will be at 4 and 8 months post-therapy, semiannually for the remainder of the first 2 years, and than annually for the next 3 years.

PROGRESS

((80 10 - 81 09) This protocol has been terminated by the Gynecology Oncology Group because of poor follow-up (more than 50% of patients have been lost to follow-up).

Seven patients were entered at MAMC. At last follow-up all had no evidence of disease.

STATUS: (T)

TITLE: GOG #32: A Randomized Comparison of Surgical Conization Versus Cryosurgery in Patients with Extensive Grade 3 Cervical Intraepithelial Neoplasia (CIN) Phase 3.

PRINCIPAL INVESTIGATOR: LTC Roger E. Lee, MC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 81/08

TECHNICAL OBJECTIVES

To evaluate and compare the immediate and long-term effectiveness of outpatient cervical cryosurgery to standard cone-knife conization in the treatment of extensive cervical intraepithelial neoplasia (CIN), Grade 3, in a randomized prospective study.

METHOD

To be eligible, patients must have a tissue diagnosis of cervical intraepithelial neoplasia and a histologic diagnosis of severe dysplasia or carcinoma *in sutu*. Patients must have lesion(s) which can be completely delineated through the colposcope which involve at least two quadrants of the portio with at least one quadrant diagnosed as CIN 3. Ectocervical distribution will be delineated by Lugol's staining. At least 3 directed biopsies will be taken and the endocervical curettage must be negative for CIN and invasive carcinoma. Patients previously treated for cervical intraepithelial neoplasia or who have had pelvic irradiation will be ineligible. Patients will be randomized to have outpatient cryosurgery or inpatient surgical conization as outlined in the protocol. Principal parameters employed to examine the relative therapeutic effect of the regimens will be: the duration of the progression-free interval; observed survival for all evaluable patients; and the incidence and severity of adverse effects of cyrosurgery and standard surgical management.

PROGRESS

(80 10 - 81 09) One patient was entered at MAMC.

This protocol has been cancelled by GOG due to the high number of patients lost to follow-up.

STATUS: (T)

TITLE: GOG #33: A Clinical Pathologic Study of Stages I and II Carcinoma of the Endometrium

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 81/12

TECHNICAL 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 these node metastases to other important prognostic factors. These findings will then be used as a guide for treatment protocols.

METHOD

These 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-oopherectomy, selective pelvic and para-aortic lymphadenectomy, and peritoneal cytology sampling are eligible. The following histologic types of endometrial carcinoma are acceptable: adenocarcinoma, adenocarcinoma with squamous metaplasia, adenoacanthoma, and adenosquamous carcinoma. Patients who have received preoperative radiotherapy are ineligible. Pathologic evaluation will include:

a. peritoneal washing will be evaluated for malignant cells
b. the uterus will be evaluated in regard to location of tumor, depth of myometrial invasion, differentiation of tumor, size of uterus.
c. The adnexae will be evaluated for presence of metastasis.
d. The lymph nodes (total number indicated) will be evaluated as to metastasis and location and number of lymph nodes involved.

After surgery, all patients will be entered into the appropriate protocol or receive appropriate treatment if no protocol is available.

PROGRESS

(80 11 - 81 09) Three MAMC patients have been entered all with no evidence of disease at this time.

Group-wide, 585 cases have been evaluable to date. Five percent have metastasis to pelvic lymph nodes and 4% to para-aortic lymph nodes; 2% have spread to the ovaries.

STATUS: (O)

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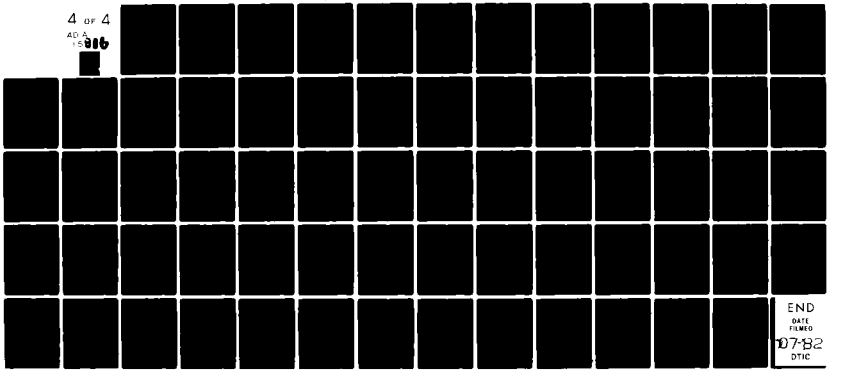

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TITLE: GOG #34: A Randomized Study of Adriamycin as an Adjuvant After Surgery and Radiation Therapy in Patients with High-Risk Endometrial Carcinoma Stage I and Occult Stage II

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 81/24

TECHNICAL OBJECTIVES

To study differences in morbidity and patient survival as functions of various tumor growth patterns as well as treatment in the high risk Stage I and, optionally, high risk Stage II occult endometrial carcinoma.

METHOD

Patients with primary, previously untreated, histologically confirmed invasive carcinoma of the endometrium, Stage I or II occult, all grades, with one or more of the following high risk criteria are eligible: (1) all lesions with equal to or greater than 1/2 myometrial involvement; (2) positive pelvic and/or para-aortic nodes; (3) microscopic evidence of cervical involvement but no gross clinical involvement of the cervix; (4) adnexal metastasis. Surgery will be followed in 2-6 weeks by "tailored" radiation therapy, pelvic and/or para-aortic, depending on node positivity. Prior to the initiation of radiation, therapy patients will be randomized to no further therapy or to adriamycin beginning 2-4 weeks after radiation therapy.

PROGRESS

(80 12 - 81 09) No entries at MAMC.

Group-wide there have been 74 evaluable cases. Ten cases (16%) have had recurrences and 7 cases (11%) have died. No other data available at this time.

STATUS: (O)

TITLE: GOG #36: Surgical-Pathologic Study of Women with Squamous Cell Carcinoma of the Vulva

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 81/67

TECHNICAL OBJECTIVES

To determine by observations of 5-year survival and disease-free interval the validity of current FIGO staging to the histopathologic prognostic factors of size of lesion, location of lesion, depth of invasion of tumor in millimeters, histologic grade, and site and number of positive lymph nodes in Stage I-IV carcinoma of the vulva; to rapidly accumulate prospectively significant surgical pathologic data which would expedite development of further protocols for sub-sets of disease identified; to determine morbidity of primary radical surgical therapy.

METHOD

Eligible patients are those with primary, previously untreated histologically confirmed invasive squamous cell carcinoma of the vulva clinically determined to be Stage I through IV. Patients will be treated with radical vulvectomy plus bilateral groin dissection. The patients will undergo a thorough pelvic examination under anesthesia to assess pelvic structures and evaluate possible pelvic node disease. Those with negative groin nodes will be followed for 5 years without therapy. Those with positive groin nodes will be transferred to GOG #37. Relevant pathologic specimens will be studied.

PROGRESS

(81 03 - 81 09) No entries at MAMC.

Group-wide there have been 322 entries of which 175 were evaluable. There have been 23 recurrences (13.1%), site: 9 vulva, 4 groin, 2 pelvis, 8 distant. Also, there were 27 deaths (15.4%), cause: 2 therapy, 16 disease, and 9 other.

STATUS: (O)

TITLE: GOG #37: A Randomized Study of Radiation Therapy Versus Pelvic Node Resection for Patients with Invasive Squamous Cell Carcinoma of the Vulva Having Positive Groin Nodes

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 81/68

TECHNICAL OBJECTIVES

To determine the benefit and morbidity of adding adjunctive radiation therapy to pelvis and groin for patients found to have positive groin nodes at the time of radical vulvectomy and bilateral groin dissection.

METHOD

Eligible patients are those with primary previously untreated histologically confirmed invasive squamous cell carcinoma of the vulva, such that radical vulvectomy suffices to remove all of the local lesion, and whose surgery revealed that there were nodes in the groin on one or both sides containing metastatic carcinoma. Patients will be randomized to receive pelvic node dissection (the dissection will be carried out only on the side containing postivie groin nodes or a bilateral if both sides are positive) or to receive bilateral groin and pelvic node irradiation. Major parameters to be studied are survival and time to recurrence. Patients will be followed quarterly for 3 years and every 6 months thereafter.

PROGRESS

(81 03 - 81 09) No entries at MAMC.

Group-wide there have been 48 entries of which 23 were evaluable. There have been 43.5% recurrences, 43.5% deaths to this point.

STATUS: (O)

TITLE: GOG #40: A Clinical-Pathologic Study of Stage I and II Uterine Sarcomas

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 81/79

TECHNICAL OBJECTIVES

The purpose of this study is to determine the incidence of pelvic and aortic lymph node metastases associated with Stage 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.

METHOD

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 pre-operative 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 ot 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:
   (1) location of involved lymph nodes and (2) number involved.

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

(81 05 - 81 09) There has been one entry at MAMC who is currently alive with no evidence of disease.

Group-wide there have been 96 patient entries of which 40 were evaluable. It is too early for any analysis.

STATUS: (O)

TITLE: GOG #41: Surgical Staging of Ovarian Carcinoma

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 81/35

TECHNICAL OBJECTIVES

To determine the spread of ovarian carcinoma to intraperitoneal structures and retroperitoneal lymph nodes by direct examination, cytologic sampling, and biopsy; to establish a surgical protocol for patients entered into GOG ovarian cancer treatment protocols; to determine the complication rate of the procedures.

METHOD

There will be no change in the surgical procedures performed. This protocol is being performed as a statistical protocol. These will be patients who have surgery as standard treatment. Eligible patients will be those who have Stages I, II, or III (optimal) ovarian carcinoma. Patients undergoing total abdominal hysterectomy, bilateral or unilateral salpingo-oophorectomy, bivalving of the other ovary, selective pelvic and para-aortic lymphadenectomy, omental biopsy, or peritoneal cytology sampling will be studied. They will not be given any preoperative treatment, but will be subjected to a complete and thorough evaluation before surgery. All patients will be explored and the steps for surgery will be as standard surgery dictates. Specific observations will be made as to the findings. If fluid is not present, washings will be taken from the inside of the abdomen to study cells. A thorough examination of all structures from the diaphragm to the pelvic floor will be carried out. After surgical staging, patients will be transferred to the appropriate treatment protocol or further treatment will be at the discretion of the investigator if no protocol is available.

PROGRESS

(81 01 - 81 09) Seven patients have been entered at MAMC; all with no evidence of disease at present.

Group-wide, there have been 97 entries and 44 evaluable cases. Data at present are insufficient to permit analysis.

STATUS: (O)

TITLE: GOG #42: Treatment of Recurrent or Advanced Uterine Sarcoma - A Randomized Comparison of Adriamycin Versus Adriamycin and Cyclophosphamide, Phase III

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, LTC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 81/69

TECHNICAL OBJECTIVES

To determine if Adriamycin alone is more effective than Adriamycin and cyclophosphamide in producing responses in advanced or recurrent uterine sarcoma; and to determine the duration of response for each different treatment arm.

METHOD

Patients with primary Stage III or Stage IV or recurrent uterine sarcoma are eligible. Patients with primary Stage III disease must have undergone exploratory laparotomy. Patients with measurable or non-measurable disease will be eligible, but they will be analyzed separately. Patients previously treated with radiotherapy to the pelvic bed are eligible provided the radiation was completed more than 3 months before entry. Patients with prior chemotherapy are ineligible. Patients will be stratified by performance status and radiation thearpy. They will be radnomized to one of two regimens. Regimen 1: adriamycin, 60 mg/M^2 IV q 3 weeks for a total dosage of 480 mg/M^2. Regimen 2: adriamycin, 60 mg/M^2, IV q 3 weeks plus cyclophosphamide 500 mg/M^2 IV q 3 weeks. Both medications will be discontinued when a total dosage of adriamycin of 480 mg/M^2 is received. Patients with progressive disease at any time will be withdrawn from the study. Patients who respond or have disease stability will remain on study until the maximum cumulative dose has been reached or until adverse effects prohibit further therapy.

PROGRESS

(81 03 - 81 09) No entries at MAMC.

Group-wide there were 111 entries of which 67 were evaluable. The most common cell type was homologous mesodermal sarcoma (40.3%); 33 cases have measurable disease. To date, there have been 1 complete response, 5 partial responses, 9 progressions, and 18 with stable disease. 24 of the 67 (35.8%) have died and 43 (64.2%) have had recurrences. There have been no statistical differences in the 2 arms of the study to this time.

STATUS: (O)

TITLE: GOG #43: A Randomized Comparison of Cis-Platinum 50 Mg/M^2 in Every Three Weeks vs Cis-Platinum 100 Mg/M^2 in Every Three Weeks vs Cis-Platinum 20 Mg/M^2 IV Daily X 5 Days Every Three Weeks in the Treatment of Patients with Advanced Carcinoma of the Cervix (Phase III)

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 81/09

TECHNICAL OBJECTIVES

To confirm the effectiveness of Cis-Platinum in advanced recurrent squamous cell carcinoma of the cervix no longer responding to radiation therapy or surgery; to compare the frequency and duration of response and adverse effects of Cis-Platinum therapy using three different doses and treatment schedules; to evaluate the role of serial determination of serum carcinoembryonic antigen (CEA) levels in determining extent of disease and response to treatment, and in predicting treatment failure.

METHOD

Patients who have histologically confirmed locally advanced, recurrent, persistent, or metastatic squamous cell carcinoma of the cervix which is resistant to curative treatment with surgery or radiotherapy are eligible Patients with previous chemotherapy are ineligible. Patients must have lesions that are measurable. Patients will be randomized to one of the following three regimens. Regimen I: cis-platinum 50 mg/M^2 IV q 3 weeks for 8 courses with follow-up every 4 weeks. Patients who progress before 8 cycles will be switched to Regimen II. After 8 cycles, when progression occurs patients will be retreated with Regimen I until progression. Patients receiving retreatment with low-dose platinum will be escalated to 100 mg/M^2 if no regression occurs after 2 cycles or if progression is noted at any point. Regimen II: cis-platinum 100 mg/M^2 IV q 3 weeks for 4 courses and follow-up every 4 weeks. If progression occurs after 4 courses, retreatment with Regimen II until progression. Regimen III: cis-platinum 20 mg/M^2 IV x 5 q 3 weeks x 4 courses with follow-up every 4 weeks. If progression after 4 courses, retreatment with Regimen III until progression.

PROGRESS

(80 10 - 81 09) Two patients have been entered at MAMC. Both have died from disease.

Group-wide: Regimen III has been terminated since there has been no significant difference from the single dose of 100 mg/M^2. Other regimens are on-going.

STATUS: (O)

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

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 81/25

TECHNICAL OBJECTIVES

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-fetoprotein 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.

METHOD

Patients with histologically confirmed malignant germ cell tumors of the ovary, Stages 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

(80 12 - 81 09) No entries at MAMC.

Group-wide there have been 31 evaluable cases; eight have failed therapy. It is too early for any conslucions to be drawn.

STATUS: (O)

TITLE: GOG #47: A Phase III Randomized Study of Adriamycin Plus Cyclophosphamide versus Adriamycin Plus Cyclophosphamide Plus Cis-Platinum in Patients with Advanced Ovarian Adenocarcinoma-Suboptimal Stage III, Stage IV and Recurrent

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 81/10

TECHNICAL OBJECTIVES

To determine if the addition of Cis-Platinum to Adriamycin plus Cyclophosphamide improves remission rate, remission duration or survival in Stage IV, Suboptimal Stage III and recurrent ovarian adenocarcinoma.

METHOD

Eligible patients are those having Stage IV and suboptimal Stage III primary cases together with all recurrent cases. Suboptimal Stage III: patients with a residual lesion $\geq$3 cm in the largest diameter at the time of surgery. Both patients with measurable disease and without measurable disease are eligible. Entry to study will be no more than 6 weeks post operative. Patients with previous radio- or chemothearpy are ineligible. Patients will be randomized to one of two regimens. Regimen I: adriamycin plus cyclophosphamide every 3 weeks for 8 courses and then second look. Complete responders at second look will receive cyclophosphamide maintenance for an additional 12 months. Patients with partial response or stable disease will have second look only if the investigators feel that significant tumor reduction may be achieved. Patients with progressive disease any time will be removed from further chemotherapy, but will continue to be followed. Regimen II: adriamycin and cyclophosphamide as in Regimen I plus cis-platinum given on the same schedule. Second-look proceudres the same as in Regimen I.

PROGRESS

(80 10 - 81 09) No entries at MAMC.

Group-wide: preliminary results show that the response rate is better with triple thearpy. Five-year survival rate is pending.

No patients are on the therapy portion and this protocol is considered to be completed.

STATUS: (C)

TITLE: GOG Protocol #48: A Study of Progestin Therapy and a Randomized Comparison of Adriamycin vs Adriamycin Plus Cyclophosphamide in Patients with Advanced Endometrial Carcinoma After Hormonal Failure (Phase III Study)

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 81/43

TECHNICAL OBJECTIVES

To evaluate the response of advanced or recurrent endometrial carcinoma to oral progestins in patients who have received no prior hormonal therapy for cancer; and to compare a combination of adriamycin and cyclophosphasmide to adriamycin alone as therapy for advanced or recurrent endometrial carcinoma which no longer responds to or has failed to respond to progestins in patients who have received no prior cytotoxic drugs.

METHOD

Patients with documented primary Stage III, Primary Stage IV, recurrent or residual endometrial adenocarcinoma, *adenoacanthoma, or adenosquamous* carcinoma, whose potential for cure by radiation therapy or surgery alone or in combination is very poor, are eligible for this study. Patients who have received previous chemotherapy are ineligible. Patients will be randomized. Regimen 1: adriamycin 60 mg/M^2 IV q 3 weeks x 8 courses. Responders will have follow-up only. Those with progression will be transferred to Protocol #26. Regimen 2: adriamycin 60 mg/M^2 IV q 3 weeks x 8 courses plus cyclophosphamide 500 mg/M^2 IV q 3 weeks x 8 courses. Responders will receive follow-up only. Those with progression will be transferred to Protocol #26. Those patients with no prior hormonal therapy will be placed on C.T. Provera for a minimum of 12 weeks. Those with progression of disease at any time after 12 weeks will be randomized as above.

PROGRESS

(81 02 - 81 09) Two patients, both with disease but alive, have been entered on the protocol at MAMC.

Group-wide there have been 91 entries with 52 evaluable cases. Of the 40 cases with measurable disease, 9 have been complete or partial responses, and 19 have been stable disease. 47 patients out of 128 (36.7%) have failed to progestin thearpy.

STATUS: (O)

TITLE: GOG #49: A Surgical-Pathologic Study of Women with Invasive Carcinoma of the Cervix Stage IB and Randomly Assigned Radiation Therapy Versus No Further Therapy in Selected Patients, Phase III

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 81/70

TECHNICAL OBJECTIVES

To determine by observations of the 5-year survival and disease-free interval, the validity of current FIGO staging to the histopathologic prognostic factors of size of lesion, location of lesion, depth of invasion of tumor in millimeters, histology and grade, growth pattern, and site and number of positive lymph nodes in Stage IB carcinoma of the cervix; to rapidly accumulate prospectively significant surgical pathologic data which would expedite development of further protocols; to determine morbidity of primary radical surgical therapy; to determine if radiation therapy will improve survival in selected patients with positive nodes.

METHOD

Patients with primary, previously untreated histologically confirmed invasive Stage IB (invasion of 3 mm or greater of lymphatic invasion) carcinoma of the cervix (squamous cell, adenocarcinoma, or adenosquamous) will be eligible. Patients must have undergone exploratory laparotomy, peritoneal fluid sampling, bilateral pelvic and para-aortic lymphadenectomy and radical hysterectomy to be eligible for the randomized portion of the study. Those with negative pelvic nodes will receive no further therapy and be followed for 5 years. Those with positive pelvic nodes, unilateral metastasis, 3 or fewer positive pelvic nodes, no parametrial involvement, and clear vaginal margins will be randomized to receive no further therapy (follow-up for 5 years) or whole pelvic radiation with follow-up of 5 years. Those with positive para-aortic nodes on paraffin section will be entered on other GOG protocols as appropriate.

PROGRESS

(81 03 - 81 09) No patients entered at MAMC.

Group-wide there were 16 entries, but insufficient therapy has taken place for any analysis.

STATUS: (O)

TITLE: GOG #50: A Study of Adriamycin as Postoperative Therapy for Ovarian Sarcoma, Primary or Recurrent, With no Prior Chemotherapy

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 81/71

TECHNICAL OBJECTIVES

To evaluate the efficacy of adriamycin in the treatment of primary ovarian sarcomas, primary or recurrent, through historic controls; and to accumulate additional surgical-pathological data relative to ovarian sarcomas.

METHOD

Patients must have histologically confirmed primary Stage I-IV or recurrent ovarian sarcoma. Cases without histologic confirmation of recurrence must be documented by submission of original slides. Optimal reductive surgery is required for cases with advanced disease, whether primary or recurrent. Patients may have measurable disease, non-measurable disease, or no residual disease postoperatively. The endometrium must be examined to exclude an endometrial origin of the tumor. Patients with prior chemotherapy are ineligible. All patients will receive chemotherapy as soon as the acute effects of surgery have resolved. After completion of a total cumulative dose of 550 mg/M^2, pateints with clinically complete responses or detectable disease which is thought to be resectable will undergo second look surgery. Those patients with progression will be entered on Protocol #26. At second look those wiht NED will have no further therapy and follow-up for 5 years; those with stable disease or progression will be entered on Protocol #26.

PROGRESS

(81 03 - 81 09) No patients were entered at MAMC.

Group-wide there were 9 entries, but insufficient time has elapsed for analysis.

STATUS: (O)

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

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 81/105

TECHNICAL OBJECTIVES

To determine, in "optimal" Stage III ovarian adenocarcinoma, if the addition of adriamycin to cyclophosphamide plus cis-platinum (Platinol) improves progression-free interval, frequency of negative second-look laparotomy and survival. This protocol replaces GOG #25.

METHOD

Eligible patients are those 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. Patient must be more than 6 weeks post-operative. Patients with prior chemo- or radiotherapy are ineligible. Patients will be randomized to cyclophosphamide plus Plantinol every three weeks for eight courses or to cyclophosphamide and Plantinol plus adriamycin every three weeks for eight courses. After eight courses those with less than clinical complete response will go off study and be followed for survival; those with clinical 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 5 years for survival rates.

PROGRESS

(81 08 - 81 09) No patients have been entered at MAMC.

Group-wide six patients have been entered. It is too early for any analysis.

STATUS: (O)

TITLE: GOG #53: A Randomized Double-Blind Clinical Trial Evaluating Cholestyramine Prophylaxis for Radiation-Induced Diarrhea, Phase II

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANTS: COL William L. Benson, MC
COL Donald Kull, MC

WORK UNIT NO: 81/115

TECHNICAL OBJECTIVES

To assess the effectiveness of cholestyramine in a randomized double-blind study in which radiotherapy plus cholestyramine will be compared with radiotherapy plus placebo.

METHOD

Patients with histologically confirmed gynecologic malignancies who undergo standard whole pelvis irradiation for at least four weeks will be randomized to receive either irradiation plus cholestyramine daily during irradiation plus 2 weeks following irradiation; or irradiation plus a placebo. The major parameter of response will be daily stool frequency for both groups. Weekly weight will also be monitored as well as radiotherapy morbidity post-treatment. Patients who have been previously treated with pelvic irradiation or who are receiving chemotherapy or immunotherapy will be ineligible. Pregnant patients or those with severe pre-existing constipation will be ineligible.

PROGRESS

(81 09 - 81 09) No MAMC patients have been registered on this protocol.

STATUS: (O)

TITLE: GOG #54: The Treatment of Women with Malignant Tumors of the Ovarian Stroma with Combination Vincristine, Dactinomycin, and Cyclophosphamide--Phase III; and a Phase II Evaluation of Adriamycin in Malignant Tumors of the Ovarian Stroma Refractory to Primary Chemotherapy

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee MC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 81/116

TECHNICAL OBJECTIVES

To evaluate the effectivensss of combined vincristine, dactinomycin, and cyclophosphamide (VAC) in treatment of malignant tumors of the ovarian stroma in patients with residual, recurrent or advanced disease; to confirm completeness of response to VAC treatment with restaging laparotomy; to evaluate response to adriamycin in patients who fail primary treatment with VAC; to evaluate the endometrium histologically to learn more about the relationship between stromal tumors and endometrial cancer.

METHOD

To be eligible, patients must have histologically confirmed malignant tumors of the ovarian stroma (granulosa cell tumor, granulosatheca cell tumor, Sertoli-Leydig cell tumor, androblastoma, gynandroblastoma, unclassified sex cord-stromal tumor, sex cord tumor with annular tubules) not amenable to cure by further surgery or radiation therapy. Patients who have received chemotherapy at any time or those who have received radiotherapy less than four weeks prior to entry are ineligible for study. Patients admitted to this study will have undergone an exploratory laparotomy with removal of as much tumor as is prudent. Chemotherapy will be followed within four weeks and not later than six weeks following surgery. Patient must have recovered from surgery. All patients will receive VAC for a minimum of three cycles or a maximum of ten cycles. Patients who exhibit a complete response or a partial response after ten cycles which makes remaining disease resectable will undergo a restaging laparotomy. If all residual disease is resected at restaging laparotomy, patients will receive adriamycin. If there is no evidence of disease at restaging laparotomy, patients will receive intermittent cyclophosphamide. If progression is observed during cyclophosphamide therapy, she will be removed from study. Patients who exhibit progression of disease after three cycles of VAC will receive adriamycin. If further progression is observed on adriamycin therapy, the patient will be removed from the study. All patients will be followed for five years or until death.

PROGRESS

(81 09 - 81 09) No MAMC patients were registered on this protocol.

STATUS: (O)

TITLE: GOG #55: Hormonal Contraception and Trophoblastic Sequelae After Hydatidiform Mole, Phase III

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 81/44

TECHNICAL OBJECTIVES

To determine whether the administration of estrogen progestrone oral contraceptives following the evacuation of a hydatidiform mole and prior to the HCG titer reaching undetectable levels affects the incidence of trophoblastic sequelae requiring chemotherapy.

METHOD

Patients with a histologically verified diangosis of hydatidiform mole evacuated at the principal investigator's institution by suction evacuation of the uterus with uterine conservation are eligible. All patients must have a pelvic ultrasound and arterial blood gases performed within 2 weeks of evacuation. Patients will be randomly assigned to Regimen 1: hormonal contraception - oral contraception to be commenced as soon as the patient has been randomized and will continue for at least 12 weeks; or Regimen 2: mechanical contraception - a. sheath and foam preparation; b. IUD inserted once the uterus has become involuted, again used with foam, c. diaphragm used with contraceptive cream or foam. The principal investigator will choose the method of mechanical contraception and it will be commenced as soon as the patient has been randomized and will continue for at least 12 weeks. At the end of 12 weeks, all patients will be evaluated for development or nondevelopment of trophoblastic sequelae. Further birth control will be at the discretion of the patient and the investigator. All patients will remain on the study for a minimum of six months after primary evacuation of the molar pregnancy.

PROGRESS

(81 02 - 81 09) Two patients have been entered on this protocol, both at MAMC. No conclusions can be made at this point.

STATUS: (O)

TITLE: GOG #59: A Randomized Comparison of Extended Field Radiation Therapy and Hydroxyurea Followed by Cisplatin or no Further Therapy in Patients with Cervical Squamous Cell Carcinoma Metastatic to High Common Iliac and/or Para-aortic Lymph Nodes--III

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANTS: COL William L. Benson, MC
COL Donald Kull, MC

WORK UNIT NO: 81/117

TECHNICAL OBJECTIVES

To determine if cis-diamminedichlorplatinum, cisplatin, given in an adjuvant setting will decrease the risk of geographic failure or improve the survival rate or progression-free interval in patients who have squamous carcinoma of the cervix with metastases to high common iliac and/or para-aortic lymph nodes, proven by either histologic or cytologic means; to evaluate the role of scalene fat pad biopsy in this group of patients before initiation of extended field irradiation therapy; to accumulate clinical/surgical pathologic data on this high-risk group of patients to expedite development of further protocols.

METHOD

Eligibility: All patients with primary, previously untreated, histologically confirmed, invasive squamous cell carcinoma of the uterine cervix, all clinical stages, with metastasis to high common iliac or para-aortic lymph nodes proven by cytologic or histologic means. Patients will undergo preoperative clinical staging (stages defined in protocol) utilizing lymphangiography, computerized axial tomography, and/or sonography as well as traditional methods. Subsequently, the patients will undergo a para-aortic lymphadenectomy and peritoneal exploration. Selected patients may be excluded from this procedure if percutaneous needle biopsy provides cytologic proof of metastasis to extra-pelvic nodes. All patients with para-arotic metastasis and negative scalene node biopsies are eligible for treatment. They will receive pelvic and para-aortic irradiation and hydroxyurea, and will be randomly assigned to receive cisplatin or no further therapy. An adequate trial will be defined as completion of the prescribed radiation therapy, completion of one course of cisplatin and survival of four weeks, or survival of eight weeks after radiation therapy for the no-further-treatment regimen. Patients will be followed quarterly for two years and every six months for three additional years.

PROGRESS

(81 09 - 81 09) No MAMC patients have been registered on this protocol.

STATUS: (O)

TITLE: GOG #60: A Phase III Randomized Study of Doxorubicin Plus Cyclophosphamide Plus Cisplatin versus Doxorubicin Plus Cyclophosphamide Plus Cisplatin Plus BCG in Patients with Advanced Suboptimal Ovarian Adenocarcinoma, Stage III and IV.

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 81/118

TECHNICAL OBJECTIVES

To determine if the addition of BCG to doxorubicin plus cyclophosphamide plus cisplatin improves remission rate, remission duration, or survival in suboptimal Stage III and IV ovarian adenocarcinoma; to determine the frequency and duration of true complete remission using these regimens as judged at second-look laparotomy.

METHOD

Eligibility: Patients with established suboptimal Stage III and Stage IV ovarian epithelial cancer. All patients must have optimal surgery for ovarian cancer, with at least an exploratory laparotomy and appropriate tissue for histologic evaluation. Patients with measurable or nonmeasurable disease will be evaluated. Patients with histologically confirmed serous adenocarcinoma, mucinous adenocarcinoma, clear-cell adenocarcinoma, endometrioid adenocarcinoma, undifferentiated carcinoma, or mixed epithelial carcinoma will be eligible. Patients who have received previous chemotherapy or radiotherapy will be ineligible. Patients will be randomized to receive either doxorubicin, cyclophosphamide, and cisplatin every 3 weeks for 8 courses; or the above regimen plus BCG (days 8 & 15 for 8 courses). Patients with complete response will have a second look laparotomy and taken off therapy if complete response if confirmed. Patients who have partial response of stable disease will be considered for a second look if, in the opinion of the investigator, significant tumor reduction may have been achieved. If resideal tumor is detected, patients will be taken off study and placed on GOG protocol #61. Patients with progressive disease at any time will be removed from the chemotherapy on this study, but will be followed.

PROGRESS

(81 09 - 81 09) No patients at MAMC have been registered on this protocol.

STATUS: (O)

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

TITLE: CCG 052 - Evaluation of Diglycoaldehyde for Previously Treated Children with Acute Leukemia (Phase II)

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: MAJ Alan D. Mease, MC

WORK UNIT NO: 79/29

TECHNICAL OBJECTIVE

To determine the therapeutic efficacy of diglycoaldehyde in acute leukemia and solid tumors of childhood.

METHOD

Patients with histologic proof of acute leukemia, with a life expectancy of at least 12 weeks, who are resistant to current standard methods of therapy are eligible for this study. Diglycoaldehyde, 1.5 gm/M^2/day x 5, I.V. over 4-6 hours, will be given every 14 days. An adequate trial will consist of a minimum of two courses. Patients with complete remission at day 28 or with complete or partial remission at day 56 will receive maintenance therapy with diglycoaldehyde, 1.5 mg/M^2/day x 5, IV, every 28 days.

PROGRESS

(80 06 - 81 09) No patients were registered on this study.

STATUS: (C)

TITLE: CCG 053 - 4'Demethyl-Epiposophyllotoxin-B-D-Ethylidene Glucoside (VP 16-213) (NSC-141540) for the Treatment of Refractory Childhood Acute Myelomonocytic, Myelocytic, Monocytic or Histiocytic Leukemias and Refractory Hodgkin's Disease and Non-Hodgkin's Lymphomas

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: MAJ Alan D. Mease, MC

WORK UNIT NO: 79/30

TECHNICAL OBJECTIVES

(1) To determine the therapeutic efficacy of VP 16-213 in refractory childhood acute myelogenous, acute monocytic and acute monomyelocytic leukemia as well as in refractory patients with lymphomas or Hodgkin's disease. (2) To determine if the specificity of response in acute myelomonocytic, monocytic, and myelocytic leukemia and non-Hodgkin's lymphomas in childhood is similar to that reported in adult patients. (3) To determine if there is any response in a variety of refractory solid tumors in childhood.

METHOD

Patients with histologic proof of acute monocytic, myelomonocytic, myelocytic, histiocytic, or erythrocytic leukemia, with a life expectancy of at least 8 weeks, who are resistant to standard therapy and who have had no prior exposure to this agent are eligible for the study. Patients will receive VP-16, 100 $mg/M^2/d$ x 5 on days 1-5; 100 mg/M^2 x 5 on days 15-20; and 125 $mg/M^2/d$ x 5 on days 29-33. At this point those patients with no response, progressive disease, or excessive toxicity will be taken off the study. Patients with complete or partial resmission or stable disease will receive maintenance therapy of VP-16 100 $mg/M^2/d$ x 2 (on consecutive days) every 14 days.

PROGRESS

(80 06 - 81 09) No patients have been registered on this protocol.

STATUS: (C)

TITLE: CCG 054 - 4'Demethyl-Epipodophyllotoxin-B-D-Thenylidene Glucoside (VM-26) for the Treatment of Refractory Childhood Malignancies, Phase II.

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: MAJ Alan D. Mease MC

WORK UNIT NO: 79/31

TECHNICAL OBJECTIVES

(1) To determine if weekly high-dose VM-26 is active in pediatric malignancies. (2) Specifically, to investigate the effectiveness of weekly VM-26 in primary or metastatic brain neoplasms, Hodgkin's disease, non-Hodgkin's lymphoma, neuroblastoma, Wilms' tumor and the sarcomas. (3) To determine if weekly VM-26 dosage can in certain instances be augmented above 130 mg/M^2 and to correlate clinical toxicity with renal and hepatic dysfunction.

METHOD

All children with any malignant disease refractory to conventional therapy will be eligible. Emphasis will be placed on trials in primary or metastatic brain tumors, all lymphomas, Wilms' tumor, neuroblastoma, and the sarcomas. Patients in hematologic relapse with acute leukemia are eligible but will not be encouraged. Patients with acute non-lymphocytic leukemia or the histiocytic types of lymphoma will be treated with VP-16-213 first. Patients will receive 130 mg/M^2/wk x 3, then 150 mg/M^2/wk x 3. Each patient will receive at least six weeks of therapy. If the disease is progressive after six weeks, VM-26 will be discontinued. On day 42 the dosage will be increased to 180 mg/M^2/wk for 3 weeks. If the patient is responding at the end of this period, the same dosage will be continued. Non-responders will be taken off the study.

PROGRESS

(80 06 - 81 09) No patients have been registered on this study.

STATUS: (C)

TITLE: CCG 061 - Evaluation of Dianhydrogalactitol for the Treatment of Refractory Childhood Malignancies

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: MAJ Alan D. Mease, MC

WORK UNIT NO: 79/23

TECHNICAL OBJECTIVE

To determine the therapeutic efficacy of dianhydrogalactitol in acute leukemia and solid tumors of childhood.

METHOD

All patients with acute leukemia or with histologic proof of malignant solid tumor resistant to standard methods of therapy who have had no prior exposure to dianhydrogalactitol, will be eligible for this study. An adequate trial will consist of a minimum of two courses of treatment. Dose schedule for acute leukemia is 50 mg/M^2/day dianhydrogalactitol x 5, IV push or fast drip every 14 days. Dose schedule for solid tumor will be 37.5 mg/M^2/day x 5 IV push or fast drip every 14 days. If in those with acute leukemia, M_1 is observed by day 28 or day 56 or M_2 is observed by day 56, the patient will continue on 50 mg/M^2/d x 5, IV every 28 days. If, in those patients with solid tumor, complete remission is observed at day 28 or day 56 or partial remission is observed at day 56, the patient will then receive 50 mg/M^2/day x 5, IV, every 28 days.

PROGRESS

(79 10 - 81 09) No patients were registered on this protocol at MAMC.

STATUS: (C)

TITLE: CCG 071 - Evaluation of Cis-Platinum Diamine Dichloride (CPDD) for Previously Treated Children with Solid Tumors, Phase II.

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: MAJ Alan D. Mease, MC

WORK UNIT NO: 79/33

TECHNICAL OBJECTIVES

To define the toxic and therapeutic effect of CPDD at 3 mg/kg administered with aggressive hydration and diuresis for various advanced pediatric solid tumors.

METHOD

Patients with any solid tumor will be eligible. Patients will be hospitalized. All patients, except osteogenic sarcomas, will have 3 mg/kg CPDD administered every three weeks. Osteogenic sarcoma patients will have 4.5 mg/kg every three weeks. If no response is obtained after three doses, the primary physician may elect t escalate the dose to 4.5 mg/kg every three weeks or remove the patient from the study.

PROGRESS

(80 06 - 81 09) No patients have been registered on this study.

STATUS: (O)

TITLE: CCG 072 - Evaluation of Vindesine for Previously Treated Children with Acute Non-Lymphocytic Leukemia and Solid Tumors, Phase II

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: MAJ Alan D. Mease, MC

WORK UNIT NO: 79/24

TECHNICAL OBJECTIVE

To determine the efficacy of Vindesine in acute non-lymphocytic and myelogenous leukemia and solid tumors of childhood in a Phase II study.

METHOD

Only patients with histologic proof of acute non-lymphocytic leukemia who are resistant to standard modalities of therapy are eligible for this study. Patients should have a life expectancy of at least 12 weeks and must have an M-3 marrow. Patients with histologic proof of malignancy who are resistant to standard modalities of therapy will be eligible for solid tumors. An adequate trial should be considered a minimum of three complete injections. Vindesine will be continued as long as there is objective or subjective response. The dosage for this study is 4 mg/M^2 IV as a bolus every week.

PROGRESS

(79 09 - 80 09) One patient was registered on this protocol. There was minimal toxicity and a partial response for two months before relapse and death from disease.

(80 09 - 81 09) No patients were entered on the protocol at MAMC.

STATUS: (C)

TITLE: CCG 075 - Evaluation of Azapicyl in the Treatment of Children with Rhabdomyosarcoma and Undifferentiated Sarcoma Resistant to Conventional Therapy, Phase II

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: MAJ Alan D. Mease, MC

WORK UNIT NO: 79/34

TECHNICAL OBJECTIVE

To determine the therapeutic effect of azapicyl in rhabdomyosarcoma and undifferentiated sarcoma which have become resistant to conventional therapy.

METHOD

Only patients with rhabdomyosarcoma or undifferentiated sarcoma (recurrent or metastatic tumor unresponsive to conventional therapy) are eligible for this study. The initial durg dose will be 350 mg/M^2/day in two divided doses orally. This dose will be continued for two weeks. If no response has begun to occur at two weeks, the dose will be increased to 400 mg/M^2/day for two weeks. If any tumor regression is apparent at four weeks, but regression is not complete, the dose will be increased to 450 mg/M^2/day for two weeks. If complete regression is present at 2, 4, or 6 weeks, the drug dose that the patient is on when complete remission occurs will be maintained until disease is recurrent or toxicity intervenes.

PROGRESS

(80 06 - 81 09) No patients were registered on this study.

STATUS: (C)

TITLE: CCG 081 - Evaluation of β-Deoxythioguanosine (β-TGdR) for the Treatment of Refractory Leukemias of Children

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: MAJ Alan D. Mease, MC

WORK UNIT NO: 79/25

TECHNICAL OBJECTIVE

To determine the effectiveness of β-TGdR in the acute leukemias of childhood that are resistant to standard methods of treatment.

METHOD

Patients with acute leukemia who are resistant to current standard methods of therapy including all non-investigational drugs effective in leukemia and having an M_3 marrow and who have had no prior exposure to β-TGdR will be eligible for the study. β-TGdR will be given at a dose of 1,750 mg/M^2/dose every 12 hour, repeated three times, which will constitute one course. The drug will be infused with 5% dextrose solution over a four hour period. Each course will be given every two weeks unless modified by toxicity. An adequate trial shall consist of three courses of β-TGdR. Those patients with M_1 on day 14, 28, or 42 or M_2 on day 42 will receive a maintenance dose of 1,750 mg/M^2/dose every 12 hours, repeated three times, every three weeks.

PROGRESS

(79 10 - 81 09) No patients were registered on this study

STATUS: (C)

TITLE: CCG 083 - Evaluation of Prednimustine in Refractory Acute Leukemia, Phase II

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: MAJ Alan D. Mease, MC

WORK UNIT NO: 79/95

TECHNICAL OBJECTIVE

To determine the therapeutic efficacy and toxicity of prednimustine in children with refractory leukemia.

METHOD

Patients with acute leukemia resistant to all conventional chemotherapy will be eligible. Patients will receive 40 mg/M^2/ day prednimustine in two divided oral doses. Administration will continue until the onset of progressive symptomatic disease or for a minimum of eight weeks. If a patient achieves a complete response, the dose will be halved and the drug continued as a single daily oral dose. In patients with no bone marrow disease during therapy, prednimustine will be discontinued temporarily for ANC less than 1,000 or platelet count less than 75,000. When counts inprove prednimustine will be started at a dose 10 mg/M^2 less than the previous dose. In patients in relapse, if the white count continues to rise at two weeks, the daily dose may be escalated 20 mg/M^2/day. Patients may be taken off study for progressive symptomatic disease after four weeks, reccurent disease after a response, or for intractible side effects. When the drug is discontinued, patients will be supported with a dose about one half the daily dose and weaned with every other day dosage. Patients will be evaluated each week with interval history, physical examination including BP and weight, urine glucose, anc CBC.

PROGRESS

(80 03 - 81 09) No patients were registered on this study.

STATUS: (C)

TITLE: CCG 172 - Vindesine or Vincristine Plus L'asparaginase and Prednisone for Reinduction, and Cyclophosphamide Plus Vindesine or Vincristine for Maintenance in the Treatment of Recurrent Acute Lymphocytic Leukemia in Children - Patients Relapsing from Other Studies, Phase III.

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: MAJ Alan D. Mease, MC

WORK UNIT NO: 79/32

TECHNICAL OBJECTIVES

To compare the relative effectiveness of vindesine and vincristine in inducing remission when used with standard prednisone and L'asparaginase; to determine the relative degrees of neurotoxicity of vindesine compared to vincristine; to determine the relative degree of thrombocytosis/leukopenia induced by vindesine compared to vincristine; to determine whether there is cross-resistance between vincristine and vindesine; and to provide data concerning the need for synchronizing timing of vinca alkaloid injections in relation to cyclophosphamide in order to determine relative length of remission.

METHOD

Patients with recurrent acute lymphocytic leukemia relapsing from other chemotherapeutic studies will be eligible. There will be two induction treatments depending upon whether vindesine (VND) or vincristine (VCR) is used. VND, L'asparaginase, and prednisone will be used for patients with VCR resistance. VCR non-resistant patients will be randomized to be treated with either VND, L'asparaginase, and prednisone or VCR, L'asparaginase, and prednisone. Patients with M_3 on day 28 will go off study. Maintenance therapy will begin on day 28. Patients will be randomized to one of six maintenance regimens based upon induction therapy. Regimen 1 will consist of cyclophosphamide (CPM) and VND, with VND administered 24 hours before CPM for VCR resistant patients. Regimen 2 will be the same as Regimen 1, but for VCR non-resistant patients. Regimen 3 will consist of CPM and VND with VND administered concurrent with CPM for VCR resistant patients. Regimen 4 will be the same as Regimen 3, but for VCR non-resistant patients. Regimen 5 will consist of CPM and VCR with VCR administered 24 hours before CPM for VCR non-resistant patients. Regimen 6 will consist of CPM and VCR with VCR administered concurrent with CPM for VCR non-resistant patients.

PROGRESS

(80 02 - 81 09) No Madigan patients were registered on this study.

STATUS: (C)

TITLE: CCG 191P - Total Sanctuary vs Conventional CNS Treatment of Newly Diagnosed Acute Lymphoblastic Leukemia for Patients with "Average Risk" and "High Risk" Prognostic Characteristics, Phase III

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: MAJ Alan D. Mease, MC

WORK UNIT NO: 79/89

TECHNICAL OBJECTIVE

To compare the effects of high-dose, protracted IV methotrexate infusions vs standard cranial irradiation plus IT methotrexate on: (1) central nervous system relapse; (2) central nervous system toxicity - both acute and delayed; (3) hematologic remission induction and duration; (4) non-CNS extramedullary relapse (e.g., testes); and (5) survival.

METHOD

Previously untreated patients less than 21 years of age with acute lymphoblastic leukemia who are (1) less than 3 years old, (2) 7 years of age or older, or (3) have an initial WBC of greater than 10,000/µl will be eligible. Patients with the diagnosis of acute undifferentiated leukemia on any initial WBC will be treated on this protocol but analyzed as a separate group. Patients will be treated initially with prednisone, vincristine, L'asparaginase, daunomycin, and central nervous system prophylaxis. They type of CNS porphylaxis will be determined by randomization and will consist either of very high doses of methotrexate IV or cranial radiation plus IT methotrexate. Most of the CNS therapy will be given during the second month of treatment, during which 6-MP will replace the daunomycin and L-asparaginase. From the third month on, remission will be maintained by a sequence of multiple drug administrations, including vincristine, prednisome, L-asparaginase, daunomycin, methotrexate, cyclophosphamide, and 6-MP. M_3 bone marrow or extramedullary leukemia at any time will be cause for removal from the study.

PROGRESS

(79 11 - 80 09) One patient was treated and did well until relapse at one year with CNS leukemia when he was removed from the study.

(80 10 - 81 09) One patient has been entered during FY 81 and is doing well at the present time.

STATUS: (O)

TITLE: CCG #251: Treatment of Newly Diagnosed Acute Non-Lymphocytic Leukemia with Multiagent Chemotherapy (Cyclic Versus Continuous) or Bone Marrow Transplantation Following Total Body Irradiation

PRINCIPAL INVESTIGATOR: LTC Alan D. Mease, MC

PROFESSIONAL ASSISTANT: None

WORK UNIT NO: 81/103

TECHNICAL OBJECTIVES

To improve remission duration and survival in children with previously untreated acute non-lymphocytic leukemia using Cytoxan and total body irradiation followed by bone marrow transplantation with compatible donor marrow for those children who achieve a complete remission with induction therapy; to compare two intensive maintenance regimens: continuous 6-thioguanine with monthly courses of Cytoxan, vincristine, 5-azacytidine, and cytosine arabinoside vs repeated cycles of 6-thioguanine and cytosine arabinoside; adriamycin and cytosine arabinoside; prednisolone, vincristine, methotrexate, and 6-mercaptopurine; 5-azacytidine and adriamycin; and BCNU and cyclophosphamide; to evaluate the induction capabilities of adriamycin and cytosine arabinoside; and to evaluate the prognostic significance of any chromosomal abnormalities in leukemic cell lines.

METHOD

Induction therapy will consist of adriamycin and ARA-C given IV. When the bone marrow by aspiration is M-1 (day 29) or M-2 (day 57), subjects will receive one of the two intensive maintenance regimens listed above with concomitant radiotherapy or bone marrow transplant preceded by two successive days of Cytoxan therapy, followed four days later by total body irradiation. Patients 21 years of age at diagnosis who have previously untreated acute non-lymphocytic leukemia will be eligible.

PROGRESS

(81 07 - 81 09) No Madigan patients have been registered on this protocol.

STATUS: (O)

TITLE: CCG 372 - Evaluation of Cis-Platinum Diamine Dichloride (CPDD) and 4'-Demethyl-Epidophyllotoxin-β-D-Thenylidene Glucoside (VM-26) for the Treatment of Recurrent Stage IV Neuroblastoma of Childhood, Phase II.

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: MAJ Alan D. Mease, MC

WORK UNIT NO: 79/35

TECHNICAL OBJECTIVE

To determine if CPDD and VM-26, both of which have been reported to produce responses in recurrent Stage IV neuroblastoma as single agents, are efficacious when given in combination.

METHOD

Patients, to be eligible, must have Stage IV neuroblastoma, i.e., remote disease involving skeleton, marrow, soft tissues, distant lymph notes, etc. Patients previously treated with CPDD and/or VM-26 are not eligible. VM-26, 150 mg/M^2 IV, will be administered on days 1, 8, and 15. CPDD, 4.5 mg/kg IV, will be administered on day 2 (24 hours after day 1 dose of VM-26). Patients will be hospitalized. Cycles will be repeated every three weeks. Two complete cycles will be considered an adequate trial. If a complete or partial response is noted, cycles will be continued until progressive disease ensues.

PROGRESS

(80 06 - 81 09) No patients were registered on this study.

STATUS: (O)

TITLE: CCG 541 - Comparison of Involved Field Radiotherapy with Involved Field Radiotherapy Plus Adjuvant Chemotherapy (MOPP: Mechlorethamine, Vincristine, Procarbazine, Prednisone) and Extended Field Radiotherapy in the Treatment of Stage I and II Hodgkin's Disease in Children

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: MAJ Alan D. Mease, MC

WORK UNIT NO: 79/38

TECHNICAL OBJECTIVES

To compare the effectiveness of involved field (IF) radiotherapy, IF radiotherapy followed by MOPP chemotherapy, and extended field (EF) radiotherapy in treating laparotomy confirmed Stage I and II Hodgkin's disease in children in terms of (a) duration of disease-free interval following completion of initial therapy, (b) the type and extent of disease extensions following initial therapy, and (c) survival. To determine the retrievability of new disease following primary therapy for each of the three regimens, using specified retrieval plans. To determine the effect of specific histology on results of primary and retrieval therapy for each of the three regimens. To determine the comparative effects of the three treatment regimens with respect to: (a) linear growth, bi-acromial, and bi-cristal diameters, (b) incidence of hypothyroidism and sterility, (c) incidence of second malignancies, (d) complications following staging celiotomy and splenectomy, immediate and remote, including fulminating infections, and (e) effectiveness of penicillin prophylaxis in the prevention of post-splenectomy infectious complications.

METHOD

Children with laparotomy confirmed Stage I and II Hodgkin's disease with no prior exposure to chemotherapy will be eligible. Patients will be randomized to three groups. Regimen I will consist of IF radiotherapy followed by IF radiotherapy plus MOPP q 28 days x 6 on first relapse. Regimen II will consist of EF radiotherapy followed by complete EF + MOPP q 28 days x 6 on first relapse. Regimen III will consist of IF + MOPP q 28 days x 6 followed by IF + MOPP q 28 days x 6 on first relapse. Patients will be removed from the study on documentation of second relapse.

PROGRESS

(80 05 - 81 09) No Madigan patients were entered on this protocol.

STATUS: (C)

TITLE: CCG 551 - A Trial of Memorial Hospital LSA_2-L_2 Treatment Regimen (Modified) Cyclophosphamide, Vincristine, Prednisone, Methotrexate, and Daunomycin for Induction; Cytosine Arabinoside, 6-Thioguanine, L-Asparaginase, Methotrexate, and BCNU for Consolidation; and 6-Thioguanine, Hydroxyurea, Cytosine Arabinoside, and Methotrexate for Maintenance vs Intermittent High Dose Cyclophosphamide, Moderate Dose Methotrexate, Vincristine, and Prednisone (COMP) and Radiation Therapy for the Treatment of Non-Hodgkin's Lymphoma in Children, With a Study of Disease Characterization, Phase III.

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: MAJ Alan D. Mease, MC

WORK UNIT NO: 79/36

TECHNICAL OBJECTIVES

To study the classification and biology of that group of childhood neoplasms included in the non-hodgkin's lymphomas. To compare the effectiveness of two combination chemotherapy programs (Memorial Hospital LSA_2-L_2 and COMP) in the control of all forms of childhood non-hodgkin's lymphoma. To determine for each of the two treatment regimens the effectiveness of standardised IT methotrexate without radiation for the control of occult CNS disease. To determine for each of the treatment regimens the effectiveness of standardised irradiation of bulk disease.

METHOD

All newly diagnosed and previously untreated patients with non-Hodgkin's lymphoma will be eligible. Multi-disciplinary treatment of the patient is required in this study. Surgical treatment will be undertaken first. For most patients this will be a biopsy procedure, but for abdominal presentation, major tumor resection may be necessary. Following the surgical phase of treatment and the initial evaluation, treatment will commence with combined chemotherapy and irradiation by random choice between Regimen I or Regimen II (see title for drugs in each regimen). Irradiation will commence during induction upon bone marrow recovery. In general, irradiation will be completed before consolidation or maintenance has commenced according to regimen. Treatment will terminate on completion of 18 months of treatment. All patients will be followed for a minimum of 5 years or until death.

PROGRESS

(80 06 - 81 10) No new patients were entered in FY 81. Two previous patients are off medication with no evidence of disease at follow-up every three months.

STATUS: (O)

TITLE: CCG 861: Surgery, Radiation Therapy, and Chemotherapy with Bleomycin, Vinblastine, Cis-Platinum Diamine Dichloride, Actinomycin-D, Cyclophosphamide, and Adriamycin in the Treatment of Local and Metastatic Malignant Germ Cell Ovarian Tumors of Childhood (Phase II Study)

PRINCIPAL INVESTIGATOR: LTC Charlene Holt, MC

PROFESSIONAL ASSISTANT: LTC Alan Mease, MC

WORK UNIT NO: 79/46

TECHNICAL OBJECTIVES

To determine, in patients with germ cell ovarian malignancy which has been completely excised by surgery, treated with 6-drug chemotherapy, and perhaps with radiation therapy, the length of disease free interval and the percentage of patients having long term survival; to determine, in patients with residual or metastatic disease treated with surgery, 6-drug chemotherapy, and radiation therapy, the effectiveness of the treatment program as indicated by percent of patients experiencing CR or PR and the length of the remission periods; to examine the relationship between age, tumor type, staging, and pathology with prognosis; and to determine if a single arm study of an infrequent childhood tumor is practical and produces significant conclusions.

METHOD

Patients will be treated with chemotherapy for 18 weeks. At week 18, a second look laparotomy is performed. If there is residual or persistent tumor present, radiation thearpy will be given. If there is no residual or persistent tumor at this time, radiation thearpy will not be administered. If at 24 weeks the patient has progressive disease, the patient will be taken off the study. Patients on study will continue chemotherapy until week 102. The patient will be taken off the study if there is progressive disease after 24 weeks of therapy or if recurrent or metastatic disease appears after six months of therapy.

PROGRESS

(78 11 - 81 09) This protocol has not been forwarded to or approved by HSC. The investigator wishes to keep it open and will submit the required volunteer agreement so that the protocol may be approved. No patients have been registered on this protocol at MAMC.

STATUS: (O)

TITLE: CCG 862: An Evaluation of Surgery, Radiation Therapy, and Chemotherapy (Vincristine, Adriamycin, Cyclophosphamide, 5-Fluorouracil) in the Treatment of Previously Untreated Primary Malignant Hepatoma in Children

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: MAJ Alan Mease, MC

WORK UNIT NO: 79/45

TECHNICAL OBJECTIVES

To determine the 2 and 5 year survival, by stage at diagnosis, of childhood hepatoma; to determine the complete and partial response rate to radiation therapy and chemotherapy in those patients who have gross residual tumor measurable by palpation, x-ray, or radionuclides; to correlate histologic appearance with response to treatment; and to determine the disease free survival interval.

METHOD

Patients will be grouped or staged according to the resectability of the tumor as follows: Group I - localized tumor, completely resected, as primary treatment - receive surgical resection plus chemotherapy. Group II/A - localized tumor rendered completely resectable by radiation and chemotherapy - receive high dose radiation to the local area combined with VCR, ADR, CPM, and 5FU, followed by complete surgical resection. Chemotherapy is continued for 12 months. Group II/B - localized residual tumor following incomplete resection - receive surgical resection (incomplete) local high dose irradiation to residual disease and chemotherapy as in II/A. Group II/C - localized tumor with no attempt at resection - biopsy only of localized lesion followed by local radiation and chemotherapy as in II/A. Group R/II - Patients with localized recurrent disease from Group I or II/A. These patients will be subclassed as Groups R II/A, R II/B, or R II/C and treated as in primary Groups II/A; B; and C, respectively. Group III/A - tumor involving both lobes of the liver - biopsy only; radiation to the entire liver, chemotherapy similar to Group II. Group R III - Patients in Groups I and II who develop generalized liver tumor - receive treatment as in III/A. Group IV - distant metastasis irrespective of the degree of liver involvement - receive biopsy only. Radiation to be used for pulmonary metastases and painful or unsightly tumors. Chemotherapy as in Group II.

PROGRESS

(78 11 - 81 09) No patients entered on this protocol at MAMC.

STATUS: (O)

TITLE: CCG 984 - Histiocytosis X: A Study of the Biology, Clinical, and Histologic Staging, Treatment, and Prognosis in Previously Untreated Children, Phase III.

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: MAJ Alan D. Mease, MC

WORK UNIT NO: 79/37

TECHNICAL OBJECTIVES

To determine if multidrug induction and maintenance regimens will improve survival in the young high-risk patient and reduce sequelae in the long-term survivors. To obtain comprehensive immunologic studies at diagnosis and at critical times during the course of the disease so as to (a) identify patients with primary immunodeficiency disorders which may simulate histiocytosis X, (b) determine if patients with histiocytosis X less than 3 years of age have acquired defects in T and B lymphocyte function, and (c) ascertain if either stage of disease or survival of these young patients can be correlated with T and B lymphocyte function. To continue to collect clinical and histologic data so that patients may be staged in a prospective fashion into those with and without organ dysfunction and those with benign or malignant histology. In addition, more detailed pathologic studies will be recommended so as to increase knowledge of the cellular infiltrates in various tissues.

METHOD

Patients 15 years of age or less with a histologic diagnosis of histiocytosis will be eligible. Patients with only a solitary bone lesion or with only two or three small well localized bone lesions or with primary immunodeficiency disease will be excluded. Induction will consist of 12 weeks of chemotherapy including prednisone, vinblastine, methotrexate, and cyclophosphamide. For pusposes of evaluating the response to therapy, an adequate trial will be at least 4 weeks of therapy. If the patient achieves complete (CR) or partial remission (PR) at 12 weeks of induction, then maintenance therapy for six months will consist of methotrexate, cyclophosphamide, and 6-MP. If there is recurrence, the 4-drug regimen will be repeated. Radiation for localized disease may be used for lesions not controlled by chemotherapy so long as other parameters of measurements of response are available.

PROGRESS

(80 05 - 81 09) No Madigan patients have been registered on this study.

STATUS: (O)

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 BRANCH PROTOCOLS

TITLE: Intrathecal Aminopterin, NSC #739-NB, Clinical Brochure

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: MAJ Alan D. Mease, MC

WORK UNIT NO: 80/50

TECHNICAL OBJECTIVES

To demonstrate that IT aminopterin is less neurotoxic in man than IT methotrexate. To show that IT aminopterin requires fewer lumbar punctures for an equivalent therapeutic effect than IT methotrexate. To compare the pharmacokinetics in man of IT aminopterin and IT methotrexate.

METHOD

Any patient with a CNS neoplasm, primary or metastatic, will be eligible provided IT methotrexate is an accepted treatment for the neoplasm. Patients with acute leukemia or non-Hodgkin's lymphoma scheduled to receive preventive IT chemotherapy will be eligible. Patients with a prior history of IT methotrexate arachnoiditis will be eligible, but patients with a prior history of myelopathy or encephalopathy associated with IT methotrexate therapy will not be eligible. Eligible patients will receive intralumbar AMT at a dose of 2.0 mg per injection at weekly intervals. For prophylaxis, six injections will be given. For treatment of established disease, the injections will be continued until the CSF is free of blast cells by cytocentrifuge analysis. Thereafter, the injections will be given weekly x 2, then q 2 weeks x 2, then monthly for 2 years.

PROGRESS

(80 09 - 81 09) No patients were registered on this study.

STATUS: (O)

TITLE: POB 76-04 - Combined Modality Treatment of Rhabdomyosarcoma

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: LTC Alan D. Mease, MC

WORK UNIT NO: 80/63

TECHNICAL OBJECTIVES

To answer the following questions: (1) Can the functional impairments of surgery be reduced by primary chemotherapy and can "radical" surgical procedures be avoided? (2) Does early use of intensive chemotherapy enhance survival for patients presenting with metastatic disease? (3) What can be learned about the kinetics, biochemistry, immunology, and etiology of childhood rhabdomyosracoma?

METHOD

Patients <25 years with rhabdomyosarcoma or undifferentiated sarcoma who have not had prior surgical debulking, radiotherapy, or chemotherapy will be eligible. STAGING: Stage I - disease limited to a single anatomic structure; State II - local continguous spread (with or without involvement of regional nodes; Stage III - metastatic disease. Stages I and II will be randomized to either Group I or or Group II. Group I will initially receive surgery followed by chemotherapy (vincristine, actinomycin, and cyclophosphamide) and radiotherapy. Group II will initially receive the same chemotherapy as above and radiotherapy. After hemotologic recovery from chemotherapy, patients will undergo surgical exploration and residual tumor will be excised. Stage III patients will be randomized to receive a standard regimen of chemotherapy or to receive an intensive regimen which is the same as standard with an extra day of chemotherapy added. Both groups will receive radiotherapy during the chemotherapy and will be evaluated for surgical excision of remaining bulk disease after recovery from chemotherapy. All patients who attain CR or PR will receive maintenance chemotherapy.

PROGRESS

(80 10 - 81 09) No Madigan patients were entered on this protocol.

STATUS: (O)

TITLE: POB 77/03 - Treatment of Metastatic Osteosarcoma

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: MAJ Alan D. Mease, MC

WORK UNIT NO: 80/51

TECHNICAL OBJECTIVES

To determine the differences in tumor response rates and drug toxicities when high dose methotrexate is given as a 6-hour bolus infusion or as a 42-hour infusion. To determine if the use of intensive chemotherapy given when tumor burden is minimal results in the complete eradication of all microscopic foci of metastatic osteosarcoma.

METHOD

Patients <30 years of age with no evidence of serious infection, active bleeding disorders, or concomitant significant complications and biopsy proven osteosarcoma are eligible. Patients must have pathologic or radiologic evidence of overt metastatic disease and must have received no previous chemotherapy, radiotherapy, or surgical therapy for metastatic disease. Patients presenting with metastatic osteosarcoma will enter a first phase which is designed to create a state in which there is no evidence of disease (NED). If possible, this will be achieved by surgery alone; if surgery alone cannot achieve NED, then chemotherapy will be used initially rather than surgery. Patients in this latter category will be randomized to receive weekly vincristine plus high dose MTX-CF given over 6 hours or methotrexate given as a 42-hour infusion. Patients who respond to this phase of methotrexate may become candidates for surgery even though resection was not possible initially. If NED can be achieved in this way, patients will proceed to Phase 2. Patients achieving NED with surgery and/or chemotherapy will enter Phase 2 of the protocol and be treated with intensive combination chemotherapy employing agents known to be active against overt metastatic disease (methotrexate, citrovorum factor, vincristine, adriamycin, cyclophosphamide, phenylalanine mustard, DTIC, cisplatinum).

PROGRESS

(80 09 - 81 09) No patients at Madigan were entered on this study.

STATUS: (O)

TITLE: POB 77/04 - Childhood Non-Hodgkin's Lymphoma

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: MAJ Alan D. Mease, MC

WORK UNIT NO: 80/62

TECHNICAL OBJECTIVES

To treat patients in as uniform a manner as possible while studying the spectrum of diseases in as much detail as possible, including clinical features, histology and cytology, surface markers, induction of differentiation in vitro, functional potential of tumor cells, distribution patterns of DNA and protein pre- and post-treatment, and possible tumor markers. From such studies, it is hoped that insights into classification and rational approaches to therapy will be forthcoming.

METHOD

Untreated patients with non-Hodgkin's lymphoma under 25 years of age, or with Brukitt's lymphoma at any age, who consent to a second biopsy procedure are eligible. Patients in whom a diagnosis of non-Hodgkin's lymphoma is strongly suspected will be admitted as soon as possible. Treatment will be commenced as soon as initial studies and biopsy have been completed and therapy should begin within 48-72 hours. Therapy will include total surgical resection wherever possible. The backbone of therapy, however, will be chemotherapy, since childhood non-Hodgkin's lymphoma is rarely a localized tumor. Drug therapy will be intensive utilizing cyclophosphamide, vincristine, adriamycin, methotrexate, and prednisone. These will be used in a sequence which should result in drugs being administered every 10 days. We propose a somewhat different approach to prophylactic therapy, in that first, an IT methotrexate boost will be given during IV 42 hour methotrexate infusion; second, Ara-C will be used as a second drug in combination with methotrexate, and third, prophylaxis will begin at the same time as systemic therapy since it is more likely that tumor cells enter the sanctuary at a time when the systemic tumor burden is high. Irradiation as part of CNS prophylactic therapy is not planned.

PROGRESS

(80 09 - 81 09) No Madigan patients were entered on this protocol.

STATUS: (O)

TITLE: POB 77/05 - Treatment of Metastatic and High Risk Ewing's Sarcoma

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: MAJ Alan D. Mease, MC

WORK UNIT NO: 80/52

TECHNICAL OBJECTIVES

To examine the efficacy of total body irradiation in combination with high dose chemotherapy in the treatment of metastatic or high-risk Ewing's sarcoma. To examine the immunological status of patients receiving total body irradiation as a function of time. To examine the utility of autologous marrow infusion in patients receiving high-dose chemotherapy who do not have marrow disease at presentation but who may have metastatic disease in other sites.

METHOD

Patients with a pathologically proven diagnosis of Ewing's sarcoma presenting with metastatic disease or with a pelvic or vertebral primary lesion, without prior radiation or chemotherapy, will be eligible. Chemotherapy to include vincristine, actinomycin D, and cyclophosphamide will be given for four weeks concomitant with irradiation to the primary site for 5 weeks. Total body irradiation will then be given weeks 6-10. High dose therapy of vincristine, adriamycin, cyclophosphamide, and DTIC will then be given for 3 days. Maintenance chemotherapy to include vincristine, adriamycin, cyclophosphamide, and DTIC will be given once every 6 weeks for 12 cycles.

PROGRESS

(80 09 - 81 09) No patients were registered on this study.

STATUS: (O)

TITLE: POB 77/06 - Treatment of Low Risk Ewing's Sarcoma

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: MAJ Alan D. Mease, MC

WORK UNIT NO: 80/53

TECHNICAL OBJECTIVES

To evaluate the efficacy of prophylactic pulmonary irradiation in conjunction with combination chemotherapy in the treatment of low risk Ewing's sarcoma. To evaluate the immunologic status and competence of patients with Ewing's sarcoma as a function of time.

METHOD

Patients with a pathologically proven diagnosis of Ewing's sarcoma presenting with distal primary lesions (but not in the pelvis or spine) without evidence of metastatic disease are eligible for this study. Patients with prior chemotherapy, radiation therapy, or surgical resection procedures other than biopsies are ineligible for the study. For initial therapy, patients will receive vincristine, actinomycin D, and cyclophosphamide (given week 1 and 4), radiation therapy to the primary site (5 treatments/week for 5 weeks), and subsequent to the completion of radiation to the primary site, pulmonary irradiation (5 treatments/week for 2 weeks). Maintenance chemotherapy will begin subsequent to pulmonary irradiation consisting of vincristine, adriamycin, and cyclophosphamide every 4 weeks for a total of 12 courses.

PROGRESS

(80 09 - 81 09) No patients were registered on this protocol.

STATUS: (O)

TITLE: POB 77/11 - A Prospective Randomized Trial of the Utility of HLA-Matched Platelet Transfusions for the Support of Thrombocytopenic Cancer Patients

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: MAJ Alan D. Mease, MC

WORK UNIT NO: 80/54

TECHNICAL OBJECTIVES

To determine what differences exist between patients initially treated with HLA-matched or HLA-mismatched platelets in the number and frequency of transfusions required; mean increments of those transfusions; frequency of transfusion reactions; number of bleeding episodes; development of anti-HLA antibodies; and length of time until patients become refractory to the treatment strategy employed. To determine how often patients refractory to one strategy will respond to the other and what differences will exist in those subsequent responses. To determine if the order of strategy makes a difference in the total length of time patients respond to platelet transfuions. To determine if the type of platelets transfused in those patients refractory to both matched and mismatched platelet transfuions makes a difference in the number of transfusions required, the mean increments of those transfusions, and the frequency and time to the development of significant bleeding episodes.

METHOD

All pediatric patients admitted to Madigan will be eligible for this study. Patients will be specifically excluded if they have received more than 5 blood component transfusions, they cannot be HLA type, or they have an inadequate number of HLA-matched donors to provide HLA-matched platelet support. Patients will be randomised into 2 groups by diagnostic categories; further, patients within each diagnostic category will be divided into those with and without known bone marrow involvement. Group 1 patients will receive platelet transfusions with matched platelets. Group 2 will receive mismatched platelets. The indications for transfusion will be the same in both groups. Patients in both groups will continue to receive platelet transfusions until the patient is judged to be refractory and then crossed into the opposite group. When patients are considered refractory to matched and mismatched platelets, they shall be randomized to receive either matched

or mismatched platelets for the remainder of the study. Following randomization, the patients will continue to receive the assigned platelet preparation until the development of a significant bleeding problem. Patients refractory to both matched and mismatched platelets who develop significant bleeding problems will be considered off-study and will be supported with the best available pletlet support.

PROGRESS

(80 09 - 81 09) No patients were registered on this study.

STATUS: (O)

TITLE: POB 78/06 - Treatment of Recurrent Lymphoma

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: MAJ Alan D. Mease, MC

WORK UNIT NO: 80/55

TECHNICAL OBJECTIVES

To investigate the utility of a combination of aggressive chemotherapy and total body irradiation (TBI) in the treatment of recurrent diseminated non-Hodgkin's lymphoma. To study the utility of flow-micro-fluorimetric techniques as a potentaial means of individualizing timed-sequence chemotherapy scheduling. To study the value of supplementary irradiation to apparently localized recurrent tumor. To study recurrent tumor for changes in morphology, surface receptors, EBV genome, and cell surface micro-viscosity as compared to the patient's primary tumor.

METHOD

Patients with recurrent non-Hodgkin's lymphoma who have relapsed on other protocols in whom autologous marrow has been stored at least 2 months prior to relapse and whose disease is not defined as small volume, local relapse will be eligible for the study. The presence of complicating factors (renal failure, infection, etc) which consitute relative contraindications to the initiation of CARAT therapy (Cytoxan, ARA-C, TBI) will be considered individually for eligibility. Patients with prior CNS disease of proven resistance to chemotherapy and cranial or craniospinal irradiation will normally be ineligibel for CARAT therapy. All patients will be treated in laminar flow rooms if available. Normally, chemotherapy will not commence until the total WBC is >4000 and granulocyte count >1500 in order to keep the period of granulocytopenia to a minimum. All patients will be vigorously hydrated prior to therapy. Treatment schemas are: cytoxan: 45 mg/kg days 1, 2, 3, 4, (IV in 100 cc D5W over 30 min; TBI: 15 rads daily x 8 commencing on day 1 omitting weekends or 400 rads on days 6 and 8; ARA-C: 300 mg/M^2/24 hours by continuous infusion days 9, 10, 11, 12, given in 5% dextrose/water; autologous marrow infusion: day 13. In the presence of CNS disease, intrathecal or intraventricular therapy will be administered. Patients also may be randomized to receive hyperalimentation.

PROGRESS

(80 06 - 81 09) No MAMC patients have been entered on this protocol.

STATUS: (O)

TITLE: POB 78/10 - A Phase II Study of Achromobacter Glutaminase in Acute Leukemia

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: MAJ Alan D. Mease, MC

WORK UNIT NO: 80/56

TECHNICAL OBJECTIVES

To determine the therapeutic efficacy of glutaminase against acute leukemia refractory to standard agents. To determine the toxicity of glutaminase administered in a fixed dosage schedule.

METHOD

Patients must have a life expectancy of least 4 weeks and cytologically documented acute lymphocytic, acute myelocytic, or acute undifferentiated leukemia (on bone marrow aspirate or biopsy specimen). In addition, patients must be proven refractory to conventional drugs considered active against their disease and must have recovered from the toxic effects of any previous therapy. The drug will be administered as a continuous infusion (10,000 IU/M^2/day) for at least 14 days with re-evaluation of the leukemia at that time. If no beneficial effect has been seen the trial will be discontinued. If there is evidence of improvement, the infusion will be continued for a total of 28 days.

PROGRESS

(80 09 - 81 09) No patients have been registered on this study.

STATUS: (O)

TITLE: POB 78/13 - Fever and Antimicrobial Therapy, Study II

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: MAJ Alan D. Mease, MC

WORK UNIT NO: 80/64

TECHNICAL OBJECTIVES

To evaluate the role of empiric antibiotic therapy in granulocytopenic cancer patients. To reduce the incidence of fever and infection in patients for whom treatment related granulocytopenia is anticipated. To evaluate and treat the granulocytopenic patient colonized with fungi.

METHOD

Patients in this study will be treated in three distinct groups. Group I (Treatment of Granulocytopenic Patients Prior to the Onset of Fever) will consist of afebrile patients receiving chemotherapy anticipated to produce granulocytopenia, irrespective of the projected duration of granulocytopenia. These patients will be randomized to a double blind study of either erythromycin and bactrim or a placebo. Group II (Evaluation and Treatment of Granulocytopenic Patients Who Become Febrile) will consist of patients with granulocytopenia who are febrile with either a documented infection or a fever of undetermined origin. Those with documented infection will receive either broad specturm antibiotics or specific therapy based on sensitivity testing. FUO patients will be treated with empiric antibiotics for 7 days and then managed according to their status (febrile/afebrile). Group III (Evaluation and Treatment of the Granulocytopenic Patient Colonized with Fungi), after 7 days of KGC will be randomized to receive amphotericin or not receive amphotericin.

PROGRESS

(80 09 - 81 09) No patients were registered on this protocol.

STATUS: (O)

TITLE: POB 79/01 - Evaluation of Human Lymphoblastoid Interferon and Poly I:C (Stabilized with Poly-L-Lysine and Carboxymethyl Cellulose (Poly{ICLC}) in the Treatment of Acute Myelocytic Leukemia, CLL, and Various Solid Tumors, Phase II.

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: MAJ Alan D. Mease, MC

WORK UNIT NO: 80/57

TECHNICAL OBJECTIVES

To determine the therapeutic efficacy of human lymphoblastoid interferon and stabilized polyriboinosinic acid-polyribocytidylic acid (poly{ICLC}) in patients with acute myelocytic leukemia (who are in their first bone marrow relapse and have received no previous induction treatment for this relapse), and in patients with various solid tumors in relapse.

METHOD

Patients 16 or over with acute myelocytic leukemia who are in their first bone marrow relapse after having been treated with standard drugs, and who have not received any other induction treatment for this relapse, are eligible. Solid tumor patients in relapse are eligible as determined by the specific protocol priority scheme for that tumor type. Patients will be randomized to receive either lymphoblastoid interferon or Poly (ICLC). An adequate trial will consist of a minimum of one month of treatment. A second month of induction with the same agent on the same schedule will be given if marrow improves by day 30 from M_3 to M_2 in the case of AML, or if, in the case of solid tumor patients, the disease is stable or improved. In no case will induction continue beyond two months. Patients with stable or improving disease at the end of two months will begin a maintenance schedule with the same agent; patients with progressive disease at the end of one or two months may, if their condition permits, corss-over to an induction attempt with the other agent.

PROGRESS

(80 09 - 81 09) No patients were registered on this study.

STATUS: (O)

TITLE: POB 79/03 - Phase II Study of 2'-Deoxycoformycin in Acute Lymphoblastic Leukemia

PRINCIPAL INVESTIGATOR: LTC Charlene P. Holt, MC

PROFESSIONAL ASSISTANT: MAJ Alan D. Mease, MC

WORK UNIT NO: 80/58

TECHNICAL OBJECTIVES

To determine the therapeutic efficacy of 2'-deoxycoformycin against acute lymphoblastic leukemia refractory to standard agents. To determine the toxicity of 2'-deoxycoformycin (2'dCF) administered in a fixed dosage schedule.

METHOD

Patients with a life expectancy of at least 4 weeks who have cytologically documented acute lymphoblastic leukemia on bone marrow aspirate or biopsy specimen are eligible. Patients must be proven refractory to those conventional drugs considered active against ALL. This protocol will investigate a dose of 0.25 mg/kg 2'dCF given IV daily for 3 consecutive days. Each patient will receive at least 2 courses of 2'dCF (toxicity permitting). The second course of 2'dCF will be given 14 days following the initial treatment. If there is no evidence of improvement on day 28 the patient will be removed from the study. Patients who have achieved either a complete or partial response after the second course will continue to receive treatment on this protocol until M_3 marrow status occurs. Upon entrance to the protocol, cell surface marker studies will be obtained on the lymphoblasts from each patient. The ALL patients will be treated and analyzed separately according to whether they have T cell or non-T cell ALL.

PROGRESS

(80 09 - 81 09) No patients were registered on this study.

STATUS: (O)

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

F O R

P R O T O C O L S

NATIONAL CANCER INSTITUTE PROTOCOLS

TITLE: NCI #I78-4: Guidelines for the Clinical Use of Streptozotocin (Group C Guidelines)

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
LTC Archie W. Brown, MC

WORK UNIT NO: 81/18

TECHNICAL OBJECTIVES

To provide an investigational drug of proven efficacy, not previously released for general use, to MAMC patients under Group C NCI Guidelines. Also, to determine extent and variety of side effects with streptozotocin that have not been previously described.

METHOD

Streptozotocin will be used for patients with malignant islet cell tumor (response rate 70%) and in metastatic carcinoid. Streptozotocin will be given IV either daily for 5 days every 4-6 weeks or weekly for approximately 4 weeks. Careful pretreatment evaluation will be accomplished and any untoward or unexpected side effects will be reported to the National Cancer Institute.

PROGRESS

(80 12 - 81 09) No MAMC patient entry on this protocol.

STATUS: (O)

TITLE: NCI #I78-10: Guidelines for the Clinical Use of Hexamethylmelamine (Group C Guidelines)

PRINCIPAL INVESTIGATOR: CCL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
LTC Archie W. Brown, MC
LTC Roger B. Lee, MC

WORK UNIT NO: 81/19

TECHNICAL OBJECTIVES

To provide an investigational drug of proven efficacy, not previously released for general use, to MAMC patients under Group C NCI Guidelines. Also to determine the extent and variety of side effects with hexamethylmelamine that have not been previously described.

METHOD

Hexamethylmelamine will be used in patients whose cancer of the ovary has become refractory to therapy with alkylating agents or in patients where therapy with alkylating agents is contraindicated. Hexamethylmelamine will be given daily by mouth, either continuously or intermittently depending on response, toxicity, and other drugs which the patient may be taking concomitantly. The treatnemt will continue for as long as the disease is stable or the tumor shrinks.

PROGRESS

(80-12 - 81 09) Hexamethylmelamine has been given to eight patients. Four of the patients had progressive disease after administration. Three others have shown stable disease from 3 to 6 months, followed by progression of disease. One patient has had eight courses of therapy (8 months) and the disease is stable at this time.

STATUS: (O)

TITLE: NCI #I80-11: VP-16-312 For Small Cell Carcinoma of the Lung (Group C Guidelines)

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
LTC Archie W. Brown, MC

WORK UNIT NO: 81/20

TECHNICAL OBJECTIVES

To provide an investigational drug of proven efficacy, not previously released for general use, to MAMC patients under Group C NCI Guidelines. To determine extent and variety of side effects with VP-16-312 that have not been previously described.

METHOD

VP 16-312 will be used in refractory or recurrent small cell cancer of the lung, usually in combination with other effective chemotherapeutic drugs. It will be administered IV over a 30-minute period either daily for 5 days every 2-3 weeks or on days 1, 3, and 5 every 4-5 weeks. The exact interval between subsequent courses will be modified, depending on the time required for recovery from toxic manifestations. Careful pretreatment evaluation and follow-up will be done. Any untoward or unexpected side effects will be reported to the NCI. The treatment will be continued for as long as the patient's tumor responds or remains stable.

PROGRESS

(80 12 - 81 09) Five patients have been treated: one complete response, 1 partial response, 1 improvement, 1 progression, and the last has not been treated long enough for evaluation.

STATUS: (O)

TITLE: NCI #I80-12: Group C Guidelines for the Use of Delta-9-Tetrahydrocannabinol

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
LTC Alan D. Mease, MC
MAJ Lauren K. Colman, MC

WORK UNIT NO: 81/102

TECHNICAL OBJECTIVES

To determine untoward side effects not previously described with THC and to make available this antinausea drug to patients on chemotherapy.

METHOD

Delta-9-THC will be used as an antiemetic therapy in cancer chemotherapy patients refractory to standard antiemetic agents. It will be administered at a starting dose of 5 mg/m^2 p.o., 6-8 hours prior to the administration of chemotherapy and for 12 hours thereafter. Should the 5 mg/m^2 dose prove to be ineffective, and in the absence of significant side effects, the dose may be excalated to 7.5 mg/m^2. Any untoward side effects will be reported to the NCI.

PROGRESS

(81 07 - 81 09) Protocol is awaiting approval from OTSG.

STATUS: (O)

TITLE: NCI #7601 - Selected Stage I Ai - I Bi Ovarian Cancer (Well and Moderately Differentiated)

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 81/45

TECHNICAL OBJECTIVES

To define the natural history of patients treated by surgery; to determine whether prophylactic, adjuvant chemotherapy with melphalan alters the natural history; to study the effect of various potential prognostic factors on the natural history of patients treated by each form of therapy; to establish the value of various staging parameters on the stage of disease and its natural history.

METHOD

To be eligible, patients must have a histopathologic diagnosis of common epithelial ovarian cancer, either serous, mucinous, or other (endometrioid, transitional, mesonephroid, adenocanthoma, mixtures and intermediate types, and unclassifiable). Patients will be stratified by histology, histologic grade, and stage. After staging laparotomy and total abdominal hysterectomy or bilateral salpingo-oophorectomy, patients will be randomized to observation with no chemotherapy or to a chemotherapy regimen of melphalen (0.2 mg/kg/day PO for 5 days). The chemotherapy will be repeated every four weeks for 18 months or after 12 cycles of therapy, whichever comes first. Chemotherapy will be discontinued for unacceptable toxicity or at 18 months if the patient is free of disease at that time. If patient relapses, she will be taken off study at that time. Second-look will occur at 18 months after randomization using peritoneoscopy or laparotomy.

PROGRESS

(81 02 - 81 09) One MAMC patient is on protocol at this time. Group-wide 46.8% of serous cell type and 29.7% of mucinous cell type have been entered with median age of 49 years; 89.3% were Stage IAi and 10.7% were Stage IBi. There has been one death from pulmonary embolus.

STATUS: (O)

TITLE: NCI #7602: All Stage IC and II (A,B,C) and Selected Stage IAii and IBii Ovarian Cancer

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 81/33

TECHNICAL OBJECTIVES

To define the natural history of patients treated by 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.

METHOD

All patients with common epithelial ovarian cancer are eligible, if after definitive staging procedures the patient is zoned to be in Stages 2A, 2B, 2C, 1Aii, 1Bii, or 1Ai or 1Bi with poorly differentiated tumors. Patients with prior therapy are ineligible. Patients will be stratified by histology, histological grade, and stage group for Regimen I. Regimen I will have staging laparotomy, total abdoninal hysterectomy and bilateral salpingo-oophorectomy with no macroscopic residual disease found. Patients will then be randomized to receive melphalan or radioisotopes. Regimen II will be stratified by histology, histological grade, and extent of disease after surgery. Patients will have staging laparotomy, total abdominal hysterectomy, and bilateral salpingo-oophorectomy. If IIB, IIC residual disease is found, patient will be randomized to pelvic radiotherapy plus melphalan or to 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

(81 01 - 81 09) One patient has been entered at MAMC and is alive at the present time.

Group-wide: there have been 78 evaluable cases; 6 have died from disease.

STATUS: (O)

APPENDIX I

GUIDING PRINCIPLES OF THE CARE AND USE OF ANIMALS

Approved by the
Council of the American Physiological Society

Only animals that are lawfully acquired shall be used in this laboratory, and their retention and use shall be in every case in strict compliance with state and local laws and regulations.

Animals in the laboratory must receive every consideration for their bodily comfort; they must be kindly treated, properly fed, and their surroundings kept in a sanitary condition.

Appropriate anesthetics must be used to eliminate sensibility to pain during operative procedures. Where recovery from anesthesia is necessary during the study, acceptable technic to minimize pain must be followed. Curarizing agents are not anesthetics. Where the study does not require recovery from anesthesia, the animal must be killed in a humane manner at the conclusion of the observations.

The postoperative care of animals shall be such as to minimize discomfort and pain and in any case shall be equivalent to accepted practices in schools of veterinary medicine.

When animals are used by students for their education or the advancement of science, such work shall be under the direct supervision of an experienced teacher or investigator. The rules for the care of such animals must be the same as for animals used for research.

APPENDIX II

Recommendations from the Declaration of Helsinki

I. Basic Principles

1. Clinical research must conform to the moral and scientific principles that justify medical research and should be based on laboratory and animal experiments or other scientifically established facts.

2. Clinical research should be conducted only by scientifically qualified persons and under the supervision of a qualified medical man.

3. Clinical research cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject.

4. Every clinical research project should be preceded by careful assessment of inherent risks in comparison to foreseeable benefits to the subject or to others.

5. Special caution should be exercised by the doctor in performing clinical research in which the personality of the subject is liable to be altered by drugs or experimental procedure.

II. Clinical Research Combined with Professional Care

1. In the treatment of the sick person, the doctor must be free to use a new therapeutic measure, if in his judgment it offers hope of saving life, reestablishing health, or alleviating suffering.

If at all possible, consistent with patient psychology, the doctor should obtain the patient's freely given consent after the patient has been given a full explanation. In case of legal incapacity, consent should also be procured from the legal guardian; in case of physical incapacity, the permission of the legal guardian replaces that of the patient.

2. The nature, the purpose, and the risk of clinical research must be explained to the subject by the doctor.

3. a. Clinical research on a human being cannot be undertaken without his free consent after he has been informed; if he is legally incompetent, the consent of the legal guardian should be procured.

b. The subject of clinical research should be in such a mental, physical, and legal state as to be able to exercise fully his power of choice.

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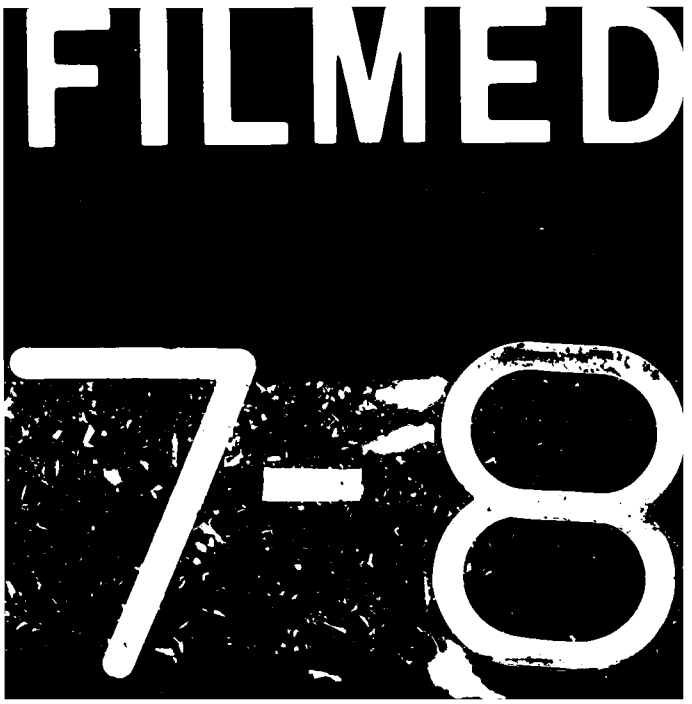
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