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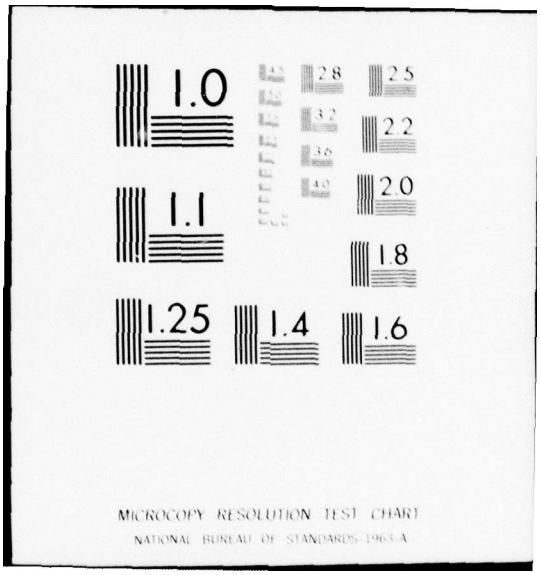
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The findings in this report are not to be construed as an official Department of the Army position unless so designated by other authorized documents.

19. KEY WORDS (Continue on reverse side if necessary and identify by block number)

Unit summary; research protocols (objective, method, progress, status); publications; presentations; exhibits, autotutorial programs; U.S. Army Preceptorship Program in Comparative Medicine

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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ANNUAL RESEARCH PROGRESS REPORT

FISCAL YEAR 1977 & 77T

CLINICAL INVESTIGATION SERVICE
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, approved by The Council of the American Physiological Society. The investigators follow the recommendations from the Declaration of Helsinki in the performance of investigations involving human subjects.

***

CODE:

C - Completed
O - Ongoing
T - Terminated

P - Publication
PR - Presentation
SP - Submitted for Publication

Work Unit Number: 77*/01**

* - Fiscal Year in Which Registered
** - Chronological Order of Registration

FOREWORD

Clinical investigations should be an integral part of every teaching hospital. It has been demonstrated that those clinical services which engage in clinical investigation develop more astute observers and more self-critical medical personnel which lead to a better clinician. Clinical investigation in order to be performed properly must be funded and supported by all members of teaching programs if it is to remain capable of assisting prospective investigators with their investigations. Clinical investigation is not a stepchild of the teaching hospitals, but is necessary if teaching programs are to show continuing improvement in advancing medical knowledge and skills. Some forethought should be given to who will work within Clinical Investigation Services. If a group of individuals who are congenial and supportive of each other are found, consideration should be given to stabilizing the members of this group as much as possible if research programs are to continue in a productive manner.

Those individuals who are conducting investigative protocols at Madigan Army Medical Center, Tacoma, Washington, are identified in this report. An abstract of each protocol giving abbreviated technical objectives, methods, and progress is presented. Readers of this report are reminded that many of these abstracts are preliminary and are not to be construed as the final report or necessarily the end result which will be obtainable at the conclusion of the investigation.

The research protocols described in this report were conducted under the provisions of AR 40-38, Clinical Investigation Program; AR 70-25, Use of Volunteers as Subjects of Research; and MAMC Supplement 1 to AR 40-38, Medical Services Clinical Investigation Program.

The staff at Clinical Investigation Service would like to express their gratitude to those investigators who responded promptly with their abstracts. We would also like to express our appreciation to the many people who have given our service support in the past fiscal year, making it possible to conduct investigative procedures in many areas. I personally would like to express my gratitude to Ms. Nancy Whitten for her assistance in compiling, typing, and proofreading this report.

JAMES W. REED, MD
COL, MC
Chief, Clinical Investigation Service

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CLINICAL INVESTIGATION SERVICE

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***

UNIT SUMMARY FY 77

1. Objective

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

2. Technical Approach

MANPOWER

DESCRIPTION	RANK	MOS
Chief Reed, James W., MC	06	61C9B8M
Microbiologist Heggers, John P., MSC	05	68A9B8Z
Vet Lab Officer Jennings, Paul B., VC	05	64F9B9Z
Staff Veterinarian Ward, George S., VC	04	64C00
Vet Precep Program Ridgway, Robert L, VC	04	64A00
Biochemist Smith, Michael L, MSC	03	68C00
NCOIC Lindstrom, Duane E.	E7	92B40
Med Lab Spec Naegle, Debbra	I-5	92B30
Oper Rm Spec Frecceri, Christopher	I-5	91D20
Vet Anim Spec Brown, Michael E.	I-5	91T20
Vet Anim Spec Lee, Donald R.	I-4	91T20
Vet Anim Spec Pack, Donald L.	I-4	91T20

DESCRIPTION	RANK	MOS
Med Tech, Supervisor Graves, James N.	GS9	00644
Med Tech Garrison, Mina J.	GS7	00644
Med Tech Matej, Louis A.	GS7	00644
Edit Asst/Steno Whitten, Nancy J.	GS6	00318
Clerk Steno Fraser, Elizabeth L.	GS4	00312
Animal Caretaker Mallouf, Jerry L.	WG6	07706

FUNDING

MEDCASE Equipment	$28,000.00
Capital Equipment	1,615.00
Personnel Services (Civ Salaries)	76,148.00
Consumable Supplies	23,543.00
Temporary Duty Travel	4,539.00
Contractual Services	3,881.00
TOTAL	$137,726.00

3. Progress

During FY77 & 77T there were 112 protocols. Of these, 84 are ongoing; 15 completed; and 13 terminated.

There were 50 publications and 21 presentations (including exhibits and autotutorials) at national meetings reporting work performed at Madigan Army Medical Center under the sponsorship of the Clinical Investigation Service.

U.S. Army Preceptorship Program in Comparative Medicine

for U.S. Army Veterinary Corps Officers

LTC Paul B. Jennings, VC
Clinical Investigation Service
Director

On 15 August 1973 the United States Army Preceptorship Program in Comparative Medicine for United States Army Veterinary Corps officers was approved by the Surgeon General's Senior Review Committee, and begun at Madigan Army Medical Center. The purposes of the program are:

1. To provide and train Veterinary Corps officers to staff the Clinical Investigation facilities.

2. To provide clinical scientists and teachers to assist in the training of physicians, dentists, and other biological scientists in research procedures and the selection and use of animal models for human disease problems.

3. To provide training for Veterinary Corps officers in laboratory animal medicine as it applies to Clinical Investigation facilities. To insure that the facilities and the health and treatment of laboratory animals in Army facilities are in accordance with American Association for Laboratory Animal Science standards.

4. To provide opportunity for clinically-oriented Veterinary Corps officers to acquire further training in veterinary medicine and surgery, especially as it applies to human public health.

5. To provide a group of experienced teachers for training nursing and medical enlisted personnel in emergency first aid procedures in a laboratory environment.

6. To increase the quality and quantity of military medicine-oriented protocols emanating from Clinical Investigation facilities.

7. To foster military-civic affairs in the communities surrounding military medical facilities.

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The first graduate of the program (1 May 1975) has entered (July 1977) a two-year residency program in surgery at Colorado State University, Ft. Collins, Colorado.

The second graduate of the program (May 1976) is presently assigned to Clinical Investigation Service, Fitzsimons Army Medical Center, and is pursuing a graduate program in surgery (part-time) at Colorado State University.

The third preceptee completed the program in June 1977. Subsequently, he has entered a two-year residency program in internal medicine at the University of California at Davis.

PUBLICATIONS AND PRESENTATIONS FROM CMP PROGRAM

PUBLICATIONS

1. Jennings, P.B.: Involvement in Hospital Clinical Research. Editorial Viewpoint. JAVMA 170:258, 1 Feb 1977.

2. Jennings, P.B.: Military Comparative Medicine: Training the Army Veterinarian for an Expanding Role in the 1970's. Military Medicine 142:294-296, April 1977.

3. Jennings, P.B.: U.S. Army Preceptorship Program in Comparative Medicine. JAVMA 170:874-878, 1 May 1977.

4. Jennings, P.B.: Veterinary Medical Participation in Hospital Clinical Research. Military Medicine 141:555-556, Aug 1976.

5. Ridgway, R.L.: Spontaneous Myxoma in a Pet Hamster. VMSAC 72:75, 1977.

6. Ridgway, R.L.: Oral Xanthoma in a Budgerigar (*Melopsittacus undulatus*). VMSAC 72:266-268, Feb 1977.

7. Ridgway, R.L.: Feline Poisoning Due to the Mushroom *Amanita pantherina*. JAVMA (in press).

8. Ridgway, R.L., Heggers, J.P., Jennings, P.B., and Hunter, W.J.: Hematogenous *Bacteroides fragilis* and *Proteus mirabilis* in a Dog with Splenic Lymphocytic Lymphoma. JAVMA (in press).

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9. Ridgway, R.L.: Plant Selenium Poisoning in Grazing Animals on Military Reservations. Military Medicine (in press).

10. Ridgway, R.L. and Zielke, D.R.: Canine Endodontics - A Nonsurgical Technique. JAVMA (in press).

11. Ridgway, R.L. and Graves, J.N.: Automated Freezing of Human Platelets Using a Controlled-Rate Freezer. Submitted to Cryobiology, 1977.

12. Ridgway, R.L., Graves, J.N., and Usry, R.: Testing and Cryopreservation of Human Platelets for Transfusion Using Glycerol-Glucose Technique. Submitted to Cryobiology, 1977.

13. Ridgway, R.L. and Rowe, A.W.: Detailed Step-by-Step Procedure for Preparing Human Platelets for Freezing and Thawing in Glycerol-Glucose. Submitted to Cryobiology, 1977.

PRESENTATIONS

1. Jennings, P.B.: Preparation of Veterinarians for Human-Oriented Clinical Research by Preceptorship Training in Comparative Clinical Medicine. 12th Annual Meeting, American College of Veterinary Surgeons, Des Moines, Iowa, 2-4 Feb 1977.

2. Ridgway, R.L. and Zielke, D.R.: Canine Endodontics - A Nonsurgical Technique. Autotutorial Presentation. Annual Meeting, American Animal Hospital Association, and Annual Meeting, American Veterinary Medical Association, 1977.

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PUBLICATIONS FY77

CLINICAL INVESTIGATION SERVICE

Heggers, J.P., Barnes, S.T., and Talmage, J.B.: Cellular Immune Response to Methylmethacrylate in Experimentally Sensitized Guinea Pigs. Mil Med (in press).

Heggers, J.P., Jennings, P.B., Smith, M.L., and Fariss, B.L.: Dimethyl Sulfoxide (DMSO) An Adjunct to Topical Antimicrobial Therapy. A Preliminary Report. (Abstract) Abstracts of the Northwest Branch Meeting, American Society for Microbiology, 24-25 June 1976, #27.

Heggers, J.P.: Food Borne Diseases - A Food Service Supervisor's Dilemma. Mil Med (in press).

Heggers, J.P.: Microbial Invasion - The Major Ally of War (Natural Biological Invasion). Mil Med (in press).

Heggers, J.P., Jennings, P.B., Yetter, J.F., Krieg, Jr., R.E., and Robson, M.C.: The Effect of Mycobacterium ulcerans Toxin on Mammary Gland Adenocarcinoma Implants in C3H/HeJ Mice. (Abstract) ASM Abstracts, p 93, # E-75, Apr 77.

Jennings, P.B., Wettlaufer, J.N., and Paulsen, C.A.: Absence of Circulating HLA Lymphocytotoxic Antibodies in Men 21-44 Months After Vasectomy. Fertil Steril 28:446-47, Apr 77.

Jennings, P.B.: Involvement in Hospital Clinical Research. JAVMA 170:258, 1 Feb 77.

Jennings, P.B.: Military Comparative Medicine - Training the Army Veterinarian for an Expanding Role in the 1970's. Mil Med 142(4):294-96, Apr 77.

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SOCIAL WORK SERVICE

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PRESENTATIONS FY 76

CLINICAL INVESTIGATION SERVICE

Heggers, J.P.: Food Borne Diseases - A Food Service Supervisor's Dilemma. Presented to American Society of Hospital Food Service Administrators, Puget Sound Chapter, 10 Nov 76, Madigan Army Medical Center, Tacoma, WA.

Heggers, J.P., Jennings, P.B., Yetter, J.F., Krieg, Jr., R.E., and Robson, M.C.: The Effect of Mycobacterium ulcerans Toxin on Mammary Gland Adenocarcinoma Implants in C3H/HeJ Mice. Presented to American Society of Microbiology Annual Meeting, 8 May 1977, New Orleans, LA.

Jennings, P.B.: Evaluation of Septic Shock in the Small Animal Patient. Presented to the 1976 Veterinary Surgical Forum, Shock Program, 27 Oct 76, Chicago, IL.

Jennings, P.B.: Use of Antibiotics in the Treatment of Shock. Presented to the 1976 Veterinary Surgical Forum, Shock Program, 27 Oct 76, Chicago, IL.

Jennings, P.B.: Veterinary Medical Participation in Hospital Clinical Research. Presented to Clinical Investigation Services Conference, 7 Dec 76, Academy of Health Sciences, Fort Sam Houston, TX.

Jennings, P.B.: Preparation of Veterinarians for Human-Oriented Clinical Research by Preceptorship Training in Comparative Clinical Medicine. Presented to the 12th Annual Meeting of the American College of Veterinary Surgeons, 2-4 Feb 77, Des Moines, IA.

Jennings, P.B., Heggers, J.P., Smith, M.L., and Fariss, B.L.: Use of Dimethyl Sulfoxide as an Adjunct to Topical Antimicrobial Therapy. Presented to the 12th Annual Meeting of the American College of Veterinary Surgeons, 2-4 Feb 77, Des Moines, IA.

Krieg, R.E., Wolcott, J.H., Meyers, W.M., and Heggers, J.P.: Comparison of Treatment Effectiveness with Severity of Mycobacterium ulcerans Infection. Presented to Annual Meeting of the American Society for Microbiology, 8 May 77, New Orleans, LA.

Ridgway, R.L.: Inflammation. Presented to General Dental Residency Wound Healing Symposium, Madigan Army Medical Center, 26-30 Jul 76, Tacoma, WA.

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Thomas, S.R., Heggers, J.P, Morrison, R., and Garrison, M.: Evaluation of the Antiseptic, Sanitary, and Practical Utilization of Septisol, Alcare, and Triclean Under Simulated Combat Conditions. Presented to Vestal Laboratories Seattle District Sales Meeting, 5 Mar 77, Seattle, WA.

DEPARTMENT OF OB GYN

Biggerstaff, E.D.: Management of the Post-Date Pregnancy. Presented to Armed Forces Seminar - OB GYN, 20-23 Sep 76, Las Vegas, NV.

Sakakini, J., Capen, C.V., and Killam, A.P.: Assessment of Fetal Lung Maturity by Utilization of the Serum Unconjugated Estriol Level. Presented to Armed Forces District Meeting, American College of Obstetricians and Gynecologists, Las Vegas, NV, Sep 76.

DEPARTMENT OF PATHOLOGY

Oberhofer, T.R., Rowen, J.W., Cunningham, G.H., and Higbee, J.W.: Comparison of Three Methods for Presumptive Identification of Group B Streptococci. Presented to Annual Meeting of the American Society of Microbiology, 8 May 77, New Orleans, LA.

SOCIAL WORK SERVICE

Lanier, Daniel, Jr.: A Retrospective Analysis of Child Abuse and Neglect Among Military Families. Presented to the Military Family Research Conference, Naval Health Research Center, San Diego, CA, 31 Aug - 3 Sep 77.

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EXHIBITS FY77

CLINICAL INVESTIGATION SERVICE

Jennings, P.B., Henderson, R.W., Alden, E., and Hofmann, J.R.: Teaching Models for Neonatal Resuscitation. Exhibited at:

1. American Academy of Pediatrics Meeting, Chicago, IL, 16-21 Oct 76 - Gold Award for Exhibits.

2. Annual Meeting of the American Medical Association, June 1977, San Francisco, CA - Certificate of Merit.

3. American Veterinary Medical Association Meeting, Atlanta, GA, 10-14 Jul 77.

AUTOTUTORIAL PROGRAMS FY77

CLINICAL INVESTIGATION SERVICE

Ridgway, R.L. and Zielke, D.R.: Instrumentation, Nonsurgical Repair, and Preservation of Fractured Anterior Teeth in Dogs - Canine Endodontics. Presented to:

1. American Animal Hospital Association Annual Meeting, 1-6 May 77, Boston, MA.

2. American Veterinary Medical Association Annual Meeting, 11-14 Jul 77, Atlanta, GA.

3. Arkansas Veterinary Medical Association Meeting, by request, 20-22 Feb 77, Little Rock AR.

4. Chicago Veterinary Medical Association Meeting, by request, 1977, Chicago, IL.

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SUBMITTED FOR PUBLICATION FY76

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Heggers, J.P., Robson, M.C., Yetter, J.F., Krieg, R.W., and Jennings, P.B.: Tumoricidal Effects of Mycobacterium ulcerans Toxin on Murine Adenocarcinoma (C3HBS). Submitted to Cancer, Sep 77.

Ridgway, R.L. and Graves, J.N.: Automated Freezing of Human Platelets Using A Controlled-Rate Freezer (A Brief Report). Submitted to Cryobiology, Mar 77.

Ridgway, R.L. and Rowe, A.W.: Detailed Step by Step Procedure for Preparing Human Platelets for Freezing and Thawing in Glycerol-Glucose (A Brief Report). Submitted to Cryobiology, May 77.

Ridgway, R.L., Graves, J.N., and Usry, R.: Testing and Cryopreservation of Human Platelets for Transfusion Using Glycerol-Glucose Technique. Submitted to Cryobiology, Jun 77.

Smith, M.L., Hand, R.E., and Harrison, J.W.: Analysis of the Effect of Dilution on the Necrotic Tissue Dissolution Property of Sodium Hypochlorite. Submitted to J Endodontics, Jun 77.

SOCIAL WORK SERVICE

Egnew, T.R.: Behavioral Science Training in an Army Family Practice Residency Program. Submitted to J Med Ed, Sep 77.

DEPARTMENT OF DENTISTRY

Harrison, J.W., Svec, T.A., and Baumgartner, J.C.: An Analysis of the Clinical Toxicity of Endodontic Irrigants. Submitted to J Endodontics, Jul 77.

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

PRINCIPAL INVESTIGATOR: COL Bruce L. Fariss, MC

WORK UNIT NO: 69/01

TECHNICAL OBJECTIVE

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

METHOD

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

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

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

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

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

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

Day 6: Day of rest.

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Renal Glycosuria - Fariss

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

Day 8, 9, and 10: NH_4Cl loading p.o. with measurement of hydrogen secretory capacity, net acidification and ammonia production each day.

PROGRESS

(76 06 - 77 09) - This study includes 49 individuals with renal glycosuria. Three individuals have developed diabetes mellitus over a period of nine years.

STATUS: (O)

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

PRINCIPAL INVESTIGATOR: COL Bruce L. Fariss, MC

WORK UNIT NO: 74/08

TECHNICAL OBJECTIVE

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

METHOD

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

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

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

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

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

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The Effects of Chronic Hyperglycemia - Fariss

PROGRESS

(76 06 - 77 09) Approximately 99% of the pancreas was resected in 13 sheep. Intravenous glucose tolerance tests were abnormal. All fetuses died within two weeks after delivery. No histological or pathological abnormalities were found.

It was observed that total pancreatectomy in twelve sheep was not associated with hyperglycemia; however, intravenous glucose tolerance tests were abnormal. Alloxan does produce hyperglycemia.

STATUS: (O)

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TITLE: Suppression of ACTH in Patients with Bilateral Adrenalectomies

PRINCIPAL INVESTIGATOR: COL Bruce L. Fariss, MC

WORK UNIT NO: 75/28

TECHNICAL OBJECTIVE

An attempt will be made to determine if substances other than cortisol suppress ACTH in patients who have had bilateral adrenalectomies.

METHOD

Plasma ACTH levels will be performed at the Metabolic Research Unit, University of California, San Francisco, by a radioimmune method. The patient group is to be composed of four individuals who have had bilateral adrenalectomies for treatment of Cushing's disease. Two of these patients have Nelson's syndrome manifested by an abnormal sella turcica and increased pigmentation while taking replacement steroids.

Plasma ACTH and cortisol levels will be performed at 0800 hours and 1800 hours on several occasions while the patients are taking replacement steroids. When each test is performed, each patient will come to the Clinical Investigation Service at 0800 hours without taking their steroids that morning. Blood for ACTH and cortisol determinations will be drawn at intervals of one hour for eight hours. Each patient will have one of the following procedures performed at intervals of one to two weeks.

1. Intramuscular injection of cortisone acetate, 25 mg, to correspond to the routine dose of cortisone acetate.

2. Infusion of 100 ml of hydrocortisone in normal saline intravenously over four hours.

3. Dexamethasone, 21 phosphate, to be infused intravenously at the rate of 0.2 mg/kilogram/hour for four hours.

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Suppression of ACTH - Fariss

PROGRESS

(76 06 - 77 09) Cortisone acetate given intramuscularly is not absorbed. There is no rise in plasma cortisol and no suppression of ACTH. Conversely, hydrocortisone given intramuscularly does cause suppression of ACTH and a rise in plasma cortisol levels. When cortisone acetate and hydrocortisone are given orally, there are comparable suppression of ACTH levels and rises of plasma cortisol.

STATUS: (C)

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TITLE: Prevalence of Varicocele and Semen Analysis in a Group of Young Men

PRINCIPAL INVESTIGATOR: COL Bruce L. Fariss, MC

WORK UNIT NO: 76/17

TECHNICAL OBJECTIVE

1. To determine the prevalence of varicocele among a group of two thousand healthy young males.

2. To evaluate the semen of the individual with a varicocele for sperm count, motility, and morphology.

METHOD

1. Individuals undergoing physical examinations at the physical examination section will be examined by one of the investigators for the presence of a varicocele. The varicocele will be graded in size as small, moderate, or large.

2. When a varicocele is detected, the individual will be requested to have a semen analysis performed.

3. The individual will be given the telephone number for the Clinical Investigation Service Laboratory and will be advised that he can obtain the results of his semen analysis if he desires.

4. Men who attend the Obstetrical Clinic with their wives who are pregnant will be utilized as controls. Individuals will be solicited for submission of a semen specimen for analysis; a total of one hundred samples.

PROGRESS

(76 06 - 77 09) A comparison of semen analyses in individuals with varicocele shows the same distribution of counts when compared to a normal group of young men.

STATUS: (C)

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TITLE: Bacillus Species as a Possible Vector for Neoplasm Producing Agents

PRINCIPAL INVESTIGATOR: LTC John P. Heggers, MSC

WORK UNIT NO: 75/19

TECHNICAL OBJECTIVE

To demonstrate neoplastic producing agents are transmitted to man by Bacillus species.

METHOD

It is proposed to continue studying the possibility that Bacillus species isolated from clinical exudates and biopsies may be vectors for neoplasm-producing agents. The Bacillus species specimens, isolated from patients with and without neoplastic disease, will be sent to us from the Department of Surgery, Chicago University School of Medicine. The isolates will be subjected to the following procedures according to standard methods.

a. Subculturing - for propagation of the isolate.

b. Sonication - to disrupt the cells and free any intracellular entities.

c. Tissue culture passage of the filtrate to determine its effect on various cell lines.

Isolates showing CPE production in tissue culture will be further studied in vivo using mice as the host animal.

PROGRESS

(76 06 - 77 09) This project was terminated primarily due to the departure of the principal investigator. Work completed reveals no indication that neoplastic agents can be isolated from Bacillus species. Primarily, contamination problems in tissue cultures have been the major barrier in the study and have abrogated the isolation of the potential agents.

STATUS: (T)

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TITLE: Mycobacterium ulcerans Lipoprotein as a Therapeutic Antitumor Agent in Mice

PRINCIPAL INVESTIGATOR: LTC John P. Heggers, MSC

WORK UNIT NO: 75/37

TECHNICAL OBJECTIVE

To test the efficacy of Mycobacterium ulcerans as an antitumor agent.

METHOD

Two groups of 100 C3H/NeJ mice (mammary tumor susceptible mice) will be established. Each group will be inoculated with a homogenized tumor tissue from C3H/HeJ tumor bearing mice. One group will act as a control group and will remain untreated. The remaining group will receive intratumoral injections of M. ulcerans toxin when the tumor is palpable. They will receive 0.1 ml every third day until complete regression or death, whichever comes first. Tissue sections of tumors from both animals will be examined histologically to determine the mechanism of action for regression.

PROGRESS

(76 06 - 77 09) To date, 92 mice have been studied utilizing the toxin, and it has been demonstrated that the toxin is an effective tumoricidal agent and does increase the survival rate of those mice that have been treated with the toxin. This material has been presented at two annual meetings, and a request for an exhibit has been submitted.

STATUS: (C)

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TITLE: The Hormonal and Metabolic Consequences of Vasectomy

PRINCIPAL INVESTIGATOR: LTC Paul B. Jennings, VC

WORK UNIT NO: 73/15

TECHNICAL OBJECTIVE

The purpose of this project is to systematically follow parameters of hormonal and metabolic function in normal males undergoing elective vasectomy. Specifically, we plan to follow testosterone, gonadotropins, blood sugar, cholesterol, and uric acid. All of these have been said to rise post-vasectomy.

METHOD

Volunteers for this study will be solicited from normal males presenting to the Urology Clinic for elective vasectomy. Prior to vasectomy, a semen sample and blood for testosterone, FSH, LH, and SMA/12 serums will be obtained. At three month intervals after vasectomy, these studies will be repeated for three years. FSH, LH, and testosterone will be analyzed by radioimmunoassay in the US Public Health Service Hospital Laboratory, Seattle, Washington. The semen analyses will be performed in the Clinical Investigation Service Laboratory using the Coulter Counter technique.

PROGRESS

(76 06 - 77 09) - Nineteen vasectomized men were followed for 21 to 42 months after surgery, and their sera were tested for the presence of HL-A lymphocytotoxic antibodies. In a previous study, the sera of two of these men had shown a definite increase in serum reactivity 6 to 12 months after surgery. Only one of the nineteen tested in the study demonstrated a single weakly positive reaction 24 months after surgery. It was considered that the initial stimulus for lymphocytotoxic antibody production was related to surgery. There was no evidence of antibody stimulation 21 to 44 months postoperatively.

STATUS: (C)

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

PRINCIPAL INVESTIGATOR: 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 through 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

(76 06 - 77 09) Training sessions for Madigan Army Medical Center personnel were held six times during this period. In addition, the teaching model was taken to several civilian hospitals in the Tacoma area.

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A Teaching Model for Pediatric Intubation - Jennings

The teaching model was incorporated into a scientific exhibit, entitled "Teaching Models for Neonatal Resuscitation" which was presented at the following meetings:

October 1976 - Academy of Pediatrics, Chicago, IL - winner of Gold Award

June 1977 - American Medical Association Annual Meeting, San Francisco, CA - winner of Certificate of Merit

July 1977 - American Veterinary Medical Association Annual Meeting, Atlanta, GA

In July and August, 1977, the exhibit was displayed at Madigan Army Medical Center.

In November 1977, it will be displayed at the Annual Meeting of the Association of Military Surgeons of the United States, Washington, DC.

STATUS: (O)

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TITLE: Use of Dimethyl Sulfoxide Plus Antibiotics for Topical Antimicrobial Therapy in Contaminated Wounds

PRINCIPAL INVESTIGATOR: LTC Paul B. Jennings, VC

WORK UNIT NO: 76/23

TECHNICAL OBJECTIVE

To determine if the solvent, dimethyl sulfoxide (DMSO), in conjunction with topical antimicrobial agents is capable of inhibiting bacterial growth in contaminated wounds longer than the 3-6 hour "golden period."

METHOD

Fifty adult New Zealand white rabbits will be utilized in these experiments for a total of two procedures each. The rabbits will be sedated with ketamine and anesthesia will be maintained with halothane O_2. A "window" will be created over the thigh muscles and a standard wound will be created. During the procedure, 1×10^8 Pseudomonas aeruginosa (ATCC10145) will be instilled into the wound. After the microorganisms have remained in the wound one hour, rabbits will be paired. Each rabbit will receive one of the following; (a) decreasing concentrations of DMSO (100%, 90%) in 1 cc total volume - 25 rabbits; (b) 1 cc volumes of DMSO and antibiotics (varying concentrations of gentamycin or tobramycin plus DMSO) - 25 rabbits; (c) 1 cc volumes of antibiotics alone (gentamycin or tobramycin) - 25 rabbits.

Twenty-five control rabbits will receive equal volumes of normal saline as the test rabbits. Blood samples for culture and tissue biopsy samples will be taken before wounding, and at 3 hour intervals for 24 hours. Following the 24 hour sample, the window will be removed and the wound allowed to heal. Rabbits may be reused after one month.

DMSO alone and DMSO and antibiotics will be tested for activity in vitro against the Pseudomonas aeruginosa (tube dilution, sensitivity discs, etc.).

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Use of Dimethyl Sulfoxide Plus Antibiotics - Jennings

PROGRESS

(76 06 - 77 09) A 45% concentration of DMSO improved the efficacy of gentamycin in experimentally-created contaminated wounds in rabbits. When the concentration of antibiotic or DMSO was increased, little difference was seen between control (antibiotic alone) and test (antibiotic and DMSO) animals. Increasing the frequency of application of the antimicrobial agents was more effective than single dose application whether DMSO was utilized or not. Further studies are needed to determine the optimum ratio, pH, and application schedule for the antibiotics-DMSO combination.

STATUS: (C)

PRESENTATION: Jennings, P.B., Heggers, J.P., Smith, M.L., and Garrison, M: Use of Dimethyl Sulfoxide as an Adjunct to Topical Antimicrobial Therapy. 12th Annual Meeting, American College of Veterinary Surgeons, Des Moines, IA, February 1977.

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TITLE: Clinical Trials of a Peripheral Capillary Blood Culture Sampling Technique

PRINCIPAL INVESTIGATOR: LTC Paul B. Jennings, VC

WORK UNIT NO: 76/28

TECHNICAL OBJECTIVE

To compare the effectiveness of a new peripheral capillary blood culture sampling technique with standard blood culture methods in human neonatal and adult patients. This technique has been demonstrated effective in three animal species and needs clinical trials to determine whether it may be used as a supplemental sampling method in man.

METHOD

GROUP I - Neonatal Patients

Infants suspected of having transient bacteremia or frank sepsis will be sampled for blood culture in the usual manner. In addition, peripheral capillary blood will be sampled at the same time via heel stick, and the results will be compared to those achieved by the standard method. Blood for pour plates will also be drawn.

GROUP 2 - Adult Patients

The capillary blood culture technique (finger stick) consists of meticulous skin preparation and drawing of 0.1 - 0.2 ml of blood into a heparinized tuberculin syringe with 20 gauge needle attached. The needle is changed and the blood is injected into a standard blood culture bottle. Results are read at 24 and 48 hours and subcultures are performed where necessary.

Routine blood culture will also be performed in each case.

A population of adult patients undergoing urological instrumentation in the Urology Service will be sampled before their procedure and at 5, 15, and 30 minutes following the procedure,

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Clinical Trials of a Peripheral Capillary Blood Culture Sampling Technique - Jennings

comparing standard blood culture technique and the capillary blood culture sampling technique. Patients undergoing trans-urethral resection of the prostate, urethral dilation, prostatic biopsy, cystoscopy, and other urological manipulations are felt to have a relatively high incidence of bacteremia.

PROGRESS

(76 06 - 77 09) Due to the departure of CPT John R. Hofmann, VC, the principal investigator was changed to LTC Paul B. Jennings, VC.

Clinical trials have begun in both pediatric and adult patients. A new sampling kit, which can be sterilized rapidly, has been developed to facilitate transfer of the microblood sample to the blood culture bottle. Preliminary results in newborns have shown a good culture correlation between the micro-sampling method and the standard technique. Further patients are needed to provide a good statistical sample population. An exhibit is in preparation to demonstrate the development and refinement of the technique for clinical use.

STATUS: (O)

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TITLE: Adrenocortical Reserve in Patients with Metastatic Carcinoma

PRINCIPAL INVESTIGATOR: MAJ K. David McCowen, MC

WORK UNIT NO: 76/05

TECHNICAL OBJECTIVE

To evaluate the adrenocortical reserve in patients with metastatic carcinoma by alpha 1-24 ACTH stimulation.

METHOD

Patients with documented metastatic carcinoma (lungs, bone, etc.) will be tested with alpha 1-24 ACTH (Cortrosyn^{R}) according to common clinical procedures after baseline serum cortisol levels have been obtained. In those patients demonstrating a suboptimal adrenal reserve, repeat stimulation will be performed after chemotherapy has been given to detect improvement in the reserve function of the adrenal gland.

PROGRESS

(76 06 - 77 09) Ten patients have thus far been completely studied. The rough data so far have failed to document any degree of adrenal impairment.

STATUS: (O)

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TITLE: The Role of Thyroid Suppression in the Treatment of Thyroid Cysts

PRINCIPAL INVESTIGATOR: MAJ K. David McCowen, MC

WORK UNIT NO: 76/18

TECHNICAL OBJECTIVE

To evaluate the efficacy of thyroid suppression in the treatment of benign thyroid cysts.

METHOD

All patients with suspected thyroid nodules will be referred to the Thyroid Clinic where evaluation of the nodule with palpation, radionuclide scanning, and ultrasonography will be performed. Blood studies to include T_3RAIU, T_4CPB, Serum T_3, and thyroid antibodies will be done.

Those patients with cystic lesions as shown by these studies will undergo percutaneous needle aspiration of these cysts. Aspiration of thyroid cysts is performed routinely in our clinic. The aspirated fluid will be evaluated with cytological examination.

The patients with successful aspirations will be entered into the experimental protocol as follows. Patients in sequence will be referred to a disinterested party who will have a series of sequenced random numbers. If the patient's random number is even, he will be started on an equivalent of three grains of desiccated thyroid hormone, and, if his random number is odd, he will be started on an identical placebo. The patients will be followed for a minimum of one year. A minimum of 20 patients will be utilized for the study. All patients not entered into the study will undergo appropriate therapy in the conventional manner.

PROGRESS

(76 06 - 77 09) Fifteen patients are currently entered in this study. The double-blind code has not been broken, and an assessment of the efficacy of thyroid suppression in this situation has therefore not yet been determined.

STATUS: (O)

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TITLE: Testicular Dehydrotestosterone (DHT) and Testosterone (T) Levels in Oligospermic Patients with Varicoceles

PRINCIPAL INVESTIGATOR: MAJ K. David McCowen, MC

WORK UNIT NO: 77/02

TECHNICAL OBJECTIVE

To determine if a difference in the testicular tissue level of T and DHT exists between the affected and normal testes of oligospermic varicocele patients.

METHOD

Patients requiring high ligation of the spermatic vein will be identified. Preparatory studies will include a semen analysis, serum testosterone, FSH and LH levels. After counseling the patient and after being granted informed consent, biopsy of both the affected and normal testes will be done at the time of the indicated surgery for varicocele repair. The tissue (50-100 mg per biopsy) will be received by the principal investigator or his designee for analysis. The tissue will be examined by extraction, separation, and radioimmuno assay of the T and DHT. A total of 20-25 patients will be studied and the comparison of these steroids from each of the patient's testes will be made, with the patient serving as his own control.

PROGRESS

(76 11 - 77 09) The data thus far indicate no clear cut significant difference in these steroid levels of the varicocele affected testis when compared to the non-affected testis.

STATUS: (O)

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TITLE: The Effect of Aspirin on Blood and Urine Thyroxine in Induced Canine Hyperthyroidism

PRINCIPAL INVESTIGATOR: MAJ K. David McCowen, MC

WORK UNIT NO: 77/03

TECHNICAL OBJECTIVE

To evaluate the effect of aspirin on the fate of serum and urine thyroxine in mongrel dogs with induced hyperthyroidism.

METHOD

Ten mongrel dogs will be utilized. The dogs will be paired and given 1.0 mg LT_4 intravenously 24 hours before receiving 1.2 mg ASA, orally, on the morning of the study. One dog will receive the ASA with the other receiving only LT_4. Baseline serum T_4 levels will be drawn and repeated at 30 minute intervals, 2 hours to 4½ hours after the ASA is given. Urine T_4 levels will be determined at 30 minute intervals, 2 hours to 4½ hours after the ASA is given, and serum ASA levels will be determined at 3 hours after administration. Six weeks later, the same pair of dogs will be studied in identical fashion, with the exception that control dogs will receive the ASA with the other dog serving as the control. T_4 levels will be determined by RIA in the Clinical Investigation laboratory.

PROGRESS

(76 08 - 77 09) The first series of paired dogs have thus far been studied. Urinary thyroxine levels are in the process of being assayed. There is no evidence, thus far, of significant differences in the serum total thyroxine values.

STATUS: (O)

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TITLE: The Effect of Exogenous Glucocorticoids on FSH-LH Levels in Post-Menopausal Females

PRINCIPAL INVESTIGATOR: MAJ K. David McCowen, MC

WORK UNIT NO: 77/04

TECHNICAL OBJECTIVE

To determine if oral glucocorticoids suppress gonadotropin excretion by their action on the hypothalamic-pituitary axis.

METHOD

Post-menopausal patients with intact ovaries who are not ingesting exogenous estrogens will be studied. These patients will be selected in the Rheumatology Clinic from those patients requiring treatment with oral glucocorticoids for non-endocrine related disease, such as rheumatoid arthritis, SLE, and polymyalgia rheumatica. After obtaining informed consent, blood will be drawn before, during, and after glucocorticoid therapy for FSH-LH determinations. The effect of these exogenous glucocorticoids on the high endogenous post-menopausal FSH-LH levels will then be determined.

PROGRESS

(76 10 - 77 09) No data for this protocol is as yet available.

STATUS: (O)

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TITLE: Instructional Nonsurgical Endodontic Technique and Endodontic Instrumentation

PRINCIPAL INVESTIGATOR: MAJ Robert L. Ridgway, VC

WORK UNIT NO: 77/05

TECHNICAL OBJECTIVE

To outline a step-by-step nonsurgical endodontic technique for the treatment of fractured anterior teeth in dogs that can be readily accomplished by a Veterinary Corps officer with his normal armamentarium.

METHOD

Anesthetize dog, section crown, and complete nonsurgical endodontics extensively documenting each step pictorally. It is anticipated that the project will be completed after eight endodontic procedures.

PROGRESS

(76 08 - 77 01) This project was completed in January 1977 with the preparation of an autotutorial entitled "Instrumentation, Nonsurgical Repair, and Preservation of Fractured Anterior Teeth in Dogs - Canine Endodontics." Copies of this autotutorial are available on a loan basis, free of charge, from Clinical Investigation Service, Box 99, Madigan Army Medical Center.

PUBLICATION: Ridgway, R.L. and Zielke, D.R.: Canine Endodontics - A Nonsurgical Technique. JAVMA (in press).

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Instructional Nonsurgical Endodontic Technique - Ridgway

PRESENTATIONS: American Veterinary Medical Association Annual Meeting, 11-14 July 1977, Atlanta, GA.

American Animal Hospital Association Annual Meeting, 1-6 May 1977, Boston, MA.

Chicago Veterinary Medical Association Annual Meeting, 1977.

Arkansas Veterinary Medical Association Meeting, 20-22 February 1977, Little Rock, AR

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TITLE: Cryopreservation of Human Platelets for Transfusion

PRINCIPAL INVESTIGATOR: CPT Rob R. Roth, MC

WORK UNIT NO: 77/06

TECHNICAL OBJECTIVE

To preserve platelets for transfusion by freezing.

METHOD

Phase I. Freeze and recover platelets.

a. Screen 10 healthy routine blood donors of O positive blood including:

(1) normal donor criteria
(2) platelet count
(3) salicylate level

b. Draw one unit of blood from each donor.
c. Red cells and other components to be used routinely by the Blood Bank.
d. Preparation of platelets for freezing in accordance with the Dayian and Rowe procedure.
e. Aliquot each prepared platelet pack to be used as control and for testing.
f. Thaw platelets after 36 hours by submersion in a 40°C water bath with mild agitation for 20 seconds.
g. Sample control and test for bacteriologic control. Culture by the automated bacterial detection method on blood agar and peptone broth.
h. Test both test and control samples for platelet count, and osmolality of platelet concentration.

Phase II.

a. Screen 20 healthy routine blood donors of O positive blood including:

(1) normal donor criteria
(2) platelet count
(3) partial thromboplastin time
(4) salicylate level

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Cryopreservation of Human Platelets for Transfusion - Roth

b. Draw one unit of blood. Red cells and other components minus PRP to be used routinely by blood bank.

c. Preparation of platelets for freezing (see #4 through #7, Phase I.)

d. Test platelets, frozen and nonfrozen, for viability of recovered platelets in accordance with criteria established by Dayian, G. and Rowe, A.W., Cryobiology 13:1-8, 1976.

(1) uptake of ^{14}C serotonin
(2) (a) ADP induced aggregation
    (b) epinephrine induced aggregation
    (c) collagen induced aggregation
(3) clot reaction
(4) response to hypotonic shock
(5) platelet recovery and size distribution
(6) osmolality of platelet concentration

PROGRESS

(76 08 - 77 09) Due to the departure of MAJ Robert L. Ridgway, VC, the principal investigator was changed to CPT Rob R. Roth, MC, Department of Pathology.

Because of inconsistent yields, the project has remained in Phase I. Since July 1977, 25 units of platelets have been frozen and thawed with minor adjustments of technique. This has produced a more consistent result. Although the range of percentage yield of platelets is still somewhat wide (47%-100%), the mean yield is 73.72% and the median yield is 73.50%. Of these 25 units, 16 units produced a yield between 70 and 80%. Six units yielded less than 70% of the original platelets, while 3 units yielded greater than 80%. With the higher and more consistent percentage yields of platelets now being obtained, the project is progressing to Phase II.

Platelets from before and following freezing and thawing are being evaluated morphologically by examination of Wright's stained smears and by electron microscopy. The former technique demonstrates platelets having only minor morphologic differences following the freezing and thawing process. Although still in the preliminary stages, electron microscopic examination of frozen and thawed platelets show them to be essentially intact ultrastructurally.

STATUS: (O)

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TITLE: Zinc, Copper, Arginine, Carnitine and Total Proteolytic Enzyme Concentration in the Seminal Fluid of Infertile Patients

PRINCIPAL INVESTIGATOR: CPT Michael L. Smith, MSC

WORK UNIT NO: 77/76

TECHNICAL OBJECTIVE

To measure the concentration of several components in the semen of a population of fertile and infertile patients and to compare the values. This information will add to our understanding of the role of these elements and compounds in fertility and may help in the management of infertile patients. A finding of abnormal values may also yield diagnostic tests for specific fertility problems.

METHOD

Semen will be collected from at least thirty patients who have fathered a child and these patients will be considered fertile and used as controls. Samples will also be collected from 30 patients whose wives have had a favorable OB-GYN checkup but the couple cannot conceive. These patients will constitute an infertile population. A sperm count, motility, volume, viscosity, and morphology will be established for each sample one hour after collection. The samples will be frozen at -70°C and the zinc, copper, arginine, carnitine, and proteolytic enzyme concentration will be determined at a convenient time. When all data are collected, the mean values for the fertile group will be compared with those of the infertile group.

PROGRESS

(77 07 - 77 09) Eighty-nine prevasectomy semen samples have been collected and are being used as controls. A sperm count, motility, volume, viscosity, morphology, and proteolytic enzyme concentration have been determined for each of these samples.

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TITLE: Polymethylmethacrylate, Self Curing Acrylic Cement, as a Stimulator of Cellular Immunity

PRINCIPAL INVESTIGATOR: LTC Stephen R. Thomas, MC

WORK UNIT NO: 75/26

TECHNICAL OBJECTIVE

The main purpose of this project is to determine if component loosening after total hip replacement where bacterial involvement is not indicated is, in fact, a cellular immune response (tissue rejection phenomenon).

METHOD

This study will be conducted in two phases:

Phase I - Guinea pig stimulation phase in an attempt to promote an immune reaction. Procedure as outlined in protocol.

Phase II - Pheripheral blood from two groups of humans will be collected. Group I will be those individuals who have never experienced any surgical procedure which required the use of methylmethacrylate (control group). Group II will be those individuals who have experienced any surgical procedure which required the installation of methylmethacrylate cement. Procedure as outlined in protocol.

Ancillary Investigative Procedures - Sheep RBC properly treated as well as polystyrene latex particles could be employed to demonstrate the probable humoral antibody response. Potential development of a microagglutination procedure is feasible.

PROGRESS

(77 06 - 77 09) Phase I - Animal studies utilizing in vitro migration inhibition tests have demonstrated that 67% of all animals stimulated with methylmethacrylate do develop an immune response. A scientific article addressing these results has been accepted for publication in Military Medicine.

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Polymethylmethacrylate, Self Curing Acrylic Cement - Thomas

Phase II - Presently, 17 patients have been evaluated for a delayed hypersensitive reaction to methylmethacrylate implants, and two of the seventeen have, in fact, demonstrated cellular immunity with the aid of the lymphocytic stimulation test.

Due to the departure of LTC John P. Heggers, MSC, the project has been turned over to LTC Stephen R. Thomas, MC, Assistant Chief, Orthopedic Service, who will continue the protocol.

STATUS: (O)

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TITLE: Evaluation of the Antiseptic and Sanitary Capabilities of Septisol, Triclean, and Alcare under Simulated Combat Conditions

PRINCIPAL INVESTIGATOR: LTC Stephen R. Thomas, MC

WORK UNIT NO: 77/01

TECHNICAL OBJECTIVE

To evaluate the antiseptic and sanitary capabilities of the subject products under field conditions. The major parameters to be measured are microbial flora of skin, decrease in infection rates, dermatological problems, and gastrointestinal involvement. Two brigades will be utilized; one will be a test group, the other a control group.

METHOD

Two brigades, while conducting war games at Yakima, will be utilized. The 3rd Brigade will be a control group and will employ routine procedures normally followed while in the field. The 2nd Brigade will be the test group. Each of the four battalions will be utilized to evaluate one or more of the products. Medical personnel will utilize Septisol, and mess and troop personnel will employ Triclean and Alcare for personal hygiene. The remaining battalions will utilize all products. Medical officers and medical personnel assigned to the brigades will monitor the operation, recording all pertinent information concerning infection rates and frequency of gastro-enteritis. Random bacteriological hand samples will be taken before and after washing to enumerate the numbers of bacteria present and to isolate organisms for identification. These samples will be taken during the last handwashing of the day. Approximately 250 samples per battalion will be required. Particular attention will be given to S. aureus (potential enterotoxin producer) and Ps. aeruginosa (resistant Gram-negative infectious agent). Septisol cans will be issued to each individual involved in the study. Triclean and Alcare dispensers will be made available to all mess personnel and placed by all latrine facilities. All personnel will be briefed prior to departure to Yakima Training Area by LTC Stephen Thomas, MC, 9th Infantry Division, Division Surgeon.

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Evaluation of the Antiseptic and Sanitary Capabilities of Septisol, Triclean, and Alcare - Thomas

PROGRESS

(76 08 - 77 07) Investigations indicate that Septisol and Alcare effectively reduce the resident microflora of the soldier under simulated combat conditions. It was found that Septisol foam reduced the microbial population by 82.9%. Alcare reduced the microbial population by 82.9%, also. Triclean, on the other hand, was minimally effective. A paper has been submitted and accepted for publication in Military Medicine.

STATUS: (C)

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TITLE: Effect of Chronic Oral Propranolol on Glucose Tolerance

PRINCIPAL INVESTIGATOR: MAJ Gary L. Treece, MC

WORK UNIT NO: 76/26

TECHNICAL OBJECTIVE

To determine what effect propranolol given orally for the treatment of hypertension and angina pectorus has on intravenous and oral glucose tolerance tests in light of recent case reports of hyperglycemia nonketotic coma attributed to propranolol therapy.

METHOD

Patients will be obtained by referral from Madigan Army Medical Center's Cardiology and Endocrinology Clinics where it will be determined that these patients require treatment with outpatient oral propranolol for hypertension, angina pectorus or control of arrhythmias. Patients with a history of bronchial asthma or congestive heart failure will be excluded from the study as well as patients with emphysema and insulin-dependent diabetes mellitus.

It is proposed that 30 such patients will voluntarily be submitted to an intravenous GTT and a three-hour oral GTT before and after two and six weeks of oral propranolol alone, and four weeks after propranolol and hydrochlorothiazide in combination (ten weeks after institution of propranolol). Patients will have ingested at least 150 gm of carbohydrate for three days prior to any GTT. Patients will be NPO after 2400 hours the evening before the day of any GTT. Other nonessential medications will be discontinued three days prior to any GTT. Doses of propranolol to be used will be 40 mg, q.i.d. (p.o.).

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Effect of Chronic Oral Propranolol - Treece

PROGRESS

(76 06 - 77 09) Five patients have completed six weeks of Inderal therapy during which time their carbohydrate metabolism was monitored as per the protocol design. Two of these patients completed an additional four weeks of combined Inderal and hydrochlorothiazide therapy. Because of the small number of patients studied so far, only three general observations can be made. All of the patients studied had normal fasting blood glucoses. Two patients with glucose intolerance, manifested in the initial OGTT, had improvement in glucose tolerance during Inderal therapy, reflected in improved OGTT's and IVGTT's. Of the three patients with normal basal glucose tolerance, two patients showed a slight worsening of glucose tolerance but retained glucose tolerance within normal limits. Hydrochlorothiazide caused no additional effects in the patients studied. In most patients, the insulin response to both oral and IV glucose diminished regardless of whether glucose intolerance improved or worsened.

STATUS: (O)

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TITLE: Hypertension in Children and Youth and Family Profile of Hypertension

PRINCIPAL INVESTIGATOR: CPT Douglas L. Attig, MC

WORK UNIT NO: 77/09

TECHNICAL OBJECTIVE

To identify all Family Practice Clinic patients who meet the following criteria:

1. Are under the age of 18 years.
2. Whose systolic and/or diastolic blood pressures fall above two standard deviations of the mean of the general population by commonly accepted criteria.
3. Are expected to remain in the area for the next full year.

Analyses of age and race distribution and familial aggregation of hypertension will be made. Special studies on those patients with persistent hypertension will be done at a later date.

METHOD

All patients under the age of 18 who are seen in the Family Practice Clinic will have their blood pressures taken by nursing personnel. Family physicians will examine the blood pressure values according to criteria for the study. A computerized listing of all Family Practice patients with diagnoses of uncomplicated hypertension, labile hypertension, hypertension with target organ involvement or hypertension NOS will be obtained. Those patients with children under the age of 18 will receive a form letter describing the study and requesting them to make arrangements to have their children screened at the clinic.

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Hypertension in Children and Youth - Attig

PROGRESS

(76 09 - 77 09) Five hundred (500) children were screened for hypertension on routine physical examination. Approximately 10% have BP higher than the standard deviation from the mean. Because of this high incidence, a mass screening program is being developed for use in our clinic. It is anticipated that 2/3 of those children with isolated elevated BP will be normal on repeat examination.

STATUS: (O)

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

PRINCIPAL INVESTIGATOR: CPT Robert R. Byland, MSC

WORK UNIT NO: 77/72

TECHNICAL OBJECTIVE

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

METHOD

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

PROGRESS

(77 04 - 77 09) The basic equipment needed for conducting the test is in the process of procurement.

STATUS: (O)

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TITLE: The Incidence of Paraspinal Musculature EMG Abnormalities in Cancer Patients with Known Spinal Metastasis

PRINCIPAL INVESTIGATOR: MAJ Surinderjit Singh, MC

WORK UNIT NO: 77/37

TECHNICAL OBJECTIVE

To systematically evaluate paraspinal skeletal musculature in cancer patients with bone scan evidence of spinous metastasis by electromyographic techniques to determine the incidence of abnormal findings and to see if a specific pattern of abnormality exists which might be useful as a diagnostic screening technique.

METHOD

Patients who have specific cancer types that frequently metastasize to bone, such as breast carcinoma, prostatic carcinoma, lung carcinoma and/or multiple myeloma, will be eligible for this study. Only those patients who have documented scan evidence of metastasis will be included in the initial study. EMG will be performed on the back musculature, looking for abnormalities. If abnormalities are noted, then the skeletal musculature of the legs will be examined using the same technique. The number and percentage of electromyogram abnormalities will be analyzed as to distribution and the data will be evaluated to see if a particular EMB abnormal pattern is present. Statistical analysis employing the Chi square method will be utilized between the various diagnostic cancer groups. Significance will be determined to the 5% level.

PROGRESS

(77 03 - 77 09) Very few patients so far have met the criteria as stated in the protocol, and those patients which have met the criteria have been unable to come for the study. Therefore, the search for these patients is still in progress.

STATUS: (O)

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TITLE: Periapical Healing Potential in Canals Obturated with Gutta Percha versus Silver Cones

PRINCIPAL INVESTIGATOR: MAJ William H. Fowler, DC

WORK UNIT NO: 76/14

TECHNICAL OBJECTIVE

There are several techniques and materials with which the root canal system can be obturated. These include the use of gutta percha, silver cones, and various paste fillers. Gutta percha and silver cones were chosen for this study because they are utilized by the dental profession. A recent in vitro investigation by Seltzer, et al, suggests a high toxicity potential for silver cones.

The purpose of this investigation is to compare the periapical healing following instrumentation and obturation, short of the anatomical apex, with gutta percha versus periapical healing following instrumentation and obturation, short of the anatomical apex, with silver cones.

METHOD

Eighteen noncarious, nonperiodontally involved monkey teeth were used in this study. The involved teeth were isolated with a rubber dam, and an aseptic technique commonly employed by endodontists was followed.

Following pulp extirpation and instrumentation short of the apex, six teeth were obturated with gutta percha, six teeth were obturated with silver cones, and six teeth served as a control and had no obturating material in the canal system. The latter were sealed from the oral environment with amalgam and copalite. Surgical block sections of the periapical region were taken after four months. Histologic examination will be used to determine the status of the periapical tissues.

PROGRESS

(76 06 - 77 09) Serial sectioning and staining has been completed. Data are being analyzed.

STATUS: (O)

TITLE: The Use of Silastic as an Injectable Root Canal Obturating Material

PRINCIPAL INVESTIGATOR: MAJ Griffith B. Jones, DC

WORK UNIT NO: 77/12

TECHNICAL OBJECTIVE

To determine the clinical effectiveness of Silastic 382 Medical Grade Elastomer for root canal obliteration.

METHOD

Extracted human teeth will be prepared with an accepted endodontic technique and Silastic 382 Medical Grade Elastomer injected into the extracted teeth as the obturating material. The teeth will then be subjected to SEM analysis and tagged iodine to determine the effectiveness of its sealing properties.

PROGRESS

(76 10 - 77 09) Following the above methodology all results have been gathered and are presently being statistically evaluated. The paper should be ready for publication by February 1978.

STATUS: (O)

TITLE: A Comparative Evaluation of the Relative Debriding Efficiency of the Type K and H Files Utilizing 5.25% or 1.00% Sodium Hypochlorite for Irrigation

PRINCIPAL INVESTIGATOR: MAJ W. Richard Liggett, DC

WORK UNIT NO: 76/10

TECHNICAL OBJECTIVE

The goal of endodontic therapy is to debride and completely obturate the pulp canal system. Since it is the desire of the practitioner to perform his therapy as effectively, efficiently, and with as little threat of toxicity to the patient as possible, the purpose of this study will be twofold. First, to study the relative ability of the Kerr File versus the Hedstrom file in debriding and smoothing the pulp canal wall, and, secondly, to see if there is any significant difference in canal cleanliness when utilizing a 5.25% or 1.00% solution of sodium hypochlorite as pulp canal irrigant.

METHOD

Forty-eight single-rooted extracted human teeth will be used. These teeth will be frozen as soon as possible following extraction and kept frozen until utilized in the experiment. The 48 teeth will be separated into three groups of 16 teeth each. One-half of the teeth in each group will be instrumented with a series of Kerr files and the other half with Hedstrom files. Group I will be irrigated with a 5.25% solution of NaOCl; Group II will be irrigated with a 1.00% solution of NaOCl; Group III will be irrigated with saline which will serve as a control. The teeth will then be prepared for histologic examination and evaluation of the debrided and smoothed pulp canal wall.

PROGRESS

(76 06 - 77 09) Data are presently being analyzed. The results will be published in the Journal of Endodontics.

STATUS: (O)

TITLE: The Immediate Sealing Properties of Cavit

PRINCIPAL INVESTIGATOR: MAJ Maylon J Todd, DC

WORK UNIT NO: 76/09

TECHNICAL OBJECTIVE

Temporary filling materials are used in endodontics to seal the access cavity between treatments. The purpose of this study is to investigate the immediate sealing ability of Cavit.

METHOD

Eighteen extracted human teeth were separated into three groups, each containing six teeth. Access openings were prepared and sealed with Cavit. Group I teeth were immediately immersed in an S^{35} radioisotope solution. Group 2 teeth were placed in the isotope solution after a five-minute period to allow for maturation of the Cavit restoration. Group 3 teeth were immersed in the isotope solution after a 15-minute "maturation" period. After 24 hours in the isotope solution, a central longitudinal section (300 micrometers in thickness) was made from each tooth with a Bronwill thin sectioning machine. From these central sections, autoradiographs were made and the level of isotope penetration determined.

PROGRESS

(76 06 - 77 09) Data are presently being analyzed. Findings will be published in the Journal of Endodontics.

STATUS: (O)

TITLE: The Effect of Root Resection on the Apical Seal

PRINCIPAL INVESTIGATOR: MAJ Maylon J. Todd, DC

WORK UNIT NO: 76/13

TECHNICAL OBJECTIVE

The purpose of this study is to determine if root resection affects the integrity of the apical seal of previously obturated canals.

METHOD

Twenty-four extracted single rooted human teeth were used in this study. Twelve teeth were obturated with gutta percha and sealer, and twelve teeth were obturated with silver points and sealer. Six teeth with each type of obturating material were subjected to the root resection procedure, using a high-speed handpiece and straight-fissure bur. The remaining twelve teeth were not resected and served as controls.

All teeth were placed in an S^{35} radioisotope solution for twenty-four hours. A central longitudinal section was made from each tooth with a Bronwill thin sectioning machine. From these central sections, autoradiographs were made and the level of isotope penetration determined.

PROGRESS

(76 06 - 77 09) Data are presently being analyzed. Findings will be published in the Journal of Endodontics.

STATUS: (O)

TITLE: A Clinical Determination of the Effectiveness of Endodontic Chemomechanical Sterilization

PRINCIPAL INVESTIGATOR: LTC David R. Zielke, DC

WORK UNIT NO: 75/22

TECHNICAL OBJECTIVE

The objective of this study is to evaluate the efficacy of an accepted root canal preparation technique in producing sterilization of the root canal system.

METHOD

The plan is to endodontically treat single rooted asymptomatic teeth that have roentgenographic evidence of periapical pathosis. All teeth will be isolated with a rubber dam and a conventional access preparation made. Two microbiological samples from each canal system will be made prior to instrumentation and at the completion of instrumentation. One will be incubated in pre-reduced sterilized medium and the other in trypticase soy broth with 0.1% agar as the control. Canal preparation will now be completed in a conventional manner.

At each subsequent appointment, two additional microbiological samples will be obtained before and after instrumentation. All canals will be obturated by the lateral condensation of gutta percha and sealer.

The patients will be reexamined at 6 and 12 month intervals. Another roentgenograph will be made. They will be placed in success or failure categories as defined by Storms. The findings will be correlated with the culture results.

PROGRESS

(76 06 - 77 09) An analysis of 244 paired samples in 61 patients revealed that when the anaerobic pre-reduced medium is not re-reduced after insertion of the culture sample, it is not more sensitive in supporting bacterial growth than trypticase soy broth medium. It was significant that the unrereduced anaerobic culture medium became positive for the growth of microorganisms quicker than trypticase soy broth medium, but after five days they were equal. This portion of the study is complete and the results are being prepared for publication in Oral Surgery, Oral Medicine, Oral Pathology.

A Clinical Determination of the Effectiveness of Endodontic Chemomechanical Sterilization - Zielke

Bacterial flora found as a direct result of endodontic manipulation is in the process of being analyzed and tabulated and the results will be forthcoming.

STATUS: (O)

PUBLICATION: Zielke, D.R., Heggers, J.P., and Harrison, J.W.: A Statistical Analysis of Anaerobic versus Aerobic Culturing in Endodontic Therapy. Oral Surg 42:830-37, Dec 76.

TITLE: Early Detection and Prevention of Thrombophlebitis

PRINCIPAL INVESTIGATOR: MAJ Henry D. Covelli, MC

WORK UNIT NO: 77/50

TECHNICAL OBJECTIVE

The incidence of thrombophlebitis in bedridden or post-operative patients approaches 20-40% when sensitive diagnostic techniques to detect venous thrombosis are utilized. Since pulmonary emboli originate from these lesions, many investigators have recommended prophylactic anticoagulation for all high risk patients. The purpose of this study is to further define these high risk groups by use of radioiodinated fibrinogen, venous Doppler exam and hypercoagulable screening tests. Concurrently, the utility of thromboembolic disease (TED) stockings would be determined by randomly allocating a TED stocking to only one leg, thereby allowing each patient to serve as his own control.

METHOD

A group of patients at high risk for developing thrombophlebitis would undergo fibrinogen scanning. Abbott Laboratory is the only source of FDA approved 125 I fibrinogen. Their protocol will be followed:

1. Blockade of the thyroid gland to prevent uptake of 125 I.
2. Intravenous administration of less than 140 μci 125 I fibrogen.
3. Scintillation counting at the bedside.

This group of patients would receive, by random allocation, a TED stocking on either right or left leg, to be worn for approximately one week while being studied. This group would include: elderly patients undergoing major surgical procedures, elderly patients with suspected myocardial infarcts and bedridden patients undergoing prolonged hospitalization. On admission, an extra blood sample would be drawn with routine studies for measurement of antithrombin III levels. Venous Doppler exam and venogram would only be done if clinically indicated.

Early Detection and Prevention of Thrombophlebitis - Covelli

PROGRESS

(77 04 - 77 09) The progress of this study depends on the accuracy of the scanning method in detecting occult venous thrombosis. To date, the method has only been fair in detection of overt disease, and we will not proceed until the technique improves.

STATUS: (O)

TITLE: Immunological Mechanism of Gold Hypersensitivity

PRINCIPAL INVESTIGATOR: MAJ Henry D. Covelli, MC

WORK UNIT NO: 77/79

TECHNICAL OBJECTIVE

Approximately 50 patients receive gold therapy in our Rheumatology Clinic in any one year. The frequency of side effects causing cessation of this therapy is approximately 25%. Many of these reactions will not persist if gold therapy is restarted; however, the morbidity to those patients that are rechallenged may be significant. Therefore, it is important to define this population. Lymphocyte transformation tests have been used to determine patients' idiosyncratic reactions to various drugs, including gold; however with conflicting results. The purpose of this study will be to define those patients who would develop delayed hypersensitivity reactions to gold. More importantly, it will help define those patients who should not be rechallenged with gold after initial cessation of therapy because of a hematologic, renal, or integumentary reaction.

METHOD

Approximately 15 cc of blood will be obtained by venipuncture from patients with seropositive rheumatoid arthritis who have been started on gold therapy or have previously been exposed to gold therapy which had to be discontinued due to side effects. These venous samples will be used to perform in vitro lymphocyte transformation to PHA and gold and serum IgE levels.

PROGRESS

(77 07 - 77 09) This protocol has been scheduled; however, we cannot proceed until our lymphocyte incubator has been repaired or replaced. A purchase request has already been obtained, and the protocol will proceed when the incubator is obtained.

STATUS: (O)

TITLE: ^{67}Gallium Citrate Body Scanning for Tumor or Abscesses

PRINCIPAL INVESTIGATOR: LTC John L. Espinosa, MC

WORK UNIT NO: 74/16

TECHNICAL OBJECTIVE

Clinical evaluation of ^{67}gallium citrate to detect the presence of known suspected areas of tumor or abscess involvement.

METHOD

The radiopharmaceutical was obtained in a sterile pyrogen-free form from Medi-Physics, Inc. Two and three days following the intravenous injection of the radiopharmaceutical, the patients were examined on the whole-body scanner and/or gamma scintillation camera for areas of increased uptake to determine the clinical efficacy of this drug. Two to five mci gallium citrate was given to non-pregnant adults over 18 years old with demonstrated or suspected tumors or occult abscesses.

PROGRESS

(76 06 - 77 09) The use of ^{67}gallium citrate to detect the presence of occult tumor or abscess has proven to be effective, and it has been approved for routine clinical use.

STATUS: (C)

TITLE: Clinical Evaluation of Indium-III DTPA for Intrathecal Injection for the Study of Cerebrospinal Fluid Pathways

PRINCIPAL INVESTIGATOR: LTC John L. Espinosa, MC

WORK UNIT NO: 74/17

TECHNICAL OBJECTIVE

The objective of this study is to establish the efficacy of Indium-III DTPA to study the cerebrospinal fluid pathways in patients demonstrated to have or suspected to have altered cerebrospinal fluid flow, such as hydrocephalus, cerebrospinal fluid leaks, porencephalic cysts, ventriculosomatic shunts and ventricular obstruction lesions.

METHOD

Approximately 0.5 mCi Indium-III DPTA (dependent on body weight) supplied by Medi-Physics, Inc., was administered by intrathecal injection. Scintiscans were performed at 2, 6, 24, and 48 hours following the injections.

PROGRESS

(76 06 - 77 09) There have been no adverse reactions and the overall quality of the images has been satisfactory. The use of this agent has been approved for routine use at this institution.

STATUS: (C)

TITLE: Determination of Normal Range for Six-Hour Radioactive Iodine Uptake Using 123 Iodine in Order to Eliminate Need for Most 24-Hour RAIU

PRINCIPAL INVESTIGATOR: LTC John L. Espinosa, MC

WORK UNIT NO: 77/56

TECHNICAL OBJECTIVE

123 iodine is a recently available radionuclide of iodine. Its physical properties make it far superior to the presently used 131 iodine for thyroid imaging and uptake. There is a 20-100 fold decrease in radiation to the patient using 123 iodine rather than 131 iodine. With 123 iodine the scan and uptake can be performed six hour after dosing, while with 131 iodine, uptake and scan is usually performed 24 hours after dosing, requiring appointments on two consecutive days. The normal 6-hour uptake with 123 iodine is unknown. We plan to determine the normal range for 6-hour uptake using 123 iodine and compare this with the 24-hour uptake. When this normal range is known, most 24 hour uptakes will not be necessary.

METHOD

Patients who have had a routine thyroid uptake or scan ordered by physicians other than those involved in the investigation will be screened for adequacy of inclusion into the study. Informed consent will be obtained on all patients. Many thyroid uptakes and scans are ordered in patients who do not have thyroid disease, e.g., patients with past history of head and neck irradiation, patients with thyroglossal duct cysts, and patients with cervical lymphadenopathy. These would be suitable patients for the study. All patients must be diagnosed as either euthyroid, hyperthyroid or hypothyroid by clinical evaluation and the following laboratory tests: T3 uptake, T4 by RIA, T3 by RIA, thyroid and microsomial antibodies. One of the three investigators will evaluate each of the patients to rule out thyroid disease. A dose of from 300 to 400 uCi of 123 iodine will be administered to the patient orally. Radioactive iodine uptake will be determined at 6 and 24 hours. A thyroid image will be performed six hours following dosing. This will decrease irradiation to the patient's thyroid from approximately 100 rads using 131 iodine to 2-3 rads using 123 iodine.

Determination of Normal Range for Six Hour Radioactive Iodine Uptake - Espinosa

Those patients who are clinically and chemically euthyroid will be evaluated to determine the normal range of thyroid uptake of 123 iodine at 6 hours, and this will be compared to their 24-hour uptake. It is anticipated that a range of normals can be determined at 6 hours which will exclude all hypo and hyperthyroid patients. In a few patients who have borderline low or high 6-hour uptakes, a 24-hour uptake will have to be determined. From evaluation of the chemical data, a normal range for T3 uptake, T4 by RIA, T3 by RIA, and TSH will be determined. It is anticipated that approximately 100 patients should be evaluated to obtain reliable statistical information. At four patients per week, this will take approximately 6 months.

PROGRESS

(77 04 - 77 09) Patients are still being gathered for the study, which is 1/4 completed. Preliminary results indicate that a 6-hour RAIU is sufficient in diagnosing most patients as hyperthyroid.

STATUS: (O)

TITLE: Development of Radionuclide Angiocardiography as a Clinical Diagnostic Tool for the Quantification of Left to Right Cardiopulmonary Shunts

PRINCIPAL INVESTIGATOR: LTC John L. Espinosa, MC

WORK UNIT NO: 77/57

TECHNICAL OBJECTIVE

The objective of this project is the local development of an existing radionuclide angiocardiography technique to be used in the diagnosis and management of patients with left to right cardiopulmonary shunts. A correlation between results obtained by this technique and those obtained by oximetry during cardiac catheterization will be established and findings from this study will be published.

METHOD

Patients will be those who will undergo or who have recently undergone cardiac catheterization and whose clinical condition will allow them to be safely included in this project. Of these patients, some will be studied twice in order to correlate peripheral injection with injection through a pre-existing catheter. Patients undergoing other nuclear medicine procedures involving appropriate isotopes in which the immediate flow study is not of benefit will also be used.

Each study will be performed using procedures similar to a brain scan except that the camera will be positioned over the heart and lungs. The data base for each study is the quantized sequential time pictures of the distribution of radioactivity in the patient's heart and lungs. Entry to the venous system for the injection will be gained by peripheral venipuncture or through a preexisting catheter.

From the data base, a time versus activity curve will be generated for various regions of the lungs. This curve will then be mathematically analyzed to determine the ratio of pulmonary to systematic blood flow (Qp/Qs). Results from patient studies using the two methods of injection will be compared to establish the validity of the peripheral venipuncture. Finally, the pair of Qp/Qs ratios for each patient obtained by oximetry and by the radionuclide technique with peripheral injection will be statistically correlated.

Development of Radionuclide Angiocardiography - Espinosa

PROGRESS

(77 04 - 77 09) The technical portion of this study has been completed. Correlation between results obtained by this technique and those obtained by oximetry during cardiac catheterization was quite good. The Department of Pediatrics and Nuclear Medicine Service are in the process of writing up the results for publication in the pediatric literature.

STATUS: (O)

TITLE: Daunomycin Therapy in Acute Leukemia

PRINCIPAL INVESTIGATOR: LTC H. Irving Pierce, MC

WORK UNIT NO: 73/47

TECHNICAL OBJECTIVE

The purpose of this project is to institute the use of Daunomycin, a potent chemotherapeutic agent, as a second order drug in the treatment of acute childhood or adult leukemias for chemotherapeutic regimens.

METHOD

Daunomycin will be used for purposes of an induction and consolidation therapy in cases of acute childhood or adult leukemias or in those who have clearly relapsed on other drug regimens or patients not responding to such chemotherapeutic regimens as Vincristine and Prednisone, OAP, or the combination of Cytosine Arabinoside and 6-Thioguanine. Daunomycin will be given in one of the following three schedules depending on the type and extent of previous chemotherapy:

1. Daunomycin, 1-2 mg/kg IV every week

2. Daunomycin, 1 mg/kg IV x 5 days
   Vincristine, 2.0 mg IV on day 1
   Prednisone, 60 mg/day x 5 days po

3. Vincristine, 2.0 mg IV on day 1
   Prednisone, 25 mg qid po x 5 days
   Cytosine Arabinoside, 100 mg/M^2/day as continuous IV x 5 days
   Daunomycin, 60 mg/M^2 IV on day 1 only

The dosage and duration of therapy with Daunomycin and other combination drugs will be prorated according to the degree of response and bone marrow cellularity (as determined by weekly or bi-monthly marrow aspirates). Upon achievement of a complete remission, 2-3 additional courses of therapy will be given for purposes of consolidation, followed by maintenance therapy with other forms of drug agents.

Daunomycin Therapy in Acute Leukemia - Pierce

Prior to institution of therapy, an electrocardiogram will be obtained and also prior to subsequent courses of therapy. Peripheral blood counts will be performed 3 times weekly in all cases. Side effects such as myelotoxicity, nausea, and vomiting following administration, skin rashes, alopecia, cardiotoxic effects such as congestive heart failure or cardiac arrhythmias, will be evaluated and noted in all patients placed on the drug.

PROGRESS

(76 06 - 77 09) During the past year, Daunomycin has been used in combination with other chemotherapeutic agents in three subjects, including one with acute monocytic leukemia, one with acute undifferentiated leukemia, and the third with acute myeloblastic leukemia. In all instances, Daunomycin was administered with Cytosine Arabinoside, 6-Thioguanine, Prednisone, and Vincristine in previously described dosages for one to two courses during the induction phase as well as an additional one to two courses for consolidation. After partial remissions, all three patients relapsed and expired.

STATUS: (O)

TITLE: Survey of Hematologic Disorders in a Military Population

PRINCIPAL INVESTIGATOR: LTC H. Irving Pierce, MC

WORK UNIT NO: 75/08

TECHNICAL OBJECTIVE

The purpose of this study is to determine the feasibility of testing a large number of healthy subjects for abnormalities of blood counts or the presence of various hemoglobinopathies.

METHOD

Participation was not limited to any specific racial group. At the time of sickle cell testing, a duplicate anti-coagulated (EDTA) blood sample approximating 2.5 ml was obtained by venipuncture. When abnormal results were noted, the participant was recalled to the Hematology Clinic and the following parameters were determined on the anti-coagulated specimen: white blood cell count, hematocrit, hemoglobin, red blood cell indices (including MCV, MCH, MCHC), and red blood cell count, utilizing the Coulter Counter, Model S. Where a white cell count of less than 4000 was observed or abnormalities of hematocrit or indices were noted, a peripheral blood smear was made for further evaluation including red cell morphology and the 200 white blood cell differential count. The second anti-coagulated blood tube utilized by the Tacoma-Pierce County Sickle Cell Testing Program was sent to the state laboratory in Seattle for the determination of a hemoglobin electrophoresis. Any subsequent abnormalities noted were further evaluated by the Medical Genetics Department at the University of Washington School of Medicine. Upon demonstration of an abnormal hemogram, individuals were recalled for further evaluation.

PROGRESS

(76 06 - 77 09) Between July 1974 and May 1976, 1,967 military personnel were examined by routine CBC testing as provided by a Model S Coulter Counter, and results were analyzed. No further progress has been made on this study during the past year, and it has been terminated.

STATUS: (T)

TITLE: Cooperative Study for the Analysis of Risk Factors in Young Coronary Patients

PRINCIPAL INVESTIGATOR: COL James W. Reed, MC

WORK UNIT NO: 72/06

TECHNICAL OBJECTIVE

A unique opportunity exists in the Army to study a large group of young coronary patients by pooling together the case material of all the Class II hospitals. It is the purpose of this study to investigate these patients in comparison to age-matched controls for the following: obesity, hypertension, family history of coronary disease, plasma lipid classification, smoking history, carbohydrate intolerance, and insulin response to glucose load.

In the study of these parameters in young coronary patients, those factors of major importance in the development of coronary disease should be detected because they have caused the disease to manifest at a young age.

METHOD

All patients who develop proven coronary disease under the age of 40 who are patients at any of the Class II Army hospitals are subjects for the study. Age-matched individuals without coronary disease from the same institution will serve as controls. Patients and controls will be studied for the parameters as listed above.

PROGRESS

(76 06 - 77 09) Nineteen patients, ages 27-39, were initially studied. A high proportion was found to have lipid abnormalities. Of the 17 who completed the study, four had normal lipid profiles, seven had Type IV hyperlipoproteinemia, four had Type IIa, and one had Type III. The study is now being statistically analyzed. No more patients are to be entered.

STATUS: (O)

TITLE: The Detection of Mental Aberration in Patients with Hypercalcemia and Response to Treatment

PRINCIPAL INVESTIGATOR: COL James W. Reed, MC

WORK UNIT NO: 76/30

TECHNICAL OBJECTIVE

The objective of this study is to quantitate the degree of mental aberration in hypercalcemia and to quantitate the response following treatment of the hypercalcemic state.

METHOD

All patients entered in the study must have chronic hypercalcemia and be a candidate for surgical treatment. This will be done by measurement of serum calcium and phosphorus x 5, serum chloride, serum PTH, urinary calcium and phosphorus, and TRP. Following an established diagnosis of hyperparathyroidism, multiphasic testing with the Minnesota Multiphasic Personality Inventory will be done by Department of Psychiatry under direction of Dr. Raymond Parker. Surgical exploration of neck will be performed by Dr. Praeger, Department of Surgery. At intervals of 2 weeks, 6 weeks, and 6 months, multiphasic testing will be repeated by Department of Psychiatry. Numerical quotients will be established for each test and degree of change will be established.

PROGRESS

(76 06 - 76 09) Fourteen patients have been entered. Seven patients have completed the one-week follow-up, and four patients have completed the six-month follow-up. Statistical analysis will start when the first ten patients have completed the six-month testing.

STATUS: (O)

TITLE: An in Vitro Model of Meningococcal Meningitis: A Study of Basic Mechanisms of Leukocyte Chemotaxis in Meningeal Inflammation

PRINCIPAL INVESTIGATOR: MAJ Jacob J. Schlesinger, MC

WORK UNIT NO: 76/19

TECHNICAL OBJECTIVE

To elucidate the factors governing inflammation of the meninges during meningococcal infection and how these may be modified.

METHOD

A modification of the Boyden chamber was used as a model of the leptomeninges during inflammation.

1. Construction of the chemotaxis model using the 5 micron millipore filter as the "meningeal membrane."

2. Control system: leukocytes were collected during routine blood bank collections from volunteer donors.

3. Excess cerebrospinal fluid collected during the course of routine diagnostic taps on the wards and radiology service at pneumoencephalography were utilized.

4. Meningococcal cultures were obtained from the hospital microbiology laboratory. ATCC strains were maintained at the Clinical Investigation Service Laboratory.

5. Cell wall polysaccharide fractions available from WRAIR.

6. With these materials, the interaction of the meningococcus and cerebrospinal fluid were studied as a model of meningeal inflammation.

PROGRESS

(76 06 - 77 06) None - this study was terminated due to the departure of the principal investigator.

STATUS: (T)

TITLE: Eosinopenia and Acute Bacterial Infection

PRINCIPAL INVESTIGATOR: MAJ Jacob J. Schlesinger, MC

WORK UNIT NO: 76/22

TECHNICAL OBJECTIVE

To elucidate the mechanism of eosinopenia during acute bacterial infection.

METHOD

To demonstrate potential eosinophil chemotactic inhibitors present in the blood of patients with acute bacterial infections and their disapperance on recovery, eosinophils from an appropriate donor were incubated with the sera from these patients and tested for chemotaxis to a standard attractant ($C5_a$, ECF-A) utilizing a 5 micron millipore filter.

PROGRESS

(76 06 - 77 06) No further progress was made in the past year due to the lack of equipment and donors, and the protocol has been terminated due to the departure of the principal investigator.

STATUS: (T)

TITLE: Neonate Neutrophil Function: An in Vitro Evaluation of Neonate Neutrophil Chemotaxis and Phagocytosis with Emphasis on the Group B Streptococcus, S. aureus and E. coli

PRINCIPAL INVESTIGATOR: MAJ Jacob J. Schlesinger, MC

WORK UNIT NO: 76/25

TECHNICAL OBJECTIVE

To quantitate, from discarded cord and placental blood, the ability of the newborn's neutrophil to reach (chemotaxis), engulf (phagocytosis) and destroy each of the three bacterial agents most often implicated in neonatal sepsis. Special attention was given to infants born of mothers with illnesses known to predispose their newborn to infection. Comparisons were made between normal gestational periods, pre and post-maturity and normal adult controls. Newborns studied were followed for evidence of perinatal infection.

METHOD

During the course of normal deliveries otherwise discarded cord blood was collected for isolation of neutrophils. A standardized assay of chemotaxis and phagocytosis currently in operation in our laboratory was used to evaluate these neutrophils. Adult control neutrophils were obtained from discarded blood bank blood. Additional data obtained included vaginal cultures immediately before delivery, culture of the suction bulb contents of the newborn's mouth and of the skin. Additional data recorded included birth weight, estimated gestation, APGAR score, duration of labor and complications if any. Infants studied were followed prospectively while in hospital, and special attention was focused on those with abnormal neutrophil function at birth.

PROGRESS

(76 06 - 77 06) None - the protocol was terminated due to the departure of the principal investigator.

STATUS: (T)

TITLE: The Effect of Pregnancy and Hormonal Birth Control on the Tuberculin Skin Test and in Vitro Delayed Hypersensitivity to PPD

PRINCIPAL INVESTIGATOR: MAJ Jacob J. Schlesinger, MC

WORK UNIT NO: 77/07

TECHNICAL OBJECTIVE

The fact that tuberculous infection may be indolent during pregnancy and may be followed by rapid acceleration in the puerperium poses a major threat to both mother and child. Anecdotal and inadequately controlled experience with skin testing for TB during pregnancy has resulted in conflicting opinions concerning the validity of the tuberculin skin test in detection of human strain TB in pregnancy. There is little information on this matter with the current standard Tween 80 stablized PPD and no information concerning the use of oral contraceptives on tuberculin testing of any kind. The addition of sensitive in vitro methods to detect and quantitate delayed hypersensitivity will further clarify the role of pregnancy in this matter.

METHOD

Pregnant women were interviewed and skin tested when routine outpatient care was begun. Selected for study were those women with a past history of tuberculosis using as criteria: documented positive i-PPD. Old chest x-rays were reviewed when available. Anti-tuberculous medication(s) were recorded. The population was divided into three trimesters. Skin testing with i-PPD (single batch) was done at the beginning of each trimester and at six week postpartum routine exam. Aliquots of routine blood samples were utilized for lymphocyte PPD stimulation. Tuberculin positive women evaluated in the GYN Clinic were skin tested and PPD induced lymphocyte transformation was studied prior to starting oral contraception and again at 3 months. Control groups (age matched): (1) PPD positive women attending GYN Clinic for contraception other than oral; (2) PPD positive women followed in community health facility not taking anti-tuberculous medication.

The Effect of Pregnancy and Hormonal Birth Control - Schlesinger

PROGRESS

(76 09 - 77 09) This study has been completed. It was found that hypersensitivity to PPD occurred during pregnancy. This hypersensitivity increased as the women neared the time of delivery, after which the PPD hypersensitivity returned to normal.

STATUS: (C)

TITLE: Single Drug Chemotherapy with CCNU

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 76/20

TECHNICAL OBJECTIVE

To use a clinically helpful cancer chemotherapeutic agent (CCNU) as reported in many professional papers, but has not as yet been released by the FDA.

METHOD

CCNU will be administered orally in dosage of 100 to 130 mg/M^2 every 6 to 8 weeks to selected patients (dosage will be modified when required). Evaluable patients will have at least two courses of medication. Duration of treatment: (a) Subjective or objective response - to relapse or for two years; (b) No change - to progression or response; (c) Progressive disease - two courses; only one course may be given if the disease shows rapid progression.

PROGRESS

(76 11 - 77 04) All patients had progression of their disease while on treatment and expired. If progression of disease was slowed, this cannot be judged on these few patients (three patients were entered). The protocol has been terminated.

STATUS: (T)

TITLE: SWOG 7410, Chronic Lymphocytic Leukemia Protocol Utilizing Cyclophosphamide, Adriamycin, and Prednisone.

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/13

TECHNICAL OBJECTIVE

1. To determine the response rate, both complete and partial, in chronic lymphocytic leukemia, to combination chemotherapy with:

   A. Cyclophosphamide, adriamycin, and prednisone (CAP) as primary therapy in patients who have had no prior chemotherapy.

   B. CAP as secondary therapy for those patients who have previously received low dose chlorambucil.

2. To assess the effectiveness of intermittent cyclophosphamide and prednisone in maintaining a remission.

METHOD

After meeting stringent criteria, all untreated patients with CLL or patients previously treated with a low dose of chlorambucil only, at least four weeks prior to start of therapy, will be entered in the study.

Remission Induction: cyclophosphamide - 500 mg/M^2, I.V., on day 1
adriamycin - 50 mg/M^2, I.V., on day 1
prednisone - 100 mg/day, p.o., for 5 days

After eight courses of induction therapy (or those having attained remission between three & eight courses), those patients who have attained complete or partial remission will receive maintenance therapy consisting of:

cyclophosphamide - 750 mg/M^2, I.V., on day 1
prednisone - 100 mg/day, p.o., for 5 days

Course will be repeated every three weeks until relapse in cases in complete remission or increasing disease is evident in cases in partial remission.

SWOG 7410 - Stutz

PROGRESS

(76 12 - 77 09) No patients have been registered on this protocol.

STATUS: (O)

TITLE: SWOG 7416/17, The Chemoimmunotherapy of Acute Leukemia

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/14

TECHNICAL OBJECTIVE

1. To determine whether with the use of sequential or simultaneous adriamycin and Ara-C there is significant difference in their ability to induce complete remission.
2. To study the effects of combination chemotherapy and immunotherapy on the duration of remission and survival in patients with acute leukemia.
3. To identify those patients with ALL vs AML who are vincristine and prednisone responsive.

METHOD

Patients fulfilling the criteria for treatment will be divided into two different categories, depending on their peripheral circulating blast count. Category 1 (blast count less than 30,000) will be treated with vincristine and prednisone. Category 2 (blast count 30,000 or more) will be treated with vincristine and prednisone in combination with either simultaneous or sequential adriamycin and Ara-C. Patients achieving complete remission with acute myeloblastic disease and those patients not clearly in acute undifferentiated or lymphoblastic disease will receive 3 courses of consolidation therapy and then be randomized to receive either OAP, BCG, or OAP alone on a 5-day subcutaneous q 6-hour administration.

PROGRESS

(76 12 - 77 02) No patients were entered on this protocol and it has been terminated.

STATUS: (T)

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CLINICAL INVESTIGATION SERVICE ANNUAL RESEARCH PROGRESS REPORT,--ETC(U)
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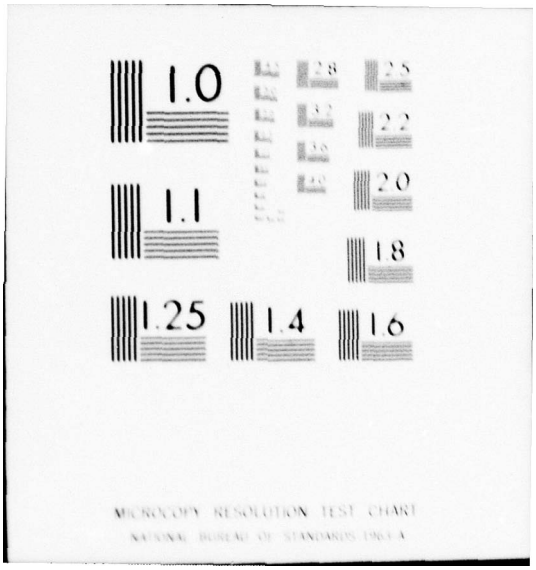
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TITLE: SWOG 7438, Cis-platinum for GU-GYN Malignancies, Phase II

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/15

TECHNICAL OBJECTIVE

To evaluate the activity of cis-diamminedichloroplatinum (II) (NSC 119875, CACP) in patients with malignant diseases of the genitourinary and gynecologic organs.

METHOD

Patients who meet the criteria as stated in the protocol will be given CACP, 75 mg/M^2, as a single rapid intravenous injection every three weeks. An adequate trial will be considered a minimum of two courses. All patients will be followed for a six-week period. If there is evidence of a tumor response or stable disease, the drug may be continued at three-week intervals indefinitely. With evidence of progression after two courses of the agent, the patient will go off study. Patients may receive other therapy as necessary to control reversible medical complications.

PROGRESS

(76 12 - 77 02) No patients were entered on this protocol and it has been terminated.

STATUS: (T)

TITLE: SWOG 7434, 5-FU+Mitomycin C vs 5-FU+MeCCNU in GI Malignancies

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/16

TECHNICAL OBJECTIVE

1. To determine and compare the effectiveness of two combination chemotherapies in gastrointestinal carcinomas: 5-Fluorouracil infusion and Mitomycin C vs 5-Fluorouracil infusion and Methyl CCNU.
2. To compare the toxicities produced by these two combinations to allow the decision as to which of the two regimens is superior.
3. To compare the results of this study with the results observed in the SWOG 7302 protocol, which was 5-FU bolus vs 5-FU bolus + Methyl CCNU.

METHOD

After randomization, patient will receive one of the above drug combinations. Initial treatment, subsequent dosage adjustment, dose levels, and treatment schema are as outlined in the protocol.

PROGRESS

(76 12 - 77 09) No patients have been registered on this protocol.

STATUS: (O)

TITLE: SWOG 7440, Adjuvant Chemotherapy for Osteogenic Sarcoma

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/17

TECHNICAL OBJECTIVE

1. To determine the efficacy of combination chemotherapy with CY-VA-DIC (cyclophosphamide, vincristine, adriamycin, and DIC) in preventing the development of metastases in patients with osteogenic sarcoma who have received definitive surgery for their primary lesions and who have no evidence of residual disease.

2. To determine the survival and disease-free interval pattern of patients on this study to be compared to historic controls in the medical literature.

METHOD

Patients with a confirmed diagnosis of osteogenic sarcoma who have received definitive surgical therapy and have no evidence of metastases following surgery and who have not received any prior therapy (other than surgery) shall be treated with a chemotherapy regimen consisting of vincristine, adriamycin, cyclophosphamide, and DIC as outlined in paragraph 5.0 of the protocol.

PROGRESS

(76 12 - 77 09) No patients have been registered on this protocol.

STATUS: (O)

TITLE: SWOG 7510, Intensive Adjuvant Chemotherapy with or Without Oral BCG Immunotherapy for Patients with Locally Advanced Adenocarcinoma of the Large Bowel

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/18

TECHNICAL OBJECTIVE

To determine the efficacy of adjuvant chemotherapy with the highly effective combination of Methyl CCNU (MeCCNU) and 5-Fluorouracil (5-FU) and to determine whether this is added to by immunotherapy with oral Bacillus Calmette-Guerin (BCG) on the disease-free interval and survival of patients with Duke C large bowel adenocarcinoma.

METHOD

Patients will be randomly assigned to either of the two following regimens:

Chemotherapy alone - Methyl CCNU, given orally on day 1, plus intravenous 5-Fluorouracil, given intravenously weekly for three doses would constitute one course. Courses would begin every eight weeks.

Chemotherapy plus immunotherapy - Chemotherapy as described above plus immunotherapy in the form of oral BCG given every two weeks.

PROGRESS

(76 12 - 77 09) Six patients have been treated on this protocol and all remain in remission. (Duration of Treatment: 9, 8, 8, 5, 3, and 2 months.)

STATUS: (O)

TITLE: SWOG 7610, Chemotherapy of Disseminated Testicular Cancer with Vinblastine, Bleomycin, Cis-Diammine-dichloroplatinum, Chlorambucil, and Actinomycin-D

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/19

TECHNICAL OBJECTIVE

1. To determine the effectiveness of the drug combination vinblastine, bleomycin, and cis-diamminedichloroplatinum (11) (CACP) in the remission induction of disseminated testicular carcinoma.

2. To determine the duration of remission with a maintenance drug combination of chlorambucil and actinomycin-D, alternating with vinblastine.

METHOD

All patients meeting certain criteria are to receive vinblastine, bleomycin, and CACP for two months. At that point, patients judged to be in complete remission, partial remission, or stable will receive an additional two months of therapy. All partial and complete responders at four months will then enter the remission maintenance program. Patients with increasing disease at two months, or stable or increasing disease at four months are to be taken off study.

PROGRESS

(76 12 - 77 09) No patients have been entered on this protocol.

STATUS: (O)

TITLE: SWOG 7404, Radio Therapy, CCNU and Procarbazine in Malignant Gliomas of the Brain

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/21

TECHNICAL OBJECTIVE

To determine whether the addition of procarbazine to CCNU and radiation therapy adds to the response rate and duration of response as compared to CCNU and radiation therapy alone in the treatment of malignant gliomas. The survival time of patients treated with procarbazine and CCNU in combination with radiation therapy will be compared with that of patients who are treated with CCNU and radiation therapy alone initially and who receive procarbazine sequentially after relapse.

METHOD

Patients who meet the criteria will be randomly allocated to one of two programs: radiation therapy plus CCNU or radiation therapy plus CCNU and procarbazine. The patients must be entered and randomized and therapy initiated within three weeks of surgery and histologic diagnosis.

PROGRESS

(77 09 - 77 09) No patients were entered on this protocol, and it has been terminated.

STATUS: (T)

TITLE: SWOG 7405, Adriamycin, 5-FU, Cytoxan and Methotrexate in Breast Cancer

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/22

TECHNICAL OBJECTIVE

To test three different drug combinations utilizing adriamycin as the base drug in the treatment of patients with breast cancer who have received no prior chemotherapy in order to: (1) determine the relative efficacy of adding drugs singularly or in combination to adriamycin; (2) determine the comparative toxicity of the regimens.

METHOD

Patients who meet the criteria will be placed on the following randomization schedules:

INDUCTION

Limb 1 - adriamycin + cyclophosphamide
Limb 2 - adriamycin + 5-FU + cyclophosphamide
Limb 3 - adriamycin followed by weekly 5-drug combination (vincristine, methotrexate, 5-FU, cyclophosphamide prednisone)

All patients who have responded or have stable disease at the completion of induction therapy will receive maintenance therapy.

Limb 1 - cyclophosphamide
Limb 2 - 5-FU + cyclophosphamide + methotrexate
Limb 3 - methotrexate + 5-FU + cyclophosphamide + prednisone

PROGRESS

(77 04 - 77 09) No patients have been entered on this protocol, and it has been terminated.

STATUS: (T)

TITLE: SWOG 7432, Vincristine, BCNU, Adriamycin, and Prednisone (VBAP) in Previously Treated Myeloma Patients

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/23

TECHNICAL OBJECTIVE

To evaluate the frequency and degree of response with Vincristine-BCNU-Prednisone-Adriamycin combination (VBAP) in patients who failed to respond on alkylating agents with or without Prednisone.

METHOD

VBAP will be administered as outlined in the protocol. The minimum duration of the initial induction treatment is 4 months; the maximum duration 9 months. If remission is confirmed, the patient will continue treatment to disappearance of "M" peak or exacerbation of disease. If no response is confirmed after 9 months or if there is progression of disease at 4 months, the study should be terminated.

PROGRESS

(77 04 - 77 09) Two patients were registered on this protocol. One patient had progression of disease and expired after 30 days on the study. The other patient showed mixed results; axillary nodes disappeared, inguinal nodes essentially unchanged.

STATUS: (O)

TITLE: SWOG 7436, Combined Modality Therapy of Breast Carcinoma

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/24

TECHNICAL OBJECTIVE

To compare the effect of two adjuvant chemotherapy programs upon the time to recurrence and upon the percentage of recurrences in post-operative breast carcinoma patients who have a high risk of developing metastases. To compare the effect of these adjuvant chemotherapy programs upon the survival pattern of such patients.

METHOD

Melphalan and combination (5-Fluorouracil, Methotrexate, Vincristine, Cyclophosphamide, Prednisone) will be used as chemotherapy as outlined in the protocol. The adjuvant chemotherapy will be instituted (regardless of radiation therapy) two weeks after radical mastectomy, unless local or systemic post-operative complications of surgery contraindicate onset of therapy. In such cases, therapy will be instituted when the primary physician involved feels it is not contraindicated by the clinical condition of the patient. The interval between surgery and the institution of adjuvant chemotherapy cannot be greater than six weeks for entry into the study. All therapy will be discontinued after one year.

PROGRESS

(77 09 - 77 09) No patients have been registered on this protocol.

STATUS: (O)

TITLE: SWOG 7509, 5-FU, MeCCNU + Radiotherapy With or Without Testolactone for Localized Adenocarcinoma of the Exocrine Pancreas

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/25

TECHNICAL OBJECTIVE

To evaluate the effect on survival of intensive radiotherapy and chemotherapy (5-FU and MeCCNU) of localized pancreatic adenocarcinoma. To evaluate, in a randomized manner, any beneficial effect of testolactone when added to the above regimen.

METHOD

Patients will be stratified according to the type of surgery performed: biopsy only, palliative bypass procedure, or resection. They will then be randomized to receive either testolactone, 5-FU, MeCCNU, and radiation therapy, or 5-FU, MeCCNU, and radiation therapy without testolactone. Patients surviving for one year will be offered a second-look operative procedure at the discretion of the attending physician for the purpose of restaging, resecting or palliating appropriately. Patients without evidence of disease at this second-look procedure will continue chemotherapy for one more year only. Those who are found to have tumor will also receive chemotherapy for one year but, at the end of this period, another re-exploration will be offered and patients found to be free of disease will be given an additional year of chemotherapy. Patients with persistent tumor at this time (third operation) will continue on chemotherapy indefinitely.

PROGRESS

(77 04 - 77 09) No patients have been entered on this protocol.

STATUS: (O)

TITLE: SWOG 7517, Therapy of Squamous Cell Carcinoma of the Head and Neck Using Combination Bleomycin, Vincristine, and Methotrexate

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/26

TECHNICAL OBJECTIVE

To determine the toxicity and effectiveness of various dosage levels of a combination of bleomycin, oncovin, and methotrexate in the treatment of patients with squamous cell carcinoma of the head and neck.

METHOD

A total of thirty patients with squamous cell carcinoma of the head and neck will be treated with a combination of bleomycin, vincristine, and methotrexate as outlined in the protocol. Patients must receive two complete cycles of therapy to be evaluable for response. The duration of response shall be measured from the time that a partial response is achieved to the time at which progression is apparent.

PROGRESS

(77 09 - 77 09) No patients have been registered on this protocol.

STATUS: (O)

TITLE: SWOG 7519, Phase III Study of Squamous Cell Carcinoma of the Head and Neck Region

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/27

TECHNICAL OBJECTIVE

To determine whether a three-drug combination treatment program will give a superior response rate and/or a longer remission duration than methotrexate alone in patients with squamous cell carcinoma of the head and neck region.

METHOD

Patients who meet the criteria as outlined in the protocol will be randomized to receive one of the following treatment plans:

Plan I: Methotrexate 15 mg/M^2 IM daily x 3 (3 week cycles)

Plan II: Methotrexate 15 mg/M^2 IM daily x 3
Methyl CCNU 200 mg/M^2 PO day 1
Bleomycin 12.5 units/M^2 IM on days 25, 29, 32, 36
(6 week cycles)

Dose modifications will be made as needed for each individual patient. Patients will be followed until remission or relapse in an effort to identify the duration of response within the two study arms.

PROGRESS

(77 04 - 77 09) Two patients were entered on this study. Patient #1 asked to be taken off the study after one month of treatment with no results. Patient #2 was transferred to SWOG 7629 after 4 months of treatment with no results.

STATUS: (O)

TITLE: SWOG 7524, Chemotherapy in Stages III & IV Ovarian and Endometrial Carcinoma

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/28

TECHNICAL OBJECTIVE

Primary: 1. To compare the effectiveness of chemotherapy alone (adriamycin-cyclophosphamide) vs chemoimmunotherapy (adriamycin-cyclophosphamide plus BCG) for remission induction in patients with Stages III and IV ovarian and endometrial carcinoma who have had no previous cytotoxic chemotherapy.
2. To test the effectiveness of continued chemoimmunotherapy vs chemotherapy in maintaining complete remissions (documented) achieved during the initial 12-month induction therapy.
3. To test the effectiveness of continued chemoimmunotherapy vs chemotherapy in inducing complete remissions or maintaining partial remissions in patients with occult disease at the time of restaging for complete response or in patients achieving only partial clinical remission during the initial 12-month induction therapy.

Secondary: 1. To establish baseline and serial data on immunologic status in both chemotherapy and chemoimmunotherapy groups.
2. To evaluate systematic restaging of patients judged to be in complete clinical remission.

METHOD

Patients meeting the criteria will be randomized to two treatment plans for both remission induction and maintenance. Treatment 1 will consist of adriamycin and cytoxan; treatment 2 will consist of adriamycin and cytoxan plus BCG. For maintenance, treatment 1 will consist of cytoxan, and treatment 2 will consist of cytoxan plus BCG. Twelve courses of treatment will constitute the remission induction phase of the protocol. If residual tumor is detected following the 12 courses of therapy, BCG plus cyclophosphamide for the chemoimmunotherapy patients or cyclophosphamide alone for the chemotherapy patients may be continued at 4-week intervals until a total of 2 years of therapy has been achieved

or there is documented evidence of recurrence or progression of disease. Those patients who have no detectable postinduction disease or who have occult disease or only clinical partial responses after the initial 12 courses of induction therapy are to be continued on maintenance therapy as outlined in the protocol.

PROGRESS

(77 04 - 77 09) No patients have been registered on this protocol.

STATUS: (O)

TITLE: SWOG 7611, Cis-Platinum for Refractory Sarcomas

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/29

TECHNICAL OBJECTIVE

This study proposes to determine the efficacy of cis-diammine-dichloroplatinum (II) (NSC-119875, CACP) in the treatment of patients with advanced sarcomas refractory to adriamycin combinations.

METHOD

Patients with a biopsy confirmed diagnosis of soft tissue or bony sarcoma, who meet other criteria as specified in the protocol, will be started on the following treatment: 50 cc of 25% Mannitol is to be given as a 30-60 minute infusion followed by CACP 15 mg/M^2 IV bolus days 1-5, repeated at 28-day intervals. If there is evidence of a tumor response or acceptable stable disease, the drug will be continued at 4-week intervals indefinitely. With evidence of progression after two courses, the patient will go off study. An adequate trial will consist of two courses of chemotherapy.

PROGRESS

(77 04 - 77 09) No patients have been registered on this protocol.

STATUS: (O)

TITLE: SWOG 7624, ADR vs ADR+CACP in Transitional Cell Bladder Carcinoma

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/30

TECHNICAL OBJECTIVE

To compare the efficacy of adriamycin vs adriamycin plus cis-diamminedichloroplatinum (II) in recurrent or disseminated transitional cell bladder carcinoma.

METHOD

Patients with histologically proven transitional cell bladder carcinoma, who meet other criteria as outlined in the protocol, will be randomized to receive ADR alone or ADR+CACP. ADR will be given in a dose of 50 mg/M^2 I.V. on day 1 of each course for Treatment Plan I. On Treatment Plan II, adriamycin will be given in a dose of 50 mg/M^2 I.V. on day 1 of each course; CACP will be given in a dose of 50 mg/M^2 I.V. on day 2 of each course; immediately prior to the administration of CACP, the patient is to be given an I.V. injection of 12.5 grams of Mannitol. An adequate trial will be two courses. All patients must be observed for a minimum of six weeks. Courses will be repeated every three weeks.

PROGRESS

(77 04 - 77 09) Two patients entered on protocol.
Patient I: duration of treatment - 5 months, results - none
Patient II: duration of treatment - 2 months, results - none, asked to be taken off protocol.

STATUS: (O)

TITLE: SWOG 7613, Combination Chemotherapy for Advanced Soft Tissue Sarcomas Utilizing Adriamycin, DIC, Cyclophosphamide and Dactinomycin. Phase III.

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/34

TECHNICAL OBJECTIVE

To determine the maximal effective chemotherapy induction regimen for patients with disseminated soft tissue sarcomas who have probability of response $\geq$50%. To determine if cycling the use of adriamycin and maintenance with CY-DIC-DACT increases the duration of CR's treated initially with A-DIC.

METHOD

Patients with biopsy confirmed diagnosis of soft tissue sarcoma with evidence of metastatic disease, who meet the other criteria as outlined in the protocol, will be stratified according to adequate or inadequate marrow reserve. These groups will then be randomized to receive adriamycin + DIC; adriamycin + DIC + Cytoxan; or adriamycin + DIC + Dactinomycin, in dosages as specified in the protocol. For both adequate and inadequate bone marrow reserve patients, a complete cycle of chemotherapy shall be repeated every 22 days, counting the first day of therapy as day 1. If on day 22 the white blood count is still less than 2,000 and/or platelet count still below 75,000, the start of the next course shall be delayed until these levels have been reached. In addition a new cycle of chemotherapy shall not be initiated unless stomatitis from previous therapy has been resolved. Dose changes and continuation of treatment shall be determined on an individual patient basis.

PROGRESS

(77 04 - 77 09) No patients have been registered on this protocol.

STATUS: (O)

TITLE: SWOG 7620, Treatment of Early Squamous Cell Carcinoma of the Head and Neck with Chemotherapy or Chemoimmunotherapy Following Initial Surgery and/or Radiotherapy

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/35

TECHNICAL OBJECTIVE

To determine if the disease-free interval and survival of patients in high risk categories of squamous head and neck cancer can be improved by adjuvant chemotherapy or chemoimmunotherapy after initial surgery, radiotherapy, or combination approach have resulted in no clinically evident disease. To accumulate immunologic data in treated and untreated patients with this malignancy.

METHOD

Patients will be registered and randomized after the reaction from the initial operative or radiotherapeutic intervention has settled and when they have achieved no clinically evident disease. The randomization process must be accomplished no later than three months after the completion of the surgery or irradiation. The tumor will be stratified into one of the four broad anatomic regions: oral cavity, larynx, pharynx, nasal cavity, and paranasal sinuses. The control group will receive no further therapy after initial surgery and/or irradiation. The chemotherapy group will consist of methotrexate 12 mg/M^2 IM daily x 3 days every 21 days for one year. The chemotherapy-immunotherapy arm will consist of methotrexate 12 mg/M^2 IM daily x 3 days every 21 days for one year with BCG scarifications administered on day 8 and 14 for eight doses of BCG. Following eight doses, the BCG may then be administered on day 14 only and continued for the remainder of the year. BCG will not be applied to the neck.

PROGRESS

(77 09 - 77 09) No patients have been registered on this protocol.

STATUS: (O)

TITLE: SWOG 7629, Cis-Diamminodichloroplatinum (II) in the Treatment of Refractory Epidermoid Carcinomas of the Head and Neck Region. Phase II Study.

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/36

TECHNICAL OBJECTIVE

The purpose of this study is to determine with some degree of precision, the efficacy and toxicity of a particular program utilizing Cis-Diammine Dichloride Platinum (II) (NSC-119875, CACP) and mannitol in the treatment of diuresis patients whose epidermoid carcinomas of the head and neck region have demonstrated refractoriness to more standard chemotherapy.

METHOD

Patients who have a biopsy-confirmed diagnosis of epidermoid carcinoma of the head and neck region and meet the criteria as outlined in the protocol shall be registered on the study. The initial course will be given at a dose of 50 mg/M^2 IV by bolus both on day 1 and day 8 of the course. For subsequent courses, the dose will be modified based on the effects of the immediately previous course. All patients will receive mannitol diuresis at the time of the cis-platinum injection (bolus injection of 12.5 gm mannitol followed by 25 gm of mannitol in 1000 cc of D5W infused over two hours). The bolus of CACP will be injected into the IV line. This procedure will be repeated each time CACP is administered. Allopurinol prophylaxis should be used to prevent hyperuricemia. Therapy is to be repeated at four week intervals or as soon thereafter as the BUN level is no greater than 30 mg%, the serum creatinine no greater than 2.0 mg%, and the WBC and platelet count are above 4,000 and 150,000 respectively. As long as there is evidence of tumor regression or disease stability at an acceptable level, the drug will be continued at approximate intervals indefinitely. Disease progression after two courses of therapy will constitute an adequate trial, and the patient will be taken off study.

SWOG 7629 - Stutz

PROGRESS

(77 04 - 77 09) One patient has been registered on the protocol and treated for 5 months with partial response.

STATUS: (O)

TITLE: SWOG 7521, Adjuvant Melanoma Protocol

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/38

TECHNICAL OBJECTIVE

1. To determine the efficacy of BCNU, hydroxyurea, and imidazole carboxamide (BHD) in preventing the recurrence of disease and prolonging the survival of patients with primary malignant melanoma who have received definitive surgical treatment for their primary lesions, have no evidence of residual disease, but in whom by the clinical and pathological characteristics of the primary lesion can be predicted to have a high incidence of recurrence. 2. To determine the efficacy of combination chemotherapy (BHD) with and without BCG in preventing the development of metastases and prolonging the disease-free interval and survival of patients with recurrent malignant melanoma which has been surgically excised ("minimal residual disease"). 3. To determine the immunocompetence of patients with malignant melanoma and any correlation with prognosis. 4. To determine the influence of chemotherapy and chemoimmunotherapy upon the immunocompetence of these patients with malignant melanoma.

METHOD

Patients who have a histologically confirmed diagnosis of malignant melanoma and have not been previously treated with chemotherapy or radiation therapy and meet the other criteria as outlined in the protocol shall be entered in the study. Patients will be classified as follows for randomization: Class I - localized disease; Class II - regional and solitary distant metastatic disease. Patients with Class I disease will be randomized between BHD and no treatment. Patients with Class II disease will be randomized to either BHD or BHD + BCG. Patients will be treated for one year or until recurrent disease develops. Patients randomized to no treatment will be followed in a similar fashion. After one year of treatment patients are to remain on study and be followed on no treatment.

PROGRESS

(77 04 - 77 09) No patients have been registered on this protocol.

STATUS: (O)

TITLE: SWOG 7603, Effect of Schedule on Activity of 5-Azacytidine in Acute Leukemia. Phase III Protocol

PRINCIPAL INVESTIGATOR: LTC FRIEDRICH H. STUTZ, MC

WORK UNIT NO: 77/39

TECHNICAL OBJECTIVE

This study will compare the activity and toxicity of single dose vs continuous 5-day infusions of 5-azacytidine in patients with acute leukemia.

METHOD

Patients will be randomized to one of the following regimens:

1. Single day infusion of 750 mg/M^2. 5-azacytidine will be given in 3 divided doses (250 mg/M^2 administered in 200 ml of Ringer's lactate solution over 2 hours) at 4 hour intervals (2 hours on therapy, 2 hours off therapy).

2. Five day infusion of 300 mg/M^2/day. 5-azacytidine will be administered in 4 divided doses in 200 ml Ringer's lactate solution as a continuous infusion over each 6 hour period. Each 6 hour dose should be prepared within 2 hours before use, and preferably immediately before administration.

Courses will be repeated at 3 week intervals unless the bone marrow cellularity remains less than 10%. The dosage of subsequent courses of 5-azacytidine will be based upon the patient's response to the previous course.

PROGRESS

(77 04 - 77 09) One patient was treated for three days on this protocol. The patient died while on protocol due to disease and infection.

STATUS: (O)

TITLE: SWOG 7426/27, Chemoimmunotherapy for the Non-Hodgkin's Lymphomas. CHOP-Bleomycin vs CHOP + BCG vs COP + Bleomycin Induction Therapy. No Maintenance vs BCG for Maintenance

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/41

TECHNICAL OBJECTIVE

1. To compare the effectiveness of two chemotherapy regimens (CHOP + bleomycin) or chemoimmunotherapy (CHOP + BCG) for remission induction in previously untreated patients with non-Hodgkin's lymphomas.
2. To establish baseline and serial data on immunologic status in both chemotherapy and chemoimmunotherapy groups.
3. To evaluate systematic restaging of patients judged to be in complete clinical remission (CR).
4. For patients proven to be in complete remission after induction, to test the value of continued maintenance immunotherapy (BCG) vs no maintenance treatment.
5. For patients who only achieve a partial remission during induction, to test the effectiveness of continued treatment with chemoimmunotherapy.

METHOD

Patients with any histologic type of stage III or IV non-Hodgkin's lymphoma established by biopsy will be randomized to one of the three induction programs. The schema for the study is given in the protocol. Remission Induction: Eight courses of treatment will constitute remission induction. If induction results in a CR and this is confirmed by restaging, then the patient is eligible for a second randomization into the maintenance phase of this study. If residual lymphoma is detected during restaging, an additional three courses of treatment will be administered, restaging repeated, and patients in CR will be eligible after 11 courses of induction for the maintenance phase. Patients who are only in a partial remission after 11 courses of treatment are eligible for continued treatment with chemoimmunotherapy.

SWOG 7426/27 - Stutz

PROGRESS

(77 04 - 77 09) One patient has been registered on this protocol. Duration of treatment: 3 months; results of treatment: objective - partial, decrease in size of measurable lesions; subjective - no change.

STATUS: (O)

TITLE: SWOG 7628, Combined CT/RT/IT for Oat Cell Cancer of the Lung (Chemotherapy, Radiation Therapy, Immunotherapy).

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/46

TECHNICAL OBJECTIVE

1. To use combination chemotherapy, local radiotherapy, and maintenance chemotherapy or chemoimmunotherapy in the treatment of oat cell carcinoma of the lung in order to improve the quality of survival and the duration of survival.
2. To compare the effectiveness of two combination chemotherapy induction regimens in a randomized fashion prior to radiotherapy of the primary.
3. To test the effectiveness of continued chemoimmunotherapy vs chemotherapy in maintaining complete or partial remissions.
4. To test the effectiveness of continued immunotherapy vs no maintenance treatment in patients achieving long-term complete remissions.
5. To establish baseline and serial data on immunologic status in both chemotherapy and chemoimmunotherapy groups.

METHOD

Patients with histologically proven diagnosis of oat cell carcinoma or small cell undifferentiated carcinoma of the lung with no prior chemotherapy or radiotherapy, who meet the other criteria as outlined in the protocol, will be entered on this study. Patients will be randomized into four treatment arms with different combinations of CT, RT, and IT as specified in the treatment plan of the protocol. Cyclophosphamide, vincristine, methotrexate, 5-fluorouracil, and adriamycin are the drugs to be used. BCG vaccine will be used for immunotherapy.

PROGRESS

(77 04 - 77 09) One patient has been treated on this study for one month. There has been progression of disease with initial decrease in cervical and axillary nodes by 50%, then enlargement.

STATUS: (O)

TITLE: M-77-1, Forty-Two Hour Methotrexate Infusions with Citrovorum Rescue - A Cliniopharmacokinetic Analysis (A Phase I-II Study)

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/48

TECHNICAL OBJECTIVE

1. To determine the maximal tolerated dose (MTD) of methotrexate (MTX) which will maintain a constant plasma antifolate concentration for 42 hours.
2. To identify what clinical factors alter renal clearance of MTX.
3. To evaluate the antitumor effect of 42-hour MTX infusions with citrovorum.
4. At Madigan Army Medical Center this treatment is being used only in patients with tumors that have shown response to it, e.g., sarcoma.

METHOD

Patients with any cancer resistant to conventional therapy who meet the other criteria as outlined in the protocol will enter the study in sequence, four patients being treated at each plasma MTX level as outlined in the protocol. A course of treatment will consist of a priming dose of MTX over the first hour, an infusion of MTX over the subsequent 41 hours, and citrovorum factor rescue thereafter, beginning at the time MTX is discontinued. Courses are repeated every two weeks.

PROGRESS

(77 08 - 77 09) One patient has been treated on this protocol with a partial remission.

STATUS: (O)

TITLE: SWOG 7630, Protocol for Chemotherapy of Advanced Prostatic Cancer (Stage D), Phase III

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/51

TECHNICAL OBJECTIVE

1. To compare the rate of response of hydroxyurea to a two-drug combination of adriamycin and cyclophosphamide in patients with advanced carcinoma of the prostate who have measurable disease (Stage D - bone metastases or extra-pelvic disease).
2. To compare the duration of survival in patients with nonmeasurable disease treated with one of the treatment regimens.
3. To estimate the response rate to each crossover regimen in patients that have been treated and did not respond to one of the regimens.

METHOD

Patients with advanced Stage D prostatic cancer (disease in bone or other extra-pelvic site) who have not received any of the protocol agents and who meet the other criteria as listed in the protocol will be randomized to Treatment #1 (hydroxyurea) or Treatment #2 (adriamycin and cyclophosphamide) with dosages as outlined in the protocol. Failure on either of the treatment programs will result in crossover to the other program. Progression as defined in the protocol may occur as early as one treatment course or 3 weeks of hydroxyurea.

PROGRESS

(77 08 - 77 09) No patients have been registered on this protocol.

STATUS: (O)

TITLE: SWOG 7518, Stage III A and B Hodgkin's Disease Remission Induction by Radiation Therapy Plus Chemotherapy Combination versus Chemotherapy Alone. Phase III

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/52

TECHNICAL OBJECTIVE

1. To compare the effectiveness of 10 courses of a five-drug combination chemotherapy (including nitrogen mustard, vincristine, procarbazine, prednisone, and bleomycin) program against the combined three courses of chemotherapy followed by total nodal irradiation therapy program for complete remission induction in patients with Stage III asymptomatic -A or symptomatic -B disease.
2. To evaluate the systematic "restaging" of patients in apparent complete remission.
3. To assess the length of unmaintained remission after intensive induction with ten courses of chemotherapy treatment versus the combination chemoradiation therapy, after documentation of complete remission status by careful "restaging".
4. To assess the toxicity of the chemotherapy alone portion of the study versus the toxicity of the combination of chemotherapy and radiation therapy.
5. To intercompare the results of this program with those to be obtained by SWOG 7406 (ongoing).

METHOD

Patients with any histopathologic type Stage III Hodgkin's disease and no prior chemotherapy or radiation therapy who meet the other criteria as outlined in the protocol will be randomized to either Treatment 1 or Treatment 2. Treatment 1: chemotherapy alone (nitrogen mustard, vincristine, procarbazine, and prednisone plus bleomycin). Treatment 2: chemotherapy plus radiation therapy (chemotherapy as above followed by total nodal radiotherapy). At the completion of ten courses of chemotherapy or of the total combination chemotherapy, radiation therapy program, a thorough evaluation for evidence of persistent Hodgkin's disease is required. If complete remission is confirmed by this evaluation, no further treatment will be given until relapse occurs. If remission is not confirmed, appropriate treatment will be given on an individual basis.

SWOG 7518 - Stutz

PROGRESS

(77 08 - 77 09) No patients have been registered on this protocol.

STATUS: (O)

TITLE: SWOG 7433, Non-Hodgkin's Lymphomas (Stages I, I_E, II and II_E). A Phase III Study

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/53

TECHNICAL OBJECTIVE

To compare the remission rate, remission duration, and survival in patients with non-Hodgkin's lymphoma, pathologic stages I, I_E, II and II_E treated with extended field radiotherapy (supra-diaphragmatic mantle or abdominal field) alone or with extended field radiotherapy plus combination chemotherapy (Cytoxan, Hydroxyl-daunorubicin(adriamycin), Oncovin (vincristine), and prednisone).

METHOD

Patients newly diagnosed (no type of prior therapy) with non-Hodgkin's lymphoma except mycosis fungoides and diffuse lymphocytic well differentiated lymphoma will be thoroughly evaluated for extent of disease and then randomized to either radiation therapy or radiation therapy plus chemotherapy. If the patient does not achieve a complete remission after completion of his treatment course, he will be removed from the study. Those achieving complete remission will be followed for two years or until relapse.

PROGRESS

(77 08 - 77 09) No patients have been entered on this protocol.

STATUS: (O)

TITLE: SWOG 7406, Advanced Hodgkin's Disease: Remission Induction (MOPP #5). Phase III

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/54

TECHNICAL OBJECTIVE

1. To compare the effectiveness of two MOPP (nitrogen mustard, vincristine, procarbazine, and prednisone) + bleomycin + adriamycin combinations against MOPP + bleomycin for remission induction in patients with advanced Hodgkin's disease without prior chemotherapy.
2. To evaluate systematic restaging of patients in apparent complete remission.
3. To assess the length of unmaintained remission after intensive induction with ten courses of treatment and after documentation of complete remission (CR) status by careful restaging.
4. To evaluate by crossover design the remission induction potential of the other study combinations for patients who relapse during unmaintained remission.

METHOD

All previously untreated patients with Ann Arbor Stages IIIB or IV A+B Hodgkin's disease who meet the other criteria as outlined in the protocol will be randomized to one of the induction programs as specified in the protocol. Ten courses of treatment at 4-week intervals will constitute remission induction. If induction results in a CR and this is confirmed by restaging, then no further treatment will be given. If at least a partial remission (PR) is indicated another four courses will be administered in a second attempt to achieve a CR. Persistence of disease after 14 courses will constitute an induction failure and the patient will be taken off study. Relapsing patients will be crossed over to one of the other induction combinations.

PROGRESS

(77 08 - 77 09) One patient treated on this protocol with a partial remission.

STATUS: (O)

TITLE: SWOG 781, Phase III Protocol - Radiotherapy-Chemotherapy (MOPP) for Stages I and II, A and B Hodgkin's

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/55

TECHNICAL OBJECTIVE

To compare total nodal radiotherapy (TN-XRT) or "mantle" and para-aortic radiotherapy to involved field radiotherapy (IF-XRT) plus MOPP (nitrogen mustard, vincristine, prednisone, and procarbazine) chemotherapy in patients with stages I and II, A and B disease.

METHOD

Patients with biopsy-proven Hodgkin's disease who have received no prior chemotherapy or radiotherapy and who meet other criteria as outlined in the protocol will be randomized to one of two treatment programs: (1) TN-XRT; (2) IF-XRT followed by MOPP chemotherapy. Following completion of the IF-XRT, a rest period of four weeks will be interposed before chemotherapy is started. Dosages for chemotherapy and radiotherapy and length of courses of treatment as specified in the protocol.

PROGRESS

(77 08 - 77 09) No patients have been registered on this protocol.

STATUS: (O)

TITLE: SWOG 7618, Combined Preoperative Adjuvant Therapy in Rectal Carcinoma

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/58

TECHNICAL OBJECTIVE

1. To determine if adjuvant preoperative irradiation and combination chemotherapy will yield a higher incidence than expected of Duke A lesions in a high risk group of patients with rectal carcinoma.
2. To determine the survival of patients with rectal carcinoma, both those with and without regional node metastasis, following the combined treatment stated in #1.

METHOD

Patients with histologically proven carcinoma of the rectum who meet the other criteria as listed in the protocol will be randomized to one of two treatment modalities: (1) radiotherapy followed by surgery; (2) radiotherapy and chemotherapy followed by surgery. For both treatment arms, the preoperative irradiation and surgery will be identical. Radiotherapy: 2000 rads at the rate of 1000 rads per week, five treatments per week. Chemotherapy: mitomycin-C, 10 mg/M^2, given once IV through a running IV as a bolus injection, or a 20-30 minute infusion; 5-fluorouracil 1000 mg/M^2/day as a continuous 24 hour infusion via a central venous pressure indwelling intracath for 4 days. Both 5-fluorouracil and mitomycin will be started on the first day within eight hours of the completion of the first radiation treatment. The 4-day 5-fluorouracil administration will be repeated starting on day 28. The patient will undergo an abdominoperineal resection 6-8 weeks after completion of the radiotherapy.

PROGRESS

(77 09 - 77 09) One patient registered on protocol - too early for evaluation.

STATUS: (O)

TITLE: SWOG 7619, Evaluation of Ftorafur in the Treatment of Metastatic Adenocarcinoma of the Colon and Rectum, Phase II

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/59

TECHNICAL OBJECTIVE

To determine the efficacy of Ftorafur in disseminated adenocarcinoma of the colon and rectum.

METHOD

Patients who have biopsy proven adenocarcinoma arising from the colon or rectum who meet other criteria as outlined in the protocol will be entered on the protocol in two categories (with or without liver metastasis) for evaluation purposes. Dose schedule: Ftorafur 2.25 gm/M^2 over a 2-hour infusion daily x 5 days. Reconstituted solution may be administered in 250 cc of 5% dextrose/ normal saline. Repeat courses every 21 days provided patient has recovered from toxicity from the previous course. Adequate trial consists of two courses of therapy.

PROGRESS

(77 09 - 77 09) One patient entered on protocol. Too early for evaluation.

STATUS: (O)

TITLE: SWOG 7622, Combined Modality for Mycosis Fungoides -- Stage I (Phase II)

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/60

TECHNICAL OBJECTIVE

1. To compare the effectiveness of combined electron beam therapy and adjuvant chemotherapy vs electron beam therapy alone for patients with Stage I mycosis fungoides to determine the time to recurrence and to determine the percentage of recurrence.
2. To determine the effectiveness of adjuvant chemotherapy and survival patterns of such patients.
3. To determine the value of staging laparotomy in the management of mycosis fungoides.

METHOD

Patients who have two or more skin biopsies read as mycosis fungoides by a pathology panel and who meet other criteria as listed in the protocol will be randomized to receive electron beam therapy alone or electron beam therapy and adjuvant chemotherapy. Electron beam total body irradiation will be given via the Stanford Technique to a dose of 3000-5000 rads/40-60 days. Following the completion of electron beam therapy a rest period of four weeks is completed before chemotherapy is started. Chemotherapy will consist of: Cytoxan, 450 mg/M^2 IV on day 1 only; adriamycin, 30 mg/M^2 on day 1 only; vincristine, 1.4 mg/M^2 on day 1; prednisone, 100 mg orally for 5 days; and bleomycin, 2 units/M^2 IV 30" after vincristine on day 1. A total of 8 cycles at 3-week intervals will be delivered. Patients will be followed indefinitely or to a point of relapse.

PROGRESS

(77 08 - 77 09) No patients have been registered on this protocol.

STATUS: (O)

TITLE: SWOG 7625, Combination Chemotherapy for Advanced Sarcomas of Bone and Mesothelioma Utilizing Rubidazone and DIC (Dimethyl Triazeno Imidazole Carboxamide)

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/61

TECHNICAL OBJECTIVE

1. To determine the efficacy in terms of rate of response of combination chemotherapy with the 2-drug regimen RubiDIC (Rubidazone + DIC) in patients with metastatic sarcomas of bone and mesothelioma.
2. To determine the duration of remission and survival pattern of patients on this study and compare them with that of patients with metastatic bone sarcomas and mesothelioma on previous Southwest Oncology Group or M.D. Anderson Hospital protocols using adriamycin containing regimens.
3. To determine the toxicity of the regimen especially with regard to cardiac toxicity.

METHOD

Patients with a biopsy-confirmed diagnosis of bony sarcoma or mesothelioma with measurable metastases who have already received appropriate surgical therapy, who have not received prior adriamycin, daunorubicin, rubidazone, DIC, or BIC, and who meet other criteria as outlined in the protocol will be entered in the protocol on two treatments. Treatment I (adequate marrow reserve) will consist of rubidazone, 150 mg/M^2 IV on day 1 and DIC, 250 mg/M^2/day IV on days 1-5 inclusive. Treatment II (inadequate marrow reserve) will consist of rubidazone, 120 mg/M^2 IV on day 1 and DIC, 200 mg/M^2/day IV on days 1-5 inclusive. For both treatments, a complete cycle of chemotherapy shall be repeated every 22 days. Patients who remain in complete remission having received a total of two years of chemotherapy will have the chemotherapy discontinued, but will continue to be followed.

PROGRESS

(77 09 - 77 09) No patients have been registered on this protocol.

STATUS: (O)

TITLE: SWOG 7626, ROAP Induction Chemotherapy of Acute Leukemia in Patients Over the Age of 50

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/62

TECHNICAL OBJECTIVE

To determine the efficacy of the 4-drug combination chemotherapy regimen ROAP (rubidazone, vincristine, arabinosyl cytosine and prednisone) in remission induction chemotherapy in patients with acute leukemia over the age of 50. To determine the toxicity of the regimen.

METHOD

Patients age 50 or greater with a diagnosis of acute leukemia who have received no extensive prior therapy who meet other criteria as outlined in the protocol will be divided into two groups; Group I - a circulating blast count of less than 30,000; Group II - circulating blast count $\geq$ 30,000/cu ml. Both groups will receive identical treatment: rubidazone, 200 mg/M^2, IV on day 1; vincristine, 2 mg, IV day 1; arabinosyl cytosine, 70 mg/M^2, continuous IV infusion days 1-7; and prednisone, 100 mg, PO qd days 1-5. Courses repeated approximately every 20 days. Patients showing response more than 50% reduction in leukemic infiltrate after three courses will receive chemotherapy as long as improvement persists. When subsequently progressive disease follows, patients will be removed from study. Separate protocols will be devised for maintenance therapy.

PROGRESS

(77 09 - 77 09) No patients have been registered on this protocol.

STATUS: (O)

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

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, 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. Determine the efficacy of a response to the antiestrogen Tamoxifen in predicting response to ablative surgery.
3. 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 and Tamoxifen. Group II (prior castration) will receive Tamoxifen, 10 mg BID. Duration of therapy: 3 weeks (a) increasing disease, oophorectomy and continue Tomoxifen; (b) response, continue to relapse; (c) stable disease, continue until 10 weeks is reached; 10 weeks - (a) increasing disease, oophorectomy and continue Tamoxifen; (b) response, continue to relapse, (c) acceptable stable disease, continue to relapse; (d) unacceptable stable disease, oophorectomy and continue Tamoxifen. Surgical guidelines and chemotherapy as outlined in protocol.

PROGRESS

(77 08 - 77 09) No patients have been registered on this protocol.

STATUS: (O)

TITLE: SWOG 7633, A Study of Rubidazone (NSC 164011) in Adults with Previously Treated Acute Leukemia and in Patients with CML Blast Transformation. Phase II

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/64

TECHNICAL OBJECTIVE

1. To determine the efficacy of rubidazone in adult patients with previously treated acute leukemia and in patients with CML blast transformation.
2. To determine the toxicity of the drug in the above patients, with special reference to patients having prior therapy with adriamycin.

METHOD

Adult patients with acute leukemia having had prior chemotherapy and patients with CML blast transformation will be entered on the study, if other criteria as outlined in the protocol are met. Starting dosage - Day 1: Good risk patients - 450 mg/M^2 IV; poor risk (over age 50 and infected or with less than 50% leukemic infiltrate) - 300 mg/M^2 IV. Subsequent doses and time intervals between doses will be determined by individual progress as outlined in the protocol. Maintenance doses of approximately 150 mg/M^2 of rubidazone may be given every three weeks after remission is reached. At the termination of rubidazone treatment, patients in remission will be maintained in any fashion deemed appropriate by the investigator.

PROGRESS

(77 09 - 77 09) One patient was entered on protocol and expired shortly thereafter.

STATUS: (O)

TITLE: SWOG 7634, Evaluation of MeCCNU Plus B-2'-Deoxythioguanosine and Mitomycin-C Plus B-2'-Deoxythioguanosine in the Treatment of Refractory Disseminated Colorectal Carcinoma. Phase III Study

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/65

TECHNICAL OBJECTIVE

1. To evaluate the effectiveness of MeCCNU plus B-2'-deoxythioguanosine (BTGdR) for remission induction in disseminated colorectal carcinoma for patients failing to respond or relapsing from chemotherapy with Mitomycin-C plus 5-FU or Mitomycin-C plus Ftorafur, 5-FU alone, or Ftorafur alone.
2. To evaluate the effectiveness of MITO-C plus BTDdR for remission induction for patients failing to respond or relapsing from chemotherapy with MeCCNU plus 5-FU of MeCCNU plus Ftorafur, 5-FU alone, or Ftorafur alone.

METHOD

Patients with histologically proven disseminated colorectal carcinomas who meet the other criteria as outlined in the protocol will be treated as follows:

Treatment 1: Patients with prior exposure to MeCCNU + 5 FU or MeCCNU + Ftorafur, 5-FU alone or Ftorafur alone.

Good risk: MITO-C, 15 mg/M^2 IV days 1 and 56
BTGdR, 60 mg/M^2 days 1-5, 28-32, 56-60

Poor risk: MITO-C, 10 mg/M^2 IV on days 1 and 56
BTGdR, 50 mg/M^2 on days 1-5, 28-32, 56-60

Treatment 2: Patients with prior exposure to Mitomycin-C + 5-FU or Mitomycin + Ftorafur, 5-FU alone or Ftorafur alone.

Good risk: MeCCNU, 130 mg/M^2 PO on days 1 and 56
BTGdR, 60 mg/M^2 on days 1-5, 28-32, 56-60

Poor risk: MeCCNU, 100 mg/M^2 PO on days 1 and 56
BTGdR, 50 mg/M^2 on days 1-5, 28-32, and 56-60

Patients without prior exposure to MeCCNU or Mitomycin-C will be randomized to receive Treatment I or Treatment II.

SWOG 7634 - Stutz

PROGRESS

(77 09 - 77 09) No patients have been registered on this protocol.

STATUS: (O)

TITLE: SWOG 7639, Two Adriamycin, Mitomycin C and 5-Fluorouracil Combinations in the Management of Gastric Adenocarcinoma. A Phase III Study

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/66

TECHNICAL OBJECTIVE

1. To determine and to document both the response rates and the toxicities of two different combinations of adriamycin, mitomycin C and 5-fluorouracil in the management of surgically incurable adenocarcinoma of the stomach.
2. To compare the effectiveness of these two regimens.

METHOD

Patients who have unresectable gastric adenocarcinoma and an objectively measurable lesion with no prior exposure to adriamycin, daunomycin, mitomycin C, or porfiromycin, and who meet other criteria as outlined in the protocol will be randomized to one of the two treatments.

Treatment 1: sequential regimen
adriamycin, 50 mg/M^2 day 1
mitomycin C, 10 mg/M^2 day 3
5-fluorouracil, 600 mg/M^2 day 29

Treatment 2: simultaneous regimen
adriamycin, 30 mg/M^2 per dose, day 1 and 19
mitomycin, 10 mg/M^2 day 1
5-fluorouracil, 600 mg/M^2 per dose, day 1,8,29, 36

Although one single course of therapy (8 weeks on study) would be considered as an adequate trial, an attempt should be made to administer at least two courses of therapy where possible. Patients whose disease has remained stable or has regressed on therapy will be continued on this combination for a total of two years unless the adriamycin dose limitation or drug toxicity precludes such continuation of therapy.

SWOG 7639 - Stutz

PROGRESS

(77 09 - 77 09) One patient registered on protocol. Too early for evaluation.

STATUS: (O)

TITLE: SWOG 7703, Radiation Therapy in Combination with BCNU, Dimethyl Triazeno Imidazole Carboxamide (DTIC) or Procarbazine in Patients with Malignant Gliomas of the Brain. Phase III

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/74

TECHNICAL OBJECTIVE

To compare the effectiveness of radiation therapy plus BCNU, radiation therapy plus DTIC, and radiation therapy plus procarbazine for remission induction, duration of remission, and survival in patients with malignant gliomas of the brain.

METHOD

Patients with histologically confirmed primary central nervous tumors of the following histologic types will be entered on the study: astrocytoma, grades 3 and 4 (glioblastoma multiforme). Other criteria: surgery with histologic diagnosis within the prior four weeks and no prior chemotherapy of any type with the exception of corticosteroids. Patients will be randomly allocated to one of the three programs: (1) radiation therapy plus BCNU; (2) radiation therapy plus procarbazine; (3) radiation therapy plus DTIC (dosage as outlined in the protocol). Since survival time is an important end point of this study, each investigator will be required to follow each patient until death and to report the death.

PROGRESS

(77 09 - 77 09) No patients have been entered on this protocol.

STATUS: (O)

TITLE: SWOG 7704, Chemoimmunotherapy for Multiple Myeloma - VMCP + VCAP vs VMCP-VBAP vs MP for Remission Induction Therapy: VMCP vs VMCP + Levamisole for Maintenance After Remission Induction. Phase III

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/75

TECHNICAL OBJECTIVE

1. To compare the effectiveness of three intermittent pulse chemotherapy combinations, VMCP + VCAP vs VMCP + VBAP vs MP for induction of remissions in previously untreated patients with multiple myeloma. (V = vincristine, M = melphalan, C = cyclophosphamide, P = prednisone, A = adriamycin, B = BCNU, L = levamisole) Results will also be compared with other combination chemotherapy treatments in previous SWOG studies, especially VMCP treatment in SWOG 7418 and previous studies of MP combinations.
2. For patients proven to have at least a 75% tumor regression after induction, to compare the value of 12 months of chemoimmunotherapy maintenance VMCP + Levamisole in comparison to VMCP alone.
3. To establish baseline and serial data on immunologic status in these patient groups.

METHOD

Patients with previously untreated multiple myeloma who meet other criteria as outlined in the protocol will be randomized to one of the following treatments. For induction:

Treatment 1: regular alternating combinations VMCP (1 cycle) then VCAP (1 cycle) alternating q 3 weeks
Treatment 2: sequential alternating combinations VMCP (3 cycles) then VBAP (3 cycles)
Treatment 3 single combination - MP 3 week cycles

For maintenance:
Treatment 1: VMCP
Treatment 2: VMCP + Levamisole

Patients still in remission at the end of 12 months of maintenance with either VMCP or VMCP plus levamisole will be followed in an unmaintained remission state. Upon relapse from unmaintained

remission, patients should be reinduced with the previously used maintenance treatment and this program should be continued until relapse.

PROGRESS

(77 09 - 77 09) One patient registered on this protocol. Too early for evaluation.

STATUS: (O)

TITLE: SWOG 7522, Chemotherapy, Splenectomy With or Without Immunotherapy in the Treatment of Chronic Myelogenous Leukemia. Phase III

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/78

TECHNICAL OBJECTIVE

To study the effects of chemotherapy, splenectomy, and/or immunotherapy on leukemic cytogenetics, immune status, appearance of blastic transformation, and any influence in overall survival.

a. To treat and control the early benign phase of chronic myelogenous leukemia with cytoxan, cytosine arabinoside, vincristine and prednisone and to study the influence of chemotherapy on bone marrow morphology, cytogenetics, and leukocyte alkaline phosphatase.

b. To study nonspecific cell mediated immunity prior to and following therapy.

c. To determine if immunotherapy with BCG will augment general immunocompetence of CML patients.

d. To remove extra tumor burden, avoid possible complication of splenic infarction and hypersplenism through surgical splenectomy.

METHOD

Splenectomy for patients entering this study will be elective. Within each group (splenectomy or no splenectomy) patients will be randomized to receive chemotherapy alone or chemotherapy + BCG immunotherapy. Hence, there will be four groups of patients.

Induction Treatment:

Treatment 1: Cytosar 100 mg/M^2 day x 5, subcutaneous
Oncovin 1.0 mg IV day 1
Cytoxan 500 mg/M^2 IV day 1
Prednisone 100 mg PO day x 5
Tice BCG scarification on days 8 and 15

Treatment 2: COAP only (same dosages as for Treatment 1)

Following three courses of induction treatment, patients will be evaluated for splenectomy. For patients not undergoing splenectomy, maintenance chemotherapy will be initiated. Splenectomy will be planned during days 21-28 after COAP #3, when the peripheral

circulating WBC is between 5 and 20,000/mm^3.

Maintenance Treatment
Treatment 1: Hydroxyurea PO in 4 divided dosages daily.
Dosage depends upon the WBC.
BCG weekly between hydroxyurea courses.
Treatment 2: Hydroxyurea PO in 4 divided dosages daily.

PROGRESS

(77 07 - 77 09) One patient treated for eight days. Not evaluable due to early death.

STATUS: (O)

TITLE: SWOG 7635, Combined Modality Treatment of Limited Squamous Carcinoma of the Lung. Phase III

PRINCIPAL INVESTIGATOR: LTC Friedrich H. Stutz, MC

WORK UNIT NO: 77/82

TECHNICAL OBJECTIVE

1. To determine whether chemotherapy with adriamycin and/or immunotherapy with levamisole improve median survival of split-course radiotherapy used alone in the treatment of patients with limited extent, squamous bronchogenic carcinoma.
2. To determine the qualitative and quantitative toxicity of each treatment regimen.

METHOD

Patients with a histologically confirmed diagnosis of limited squamous carcinoma of the lung with no previous chemotherapy or radiation therapy will be randomized to one of the following regimens:

Regimen A: Radiation therapy plus levamisole.
Regimen B: Radiation therapy plus adriamycin.
Regimen C: Radiation therapy plus adriamycin and levamisole.
Regimen D: Radiation therapy alone.

Dosages for both chemotherapy and radiotherapy and courses of treatment are detailed in depth in the protocol.

PROGRESS

(77 08 - 77 09) One patient was registered on this protocol, but was never treated because he was found, on tomograms, to have metastatic disease after registration, but before the planned start of treatment.

STATUS: (O)

TITLE: In vitro Identification of Tumor Associated Antigens

PRINCIPAL INVESTIGATOR: COL Clarence M. Virtue, MC

WORK UNIT NO: 75/14

TECHNICAL OBJECTIVE

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

METHOD

Phase I: Ten C3H-strain mice with implanted murine breast carcinoma will be obtained, and, after tumor growth has progressed beyond palpable stage, the mice will be sacrificed, and tumor tissue removed. Tissue treatment as listed in protocol.

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

Phase III: Once the specific tumor associated antigens from mouse breast carcinoma are separated (Phase I), the antigens will be pooled and held at -80°C. Forty C3H-strain mice with implanted murine breast carcinoma will be obtained. Ten of these mice will be separated and have no further procedures. Twenty other mice will undergo resection of the tumor mass, and ten will subsequently receive an injection of the specific murine tumor associated antigens (obtained in Phase I) combined with Fruend adjuvant, followed by a booster injection with tumor associated antigen without tumor resection. The mice will then be observed and compared.

PROGRESS

(76 06 - 77 09) Breast carcinoma tissue from surgical specimens has been extracted in saline and fractionated by G-200 column. Preparative electrophoretic apparatus has been assembled and is in the process of testing for further fractionation.

STATUS: (O)

TITLE: Serum RAST Titer Changes in Allergic Patients on Desensitization and the Correlation with Skin Test Changes

PRINCIPAL INVESTIGATOR: COL Clarence M. Virtue, MC

WORK UNIT NO: 77/67

TECHNICAL OBJECTIVE

It is the objective of this investigation to study the changes in serum IgE reagenic antibody at various times during desensitization and compare these changes with the clinical course and skin test results.

METHOD

Patients seen by the Allergy Service will be given the usual allergy evaluation to include clinical history, physical examination, appropriate skin tests, laboratory blood tests and pulmonary function spirometry. A 5 cc aliquot of serum will be reserved and tested for specific IgE reagenic antibody titers by the RAST technique, performed by the Nuclear Medicine Service. Those patients who are placed on desensitization treatment will be reevaluated at appropriate intervals by the Allergy Service, at which time serum will again be drawn for repeat RAST titers and compared with skin test results and correlated with the clinical course.

PROGRESS

(77 06 - 77 09) Pre-treatment skin tests and serum for RAST titers have been obtained on ten atopic patients.

STATUS: (O)

TITLE: Immunotherapy of Murine Mammary Carcinoma

PRINCIPAL INVESTIGATOR: COL Clarence M. Virtue, MC

WORK UNIT NO: 77/77

TECHNICAL OBJECTIVE

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

METHOD

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

PROGRESS

(77 05 - 77 09) A line of mammary carcinoma C3H mice has been established. Tumor has been removed and is in the process of extraction and fractionation.

STATUS: (O)

TITLE: Comparison of Three Methods for Presumptive Identification of Group B Streptococci

PRINCIPAL INVESTIGATOR: LTC Thomas R. Oberhofer, MSC

WORK UNIT NO: 77/47

TECHNICAL OBJECTIVE

To compare the sodium hippurate test, the rapid hippurate test and the CAMP test for ease of performance, rapidity of performance, and accuracy in the presumptive identification of group B streptococci.

METHOD

All isolates of hemolytic streptococci suggestive of group B organisms, based on morphology and hemolytic reactions, will be subjected to the three tests. Additional tests, routinely used for identification of streptococci, will also be used. These are the bacitracin test for group A and the bile-esculin and 6.5% NaCl tests for group D. Randomly selected isolates of groups A and D streptococci and organisms deemed to be non-group A, B, or D will also be tested by the three methods. Most, but not all of the test organisms, will be sent to the reference microbiology laboratory, BAMC, for serogrouping as the final determination of identity. Results of seroidentification will be correlated with those of each of the three presumptive tests. Accuracy of identification, ease and rapidity of performance of each presumptive test, and discrepancies in results will be examined.

PROGRESS

(77 01 - 77 08) Three non-serologic tests used for the presumptive identification of group B streptococci were evaluated for performance. These were the sodium hippurate, rapid hippurate, and CAMP tests. The rapid hippurate test can be used as an alternative to the sodium hippurate test providing that large inocula and pure cultures are available for testing. The CAMP test is suited for selecting organisms from mixed cultures since only a small inoculum is required. A manuscript has been accepted for publication by the Journal of Clinical Microbiology.

STATUS: (C)

TITLE: Rejuvenation of Outdated Human Erythrocytes and Evaluation of Frozen Blood Techniques

PRINCIPAL INVESTIGATOR: MAJ Robert T. Usry, MSC

WORK UNIT NO: 77/45

TECHNICAL OBJECTIVE

To determine the safety and efficacy of human red cells stored at 4°C for 22-28 days that are biochemically modified (rejuvenated) prior to freeze-preservation; and to evaluate two techniques to freeze and deglycerolize human erythrocytes for utilization at Madigan Army Medical Center.

METHOD

Phase I: Rejuvenate and refreeze (as outlined in protocol) 30 units outdated O-positive or O-negative red cells and ship in dry ice to the Naval Blood Research Laboratory, Boston, MA, for complete freeze-thaw-wash recoveries on the red cells, bacterial cultures, and measurement of the red cell 2, 3 DPG, ATP, and potassium ion levels in addition to in vitro P_{50} levels. Red cell survival measurements will be performed on selected units.

Phase II: Rejuvenate and refreeze 30 units of expired blood, the same as Phase I with the exception of the removal of the supernatant solution containing glycerol, the solution used for biochemical modification, and plasma that is present in the concentrated red cells prior to freezing. These units will be shipped and evaluated as in Phase I.

Phase III: Same procedures as in Phase II with the exception that freezing will be accomplished in the original blood bag and shipped as in Phase I and II.

PROGRESS

(77 01 - 77 09) Work on this research protocol continues with encouraging results. Mrs. Dolores LaBarge worked with Dr. Valeri in Boston rejuvenating, freezing, and thawing human red cells, and Phases I and II were completed with highly acceptable results.

STATUS: (O)

TITLE: Early Detection of School Learning Problems During Kindergarten School Physicals Using Volunteer Staff and New Techniques

PRINCIPAL INVESTIGATOR: LTC James H. Nelson, MC

WORK UNIT NO: 77/11

TECHNICAL OBJECTIVE

To determine if the newly devised PDQ (Denver Prescreening Questionnaire) is an accurate, rapid, and effective tool in the identification of the anticipated 10-15% of children entering kindergarten who will have school learning problems. Such information, necessary for comprehensive pediatric care, would be most valuable to physicians, school, and family before rather than after the problem becomes manifest.

METHOD

All children receiving a physical examination at Madigan on a mass scale basis for kindergarten will be given a PDQ (to be completed by parents) and a Goodenough Draw-A-Person (to be completed by child), supervised by pediatric clinic volunteer staff. Total number anticipated is 400. After analysis, this material will be added to the individual child's outpatient medical chart, as it is information helpful to future care of the child and has many of the same items to be found on the DDST's now added to the chart, and may be compared to growth charts. Normal PDQ's will have no follow-up, questionables will be phoned for repeat screening, and abnormals will have more thorough screening before referral to other resources, such as Child Guidance Clinic, or the actual classroom performance in school after 5 months will be determined.

PROGRESS

(77 02 - 77 09) The PDQ appears quite successful in the early detection of school disorders and has resulted in the addition of the PDQ to kindergarten physicals given at MAMC. The results of this information are being collected to determine if there was adequate follow-up and intervention with any abnormal results.

STATUS: (O)

TITLE: A Prospective Analysis of the Current Pediatric Screening Program (PSP) to Critically Evaluate Its Effectiveness and Application to Other Military Pediatric Clinics.

PRINCIPAL INVESTIGATOR: LTC James H. Nelson, MC

WORK UNIT NO: 77/44

TECHNICAL OBJECTIVE

To determine through a comprehensive data analysis the effectiveness of the PSP to identify and treat pediatric patients who prior to its conception had not been receiving comprehensive, organized health care past the first year of life. In addition, this project will detail the PSP organization, methodology, and availability of application to other military clinics using the paraprofessional services of local Red Cross volunteers.

METHOD

A prospective study of 100 routine screenings was conducted, including information concerning early detection of vision, speech and hearing deficiencies, deviant physical and psychomotor development, dental disease, high blood pressure, anemia, bacteriuria, significant family history and environmental influences, immunization lags, and potential learning disabilities. The statistics were analyzed to document the need and effectiveness of the PSP. An analysis of the follow-up treatment necessary for those individuals identified with abnormalities will be conducted. A detailed report will be submitted concerning the present PSP and the utilization of Red Cross volunteers to provide a reference source for other military hospitals interested in the establishment of such a program. In addition, the paper will relate the results of the prospective study and its significance in detecting the implementation of quality health care for pediatric patients. In conjunction with assisting other military hospitals in program implementation, a video tape of a representative family and medical history intake and routine screening appointment will be made using existing Madigan audio-visual facilities.

A Prospective Analysis of the Current Pediatric Screening Program - Nelson

PROGRESS

(77 01 - 77 09) Intake evaluations of 100 children have been examined. This survey shows that primary medical care is often fragmented and that basic screening for anemia, dental care, immunizations, vision, etc. has been deficient for many of our pediatric patients. Lack of professional time, inadequate medical records, a need for better education of the parents about the need for preventive pediatrics, lack of proper equipment, growth charts, and the constant confusion of changing health professionals and clinic settings at each visit are often apparent. This program has helped us to correct some of these problems. The suvey indicates that the Madigan PSP is indeed valuable and provides an upgrading of medical care for over a thousand children a year. If time and funding are available, another 400 prospective cases will be reviewed to provide data to submit to the computer at University of Washington School of Medicine for statistical analysis.

STATUS: (O)

TITLE: Variations in the Oxygen Consumption of Newborns in Different Artificial Warming Devices

PRINCIPAL INVESTIGATOR: MAJ Amil Ortiz, MC

WORK UNIT NO: 76/32

TECHNICAL OBJECTIVE

To establish some normal values of the oxygen consumption of newborns during the first three days of life and to observe the difference in the oxygen consumption of newborns in different artificial warming devices.

METHOD

Fifty full term infants with birth weight above 2,500 gm, apgars at birth above 8, and blood pH of 7.25 or above will be randomly selected for this study. Each infant will be randomly assigned to one of two groups. Group A will consist of 25 infants, each placed in a radiant warmer for a period of 30 minutes. The first 15 minutes will be for equilibration and the last 15 to obtain the oxygen consumption. Two hours later the patient will be placed in a conventional isolette and the same method for oxygen consumption determination will be utilized. Group B will differ from Group A only in that the first determination of oxygen consumption will be in the isolette followed by the radiant warmer. The method to be utilized in the determination of the oxygen consumption will be the "closed system" as outlined in the protocol.

PROGRESS

(76 06 - 77 09) Oxygen consumption was measured in eight normal, term infants during quiet sleep while on a radiant energy warmer and in a conventional incubator. The use of the radiant energy warmer was associated with a 14.9% increase in oxygen consumption as compared to the incubator. This increase may be critical in the care of some neonates.

STATUS: (C)

TITLE: Genetic Studies of a Family with Chromosomal Anomalies in Both Parents and Their Children

PRINCIPAL INVESTIGATOR: CPT Isaac S. Pope, MC

WORK UNIT NO: 76/07

TECHNICAL OBJECTIVE

The purposes of this project are: (1) To identify members of the maternal family who carry inverted #3 and #9 chromosomes; to evaluate effect of the carrier state on results of pregnancy; to assess the magnitude of the risk for a malformed child to be born to a carrier and to give the information to those affected. (2) To attempt confirmation of assignment for the gene galactose-1-phosphate-iridyl-transferase (the gene mutant in galactosemia) to the long arm of chromosome-3 and to further refine the localization of the gene. (3) To obtain pedigree data and chromosomal studies for members of the paternal family to assess: (a) whether the "Premature Centromere Division" (PCD) is present; (b) whether the PCD exhibits characteristics of Mendelian inheritance; and (c) whether the CYY karyotype of the father and other chromosomal anomalies, if found in the family, may reasonably be related to the PCD syndrome.

METHOD

The principal investigator will visit both maternal and paternal families to obtain family histories and blood samples and to perform chromosomal studies. Cytogenic and enzyme studies will be done in conjuntion with the Birth Defects Study and Counseling Program, State of Washington.

PROGRESS

(76 12 - 77 09) This study has been completed and the results are being analyzed at present.

STATUS: (C)

TITLE: Prospective Study of the Incidence and Manifestations of Allergy to Foods in the First Year of Life in a Well Child Clinic Population

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

WORK UNIT NO: 75/31

TECHNICAL OBJECTIVE

The study will ascertain the incidence of allergy to foods in a large general clinic population of infants and attempt to clarify the clinical patterns. This would assist in early identification of allergy problems and early institution of appropriate therapy.

METHOD

Two thousand infants seen in the Well Child Clinic will be followed to age one year or longer in the customary clinic visits at 1, 2, 6, and 12 months. Members of the Pediatric Department and Family Practice Service will be requested to refer infants who develop wheezing or recurrent pulmonary problems to the Allergy Clinic and infants who develop eczema, persistent severe rhinitis or gastrointestinal intolerance to cow's milk formula to the Well Child Clinic. Symptomatic infants will be evaluated by complete allergy history and examination, as indicated, with dietary alteration and food challenges, environmental controls, nasal smear, skin testing, serum precipitin test and other customary tests for those with pulmonary problems. Charts of study patients will be analyzed at 6 and 12 months. Statistical analysis will be done when the first 1,000 infants have been followed for 1 year, when the next 1,000 infants have been followed for 1 year, and further as indicated.

PROGRESS

(76 06 - 77 08) Of the initial enrollment of 1820 infants, 670 remained on the study for a full year. The study indicates that true and persisting allergy occurs with a frequency below 1% in the period of infancy. Due to the high mobility of the base population, a longer term study does not appear feasible.

STATUS: (C)

TITLE: Preventive Care Services for Infants: Evaluation of Problems and Outcomes

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

WORK UNIT NO: 77/08

TECHNICAL OBJECTIVE

To evaluate both process and outcomes of preventive care services provided in a large clinic to infants from one month of age up to and including the one year checkup.

METHOD

Infants enrolled in the Well Child Clinic for the initial one month checkup and remaining in care at MAMC through the first year checkup, who are healthy single births, will have their records surveyed. We will assess time, personnel and funds required to provide customary preventive services to the normal infant population; level of completion of recommended available services, particularly routine immunization; compliance with instructions regarding safety measures, particularly provision of a safe restraint device for the infant in the family automobile; and frequency of consultations to other departments and of visits to other clinics for care of illness. Also assessed will be incidence of accidents or other preventable type of illness; incidence of significant problems detected; overall maintenance of good health; relation of demographic characteristics to health problems. A survey will be made of other military pediatric facilities by mail for purposes of comparison of the scope of preventive care services provided.

PROGRESS

(76 09 - 77 09) Analysis of data has been completed and a full report is being prepared for publication. Preventive services have proven valuable and the benefits of increased emphasis on creating a safe environment are now obvious.

STATUS: (O)

TITLE: A Clinical Validation Study of the Walter Reed Neuropsychological Screening Battery

PRINCIPAL INVESTIGATOR: CPT Raymond A. Parker, MSC

WORK UNIT NO: 75/35

TECHNICAL OBJECTIVE

To determine empirically the clinical usefulness of the Walter Reed Neuropsychological Screening Battery, a multi-test battery designed to permit certain inferences concerning the organic integrity of an individual's cerebral cortex.

METHOD

Patients will be referred to Neuropsychology from Neurology with (a) clear-cut unequivocal evidence of cortical lesions with an established neurological diagnosis and (b) with no CNS pathology that can be demonstrated (control group). After establishing a final diagnosis on a patient, Neurology will fill out a validation study data sheet and hold the data sheet for the final analysis. Neurology will then contact Neuropsychology and arrange for the patient to be assessed with the Walter Reed Neuropsychological Screening Battery. After approximately ten patients have been evaluated for each of the two groups, the data sheets will be obtained from Neurology, and a comparison of the impressions from Neuropsychology and Neurology will be made. The neurological impression will be the validation criterion for each patient. Contingency tables such as illustrated in the protocol will be used to illustrate the results for each of the two neuropsychologists and Neurology. An appropriate Chi-square statistic will be used to evaluate the statistical significance of the agreement between Neuropsychology and Neurology. The results will be interpreted and discussed appropriately.

PROGRESS

(76 06 - 77 09) Significant procedural and theoretical revisions in the structure of this project are being carried out. Currently, the data necessary to complete the project has been gathered, and, as soon as the procedural revisions and theoretical changes are made, completion of the project will follow shortly.

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: LTC William H. Gernon, 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, initia[illegible]on an experimental basis.

METHOD

The surgical anatomy of the guinea pig ear is well known with two good approaches. 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

(77 08 - 77 09) Investigators presently are assembling the materials to be used in this study.

STATUS: (O)

TITLE: Evaluation of One Stage Longitudinally Reduced Ileal Ureters with the Use of the Auto Suture in Dogs

PRINCIPAL INVESTIGATOR: LTC Dietrich W. Geschke, MC

WORK UNIT NO: 77/69

TECHNICAL OBJECTIVE

To determine the chemical aberrations that occur in the urine and serum between an ileal ureter and its contralateral in situ ureter; to compare quantitatively the changes that occur in the urine of longitudinally reduced ileal ureters and its contralateral in situ ureter; to observe radiographically the function of ileal ureters and longitudinally reduced ileal ureters; to evaluate the applicability of the Auto Suture, Models TA-55 and GIA, in intestinal urinary conduit and urinary bladder surgery; and to study the long-term effects of variably longitudinally reduced ileal ureters on renal function and on qualitative and quantitative changes in urine and serum.

METHOD

Phase I - divide the urinary bladder in a female dog with the GIA Auto Suture; obtain baseline split renal collections for volume, electrolytes, BUN, creatinine, Ca, phosphorus, protein, glucose, oxalate, pH, and osmolality determinations; obtain simultaneous serum samples for electrolyte, BUN, creatinine, Ca, phosphorus, glucose, and protein determinations; and determine the renal function by excretory urogram.

Phase II - Group I - one ureter will be replaced with a pedicled vascularized distal ileal segment according to techniques used by Goldstein and others. Group II - will have an appropriate segment of ileum isolated on a vascular pedicle. An ileo-ileostomy is carried out to reestablish bowel continuity. The pedicled ileal segment is sutured longitudinally parallel to the mesenteric border of the ileum by applying the TA-55 or GIA Auto Suture, longitudinally bisecting the ileum between its mesenteric and antimesenteric borders. The sequence is repeated until the ileal segment is longitudinally bisected and a 50% reduction in surface area is noted. A proximal ileo-pyelo and a distal ileo-vesicle anastomosis is carried out. Group III - will

undergo the same procedure as Group II dogs except that the ileal segment will be reduced to an even smaller lumen, i.e., a 24 French caliber ileal tubular segment.

Qualitative and quantitative split urine collections and serum determinations are repeated as in Phase I in the postoperative period. Radiologic contrast studies, consisting of intravenous pyelograms, retrograde cystograms and fluoroscopic evaluation of the upper and lower urinary tracts, will be done. Urine collections, serum determinations, and radiologic contrast studies will be repeated at 6 weeks, 3, 6, and 12 months post-ureteral replacement surgery. Following initial evaluation of what appears to be the more ideal ileal segment for ureteral replacement, a contralateral nephrectomy will be considered in order to simulate more effectively the patient who has only one functioning kidney remaining. At completion of the investigation, perform unilateral nephrectomies with hemicystectomies or sacrifice the dogs for gross and microscopic evaluation of kidneys, ileal ureters, and bladder.

PROGRESS

(77 05 - 77 09) Initial surgery has commenced and the protocol is proceeding according to the plan.

STATUS: (O)

TITLE: Nonsurgical Recording of Human Acoustic Nerve Action Potentials in Differential Diagnosis of Auditory Problems in Patients with Hearing Loss

PRINCIPAL INVESTIGATOR: CPT S. Dean Harmer, MSC

WORK UNIT NO: 73/33

TECHNICAL OBJECTIVE

Objective assessment of cochlear reserve on patients with hearing loss of sudden onset. To determine if the acoustic nerve action potential produced by click stimulus demonstrates cochlear hair cell reserve more accurately than does tone audiometry and if acoustic nerve action potential indicates recovery rate of sudden hearing loss more accurately than does pure tone audiometry.

METHOD

Perfect the measurement procedure on normals measuring whole nerve action potentials. Perform procedure on conductive and sensorineural loss to obtain standard for differential diagnosis with our specific equipment. Perform procedure on all patients entering ENT Clinic, Madigan Army Medical Center, with complaint of hearing loss of sudden onset. An active electrode wrapped in cotton soaked with sterile saline is gently lowered into the canal to finally rest against the tympanic membrane. This wire electrode is held in a stationary position by taping the wire to the ear lobe. The testing procedure involves presenting a number of clicks at specific intensity levels to the ear from a distance of 12 inches through a small speaker. The last procedure will consist of comparing pure tone audiometry and action potential results during the treatment procedure utilized by the ENT physician.

PROGRESS

(76 06 - 77 08) The principal investigator was changed from CPT David G. Cyr, MSC, to CPT Harmer. During FY76, approximately 60% of the total projected patients had been run. No further work was accomplished in FY77. This protocol has been terminated and combined with the protocol "Nonsurgical Recording of Human Acoustic Nerve Action Potentials in Differential Diagnosis of Auditory Problems in Normals" to form a new protocol entitled "Brainstem Electric Response Audiometry with High Frequency Hearing Loss" which is awaiting approval to proceed from the HSRRB.

STATUS: (T)

TITLE: Nonsurgical Recording of Human Acoustic Nerve Action Potentials in Differential Diagnosis of Auditory Problems in Normals

PRINCIPAL INVESTIGATOR: CPT S. Dean Harmer, MSC

WORK UNIT NO: 73/36

TECHNICAL OBJECTIVE

Objective test procedure for patients demonstrating pseudohypoacousis. To determine if the acoustic nerve action potential procedure by click stimulus demonstrates threshold levels more accurately than pseudohypoacousis and if acoustic nerve action potential procedure by click stimulus speeds up the diagnostic process as opposed by psychogalvonic skin response audiometry in the diagnosis of pseudohypoacousis.

METHOD

Perform the measurement procedure on normals measuring whole nerve action potentials. Perform procedure on all patients entering the ENT Clinic with complaint of hearing loss and suspect of pseudohypoacousis. An active electrode wrapped in cotton soaked in sterile saline is gently lowered into the canal to finally rest against the tympanic membrane. This wire electrode is held in a stationary position by taping the wire to the ear lobe. The testing procedure involves presenting a number of clicks at specific intensity levels to the ear from a distance of 12 inches through a small speaker. The responses are then amplified and averaged by a signal averaging computer to obtain the test findings.

PROGRESS

(76 06 77 08) The principal investigator was changed from CPT David G. Cyr, MSC, to CPT Harmer. During FY76, approximately 40% of the total projected patients had been tested. No further work was accomplished in FY77. This protocol has been terminated and combined with the protocol "Nonsurgical Recording of Human Acoustic Nerve Action Potentials in Differential Diagnosis of Auditory Problems in Patients with Hearing Loss" to form a new protocol entitled "Brainstem Electric Response Audiometry with High Frequency Hearing Loss" which is awaiting approval to proceed from the HSRRB.

STATUS: (T)

TITLE: Parent-Infant Screening Program

PRINCIPAL INVESTIGATOR: CPT S. Dean Harmer, MSC

WORK UNIT NO: 77/80

TECHNICAL OBJECTIVE

To accurately identify those newborns suspected of having significant hearing loss since much can be done to help the hearing impaired child if the loss is detected early in life.

METHOD

A questionnaire concerning response to sound will be given to the mother of each newborn child when she takes the child home for the first time. The mother will return the questionnaire to the baby's first checkup. It will be reviewed by the examining physician who will note the results in the baby's record. Abnormal findings will be referred to Audiology Clinic for audiometric testing, and the questionnaire will be returned to the Audiology Clinic for a compilation of results.

PROGRESS

(77 05 - 77 09) Distribution of the questionnaire has begun. No evaluation is possible at this time.

STATUS: (O)

TITLE: Medical Treatment of the Frey Syndrome

PRINCIPAL INVESTIGATOR: LTC Leonard L. Hays, MC

WORK UNIT NO: 76/06

TECHNICAL OBJECTIVE

To study objectively the true incidence of the Frey Syndrome in post-parotidectomy patients by means of the Minor Starch Iodine Test; to determine the effect of and patient satisfaction with medical management; to investigate the value and practicality of iontophoresis of the above agents; to investigate the value of surgical correction such as tympanic neurectomy, etc.; to compare electromygraphic studies of severely involved cases of Frey syndrome to a comparable group of asymptomatic cases using the unoperated side as a control; other studies as time permits.

METHOD

Phase I - Double-blind treatment with ½%, 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 failed 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.

PROGRESS

(76 06 - 77 09) Approximately 20 patients have been treated (one patient requested tympanic neurectomy). Scopolamine in particular was noted to have a great variation in efficacy between individual patients, necessitating adjustment in dosage

from 0.25% or less to at least 3% in some patients with thicker skin. Individual variation of dosage was necessary to reduce the incidence of systemic side effects, particularly oral dryness or dry eyes.

Glycopyrrolate in concentrations of 0.5% and 1% provided complete effective control of at least several days duration after a single application. Accurate topical placement of the drug is emphasized, using a sketch of the patient's Minor Starch Iodine Test. There have been no significant side effects with the use of glycopyrrolate.

A technique for the iontophoresis of 0.1% glycopyrrolate solution was developed in order to compare the efficacy of iontophoretic application of glycopyrrolate to topical application. Iontophoresis resulted in immediate complete inhibition of gustatory sweating but often produced the systemic side effect of significant oral dryness without increasing duration of inhibition, and, therefore, was not further investigated.

At present research efforts involve ten of the original patients comparing glycopyrrolate in an improved cream base (HEB base) to a roll on (deodorant type) dispenser application.

STATUS: (O)

TITLE: Teaching Program for Practical Microsurgery

PRINCIPAL INVESTIGATOR: MAJ Stanley Jackson, MC

WORK UNIT NO: 77/92

TECHNICAL OBJECTIVE

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

METHOD

The teaching program will be established at Clinical Investigation Service, 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

(77 09 - 77 09) Assemblage of equipment has begun.

STATUS: (O)

TITLE: Split Renal Determination of Protein Following Unilateral Ligation of Renal Vein

PRINCIPAL INVESTIGATOR: MAJ Patrick W. Kronmiller, MC

WORK UNIT NO: 76/27

TECHNICAL OBJECTIVE

To attempt to produce the nephrotic syndrome (proteinuria) by ligation of a single or both renal veins and determine the relative time between ligation and onset of proteinuria. To quantitate, by split renal collection, the proteinuria and determine unilateral predominance. To examine renal biopsy specimens with light microscopy and electron microscopy and correlate clinical findings with microscopic changes. To study collateral venous circulation post renal vein ligation.

METHOD

Divide the urinary bladder in a female dog and obtain baseline serum and urine studies to include serum total protein, albumin, cholesterol, creatinine and BUN, and urine protein, lipid, creatinine, urea, and glucose. Two weeks following bladder division, ligate the right renal vein, and measure serum and urine values serially, post ligation. If results are inconclusive after a period of ten days, perform ligation of the left renal vein at the junction with the vena cava and repeat serial serum and urine determinations. Consistent with the incidental objective, perform left renal venography using the proximal renal vein on the left to observe and identify collateral circulation. If venograph or arteriography is satisfactory, right sided studies may also be attempted. A total of seven dogs will be studied.

PROGRESS

(77 06 77 09) Findings: Proteinuria can be produced with unilateral renal vein occlusion. Complete ligation of the renal vein results in marked contralateral proteinuria. Complete ligation results in persistent proteinuria. Partial occlusion of the renal vein results in moderate proteinuria

which resolves with the formation of adequate collateral circulation, usually within six weeks following ligation.

The observations in this study have resulted in publication and presentations at the Kimbrough Urologic Seminar, San Diego, CA (1976) and the Western Section of the American Urologic Association, San Francisco, CA (1977).

STATUS: (C)

TITLE: Jejuno-ileal Bypass Surgery for Morbid Obesity

PRINCIPAL INVESTIGATOR: COL Joseph C. McDonald, MC

WORK UNIT NO: 77/81

TECHNICAL OBJECTIVE

To reduce the morbidity and mortality of morbidly obese patients by achieving weight reduction through partial defunctionalizing of the small bowel.

METHOD

Criteria: Subjects must demonstrate a minimum of 100% above ideal body weight; a weight problem for five years; evidence of failure of dietary and/or group therapy measures for weight reduction; age under 50 years; absence of causative endocrine or metabolic dysfunction or unrelated medical disease which would contraindicate operation; presence of complications of obesity; no history of ethanol abuse and a commitment to avoid ETOH for three years postoperatively; mental and emotional stability to tolerate the operation and its postoperative sequelae; and assurance of cooperation in the conduct of necessary pre- and postoperative studies. Once selected for jejunoileal bypass, the patient will undergo extensive pre-operative evaluation by the Gastroenterology Service, followed by jejunoileal bypass and ileo-cecostomy. Immediate postoperative care will be carried out by the surgeons with appropriate consultation. Long term follow-up care will be conducted by each involved service.

PROGRESS

(77 06 - 77 09) The present status of this procedure is controversial; therefore, the protocol was activated per a message from HQDA, DASG-HCP, 180800Z, Mar 77. One patient has had surgery on this study. There were no complications, but no weight loss had been reported to date.

STATUS: (O)

TITLE: A Teaching Model for Vascular Anastomoses, Arterial and Venous

PRINCIPAL INVESTIGATOR: LTC William H. Martin, MC

WORK UNIT NO 75/11

TECHNICAL OBJECTIVE

To teach surgical residents correct technique and approach to vascular anastomoses of various sizes. To evaluate the success of such anastomoses on short term patency.

METHOD

Preliminary vascular anastomoses will be performed on a bench test model from cadaver vessels. In the second stage, various anastomoses will be made in dogs under general anesthesia in the extremities and then in the abdomen and finally in the chest. Regular teaching sessions will be scheduled for the residents weekly for those who are in off-service rotation and on the Clinical Investigation Service. The residents will thus throughout the year have first hand opportunity to perform these anastomoses and later apply them in the operating room. It is anticipated that the length of the program will be nine months. Facility to be used is the Clinical Investigation Service operating room.

PROGRESS

(76 06-77 09) None. This study was terminated due to the departure of two consecutive principal investigators - COL Frances J. Heck, MC, and LTC William H. Martin, MC.

STATUS: (T)

TITLE: Lid Magnets for Correction of Orbicularis Palsy

PRINCIPAL INVESTIGATOR: COL Stanley C. Sollie

WORK UNIT NO: 75/27

TECHNICAL OBJECTIVE

To study the effects of the insertion of lid magnets on the tarsal plates of the lids involved in seventh nerve palsy.

METHOD

Patients with seventh nerve palsy will be evaluated, and, if the palsy persists longer than six months without showing improvement and if the eye is affected by the lack of lid closures, these patients will be considered for the surgery. The surgery consists of implanting lid magnets, supplied through Wolfgang D Muhlbauer, Department of Plastic and Reconstructive Surgery, Klinikum rechts der Isar of the Technical University, Munich, Germany. A skin incision is made in the upper and lower lid and the magnets are sutured to the tarsus. The skin incision is then closed.

PROGRESS

(76 06 - 77 09) Lid magnets have been inserted in five patients at Madigan Army Medical Center with good success. This is an ongoing project, and it is hoped that other patients will be included in the study.

STATUS: (O)

TITLE: An Investigation To Compare the Effect on Renal Function of Conservative versus Surgical Management of Blunt Renal Trauma in Canines

PRINCIPAL INVESTIGATOR: CPT Jonathan S. Vordermark, MC

WORK UNIT NO: 76/16

TECHNICAL OBJECTIVE

To compare the morbidity and mortality of conservative (non-operative) versus surgical treatment of cortical lacerations analagous to those produced by non-penetrating trauma in man; to compare pre- and post-trauma renal function in these two groups and determine the therapy that provides the maximum preservation of renal function; and to determine the effect of these two therapeutic modalities on the development of hypertension via the renin-angiotensin system.

METHOD

Ten dogs weighing 25-35 pounds will be used for long term management. These dogs will be divided into two groups (surgical and conservative). Baseline CSC, Na, BUN, creatinines will be drawn. After the induction of anesthesia, pre-trauma urograms will be obtained in addition to urinalysis, urine culture and blood pressure. Only one renal unit will be studied so that each dog can act as his own control. Trauma will be induced through a flank incision by driving a dull cold chisel one cm into the lower pole cortex to form a cross-shaped laceration. The kidneys will be replaced and a 30-minute post-trauma arteriogram will be obtained. The dogs to be treated surgically will undergo heminephrectomy and the remainder will be observed. Three months post-trauma repeat laboratory studies to include renins, BP, urograms, and arteriograms will be taken. The animals will then be sacrificed and the kidneys examined both grossly and microscopically.

PROGRESS

(76 06 - 77 09) All preliminary work has been completed. The main body of the project will be completed in February. All necessary funds have been allocated.

STATUS: (O)

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