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DEPARTMENT

OF

CLINICAL INVESTIGATION

ANNUAL RESEARCH PROGRESS REPORT

FISCAL YEAR 1982



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ANNUAL PROGRESS REPORT

30 September 1982

DEPARTMENT OF CLINICAL INVESTIGATION

MADIGAN ARMY MEDICAL CENTER

TACOMA, WASHINGTON 98431

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number) Subject report identifies those individuals who are conducting investigative protocols at Madigan Army Medical Center. An abstract of each protocol giving abbreviated technical objectives, methods, and progress is presented.		

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MADIGAN ARMY MEDICAL CENTER
TACOMA, WASHINGTON 98431

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

ACKNOWLEDGEMENTS

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



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FORWARD

The mission for the Department of Clinical Investigation is to encourage and support research endeavors by the professional staff assigned to Madigan Army Medical Center. The Department of Clinical Investigation must become more efficient and streamline the necessary paperwork which is required by regulations in an effort to assist all prospective and actual investigators. However, the staff of the Department of Clinical Investigation must continuously be on guard not to create such a bureaucracy that the Department exists for the sake of the bureaucratic organization. The Department of Clinical Investigation exists for the investigator and must be willing to offer assistance to support justifiable research endeavors. It is hoped that the Department of Clinical Investigation will never become so submerged in the wellspring of bureaucracy that the investigator is not assisted in his effort to further scientific knowledge.

One of the problems today in encouraging research is exemplified by a quote from The Water Babies.¹ "For as fast as I learn things I forget them again. So my mama says that my intellect is not adapted for methodic science, and says that I must go in for general information." There is an increasing tendency for physicians of today to do less methodic science, *research*, and to be more concerned about general information, *patient care*. It should be pointed out that the simplest question is the most profound and that "learning is finding out what you already know, doing is demonstrating that you know it, teaching is reminding others that they know just as well as you."² The Department of Clinical Investigation encourages the staff to find out what they already know, do it, then teach it by utilizing our facilities and expertise in answering posed questions.

Concern about what his peers may think is one of the difficulties when encouraging an investigator to enter into new areas or to ask questions that he thinks have been answered previously. To quote Jonathan Livingston Seagull when he tried to tell his flock of new findings, "Irresponsibility? My brothers! he cried. Who is more responsible than a gull who finds and follows meaning, a higher purpose for life? For a thousand years we have scabbled after fish heads, but now we have a reason to live--to learn, to discover, to be free! Give me one chance, let me show you what I've found..."³ The researcher must be prepared to meet with skepticism and occasionally downright disbelief. This can only be met with self-assurance of knowing oneself. In doing research one must first learn how to judge oneself. Even the Little Prince was told, "It is much more difficult to judge oneself than to judge others. If you succeed in judging yourself rightly then you are indeed a man of true wisdom."⁴ So must the researcher learn how to judge himself, hence, his work and the results, and finally to be able to compile the data in a meaningful manner. Each of us is born a researcher but many hours of diligent hard work and self questioning are required in efforts to find answers to questions.

The researcher must be ever on guard not to lose sight of the objective. In Frank Herbert's *Dune*,⁵ a Bene Gesserit proverb states, "Any road followed precisely to its end leads precisely nowhere. Climb the mountain just a little bit to test that it's a mountain. From the top of the mountain you cannot see the mountain." Hence, the researcher must be continuously alert when the objective is no longer in sight less the sands of the mountain become of paramount importance. The staff of Clinical Investigation stands ready to give support and direction when the researcher has reached the mountain of his question, helping to guard against the sands until an answer, the pinnacle of success, is achieved.

This report can be best summarized by a poem by George Stewart⁶:

*Here, silent, speak the great of other years,
the story of their steep ascent from the
unknown to the known, erring perchance
in their best endeavor, succeeding often,
where to their fellows they seemed most
to fail;*

*Here, the distilled wisdom of the years, the
slow deposit of knowledge gained and writ
by weak, yet valorous men, who shirked not
the difficult emprise;*

*Here is offered you the record of their days
and deeds, their struggle to attain that
light which God sheds on the mind of man,
and which we know as Truth.*

*Unshaved must be their genius; it was their
own; but you, be you but brave and diligent,
may freely take and know the rich compan-
ionship of others' ordered thought.*

Bruce L. Fariss

BRUCE L. FARISS, M.D., COL, MC

- 1 Kingsley, Charles: *The Water Babies*. Houghton Mifflin Company, Boston & New York, p 287.
- 2 Bach, Richard: *Illusions: The Adventures of a Reluctant Messiah*. Delaconte Press/Eleanor Friede, 1977, p 46.
- 3 Bach, Richard: *Jonathan Livingston Seagull: A Story*. The MacMillan Company, New York, New York, 1970, p 35.
- 4 De Saint-Exupéry, Antonine: *The Little Prince*. Harcourt, Brace & World, Inc., New York, 1943, p 39.
- 5 Herbert, Frank: *Dune*. Chilton Book Company, Philadelphia, Pennsylvania, 1965, p 68.
6. Fulton, John F.: *Harvey Cushing, A Biography*. Charles C. Thomas, Publisher, Springfield, Illinois, 1946, p 715.

UNIT SUMMARY FY 82

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

<u>DESCRIPTION</u>	<u>MANPOWER</u>	<u>RANK</u>	<u>MOS</u>
Chief, FARISS, Bruce L., M.D., COL, MC		O6	61C9A
C, Clin Studies Svc FLYMATE, Stephen R., M.D., LTC, MC		O5	61C9B
C, Surg & Animal Care Svc LIEBENBERG, Stanley, D.V.M., MAJ, VC		O4	64C9B
C, Microbiology Svc HIGBEE, James W., Ph.D., MAJ, MSC		O4	68A9B
C, Physiology Svc JACOB, Willis H., Ph.D, MAJ, MSC		O4	68J9B
C, Biochemistry Svc LITTLE, James S., Ph.D., MAJ, MSC		O3	68C9C
NCOIC MCDONALD, Karl O.		E5	91T2R
Med Lab Spec JONES, Richard E.		E7	92B4R
OR Tech SATTEFIELD, Thomas		E4	91D1R
Vet Animal Spec PADILLA, Hector		E5	91T2R
Vet Animal Spec MORMILE, Andrea K.		E4	91T1R
Vet Animal Spec FRYSLIE, Paul M.		E3	91T1R

<u>DESCRIPTION</u>	<u>RANK</u>	<u>MOS</u>
Med Tech GARRISON, Mina J.	GS9	0644
Med Tech KETTLER, Thomas M.	GS9	0644
Med Tech MATEJ, Louis A.	GS9	0644
Edit Asst/Steno WHITTEN, Nancy J.	GS6	1087
Sec/Steno HOUGH, Eugenia R.	GS4	0318
Maintenance Worker MALLOUF, Jerry	WG7	4749

FUNDING

MEDCASE Equipment	\$ 135,179.00
Capital Equipment	1,460.00
Civilian Salaries	116,785.00
Consumable Supplies	81,688.00
Contractual Services	<u>5,323.00</u>
TOTAL	\$ 340,435.00

3. Progress

During FY 82 there were 236 active protocols that received administrative and/or technical support during the year. Of these, 158 are presently ongoing; 65 were completed; and 13 were terminated.

There were 36 publications, 7 papers are in press, and 30 papers have been submitted to journals for possible publication. There were 28 presentations at regional, national or international meetings resulting from these protocols.

Five theses from research protocols were presented and accepted as partial fulfillment of the requirements of the USA Health Services Nurse Anesthetists Course.

4. Committee Members

Commander

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

CLINICAL INVESTIGATION COMMITTEE

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PUBLICATIONS.....FY 82

DEPARTMENT OF CLINICAL INVESTIGATION

Publications:

Little, J.S.: Effect of *Streptococcus pneumoniae* Infection on the Synthesis of Rat Liver Plasma Membranes. Proc Soc Exp Bio Med 167: 284-89, 1981.

Little, J.S. and Canonico, P.G.: Biochemical and Cytological Aspects of Liver Cell Function During Infection. In The Physiologic and Metabolic Response of the Host. Powanda, M.C. and Canonico, P.G. (ed), Elsevier/North-Holland Biomedical Press, 1981, pp 97-129.

Plymate, S.R., et al: Receptors Reconsidered: A 20 Year Perspective (Chapter 1); Mullerian-Inhibitin Substance: An Update (Chapter 8); and The Serum Transport of Steroid Hormone (Chapter 11) in Recent Progress in Hormone Research, Vol 38, Proceedings of the 1981 Laurentian Hormone Conference, Roy O Greep (ed), Academic Press, New York, 1982.

Smith, M.L. and Lugman, W.A.: Prolactin in Seminal Fluid. Arch Andrology 9(2): 105-13, 1982.

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. JCEM 53(5):1021-24, 1981

Ward, G.S. and Byland, R.R.: Concentrations of Halothane in Veterinary Operating and Treatment Rooms. JAVMA 180:174-77, 1982.

Ward, G.S. and Byland, R.R.: Concentrations of Methoxyflurane and Nitrous Oxide in Veterinary Operating Rooms. Amer J Vet Res 43(2): 360-362, 1982.

Ward, G.S., Guiry, C.C., Alexander, L.L.: Tetracycline-Induced Anaphylactic Shock in a Dog. JAVMA 180:770-771, 1982.

Accepted for Publication:

Liebenberg, S.P.: Bone Marrow Depletion as a Coincidental Finding to Hypothermia in *Macaca mulatta*. Accepted by J Med Primatology July 1982

Submitted for Publication: (Dept Clinical Investigation - Cont)

Jacob, W.H., Smith, M.L., Plymate, S.R., Fariss, B.L., Darrow, R.: Variations in the Composition of Human Semen. Submitted to Fertil Steril, Feb 82.

Hauer, E.C. and Little, J.S.: An Assay of RNA Synthesis in Hepatic Nuclei from Control and *Streptococcus pneumoniae* Infected Rats. Submitted to Proc Soc Exp Bio Med, Jul 82.

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 Reticuloendothelial Society, Aug 82.

Plymate, S.R., Fariss, B.L., Leonard, J.M., and Paulsen, C.A.: Sex Hormone Binding Globulin Changes with Androgen Replacement. Submitted to JCEM, Aug 82.

Plymate, S.R., Smith, W.D., and Fariss, B.L.: Recovery of Fertility Following Vasovasotomy. Submitted to Andrologia, Apr 82.

Plymate, S.R. and Ward, G.S.: The Effect of Lowered Prolactin on Hypothalamic Pituitary Testicular Function in the Male Rat. Submitted to Endocrinology, Apr 82.

DEPARTMENT OF EMERGENCY MEDICINE

Publication:

Dice, W.H., Ward, G.S., Kelley, J., and Kilpatrick, W.R.: Pulmonary Toxicity Following Gastrointestinal Ingestion of Kerosene. Ann Emerg Med 11(3):138-142, 1982.

Submitted for publication:

Benjamin, G.C.: Sickle Cell Anemia - Therapeutic Approaches. Submitted to Mil Med, Aug 82.

DEPARTMENT OF FAMILY PRACTICE

Submitted for Publication:

Madlon-Kay, D.J. and Crumrine, M.R.: Gonorrhea Screening in Women: When Is It Cost Effective? Submitted to JAMA, Feb 82.

DEPARTMENT OF MEDICINE

Publications:

Riesbroeck, R.C., Albers, J.J., Wahl, P.W., Weinberg, C.R., Bassett, M.L., and Bierman, F.F.: Abnormal Composition of High Density Lipoproteins in Non-Insulin Dependent Diabetics. Diabetes 31:126, 1982.

Covelli, H.D., Beekman, J., and Weled, B.: Efficacy of Continuous Positive Airway Pressure Administered by Face Mask. Chest 81: 147-50, 1982.

Covelli, H.D., Black, J.W., Olson, M.S., and Beekman, J.F.: Respiratory Failure Precipitated by High Carbohydrate Loads. Ann Int Med 95: 879-81, 1981.

Gibbons, R.R.: Design for A Successful Morning Report. Mil Med 147: 678-70, 1982.

Harris, J.M., Jr.: The Hazards of Bedside Bayes. JAMA 246: 2607-09, 1981.

Harris, J.M., Mergel, M.B., and Malik, A.H.: Mega Cisterna Magna: diagnosis Using Metrizamide Computed Tomographic Cisternography. Spinal Cord 20: 260-262, 1982.

Hughes, D.R. and McWaters, F.J.: Abdominal Aortic Aneurysm with Central Obstruction of Superior Mesenteric Artery. Amer J Gastroenterol 74: 88-98, 1981.

Kroedel, A.R., et al: Unexplained Fevers in Patients with Naso-
pharyngeal Carcinoma. JAMA 246: 808-808, 1982.

Accepted for publication: (Dept Medicine - Cont)

Hough, D.R., Chan, A., and Davidson, H.: Von Recklinghausen's Disease Associated with Gastrointestinal Carcinoid Tumors. Accepted by Cancer, Apr 82.

Sullivan, M.J., Hough, D.R., and Agodoa, L.C.Y.: Peripheral Arterial Thrombosis Associated with the Nephrotic Syndrome: A Review of the Clinical Spectrum. Accepted by South J Med, Jun 82.

Submitted for Publication:

Bassett, M.L., Przasnyski, E.J., McCowen, Fariss, B.L., and Plymate, S.R.: Serum Angiotensin Converting Enzyme (ACE) Levels in Thyroid Disease. Submitted to Acta Endocrinol, Apr 82.

Colman, L.K. and Baker, T.M.: Lactic Acidosis Associated with Extensive Oat Cell Carcinoma of the Lung - Not Necessarily a Poor Prognostic Sign. Submitted to Ann Int Med, Jan 82.

DEPARTMENT OF NURSING

Publication:

Glor, B.A. and Barko, W.F.: Sociotechnical Systems Using an Industrial Tested Technology to Design Quality Assurance Standards in Health Care Systems. Mil Med 147(4):313-317, 1982.

Theses Accepted as a Requirement of the Nurse Anesthetists Course:

Anderson, C.E. and Patrick, R.E.: A Comparison of the Bain's Anesthesia Circuit to the Circle Absorber System in Relation to Changes in Oxygen Measurements.

Collar, L.D. and Allen, S.D.: A Research Proposal to Study the Effects of Pretreatment with Gallamine, Pancuronium, and Curare on the Action of Succinylcholine.

Kelsch, S.P.: Effect of Hemoglobin Concentration on Depth of Anesthesia Using Enflurane.

Muench, M.L.: The Effects of Anesthetic Waste Gases on Army Nurse Corps Anesthetists.

Plumlee, C.D.: The Effect of Laryngoscopy with Intubation at Variable Time Periods After Lidocaine Spray on Blood Pressure and Heart Rate.

Submitted for Publication:

Frost, J.C. and Herrick, K.H.: Marketing + Innovation: A Proactive Approach to Enhance A Major Hospital Resource. Submitted to Hosp Health Svcs Admin, Mar 82 .

DEPARTMENT OF OB/GYN

Publications :

Lee, R.B. and Park, R.C.: Bladder Dysfunction Following Radical Abdominal Hysterectomy. *Gynecol Oncol* 11:304-08, 1981.

Lee, R.B., Neglia, W., and Park, R.C.: Cervical Carcinoma in Pregnancy. *Obstet Gynecol* 58:584-89, 1981.

Submitted for Publication:

Benson, W.L., Brown, R.L., and Schmidt, P.M.: A Comparison of Short and Long Courses of Ampicillin for Vaginal Hysterectomy. Submitted to *Obstet Gynecol*, Oct 81.

DEPARTMENT OF PATHOLOGY

Publications:

Oberholzer, T.R.: Characteristics of Human Isolates of Unidentified Fluorescent Pseudomonads (UFP) Capable of Growth at 42°C. *J Clin Microb* 14:492-95, 1981.

Oberholzer, T.R. and Back, A.E.: Isolation and Cultivation of *Stenotrophomonas maltophilia*. *J Clin Microbiol* 10: 625-29, 1982.

Oberholzer, T.R. and Polgore, J.K.: Frea-Hydrolyzing *Vibrio parahaemolyticus* Associated with Acute Gastroenteritis. *J Clin Microbiol* 16: 581-83, 1982.

Oberholzer, T.R. and Fowler, D.W.: Evaluation of the Rapid Penicillinase Paper Strip Test for Detection of Beta-lactamase. *J Clin Microbiol* 15: 496-99, 1982.

Submitted for Publication:

Oberholzer, T.R. and Fowler, D.W.: Interactions Between Aminoglycosides, Ethanol, and Phosphate, and Polyamines *lysine* in Bacteria, and Patients. June 1982.

Oberholzer, T.R.: Identification of Nonfermentative Bacteria. (book) Submitted to University Park Press, Baltimore, MD; Mar 82.

Oberholzer, T.R.: Methods for Clinical Bacteriology. (book) Submitted to University Park Press, Baltimore, MD; Mar 82.

Oberholzer, T.R. and Polgore, J.K.: Urine-Positive *Vibrio parahaemolyticus*. Submitted to *J Clin Microbiol*, March 82.

Submitted for publication: (Dept of Pathology - Cont)

Podgore, J.K., Holmes, K.K., and Alexander, E.R.: Asymptomatic *Chlamydia trachomatis* Urethral Infection in Male Military Personnel. Submitted to JAMA, March 82.

Robinson, M.J. and Oberholzer, T.R.: Identification of Pathogenic *Yersinia* Species Using the Kap-ID NHTM System. Submitted to J Clin Microbiol, Sep 82.

DEPARTMENT OF PEDIATRICS

Publications:

Marinelli, G.V. and Pettett, E.G.: The Effect of Sampling Sites on White Blood Cell Count in Healthy Newborns. Clin Research 30(1): 148, 1982.

Marinelli, G.V. and Pettett, E.G.: The Effect of Identical Ventilator Settings in Different Disease States. Clin Res 30:145A, 1982.

Moore, D.C., Ruvalcaba, R.H.A., Smith, E.K., and Felley, V.C.: Plasma Somatomedin-C as a Screening Test for Growth Hormone Deficiency in Children and Adolescents. Hormone Research 16: 49-55, 1982

Accepted for Publication:

Stephan, M., Britz, J., Smith, E., and Aiken, E.K.: Early Corticosteroid Administration in Neonates. J Pediatr, 1982.

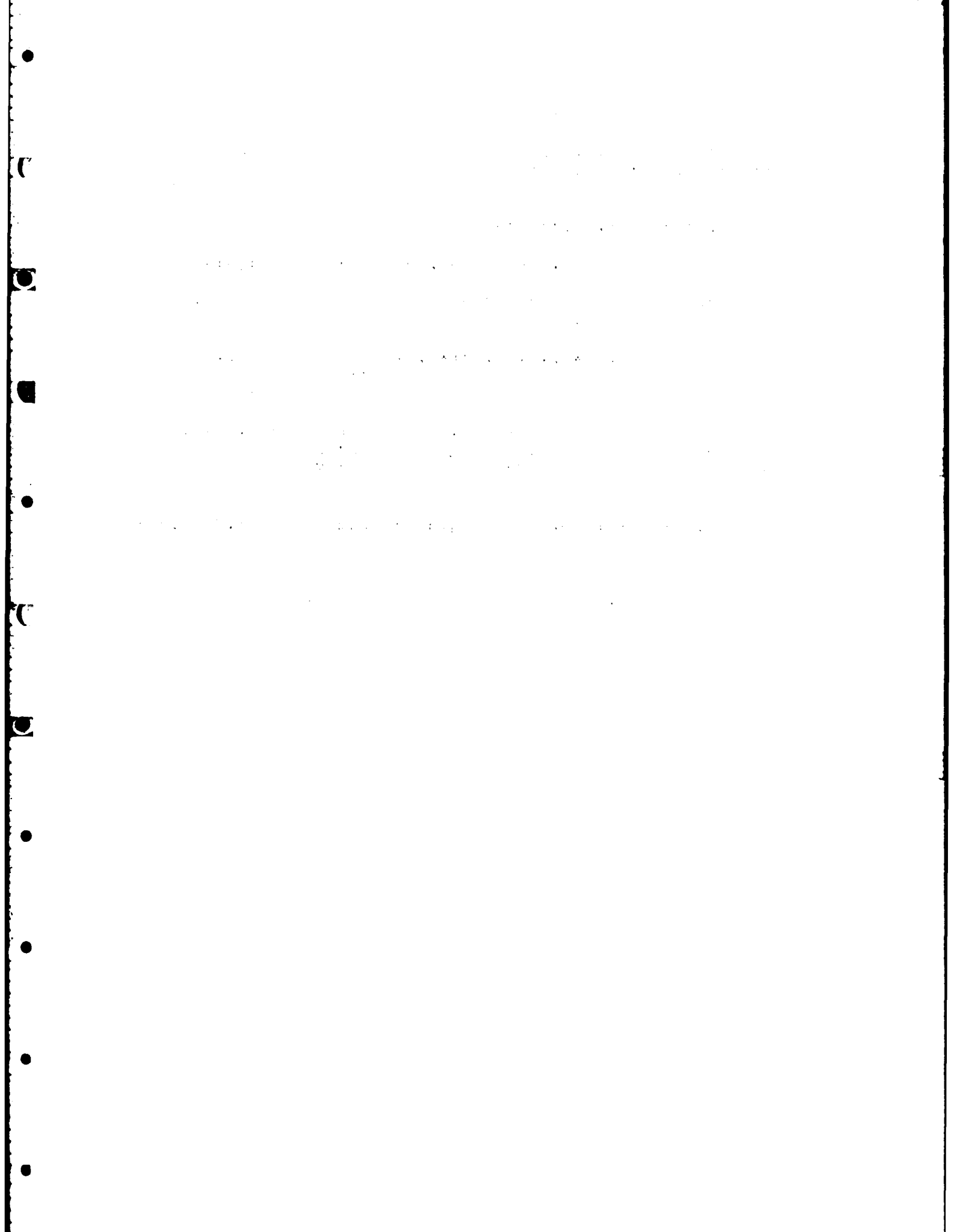
Stephan, M., and Moore, D.C.: Growth Hormone Deficiency in Adolescents - Detection and Treatment. Abstracted from the Proceedings of the 1982 Annual Meeting of the Pediatric Endocrine Society, M.D. Smith, Editor, and Paul W. H. Company, Accepting August 1982.

Submitted for Publication:

Marinelli, G.V., and Pettett, E.G.: White Blood Cell Count in the Neonate - A Study of the Effect of Sampling Sites. Submitted to JAMA, 1982.

Marinelli, G.V., and Pettett, E.G.: The Effect of Identical Ventilator Settings in Different Disease States. Submitted to Clin Res, 1982.

Moore, D.C., Ruvalcaba, R.H.A., Smith, E.K., and Felley, V.C.: Plasma Somatomedin-C as a Screening Test for Growth Hormone Deficiency in Children and Adolescents. Submitted to Hormone Research, August 1982.



Submitted for Publication: (Dept Physical Medicine - Cont)

Saeed, M.A., Dresner, M.L., and Gatens, P.F.: Electromyography of the Bulbocavernosus Muscle in the Evaluation of Neurogenic Bladder. Submitted to J Urology. Jan 81

Saeed, M.A., Dresner, M.L., and Singh, S.: The Bulbocavernosus Reflex in Impotence. Submitted to Arch Phy Med Rehab. Mar 81

DEPARTMENT OF SURGERY

Publication:

Babcock, T.L. and Snyder, B.A.: Spontaneous Pneumothorax Associated with Tuberos Sclerosis. J Thorac Cardiovas Surg 83(1):100-104, 1982.

Dresner, M.L.: Surgical Revision of Scrotal Engulfment. Urol Clin North Am 9:305-310, 1982.

Hays, L.L., Luqman, W.A., Davis, R.K., and Smith, D.R.: Medullary Carcinoma of the Thyroid Masquerading as Idiopathic Vocal Cord Paralysis. Otolaryngol Head neck Surg 90:81-84, 1982.

Hays, L.L., Novack, A.J., and Worsham, J.C.; The Frey Syndrome: A Simple, Effective Treatment. Otolaryngol Head Neck Surg 90: 419-25, 1982.

Accepted for Publication:

Schoenfeld, R.H., Belville, W.D., Jacob, W.H., Buck, A.S., Dresner, M.L., Insalaco, S.J., and Ward, G.S.: The Effect of Dimethyl Sulfoxide on the Uptake of Cisplatin From the Urinary Bladder of the Dog. Accepted by J Amer Osteo Assoc, Sep 82.

Submitted for Publication:

Taylor, W.E., Myer, C.M., Hays, L.L., and Cotton, R.T.: Acute Suppurative Thyroiditis in Children. Submitted to The Laryngoscope, Jan 82.

PRESENTATIONS.....FY 82

DEPARTMENT OF CLINICAL INVESTIGATION

Fariss, B.L. and Plymate, S.R.: Renal Glycosuria: The Evaluation of Blood Sugar and Insulin Responses to Glucose and Tolbutamide. Presented to 3rd Annual Military Endocrinologists Meeting, San Francisco, CA, 15 June 1982, page 12 of the Program and Abstracts of the meeting. (Poster session)

Fariss, B.L., Mallouf, J., Ward, G.S., Liebenberg, S.P., and Plymate, S.R.: Evaluation of the Pituitary-Adrenal Axis in the Pacific Coast Silver Salmon (*Oncorhynchus kisutch*). Presented to the 3rd Annual Military Endocrinologists Meeting, San Francisco, CA, 15 June 1982, page 13 of the Program and Abstracts of the meeting. (Poster session)

Hauer, E.C. and Little, J.S.: Infection Induced RNA Synthesis in Isolated Nuclei. Federation of American Society for Experimental Biology. 15 Apr 82, New Orleans, LA. Abstract 3950, Fed Proc 11(4):945, 1982.

Liebenberg, S.P. and Linn, J.M.: Seasonal and Sexual Influences on Rabbit Atropinesterase. West Coast Meeting, Amer Assoc Lab Animal Sci, Eugene, OR, June 1982.

Liebenberg, S.P., Stills, H.F., and Balady, M.A.: A Comparison of Bacterial Flora Isolated by Transtracheal Aspiration and Pharyngeal Swabs in *Mus mus domesticus*. West Coast Regional Meeting, Amer Assoc Lab Animal Sci, Eugene, OR, June 1982.

Plymate, S.R., Aybel, A., and Fariss, B.L.: Effects of Hyperthyroidism on Intratesticular Testosterone and Androgen Binding Protein. Reproductive Biology Section, Univ Washington, Seattle, WA May 1982.

Plymate, S.R., Ward, G.S., Sailor, K., and Fariss, B.L.: Morphine Sulfate (MS) Addiction Suppresses Gonadotropin Secretion in the Female *Mus mus domesticus*. Presented to The Endocrine Society Meeting, 16-18 June 1982, San Francisco, CA, Abstract #579.

Plymate, S.R., Ward, G.S., Sailor, K., and Fariss, B.L.: Morphine Sulfate (MS) Addiction Suppresses Gonadotropin Secretion in the Female *Mus mus domesticus*. Presented to the 3rd Annual Military Endocrinologists Meeting, 15 June 1982, San Francisco, CA, page 14 of the Program and Abstracts of the meeting. (Poster session)

Plymate, S.R., Leonard, J.M., Paulsen, C.A., and Fariss, B.L.: Effect of Androgen Therapy on Free Testosterone and Testosterone Binding Globulin in Hypogonadal Males. Presented to American Society of Andrology Meeting, Hilton Head Island, SC, February 1982.

DEPARTMENT OF FAMILY PRACTICE

Madlon-Kay, D.J.: Gonorrhea Screening in Women: When Is It Cost Effective? 9th Annual Scientific Meeting, Uniformed Services Academy of Family Physicians, 26 May 82, Seattle, WA. Outstanding presentation of a scientific paper by a resident.

DEPARTMENT OF MEDICINE

Avbel, A., Plymate, S.R., Harwood, J.P., and Fariss, B.L.: Influence of Long Term Testosterone and Human Chorionic Gonadotropin Administration on Intratesticular Testosterone. Presented to Third Annual Military Endocrinologists Meeting, San Francisco, CA, 15 June 82, page 5 of Program and Abstracts for the meeting.

Avebl, A., Plymate, S.R., Fariss, B.L., Ward, G.W., and Garrison, M.J.: Effect of Chronic Administration of Testosterone and Human Chorionic Gonadotropin on Testicular Function. Pacific Coast Fertility Society, 18 Oct 81, Palm Springs, CA. Abstract #48.

Hill, J.C.: Intracoronary Thrombolysis with Streptokinase in the Hyperacute Phase of Myocardial Infarction. Army Association of Cardiology, May 1982.

Treece, G.L.: Medical Boards and the Active Duty Diabetic. Presented to the 3rd Annual Military Endocrinologists Meeting, 15 June 1982, San Francisco, CA, page 9 of the Program and Abstracts for the meeting.

Treece, G.L.: The Integration of Purified Pork Insulin Into the Military Health Care Systems. Presented to the 3rd Annual Military Endocrinologists Meeting, 15 June 1982, San Francisco, CA, page 10 of the Program and Abstracts for the meeting.

DEPARTMENT OF NURSING

Hogeland, S.C.: Measurement of Lymphedema of the Arm. Presented to 13th International Cancer Congress, Seattle, WA, 13 Sep 82.

DEPARTMENT OF PEDIATRICS

Marinelli, P.V. and Pettett, P.G.: The Effect of Identical Ventilator Settings in Different Disease States. Western Conference on Perinatal Research, San Diego, CA, 10-12 Jan 82.

Marinelli, P.V. and Pettett, G.: The Effect of Sampling Sites on White Blood Cell Counts in Healthy Newborn Infants. Amer Acad Pediatrics, District VIII, 7th Annual Conference on Perinatal-Neonatal Medicine, Jackson Hole, Wyoming, May 26-29, 1982.

Mordell, R., Marinelli, P.V., and Pettett, G.: Timing and Evolution of ICH in Infants Weighing less than 2000 grams. Aspen Military Perinatal Conference, Aspen, CO, 18-21 Jul 1982.

Pettett, G.: Army Followup in a Regional Neonatal Referral Program. Amer Acad Pediatrics, District VIII, 7th Annual Conference on Perinatal-Neonatal Medicine, Jackson Hole, Wyoming, May 26-29, 1982.

Rawlings, J.S., Pettett, G., Wiswell, T.E., and Clapper, J.: Estimated Blood Volumes in Polycythemic Neonates as a Function of Birth Weight. 13th Annual Uniformed Services Pediatric Seminar, Bethesda, MD, March 1981.

Ryan, R.M.: Microcomputer Graphics of Neonatal Data. Presented at: Second Symposium on Computers in Perinatal Medicine, May 24-26, 1981. Cleveland, OH.

DEPARTMENT OF SURGERY

Dreger, M.L., Saeed, M.A., Kelville, W.D., and Buck, A.S.: Evaluation of the Pediatric Neurosection of the American Neurological Association. J Neurosurg, 56:1, 1981.

Dreger, M.L., Saeed, M.A., Kelville, W.D., and Buck, A.S.: Evaluation of the Pediatric Neurosection of the American Neurological Association. J Neurosurg, 56:1, 1981.

Dreger, M.L., Saeed, M.A., and Kelville, W.D.: Bulbocavernosus Reflex and the Pediatric Neurosection. J Neurosurg, 56:1, 1981.

Dreger, M.L.: The Pediatric Neurosection: A Review and Critical Evaluation of the Neurosection of the American Neurological Association. J Neurosurg, 56:1, 1981.

Presentations: (Dept Surgery - Cont)

Reid, H.S.: Tourniquet Hemostasis: A Clinical Study.
Presented Annual Meeting Society of Military Orthopaedic Surgeons,
Bethesda, MD, 9 Nov 81.

Schoenfeld, R.H., Belville, W.D., Jacob, W.H., Buck, A.S., Dresner,
M.L., Insalaco, S.J., and Ward, G.S.: The Effect of Dimethyl
Sulfoxide on the Uptake of Cisplatin From the Urinary Bladder of
the Dog. Kimbrough Urologic Seminar, Denver, November 1981.

THE BYRON L. STEGER RESEARCH AWARD

1982 saw the development of a new award at Madigan - the Byron
L. Steger Research Award. The submissions are judged on their
scientific merit, relevance, objectivity of evaluation, inter-
pretation of results, and the potential importance of the
subject of the research. The recipient of this award for 1982
was CPT Hubert S. Reid, MC, for his project entitled "Tourniquet
Hemostasis - a Clinical Study."

Other nominees were:

MAJ William H. Dice, MC - Pulmonary Toxicity following
Gastrointestinal Ingestion of Kerosene

MAJ Richard C. Keniston, MC - Biochemical Correlates of Mortality
Hypoalbuminemia and Vitamin B6 Deficiency

MAJ Arthur R. Knodel, MC - Are Outpatients' Theophylline Levels
Useful? A Clinical Evaluation

MAJ Diane J. Madlon-Kay, MC - Gonorrhea Screening in Women: When
is it Cost-Effective?

MAJ Philip Marinelli, MC - Mechanical Properties of the Premature
Lamb Lung After Antepartum Exposure to Betamethasone

LTC John K. Podgore, MC - Asymptomatic *Chlamydia trachomatis*
Urethral Infection in Male Military Personnel

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1979	CCG 372: Evaluation of Cis-Platinum Diamine Dichloride (CPDD) and 4'-Dimethyl-Epidophyllotoxin-Beta-D-Thenylidene Glucoside (VM-26) for the Treatment of Recurrent Stage IV Neuroblastoma of Childhood, Phase II. LTC Holt (O)	287
1979	CCG 551: A Trial of Memorial Hospital ISA 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, Hydroxycurea, 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. LTC Holt (O)	288
1979	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). LTC Holt (O)	289
1979	CCG 862: An Evaluation of Surgery, Radiation Therapy, and Chemotherapy (Vincristine, Adriamycin, Cyclophosphamide, 5-FU) in the Treatment of Previously Untreated Primary Malignant Hepatoma in Children. LTC Holt (T)	290
1979	CCG 984: Rhabdomyosarcoma X: A Study of the Biology, Clinical, and Histologic Staging, Treatment, and Prognosis in Previously Untreated Children, Phase III. LTC Holt (O)	291

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1980	POB 77/11: A Prospective Randomized Trial of the Utility of HLA-Matched Platelet Transfusions for the Support of Thrombocytopenic Cancer Patients. LTC Holt (O)	299
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1980	POB 78/10: A Phase II Study of Achromobacter Glutaminase in Acute Leukemia. LTC Holt (O)	301
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1980	POB 79/01: Evaluation of Human Lymphoblastoid Interferon and Poly I:C (Stabilized with Poly-L-Lysine and Carboxymethyl Cellulose [Poly(1CLC)]) in the Treatment of Acute Myelocytic Leukemia, CLL, and Various Solid Tumors, Phase II. LTC Holt (O)	303
1980	POB 79/03: Phase II Study of 2'Deoxycoformycin in Acute Lymphoblastic Leukemia. LTC Holt (O)	304

DETAIL SHEETS
FOR
PROTOCOLS

DEPARTMENT OF CLINICAL INVESTIGATION

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 effects 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 libitum*. Group I: This will be the control group of six animals with no treatment. Group II: 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. Group III: 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 pounds 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.

PROGRESS

(81 10 - 82 09) It has been shown that pancreatectomy will not cause diabetes mellitus in the sheep. Fasting blood sugars continue to be normal basally, but IV administration of glucose does show an abnormal utilization factor. Pancreatectomy in the sheep does not interfere with fetal growth and development but lactation is reduced.

STATUS: (0)

TITLE: Adrenal Hyperplasia in Pacific Salmon

PRINCIPAL INVESTIGATOR: COL Bruce L. Fariss, MC

PROFESSIONAL ASSISTANT: 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

(81 10 - 82 09) ACTH stimulation tests and insulin tolerance tests have been done in the salmon and the rainbow trout. The maximal rise following ACTH administration occurs 30 minutes later. The insulin tolerance test is associated with hypoglycemia in 7-8 hours, at which time a rise in cortisol occurs.

PRESENTATION: Fariss, B.L., Mallouf, J., Ward, G.S., Liebenberg, S.P., and Plymate, S.R.: Evaluation of Pituitary-Adrenal Axis in the Pacific Coast Silver Salmon (*Oncorhynchus kisutch*). Society of Military Endocrinologists, poster session, 15 Jun 82, San Francisco, CA.

STATUS: (O)

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

PRINCIPAL INVESTIGATOR: COL Bruce L. Fariss, MC

PROFESSIONAL ASSISTANTS: LTC George S. Ward, VC
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 norepinephrine. The differences between the restrained and non-restrained values will be compared by the paired t-test method of statistical analysis.

PROGRESS

(81 10 - 82 09) The restrained rabbit has been found to develop hyperglycemia which continues to rise for three hours and then plateaus. There is an associated rise in plasma catecholamines but poor correlation to the blood sugar levels.

STATUS: (0)

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: A Comparison of the Effect of Glucose vs Sodium Butyrate
on the Levels of Insulin and Glucagon in Normal and
Pancreatectomized Sheep

PRINCIPAL INVESTIGATOR: COL Bruce L. Fariss, MC

PROFESSIONAL ASSISTANTS: MAJ Stanley P. Liebenberg, VC
CPT Duane J. Jeffers, MC

WORK UNIT NO: 82/18

TECHNICAL OBJECTIVE

To delineate additional mechanisms of insulin and glucagon release in sheep, with specific attention directed at the role of the pancreas in the secretion of these two hormones.

METHOD

Six adult female sheep will be fasted for 24 hours and then given 25 gm IV glucose. Blood samples will be drawn every 10 minutes for 90 minutes and glucose, insulin, and glucagon levels will be measured in these samples. Two weeks later, the animals will again be fasted for 24 hours and then receive 0.2 mmole/kg body weight of a solution of sodium butyrate adjusted to pH of 7.4. Again blood samples will be obtained every 10 minutes for 90 minutes as above. Approximately 3 weeks or as soon as technically possible after the first administration of sodium butyrate, all sheep will undergo complete pancreatectomy. Glucose and sodium butyrate in the same amounts used previously will be administered and the same measurements of glucose, insulin and glucagon will be performed.

PROGRESS

(82 01 - 82 09) The administration of sodium butyrate to non-pancreatectomized sheep causes a marked rise in insulin and glucagon levels. There is a rise in blood sugar levels, likewise. In the pancreatectomized sheep, there is no rise of glucose, insulin, or glucagon.

STATUS: (O)

TITLE: The Effects of Alloxan and Streptozotocin in
Pancreatectomized Sheep

PRINCIPAL INVESTIGATOR: COL Bruce L. Fariss, MC

PROFESSIONAL ASSISTANTS: LTC Preston Carter, MC
MAJ Michael Fincher, MC
MAJ Robert Jackson, MC
MAJ Stanley Liebenberg, VC

WORK UNIT NO: 82463

TECHNICAL OBJECTIVE

To further elucidate the mechanisms of hyperglycemia following the administration of alloxan or streptozotocin.

METHOD

Twelve (12) adult ewes given food and water *ad libitum* will be subjected to total pancreatectomy utilizing a modification of the method described by Jarret, et al. Prior to administration of the alloxan or streptozotocin, sodium butyrate in a dose of 1.25 mM/kg pH 7.0 will be administered intravenously to substantiate the completeness of the pancreatectomy. Basal and then 10 minute-interval for 90 minutes blood samples will be drawn for glucose, glucagon, and insulin determinations. Glucagon will be determined, using an RIA method and the antibody of Uniger. The insulin will be determined utilizing an RIA method. Glucose will be determined by an alkaline ferricyanide method utilizing a Technicon instrument. One week following pancreatectomy, six of the pancreatectomized sheep will be given 65 mg/kg body weight of alloxan as a bolus, intravenously. The other six pancreatectomized sheep will be given streptozotocin freshly dissolved in 0.01 M citrate buffer, pH 4.3, 100 mg/kg body weight. Daily blood samples for glucose will be drawn in both groups. Statistical analysis will be performed by the appropriate Student's t Test. The primary analysis, though, will be whether there is the development of diabetes mellitus, following the addition of alloxan or streptozotocin in the pancreatectomized sheep.

PROGRESS

(82 07 - 82 09) The supplies for the performance of this study have been obtained. No animals have been studied to this date.

STATUS: (0)

TITLE: Evaluation of the Cyclic Nature of Human Semen Content

PRINCIPAL INVESTIGATOR: MAJ Willis H. Jacob, MSC

PROFESSIONAL ASSISTANTS: MAJ 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

Test Subjects: Twenty to thirty healthy volunteers will be selected 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.

Semen Collection and Analysis: Semen samples will be collected daily for a period of 20-25 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 (24°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.

PROGRESS

(78 04 - 82 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

Evaluation of the Cyclic Nature of Human Semen Content - Jacob

correlations were found between sperm density and total counts in ten 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 are now attempting to determine whether a cyclic pattern can be seen in long term studies. In addition, some consideration is being given to determining extratesticular factors which may influence sperm count.

Two manuscripts are now in preparation.

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

STATUS: (O)

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 - 82 09) Efforts are continuing to obtain a sufficient number of subjects to complete this study. In addition, comparisons between various methods for measuring prostaglandins and other semen components are being made to determine the most efficacious assay method.

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.

STATUS: (O)

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

PRINCIPAL INVESTIGATOR: MAJ Willis H. Jacob, MSC

PROFESSIONAL ASSISTANTS: LTC George S. Ward, VC
MAJ John B. McClain, MC
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 1 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 - 82 09) Six female monkeys and one male monkey studied at this time. No change in blood pressure could be detected in the female monkeys under the conditions of this study. However, there was a noticeable decrease in systolic, diastolic, and mean pressures in the male. The number of male monkeys studied will be expanded to attempt to validate this finding in the single animal. We are now awaiting additional animals and powered naloxone to complete this study. Due to the departure of LTC Ward, MAJ Jacob has become the principal investigator on this protocol.

STATUS: (0)

TITLE: Use of the CO₂ Laser in Pharyngeal Surgery in the Dog

PRINCIPAL INVESTIGATOR: MAJ Stanley P. Liebenberg, VC

PROFESSIONAL ASSISTANTS: COL Leonard L. Hays, MC
MAJ Del Ray Maughan, MC
CPT Wallace E. Taylor, MC

WORK UNIT NO: 82/54

TECHNICAL OBJECTIVE

To define a better technique for achieving a more complete excision of vocal cord tissue in the canine.

METHOD

Twelve large mongrel dogs will be anesthetized with ultra-short acting barbiturate and placed in dorsal recumbancy. Suspension laryngoscopy will then be employed to visualize the larynx. The CO₂ laser will then be used to perform a partial laryngectomy. Supplemental oxygen will be administered to the animal using the Saunders jet ventilating device to displace CO₂ from the lower airways and to facilitate viewing of the operative site during actual tissue removal with the laser. The opposite hemilarynx will be left unoperated to serve as a control. Each dog will be placed on a liquid diet for 24 hours post-op and will then be fed a semi-soft diet for the next 5 days. Each dog will be endoscoped at weekly intervals until healing is completed. At 14 days post-op two dogs will be reanesthetized in the same manner and tissue specimens will be collected from the operative site for histopathologic studies. The vocal cord will then be removed from the opposite side, the skin and larynx will be sutured and the dog allowed to recover. At 30 and 60 days post-op, two additional dogs at each time will have similar laryngeal tissues biopsied and complete debarking performed. The remaining six dogs will not have the operative site biopsied but will be released following the 60 day post-op exam and debarking of the side not performed initially. Thirty-five mm photographs will be taken of the operative and post-op procedures and of all post-op endoscopies.

PROGRESS

(82 05 - 82 09) Using the CO₂ laser, total ventriculocordectomies and hemilaryngectomies were performed on several dogs of mixed ages and sizes. The results in all cases performed were totally favorable. A paper from this protocol has been accepted for presentation at the annual meeting of the American Association for Laboratory Animal Science in the fall of 1982, and a paper is being prepared for submission for publication.

STATUS: (C)

TITLE: Effect of *Streptococcus pneumoniae* Infection on the Binding of Insulin to Plasma Membranes Isolated from Rat Liver

PRINCIPAL INVESTIGATOR: MAJ James S. Little, MSC

PROFESSIONAL ASSISTANTS: MAJ James Anderson, MC
CPT Jerald Merrill, MSC

WORK UNIT NO: 82/24

TECHNICAL OBJECTIVE

To determine if *Streptococcus pneumoniae* infection affects the binding of insulin to hepatic plasma membranes and to determine if observed results can be correlated with hepatic alterations known to occur during this infection.

METHOD

Male albino rats (150-250 gm) of the Sprague-Dawley strain will be maintained on stock lab chow and tap water, *ad libitum* and acclimatized to a 12-hr day/night cycle for at least 12 days prior to experimentation in order to eliminate circadian variations. Rats will be inoculated subcutaneously with 3×10^5 to 6×10^5 heat-killed or virulent *S. pneumoniae* serotype I, A5 strain organisms. At 40 hr post inoculation, plasma membranes will be prepared from both groups of rats. These membranes, which have been shown to be essentially devoid of other cellular contaminants, will be washed by suspension and recentrifugation to remove absorbed cytoplasmic proteins. Preliminary experiments conducted at BAMC will be designed to determine optimum plasma membrane protein concentration, time, pH, and temperature for the binding of labeled insulin to isolated plasma membranes. In a total incubation volume of 450 microliters, buffer, plasma membranes, cold standards, and labeled hormone will be incubated at the predetermined temperature, pH, and time. Non-specific binding is determined by parallel incubation with excess cold hormone. Scatchard analysis will be used to assess affinity and binding capacity of 125 I insulin to plasma membranes isolated from 10 control and 10 infected animals. Group mean values will be compared by the unpaired Student's t test and differences will be considered significant at $P < 0.05$.

PROGRESS

(82 01 - 82 09) The start of this protocol was delayed due to the departure of the assistant who was to do the insulin binding. However, purified plasma membranes have been prepared from both control and infected rats. Infection did not alter the membrane purity or yield. Preliminary studies have determined the optimum time, temperature, and pH of binding. Scatchard analysis will now be performed to determine if maximum binding capacity and affinity of the receptor for insulin is altered during infection.

STATUS: (O)

TITLE: The Effect of *Streptococcus pneumoniae* Infection on the Binding of Thyroxine (T₄) to Purified Rat Liver Plasma Membrane

PRINCIPAL INVESTIGATOR: MAJ James S. Little, MSC

PROFESSIONAL ASSISTANT: MAJ Stanley P. Liebenberg, VC

WORK UNIT NO: 82/65

TECHNICAL OBJECTIVES

To determine if there are specific receptors for T₄ on hepatic plasma membranes; if these receptors are affected by *S. pneumoniae* infection; and if receptor changes can be correlated with alterations known to occur in hepatic metabolism during infection.

METHOD

Male Sprague-Dawley rats (200-250 g) will be maintained on stock Purina lab chow and tap water *ad libitum*. All rats will be acclimated to a 12-hour day-night cycle for 14 days before experimentation to standardize circadian variations. Rats will be inoculated with varying doses (3×10^4 - 3×10^5 ; 6×10^5 - 1×10^6 ; and 6×10^6) of heat-killed (control) or virulent (infected) colony-forming units of *S. pneumoniae*, serotype I, A-5 strain. After inoculation, all rats will be fasted but allowed access to water and euthanized 40 hours after inoculation, a time corresponding to the midpoint of the night cycle. Fasting of controls will be necessary because infected rats are anorectic. Hepatic plasma membranes will be isolated and the purity assessed. For initial studies to determine optimum time, temperature, protein concentration, and pH, plasma membranes from control or infected animals will be pooled. Once the binding assay has been optimized with respect to time, temperature, plasma membrane protein concentration, and pH, plasma membranes will be prepared from individual control and infected animals. Each control or infected group will contain at least 6 animals. Three groups of infected animals will be studied with each group receiving an increasingly larger dose of *S. pneumoniae*. Receptor assays will be performed in a total volume of 0.2 ml contained in 10x75 mm borosilicate glass test tubes. The assay will contain ¹²⁵I T₄ (50,000 to 100,000 counts per minute), from 0 to 10⁻⁵ M cold T₄, and plasma membranes at the determined concentration. All components will be diluted in buffer (T₄ Buffer) containing 0.25 M sucrose, 20 mM Tris-Cl, 1 mM MgCl₂, 2 mM EDTA, 50 mM NaCl, 1 mM dithiothreitol, and 5% (v/v) glycerol. Assays will be performed in triplicate at the optimal temperature and time. Assays will be stopped by the addition of 1.0 ml of ice cold T₄ buffer and centrifugation at 2200 g for 15 minutes. Following centrifugation, the supernatant will be aspirated and the plasma membrane pellets washed by the addition of 1.0 ml of ice cold T₄ buffer. The

The Effect of *Streptococcus pneumoniae* Infection on the Binding of Thyroxine (T₄) to Purified Rat Liver Plasma Membrane - Little

membranes will again be pelleted as described above, the supernatants aspirated, and the membranes counted. Non-specific binding will be determined by parallel incubation with excess cold hormone (10^{-5} M). Scatchard analysis will be used to assess the affinity and maximum binding capacity of the receptor for T₄. Counting efficiency will be determined by the channel ratio method.

PROGRESS

Hepatic plasma membranes were isolated and purified from control and *Streptococcus pneumoniae* infected rats by differential and isopycnic density gradient centrifugation. Infection did not affect the purity of the isolated membranes or the yield. Infection caused a significant decrease in both total and free serum thyroxine (T₄). The mechanism of this decrease has not been determined. The binding of T₄ to plasma membranes isolated from control and infected rats was optimized with respect to time, temperature, and pH. Scatchard analysis of membrane binding confirmed high affinity, low capacity sites as well as lower affinity sites for T₄. Hepatic plasma membranes from rats inoculated with varying doses of virulent *S. pneumoniae* were compared to those from rats inoculated with heat-killed organisms. In infected plasma membranes, T₄ maximum binding capacity (MBC) of the high affinity site decreased significantly as the infection progressed. The affinity of the receptor for T₄ did not change. Neither MBC nor affinity of the lower affinity site was altered by infection. In summary, (1) there is saturable high affinity binding of T₄ to purified rat liver plasma membranes; (2) during *S. pneumoniae* infection, serum total and free T₄ are significantly decreased and the MBC of the high affinity site for T₄ is decreased; (3) altered receptor number or affinity cannot explain the decreased serum T₄ values or the observed hepatic metabolic alterations known to occur during *S. pneumoniae* infection.

A paper is being prepared for submission for presentation at the annual meeting of The Federation of American Societies for Experimental Biology.

PLATE: (0)

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

TECHNICAL OBJECTIVE

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

METHOD

Three groups of male rats >90 days old (20 rats/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 propionate 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 propionate and Group 3 will also receive the HCG at a dose of 6 U/100 gm 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

(81 10 - 82 09) The technical portion of this protocol was completed and a manuscript is in preparation. The study demonstrated that testosterone and HCG are additive in depressing testicular steroidogenesis and seminiferous tubule function.

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

Effect of Chronic Administration of Testosterone and Human Chorionic Gonadotropin on Testicular Function. Pacific Coast Fertility Society, Palm Springs, CA, 16 Oct 81; abstract #48.

STATUS: (O)

TITLE: Testosterone and HCG Effects on Testicular Steroidogenesis

PRINCIPAL INVESTIGATOR: LTC Stephen R. Plymate, MC

PROFESSIONAL ASSISTANTS: COL Bruce L. Fariss, MC
MAJ Stanley 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 intratesticular 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 epididymus removed, weighed, and frozen. Intratesticular DHT, E_2 , and ARB 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 10 - 22 09) The technical portion of this protocol was completed and a manuscript is in preparation. This study demonstrated that administration of testosterone and HCG had a greater effect on suppression of testicular testosterone levels than administration of testosterone alone. Testosterone alone lowered intratesticular testosterone by LH suppression and increased

Testosterone and HCG Effects on Testicular Steroidogenesis -
Plymate

intratesticular E₂. The combined effect of HCG and testosterone appeared to be by further increases in intratesticular E₂ as well as greater suppression of serum LH.

STATUS: (O)

PRESENTATION: Influence of Long Term Testosterone (T) and Human Chorionic Gonadotropin (HCG) Administration on Intratesticular Testosterone. 3rd Annual Military Endocrinologists Meeting, San Francisco, CA, 15 June 1982.

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 minutes. Next, a bolus of naloxone will be given and samples drawn for 120 minutes. 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 minutes. 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. 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 10 - 82 09) The technical portion of this protocol was completed and a manuscript is in preparation. This study demonstrated a significant suppression of LH by chronic morphine sulphate addiction unrelated to weight loss and this suppression was also seen with acute morphine sulphate administration when a sensitive bioassay for LH was used. This suppression is reversed by Naloxone.

STATUS: (0)

The Effect of Opiates on the Release of Gonadotropins in the
Macaca nemestrina - Plymate

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

Morphine Sulfate Addiction Suppresses Gonadotropin
Secretion in the Female *Macaca nemestrina* .
64th Annual Meeting, The Endocrine Society, San
Francisco, CA, 16 June 1982. Abstract #579,
Abstracts of the 64th Annual Meeting of The
Endocrine Society, June 1982, page 224.

IBID, 3rd Annual Meeting, Military Endocrinologists
Society, San Francisco, CA, 15 June 82, poster
session, page 14 of the abstracts.

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

PRINCIPAL INVESTIGATOR: LTC Stephen R. Plymate, MC

PROFESSIONAL ASSISTANTS: COL Bruce L. Fariss, MC
MAJ Willis H. Jacob, MSC

WORK UNIT NO: 82/23

TECHNICAL OBJECTIVE

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

METHOD

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

PROGRESS

(82 01 - 82 09) H^+ DHT linked to SHBG, using P-125 columns in tandem, has been separated. Using a high salt gradient, SHBG has successfully been isolated.

STATUS: (0)

TITLE: The Incidence of Varicocele in an Unselected Male Population

PRINCIPAL INVESTIGATOR: LTC Stephen R. Plymate, MC

PROFESSIONAL ASSISTANTS: COL Bruce L. Fariss, MC
LTC William D. Belville, MC
MAJ Willis H. Jacob, MSC
Alton B. Peyton, M.D., (COL Ret), DAC
William J. Bremner, M.D., VA Hospital, Seattle

WORK UNIT NO: 82/42

TECHNICAL OBJECTIVE

To determine the incidence and functional significance of a testicular varicocele in an unselected male population.

METHOD

One thousand (1000) ROTC cadets will be examined during summer physicals for the presence of varicocele. Twenty men in whom a varicocele is found will be randomly selected as subjects. Blood will be drawn for LH, FSH, and prolactin. A LH-RH stimulation test will be performed by giving 100 µg of LH-RH and drawing baseline and 45-minute LH and FSH levels. Sperm counts will be obtained on all subjects and a fertility history will be obtained. A group of 20 normal volunteers will have sperm counts and the LH-RH test performed. Data will be analyzed by the appropriate statistical analysis using the non-paired t-test and analysis of variance where appropriate.

PROGRESS

(82 03 - 82 09) This was terminated due to the inability of the investigators to obtain a population.

STATUS: (T)

TITLE: Effect of HCG and T on Regulation of Leydig Cell Function

PRINCIPAL INVESTIGATOR: LTC Stephen R. Plymate, MC

PROFESSIONAL ASSISTANTS: COL Bruce L. Fariss, MC
MAJ James S. Little, MSC
Mina Garrison, M.T.
John White, Ph.D.
Louis Matej, M.T.

WORK UNIT NO: 82/67

TECHNICAL OBJECTIVE

To expand further the studies which the investigators have reported showing the relationship between LH and testosterone (T) in regulating testosterone production. The current study is designed to determine the time course of events following HCG administration to testosterone suppressed animals by determining changes in intratesticular testosterone and LH receptors at specified intervals following HCG administration.

METHOD

Male Wister rats >90 days and weighing 200-250 gms will be given testosterone enanthate 150 µgm/100 gm body weight IM biweekly for six weeks and control animals will be injected with sesame oil. This will be time zero time. Eight control and eight treatment animals will be sacrificed at this point. Then HCG 18 IU each day will be started on all animals treated with T and control animals will be injected daily with saline. Eight control and eight treatment animals will be sacrificed at 3, 7, 14, 28, and 56 days after zero time and trunk blood collected. Testes and epididymae will be removed, trimmed of fat, weighed, and frozen at -70°C until assayed. Serum will be separated and frozen until assayed. Serum will be analyzed for T and LH. Testes will be analyzed for T, E₂, ABP, and HCG receptors. Testes from six control and six treatment animals sacrificed at 7, 28, and 56 days will be prepared for electron-microscopy. Electron-microscopy and stereological analysis of the smooth endoplasmic reticulum in the Leydig cells will be performed. Serum T and LH will be performed by RIA. The testes, while still frozen, will be cut in half. One half along with the epididymis, will be thawed and homogenized in a phosphosaline buffer pH 7.4 with 6 ml used per gm of tissue. This homogenate will then be assayed for T, E₂, and ABP and results expressed per ng of protein. The other half of the testes will then be assayed for HCG/LH receptors. Comparison between groups will be made using the non-paired Student's T test or a non-parametric test such as the Mann Whitney test.

PROGRESS

(82 08 - 82 09) Supplies have been ordered. This project will begin as soon as they are received.

STATUS: (0)

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 Lower Body Positive Pressure on Tissue Perfusion

PRINCIPAL INVESTIGATOR: CPT Carey D. Chisholm, MC

PROFESSIONAL ASSISTANTS: None

WORK UNIT NO: 82/22

TECHNICAL OBJECTIVE

Lower extremity ischemia and compartment syndromes have recently been attributed to the use of pneumatic trousers. These detrimental effects may be related to the quantity and duration of pressure applied. The purpose of this protocol is to study the effect of lower body positive pressure over time and at different pressures in normal volunteers.

METHOD

Intramuscular compartment pressure will be monitored throughout the study by the wick catheter technique. Military-Anti-Shock Trousers (MAST) will be inflated to 30 mm Hg for 60 minutes, increased to 60 mm Hg for 20 minutes, decreased to 30 mm Hg for 10 minutes, and finally deflated. Peripheral blood samples for venous pH, lactate, CPK, myoglobin, and K+ will be obtained prior to inflation of the MAST and upon deflation from 60 mm Hg to 30 MM Hg. Blood pressure will be monitored at 10 minute intervals throughout the study.

PROGRESS

(82 01 - 82 09) The study has been completed and a paper is in the final draft stage. The anterior tibial compartment pressures of 8 healthy volunteers were studied at varying PASG inflation pressures. A linear correlation between PASG pressure and IMP exists with >90% of the externally applied pressure being transmitted to the muscle compartment. All subjects developed IMP >50 mm Hg at PASG inflation of 60 mm Hg. Externally applied pressure appears to create a condition which may stimulate or lead to a compartment syndrome. Inflation pressure should be closely monitored during PASG application as IMP may be assumed to be at least as high as inflation pressure. The lowest effective PASG pressure should be utilized.

STATUS: (C)

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
MAJ 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 inadequate. 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 initiation 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

(81 10 - 82 09) 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 suggested and subsequent experiments confirmed that the ethanol treated animals were not any more susceptible than the controls and, in fact, may be less susceptible. It was confirmed that serum enzyme levels were not altered by ethanol treatment and that ethanol had a protective effect when animals were subsequently intubated with acetaminophen.

STATES: (C)

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 three 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 medication 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 the 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 followup of their condition. If the patient was admitted, the physician will be asked for his reasons for admission.

PROGRESS

(81 02 - 82 06) Data has been collected and has been analyzed. A manuscript is being prepared.

STATUS: (C)

TITLE: Emergency Room Procedure Training

PRINCIPAL INVESTIGATOR: CPT Steven C. Dronen, MC

PROFESSIONAL ASSISTANTS: LTC George S. Ward, VC
MAJ Wilson R. Kilpatrick, MC
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; cricothyrotomy; 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

(81 99 - 82 02) Three residents practiced techniques on this program. In February 1982, the protocol was rewritten and approved by the Committees under the same name as MAMC #82/25.

STATUS: (C)

TITLE: Emergency Room Procedure Training

PRINCIPAL INVESTIGATOR: CPT Steven C. Dronen, MC

PROFESSIONAL ASSISTANTS: LTC Samuel T. Coleridge, MC
MAJ Stanley P. Liebenberg, VC

WORK UNIT NO: 82/25

TECHNICAL OBJECTIVE

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

METHOD

The procedures listed below will be performed in two separate sessions under the supervision of a staff member and the veterinarian assigned to Clinical Investigation. All animals will be anesthetized and then will be sacrificed immediately after the procedures. All participants will be instructed concerning the importance of humane and professional treatment of the animals and the involvement of any participant who does not adhere to these principles will be terminated.

PART I:

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

PART II:

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

PROGRESS

(82 02 - 82 09) Incoming Emergency Medicine Residents have been trained in the first part of the procedures protocol. The second phase will be completed later in the calendar year.

STATUS: (0)

TITLE: Hemodynamic Responses to Application and Removal of Nitroglycerin Ointment in Normal Subjects

PRINCIPAL INVESTIGATOR: MAJ Kenneth Frumkin, MC

PROFESSIONAL ASSISTANTS: CPT Ted A. McMurry, MC

WORK UNIT NO: 82/17

TECHNICAL OBJECTIVE

To determine the temporal characteristics of the action of topically applied nitroglycerin on pulse and blood pressure volunteers. The onset of action, time required for maximal hemodynamic response, and the time for return to baseline values after the ointment has been removed will be measured.

METHOD

Sixteen (16) healthy male volunteer subjects with a normal blood pressure and pulse without orthostatic changes during the baseline phase of the experiment will be used. An automated Critikon blood pressure cuff and an automatic dental chair in the fully erect position will be used. Initially, orthostatic vital signs will be taken. Patients will then have pulse and blood pressure taken after being supine for two minutes and again after two minutes of standing. Those with a decrease in systolic blood pressure of 20, a decrease in diastolic blood pressure of 10, or a rise in pulse of >20 beats /minute will be excused from the study. Non-orthostatic patients will then sit erect in the chair and pulse and blood pressure will be recorded automatically by the device every two minutes for 14 minutes (baseline). Two inches (30 grams) of 2% nitroglycerin ointment will then be applied to a 53 cm² area at the left costal margin in the midclavicular line. Blood pressure and pulse will be recorded every two minutes by the machine and also by a physician. Symptomatic hypotension will be treated by Trendelenberg position and other standard means. After 40 minutes of continuous monitoring, one half of the patients (randomly assigned) will have the nitroglycerin paste completely wiped off with a clean terrycloth towel. Monitoring of these patients will continue for another 60 minutes. The control subjects will have the paste left on and will be monitored for the same period of time.

PROGRESS

(81 11 - 82 09) Four of the proposed sixteen subjects have been tested. There have been no adverse reactions. Preliminary analysis suggests that the effects of nitroglycerin ointment on pulse and blood pressure in normal subjects is not as predictable as the literature implies.

STATUS: (0)

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 ASSISTANTS: 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 assistant 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 was completed and data has been analyzed. Many of the patients who came to the ER did not have a good idea of how severe their illness was. A paper has been written and is being reviewed by the various authors before submission.

STATUS: (C)

DETAIL SHEETS
FOR
PROTOCOLS

DEPARTMENT OF FAMILY PRACTICE

TITLE: Diamine Oxidase Levels and Asthma in Pregnancy

PRINCIPAL INVESTIGATOR: CPT Julie Ducey, MC

PROFESSIONAL ASSISTANTS: MAJ James S. Little, MSC
MAJ Rebecca Sullivan, MC
CPT Diane J. Madlon-Kay, MC

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 postpartum both the control and asthmatic patients will have spirometry and diamine oxidase determinations. The asthmatic patients' clinical conditions during pregnancy will be classified as worse, unchanged, or improved by evaluating the change in respiratory symptoms, severity of wheezing on physical exam, medication changes required, and spirometry. A chi-square analysis will be done to determine if any correlation exists between the diamine oxidase levels and the asthmatic patients' clinical conditions.

PROGRESS

(81 10 - 82 09) Fourteen asthmatics and nine matched control patients have been enrolled. Of the 19 asthmatics, ten have completed the study, three are still pregnant, and six have dropped out of the study. Of the controls, five are still pregnant and four were dropped from the study. Fourteen of the asthmatics and all of the controls enrolled during FY 82.

An Attempt has been made to correlate the diamine oxidase levels in these pregnant asthmatics with their clinical status as determined by FEV₁/FVC and clinical histories. There has been no difference in the diamine oxidase levels in patients placed

Diamine Oxidase Levels and Asthma in Pregnancy - Ducey

in three different groups "improved", "no change", and "worse" by virtue of their clinical status. However, in four of the nine asthmatic patients, there has been a direct relationship between diamine oxidase levels and FEV₁/FC. Data collection is continuing.

Due to the departure of Dr. Madlon-Kay in June 1982, Dr. Julie Ducey is now the principal investigator on this protocol.

STATUS: (0)

TITLE: Exercise Prescription and Dietary Restriction for the
Reduction of Weight and Cardiovascular Risk Factors

PRINCIPAL INVESTIGATOR: CPT Gaspar Giorgi, MC

PROFESSIONAL ASSISTANT: MAJ Diana M. Barefoot, SP

WORK UNIT NO: 82/61

TECHNICAL OBJECTIVE

To establish through the aegis of the Family Practice Clinic a program of exercise therapy coupled with dietary restriction for the reduction of weight and other cardiovascular risk factors.

METHOD

Thirty (30) obese patients will be enrolled. Obesity will be defined according to the Metropolitan Life Insurance Tables. Patients 20-60 years of age are eligible; patients >35 will be screened by treadmill to determine functional capacity and the presence of latent cardiovascular disease; patients with established cardiovascular disease after a myocardial infarction or coronary bypass will not be allowed into the program; screening history and physical and labs pertinent for cardiovascular risk factors will be obtained before and after the program; routine chest x-ray and spirometry will be obtained in patients with a history of pulmonary disease. Laboratory screen will include CBC, SMA-20, HDL-cholesterol, triglycerides, and urinalysis. This will be an individual, rather than a group, exercise program and will consist of swimming or running. Patients will be admitted into the program bi-monthly. Exercise prescriptions utilizing a training heart rate zone for 20 minutes, 3 times a week, coupled with diet therapy appropriate for age and weight will be given at that time. Follow-up will be at 1 week and 2 weeks, and then monthly. Weight, compliance, and various cardiovascular performance and risk factors will be checked at each follow-up with further dietary and risk factor counselling at that time. Data from the program analyzing its success will be taken in 12 months.

PROGRESS

(82 06 - 82 09) Fifteen subjects were enrolled on 11 Sep 82. All had initial blood work and EKG and stress tests performed according to the screening criteria established by prescription based on age and then issued an exchange diet. Follow-up meeting one week later showed that all patients lost weight (2-5 lbs). However, only 70% of the initial number returned for the next follow-up. No problems were reported. Follow-up will continue on a monthly basis with periodic induction of further subjects.

STATUS: (0)

TITLE: Metronidazole Therapy for Nonspecific Vaginitis: 3 vs 7 Days

PRINCIPAL INVESTIGATOR: CPT Mark B. Mengel, MC

PROFESSIONAL ASSISTANTS: MAJ Shannon Harrison, MC
MAJ James Higbee, MSC
CPT William Watson, MC

WORK UNIT NO: 82/66

TECHNICAL OBEJCTIVES

To determine the effectiveness of 3 days of metronidazole therapy (500 mg po bid) vs 7 days (500 mg po bid) in the treatment of nonspecific vaginitis (NSV) and to determine if treatment of the male sexual partner of a woman with NSV reduces the rate of recurrence of that disease in previously cured women.

METHOD

Women 18-50 years of age who complain of abnormal vaginal discharge or vulvar itching, are non-pregnant, non-menopausal, have not used oral antibiotics or vaginal medications in the previous month, do not have clinical evidence of a mucopurulent cervical discharge or genital herpes, but do have negative wet-mounts for *Trichomonas vaginalis* and negative KOH prep for *Candida albicans* will be admitted to the study if their vaginal discharge fulfills two of the following four criteria: grey, homogenous discharge that adheres to the vaginal wall; pH >4.5; positive "clue cells" on wet mount or gram stain; or release of a "fishy" amine odor on addition of 10% KOH. Cultures will be taken from the vaginal vault for *C. vaginalis*, *T. vaginalis*, *C. albicans*, and *N. gonorrhoea*. Women with positive cultures for the latter 3 organisms or negative cultures for *G. vaginalis* will be excluded from the study at the first follow-up visit. Epidemiologic data will include age, race, number of sex partners, marital status, contraceptive use, number of pregnancies, and rank. All women will then be given a 3-day supply of metronidazole and a 3 day supply of placebo or metronidazole for their sexual partner. Women will be asked to abstain from sexual intercourse during the 1-week treatment period.

Thirty asymptomatic women will be used as controls and asked to have a clinical assessment done, cultures taken, and to provide epidemiologic data.

The first follow-up visit will be conducted at 3 days. A clinical assessment and cultures will again be taken. Patients will then be randomized to receive 4 additional days of metronidazole or 4 days of placebo. Sexual partners of the 7-day treatment group will be randomized to receive 4 days of placebo or 4 days of metronidazole. Because of the randomization process the sexual partners of the 7-day treatment group will be divided into those that receive placebo, those that receive a 3-4 day course, and those that receive a 7-day course.

Metronidazole Therapy for Nonspecific Vaginitis: 3 vs 7 Days -
Mengel

A follow-up visit at one week after the start of therapy will be conducted to judge cure. A full clinical assessment and cultures will be taken. Cure will be judged by culture results and lack of symptoms. Cultures will not be taken from the male sexual partner as evidence of eradication of the organism from the male can be judged by the rate of recurrence in the female. Follow-up visits will occur at 3 and 6 weeks post start of therapy. A full clinical assessment and cultures will be taken at these visits as well. Recurrences will be treated with a 7-day course of metronidazole for both patient and partner.

Appropriate statistical techniques will then be used to analyze the data. A minimum of 60 women in each treatment group will be used in order to assure statistical significance.

PROGRESS

(82 08 - 82 09) The principal investigator is in the process of getting necessary paperwork completed in order to obtain the drug from the supplier. The study will begin as soon as the drug is received.

STATUS: (0)

TITLE: Post-Partum Weight Loss in Lactating and Non-Lactating Females

PRINCIPAL INVESTIGATOR: CPT Richard Turner, MC

PROFESSIONAL ASSISTANTS: MAJ Philip Marinelli, MC
CPT Cathy Canny, AMSC
CPT Kevin Kiley, MC
Catherine Yokan, M.D., DAC

WORK UNIT NO: 82/44

TECHNICAL OBJECTIVE

To examine the short term post-partum weight reduction in lactating and non-lactating females, specifically to see if the caloric expenditure of the mother for the infant is clinically effective in allowing lactating women to return to pre-pregnancy weight sooner, in greater numbers, or with less dietary restriction than non-lactating women. Demographic data to more closely define the military post-partum population and examine how mothers make the decision to breast feed or bottle feed their newborn infants will also be studied.

METHOD

The weights of patients will be taken after a positive urine HCG, at time of admission for delivery, at discharge from hospital, and at 2 weeks, six weeks, 2 months, and 6 months. A questionnaire to obtain demographic data and determine the reasons for breast versus bottle feeding will be filled out on the post-partum ward. An ideal body weight will be estimated and compared with height and weight curves to check its validity. A dietary and activity questionnaire will be filled out at six months to obtain an estimate of caloric intake and activity levels, and the mother will be asked if she is still breast feeding and if she has stopped the reason why. The data will be analyzed to determine if a statistically significant difference in post-partum weight loss exists between breast and bottle feeders and to determine if any other correlations exist between post-partum weight loss and the maternal age, education, and socioeconomic status. The normal expected rate of weight loss following parturition will be documented.

PROGRESS

(82 04 - 82 09) A total of 230 patients has been registered on the protocol and weights have been obtained and questionnaires completed according to the protocol. The investigators are still in the process of gathering data and no analysis has been done at this point.

STATUS: (O)

DETAIL SHEETS
FOR
PROTOCOLS

DEPARTMENT OF MEDICINE

TITLE: Comparison of Captopril 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, myocardial 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 anti-hypertensive 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.

PROGRESS

(80 10 - 81 09) The start of this protocol was delayed for almost a year due to complications in getting an IND number. Within a few weeks of approval, both investigators at MAMC were reassigned; therefore, the protocol at MAMC has been terminated.

STATUS: (T)

TITLE: *In vivo* Uptake of $^{131}\text{I}^-$ by Semen and other Body Fluids

PRINCIPAL INVESTIGATOR: MAJ Allan Avbel, MC

PROFESSIONAL ASSISTANTS: COL Bruce Fariss, MC
COL Stanton Brown, MC
MAJ Willis Jacob, MSC
CPT Michael Smith, MSC
James Graves, DAC

WORK UNIT NO: 80/44

TECHNICAL OBJECTIVE

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

METHOD

Twelve hyperthyroid men and 6 men with thyroid cancer receiving $^{131}\text{I}^-$ 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. Five cc of blood will be drawn into an EDTA tube and $^{131}\text{I}^-$ 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. $^{131}\text{I}^-$ activity will be determined in one ml. Sweat will be collected utilizing pilocarpine for stimulation. Twenty-four hour urine will be collected in 3 liter plastic bottles. $^{131}\text{I}^-$ activity in 2 ml will be determined. After data is collected, the distribution of $^{131}\text{I}^-$ body fluids at various periods after oral dosing 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.

PROGRESS

(80-05 - 82 06) A literature review and experimentation with methods were performed on this protocol. Due to the departure of the principal investigators during both years the protocol was open and an inability to obtain subjects, the protocol had to be terminated.

STATUS: (T)

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

PRINCIPAL INVESTIGATOR: MAJ 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 E₂ 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 E₂ levels. Testicular samples will be analyzed for T, DHT, E₂ and SSBG.

PROGRESS

(81 08 - 82 06) This protocol has been completed and data are being analyzed. An initial presentation was made from the preliminary results.

STATUS: (C)

PRESENTATION: Plymate, S.R., Avbel, A., and Fariss, B.L.;
Effects of Hyperthyroidism on Intratesticular
Testosterone and Androgen Binding Protein
Production. Reproductive Biology Section,
University of Washington, Seattle, WA, May 1982.

TITLE: Cis-Platinum, 5-FU Chemotherapy of Advanced Head and Neck Squamous Cell Carcinoma (Stage III and Stage IV)

PRINCIPAL INVESTIGATOR: CPT Thomas M. Baker, MC

PROFESSIONAL ASSISTANTS: COL Donald Kull, MC
COL Frederick 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/M², given with hydration and manitol diuresis, followed by 5-FU, 1000 mg/M² 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 - 09) Twelve (12) patients have been registered (all in FY 82). These patients can be divided into those who had this form of chemotherapy as their initial treatment of advanced stage carcinoma subsequently followed by radiation and/or surgery or those patients who have relapsed after having had prior treatment (radiation and/or surgery). The findings concerning those patients in which this form of chemotherapy was used initially are too early to evaluate. Preliminary findings for those patients who received this form of chemotherapy after relapse show that a proportion of patients can be palliated with this form of chemotherapy.

STATUS: (0)

TITLE: Dexamethasone vs Standard Antiemetic Drugs in the Treatment of Chemotherapy-Induced Nausea and Vomiting

PRINCIPAL INVESTIGATOR: CPT Thomas M. Baker, MC

PROFESSIONAL ASSISTANTS: COL Friedrich H. Stutz, MC
LTC James E. Congdon, MC
LTC Irwin B. Dabe, MC
MAJ Lauren K. Colman, MC
MAJ Howard Davidson, MC
CPT Alfred H. Chan, MC

WORK UNIT NO: 82/20

TECHNICAL OBJECTIVE

To determine the antiemetic effect of dexamethasone as compared to the present "best" standard therapy for the nausea and vomiting caused by cancer chemotherapy; to determine type and severity of adverse effects of dexamethasone as an antiemetic; and to determine if there is any additive effect of dexamethasone with the "best" standard therapy for nausea and vomiting.

METHOD

Any patient who is undergoing 3 or more courses of chemotherapy with drugs thought to be strongly emetic who does not have an underlying or active psychiatric problem, diabetes mellitus, or osteoporosis will be eligible. Patients will receive a different antinausea regimen for each course of similar chemotherapy following numeric order (Arm 1 to Arm 2 to Arm 3; or Arm 2 to Arm 3 to Arm 1; or Arm 3 to Arm 1 to Arm 2) until the 3 regimens have been utilized with each patient. The patient (and physician if present) will be asked to quantify the nausea and vomiting experienced with each course. The patient will subsequently continue the antiemetic regimen which is most effective and be continued on study to check for the development of resistance to the antiemetic therapy. Those thought equally effective will continue to alternate antiemetic therapy. Arm I: standard antiemetic regimens; (a) after doxorubicin, daunorubicin, DTIC, mechlorethamine, or actinomycin-D: compazine 10 mg po just prior to chemotherapy and q 6 hr po x 24 hrs prn after chemotherapy and reglan 20 mg IV just prior to chemotherapy; (b) after cisplatin: thorazine 25-50 mg po 1 hr prior to chemotherapy and q 6 hr thereafter x 4 doses, valium 5-10 mg po 1 hr prior to chemotherapy and q 6 hr thereafter x 4 doses, and reglan 20 mg IV just prior to chemotherapy. Arm II: Dexamethasone regimen: 4 mg po q 6 hr starting the AM of chemotherapy treatment x 48 hrs and 10 mg IV just prior to chemotherapy. ARM III: standard + dexamethasone. This regimen will contain the drugs described in both Arms 1 and 2 in the same doses.

PROGRESS

(32 91 - 82 09) Due to lengthy approval procedures and lack of time of the investigators, this protocol was terminated.

STATUS: (T)

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 followup. The data will be analyzed using the objective and subjective evaluation of patients after the placebo code is broken.

PROGRESS

(81 07 - 82 09) This protocol has not received final approval from HSC since required changes have not been forwarded. The protocol has been in a temporarily inactive status due to the change of the duty assignment of the principal investigator within MAMC. With the addition of new staff in the Pulmonary Service, the protocol is now being revised in accordance with HSC and should become active within the next two months.

STATUS: (O)

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 through a heparin lock. Phlebotomy of 10cc will again be done at 0, 15, 30, 60, 90, 120, 150, and 180 minutes. Five cc will be spun and sent for prolactin analysis. The following week, patients will be given 2.5 mg bromocryptine PO and phlebotomy will 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 - 82 09) Due to the lengthy approval procedures associated with this protocol and the imminent departure of the principal investigator upon its approval, no patients were entered on the protocol. The principal investigator had planned to transfer this protocol to Eisenhower Army Medical Center. However, due to the lack of time he has been unable to do so, and it has been terminated.

STATUS: (T)

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 ASSISTANTS: 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 stabilizing 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 - 82 09) Due to the departure of the principal investigator no patients were entered on this protocol. The principal investigator had hoped to continue this study at his new assignment; however, he was unable to do so because of time restrictions. The protocol has been terminated.

STATUS: (T)

TITLE: Vinblastine - Continuous 5-Day Infusion in Refractory
Advanced Solid Tumors

PRINCIPAL INVESTIGATOR: CPT Alfred H. Chan, MC

PROFESSIONAL ASSISTANTS: COL Friedrich H. Stutz, MC
LTC James E. Congdon, MC
LTC Irwin B. Dabe, MC
MAJ Lauren K. Colman, MC
MAJ Howard Davidson, MC
CPT Thomas M. Baker, MC

WORK UNIT NO: 82/10

TECHNICAL OBJECTIVE

To determine the response rate and remission duration using Velban as a continuous IV infusion in patients with advanced solid tumors refractory to all effective forms of conventional treatment; and to define further the qualitative and quantitative toxicity of the continuous infusion of Velban.

METHOD

Since the response rate of these tumors at this stage to any particular agent or combination of agents has been dismal in the past, it would be meaningful, if a response rate of >15% can be established, to add this method to the existing regimens for the treatment of refractory solid tumors such as breast cancer, non-seminomatous testicular germ-cell cancer, small cell undifferentiated cancer of the lung, renal cell cancer, ovarian cancer, and lymphomas. This will be a single-armed study. The results will be compared with historical data whenever available. All patients registered on this study will be considered evaluable and be analyzed. Patients will be stratified according to tumor cell types. In the case of breast cancer, further substratification into ER+/- and pre- vs post-menopausal status will be carried out. Vinblastine will be given as a continuous infusion over five days every three weeks, provided there has been recovery from hematologic toxicity.

PROGRESS

(81 11 - 82 09) Five patients have been accrued. This included one patient with metastatic breast carcinoma and extensive prior treatments who attained a remarkably lengthy period of stable disease exceeding nine months. Response in the remainder of the patients was variable. At present, the number of patients accrued is insufficient for meaningful statistical analysis.

STATUS: (0)

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 - 82 07) Rats were injected with Freund's adjuvant and either gold thiomalate 0.7 mg/kg or 10 mg/kg. Comparison of IM vs oral gold was not possible as the investigators were unable to obtain the oral gold preparation. The low dose gold had no effect on the severity of the arthritis induced by the adjuvant. The high dose gold did ameliorate the severity of the arthritis. This effect, however, may have been caused by nonspecific toxic factors rather than specific effect on the disease. There was a 20% mortality in the high dose gold animals including the high dose gold control group. The second part of the study was to determine the tissue distribution of the gold in animals with and without arthritis. The plan was to use an atomic absorption technique. Thus far attempts to modify existing methods of gold analysis have been unsuccessful. As the investigators have been reassigned it was necessary to forego this part of the study.

STATUS: (C)

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 ASSISTANTS: 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). Cultures will be done in triplicate in microtiter plate. Initially the effect of d-penicillamine (d-Pen) and chloroquine (AM) added to the cultures prior 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 concentrations 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 paired t test and χ^2 analysis to compare stimulated to non-stimulated values and the response of treated vs untreated controls.

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

PROGRESS

(80 05 - 82 07) The study shows that chloroquine, primaquine, and d-penicillamine have a dose-related ability to suppress lymphocyte stimulation by T & B cell mitogens of phytohemagglutinin, concanavalin A, and pokeweed mitogen. D-penicillamine also suppressed lymphocyte stimulation but to a much smaller degree. The addition of sulfate in amounts not toxic to the lymphocytes greatly increased the suppressive effect of d-penicillamine. This study shows that suppression of lymphocyte function could be a mechanism of drug action in the treatment of rheumatoid arthritis.

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 (myochrysin), saline, or thiomalate (the vehicle in myochrysin). 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 then be killed and transplantation sites harvested for histopathology. The presence of humoral antibodies will be evaluated by either complement fixation or hemagglutination inhibition.

PROGRESS

(81 03 - 82 07) Cross skin grafts were done among two outbred rat strains. Autografts were done on each animal for controls and gold was given to 7 out of each group of animals. Histologic examination of the grafts by a pathologist who was blinded as to treatment of the animals was done. Fibrosis and inflammation were in all grafts with no difference as to degree of reaction whether the graft was homograft or heterograft or whether the animal had gold or not. It is felt the changes were all related to technique rather than immune rejection. Further studies could not be done due to the reassignment of three of the investigators.

STATUS: (C)

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

PRINCIPAL INVESTIGATOR: LTC Henry D. Covelli, MC

PROFESSIONAL ASSISTANTS: 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 will also be used to assess therapeutic results.

PROGRESS

(81 10 - 82 09) Fifteen patients (seven entered during FY 82) were entered on this protocol with no adverse effects. Data have been collected, but it is too early for evaluation of results.

STATUS: (0)

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 energy 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 biopsied 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.

PROGRESS

(81 10 - 82 09) Thirty patients have been entered - five during FY 82 - with no adverse effects. Investigators are continuing to collect data.

STATUS: (0)

TITLE: Evaluation of High Dose vs Low Dose Corticosteroid in the Treatment of Acute Bronchospasm

PRINCIPAL INVESTIGATOR: LTC Henry D. Covelli, MC

PROFESSIONAL ASSISTANTS: COL Bruce L. Fariss, MC
LTC J. Waylon Black, MC
LTC Gary Treece, MC
CPT Arthur R. Knodel, MC
CPT James Wallingford, MC

WORK UNIT NO: 82/64

TECHNICAL OBJECTIVES

To evaluate the optimal dose of corticosteroids used in the treatment of acute exacerbations of bronchospasm and to assess the difference in the duration of adrenal suppression between low and high dose corticosteroid therapy.

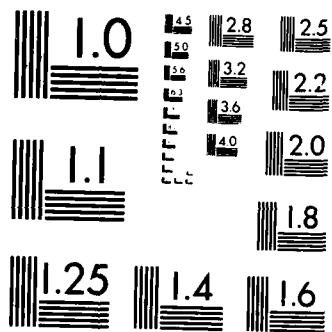
METHOD

Approximately 50 patients hospitalized for an acute exacerbation of bronchospasm from either chronic obstructive lung disease or asthma will be evaluated in a double blind randomized trial. Treatment will consist of the usual therapeutic measures of IV aminophylline and orally inhaled bronchodilators. Then one of four corticosteroid regimens will be used. Regimen 1: 125 mg of IV methylprednisolone (MP) q 6 hrs x 3 days with a weaning oral prednisone dose of 60 mg x 3 days, 40 mg x 3 days, and 20 mg x 3 days. Regimen 2: 125 mg of IV MP q 6 hrs x 3 days with a weaning dose of oral prednisone of 30 mg x 3 days, 20 mg x 3 days, and 10 mg x 3 days. Regimen 3: 125 mg MP q day x 3 days, then a weaning dose of oral prednisone of 60 mg x 3 days, 40 mg x 3 days, and 20 mg x 3 days. Regimen IV: 125 mg MP q day x 3 days, then a weaning dose of oral prednisone of 30 mg x 3 days, 20 mg x 3 days, and 10 mg x 3 days. A placebo of IV glucose will be given q 6 hrs to patients receiving regimens 3 and 4. Routine studies such as eosinophil counts and peak expiratory flow rates (spirometry) will be performed during this time. After discharge, patients will be evaluated with a cortrosyn stimulation test one or two weeks after discontinuing a weaning dose of oral prednisone. If the cortrosyn stimulation test is abnormal, a repeat study will be performed weekly until it normal.

PROGRESS

(82 08 - 82 09) No patients accrued at this time.

STATUS: (0)



MICROCOPY RESOLUTION TEST CHART
NATIONAL BUREAU OF STANDARDS 1963 A

TITLE: 5-Azacytadine in Acute Leukemia

PRINCIPAL INVESTIGATOR: LTC Irwin Dabe, MC

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

PROGRESS

(80 02 - 82 07) Two patients were treated on this study in FY 80 with very little response to the drugs, followed by death from uncontrolled leukemia. No patients were entered during FY 81 or FY 82.

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 OBJECTIVE

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/M² per day by continuous IV infusion for 5 days. One half of the daily dose (45 mg/M²) 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 leukemic 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/MM³ and platelets are >100,000/MM³.

PROGRESS

(81 03 - 82 07) The investigators were unable to obtain the necessary drugs from the NCI since this was an individual rather than a group protocol; therefore, the protocol had to be terminated.

STATUS: (T)

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 Clinic 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 clinical 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 - 82 06) All data has been collected for the study and has been sent to Dr. Harris in San Francisco for statistical analysis. The principal investigator is being reassigned to Europe, but will forward results when they are available.

STATUS: (C)

TITLE: The Effects of Thyroid Hormone on Sex Steroid Binding Globulin

PRINCIPAL INVESTIGATOR: MAJ Michael E. Fincher, MC

PROFESSIONAL ASSISTANTS: COL Bruce Fariss, MC
LTC Stephen Plymate, MC
LTC Gary Treece, MC
MAJ Allan Avbel, MC
MAJ Robert Jackson, MC

WORK UNIT NO: 82/06

TECHNICAL OBJECTIVE

To determine the effects of thyroid hormone on sex-steroid binding globulin (SSBG).

METHOD

Male and female patients (approximately 20 total) will have plasma estradiol, testosterone, and SSBG levels drawn as well as LH and FSH when first presenting with hyperthyroidism before any treatment except propranolol. Following treatment, SSBG levels will be drawn every two weeks until the patient becomes euthyroid or until he becomes hypothyroid. In addition to the SSBG parameters, TSH, T₄, T₃ uptake and T₃ by RIA will be drawn at each visit. The results will be analyzed by linear regression analysis.

PROGRESS

(81 11 - 82 09) Six patients have been entered in the study. MAJ Avbel initiated this protocol. Due to his reassignment, MAJ Fincher was assigned as principal investigator.

STATUS: (0)

TITLE: Coronary Arteriography in the Army

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

PROFESSIONAL ASSISTANTS: 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 analyzed 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. The data has been analyzed and a paper has been prepared. It has now been sent for local review of participants. It will be submitted for publication when this review is completed. A paper has been accepted for presentation at the Robert Wood Johnson Foundation Seminar, Scottsdale, AZ, November 1982.

STATUS: (C)

TITLE: Metronidazole Pharmacokinetics and Metabolism in Liver Disease, Aging, and Drug-Drug Interactions

PRINCIPAL INVESTIGATOR: MAJ Shannon Harrison, MC

PROFESSIONAL ASSISTANTS: CPT David W. Towle, MSC
Lawrence L. Pelletier, Jr., M.D.,
American Lake VA Medical Center
Robert Vestal, M.D.,
Boise VA Medical Center

WORK UNIT NO: 82/33

TECHNICAL OBJECTIVE

To compare the levels of metronidazole and its two major metabolites to see if metabolites accumulate in liver patients with liver disease; to attempt to define the contribution of active metabolites to the therapeutic outcome in patients with serious anaerobic infections; and to develop guidelines for metronidazole dosage in patients with liver disease.

METHOD

This protocol will be done in conjunction with the American Lake VA Medical Center, Tacoma, WA, and the Boise VA Medical Center. Twenty patients with liver disease and ten controls with proven or suspected anaerobic infection requiring in-hospital antimicrobial therapy will be enrolled. Metronidazole will be administered IV and serum levels of metronidazole and its two major metabolites will be determined. Serum levels will be correlated to the minimum inhibitory concentration of metronidazole and the two metabolites, results of serial cultures, and clinical outcome. Dosage will be adjusted to maintain therapeutic serum levels and any reduction in dosage correlated with the type and severity of liver disease. In subsequent studies, the investigators will determine whether metronidazole metabolism is altered in patients over 70 years and in individuals receiving phenytoin or cimetidine.

PROGRESS

(82 03 - 82 09) The progress on this protocol has been deterred due to the departure of the co-investigator from the American Lake VA Hospital. All of the materials and techniques necessary for the *in vitro* determination of metronidazole levels and metronidazole metabolites and the reagent drug requirements necessary for the *in vitro* determination of anaerobic sensitivities are ready for use. The investigators will now begin to enroll subjects in the study.

STATUS: (0)

TITLE: Patterns of Angina and Primary Care Utilization After Myocardial Infarction: Implications for Cardiac Rehabilitation

PRINCIPAL INVESTIGATOR: COL John C. Hill, MC

PROFESSIONAL ASSISTANTS: CPT Sandra F. Yancy, ANC, USAR

WORK UNIT NO: 81/112

TECHNICAL OBJECTIVE

To determine the prevalence and characteristics of chest pain or other symptoms perceived by the client as being anginal at two and four months after uncomplicated MI and to describe the incidence and disposition of urgent primary care utilization for chest pain or symptoms during this period.

METHOD

The Cardiac Care Unit Admission Book will be reviewed and patients 30-65 years of age who meet the other criteria as listed in the protocol will be asked to participate. The information will be collected via telephone interviews at two and four months post-cardiac episodes. The subject's health record will be reviewed for primary care utilization the same day as the telephone interviews. Frequencies of responses and weighted scores will be calculated for questionnaires. Group and individual patterns will be reported and compared. Ordinal values will be assigned to questionnaire responses in order to quantify symptom evolution as stable, regressive, or accelerating.

PROGRESS

(81 08 - 82 10) Six patients have been studied, and the data collection is complete. The data is being analyzed at this time.

STATUS: (C)

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.

PROGRESS

(81 09 - 82 09) Seven treatment and three control patients were studied at MAMC. There were no complications. After assessment of the first 100 cases (from the 13 hospitals participating in the study the recommendation was made to continue to 250 cases. The initial experience would suggest salvage of myocardium by the therapy in those patients treated within the first five hours.

PRESENTATION: Army Association of Cardiology, May 1982.

STATUS: (O)

TITLE: An Evaluation of Hemodialysis Blood Loss

PRINCIPAL INVESTIGATOR: CPT Douglas R. Hough, MC

PROFESSIONAL ASSISTANTS: COL Stanton Brown, MC
LTC Poong S. Shim, MC
MAJ Howard Davidson, MC
William K. Tuttle, Ph.D.

WORK UNIT NO: 82/41

TECHNICAL OBJECTIVE

To measure accurately the blood loss due to residual blood remaining in the dialyzer membrane and document the efficiency of the Gambro hollow fiber dialyzer. Related objectives would include answering the following questions: (1) Is there significant variation in the amount of residual blood loss between individual patients; (2) does the dialysis blood loss correlate with the severity of the anemia; and (3) can the amount of blood loss be reduced?

METHOD

Twenty-five (25) ml of blood will be withdrawn from each patient and placed in an oxalate tube for hematocrits. The remainder will be placed in a sterile prewarmed (37°C) 30cc bottle containing acid citrate dextrose. Then 50 mCi of ⁵¹Chromium will be added and incubated for 45 min with swirling every five min to mix. Then 50 mg of ascorbic acid will be added to reduce the unbound ⁵¹Chromium and inhibit further labeling of the red blood cells. With a calibrated syringe, 20 ml of the ⁵¹Chromium whole blood will be injected IV. After 15 Min, 10-20 ml of blood will be withdrawn and the red blood cell volume measured. The patient will then undergo hemodialysis after which the hollow fiber dialyzer and all connecting tubing will be cleared by the usual backwash techniques. The disconnected dialyzer and tubing will then be measured for residual blood loss.

PROGRESS

(82 03 - 82 06) This protocol was terminated due to the transfer of the principal investigator.

STATUS: (T)

TITLE: Effects of Somatostatin on Plasma Insulin and Glucagon in Sheep

PRINCIPAL INVESTIGATOR: MAJ Robert Jackson, MC

PROFESSIONAL ASSISTANT: COL Bruce L. Fariss, MC

WORK UNIT NO: 82/62

TECHNICAL OBJECTIVE

To examine the effects of somatostatin on insulin and glucagon release from the sheep pancreas.

METHOD

Six adult female sheep, after a 24-hr fast, will be immobilized and an intravenous catheter inserted into the jugular vein for the introduction of test substances. Another catheter will be inserted into the contralateral jugular vein for withdrawal of blood samples. Each sheep will receive an infusion of a solution of sodium butyrate 1.25 mM/kg of body weight adjusted to a pH of 7.4. Blood samples will be drawn every 10 min for the next 90 min and analyzed for insulin, glucagon and glucose. Two weeks later the sheep will receive an infusion of somatostatin 0.8 mcg/kg/min and blood specimens drawn every 10 min for 90 min for insulin, glucagon, and glucose. While the somatostatin is infusing, the sheep will be given sodium butyrate 0.2 nmole/kg body weight and blood samples again drawn every 10 min for 90 min and sent for glucagon, insulin, and glucose. Plasma glucose will be measured by the glucose oxidase method.

PROGRESS

(82 07 - 82 09) The samples have been drawn and will be processed within the next few weeks.

STATUS: (0)

TITLE: Theophylline Induced Seizure: Increased Susceptibility
with Prior Episode

PRINCIPAL INVESTIGATOR: CPT Arthur R. Knodel, MC

PROFESSIONAL ASSISTANTS: LTC Jerome F. Beekman, MC
LTC Henry D. Covelli, MC
LTC Georgio Turella, MC
MAJ Stanely 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 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 min 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 - 82 09) Initially, beagle dogs were the experimental animals used in this study. Utilizing curare, the first dog died approximately 15 minutes after he was paralyzed and placed on mechanical ventilation. During the study on the second dog, in which pavalon was used, the animal experienced cardiopulmonary instability, but was fortunately resuscitated. At this time, it was elected to change the experimental animal from a paralyzed dog to an awake sheep which would be suspended in a sling, which required an implantable electrode in the brain to obtain an EEG. There has been difficulty in obtaining the materials in order to do this. Once the problem with the EEG monitoring with implanted electrodes has been resolved, the protocol will be carried out.

STATUS: (0)

TITLE: Face Mask CPAP for Prevention of Post-Op Atelectasis

PRINCIPAL INVESTIGATOR: MAJ Arthur R. Knodel, MC

PROFESSIONAL ASSISTANTS: COL Waylon J. Black, MC
LTC Henry D. Covelli, MC
LTC Michael Moon, MC
CPT Richard Dearman, MC
CPT William Weaver, MC
Donald Winfrey, DAC

WORK UNIT NO: 82/72

TECHNICAL OBJECTIVE

To evaluate the usefulness of continuous positive airway pressure (CPAP) delivered by a face mask as a prophylactic measure in the prevention of post-operative pulmonary atelectasis.

METHOD

One hundred patients undergoing elective abdominal or thoracic surgery will be studied: Patients with acute pulmonary diseases, including ARDS, CHF, and pneumonia, diagnosed immediately post-operatively, will be excluded. No intubated patient will be included in the study. The patients will be randomly assigned to one of three groups: (1) control group - conservative therapy of cough deep breath; no device; (2) incentive spirometry (3) CPAP by mask at a level of 10. All patients will get pre-operative instructions on the modality of the post-operative therapy they will receive. Pre-operative evaluation will include pulmonary function test, arterial blood gas, and chest x-ray. Four hours post-operatively all of these studies will be repeated. The patient will then be given a treatment followed in 15-30 minutes by repeat pulmonary function test and arterial blood gas. During waking hours the patient will receive the treatment for 15 minutes every four hours. Pulmonary function test, arterial blood gas, and chest x-ray will be done at 24, 48, and 72 hours. At that time the study will be completed.

PROGRESS

(82 09 - 82 09) New protocol; investigators are assembling supplies and materials.

STATUS: (0)

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

PRINCIPAL INVESTIGATOR: LTC Michael S. Olsen, MC

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

WORK UNIT NO: 81/95

TECHNICAL OBJECTIVE

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

METHOD

Increased CO₂ 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 response to the larger CO₂ 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, VO₂, VCO₂, and VE will be measured at regular intervals while the animal is on the ventilator.

PROGRESS

(81 07 - 82 09) Due to difficulties controlling the anesthesia given to the dogs, no meaningful data could be obtained from this study. The investigator has been transferred to Letterman Army Medical Center, and hopes to attempt the protocol again at that institution when time permits.

STATUS: (T)

TITLE: Rat Liver Membrane Binding of Thyroid Hormones

PRINCIPAL INVESTIGATOR: MAJ Louis Pangaro, MC

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

WORK UNIT NO: 81/16

TECHNICAL OBJECTIVE

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 sub-cellular characterization, and radioreceptor assay methods as outlined in the protocol. Ten male Sprague-Dawley rats used as controls for T₃ and T₄ displacement analysis will be fed *ad libitum*, fasted overnight (6 with daily intraperitoneal saline). The experimental groups will be: 6 female rats; 6 male rats fed *ad libitum* (not specifically fasted); 6 male rats fasted four days (water *ad libitum*); 10 male rats made hyperthyroid by daily intraperitoneal injection of T₄; 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 naphthalene, ipodate, iopanoic acid, propranolol, tyropanoate, propylthiouracil, methimazole, and amiodarong. Thyronine analogue displacement curves are compared with the addition of T₄; T₃; reverse T₃ (3'3'5'T₃); Tetrac; triac; D-T₄; D-T₃; 3'5'T₂; 3,5T₂; 3,3'T₂; 3-T₁; T₀.KI.

PROGRESS

(80 11 - 82 09) Study is completed. Conclusions: (1) there is saturable, high affinity binding of T₄ and T₃ to purified rat liver plasma membranes; (2) hyperthyroidism decreased maximal binding capacity (MBC) for T₄; (3) fasting increased MBC for T₃; and (4) 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. A manuscript is in preparation.

PRESENTATION: Pangaro, L.N., Little, J.S., Fariss, B.L., and Burman, K.D.: Binding of L-Thyroxine (T₄) and L-Triiodothyronine (T₃) to Purified Rat Liver Plasma Membranes: Changes in Hyperthyroidism and Fasting. Amer Thyroid Assoc, 57th Meeting, Minneapolis, MN, 18 Sep 81, Abstract # T-17.

STATUS: (C)

TITLE: The Role of Phosphate in the Anemia of Chronic Renal Failure.

PRINCIPAL INVESTIGATOR: LTC Poong S. Shim, MC

PROFESSIONAL ASSISTANTS: LTC Stephen R. Plymate, MC
CPT Wayne R. Heaton, MC
CPT Douglas R. Hough, MC

WORK UNIT NO: 82/60

TECHNICAL OBJECTIVE

To study the role of serum phosphate levels in the anemia of chronic renal failure patients on maintenance hemodialysis. It has been proposed that parathyroid hormone is a uremic toxin. The contribution of secondary hyperparathyroidism to the anemia of hemodialysis patients will be studied. The elevated serum phosphate levels and parathyroid hormone levels of secondary hyperparathyroidism are expected to be reduced with low phosphate diet, oral phosphate binders, and Rocaltrol. The response of the anemia to the treatment of the secondary hyperparathyroidism will be evaluated.

METHOD

PATIENTS TO BE STUDIED: Subjects (N=14) undergoing hemodialysis and those patients with chronic renal failure and evidence of secondary hyperparathyroidism. Patients with chronic constipation or documented non-compliance will be excluded. PROCEDURES: Pre-study bloodwork for each patient will include SMA-20, CBC, serum iron/TIBC, serum ferritin, folate, B-12, and PTH level. Radiographs of the hands for evidence of secondary hyperparathyroidism will be done. All patients will receive written and verbal instructions describing the study and the need for compliance with a low phosphate diet, oral phosphate binders, and Rocaltrol, a potent metabolite of vitamin D given to manage the hypocalcemia and reduce the elevated parathyroid hormone levels. Serum phosphate and calcium levels will be monitored monthly during the study; the calcium phosphate product will be maintained at <70. Alucaps or aluminum hydroxide will be given to control serum phosphate levels. Patients will be examined every two weeks for adverse side effects. The study duration will be for a minimum of six months. At the end of the study, all the pre-study bloodwork will be repeated. Radiographs will be repeated only for patients with pre-study evidence of bone cysts or subperiosteal resorption. Each patient will serve as his own control with pre-study values compared with study values using the Student's t Test. Also each individual will be compared with the group.

PROGRESS

(82 06 - 82 09) The investigators are in the process of coordinating supplies and personnel. No subjects have been entered. Dr. Hough, the original principal investigator, was replaced by Dr. Shim due to the reassignment of Dr. Hough.

STATUS: (0)

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

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: Suresh B. Katakhar, 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

(70 10 - 82 09) Six patients were entered by MAMC and 18 by other institutions for the pilot study, and it was felt that the study was feasible. Since then the protocol has been revised and submitted for NCI funding as a SWOG study. However, the NCI did not appropriate funds for this study in the framework of the SWOG because this was an epidemiological study which is not normally performed by the cooperative cancer groups.

STATUS: (C)

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 - 82 09) No patients entered on this protocol.

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; subjects with hyperthyroidism; with hypothyroidism, primary untreated; with hypothyroidism treated for one month with L-thyroxine; with the nephrotic syndrome; subjects with the nephrotic syndrome treated for one month with L-thyroxine. A 24-hour urine for volume, creatinine, total protein, urine protein, electrophoresis, T₄, and T₃ will be completed, and the following day, after an overnight fast, blood will be drawn for SMAC-20, T₄, T₃ resin, T₃ by RIA, TSH, THAT (an extra tube will be drawn for free T₄, reverse T₃, and TBG). 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 T₄ 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 - 82 09) Three patients with the nephrotic syndrome, but euthyroid, have been studied, and one patient with the nephrotic syndrome and pre-existing treated hypothyroidism and one hypothyroid patient are currently under study. The three former patients have normal serum thyroid function (consistent with previous studies) and normal TRH responses. Urinary thyronines will be measured utilizing a RIA, which uses a Sephadex column for both extracting and separation of free and antibody bound hormone. This assay is to be established in the near future. In addition to the stated objectives, it is anticipated that new insights into urinary thyronine will be made through this protocol.

STATUS: (O)

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

PRINCIPAL INVESTIGATOR: LTC Gary L. Treece, MC

PROFESSIONAL ASSISTANTS: COL Bruce Fariss, MC
MAJ Robert Jackson, MC

WORK UNIT NO: 82/05

TECHNICAL OBJECTIVE

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

METHOD

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

PROGRESS

(81 11 - 82 09) Two patients have completed the protocol. One patient has well documented spontaneous primary adrenal insufficiency; the other has surgically induced adrenal insufficiency (as treatment for Cushing's disease) complicated by Nelson's syndrome requiring transphenoidal hypophysectomy. The patient tolerance of the protocol has been good.

STATUS: (0)

TITLE: An Evaluation of Local Anesthetic Skin Testing and Progressive Challenge in Patients with a History of an Adverse Reaction to Local Anesthetics

PRINCIPAL INVESTIGATOR: LTC Richard Weber, MC

PROFESSIONAL ASSISTANTS: COL H.S. Nelson, MC
LTC John M. Piersol, MC
Bonnie Baswell, M.D.
Richard deShazo, M.D.
Richard Summers, M.D.

WORK UNIT NO: 82/21

TECHNICAL OBJECTIVE

To confirm the safety and usefulness of local skin testing and progressive challenge in a large number of patients with histories of previous suspected adverse reactions to local anesthetics.

METHOD

After a history is taken, skin tests will be performed as described in the protocol and the 20 minute results recorded. If the history suggests a severe prior reaction, skin tests and progressive dose testing (PDT) may not be performed at the discretion of the attending physician. If PDT is indicated, a LA that does not cross-react with the LA implicated in the prior reaction will be used for PDT. If the prior LA is unknown, a Group II LA will be chosen. If the history suggests a delayed LA reaction, the patient will be evaluated at 24 hours after initial evaluation. The patient will be questioned for any delayed symptoms and examined for delayed physical findings at this time. An attempt will be made to obtain follow-up on the subsequent clinical history in each patient regarding the LA use and the presence or absence of a reaction. Serum (5cc) will be obtained from all patients with positive skin tests or with reaction to PDT or subsequent LA administration and frozen for subsequent analysis, including RAST or P-K testing.

PROGRESS

(82 01 - 82 09) Thirteen patients have been studied at MAMC. A total of 50 patients has been studied group-wide. The study is approximately 20% complete. No analysis has been attempted as the numbers are too small for statistical significance. Dr. John Piersol has been added to the protocol as the investigator directing the studies at MAMC due to Dr. Weber's reassignment.

STATUS: (0)

DETAIL SHEETS
FOR
PROTOCOLS

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
LTC 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 11) 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 pO_2 .

A thesis was written and accepted as partial fulfillment of the requirements for the Academy of Health Sciences, Anesthesiology for ANC Officers Course.

STATUS: (C)

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 Leo A. Le Bel, ANC
LTC Michael R. Moon, MC

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 ten 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, or d-tubocurarine, respectively.

PROGRESS

(81 03 - 81 11) A total of 20 patients was 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. A thesis was written and accepted as partial fulfillment of the requirements for the Academy of Health Sciences, Anesthesiology for ANC Officers Course.

STATUS: (C)

TITLE: Social Support and Symptomatology: A Study of First Time Expectant Parents

PRINCIPAL INVESTIGATOR: MAJ Jan Graham, ANC

PROFESSIONAL ASSISTANT: Marie Annette Brown, R.N.

WORK UNIT NO: 82/47

TECHNICAL OBJECTIVE

To describe the dimensions of social support perceived by expectant mothers and fathers; to compare the similarities and differences between expectant mothers and fathers in their experience of the dimensions of support; to explore the relationship between social support and symptomatology in expectant parents; to explore the effect of marital quality on the relationship between social support and symptomatology; and to gather data for a possible later longitudinal study.

METHOD

The data will be collected using a questionnaire designed by the investigator which takes about 45 minutes to complete. The sample will include 125 couples (at least 250 individuals) who are living together and expecting their first child. Subjects will be recruited during either prenatal classes or during their routine visits to the prenatal clinics. When the woman checks in for her appointment she will be approached by either the investigator or a staff person and asked if she is interested in participating in a study of expectant parents. If she indicates an interest, the study will be explained to her. If she desires to participate, the questionnaire and a consent form will be given or mailed to her and the questionnaire and a consent form will be given or mailed to the father in a separate packet. The questionnaires will be coded and will not include names. Only the investigator will have access to the code. The expectant parents will be asked to fill out the questionnaire and the consent form separately with no consultation or discussion between themselves and to return the questionnaire in a prepaid envelope at their convenience. All data will be confidential. Subject numbers will be assigned and questionnaires will be numbered.

PROGRESS

(82 05 - 82 09) Questionnaires were distributed to approximately 400 couples with 125 responses. The data has been coded and is now being entered into the computer. Analysis will begin within a few weeks.

STATUS: (O)

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

PRINCIPAL INVESTIGATOR: CPT Steven P. Kelsch, ANC

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

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 (minimum 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, height, and weight. Preoperative measurements: hemoglobin level and preinduction pulse and blood pressure base line. Induction with sodium pentothal and intubation following curare and anectine. Maintenance with N₂O, O₂, Enflurane. Record Enflurane concentration required to maintain pulse and blood pressure within 20% of base line for 75% of procedure.

PROGRESS

(81 03 - 81 11) Twenty-five (25) ASA class I patients admitted for elective orthopedic procedures on an upper or lower extremity were studied. There was no relationship between the preoperative hemoglobin levels and the percent concentration of Enflurane required for anesthesia. A thesis was written and accepted as partial fulfillment of the requirements for the Academy of Health Sciences, Anesthesiology for ANC Officers Course.

STATUS: (C)

TITLE: Arterial Blood Gas Analysis: A Study of Sampling
Techniques From Indwelling Arterial Catheter Systems

PRINCIPAL INVESTIGATOR: MAJ Nancy C. Molter, ANC

PROFESSIONAL ASSISTANTS: COL Beverly A.. Glor, ANC
LTC Henry D. Covelli, MC

WORK UNIT NO: 82/40

TECHNICAL OBJECTIVE

To ascertain the least amount of blood required to be withdrawn and discarded from the indwelling arterial catheter flush system prior to sampling for accurate arterial blood gas (ABG) values.

METHOD

Samples (at least 30 sets of four specimens per set) will be taken from patients with an indwelling arterial catheter whose condition does not warrant removal of nine ml of blood for study purposes only. All samples will be drawn with a standardized kit and immediately placed on ice. A baseline ABG sample (#A) of 2 ml will be obtained by direct puncture. The arterial catheter flush system will be cleared of one ml of solution by withdrawing at the first stopcock nearest the catheter. A standard calibrated syringe will be used. The solution obtained will be discarded. A 2 ml blood specimen for ABG # 1 will be drawn, and then a second and third sample of two ml will be drawn for ABG's #2 and #3. Each sample from the arterial line represents specimens obtained after 1 ml of clearing, 3 ml clearing, and 5 ml clearing, respectively. All ABG specimens will be analyzed by a skilled technician on approved laboratory equipment for pH, PCO₂, and PO₂ values. The differences in values between ABG #A and #1, #2, and #3 respectively will be analyzed by analysis of variance.

METHOD

(82 03 - 82 09) Thirty (30) sets of specimens were studied. There was no statistical significance between the specimens. As little as 1 cc could be withdrawn and discarded with accurate results obtained. A paper has been submitted for presentation at a national meeting in the spring of 1983.

STATUS: (C)

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

PRINCIPAL INVESTIGATOR: CPT Mary L. Muench, ANC

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

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 11) Twenty-eight couples were studied. The general conclusion drawn from this study is that there is no significant difference in the spontaneous abortion rate between the wives of active duty Army anesthetists and the wives of general duty male nurses. However, since only a small number of a select population was studied, it is felt that further study is definitely needed in this area. A thesis was written and accepted as partial fulfillment of the requirements for the Academy of Health Sciences, Anesthesiology for ANC Officers Course.

STATUS: (C)

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 Leo A. Le Bel, ANC
LTC Michael R. Moon, MC

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 O₂ 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% O₂ 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

(81 03 - 81 11) Fifteen adult subjects from a random convenient sample or those patients scheduled for elective surgery were studied. There was not a significant difference in the three treatment groups for either mean arterial pressure or heart rate. A thesis was written and accepted as partial fulfillment of the requirements for the Academy of Health Sciences, Anesthesiology for ANC Officers Course.

STATUS: (C)

TITLE: Hemoglobin Saturation During Spinal Anesthesia

PRINCIPAL INVESTIGATOR: CPT William A. Richling, ANC

PROFESSIONAL ASSISTANTS: LTC Leo A. Le Bel, ANC
LTC Michael R. Moon, MC
MAJ Donald Christensen, ANC
CPT Martha Downs, ANC
CPT James Spivery, ANC

WORK UNIT NO: 82/43

TECHNICAL OBJECTIVE

To determine whether subarachnoid block anesthesia significantly alters oxygen saturation of hemoglobin.

METHOD

Approximately 30 subjects undergoing elective surgery, subarachnoid block anesthesia, ASA classification I or II, whose surgical position will be supine will be studied. The subjects will receive no premedication. Oxygen-hemoglobin saturation will be measured by oximetry before administration of subarachnoid block anesthesia and thirty minutes after the administration of the subarachnoid block anesthesia. Data will be examined to determine if there is a significant change in oxygen-hemoglobin saturation resulting from the subarachnoid block anesthesia.

PROGRESS

(82 04 - 82 09) Eleven (11) subjects were studied during Fy 82. Patients were counselled preoperatively. Oxygen-hemoglobin saturation was painlessly measured by ear oximetry before administration of subarachnoid block anesthesia and thirty minutes after administration of the subarachnoid block. Data has been examined to determine if there was significant change in oxygen-hemoglobin saturation resulting from the subarachnoid block anesthesia. No significant change was noted. The final draft of a paper is now being prepared.

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 OB/GYN

TITLE: Ritodrine Hydrochloride Applications to Fetal Distress

PRINCIPAL INVESTIGATOR: LTC Edward Dashow, MC

PROFESSIONAL ASSISTANTS: COL Joseph Sakakini, MC
LTC Roger A. Spencer, 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 made 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 - 82 09) Thus far only two patients have been entered into this protocol, both in FY 81. Because of the double-blind method, the effect of ritodrine hydrochloride used thus far is not known. The two patients entered had unremarkable postpartum courses along with their infants.

STATUS: (O)

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

PRINCIPAL INVESTIGATOR: LTC Edward E. Dashow, MC

PROFESSIONAL ASSISTANT: COL Joseph Sakakini, 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 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 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 - 82 09) Five patients have been entered, and it would appear that in only one case did the protocol medication cause cessation of bleeding. It is thought that better results might have been obtained had there not been a problem with a possible impotent batch of medicine. The medication has had no adverse effect in any of the patients.

STATUS: (0)

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 OBJECTIVE

To review all pregnancies where antepartum monitoring was used and assess the following: (1) the outcome 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 seemingly 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 - 82 09) Two thousand charts have been reviewed with 16 charts being positive. All positives have been associated with fetal jeopardy. A paper has been submitted for publication. A paper has been accepted for presentation at the Armed Forces District Meeting of the American College of Obstetrics and Gynecology, Portland, OR, October 1982.

STATUS: (C)

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 OBJECTIVE

(1) To ascertain whether a decreased caesarean section rate will result with conservation 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 conservation 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 - 82 09) Nineteen patients have been entered in the conservative treatment group. There has been one Cesarean section secondary to failure to progress in labor. This was felt to be secondary to cephalo-pelvic disproportion. There are eleven subjects in the immediate induction group. There is no indication that infection has been a problem. There has been one Cesarean section in this group for failure to progress in labor.

STATUS: (0)

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 OBJECTIVE

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

The implementation of this protocol has been delayed

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 ASSISTANTS: 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 objective 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 poke-weed) 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 - 82 09) Equipment and supplies have now be assembled. Actual inoculation of the animals will begin in late November.

STATUS: (0)

TITLE: Impact on Fetal Monitoring on the Premature Infant

PRINCIPAL INVESTIGATOR: COL David Sa'Adah, MC

PROFESSIONAL ASSISTANTS: COL Joseph Sakakini, MC
MAJ Alexander Smythe, 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 compared to randomized traditional auscultation fetal heart rate. Comparisons of fetal outcome and well-being will be made. A comparison will be made of infants <1100 gm and >1100 gm. Infants will be followed and evaluated for evidence of retardation, cerebral palsy, and hearing loss at 6 months, 1 year, 1 1/2 years, and 2 years.

PROGRESS

(80 06 - 82 09) Nineteen patients have been enrolled. It is too early for any analysis of data.

Due to the departure of MAJ Smythe, COL David Sa'Adah has become the principal investigator.

STATUS: (0)

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

D E P A R T M E N T O F P A T H O L O G Y

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 ³H-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., B ₆ assay, begin multivitamins, p.o. 2 mg B ₆ , q.d.
4 wks	- L.T., B ₆ assay, begin B ₆ vitamins p.o. 50 mg q.d.
6 wks	- L.T., B ₆ assay
12 wks	- L.T., B ₆ assay
14 wks	- L.T., B ₆ assay, end B ₆ supplementation
20 wks	- L.T., B ₆ assay, end multivitamin supplementation
24 wks	- L.T., B ₆ 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 deficient 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

(78 11 - 82 09) The data show that dietary vitamin B₆ supplementation markedly stimulates the (methyl-³H) 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. 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. Studies were also 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. Vitamin B₆ reverses this depletion. A previously unreported toxic effect of the aminoglycoside antibiotics is the apparent exacerbation of pre-existing vitamin B₆ deficiency, causing patients to become comatose. A manuscript has been submitted on this latter study.

PUBLICATION: 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 Springs, BC.

STATUS: (C)

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

PRINCIPAL INVESTIGATOR: COL 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 coliform 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 *M. 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. Radioisotope scrotal scans will be done on all patients within 48 hours to rule out testicular torsion.

The Role of Bacterial and Chlamydial Agents - Podgore

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 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*, *N. 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 - 82 09) Preliminary results have been tabulated and were presented at the American Public Health Association Meeting in November 1980.

Due to the departure of the investigators, the entire protocol could not be completed. However, a paper entitled "Asymptomatic *Chlamydia trachomatis* Urethral Infection in Male Military Personnel" has been submitted for consideration for publication. *Chlamydia trachomatis* alone was isolated from the urethra from 10 of 97 asymptomatic sexually active U.S. Army enlisted men undergoing routine physical examinations. *Neisseria gonorrhoeae* alone was isolated from one man, and both *N. gonorrhoeae* and *C. trachomatis* were isolated from another subject. The presence of *C. trachomatis* was associated with a previous history of urethritis, but not with age, presence of pyuria, or the number of sexual partners in the previous six months. The asymptomatic male enlisted population may comprise a significant reservoir of *C. trachomatis* infection that has been previously unrecognized.

STATUS: (C)

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: COL John K. Podgore, MC

PROFESSIONAL ASSISTANTS: LTC Richard Belts, MC

WORK UNIT NO: 80/72

TECHNICAL OBJECTIVE

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

Pregnant women who have *C. trachomatis* isolated from their cervical culture at the routine 32-week gestation exam and their spouses will be studied. The women will receive either 250 mg erythromycin q.i.d. for 14 days or amoxicillin, 500 mg q.i.d. for 14 days. The spouses will receive doxycycline 100 mg twice a day for 14 days. A repeat cervical culture will be obtained. Spouses will have an anterior urethral culture for *C. trachomatis*. Other necessary specimens will be obtained. Conjunctival and nasopharyngeal specimens will be obtained on all study infants 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 - 82 09) All data has been collected. A manuscript is in preparation.

STATUS: (C)

TITLE: Use of a Microwave Oven to Thaw Fresh-Frozen Plasma (and Cryoprecipitate).

PRINCIPAL INVESTIGATOR: CPT Dennis E. Urban, MSC

PROFESSIONAL ASSISTANTS: CPT Robert M. Melmoth, MSC

WORK UNIT NO: 82/03

TECHNICAL OBJECTIVE

To demonstrate that the use of a microwave oven does not significantly deteriorate labile coagulation factors when thawing fresh frozen plasma (FFP) or cryoprecipitate.

METHOD

A minimum of 40 split samples of FFP from the same donor will be prepared. Twenty will be thawed in a waterbath and twenty will be thawed in a microwave oven with revolving carousel and a temperature probe to monitor maximum temperature, followed by coagulation factor assay and the results compared. If the microwave oven method is successful, the FFP will be thawed by this method and transfused to patients, with two units per month assayed for quality assurance purposes.

A minimum of 50 units of cryoprecipitate will be compared in the same manner as above and transfused in the same manner as above if the preliminary study is successful.

PROGRESS

(81 11 - 82 09) This protocol has been terminated. The investigators were unable to obtain the necessary equipment before being reassigned.

STATUS: (T)

TITLE: Use of a Syringe and Blood Filter for Neonatal Transfusions.

PRINCIPAL INVESTIGATOR: CPT Dennis Urban, MSC

PROFESSIONAL ASSISTANTS: Marlene Bartram, M.T.
Delores Dilks, M.T.
Hollis Smith, M.T.

WORK UNIT NO: 82/04

TECHNICAL OBJECTIVE

To provide better utilization of Group O, Rh negative red blood cells, when small amounts (10-20 ml) are needed for neonatal replacement transfusions. The investigators will attempt to obtain (a) the incidence of culture positive fresh frozen plasma (FFP) on whole blood; (b) correlation with neonatal bacteremia/septicemia; and (c) comparison of blood utilization rate with new and old methods.

METHOD

Thirty (30) ml syringes will be filled with 8 ml fresh AB plasma and frozen in a sealed plastic bag. When blood is needed, syringe will be thawed and 16 ml of O negative packed red blood cells will be added and mixed. Syringe will be issued with an 18-micron syringe blood filter. Exact amount of FFP and packed red blood cells may be adjusted to provide whole blood with a hematocrit of 65%. All syringes of thawed FFP or units of reconstituted whole blood will be cultured for sterility and the NICU notified immediately of positive culture results. All transfused infants would be evaluated when FFP or reconstituted blood is culture positive.

PROGRESS

(81 11 - 82 09) Eighty-four (84) syringes of plasma have been cultured and transfused to 33 neonatal patients. Of the 84 cultures, 81 showed no growth and 3 were positive. The three positive cultures consisted of one *Staphylococcus epidermitis*, one *Pseudomonas maltophilia*, and one *Flavobacterium sp.*, all common contaminants. Extra precautions have been instituted to prevent contamination. This project should be continued for at least six months.

STATUS: (0)

DETAIL SHEETS
FOR
PROTOCOLS

DEPARTMENT OF PEDIATRICS

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 Soliders

PRINCIPAL INVESTIGATOR: COL Richard M. Graven, MC

PROFESSIONAL ASSISTANTS: 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 classification 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 - 82 09) Studies on fifty-one (51) active duty soldiers were completed. There were no significant differences between mean scores in any of the four areas evaluated.

STATUS: (C)

TITLE: Use of Folinic Acid in Prevention of Neutropenia and
Thrombocytopenia Secondary to Trimethoprim-sulfamethoxazole.

PRINCIPAL INVESTIGATOR: CPT G. William Letson, MC

PROFESSIONAL ASSISTANTS: LTC Alan D. Mease, MC
CPT Joseph High, MSC
CPT Merlin L. Robb, MC
CPT Philip L. Rogers, MC

WORK UNIT NO: 82/38

TECHNICAL OBJECTIVE

To establish whether or not folinic acid can significantly reduce reported incidence of 34% neutropenia and 12% thrombocytopenia in children treated with Trimethoprim-sulfamethoxazole.

METHOD

Pediatric patients diagnosed as having acute otitis media or urinary tract infections would be treated with Trimethoprim-sulfamethoxazole (T-S) in one group and T-S plus folinic acid in a second group. Dosage would be 40 mg/kg per day for T-S and 0.5 mg/kg per day for folinic acid divided in two daily doses and given over a ten day period. Patients would be randomized and selected to be in one or the other group with the T-S plus folinic acid as an experimental group. Drugs would be given in such a fashion as to achieve a double blind study. Results would be obtained by drawing a baseline CBC and another on the final day of treatment. Anyone developing neutropenia would be followed further with CBC's until resolution of neutropenia. Count of medication left over would be undertaken at the end of treatment to determine compliance level. The final step would be statistical analysis of data. A minimum of 30 subjects would be studied in each group.

PROGRESS

(82 03 - 82 09) Thirteen patients have been studied. As this is a double-blind study, no results have been tabulated. Only follow-up on neutropenic or thrombocytopenic patients has been done.

STATUS: (O)

TITLE: Mechanical Ventilation of Newborn Premature Lambs: The Effect of Frequency, I:E Ratio, PIP, and PEEP on Oxygenation and Ventilation

PRINCIPAL INVESTIGATOR: MAJ Philip V. Marinelli, MC

PROFESSIONAL ASSISTANTS: LTC Gary Pettett, MC
MAJ Stanley P. Liebenberg, VC
CPT Richard Meidell, MC

WORK UNIT NO: 82/26

TECHNICAL OBJECTIVE

To prospectively evaluate the effect of ventilator setting, specifically frequency, I:E ratio, PIP, and PEEP, on arterial oxygenation and minute ventilation in premature newborn lambs.

METHOD

Premature or term lambs (125-135 days gestation) will be delivered via C-section, intubated with cuffed endotracheal tubes, paralyzed with Pavulon, and ventilated with the Sechrist ventilator. All animals will have prophylactic chest tubes inserted bilaterally to prevent symptomatic pneumothoraces during the experiment. Catheters will be placed in the descending aorta through femoral artery cutdowns. The aortic blood pressure will be maintained at 50-70 mm of mercury by infusions of maternal blood and/or lactated Ringer's solution. Initially, ventilator settings will be a rate of 30, inspiratory time of 1 sec, expiratory time of 1 sec, and sufficient PIP and PEEP to deliver an adequate tidal volume while maintaining a normal P_aO_2 and P_aCO_2 . The sequential changes in rate will be made maintaining the baseline PIP and PEEP. At the completion of each change, the fetus will be returned to baseline until values are stabilized before proceeding to the next step. Subsequent changes in I:E ratio, maintaining a constant rate PIP and PEEP, will be studied. The fetus will be returned to baseline settings between each step. Third, changes in PIP will be employed with a constant rate, constant I:E ratio, and a constant PEEP. Finally, changes in PEEP will be determined by maintaining a constant rate, a constant I:E ratio, and a fixed peak inspiratory pressure. Arterial blood gases will be determined prior to and immediately following each portion of the experiment. Lung tissue will be obtained from each lamb for microscopic examination.

PROGRESS

(82 02 - 82 09) No studies have been done. The investigators are awaiting the birth of the lambs.

STATUS: (0)

TITLE: Mean Airway Pressure: Significance During Mechanical Ventilation in Neonates

PRINCIPAL INVESTIGATOR: MAJ Philip V. Marinelli, MC

PROFESSIONAL ASSISTANTS: LTC Gary Pettett, MC
CPT Richard Meidell, MC

WORK UNIT NO: 82/27

TECHNICAL OBJECTIVE

The specific aspects of the respiratory cycle during mechanical ventilation which allow optimal gas exchange are controversial. Recently, the concept of mean airway pressure as a composite of all pressures has been employed. It has been shown that mean airway pressure correlates directly with oxygenation. The purpose of this study is to examine the effect of various ventilator settings on gas exchange while maintaining a constant mean airway pressure.

METHOD

All neonates requiring intermittent mandatory ventilation will be eligible for the study. Indications for mechanical ventilation will be based on the standard criteria ($P_{aCO_2} > 60$ Torr, $pH < 7.25$ and/or $aPO_2 < 50$ Torr, $F_{iO_2} > 0.6$). A pressure limited time-cycled ventilator will be used. PIP, PEEP inspiratory time, flow rate, ventilator rate, and F_{iO_2} will be adjusted to provide a P_{aO_2} of 50-80 Torr and a $P_{aCO_2} < 60$ Torr, pH of 7.30-7.40. The initial combination of settings producing these values will be taken as the baseline ventilator settings. Mean airway pressure will be measured from the T piece of the ventilator circuit using a proximal airway ventilator monitoring system which provides a constant digital display of the mean airway pressure by sampling proximal airway pressures every 10 msec and averaging these values over time. After achieving a steady state on baseline ventilator settings, an arterial blood sample will be obtained and the following sequential changes will be made on the ventilator:

Experiment I: PIP increased by 20% of baseline value and duration of positive pressure (inspiratory time) will be decreased in order to achieve the same baseline mean airway pressure. The other ventilator settings will be maintained at baseline value. All settings will then be returned to the initial baseline values.

Experiment II: PIP will be decreased by 20% of baseline value and inspiratory time will be increased to maintain a constant mean airway pressure; the other ventilator settings will be held constant.

Following a 10 min equilibration period, arterial blood gas will be sampled. Vital signs will be continuously monitored. In

Mean Airway Pressure: Significance During Mechanical Ventilation
in Neonates - Marinelli

addition, a transcutaneous PO_2 monitor will be used to insure that no detrimental increase or decrease in P_{aO_2} occurs as the result of experimental changes. This sequence will be followed in the first 24 hours of the infant's life and repeated during the second and third day in order to observe whether the natural change in compliance of the lungs will change the significance of mean airway pressure.

Each of the infants will serve as its own control. Statistical analysis of pH and P_{aO_2} and P_{aCO_2} will be performed utilizing Student's t test for paired data. The $aAPO_2$ gradient will be calculated from each of the blood gas results in order to standardize P_{aO_2} values over a range of F_iO_2 concentrations. These ratios will be analyzed by the means of the t test for paired data.

PROGRESS

(82 02 - 82 09) Equipment for this study has just been received. The study will start within the next few weeks.

STATUS: (0)

TITLE: Modified Immune Serum Globulin in Neonates

PRINCIPAL INVESTIGATOR: MAJ Philip V. Marinelli, MC

PROFESSIONAL ASSISTANTS: LTC G. Fischer, MC
LTC Gary Pettett, MC
LTC J. Pierce, MC
MAJ Robert M. Skarin, MC
CPT Richard Meidell, MC

WORK UNIT NO: 82/28

TECHNICAL OBJECTIVE

To evaluate Modified Immune Serum Globulin (MISG) as an adjunct to antimicrobial therapy in the treatment of neonatal Group B streptococci (GBS) disease. This protocol will analyze the ability of MISG to elevate neonatal IgG levels and will specifically look at pre and post MISG sera for evidence of increased activity against Group B streptococci using *in vitro* assays for opsonic antibody.

METHOD

Human MISG will be screened to ensure activity against several strains of GBS and one lot of 5% MISG will be selected and used throughout the study. Neonates who have a clinical diagnosis of suspected or proven sepsis will be evaluated and treated in the standard fashion and will also receive MISG. Infants thought to be in need of blood products will be excluded from the study. All infants will have cultures for bacterial pathogens taken prior to antibiotic or MISG therapy which will include umbilical, gastric aspirate, urine, blood, and cerebral spinal fluid. A 2.0 ml blood sample (prespecimen) will be obtained just prior to starting antibiotics and MISG therapy. A second 2.0 ml specimen will be obtained 2 hours after the completion of MISG infusion and again at 1, 2, 3, and 6 weeks after the infusion. The material will be given as 5% human MISG in a 10% maltose solution. The dose will be 250 mg/kg or 5 ml/kg to be given as a 30 minute infusion. Standard supportive care will be given to all other neonates treated for proven or suspected sepsis. All patients receiving MISG will be required to have constant temperature, heart rate, and respiratory monitoring. Patients with an umbilical artery catheter will have continuous BP monitoring. If not, BP by the Doppler method will be obtained before infusion, every 15 minutes after infusion for at least 2 hours, and then every hour for at least 24 hours. Urine volume, protein, and reducing substances will be measured at each void for the first 24 hours after MISG administration. Serum sodium, potassium, BUN, chloride, calcium, glucose, and osmolality along with hematocrit, hemoglobin, platelets and white blood cell count with differential will be

Modified Immune Serum Globulin in Neonates - Marinelli

obtained before, 2 hours after, and twice weekly for 2 weeks following the infusion. After the blood specimen is obtained, the serum will be separated and stored at -70°C. Immunoglobulin levels will be determined by standard immunodiffusion assay and opsonic antibody to GBS will be measured using the bactericidal opsonophagocytic assay currently used in the MAMC lab. In addition, a chemiluminescent assay, which measures activation of the hexose-monophosphate shunt, is being developed and will be utilized to measure functional antibody to GBS. All patients will be followed for a minimum of 6 weeks. The infants will be evaluated for growth and development and will receive all standard immunizations and care.

PROGRESS

(82 02 - 82 09) Approval has just been received from HSC. No patients have been enrolled.

STATUS: (C)

TITLE: Intracranial Two-Dimensional Ultrasonography and
Intracranial Hemorrhage. Identifying Patients at Risk.

PRINCIPAL INVESTIGATOR: CPT Richard Meidell, MC

PROFESSIONAL ASSISTANTS: LTC Gary Pettett, MC
MAJ Philip V. Marinelli, MC
MAJ Robert M. Skarin, MC

WORK UNIT NO: 82/19

TECHNICAL OBJECTIVE

To determine incidence of intracranial hemorrhage in a selected group of neonates; to document the time of onset of intracranial hemorrhage and relate this to clinical course and outcome; and to identify the risk factors which correlate with the occurrence of the hemorrhage.

METHOD

Infants <2000 gms at birth and/or Apgar scores <5 at one minute and/or <6 at five minutes will be scanned on days 1, 3, and 5 of life. Sagittal, coronal, and, when possible, cross sectional views will be obtained via 2-D real time ultrasonography. Evidence of intracranial hemorrhage and its sequelae will be noted. Physical examination including neurological evaluation will be made on each study day. Clinical findings associated with intracranial hemorrhage will be noted. Prenatal and intrapartum history will be obtained along with blood gas studies, serum electrolytes, serum calcium, and CBC. Additional laboratory studies such as CSF will be obtained if clinically warranted. Drug therapy and other therapeutic measures, such as mechanical ventilation and fluid therapy, will be noted. CT scan will be obtained on all positive ultrasound studies as well as in those infants whose clinical course suggests intracranial hemorrhage although intracranial hemorrhage is not demonstrated by ultrasound. Incidence of intracranial hemorrhage as diagnosed by ultrasound will be determined. Those patients at risk for intracranial hemorrhage will be identified.

PROGRESS

(82 01 - 82 09) Twenty-five patients have been studied in a prospective fashion. Data has been analyzed and a paper has been submitted for presentation at the American Academy of Pediatrics Annual Meeting. A manuscript is also being prepared.

STATUS: (C)

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

TECHNICAL OBJECTIVE

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 - 82 09) The necessary laboratory apparatus has just become operational. Investigators will now begin to register infants in the protocol.

STATUS: (0)

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 - 82 09) The necessary laboratory apparatus has just become operational. Investigators will now begin to register infants in the protocol.

STATUS: (0)

TITLE: Hydrogen Breath Analysis in Children with Chronic
Nonspecific 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 midexpiration, 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 - 82 09) The necessary laboratory apparatus has just become operational. Investigators will now begin to register infants in the protocol.

STATUS: (0)

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

PRINCIPAL INVESTIGATOR: MAJ Dan C. Moore, MC

PROFESSIONAL ASSISTANTS: 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, T₄, T₃RU, 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 T₄, T₃U, thyroid antibodies, HLA type and hemoglobin A₁C.
- b. Injection of TRH, 7 µg/kg IV
- c. 30 minutes - blood sample for TSH
- d. 60 minutes - blood sample for TSH

Measurement of TSH, T₄, T₃U, thyroid antibodies, HLA type and hemoglobin A₁C are accepted tests in the management of the diabetic. The TRH test is a standard test to evaluate thyroid function.

PROGRESS

(81 07 - 82 09) Five patients have been entered in this study; all during FY 82. Data collection is continuing, but is insufficient to analyze at this point.

STATUS: (0)

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 - 82 09) A sample of 12 mothers of hypertensive adolescents and 15 mothers of normotensive adolescents matched for adolescent's age, height, and weight were studied. Hypertension was defined as diastolic BP > 2 S.D. above the mean for age and sex. Only one case of toxemia was identified in either group, thus limiting the potential for meaningful analysis. The experience in designing the study and problems in conducting it, as well as the data obtained, formed the basis of a master's thesis in nursing for co-investigator Jeanette Welker.

STATUS: (C)

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; to discern whether any of these same parameters can be used to predict response to medroxyprogesterone therapy; and to 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 puberty status according to the system of Tanner. Plasma LH, FSH, E₁, E₂, 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 - 82 09) Nineteen (19) subjects have been entered in this protocol. Preliminary analysis of data shows expected increases in sex hormone level and gonadotropins. In some cases, estrone levels are significantly higher than estradiol levels. Two cases of premature thelarche associated with elevated estrone levels have spontaneously resolved in conjunction with return of estrone levels to normal. Sex hormone binding globulin levels tend to be lower than expected for age. Somatomedin-C levels do not appear to be affected.

STATUS: (0)

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

PRINCIPAL INVESTIGATOR: LTC Gary Pettett, MC

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

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

(81 09 - 82 09) During FY 82 this protocol was utilized on two occasions as part of the regional medical education program; once at Bremerton NRMCC and once at Whidbey Island NAS. It is anticipated that this protocol will continue to be used in this manner.

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.

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

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
Atlanta, GA, Jul 1977.
- d. Annual Meeting of the Association of Military Surgeons, Washington, DC, Nov 1977.

STATUS: (O)

TITLE: Short Term Developmental Consequences of Acquiring CMV
From a Blood Transfusion Prior to Term

PRINCIPAL INVESTIGATOR: LTC Virginia F. Randall, MC

PROFESSIONAL ASSISTANTS: LTC John Podgore, MC
MAJ Carl Loovis, MSC

WORK UNIT NO: 82/16

TECHNICAL OBJECTIVE

To describe short term developmental consequences produced in infants who are CMV negative at birth and who acquire active disease as a result of being transfused CMV antibody positive blood. Principal developmental consequences to be assessed are those related to auditory and vestibular function. Short term implies less than one year. An important goal of the principal investigator is to begin screening blood prior to use in the nursery. This study will terminate collection of new infants when the blood bank adopts this procedure.

METHOD

ELISA will be used for determination of those infants who are seronegative and those seropositive from cord blood and mother's blood samples. A determination will be made of seronegative or seropositive for each unit of blood used for transfusion in the nursery. Infants who are seropositive at birth are congenitally infected and will be followed with assessments at due date, 2 months corrected age, and 4 months corrected age. At 4 months corrected age, BSER and cold calorics will be done in addition to the neurodevelopmental assessment. Seronegative infants who receive seronegative blood will be assessed at due date, 2 months, and 4 months corrected age. ELISA will be repeated at these dates as well as neurodevelopmental assessment. Seronegative infants who receive seropositive blood will have neurodevelopment at due date, 2 months and 4 months corrected age. ELISA and urine for virus culture will be repeated on these assessments. If the ELISA or viral culture suggests active infection, BSER and cold calorics will be done at 4 months. Method of neurodevelopmental evaluation: (1) due date - Brazelton, Bayley mental and motor, MAI, neurovestibular examination; (2) two and four months corrected age - Bayley mental and motor, MAI, and neurovestibular examination.

PROGRESS

(81 11 - 82 09) This project was closed when the Blood Bank at MAMC began to screen for CMV titer prior to release of blood for transfusion to nursery patients. At that time, only three patients were entered on whom the total lab work and developmental studies were available. A paper has been submitted to Child Development describing the possible developmental consequences of acquiring CMV from transfusion in the nursery and describing the method used here at MAMC to reduce that risk.

STATUS: (C)

TITLE: Comparison of Highly Skilled Professionals and Entry Level Practitioners in Assessment of Infants

PRINCIPAL INVESTIGATOR: Catherine Yokan, M.D., DAC

PROFESSIONAL ASSISTANTS: CPT Nancy Todd, ANC
Lynette S. Chandler, Ph.C.
Mary Andrews, R.N.

WORK UNIT NO: 82/46

TECHNICAL OBJECTIVE

To compare highly skilled professionals with entry level practitioners in their ability to reliably present and interpret a screening test of Movement Assessment of Infants in an effort to discover if personnel with entry level skills can be used in a screening program without compromising the care of infants.

METHOD

Twenty entry level PT and OT students and twenty NDT trained OT and PT students will be given an initial 1/2 day training on the screening test as derived from The Movement Assessment of Infants. In terms of four trainees and one supervisor, 13 infants will be screened for movement deficits with the goal of achieving inter-rater reliabilities of 80 and above. Each training sessions will last 2 1/2 days. There will be 10 sessions to complete the study involving a total of 40 trainees and 130 infant-mother dyads. Four month old infants will be screened. All sessions will be video taped, and parents will be interviewed as to their perspective on the screening session.

PROGRESS

(82 05 - 82 09) Data analysis is in progress and a manuscript is being prepared for publication.

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 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. Hotelling's Multiple t-tests for multi-variant 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 - 82 09) Six subjects have been evaluated. Four of these have completed the evaluations and the other two require another testing. No controls have been entered. Subject collection will continue.

STATUS: (0)

TITLE: Parental Discrimination in the First 2 Weeks of Life

PRINCIPAL INVESTIGATOR: MAJ Robert C. Hulsebus, MSC

PROFESSIONAL ASSISTANTS: 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 two 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 - 82 06) This study was modified to only study the fathers and infants. Twenty-one 3-day old infants were studied. Although there was a preference by 3-days old for their fathers' voices (57%), the shift was not statistically significant. Twenty-two 7-day old infants were studied and their preference for their fathers was statistically different using the chi square test. This study demonstrated that infants can discriminate their fathers within the first week of birth. More study is suggested in this area. A manuscript is in preparation from this study.

STATUS: (C)

TITLE: Psychological Variables Related to Childbirth and Early Infant Development

PRINCIPAL 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 follow-up interview to obtain mother's subjective rating of the delivery and the infant. Conduct record search for selected variables: length of labor, presence of complications, status of newborn, and the bonding rating between mother and child. At the 2-month well-baby follow-up visit, request mother to repeat the Zung Self-Rating Depression Scale and do a record search on the development of the infant. Data analysis will include descriptive statistics, correlation, and contingency table analysis.

PROGRESS

(81 03 - 82 09) The project is in the fourth of its five stages. Preliminary work has begun on stage five. Phase I, interviewed 250 women during the seventh month of pregnancy, and most of Phase II, post-partum interviews, were completed in FY 81. FY 82 work included the remaining post-partum interviews (87 patients), all of the Phase III review of inpatient records of mothers and infants and approximately 40% of Phase IV, follow-up outpatient record review. Phase V, data processing, has begun on 75 studies in order to expedite "debugging of computer programs while Phase IV is being completed.

STATUS: (0)

DE 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: Implantation of Intraocular Lenses

PRINCIPAL INVESTIGATOR: COL Stanley C. Allison, MC

PROFESSIONAL ASSISTANTS: COL Stanley C. Sollie, MC
LTC Christopher G. Knight, MC
MAJ Bruce D. Bellin, MC
CPT Lawrence E. Hannon, MC
LTC John C. Goodin, MC

WORK UNIT: 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

(81 10 - 82 09) Due to the retirement from active duty of COL Sollie, COL Allison, who initially began this protocol before a tour in Korea, is now the principal investigator. The implantation of intraocular lenses has become the standard of cataract surgery. It continues, at this time, to be an experimental procedure although general clearance is expected from the FDA in one to five years. There were 123 implants performed over the past 12 months. This rate is expected to continue for the foreseeable future.

STATUS: (O)

TITLE: Advanced Trauma Life Support Course

PRINCIPAL INVESTIGATOR: LTC Terence L. Babcock, MC

PROFESSIONAL ASSISTANTS: LTC Stanley C. Harris, MC
MAJ Kenneth Frumkin, MC
MAJ Stanley P. Liebenberg, VC

WORK UNIT: 82/32

TECHNICAL OBJECTIVE

To provide training to General Surgery, Emergency Medicine, and Family Practice residents in the proper management of the patient in the initial one hour after major trauma.

METHOD

At least twice a year, the Advanced Trauma Life Support Course as designed by the American College of Surgeons will be conducted. The course involves a hands on training session in the placement of chest tubes, tracheostomy, pericardiocentesis, peritoneal lavage, and venous cutdown utilizing the dog as the animal model.

PROGRESS

(82 03 - 82 09) Four sessions of this course have been taught. Due to the departure of LTC Babcock, LTC Stanley C. Harris has become the principal investigator.

STATUS: (0)

TITLE: Study of Delayed/Nonunion in Jones Fracture
PRINCIPAL INVESTIGATOR: COL Virginia M. Badger, MC
PROFESSIONAL ASSISTANTS: MAJ Stanley 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 stress 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 - 82 09) Technical work and histopathology have been completed. 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: LTC William Belville, MC

PROFESSIONAL ASSISTANTS: LTC Samuel J. Insalaco, MC
LTC George S. Ward, VC
MAJ Eduardo S. Blum, MC
MAJ Carl F. Cricco, MC
MAJ Willis H. Jacob, MSC
MAJ Roger Schoenfeld, MC

WORK UNIT: 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.

TECHNICAL OBJECTIVE

Thio-TEPA has been used in the management of various types of neoplasias for almost two decades. However, its use in the management of urinary bladder carcinoma has had mixed results. In addition, the cytotoxic effect 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 bladder 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.

The Effect of Dimethyl Sulfoxide - Belville

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

(81 09 - 82 10) As stated in the preceding note, cis-platinum was used in this study rather than Thio-TEPA. A manuscript has been accepted for publication by the Journal of the American Osteopathic Association. The results of the study 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 necessary, and is planned, to solidify and extend these observations.

Upon the departure of MAJ Schoenfeld in June, LTC Belville became the principal investigator.

PRESENTATION: Schoenfeld, R.H., Belville, W.D., Jacob, W.H., Buck, A.S., Dresner, M.L., Insalaco, S.J., and Ward, G.S.: The Effect of Dimethyl Sulfoxide on the Uptake of Cisplatin From the Urinary Bladder of the Dog. Kimbrough Urologic Seminar, Denver, November 1981.

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 prostate 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 04 - 82 09) A computerized system for data storage for the tumor registries of the MEDCENS is in the process of being developed at the present time at HSC. Also, MAMC will begin trial use of a new system within the next 6 months which has been ongoing at DDEAMC and will be adapted by MAMC for use here. This model can be modified to be compatible with American College of Surgeons requirements. In view of these developments, this project has been terminated.

STATUS: (T)

TITLE: End to Side Distal Gastrectomy in Dogs

PRINCIPAL INVESTIGATOR: LTC Preston L. Carter, MC

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

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 proposed for the initial trial. Large dogs will be subjected to distal gastrectomy 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 also be carried out prior to sacrifice.

PROGRESS

(81 05 - 82 09) This project demonstrated that end to side gastroduodenostomy heals reliably in the dog model following gastric resection. A paper has been accepted for exhibit at the American College of Surgeons Meeting in Chicago in October 1982.

STATUS: (C)

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 - 82 09) This protocol provided technical instruction in basic surgical skills to interns and residents in General Surgery and met its objective.

STATUS: (C)

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. Hospitalization 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 - 82 09) Nine patients have been entered into the study. Estimate completion of study (20 patients) in one year.

STATUS: (0)

TITLE: A Protocol to Compare Segmental Mastectomy and Axillary Dissection With and Without Radiation of the Breast and Total Mastectomy and Axillary Dissection.

PRINCIPAL INVESTIGATOR: LTC Preston Carter, MC

PROFESSIONAL ASSISTANTS: LTC James F. Bascom, MC
LTC Stanley C. Harris, MC
LTC Dick R. Smith, MC

WORK UNIT NO: 82/02

TECHNICAL OBJECTIVE

To begin participation by MAMC in an established national cooperative study comparing the survival, treatment failure, and cosmetic results of partial mastectomy with and without radiation compared to modified radical mastectomy.

METHOD

Patients with breast cancers under two inches in size and without fixation to the chest wall or skin will be offered randomization to three treatment arms: (a) segmental mastectomy, axillary dissection; (b) segmental mastectomy, radiation, axillary dissection; (c) total mastectomy, axillary dissection. Patients with positive axillary nodes will, regardless of the primary treatment, be given L-PAM and 5-FU chemotherapy as further treatment.

PROGRESS

(81 10 - 82 09) One patient at MAMC has been entered into this highly specialized and specific study (hence few suitable candidates).

STATUS: (0)

TITLE: Intravenous Dexamethasone to Control Post Operative Pain
in Orthopedic Patients

PRINCIPAL INVESTIGATOR: CPT Michael Q. Cosio, MC

PROFESSIONAL ASSISTANTS: COL Richard Camp, MC
LTC Thomas J. Parr, MC
MAJ Douglas Beirne, MC

WORK UNIT NO: 82/29

TECHNICAL OBJECTIVE

To determine whether intravenous dexamethasone can decrease the severity of post-operative pain in orthopedic patients.

METHOD

Patients undergoing elective surgery will be studied with the following exceptions: history of altered immune response or delayed wound healing; steroid use in past 6 months; open wounds or fractures, infected wounds/joints or abscesses; open growth plates; total joint, hip, and spine surgery, history of malignancy; pregnant or lactating female. In a prospective, randomized, double-blind study, dexamethasone or placebo (D₅W) will be given IV slow push in 3 doses: 12 mg in the OR prior to surgery, then 4 mg 6 hours and 14 hours after the first dose. The patient will fill out a questionnaire regarding his pain level throughout the hospital stay. Pain medications will be standardized as follows: Morphine 4 or 8 mg IM q 3 hr and codeine 30 or 60 mg po q 4 hr prn pain. If allergic to codeine, Zomax 1 or 2 tabs po q 4 hr prn will be used. If allergic to morphine, Stadol 1 or 2 mg IM q 3 hr with Zomax will be used. In order to eliminate nursing bias in the use of pain medications, the patient will regulate his analgesic use by informing the nurse if he desires the IM or PO medication and the amount. The use of anti-pyretics and salicylates will be withheld for one week to insure detection of fever and possible infection as early as possible. Since some surgery is more painful than others, the patients will be subdivided into regions, ie; hand and forearm (150), shoulder (50), foot (50); ankle/tibia (100), knee (100), metal removal (50), for a total of 500 patients. Patients will be followed until the sutures are removed, usually two weeks later.

PROGRESS

(82 02 - 82 09) Fifteen subjects from a mixed population have been entered.

STATUS: (0)

TITLE: Incidence and Natural History of Deep Venous Thrombosis
in Patients Undergoing Elective Knee Surgery

PRINCIPAL INVESTIGATOR: CPT Michael Q. Cosio, MC

PROFESSIONAL ASSISTANTS: COL Stanton Brown, MC
COL Joel Sim, MC
LTC Thomas J. Parr, MC
Denise Anderson, R.N.

WORK UNIT NO: 82/57

TECHNICAL OBJECTIVE

To determine the true incidence, natural history, and response to therapy and prophylaxis of DVT in patients undergoing elective knee surgery.

METHOD

Approximately 100 patients undergoing elective surgery about the knee, except for knee ligament reconstruction, total knee replacement, or pediatric patients, will have daily clinical evaluation for DVT and PE following surgery. If a patient develops signs and symptoms of DVT or PE, an immediate Doppler and venogram and/or lung scan will be performed as appropriate. Otherwise, a venogram will be performed following a Doppler evaluation of both limbs 7-10 days post op. If the incidence of DVT in the nonoperated leg is found to be <5%, venography will be done only on the operated leg. Those patients who have DVT will undergo a perfusion lung scan immediately after the venogram, at four and eight days after detection of the DVT. Those who have CVT confined to the calf will not receive any therapy. Those with DVT of the calf with proximal extension will receive a 10 day course of IV heparin. The heparin will always be given by continuous IV infusion, maintaining the PTT between one and a half to two times normal.

PROGRESS

(82 06 - 82 09) Thirteen patients have been studied. Patient collection will continue.

STATUS: (0)

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 peripheral 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 stimuli 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 07 - 82 09) Approximately 200 subjects have been studied. The investigators found that the bulbocavernosus reflex was slightly higher in patients when stimulation was done at the glans penis. More subjects are to be studied. A manuscript has been accepted for publication.

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

Dresner, M.L., Saeed, M.A., Belville, W.D., and Buck, A.S.: Evaluation of Impotence. NY Section of the American Urological Assoc, 16 Oct 82, Rome, Italy.

STATUS: (O)

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 ASSISTANTS: 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

(81 10 - 82 09) In previous years, 16 animals were studied and sacrificed. The skulls and temporal bones were sent to the ENT Section, A.F.I.P., for review, but repeated calls have only resulted in promises of completion by the end of November 1982. A paper has been submitted for publication entitled "The Guinea Pig as a Surgical Otologic Model" from the pretrial work.

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

STATUS: (0)

TITLE: Teaching Program for Practical Microsurgery

PRINCIPAL INVESTIGATOR: LTC Thomas G. Griffith, MC

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

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 liver) will be developed by the veterinary 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

(77 09 - 82 03) This protocol has been updated and replaced by Protocol 82/35 with the same name.

STATUS: (C)

TITLE: Teaching Program for Practical Microsurgery

PRINCIPAL INVESTIGATOR: LTC Thomas G. Griffith, MC

PROFESSIONAL ASSISTANTS: COL Leonard L. Hays, MC
LTC Preston L. Carter, MC
LTC Stanley Jackson, MC
MAJ Stanley P. Liebenberg, VC

WORK UNIT NO: 82/35

TECHNICAL OBJECTIVE

To establish a formal training program in clinical microsurgery at MAMC for use of surgeons desiring to develop this expertise.

METHOD

In order to perfect the techniques needed to perform clinical microsurgery, extensive practice is needed in the research laboratory. 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 veterinary 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

(82 03 - 82 09) Eight sessions were completed during FY 82. Due to the departure of LTC Griffith, LTC Stanley Jackson has been selected as the principal investigator.

STATUS: (0)

TITLE: Medical Treatment of the Frey Syndrome

PRINCIPAL INVESTIGATOR: COL Leonard L. Hays, MC

PROFESSIONAL ASSISTANTS: 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 1/4%, 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 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

(81 10 - 82 09) Twenty-two patients participated in this study. Seventeen of these have been followed for four to five years. Topical glycopyrrolate has achieved satisfactory control of the Frey syndrome in all but one patient with only rare side effects. In the past year, the investigators studied varying dose levels on patients who had borderline satisfactory responses. Owing to its more numerous side effects and greater potential toxicity, scopolamine has been excluded from investigation for the last four years. Topical antiperspirants were usually ineffective in completely controlling gustatory sweating. More patients will be studied.

PUBLICATION: Hays, L.L.: The Frey Syndrome: A Review and Double Blind Evaluation of the Topical Use of a New Anticholinergic 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 Worsham, J.C.: The Frey Syndrome, A Simple Effective Treatment. American Academy of Otolaryngology Meeting, New Orleans, LA, Sep 81.

PUBLICATION: Hays, L.L., Novack, A.J., and Worsham, J.C.: The Frey Syndrome, A Simple Effective Treatment. Otolaryngol Head Neck Surg 90:419-25, 1982.

STATUS: (0)

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 OBJECTIVE

- (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 - 82 06) Preliminary work involved microsurgical work in a rabbit model on several occasions to gain familiarity with microsurgical techniques of arterial and venous anastomoses. Because of time constraints, MAJ Lanier was unable to carry through the primary goal of the protocol before being reassigned following the completion of his residency.

STATUS: (T)

TITLE: Evaluation of a Short Course of Dexamethasone in the
Treatment of Serous Otitis Media: A Double Blind
Crossover Study

PRINCIPAL INVESTIGATOR: MAJ Del Ray Maughan, MC

PROFESSIONAL ASSISTANTS: COL William Gernon, MC
LTC William Harpster, MC

WORK UNIT NO: 82/01

TECHNICAL OBJECTIVE

To evaluate the effect of a brief course of dexamethasone on the course of serous otitis media.

METHOD

Population: Patients diagnosed as having unilateral or bilateral serous otitis media by clinical microscopic exam; type B tympanogram must be present; effusion must be unresponsive to standard medical therapy, using decongestants, for at least three weeks; adult and pediatric patients will be studied.

Double blind protocol: Group I (25 patients) - placebo
Group II (25 patients) - dexamethasone
1 mg/kg for 2 days; 0.75 mg/kg
for 2 days, and 5 mg/day for 3 days.

Follow-up clinical exam after one week and crossover then performed for patients with a persistent effusion. Patients clearing their effusion would be followed with periodic clinical exam and tympanometry for one year (every 3 months). Any patient developing acute otitis media would have his medication discontinued, be removed from the study, and receive standard therapy.

PROGRESS

(81 10 - 82 09) Six patients have been entered in the protocol. No conclusions can be made at present as the code will not be broken until fifty patients have been entered.

STATUS: (0)

TITLE: Evaluation of Calcium Sulfate (Plaster of Paris) as
an Alloplastic Implant in Mandible Reconstruction

PRINCIPAL INVESTIGATOR: MAJ Del Ray Maughan, MC

PROFESSIONAL ASSISTANTS: COL Leonard L. Hays, MC
MAJ Stanley P. Liebenberg, VC
CPT John H. McGath, MC
CPT Wallace E. Taylor, MC

WORK UNIT NO: 82/34

TECHNICAL OBJECTIVE

To evaluate the use of calcium sulfate as an alloplastic implant material in reconstruction of surgical defects of the mandible.

METHOD

Six mongrel dogs will undergo unilateral partial mandibulectomies (2-4 cm segments of hemi-mandible, depending upon dog size) under endotracheal halothane anesthesia. Three will have periosteum preserved and three will have periosteum removed. Each dog will undergo immediate reconstruction utilizing calcium sulfate as an alloplastic implant. Stabilization will be accomplished utilizing standard ASIF fixation bone plates applied to the lateral aspect of proximal and distal segments. Each animal will be placed on liquids postoperatively until intraoral mucosa is sealed and then on a soft diet for four to six weeks. Each dog will be followed with monthly roentgenograms to determine calcium sulfate resorption and osteoneogenesis. Two dogs (one with periosteum intact and one with periosteum removed) will be sacrificed at two, four, and six months postop and the reconstructed mandibles examined histologically for bone formation.

PROGRESS

(82 03 - 82 09) Three dogs have undergone partial mandibular resection with reconstruction utilizing calcium sulfate. All three dogs have required removal of exposed wire which was utilized to secure the alloplastic implant to the mandibular plates. The first dog developed the exposed wire more than three months after the initial surgery. The second and third dogs developed exposed wire at a briefer post-operative time. There has been no loss of mandibular stability due to this unexpected complication and all three dogs have been able to continue on their planned diet. Investigators are exploring alternative methods of securing the implant before proceeding with more surgery.

STATUS: (O)

TITLE: Immunologically Mediated Persistent Infertility in
Patients Following Vasovasotomy

PRINCIPAL INVESTIGATOR: LTC Michael R. Moon, MC

PROFESSIONAL ASSISTANTS: LTC William E. Belville, MC
LTC Stephen R. Plymate, MC
MAJ James W. Higbee, MSC

WORK UNIT NO: 82/68

TECHNICAL OBJECTIVE

To investigate the relationship between immunologically mediated infertility in patients after vasovasotomy and its treatment by corticosteroids.

METHOD

Thirty males who are going to have vasovasotomies performed will, prior to surgery, have serum samples analyzed for antisperm antibodies using the Isojima and Kibrick techniques as described by Linnet. They will have two serum samples measured at least one week apart. Following vasovasotomy, monthly semen analyses will be performed, and upon the first appearance of sperm in the ejaculate, serum and semen will be analyzed by the Isojima and Kibrick technique for antisperm antibodies. Monthly semen analyses will be followed, and, when sperm samples for two consecutive months are >20 million/ml with $>20\%$ motility, a sperm penetration assay (SPA) will be performed as well as a repeat antibody study. If the SPA is negative, patients will be treated with 1 mg dexamethasone three times a day for one month. One month following the dexamethasone treatment, a repeat SPA will be performed as well as serum drawn for antibodies. If the patient's spouse becomes pregnant during the study, serum and semen antibodies will be drawn and a SPA performed as soon as the pregnancy is recognized.

PROGRESS

(82 08 - 82 09) No patients have been entered as this project has just be approved.

STATUS: (0)

TITLE: A Prospective Clinical Trial Comparing Drainage or no Drainage After Acute Cholecystectomy

PRINCIPAL INVESTIGATOR: CPT Michael J. O'Reilly, MC

PROFESSIONAL ASSISTANT: LTC Preston L. Carter, MC

WORK UNIT NO: 82/58

TECHNICAL OBJECTIVE

This study will be a randomized prospective clinical trial. Patients presenting with signs and symptoms consistent with acute cholecystitis to include right upper quadrant pain, fever, and leukocytosis will have diagnosis confirmed by histological examination of the gallbladder. Cholecystectomy will be performed according to standard technique through a subcostal incision. If the surgeon determines that the patient has no contraindications for inclusion in the study, the patient will be randomly assigned to have drainage of the gallbladder bed with a Jackson-Pratt drainage system brought out through a lateral stab wound or no drainage of the gallbladder bed. A bile culture will be taken and an intraoperative cholangiogram performed when possible. Visible bile in the peritoneal cavity following cholecystectomy, presence of a frank abscess cavity in the gallbladder bed, or a common bile duct exploration will be cause for exclusion from the study. Postoperative management and follow-up will be identical in both groups. Parameters to be followed include: postoperative fever, wound infection, return of gastrointestinal tract function, and length of stay in the hospital. A SMAC-20 will be drawn on all patients on postoperative day number two.

PROGRESS

(82 06 - 82 09) No patients have been entered in this study.

STATUS: (0)

TITLE: Repair of Peripheral Meniscal Tears; A Long Term Study

PRINCIPAL INVESTIGATOR: LTC Thomas J. Parr, MC

PROFESSIONAL ASSISTANTS: CPT Michael Q. Cosio, MC

WORK UNIT NO: 82/45

TECHNICAL OBJECTIVE

To determine the long term sequelae of repair of peripheral meniscal tears.

METHOD

PATIENT POPULATION: Patients who have had symptoms of a torn meniscus for at least four months and who subsequently are found to have a peripherally torn meniscus. Patients will be excluded who have undergone a previous menisectomy, who have a torn anterior or posterior cruciate ligament, or who have worse than Grade II osetoarthritis.

If the meniscus is detached from its capsular attachment, it will be reattached with 2-0 Dexon suture going through the capsule, grabbing at least 1 mm of the body of the meniscus, then back out of the capsule and tied. If there is a tear of the body of the meniscus paralleling the capsular edge of the meniscus and leaving no more than 2 mm of meniscus still attached to the capsule, this capsular remnant will be excised, the edge of the meniscus will be abraded, and the meniscus reattached to the capsule as above. Both groups of patients will be placed in a long leg bent knee cast, partial weight bearing on crutches for six weeks before beginning knee rehabilitation. Follow-up will be every three months for the first year, six months the second year, then annually for subsequent years up to ten years. If the patient develops recurrence of the symptoms despite vigorous physical therapy and anti-inflammatory medication, he will be rearthroscoped for inspection of the repair. A final evaluation of the knee will be made at ten years that will include x-rays of the knees, assessment of the level of activity, and knee function.

PROGRESS

(82 04 - 82 09) No patients have been seen that fit the criteria.

STATUS: (0)

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: 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 than 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 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 is not statistically significant, additional numbers of children will be studied.

PROGRESS

(81 07 - 82 09) No patients have been entered in this study. Discussion with several leading researchers in the field of learning disabilities and auditory evoked response led the investigators to the conclusion that several modifications in the design of the study should be made. At the present time, these modifications are in the planning stage. They will be presented to the research committees for approval when completed.

STATUS: (0)

TITLE: Canine Training Model for Endoscopic Laryngeal Surgery
Using the CO₂ Laser

PRINCIPAL INVESTIGATOR: CPT Wallace E. Taylor, MC

PROFESSIONAL ASSISTANTS: COL Leonard L. Hays, MC
MAJ Stanley P. Liebenberg, VC
MAJ Del Ray Maughan, MC

WORK UNIT: 82/55

TECHNICAL OBJECTIVE

To train ENT residents in the use of the CO₂ laser in a non-human subject in a controlled setting simulating a human situation prior to performing in an actual clinical setting.

METHOD

Twelve large mongrel dogs will be anesthetized with ultra-short acting barbiturate and placed in dorsal recumbancy. Suspension laryngoscopy will then be employed to visualize the larynx. ENT residents will use the CO₂ laser to perform a partial laryngectomy. Supplemental oxygen will be administered to the animal using the Saunders jet ventilating device to displace CO₂ from the lower airways and to facilitate viewing of the operative site during actual tissue removal with the laser. The opposite hemilarynx will be left unoperated to serve as a control. Each dog will be placed on a liquid diet for 24 hours post-op and will then be fed a semi-soft diet for the next 5 days. Each dog will be endoscoped at weekly intervals until healing is completed. The dogs will then be used in conjunction with the protocol "Use of the CO₂ Laser in Pharyngeal Surgery in the Dog"; LTC Stanley P. Liebenberg, Principal Investigator.

PROGRESS

(82 05 - 82 09) Fifteen canine subjects underwent laser cordectomies. These animals have been closely followed with good photographic documentation of their progress.

STATUS: (0)

TITLE: Defining Blood Gas Parameters Using the Saunders Jet Ventilating Device in the Dog in Conjunction with Endoscopic Laryngeal Surgery

PRINCIPAL INVESTIGATOR: CPT Wallace E. Taylor, MC

PROFESSIONAL ASSISTANTS: COL Leonard L. Hays, MC
MAJ Willis H. Jacob, MSC
MAJ Stanley P. Liebenberg, VC
MAJ Del Ray Maughan, MC

WORK UNIT: 82/56

TECHNICAL OBJECTIVE

To define blood gas and blood pH levels in the dog using the Saunders jet ventilating device.

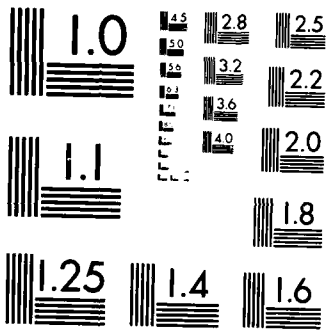
METHOD

A total of six dogs will be included in this study. After each dog has been anesthetized with ultrashort-acting barbiturate and before actual tissue excision with the CO₂ laser commences, a femoral arterial cutdown will be performed. Arterial catheterization will be made under direct visualization by insertion of an Intracath. After ligatures are securely placed around the Intracath to prevent accidental withdrawal, a 3-way stopcock will be placed on the end of the catheter, the catheter will be flushed with 10% heparinized saline to prevent clot formation, and then the catheter will be connected to a Hewlett-Packard Model 7700 8-channel physiograph machine for blood pressure and EKG monitoring. Ventilation with the Saunders device will be performed at varying rates (4, 5, 7.5, 12, and 30 times/minute) for 5 minutes each. The duration of each burst of oxygen will be approximately one second. An initial arterial blood sample will be drawn for O₂, CO₂, and pH determinations prior to any ventilation with the Saunders device. Further blood samples for the same parameters will be drawn at the end of each 5 minute ventilation period. The study will commence with the most rapid rate (30/minute) and proceed in order to the slowest rate (4/minute). After completion of all ventilation periods, the Intracath will be withdrawn. This protocol will be done in conjunction with the protocol "Use of the CO₂ Laser in Pharyngeal Surgery in the Dog"; LTC Stanley P. Liebenberg, Principal Investigator.

PROGRESS

(82 05 - 82 09) It has become obvious to the investigators that this study will need to be performed alone. Further planning to better control the results and findings will be completed before actual animal investigation begins.

STATUS: (0)



MICROCOPY RESOLUTION TEST CHART
NATIONAL BUREAU OF STANDARDS 1963-A

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: 81/18

TECHNICAL OBJECTIVE

To provide an investigational drug of proven efficacy, not previously released for general use, to MAMC patients under Group C NCI Guidelines. Also, to determine 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 pre-treatment evaluation will be accomplished and any untoward or unexpected side effects will be reported to the National Cancer Institute.

PROGRESS

(80-12 - 82 09) No entries at MAMC.

STATUS: (0)

TITLE: NCI #I78-10: Guidelines for the Clinical Use of
Hexamethylmelamine (Group C Guidelines)

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
LTC Archie W. Brown, MC
LTC Roger B. Lee, MC

WORK UNIT: 81/19

TECHNICAL OBJECTIVE

To provide an investigational drug of proven efficacy, not previously released for general use, to MAMC patients under Group C NCI Guidelines. Also to determine the extent and variety of side effects with hexamethylmelamine that have not been previously described.

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 contra-indicated. Hexamethylmelamine will be given daily by mouth, either continuously or intermittently depending on response, toxicity, and other drugs which the patient may be taking concomitantly. The treatment will continue for as long as the disease is stable or the tumor shrinks.

PROGRESS

(80 10 - 82 09) Five patients were on this protocol during FY 82. Of these, one was entered during FY 82 and four were entered during the previous year. All had recurrent ovarian carcinoma. One patient had progression, three had stable disease for 3, 4, and 7 months, and one patient has had a partial response for 4+ months. Hematological toxicity was significant but there were no drug related fatalities.

In the previous year, four patients were entered and had progressive disease after administration and were taken off study.

STATUS: (0)

TITLE: NCI #180-11: 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: 81/20

TECHNICAL OBJECTIVE

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 pre-treatment 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 - 82 09) There are eight patients on this study; seven entered during FY 82. Seven of the patients had extensive oatcell Ca and one had limited disease. Four patients died within 0-3 months after starting treatment with combination chemotherapy including VP16. Four patients are still under treatment; one with a complete (clinical) response, one with a partial response, and two are too early for evaluation.

STATUS: (0)

TITLE: NCI #180-12: 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: 81/102

TECHNICAL OBJECTIVE

To determine untoward side effects not previously described with THC and to make available this antiemetic 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/m² p.o., 6-8 hours prior to the administration of chemotherapy and for 12 hours thereafter. Should the 5 mg/m² dose prove to be ineffective, and in the absence of significant side effects, the dose may be escalated to 7.5 mg/m². Any untoward side effects will be reported to the NCI.

PROGRESS

(81 07 - 82 09) Six patients are entered on this study; five of them were entered during FY 82. Two patients with ovarian Ca and four with breast Ca were treated with oral THC (Group C drug) Four patients had some reduction of nausea and vomiting. The other two reported that the THC did not reduce severity of side effects.

STATUS: (0)

TITLE: NCI #7601 - Selected Stage I_{Ai} - I_{Bi} Ovarian Cancer
(Well and Moderately Differentiated)

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANTS: COL William L. Benson, MC

WORK UNIT: 81/45

TECHNICAL OBJECTIVE

To define the natural history of patients treated by surgery; to determine whether prophylactic, adjuvant chemotherapy with melphalan alters the natural history; to study the effect of various potential prognostic factors on the natural history of patients treated by each form of therapy; to establish the value of various staging parameters on the stage of disease and its natural history.

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 - 82 09) One patient was entered in FY 81 and is disease free at this time. No patients entered during FY 82.

STATUS: (0)

TITLE: NCI #7602: All Stage I_C and II (A, B, C) and Selected Stage IA_{ii} and IB_{ii} Ovarian Cancer

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANTS: COL William L. Benson, MC

WORK UNIT: 81/33

TECHNICAL OBJECTIVE

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, IA_{ii}, IB_{ii}, or IA_i or IB_i with poorly differentiated tumors. Patients with prior therapy are ineligible. Patients will be stratified by histology, histological grade, and stage group for Regimen I. Regimen I will have staging laparotomy, total abdominal hysterectomy and bilateral salpingo-oophorectomy with no macroscopic residual disease found. Patients will then be randomized to receive melphalan or radioisotopes. Regimen II will be stratified by histology, histological grade, and extent of disease after surgery. Patients will have staging laparotomy, total abdominal hysterectomy, and bilateral salpingo-oophorectomy. If II_B, II_C, residual disease is found, patient will be randomized to pelvic radiotherapy plus melphalan alone. If after 18 months of therapy, the patient remains free of disease, chemotherapy will be discontinued. Second look will be done if the patient is free of disease after 18 months of chemotherapy.

PROGRESS

(81 01 - 82 09) One patient entered during FY 81 and is alive at present time. No entries during FY 82.

STATUS: (0)

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 James E. Congdon, 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 stage I, I_E, II and II_E treated with extended field radiotherapy (supra-diaphragmatic mantle or abdominal field) alone or with extended field radiotherapy plus combination chemotherapy [Cytosan, 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 06 - 82 09) One patient was entered during FY 80 but was ineligible because of bone marrow involvement found at a later date; however patient is alive in complete remission for 2 1/2 years. One patient was treated from May 1978 to November 1978; continues in complete remission for four years. No new patients were entered in FY 82.

STATUS: (C)

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 James E. Congdon, 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

(77 10 - 82 09) This protocol was closed to new entries in August 1980. Of the 626 patients studied, MAMC contributed 10 patients. Nine of these are still in remission and are being followed every 6-12 months. One patient had metastasis to brain and lungs. Results from the study indicate no statistically significant difference between the two groups.

STATUS: (C)

TITLE: SWOG 7632: Combined Modality Protocol for Recurrent Breast Cancer, Phase III

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANT: LTC James E. Congdon, 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 progesterone 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 03 - 82 09) No patients registered during FY 82. Previously, one patient had progression and died 5 months later; one patient was treated for 18 months and taken off study due to other complications with progression of disease; and one patient has been on study for 30 months with complete response.

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 James E. Congdon, MC

WORK UNIT NO: 78/02

TECHNICAL OBJECTIVES

(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) to compare the duration of documented complete response obtained by continued maintenance immunotherapy in patients proven to be in complete remission after induction levamisole vs no maintenance therapy; (3) to estimate the complete response rate obtained by continued chemoimmunotherapy with COP + levamisole in patients with impaired 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; (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; and (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 disease 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 impaired 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.

PROGRESS

(77 12 - 82 09) Three patients entered study. Patient 1 had progressive disease and expired; Patient 2 with recurrent diffuse histocytic lymphoma has maintained a complete response for 36 months. Patient 3 with stage IV_A nodular poorly differentiated lymphoma obtained and has maintained a good partial response for two years. No patients were entered during FY 82.

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 James E. Congdon, 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/M²/day over 24 hr infusion in 1000 ml of D₅W 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) impaired marrow; II. (a) BHD + levamisole - normal marrow (b) impaired marrow; and III. (a) actinomycin D + high dose DTIC normal marrow (b) impaired 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 modifications are given in detail in the protocol.

PROGRESS

(78 02 - 82 09) Four patients were registered. Three had severe progressive disease, relapsed, and expired. One patient had an excellent response (first PR then CR) lasting 12 months and then relapse. No patients were entered during FY 82.

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 James E. Congdon, MC
LTC Irwin B. Dabe, MC

WORK UNIT NO: 78/42

TECHNICAL OBJECTIVE

To determine the efficacy of adjuvant chemotherapy with FAM on the disease-free interval and survival of patients with TNM stage-groups I_B, I_C, II and III gastric adenocarcinoma compared to potentially curative surgery alone.

METHOD

Patient Eligibility: patients must have TNM stage-group I_B, I_C, II, or III gastric adenocarcinoma and no microscopic or gross residual postoperatively; no prior 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) or Treatment 2:
FAM - 5-FU, 600 mg/M² IV days 1 & 8, 29 & 36
adriamycin, 30 mg/M² IV days 1 & 29
mitomycin-C, 10 mg/M² IV day 1

A total of 6 courses, one every 8 weeks, will be administered. After 12 months, the active therapy phase is completed. The patient will be followed at six month intervals for five years if remission continues.

PROGRESS

(78 06 - 82 09) No entries at MAMC.

STATUS: (0)

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 James E. Congdon, MC
LTC Irwin B. Dabe, MC

WORK UNIT NO: 78/47

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; and to determine if immunotherapy maintenance with levamisole or consolidation with low dose involved field radiotherapy will produce significantly longer remission durations over a no further treatment group when complete remission has been induced with 6 cycles of MOP-BAP in Stages III & IV Hodgkin's.

METHOD

Patients (>15 yrs) must have histologic diagnosis of Hodgkin's disease classified by the Lukes and Butler System; no prior chemotherapy. Exclusions: a history of congestive heart failure, valvular heart disease, or serious obstructive or restrictive pulmonary disease.

Treatment: All patients except those with prior radiotherapy must receive radiation therapy consultation before chemotherapy begins.

Treatment 1: Normal marrow patients will receive 6 cycles of MOP-BAP.

Treatment 2: Impaired 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.

PROGRESS

(78 07 - 82 09) Four patients entered (two during FY 82). All patients have Stage III Hodgkin's disease and are in complete remission 5, 12, 21, and 21 months after beginning treatment.

STATUS: (0)

TITLE: SWOG 7811: Brain Metastases Protocol, Phase III

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC James E. Congdon, MC
LTC Irwin B. Dabe, MC

WORK UNIT NO.: 79/03

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

(78 11 - 81 09) One patient treated. After one course of metronidazole, patient refused further treatment because of nausea and vomiting, patient later expired.

(81 09 - 82 09) No entries at MAMC.

STATUS: (C)

TITLE: SWOG 7823/24/25/26: ROAD-AdOAP in Acute Leukemia,
Phase III

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC James E. Congdon, MC
LTC Irwin B. Dabe, MC

WORK UNIT NO: 79/02

TECHNICAL OBJECTIVE

To compare the efficacy of the 4-drug combination chemotherapy regimen, ROAP (Rubidazole, Vincristine, Arabinosyl Cytosine, and Prednisone) to AdOAP (the same combination using Adriamycin in place of Rubidazole) 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

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patients will then receive late intensification therapy consisting of a combination of vincristine, prednisone, and methotrexate plus 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

(11 78 - 81 02) Five patients entered:

- (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.
- (5) patient entered FY 81 with complete remission until March 1982; relapse and reinduction; lost to follow up.

(81 10 - 82 09) No new entries at MAMC.

STATUS: (0)

TITLE: SWOG 7827: Combined Modality Therapy for Breast Carcinoma,
Phase III

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC James E. Congdon, MC
LTC Irwin B. Dabe, MC

WORK UNIT NO: 79/96

TECHNICAL OBJECTIVE

To compare the disease-free interval and recurrence rates in:
(1) estrogen receptor positive premenopausal patients with Stage II disease using combination chemotherapy alone vs combination chemotherapy and oophorectomy; (2) estrogen receptor positive postmenopausal patients with Stage II disease using combination chemotherapy plus tamoxifen vs tamoxifen alone vs combination chemotherapy alone; (3) estrogen receptor negative patients with Stage II disease using one vs two years of combination chemotherapy; and to compare the effect of the various adjunctive therapy programs upon survival patterns and to correlate the estrogen receptor status with disease-free interval and survival.

METHOD

Patients with a histologically proven diagnosis of breast cancer (Stage II or Stage III) with one or more pathologically involved axillary nodes will receive one of the following treatments: (CMFVP = cyclophosphamide, methotrexate, 5-fluorouracil, vincristine, and prednisone):

- (1) CMFVP for 1 yr - pre or postmenopausal ER- patients.
- (2) CMFVP for 2 yr - pre or postmenopausal ER- patients.
- (3) CMFVP for 1 yr - premenopausal ER+ patients.
- (4) Oophorectomy + CMFVP - premenopausal ER+ patients.
- (5) Tamoxifen alone for 1 yr - postmenopausal ER+ patients.
- (6) CMFVP for 1 yr - postmenopausal ER+ patients.
- (7) Tamoxifen + CMFVP for 1 yr - postmenopausal ER+ patients.

Patients undergoing segmental mastectomy (lumpectomy) will receive 6 wks of radiation therapy in addition to the treatment they are randomized to receive.

PROGRESS

(79 09 - 82 09) Fourteen patients on study, six entered during FY 82. Of these 14 patients, 12 remain in complete remission. One patient on R_x 2 developed metastases to liver, lung, pleura, and skin during the adjuvant chemotherapy and died 11 months after receiving first chemotherapy treatments. Another patient on R_x 3 developed local chestwall recurrence 11 months after the start of treatment. She was treated with local radiotherapy and Tamoxifen and is in complete clinical remission 14 months after her recurrence. Mild to moderate neutropenia and intermittent nausea and vomiting were the most common side effects.

STATUS: (0)

TITLE: 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: LTC James E. Congdon, MC
LTC Irwin B. 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 will 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 alternate treatment.

PROGRESS

(80 02 - 82 09) One patient registered in December 1980 with stable disease for one year with subsequent progression and removal from the study. No other patients entered.

STATUS: (C)

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/M², 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 - 82 09) No entries at MAMC.

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: LTC James E. Congdon, MC
LTC Irwin B. Dabe, MC

WORK UNIT NO: 80/23

TECHNICAL OBJECTIVES

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/m² 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 02 - 82 09) Study is now open only to bladder patients.
No entries at MAMC.

STATUS: (0)

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 James E. Congdon, MC
LTC Irwin B. Dabe, MC

WORK UNIT NO: 79/99

TECHNICAL OBJECTIVES

To determine the efficacy of m-AMSA at a dose of 120 mg/M² 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/M² in 500 cc of dextrose and water over one hour. Poor risk will receive 90 mg/M² and abnormal liver function patients will receive 60 mg/M². 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

(79 09 - 81 09) Two patients registered: (1) had progression on treatment and was taken off study after one month; (2) had progression on treatment and was taken off study after one month, expired 4 months later.

(81 10 - 82 09) No entries at MAMC.

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 James E. Congdon, MC
LTC Irwin B. Dabe, MC

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 improvement 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: (1) 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. (2) 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) Three patients were entered during this period with partial remission (8, 11, and 17 months) and subsequent progression of disease and removal from the study.

(81 10 - 82 09) Four patients registered: (1) & (2) with complete remission for 7 and 9 months then relapsed and died; (3) Partial remission for 9 months, then relapsed and has been retreated with good second partial remission (2+ months); (4) complete remission (4+ months).

STATUS: (0)

TITLE: SWOG 7927/28: Chemotherapy for Multiple Myeloma,
Phase III

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC James E. Congdon, MC
LTC Irwin B. Dabe, MC

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, Stages 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 prednisone (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 treatment 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 platelet count is at least 80,000.

PROGRESS

(80 02 - 82 09) One patient was entered in FY 81 and was treated for 7 months with some disease stabilization before subsequent progression. One patient was entered in FY 82 and treated for 8 months before subsequent progression of disease and death.

STATUS: (0)

TITLE: SWOG 7937: Evaluation of m-AMSA in Metastatic Carcinoma
of the GU Tract Except Renal Carcinoma, Phase II

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC James E. Congdon, MC
LTC Irwin B. Dabe, MC

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/M² dissolved in 500 ml of D/W infused IV over no less than one hour every 21 days. Poor risks will receive 90 mg/M². If bilirubin >2 mg%, the initial dose will be 75 mg/M². 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 - 82 09) No entries at MAMC.

STATUS: (C)

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 H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Archie W. Brown, MC
LTC Irwin B. Dabe, 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 - 82 09) No patients registered during FY 82 on this study. In FY 81, one patient was registered with stable disease for 3 months and then progression of disease.

STATUS: (C)

TITLE: SWOG 7945: Evaluation of AZQ and Metastatic Adenocarcinoma
of the Large Bowel

PRINCIPAL INVESTIGATOR: LTC James E. Congdon, MC

PROFESSIONAL ASSISTANTS: COL Friedrich H. Stutz, MC
LTC Irwin B. Dabe, MC
MAJ Lauren K. Colman, MC
MAJ Howard Davidson, MC
CPT Thomas M. Baker, MC
CPT Alfred H. Chan, MC

WORK UNIT NO: 82/12

TECHNICAL OBJECTIVE

To determine the antitumor activity of AZQ in colorectal carcinoma by determination of response rate and remission duration; and to further determine the nature and extent of AZQ toxicity in a Phase II Study.

METHOD

The starting dose of AZQ will be 7 mg/M² daily x 5 as a slow injection through the side tubing of a running IV. AZQ will be given daily x 5 and repeated every 28 days provided all toxicities have resolved by the time of the next treatment course. An adequate trial will consist of one complete 5-day course of treatment.

PROGRESS

(81 11 - 82 09) One patient registered on study on 10 May 82 who had documented progression of disease in pelvis and was removed from study after three cycles on 7 Sep 82.

STATUS: (C)

TITLE: SWOG 7958: Evaluation of m-AMSA in Metastatic or Recurrent Epithelial Carcinoma of the Female Genital Tract, Phase II

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC James E. Congdon, MC
LTC Irwin B. Dabe, MC

WORK UNIT NO: 80/37

TECHNICAL OBJECTIVES

To determine the antitumor activity of AMSA in patient 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/M²/day, IV, for three days. Dose for poor risk: 30 mg/M²/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 - 82 09) One patient with good response for 19+ months.
No entries during FY 82.

STATUS: (0)

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/M² 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 - 82 09) No entries at MAMC.

STATUS: (C)

TITLE: SWOG 7965: Chemotherapy or Chemotherapy and Immuno-
therapy 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 James E. Congdon, MC
LTC Irwin Dabe, MC

WORK UNIT NO: 80/32

TECHNICAL OBJECTIVES

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 Stages I-IV (MO); supraglottic and glottic larynx Stages II and IV and subglottic larynx Stages I-IV (MO); oral cavity Stages II-IV (MO); and nasal cavity/paranasal sinus Stages I-IV (MO). These patients will be randomized to receive either no treatment or MTX at a dose of 12 mg/M² IM daily for 3 days every 21 days for one year or until relapse or inability to tolerate drug because of toxicity.

PROGRESS

(80-02 - 82-09) No entries at MAMC.

STATES: (C)

TITLE: SWOG 7980. Study of Cis-Diammine Dichloroplatinum (DDP)
for Recurrent Gliomas, Phase II

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC James E. Congdon, MC
LTC Irwin Dabe, MC

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 (Grades I-IV) who have recurred following cranial irradiation will be eligible. The starting dose for all patients will be 35 mg/M²/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 efficacy and toxicity. A course is defined as a treatment plus a 3 week observation period.

PROGRESS

(80 05 - 82 09) No entries at MAMC.

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 - 82 09) No entries at MAMC.

STATUS: (0)

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
Suresh B. Katakhar, M.D., DAC

WORK UNIT NO: 80/66

TECHNICAL OBJECTIVES

To compare disease-free interval and survival among control groups 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 femtomoles/mg cytosol protein in order to be eligible for study (Stage I and 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 further 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 postoperative 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 - 82 09) One patient entered in FY 81 with complete remission at 9 months when lost to follow up. No patients registered during FY 82.

STATUS: (C)

TITLE: SWOG 7990: Intergroup Testicular Study

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC James E. Congdon, MC
LTC Irwin Dabe, MC

WORK UNIT NO: 80/33

TECHNICAL OBJECTIVES

To compare the disease-free survival and overall survival for surgery alone (with chemotherapy for relapsers) vs surgery plus early adjuvant chemotherapy in patients with resectable Stage II testicular cancer; to register and follow patients with nonseminoma, nonchoriocarcinoma Stage I testicular cancer to define prognostic variables which may predict recurrence in this stage group; to define the difference in disease-free rates and patterns of recurrence, based upon histologic subtypes and extent of disease on initial presentation; to evaluate the role of marker substances such as HCG, alpha-fetoprotein, and lactic dehydrogenase in the early detection and management of recurrence in patients with Stage I and Stage II testicular carcinoma; to evaluate the accuracy of lymphangiograms, CAT scans, and ultrasound studies for staging of retroperitoneal nodal involvement.

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 to 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 follow-up until recurrence. Group II: adjuvant chemotherapy with vinblastine, bleomycin, and cis-platinum. Stages I and II who were originally randomized to the follow-up group and Stage II relapsing after chemotherapy will be further treated with vinblastine, bleomycin, and cis-platinum. Patients in complete or partial remission or showing improvement after relapse induction will receive maintenance treatment with vinblastine, repeated every 4 weeks until complete remissions have received 104 weeks of therapy and partial remissions and improvements may continue indefinitely. All other patients will go off study.

PROGRESS

(80 02 - 82 09) No entries at MAMC.

STATUS: (0)

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 - 82 09) No entries at MAMC.

STATUS: (C)

TITLE: SWOG-8008: Evaluation of Dihydroxyanthracenedione (DHAD)
in Refractory Breast Cancer, Phase II

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
LTC Archie W. Brown, MC

WORK UNIT: 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/M² (good risk) or 10 mg/M² (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 - 82 09) No entries at MAMC.

STATUS: (C)

TITLE: SWOG 8009: Evaluation of Dihydroxyanthracenedione (DHAD)
in Patients with Refractory Small Cell Lung Cancer,
Phase II

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
LTC Archie W. Brown, MC

WORK UNIT: 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/M² IV infusion in 100 cc D5W over 30 minutes, repeated every 3 weeks.

PROGRESS

(80 10 - 82 09) No entries at MAMC.

STATUS: (C)

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: 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 intolerable, the patient will be removed from the protocol. Treatment will be 10 mg/M² IV infusion in 100 cc D5W (poor risk) or 12 mg/M² (good risk), repeated every 3 weeks. Patients will be stratified by prior chemotherapy.

PROGRESS

(80 10 - 82 09) No entries 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 Archie W. Brown, MC
LTC Irwin B. Dabe, MC

WORK UNIT: 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 M₁) 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 M₁) are eligible. This excludes patients who have metastases only to ipsilateral hilar nodes (N₁) and/or mediastinal nodes (N₂). Patients whose disease can be encompassed within a single radiation port are not eligible. Prior chemotherapy 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 1 (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 - 82 09) Five patients have entered this study (two during FY 82). Two were treated for one month and three months before progression of disease and death. Two have been treated for 5 and 7 months, respectively, with stable disease, and one is too early for evaluation.

STATUS: (0)

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 Archie W. Brown, MC
LTC Irwin B. Dabe, MC

WORK UNIT: 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 Cisplatinum (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 determining 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 M₁ 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. Patients who were initially treated with radiation but 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. Patients 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. Reasons for removal from the protocol are patient refusal and intolerable side effects.

PROGRESS

(80 12 - 82 09) No patients entered in previous years. One patient was entered during FY 82, but was removed because the pathology review did not bear out the diagnosis of squamous cell carcinoma.

STATUS: (0)

TITLE: SWOG 8017: 5-FU, Adriamycin, Streptozotocin, and
Cyclophosphamide (FAC-S) in the Treatment of Metastatic
Carcinoid Tumors, Phase II

PRINCIPAL INVESTIGATOR: CPT Alfred H. Chan, MC

PROFESSIONAL ASSISTANTS: COL Friedrich H. Stutz, MC
LTC James E. Congdon, MC
LTC Irwin B. Dabe, MC
MAJ Lauren K. Colman, MC
MAJ Howard Davidson, MC
CPT Thomas M. Baker, MC

WORK UNIT NO: 82/11

TECHNICAL OBJECTIVE

To determine whether combination chemotherapy employing 5-Fluorouracil, is effective in the management of metastatic carcinoid; to study the duration of survival of patients with metastatic carcinoid tumor treated with combination chemotherapy regimens; to provide further information concerning the response and/or survival of patients with metastatic carcinoid originating in different sites and having different metastatic patterns.

METHOD

All patients except those with cardiac disease will receive the combination of 5-FU, cyclophosphamide, adriamycin, and streptozotocin. Patients will be divided into good and poor risk groups with medication adjusted accordingly. Courses will be repeated at 28 day intervals as tolerated. Patients with carcinoid or other varieties of cardiac disease will not receive adriamycin. An adequate trial is considered two courses.

PROGRESS

(81 11 - 82 09) One patient entered on study during FY 82 and expired after failing to respond after two courses of treatment.

STATUS: (0)

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 Archie W. Brown, MC
LTC Irwin B. Dabe, MC

WORK UNIT: 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 entered: (1) partial response for two months with death one month after relapse and (2) patient refused treatment after one dose and expired three months later.

(81 10 - 82 09) No patients entered.

STATUS: (0)

TITLE: SWOG 8025: Combination Chemotherapy for Chronic Lymphocytic Leukemia, Phase II

PRINCIPAL INVESTIGATOR: LTC Irwin B. Dabe, MC

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

WORK UNIT: 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, Cytosan, and adriamycin; 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 documentation of the progression of the disease; and Arm II, Rai Classification 3-4, consisting of chemotherapy with a combination of prednisone, Oncovin, Ara-C, cyclophosphamide, and hydroxyduranubicin (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 chemotherapy regimen. Patients will be followed indefinitely or until death.

PROGRESS

(81 05 - 82 09) No patients registered on protocol at MAMC.

STATUS: (0)

TITLE: SWOG 8027: The Natural History of Pathological Stage T₁₋₂
N₀ M₀ ER+ Breast Cancer, Phase III

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Archie W. Brown, MC
LTC Irwin B. Dabe

WORK UNIT: 81/64

TECHNICAL OBJECTIVES

To document recurrence rates, patterns of recurrence, and survival among patients with Stage I or Stage II node negative (T₁₋₂ N₀ M₀) 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 positive are eligible. Patients undergoing local adequate excision with axillary node sampling as primary treatment must receive radiation therapy beginning 14-20 days postoperatively as outlined in the protocol. Only patients with pathologic Stage T₁₋₂ N₀M₀ with a primary tumor of ≤ 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 - 82 09) Five patients were entered into this study (four of them during FY 82). All five patients remain in complete remission at 7, 11, 11, 11, and 15 months.

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 Archie W. Brown, MC
LTC Irwin B. Dabe, MC

WORK UNIT: 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 amenable 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/M² 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 - 82 09) No patients registered on this protocol.

STATUS: (0)

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: 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 dose 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/M² 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 - 82 09) No patients registered on this protocol at MAMC.

STATUS: (0)

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: 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 - 82 09) No patients registered at MAMC.

STATUS: (C)

TITLE: SWOG 8037: Combined Therapies for Squamous Cell Cancer
of the Esophagus, Phase II

PRINCIPAL INVESTIGATOR: LTC James E. Congdon, MC

PROFESSIONAL ASSISTANTS: COL Friedrich H. Stutz, MC
LTC Irwin B. Dabe, MC
MAJ Alfred H. Chan, MC
MAJ Howard Davidson, MC
MAJ Timothy J. O'Rourke, MC
CPT Thomas M. Baker, MC

WORK UNIT NO: 82/69

TECHNICAL OBJECTIVE

To determine the feasibility and toxicity of combined radiotherapy and chemotherapy with 5-fluorouracil (5-FU) and cis-platinum followed by surgery in patients with epidermoid carcinoma of the middle or distal esophagus; to determine the time to local or distant progression in patients treated by these three combined modalities; to determine the survival of patients treated by these three combined modalities; and to determine the response rate by clinical and pathological staging at the time of surgery.

METHOD

After metastatic survey testing to determine that the patient has localized disease, the patient will be started on a simultaneous combination of chemotherapy and radiotherapy. The chemotherapy will consist of cis-platinum given through the side tubing of a freely running IV line over 2 hours followed by 5-FU given through a freely running IV by continuous infusion for 4 days. The patient will then be given a 4-week rest period and a similar chemotherapy regimen will be repeated. The exact dose of each chemotherapy agent will be determined by the patient's height and body weight. Simultaneous with the start of the chemotherapy, the patient will receive external beam radiation therapy to the esophagus in the region of the tumor. Approximately 2 weeks after the completion of the radiation and two courses of chemotherapy, the patient will be taken to surgery for definitive resection of the tumor. This will be followed by an anastomosis of the proximal remaining esophagus to the stomach.

PROGRESS

(82 09 - 82 09) No patients registered on this protocol at MAMC.

STATUS: (0)

TITLE: SWOG 8038: Vinblastine in Advanced Ovarian Cancer,
Phase II

PRINCIPAL INVESTIGATOR: COL Friedrich H. Stutz, MC

PROFESSIONAL ASSISTANTS: LTC Irwin B. Dabe, MC
LTC Roger B. Lee, MC

WORK UNIT: 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 phosphatase status.

PROGRESS

(81 04 - 82 09) One patient registered (FY 82) with stable disease for two months. Patient had mild nausea, vomiting, and severe neutropenia.

STATUS: (0)

TITLE: SWOG 8040: Evaluation of Combination Chemotherapy (FAM-S)
vs a Phase II Drug 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: 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 patient 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 - 82 09) No patients registered on study at MAMC.

STATUS: (0)

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: 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 method of the protocol will be the same as for SWOG 80/40.

PROGRESS

(81 05 - 82 09) No patients registered on this protocol at MAMC.

STATUS: (C)

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: 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 - 82 06) One patient entered (Sep 82); too early for evaluation.

STATUS: (0)

TITLE: SWOG 8049: Treatment of Resected, Poor Prognosis
Malignant Melanoma: Stage I: Surgical Excision vs
Surgical Excision + Vitamin A

PRINCIPAL INVESTIGATOR: LTC James E. Congdon, MC

PROFESSIONAL ASSISTANTS: COL Friedrich H. Stutz, MC
LTC Irwin B. Dabe, MC
MAJ Lauren K. Colman, MC
MAJ Howard Davidson, MC
CPT Thomas M. Baker, MC
CPT Alfred H. Chan, MC

WORK UNIT NO: 82/13

TECHNICAL OBJECTIVE

To determine the efficacy of surgical excision or surgical excision plus vitamin A in preventing the recurrence of high risk, Stage I malignant melanoma by determination of remission or disease-free interval; to determine the immunocompetence of patients with malignant melanoma and to determine the influence of vitamin A upon that immunocompetence.

METHOD

Patients will be equally randomized between the two treatment arms: vitamin A versus no further treatment. Patients will be stratified by depth of invasion, sex, and type of surgery. Those patients randomized to receive vitamin A will receive a dose of 100,000 I.U. daily. Treatment will continue for 18 months. Patients who receive no treatment will be followed until relapse and removal from the study.

PROGRESS

(81 11 - 82 09) One patient entered study. At present, patient in complete remission and therapy is being continued.

STATUS: (0)

TITLE: SWOG 8051: Evaluation of L-Alanosine in Acute Leukemia,
Phase II

PRINCIPAL INVESTIGATOR: LTC James E. Congdon, MC

PROFESSIONAL ASSISTANTS: COL Friedrich H. Stutz, MC
LTC Irwin B. Dabe, MC
MAJ Lauren K. Colman, MC
MAJ Howard Davidson, MC
CPT Thomas M. Baker, MC
CPT Alfred H. Chan, MC

WORK UNIT NO: 82/53

TECHNICAL OBJECTIVE

To determine the antitumor activity of L-Alanosine as determined by response rate and duration of response in patients with acute leukemia who are ineligible for higher priority studies and to determine the nature and degree of toxicity of this drug.

METHOD

This is a Phase II clinical trial of a new chemotherapy agent and is to be used in patients with acute leukemia who have not responded to the standard forms of treatment. L-Alanosine has demonstrated moderate activity against both acute lymphocytic leukemia cells and acute myelogenous leukemia blast cells in cell culture work as well as a variety of laboratory animals. It has been tested in Phase I clinical trials in human beings and its toxicities, including temporary myelosuppression, temporary nausea and vomiting, and temporary gastrointestinal toxicity consisting mainly of stomatitis and diarrhea, as well as a rare case of idiosyncratic anaphylactoid reactions, have been recognized. The patients will have met a number of performance and laboratory eligibility criteria. L-Alanosine will be administered through a freely running IV line as a continuous infusion for 5 consecutive days. Bone marrow examinations will be performed at weekly intervals and, if the bone marrow blast count remains greater than 50% of the initial count by 3 weeks, a second course will be given. The amount of L-Alanosine will be determined by the patient's body surface area.

PROGRESS

(82 05 - 82 09) One patient entered study Jun 82 with documented disease progression after two cycles. Patient died of acute leukemia relapse two months later.

STATUS: (0)

TITLE: SWOG 8077: Combined Chemotherapy and Hormonal Therapy
for Recurrent or Disseminated ER+ Breast Cancer, PACT
vs ACT, Phase II.

PRINCIPAL INVESTIGATOR: LTC James E. Congdon, MC

PROFESSIONAL ASSISTANTS: COL Friedrich H. Stutz, MC
LTC Irwin B. Dabe, MC
MAJ Lauren K. Colman, MC
MAJ Howard Davidson, MC
CPT Thomas M. Baker, MC
CPT Alfred H. Chan, MC

WORK UNIT NO: 82/14

TECHNICAL OBJECTIVE

To determine the response rate of a combined chemo-hormonal program in ER+ patients with metastatic breast cancer; to determine if the addition of prednisone will greatly increase the response rate.

METHOD

If regular menstrual periods are present, oophorectomy will be done followed within two weeks by chemotherapy. Twelve treatments, one every four weeks, with adriamycin and cyclophosphamide will be given. Half of the subjects will also receive prednisone immediately before each chemotherapy injection. After the first 12 treatments, medication will be adjusted because of the detrimental effects of adriamycin when given for longer than 12 months, and this regimen will be given once a month for 13 months. Those patients whose ovaries have been removed will receive the same regimens with the addition of tamoxifen throughout the study.

PROGRESS

(81 11 - 82 09) No patients registered on study at MAMC.

STATUS: (0)

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 Irwin B. Dabe, MC
LTC Roger B. Lee, 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 treatment, treatment recommendations will be made. All these patients should have measurable 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 - 82 09) Two patients entered; one in FY 81, the other in FY 82. There was no growth from either patient's tumor. Both patients have expired since that time.

STATUS: (0)

TITLE: SWOG 8101: VM-26 in Advanced GU Cancer

PRINCIPAL INVESTIGATOR: LTC James E. Congdon, MC

PROFESSIONAL ASSISTANTS: COL Friedrich H. Stutz, MC
LTC Irwin B. Dabe, MC
MAJ Lauren K. Colman, MC
MAJ Howard Davidson, MC
CPT Thomas M. Baker, MC
CPT Alfred H. Chan, MC

WORK UNIT NO: 82/15

TECHNICAL OBJECTIVE

To determine the response rate and duration of response of VM-26 in locally advanced or metastatic transitional cell carcinoma of the bladder, ureter, renal pelvis, and renal cell carcinoma; to determine further the quantitative and qualitative toxicity in patients treated with VM-26.

METHOD

VM-26 will be given at 100 mg/M² weekly for 4 weeks, rest 2 weeks, and then repeated when WBC and platelet counts have recovered. The VM-26 will be diluted with 100 cc of sodium chloride injection USP or 5% dextrose injection USP before administration by IV infusion. An adequate trial will be defined as completion of two evaluable courses.

PROGRESS

(81 11 - 82 09) Two patients were entered. Both experienced disease progression after 3 cycles and were removed from study.

STATUS: (C)

TITLE: SWOG 8106: Evaluation of AZQ (Carbamic Acid) in Central Nervous System Tumors, Phase II

PRINCIPAL INVESTIGATOR: LTC James E. Congdon, MC

PROFESSIONAL ASSISTANTS: COL Friedrich H. Stutz, MC
LTC Irwin B. Dabe, MC
MAJ Lauren K. Colman, MC
MAJ Howard Davidson, MC
CPT Thomas M. Baker, MC
CPT Alfred H. Chan, MC

WORK UNIT NO: 82/39

TECHNICAL OBJECTIVE

To determine the efficacy of AZQ given by intermittent bolus schedule in malignant gliomas by evaluation of response rate, duration, and survival; to determine the qualitative and quantitative toxicities of AZQ given by this schedule in a Phase II setting.

METHOD

This is a Phase II clinical trial of Aziridinybenzoquinone (AZQ) in patients with malignant, primary brain tumors who have not completely responded to surgery and/or radiation therapy. AZQ has demonstrated considerable effectiveness in controlling primary brain neoplasms in a variety of laboratory animals. The drug has been tested in Phase I trials in humans, and its toxicities, including temporary marrow suppression, nausea, emesis, alopecia, and stomatitis have been recognized. All patients in this study will have met a number of performance and laboratory eligibility criteria as listed in the protocol. AZQ will be administered through the side tubing of a freely flowing IV line in an amount determined by the patient's body surface area. The treatments will be repeated at three week intervals, unless unusual toxicities are encountered, for a minimum of two courses or until objective evidence of disease progression is ascertained.

PROGRESS

(82 03 - 82 09) No patients registered at MAMC.

STATUS: (0)

TITLE: SWOG 8112: Combination Chemotherapy of Unfavorable
Histology Non-Hodgkin's Lymphoma with CHOP and CVB,
Phase III

PRINCIPAL INVESTIGATOR: LTC James E. Congdon, MC

PROFESSIONAL ASSISTANTS: COL Friedrich H. Stutz, MC
LTC Irwin B. Dabe, MC
MAJ Lauren K. Colman, MC
MAJ Howard Davidson, MC
CPT Thomas M. Baker, MC
CPT Alfred H. Chan, MC

WORK UNIT NO: 82/59

TECHNICAL OBJECTIVE

To gain experience with a treatment program utilizing a combination of two non-cross-resistant drug regimens in the treatment of "poor prognosis" lymphomas; to determine an approximate complete remission rate to the Cyclophosphamide, Adriamycin, Vincristine, and Prednisone (CHOP)/Cis-platinum, Vinblastine, and Bleomycin (CVB) treatment program prior to initiating a group wide Phase III study utilizing this program.

METHOD

Patients will initially receive 3 cycles of CHOP chemotherapy, which is the standard treatment for poor prognosis lymphoma. In addition, he will receive a small injection of intrathecal Methotrexate at the start of each new CHOP regimen. All of these drugs have been used extensively in lymphoma patients and their response rates and various toxicities are well known. All patients will have met a number of performance and laboratory eligibility criteria as outlined in the protocol. Most of these chemotherapy agents will be administered through the side tubing of a freely flowing IV line in an amount to be determined by the patient's body surface area. One agent, Prednisone, will be given by mouth daily for 5 days at the start of each CHOP treatment regimen and one final agent, Methotrexate, will be given directly into the spinal column via spinal tap. All patients will receive a minimum of 6 cycles of combination, cross-over type chemotherapy which will be given every 3 weeks unless unusual toxicities are encountered.

PROGRESS

(82 06 - 82 09) No patients registered on the protocol at MAMC.

STATUS: (0)

TITLE: SWOG 8116: Evaluation of Bisantrene Hydrochloride in Refractory Lymphoma, Phase II

PRINCIPAL INVESTIGATOR: LTC James E. Congdon, MC

PROFESSIONAL ASSISTANTS: COL Friedrich H. Stutz, MC
LTC Irwin B. Dabe, MC
MAJ Lauren K. Colman, MC
MAJ Howard Davidson, MC
CPT Thomas M. Baker, MC
CPT Alfred H. Chan, MC

WORK UNIT NO: 82/48

TECHNICAL OBJECTIVE

To determine the response rate and response duration of malignant lymphoma treated with bisantrene hydrochloride used in a single dose, every-three-week schedule; to define the qualitative and quantitative toxicities of bisantrene administered in a Phase II study.

METHOD

This is a Phase II clinical trial of a new chemotherapy agent, bisantrene hydrochloride used in patients with malignant lymphomas of the Hodgkin's and non-Hodgkin's varieties that have not responded to standard treatment modalities. The drug has demonstrated some effectiveness in controlling lymphomas in a variety of laboratory animals. It has been tested in Phase I trials in humans, and its toxicities, including temporary bone marrow suppression, nausea, emesis, alopecia, transient hypotension, and pain at the injection site have been recognized. All patients in this study will have met a number of performance and laboratory eligibility criteria as listed in the protocol. Bisantrene hydrochloride will be administered through the side tubing of a freely flowing IV line in an amount determined by the patient's body surface area. The treatments will be repeated at three week intervals, unless unusual toxicities are encountered, for a minimum of two courses or until objective evidence of disease progression is ascertained.

PROGRESS

(82 05 - 82 09) No patients registered on the protocol at MAMC.

STATUS: (0)

TITLE: SWOG 8117: Evaluation of Bisantrone Hydrochloride in
Refractory Ovarian Cancer, Phase II

PRINCIPAL INVESTIGATOR: LTC James E. Congdon, MC

PROFESSIONAL ASSISTANTS: COL Friedrich H. Stutz, MC
LTC Irwin B. Dabe, MC
MAJ Lauren K. Colman, MC
MAJ Howard Davidson, MC
CPT Thomas M. Baker, MC
CPT Alfred H. Chan, MC

WORK UNIT NO: 82/49

TECHNICAL OBJECTIVE

To determine the response rate and response duration of refractory ovarian cancer treated with bisantrene hydrochloride used in a single dose, every-three-week schedule; to define the qualitative and quantitative toxicities of bisantrene administered in a Phase II study.

METHOD

This is a Phase II clinical trial evaluating a new chemotherapy agent, bisantrene hydrochloride, in the treatment of refractory ovarian carcinoma. Bisantrone is one of a series of new synthetic anticancer drugs in the hydrazone class which have demonstrated some in vitro activity in cell culture work against ovarian carcinoma as well as some in vivo efficacy in human volunteers. The clinical toxicities have been delineated in Phase I trials and include transient myelo suppression, nausea, emesis, transient alopecia, transient mild hypotension, and local superficial ulceration of the skin with extravasation of the drug at the IV site. The exact dosage of bisantrene that the patient will receive depends on several factors including the patient's height, body weight, and performance standards on several laboratory tests which evaluate bone marrow, hepatic, and renal function. The drug will be administered, dissolved in 500 cc of dextrose in water solution, through a freely flowing IV line over two hours. Unless unusual toxicities are encountered, the treatments will be repeated at three week intervals, for a minimum of two cycles or until objective evidence of disease progression is ascertained.

PROGRESS

(82 05 - 82 09) No patients registered on the protocol at MAMC.

STATUS: (0)

TITLE: SWOG 8118: Evaluation of Bisantrone Hydrochloride in Refractory Malignant Melanoma, Phase II

PRINCIPAL INVESTIGATOR: LTC James E. Congdon, MC

PROFESSIONAL ASSISTANTS: COL Friedrich H. Stutz, MC
LTC Irwin B. Dabe, MC
MAJ Lauren K. Colman, MC
MAJ Howard Davidson, MC
CPT Thomas M. Baker, MC
CPT Alfred H. Chan, MC

WORK UNIT NO: 82/50

TECHNICAL OBJECTIVE

To determine the response rate and response duration of malignant melanoma treated with bisantrene hydrochloride used in a single dose, every-three-week schedule; to define the qualitative and quantitative toxicities of bisantrene administered in a Phase II study.

METHOD

This is a Phase II clinical trial evaluating a new chemotherapy agent, bisantrene hydrochloride, in the treatment of malignant melanoma which has become refractory to standard treatment modalities. This drug has demonstrated some effectiveness in controlling malignant melanoma neoplasms in cell cultures and in a variety of laboratory animals. The drug has been tested in Phase I clinical trials in human beings and its toxicities, including temporary bone marrow suppression, nausea, emesis, alopecia, mild hypotension, and pain at the injection site, have been recognized. All patients entered into the study will have met a number of performance and laboratory eligibility criteria as outlined in the protocol. Bisantrone hydrochloride will be administered through the side tubing of a freely flowing IV line in an amount determined by the patient's body surface area. Unless unusual toxicities are encountered, the treatments will be repeated at three week intervals, for a minimum of two cycles or until objective evidence of disease progression is ascertained.

PROGRESS

(82 05 - 82 09) No patients registered on the protocol at MAMC.

STATUS: (0)

TITLE: SWOG 8119: Evaluation of Bisantrone Hydrochloride in
Hepatoma, Phase II

PRINCIPAL INVESTIGATOR: LTC James E. Congdon, MC

PROFESSIONAL ASSISTANTS: COL Friedrich H. Stutz, MC
LTC Irwin B. Dabe, MC
MAJ Lauren K. Colman, MC
MAJ Howard Davidson, MC
CPT Thomas M. Baker, MC
CPT Alfred H. Chan, MC

WORK UNIT NO: 82/51

TECHNICAL OBJECTIVE

To determine the response rate and response duration of hepatomas treated with bisantrene hydrochloride used in a single dose, every-three-week schedule; to define the qualitative and quantitative toxicities of bisantrene administered in a Phase II study.

METHOD

This is a Phase II clinical trial evaluating a new chemotherapy agent, bisantrene hydrochloride, in the treatment of malignant primary carcinoma of the liver. The patients will have all failed on prior standard treatments including surgery, radiation therapy, and chemotherapy. This drug has demonstrated some effectiveness in controlling primary liver cancer in a variety of laboratory animals. The drug has been tested in Phase I clinical trials in human beings and its toxicities, including temporary nausea, emesis, alopecia, transient mild hypotension, transient mild myelosuppression, and localized pain at the injection site, have been recognized. All patients entered into the study will have met a number of performance and laboratory eligibility criteria as outlined in the protocol. Bisantrone hydrochloride will be administered through the side tubing of a freely flowing IV line in an amount determined by the patient's body surface area. Unless unusual toxicities are encountered, the treatments will be repeated at three week intervals, for a minimum of two cycles or until objective evidence of disease progression is ascertained.

PROGRESS

(82 05 - 82 09) No patients registered on the protocol at MAMC.

STATUS: (0)

TITLE: SWOG 8120: Evaluation of Bisantrone Hydrochloride in
Gastric Carcinoma, Phase II

PRINCIPAL INVESTIGATOR: LTC James E. Congdon, MC

PROFESSIONAL ASSISTANTS: COL Friedrich H. Stutz, MC
LTC Irwin B. Dabe, MC
MAJ Lauren K. Colman, MC
MAJ Howard Davidson, MC
CPT Thomas M. Baker, MC
CPT Alfred H. Chan, MC

WORK UNIT NO: 82/52

TECHNICAL OBJECTIVE

To determine the response rate, response duration, and survival of gastric carcinoma treated with bisantrene hydrochloride used in a single dose, every-three-week schedule; to define the qualitative and quantitative toxicities of bisantrene administered in a Phase II study.

METHOD

This is a Phase II clinical trial evaluating a new chemotherapy agent, bisantrene hydrochloride, in the treatment of malignant primary gastric carcinoma. The patients will have all failed on prior standard treatments including surgery and standard chemotherapy agents. This drug has demonstrated some effectiveness in controlling the growth of primary gastric carcinomas in cell culture work and moderate effectiveness in several laboratory animals. The drug has been tested in Phase I clinical trials in human beings and its toxicities, including temporary nausea, emesis, alopecia, transient mild hypotension, transient mild myelosuppression, and localized pain at the injection site, have been recognized. All patients entered into the study will have met a number of performance and laboratory eligibility criteria as outlined in the protocol. Bisantrone hydrochloride will be administered through the side tubing of a freely flowing IV line in an amount determined by the patient's body surface area as well as the patient's overall performance status. Unless unusual toxicities are encountered, the treatments will be repeated at three week intervals, for a minimum of two cycles or until objective evidence of disease progression is ascertained.

PROGRESS

(82 05 - 82 09) No patients registered on the protocol at MAMC.

STATUS: (0)

TITLE: SWOG 8206: Evaluation of Aclacinomycin A in Colorectal Carcinoma, Phase II

PRINCIPAL INVESTIGATOR: LTC James E. Congdon, MC

PROFESSIONAL ASSISTANTS: COL Friedrich H. Stutz, MC
LTC Irwin B. Dabe, MC
MAJ Alfred H. Chan, MC
MAJ Howard Davidson, MC
MAJ Timothy J. O'Rourke, MC
CPT Thomas M. Baker, MC

WORK UNIT NO: 82/70

TECHNICAL OBJECTIVE

To determine the antitumor activity of aclacinomycin A in previously untreated patients with colorectal carcinoma by determination of the response rate and remission duration of two dosage schedules: a single dose, every-three-week schedule and a weekly dosage schedule for four weeks out of six; and to further define the qualitative and quantitative toxicities of this drug for each of the two dosage schedules in a phase II study.

METHOD

This is a phase II study designed to determine the efficacy of a new agent, aclacinomycin A, in the treatment of disseminated or recurrent colon carcinoma. Aclacinomycin A is in the anthracycline derivative class of chemotherapeutic agents. It has seen limited in vitro and in vivo trials but has demonstrated activity in a number of hematologic and solid tumors. Aclacinomycin A will be given by IV infusion on one of two treatment schedules: either weekly (65 mg/M^2) for four weeks followed by a two-week rest period or once every three weeks (100 mg/M^2) for two cycles. At the end of the initial treatment phase, a repeat metastatic evaluation will be performed and, if there is evidence of tumor response, the treatments will continue. Treatment will be terminated at the first evidence of tumor progression or withdrawal of patient's permission.

PROGRESS

(82 09 - 82 09) No patients registered at MAMC.

STATUS: (0)

TITLE: SWOG 8207: AZQ in Advanced Renal Cell Carcinoma,
Phase II

PRINCIPAL INVESTIGATOR: LTC James E. Congdon, MC

PROFESSIONAL ASSISTANTS: COL Friedrich H. Stutz, MC
LTC Irwin B. Dabe, MC
MAJ Alfred H. Chan, MC
MAJ Howard Davidson, MC
MAJ Timothy J. O'Rourke, MC
CPT Thomas M. Baker, MC

WORK UNIT NO: 82/71

TECHNICAL OBJECTIVE

To determine the response rate and duration of response in patients with advanced renal cell carcinoma treated with AZQ (aziridinylbenzoquinone) used in a single dose, every-three-week schedule; and to define the qualitative and quantitative toxicities of AZQ administered in a phase II study.

METHOD

This is a phase II study designed to determine the efficacy of a new agent, AZQ, in the treatment of advanced renal cell carcinoma. It has shown promising in vitro and in vivo efficacy in a number of adenocarcinomas including renal cell carcinoma. The drug will be given through the side tubing of a freely running IV every 3 weeks (good risk: 40 mg/M², poor risk: 30 mg/M²). The treatments will be continued on a 3-week basis as long as there is objective evidence of disease stabilization or regressions. Treatment will be terminated if unacceptable side effects develop or if there is objective evidence of disease progression.

PROGRESS

(82 09 - 82 09) No patients registered at MAMC.

STATUS: (0)

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 #26C: A Phase II Trial of Cis-Platinum Diamminedichloride

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANTS: COL William L. Benson, MC

WORK UNIT NO: 82/07

TECHNICAL OBJECTIVE

To screen for activity of new agents or drug combinations in patients with advanced malignancies. The intent is to determine the efficacy of chemotherapeutic agents in patients whose advanced malignancies have been resistant to high priority methods of treatment.

METHOD

All patients with measurable gynecological cancer, who have failed higher priority therapies, will be offered Cis-Platinum as a Phase II drug to determine its efficacy. The drug is given at 50 mg/M² intravenously every three weeks as toxicity permits. Patients who respond or who demonstrate disease will continue to receive the agent until progression has occurred.

PROGRESS

(81 11 - 82 09) Two patients were entered on this protocol; one had progression of disease.

STATUS: (0)

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 - 82 09) No patients entered on this protocol at MAMC.

STATUS: (C)

TITLE: GOG #26-0: A Phase II Trial of Aziridinybenzoquinone
(AZQ) in Patients with Advanced Malignancies

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANTS: COL William L. Benson, MC

WORK UNIT NO: 82/30

TECHNICAL OBJECTIVE

To determine the efficacy of chemotherapeutic agents in patients whose advanced malignancies have been resistant to high priority methods of treatment. This is a phase II study.

METHOD

Eligible patients are those with advanced gynecological malignancies who have been resistant to higher priority methods of treatment. The dosage of the AZQ is 30 mg/M² given every three weeks as toxicity permits. Medicine will be continued for as long as the tumor shows a response.

PROGRESS

(82 03 - 82 09) No patients entered at MAMC.

STATUS: (0)

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 the 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-oophorectomy, selective pelvic and para-aortic lymphadenectomy, and peritoneal cytology sampling are eligible. The following histologic types of endometrial carcinoma are acceptable: adenocarcinoma, adenocarcinoma with squamous metaplasia, adenoacanthoma, and adenosquamous carcinoma. Patients who have received preoperative radiotherapy are ineligible. Pathologic evaluation will include:

- a. peritoneal washing will be evaluated for malignant cells;
- b. the uterus will be evaluated in regard to location of tumor, depth of myometrial invasion, differentiation of tumor, size of uterus;
- c. the 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 - 82 09) Five patients have been entered on the protocol two of these during FY 82. All show no evidence of disease at this time.

STATUS: (0)

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 patient entries at MAMC.

(81 10 - 82 09) Two patients were entered with no progression of disease.

STATUS: (0)

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 Stages I-IV carcinoma of the vulva; to rapidly accumulate prospectively significant surgical pathologic data which would expedite development of further protocols for subsets 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 - 82 09) No entries at MAMC.

STATUS: (0)

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 positive groin nodes or a bilateral if both sides are positive) or to receive bilateral groin and pelvic node irradiation. Major parameters to be studied are survival and time to recurrence. Patients will be followed quarterly for 3 years and every 6 months thereafter.

PROGRESS

(81 03 - 82 09) No entries at MAMC.

STATUS: (0)

TITLE: GOG #40: A Clinical-Pathologic Study of Stages 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 Stages I and II uterine sarcomas, the relationship of these node metastases to other important prognostic factors such as mitotic index of the tumor, and the complication rate of the procedures. These findings will then be used as a guide for treatment protocols.

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 preoperative adjuvant pelvic radiation or chemotherapy will be ineligible. The following pathologic evaluation will be done:

- a. Peritoneal cytology will be evaluated for malignant cells.
 - b. The uterus will be evaluated at least in regard to:
 - (1) location of tumor; (2) depth of myometrial invasion;
 - (3) differentiation of tumor; (4) size of uterus;
 - (5) number of mitoses per 10 HPF; (6) histologic type of tumor.
 - c. The adnexa will be evaluated for presence of metastasis.
 - d. The lymph nodes will be evaluated as to metastasis and:
 - (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 - 82 09) A total of three patient entries; two during FY 82. One patient has regressed.

STATUS: (0)

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 - 82 09) A total of ten patients has been entered (three during FY 82); all with no evidence of disease at present.

STATUS: (0)

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 therapy. They will be randomized to one of two regimens. Regimen 1: adriamycin, 60 mg/M² IV q 3 weeks for a total dosage of 480 mg/M². Regimen 2: adriamycin, 60 mg/M², IV q 3 weeks plus cyclophosphamide 500 mg/M² IV q 3 weeks. Both medications will be discontinued when a total dosage of adriamycin of 480 mg/M² 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 - 82 09) No entries at MAMC.

STATUS: (C)

TITLE: GOG #43: A Randomized Comparison of Cis-Platinum 50 mg/M² in Every Three Weeks vs Cis-Platinum 100 Mg/M² in Every Three Weeks vs Cis-Platinum 20 Mg/M² 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 with histologically confirmed locally advanced, recurrent, persistent, or metastatic squamous cell carcinoma of the cervix 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/M² 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/M² if no regression occurs after 2 cycles or if progression is noted at any point. Regimen II: cis-platinum 100 mg/M² 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/M² 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 entered - both died from disease.

(81 10 - 82 09) No patients entered at MAMC.

STATUS: (C)

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-feto-protein and human chorionic gonadotropin (beta HCG), when these are present in predicting response and relapse; to determine the role of restaging laparotomy in determining response, predicting relapse, and planning further therapy.

METHOD

Patients with histologically confirmed malignant germ cell tumors of the ovary, Stage I or II, if previously untreated and completely resected, (excluding patients with pure dysgerminoma) will be eligible. Patients with Grade 2 or 3 immature teratoma are eligible. After adequate recovery from required surgery, patients will receive 6 courses of VAC chemotherapy. If progression is noted during chemotherapy, patients will be transferred to the appropriate protocol. Patients with no evidence of disease after 6 courses will then undergo a restaging laparotomy. Those showing evidence of progression will be transferred. If laparotomy reveals no evidence of disease, patients will receive an additional 3 courses of VAC and then be followed on no further therapy.

PROGRESS

(80 12 - 82 09) No entries at MAMC.

STATUS: (0)

TITLE: GOG #48: A Study of Progestin Therapy and a Randomized Comparison of Adriamycin vs Adriamycin Plus Cyclophosphamide in Patients with Advanced Endometrial Carcinoma After Hormonal Failure (Phase III Study)

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 cyclophosphamide to adriamycin alone as therapy for advanced or recurrent endometrial carcinoma which no longer responds to or has failed to respond to progestins in patients who have received no prior cytotoxic drugs.

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/M² 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/M² IV q 3 weeks x 8 courses plus cyclophosphamide 500 mg/M² IV q 3 weeks x 8 courses. Responders will receive follow-up only. Those with progression will be transferred to Protocol #26. Those patients with no prior hormonal therapy will be placed on C.T. Provera for a minimum of 12 weeks. Those with progression of disease at any time after 12 weeks will be randomized as above.

PROGRESS

(81 02 - 82 09) Two patients, both entered in FY 81, are on this protocol, with disease but alive.

STATUS: (0)

TITLE: GOG #49: A Surgical-Pathologic Study of Women with Invasive Carcinoma of the Cervix Stage I_B and Randomly Assigned Radiation Therapy Versus No Further Therapy in Selected Patients, Phase III

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 of the histopathologic prognostic factors of size of lesion, location of lesion, depth of invasion of tumor in millimeters, histology and grade, growth pattern, and site and number of positive lymph nodes in Stage I_B carcinoma of the cervix; to rapidly accumulate prospectively significant surgical pathologic data which would expedite development of further protocols; to determine morbidity of primary radical surgical therapy; to determine if radiation therapy will improve survival in selected patients with positive nodes.

METHOD

Patients with primary, previously untreated histologically confirmed invasive Stage I_B (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 entries at MAMC.

(81 10 - 82 09) Four patients entered: 3 stable and one with progression of disease.

STATUS: (0)

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, nonmeasurable disease, or no residual disease postoperatively. The endometrium must be examined to exclude an endometrial origin of the tumor. Patients with prior chemotherapy are ineligible. All patients will receive chemotherapy as soon as the acute effects of surgery have resolved. After completion of a total cumulative dose of 550 mg/M², patients with clinically complete responses or detectable disease which is thought to be resectable will undergo second look surgery. Those patients with progression will be entered on Protocol #26. At second look those with NED will have no further therapy and follow-up for five years; those with stable disease or progression will be entered on Protocol #26.

PROGRESS

(81 03 - 82 09) No entries at MAMC.

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 clinically complete response will go off study and be followed for survival; those with clinically complete response will have second-look surgery to validate the complete response or to remove residual tumor masses. Patients will then be followed for approximately 5 years for survival rates.

PROGRESS

(81 08 - 81 09) No entries at MAMC.

(81 10 - 82 09) Two entries with no progression of disease.

STATUS: (0)

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 ASSISTANT: 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 - 82 09) No entries at MAMC.

STATUS: (C)

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 effectiveness of combined vincristine, dactinomycin, and cyclophosphamide (VAC) in treatment of malignant tumors of the ovarian stroma in patients with residual, recurrent or advanced disease; to confirm completeness of response to VAC treatment with restaging laparotomy; to evaluate response to adriamycin in patients who fail primary treatment with VAC; to evaluate the endometrium histologically to learn more about the relationship between stromal tumors and endometrial cancer.

METHOD

Eligible patients must have histologically confirmed malignant tumors of the ovarian stroma (granulosa cell tumor, granulosa-theca cell tumor, Sertoli-Leydig cell tumor, androblastoma, gynandroblastoma, unclassified sex cord-stromal tumor, sex cord tumor with annular tubules) not amenable to cure by further surgery or radiation therapy. Patients who have received chemotherapy at any time or those who have received radiotherapy 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. Patients must have recovered from surgery. All patients will receive VAC for a minimum of three cycles or a maximum of ten cycles. Patients who exhibit a complete response or a partial response after ten cycles which makes remaining disease resectable will undergo a restaging laparotomy. If all residual disease is resected at restaging laparotomy, patients will receive adriamycin. If there is no evidence of disease at restaging laparotomy, patients will receive intermittent cyclophosphamide. If progression is observed during cyclophosphamide therapy, patient will be removed from study. Patients who exhibit progression of disease after three cycles of VAC will receive adriamycin. If further progression is observed on adriamycin therapy, the patient will be removed from the study. All patients will be followed for five years or until death.

PROGRESS

(81 09 - 82 09) No entries at MAMC.

STATUS: (0)

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 progesterone oral contraceptives following the evacuation of a hydatidiform mole and prior to the HCG titer reaching undetectable levels affects the incidence of trophoblastic sequelae requiring chemotherapy.

METHOD

Patients with a histologically verified diagnosis of hydatidiform mole evacuated by suction evacuation of the uterus with uterine conservation are eligible. All patients must have a pelvic ultrasound and arterial blood gases performed within 2 weeks of evacuation. Patients will be randomly assigned to Regimen 1: hormonal contraception - oral contraception to be commenced as soon as the patient has been randomized and will continue for at least 12 weeks; or Regimen 2: mechanical contraception - a. sheath and foam preparation; b. IUD inserted once the uterus has become involuted, again used with foam; c. diaphragm used with contraceptive cream or foam. The principal investigator will choose the method of mechanical contraception and it will be commenced as soon as the patient has been randomized and will continue for at least 12 weeks. At the end of 12 weeks, all patients will be evaluated for development or nondevelopment of trophoblastic sequelae. Further birth control will be at the discretion of the patient and the investigator. All patients will remain on the study for a minimum of six months after primary evacuation of the molar pregnancy.

PROGRESS

(81 02 - 82 09) Two patients entered (FY 81) with no progression of disease. No entries in FY 82.

STATUS: (0)

TITLE: GOG #56: A Randomized Comparison of Hydroxyurea Versus Misonidazole as an Adjunct to Radiation Therapy in Patients with Stage II_B, III, and IV_A Carcinoma of the Cervix and Negative Para-Aortic Nodes (Phase III)

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANTS: COL William L. Benson, MC
COL Donald Kull, MC

WORK UNIT NO: 82/08

TECHNICAL OBJECTIVE

To determine whether hydroxyurea or misonidazole is superior as a potentiation of radiation therapy in advanced cervical cancer; and to compare the toxicity of hydroxyurea versus misonidazole when given concurrently with radiotherapy.

METHOD

All patients with invasive squamous cell carcinoma of the cervix, Stages II_B through IV_A will undergo preoperative clinical staging. This will include traditional staging as permitted by FIGO rules. Extended clinical staging utilizing lymphangiography, computerized transaxial tomography, and/or sonography is required. Subsequently, patients will undergo a para-aortic lymphadenectomy and peritoneal exploration. Selected patients may be excluded from this procedure if percutaneous needle biopsy provides histologic proof of metastasis to the aortic nodes. All patients with cancer confined to the pelvis are eligible for treatment. They will receive pelvic irradiation and will be randomly assigned to receive concomitant hydroxyurea or misonidazole. Patients with metastasis outside the pelvis are not eligible for treatment.

PROGRESS

(81 11 - 82 09) No entries at MAMC.

STATUS: (0)

TITLE: GOG #57: A Randomized Comparison of Multiple Agent
Chemotherapy with Methotrexate, Dactinomycin, and
Chlorambucil versus the Modified Bagshawe Protocol
in the Treatment of "Poor Prognosis" Metastatic
Gestational Trophoblastic Disease (Phase II)

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANTS: COL William L. Benson, MC

WORK UNIT NO: 82/31

TECHNICAL OBJECTIVE

To evaluate the effectiveness and toxicity of the Modified Bagshawe Protocol (MBP) in patients with "poor prognosis" metastatic gestational trophoblastic disease (MGTD); and to compare the effectiveness and toxicity of the MBP with standard triple agent chemotherapy with methotrexate, dactinomycin, and chlorambucil (MAC).

METHOD

Patients who have a histologic diagnosis of gestational trophoblastic disease and an elevated HCT titer, who are considered "poor prognosis" on the basis of the criteria set forth in the protocol, will be randomized to either a drug combination of MAC or to a modified Bagshawe Protocol.

PROGRESS

(82 02 - 82 09) No entries at MAMC.

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 ASSISTANT: COL William L. Benson, MC
COL Donald Kull, MC

WORK UNIT NO: 81/117

TECHNICAL OBJECTIVES

To determine if cis-diamminedichloroplatinum, 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 highrisk 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-aortic metastasis and negative scalene node biopsies are eligible for treatment. They will receive pelvic and para-aortic irradiation and hydroxyurea and will be randomly assigned to receive cisplatin or no further therapy. An adequate trial will be defined as completion of the prescribed radiation therapy, completion of one course of cisplatin and survival of four weeks, or survival of eight weeks after radiation therapy for the no-further-treatment regimen. Patients will be followed quarterly for two years and every six months for three additional years.

PROGRESS

(81 09 - 82 09) No entries at MAMC.

STATUS: (0)

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 Stage 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 or Stage IV ovarian epithelial cancer. Patients must have optimal surgery for ovarian cancer, with at least an exploratory laparotomy and appropriate tissue for histologic evaluation. Patients with measurable or nonmeasurable disease will be evaluated. Patients with histologically confirmed serous adenocarcinoma, mucinous adenocarcinoma, clear-cell adenocarcinoma, endometrioid adenocarcinoma, undifferentiated carcinoma, or mixed epithelial carcinoma will be eligible. Patients who have received previous chemotherapy or radiotherapy will be ineligible. Patients will be randomized to receive either doxorubicin, cyclophosphamide, and cisplatin every 3 weeks for 8 courses; or the above regimen plus BCG (days 8 & 15 for 8 courses). Patients with complete response will have a second look laparotomy and will be taken off therapy if complete response is confirmed. Patients who have partial response of stable disease will be considered for a second look if, in the opinion of the investigator, significant tumor reduction may have been achieved. If residual tumor is detected, patients will be taken off study and placed on GOG #61. Patients with progressive disease at any time will be removed from the chemotherapy on this study, but will be followed.

PROGRESS

(81 09 - 81 09) No entries at MAMC.

(81 10 - 82 09) Three patients entered: none with progression, but one expired from pulmonary embolus.

STATUS: (0)

TITLE: GOG #61: Phase III Randomized Study of Cis-Platinum Plus Cyclophosphamide versus Hexamethylmelamine After Second-Look Surgery in Nonmeasurable Stage III Ovarian Adenocarcinoma Partially Responsive to Previous Regimens Containing Cis-Platinum and Cyclophosphamide.

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 82/09

TECHNICAL OBJECTIVE

To determine in nonmeasurable but residual Stage III ovarian adenocarcinoma, partially responsive after treatment with regimens containing cis-platinum and cyclophosphamide, if the progression-free interval and survival are improved by continuing cyclophosphamide plus cis-platinum or by changing treatment to hexamethylmelamine.

METHOD

With the increasing use of second-look laparotomy after combination chemotherapy for ovarian cancer, more Stage III patients are being identified who show a partial response or stable disease when compared with the original findings. The GOG has two studies involving cyclophosphamide and cis-platinum, but not hexamethylmelamine (Protocols #47 and #52), in which partial responders (as judged at second look) currently go off study. We propose to randomize such patients to more cyclophosphamide plus cis-platinum or to hexamethylmelamine. This additional treatment will be given for a finite period of 12 months since: (1) we do not propose a third look which might provide an endpoint for treatment but probably would not benefit most patients as there is no promising third line treatment if residual disease were found and it is unlikely that debulking surgery would be of consistent benefit at this point; moreover it may be difficult to do adequate biopsies after two prior laparotomies and (2) some of these patients may progress slowly even though they do not respond to the additional treatments.

PROGRESS

(81 11 - 82 09) One entry at MAMC with no progression.

STATUS: (0)

TITLE: GOG #63: A Clinical-Pathologic Study of Stages II_B, III,
and IV_A Carcinoma of the Cervix

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 82/36

TECHNICAL OBJECTIVES

To evaluate the sensitivity and specificity of non-invasive procedures such as sonography, computerized transaxial tomography and lymphangiography in detection of metastases; to better understand the significance of various surgical and pathologic factors involved in staging and therapy for "advanced" cervical cancer. The accumulated clinical/surgical/pathological data may then play a role in modification or design of future protocols; to determine by observations of five-year survival and disease-free interval, the validity of current FIGO staging in comparison to histopathologic prognostic factors such as size of lesion, location of lesion, histology, grade, pelvic lymph node metastases, and aortic lymph node metastases, in patients with Stages II_B, III, and IV_A carcinoma of the cervix.

METHOD

All eligible patients with invasive carcinoma of the cervix, Stages II_B through IV_A, will undergo preoperative clinical staging, including traditional staging as permitted by FIGO rules. Extended clinical staging utilizing sonography, lymphangiography, and computerized transaxial tomography are mandatory. When these tests reveal an aortic nodal metastasis, the patient will have a fine needle biopsy; however, if the tests are negative, the patient will have an aortic lymphadenectomy. Patients who have a positive fine needle biopsy or positive aortic lymphadenectomy will undergo scalene node biopsy before consideration for a GOG treatment protocol. It is anticipated that all patients will be considered for entry into a GOG protocol for which they are suitable when such protocols are available.

PROGRESS

(82 03 - 82 09) No entries at MAMC.

STATUS: (0)

TITLE: GOG #64: A Randomized Comparison of Rapid vs Prolonged
(24-Hour) Infusion of Cisplatin in Therapy of Squamous
Cell Carcinoma of the Cervix.

PRINCIPAL INVESTIGATOR: LTC Roger B. Lee, MC

PROFESSIONAL ASSISTANT: COL William L. Benson, MC

WORK UNIT NO: 82/37

TECHNICAL OBJECTIVES

(1) To determine whether the frequency and duration of objective response of squamous cell carcinoma of the cervix is altered significantly by prolonging to 24 hours the duration of the infusion of a dose of cisplatin as compared to administration at a rate of 1 mg/minute; and (2) to determine whether the administration of a dose of cisplatin as a continuous 24-hour infusion alters the frequency and/or severity of drug-related nausea and vomiting as compared to the administration of the same dose at a rate of 1 mg/minute.

METHOD

Eligible patients are those with histologically confirmed, locally advanced, recurrent, persistent, or metastatic squamous cell carcinoma of the cervix which is resistant to curative treatment with surgery or radiotherapy. Cis-platinum (50 mg/M^2) will be given as a 24-hour infusion or at a rate of 1 mg/minute IV once every three weeks. Treatment will be repeated every three weeks for eight courses unless disease progression or adverse effects dictate cessation.

PROGRESS

(82 03 - 82 09) No entries at MAMC.

STATUS: (0)

D E T A I L S H E E T S
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CHILDRENS CANCER STUDY GROUP PROTOCOLS

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: LTC 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 to escalate the dose to 4.5 mg/kg every three weeks or remove the patient from the study.

PROGRESS

(78 11 - 82 09) No entries at MAMC.

STATUS: (C)

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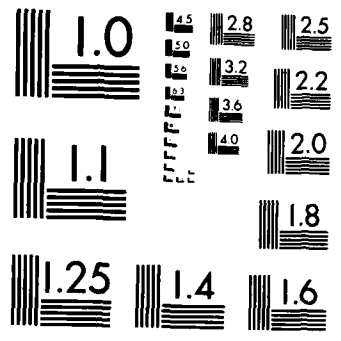
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TITLE: CCG 191P - Total Sanctuary vs Conventional CNS Treatment of Newly Diagnosed Acute Lymphoblastic Leukemia for Patients with "Average Risk" and "High Risk" Prognostic Characteristics, Phase III

PRINCIPAL INVESTIGATOR: MAJ Allen R. Potter, MC

PROFESSIONAL ASSISTANTS: LTC Charlene P. Holt, MC
LTC Alan D. Mease, MC

WORK UNIT NO: 79/89

TECHNICAL OBJECTIVES

To compare the effects of high-dose, protracted IV methotrexate infusion 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 <21 years of age with acute lymphoblastic leukemia who are (1) <3 years old, (2) >7 or (3) have an initial WBC of greater than 10,000/ μ l 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. The type of CNS prophylaxis 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, prednisone, L-asparaginase, daunomycin, methotrexate, cyclophosphamide, and 6-MP. M₃ bone marrow or extramedullary leukemia at any time will be cause for removal from the study.

PROGRESS

(79 07 - 82 09) Two patients entered on study; one was removed from study upon relapse; the other is well with no evidence of disease at present time. No new entries at MAMC during FY 82.

Due to the departure of LTC Mease, MAJ Allen R. Potter became the principal investigator on this protocol in July 1982.

STATUS: (0)

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: MAJ Allen R. Potter, MC

PROFESSIONAL ASSISTANT: LTC Alan D. Mease, MC

WORK UNIT NO: 81/103

TECHNICAL OBJECTIVES

To improve remission duration and survival in children with previously untreated acute non-lymphocytic leukemia using Cytosan 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 Cytosan, 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 Cytosan 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 - 82 09) No entries at MAMC.

Due to the departure of LTC Mease, MAJ Allen R. Potter became the principal investigator on this protocol in July 1982.

STATUS: (0)

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: MAJ Allen R. Potter, MC

PROFESSIONAL ASSISTANTS: LTC Charlene P. Holt, MC
LTC Alan D. Mease, MC

WORK UNIT NO: 79/35

TECHNICAL OBJECTIVES

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 nodes, etc. Patients previously treated with CPDD and/or VM-26 are not eligible. VM-26, 150 mg/M² 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

(78 11 - 82 09) No entries at MAMC.

Due to the departure of LTC Mease, MAJ Allen R. Potter became the principal investigator on this protocol in July 1982.

STATUS: (0)

TITLE: CCG #551: A Trial of Memorial Hospital LSA₂-L₂ 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: MAJ Allen R. Potter, MC

PROFESSIONAL ASSISTANTS: LTC Charlene P. Holt, MC
LTC 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 LSA₂-L₂ 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 standardized IT methotrexate without radiation for the control of occult CNS disease. To determine for each of the treatment regimens the effectiveness of standardized 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

(78 11 - 82 09) No new entries during FY 82. Two patients have been followed for 18+ months post-medication with no evidence of disease.

Due to the departure of LTC Mease, MAJ Allen R. Potter became the principal investigator on this protocol in July 1982.

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: MAJ Allen R. Potter, MC

PROFESSIONAL ASSISTANTS: LTC Charlene Holt, MC
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 therapy will be given. If there is no residual or persistent tumor at this time, radiation therapy will not be administered. If at 24 weeks the patient has progressive disease, the patient will be taken off the study. Patients on the study will continue chemotherapy until week 102. The patient will be taken off the study if there is progressive disease after 24 weeks of therapy or if recurrent or metastatic disease appears after six months of therapy.

PROGRESS

(78 11 - 82 09) No entries at MAMC.

Due to the departure of LTC Mease, MAJ Allen R. Potter became the principal investigator on this protocol in July 1982.

STATUS: (0)

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: LTC 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 radio-nuclides; 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 82 09) No entries at MAMC.

STATUS: (T)

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: LTC 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 purposes 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 lesion not controlled by chemotherapy so long as other parameters of measurements of response are available.

PROGRESS

(78 11 - 82 09) No entries at MAMC.

STATUS: (C)

DE T A I L S H E E T S
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PEDIATRIC ONCOLOGY BRANCH PROTOCOLS

TITLE: Intrathecal Aminopterin, NSC #739-NB, Clinical Brochure

PRINCIPAL INVESTIGATOR: MAJ Allen R. Potter, MC

PROFESSIONAL ASSISTANTS: LTC Charlene P. Holt, MC
LTC 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 cyto centrifuge analysis. Thereafter, the injections will be given weekly x 2, then q 2 weeks x 2, then monthly for 2 years.

PROGRESS

(80 06 - 82 09) No entries at MAMC.

Due to the departure of LTC Mease, MAJ Allen R. Potter became the principal investigator on this protocol in July 1982.

STATUS: (0)

TITLE: POB #76-04: Combined Modality Treatment of Rhabdomyosarcoma

PRINCIPAL INVESTIGATOR: MAJ Allen R. Potter, MC

PROFESSIONAL ASSISTANTS: LTC Charlene P. Holt, MC
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 rhabdomyosarcoma?

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; Stage II - local contiguous spread (with or without involvement of regional nodes; Stage III - metastatic disease. Stages I and II will be randomized to either Group I 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 07 - 82 09) No entries at MAMC.

Due to the departure of LTC Mease, MAJ Allen R. Potter became the principal investigator on this protocol in July 1982.

STATUS: (O)

TITLE: POB 77/03 - Treatment of Metastatic Osteosarcoma

PRINCIPAL INVESTIGATOR: MAJ Allen R. Potter, MC

PROFESSIONAL ASSISTANTS: LTC Charlene P. Holt, MC
LTC 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 06 - 82 09) No entries at MAMC.

Due to the departure of LTC Mease, MAJ Allen R. Potter became the principal investigator on this protocol in July 1982.

STATUS: (0)

TITLE: POB #77/04: Childhood Non-Hodgkin's Lymphoma

PRINCIPAL INVESTIGATOR: MAJ Allen R. Potter, MC

PROFESSIONAL ASSISTANTS: LTC Charlene P. Holt, MC
LTC Alan D. Mease, MC

WORK UNIT NO: 80/62

TECHNICAL OBJECTIVES

To treat patients in as uniform 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 <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 07 - 82 09) No entries at MAMC.

Due to the departure of LTC Mease, MAJ Allen R. Potter became the principal investigator on this protocol in July 1982.

STATUS: (0)

TITLE: POB #77/05 - Treatment of Metastatic and High Risk
Ewing's Sarcoma

PRINCIPAL INVESTIGATOR: MAJ Allen R. Potter, MC

PROFESSIONAL ASSISTANTS: LTC Charlene P. Holt, MC
LTC 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 06 - 82 09) No entries at MAMC.

Due to the departure of LTC Mease, MAJ Allen R. Potter became the principal investigator on this protocol in July 1982.

STATUS: (0)

TITLE: POB #77/06: Treatment of Low Risk Ewing's Sarcoma

PRINCIPAL INVESTIGATOR: MAJ Allen R. Potter, MC

PROFESSIONAL ASSISTANTS: LTC Charlene P. Holt, MC
LTC 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 06 - 82 09) No entries at MAMC.

Due to the departure of LTC Mease, MAJ Allen R. Potter became the principal investigator on this protocol in July 1982.

STATUS: (0)

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: MAJ Allen R. Potter, MC

PROFESSIONAL ASSISTANTS: LTC Charlene P. Holt, MC
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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 transfusions; to determine if the type of platelets transfused in those patients refractory to both matched and mismatched platelet transfusions 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

ELIGIBILITY: All pediatric patients admitted to Madigan.

EXCLUSIONS: >5 blood component transfusions, if cannot be HLA typed, or if there is an inadequate number of HLA-matched donors to provide HLA-matched platelet support. RANDOMIZATION: 2 groups by diagnostic categories; further, patients within each diagnostic category will be divided into those with or 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 platelet support.

PROGRESS

(80 06 - 82 09) No entries at MAMC.

Due to the departure of LTC Mease, MAJ Allen R. Potter became the principal investigator on this protocol in July 1982.

STATUS: (0)

TITLE: POB #78/06 - Treatment of Recurrent Lymphoma

PRINCIPAL INVESTIGATOR: MAJ Allen R. Potter, MC

PROFESSIONAL ASSISTANTS: LTC Charlene P. Holt, MC
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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 disseminated non-Hodgkin's lymphoma. To study the utility of flow-micro-fluorimetric techniques as a potential 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 constitute relative contraindications to the initiation of CARAT therapy (Cytosan, 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 ineligible 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: cytosan; 45 mg/kg days 1, 2, 3, 4, (1V 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/M²/24 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 - 82 09) No entries at MAMC.

Due to the departure of LTC Mease, MAJ Allen R. Potter became the principal investigator on this protocol in July 1982.

STATUS: (0)

TITLE: POB #78/10 - A Phase II Study of Achromobacter Glutaminase
in Acute Leukemia

PRINCIPAL INVESTIGATOR: MAJ Allen R. Potter, MC

PROFESSIONAL ASSISTANTS: LTC Charlene P. Holt, MC
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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 at least 4 weeks and cytologically documented acute lymphocytic, acute myelocytic, or acute undifferentiated leukemia (on bone marrow aspirate or the 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/M²/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 06 - 82 09) No entries at MAMC.

Due to the departure of LTC Mease, MAJ Allen R. Potter became the principal investigator on this protocol in July 1982.

STATUS: (0)

TITLE: POB #78/13 - Fever and Antimicrobial Therapy, Study II

PRINCIPAL INVESTIGATOR: MAJ Allen R. Potter, MC

PROFESSIONAL ASSISTANTS: LTC Charlene P. Holt, MC
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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 spectrum 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 07 - 82 09) No entries at MAMC.

Due to the departure of LTC Mease, MAJ Allen R. Potter became the principal investigator on this protocol in July 1982.

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: MAJ Allen R. Potter, MC

PROFESSIONAL ASSISTANTS: LTC Charlene P. Holt, MC
LTC 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 years 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 M₃ to M₂ 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, cross-over to an induction attempt with the other agent.

PROGRESS

(80 06 - 82 09) No entries at MAMC.

Due to the departure of LTC Mease, MAJ Allen R. Potter became the principal investigator on this protocol in July 1982.

STATUS: (O)

TITLE: POB #79/03: Phase II Study of 2'-Deoxycoformycin in
Acute Lymphoblastic Leukemia

PRINCIPAL INVESTIGATOR: MAJ Allen R. Potter, MC

PROFESSIONAL ASSISTANTS: LTC Charlene P. Holt, MC
LTC Alan D. Mease, MC

WORK UNIT NO: 80/58

TECHNICAL OBJECTIVES

To determine the therapeutic efficacy of 2'-deoxycoformycin (2'dCF) against acute lymphoblastic leukemia refractory to standard agents; to determine the toxicity of 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 M₃ 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 06 - 82 09) No entries at MAMC.

Due to the departure of LTC Mease, MAJ Allen R. Potter became the principal investigator on this protocol in July 1982.

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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