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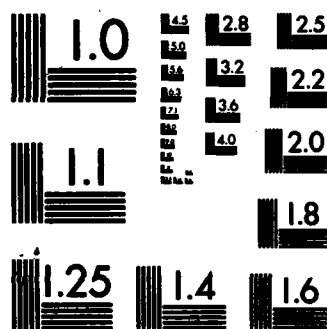
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MEDICAL CENTER SAN FRANCISCO CALIF 01 OCT 83 MED-300

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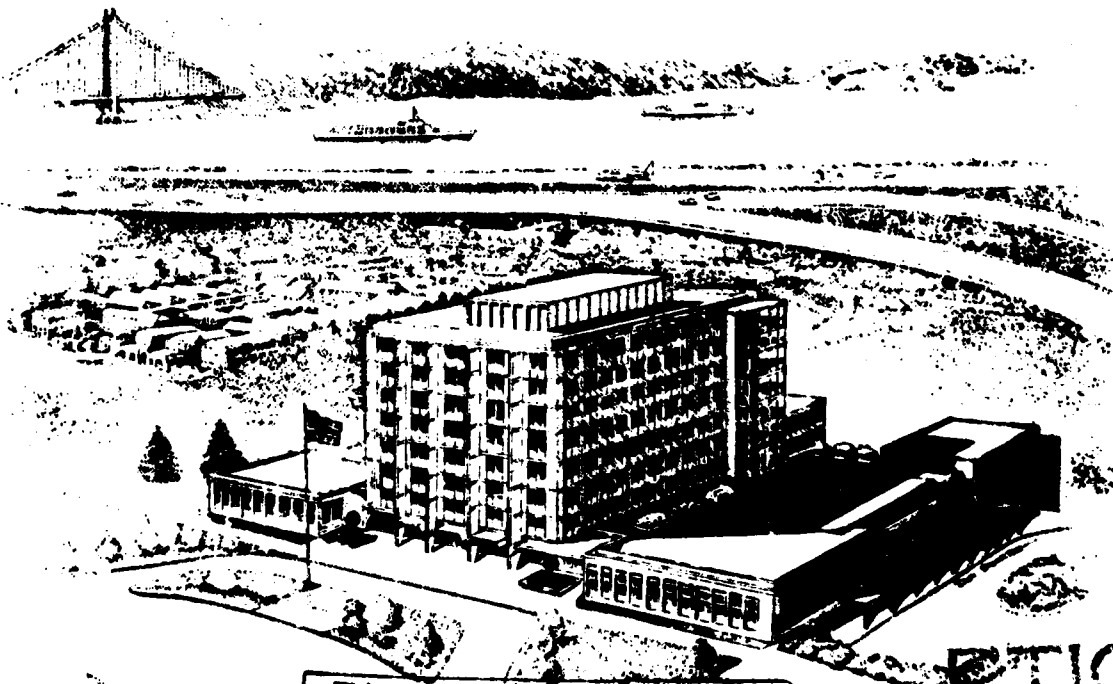
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# Department of Clinical Investigation

## Annual Progress Report

Fiscal Year 1983



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Letterman Army Medical Center

Presidio of San Francisco

California 94129

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20. ABSTRACT (Continue on reverse side if necessary and identify by block number)  ✓ This report identifies the research activities conducted by Letterman Army Medical Center investigators through protocols approved by the Clinical Investigation, Human and Animal Use Committees during FY 1983. A			

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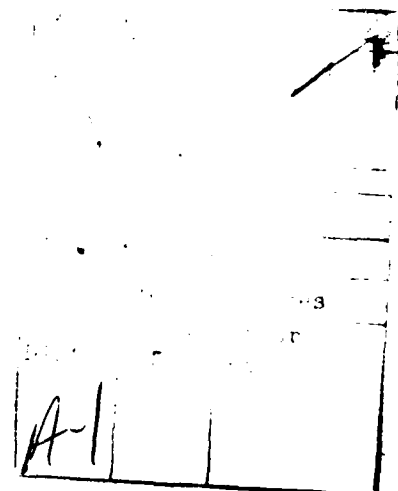
CLINICAL INVESTIGATION

PROGRAM REPORT

1 October 1983

CONTROL SYMBOL: MED-300

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## Foreward

Clinical Investigation plays a critical role in the modernization of a hospital. New equipment, medications, and procedures can safely be tested and introduced through an investigational process. Often awareness of new approaches are obtained through library research completed in preparation of a research protocol.

Research experience helps the busy clinician critically review current publications. Detection of any areas of poor design and faulty conclusions requires experience and prevents erroneous changes in practice.

Great teaching programs tend to have great clinical research programs. The linkage may be due to more than direct contributions of research to better understanding of medicine and thus better teaching. Leading clinicians and teachers tend to also be eminent researchers. It is reasonable to attribute this to the impatience of great clinicians to look ahead and start practicing tomorrow's medicine today. The brighter clinician is more apt to appreciate future needs in medicine and to perceive the gaps in knowledge that must be bridged by research.

Gifted students migrate to programs with a strong research reputation. There is a luster and magic to research that is profoundly credible to students. This is particularly true of the gifted medical student that is sensitive to the mystery of life and to the pioneer role of research in its exploration of the unknown.

Excellence in Clinical Investigation is the theme of this annual report. This medical center has set high standards of excellence in Clinical Investigation. Readers of the reports in this publication will no doubt agree.



KAY R. KYSER, M.D., Ph.D

COL, MC

Chief, Department of Clinical Investigation

## Unit Summary

Fiscal Year 1983

### A. Objectives

The objectives of the Department of Clinical Investigation are as follow:

1. To provide new information to improve the quality of care rendered to patients.
2. To assure the highest level of professional and ethical standards in the conduct of human and animal research.
3. To encourage and support participation by house and teaching staff in the conduct of clinical and applied basic science research.
4. To develop an atmosphere conducive to recruitment and retention of competent, motivated personnel.
5. To function as an important motivating force in the education of house staff.
6. To provide technical and logistical support for investigators assigned currently to regional MEDDAC units.
7. To maintain the high standards required for accreditation of advanced health programs.

### B. Technical Approach

All investigational and training activities fall within the purview of the Department of Clinical Investigation and are reviewed under the guidance of AR 40-7, AR 40-38, AR 40-25, AR 70-18 and HSC Reg 40-23. If approved for conduct and funding, all are monitored carefully to insure strict compliance with applicable regulations.

### C. Department of Clinical Investigation Staff

Kyser, Kay A.	COL 60J9B	Chief/Gynecologist
Watson, Richard A.	COL 60K9B	Assistant Chief/Urologist
Danley, David L.	CPT 68C9C	Laboratory Director/Immunologist
Monteverde, Michael	SSG 92B30	Med Lab NCOIC
Stinnett, Therese M.	SP5 01H20	Biological Sciences Assistant
Smart, Thomas P.	SP5 91T20	Animal Care Specialist
Hunt, Marjorie K.	SP4 01H10	Biological Sciences Assistant
Trom, Virginia	Sp4 01H10	Biological Sciences Assistant
Wade, Charles E.	GS12 22662S	Research Physiologist
Brooks, Daniel E.	GS9 00644	Medical Technician
Coppes, Valerie G.	GS8 00404	Biological Laboratory Animal Technician
Polakoff, Josephine A.	GS7 00644	Medical Technician
Villaflor, Marina E.	GS5 00318	Secretary/Typist

### D. Funding Data

Civilian Personnel (to include benefits)	\$ 93,387.00
Consumable Supplies	69,449.00
Other Purchased Services (LAIR)	184,496.00
Travel (conference only)	520.00
Consultants	1,516.00
MED CASE	102,000.00
Capital Expense	6,019.00
Military Pay	160,982.00
<b>TOTAL</b>	<b>\$ 618,369.00</b>

### E. Disposition of Protocols - FY 1983

97	Ongoing
29	Completed
15	Terminated
1	Transferred

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142	Total
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Department of Clinical Investigation

Annual Report

Fiscal Year 1983

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### Legend

- (O) Ongoing  
(T) Terminated  
(Tr) Transferred  
(C) Completed

Detail Summary Sheet

Date: 3 Aug 83

Prot. No.: AC-83-01

Status: Ongoing

Title: Argon laser treatment of actinic keratoses.

Start Date: Aug 83

Est Comp Date: 1984

Principal Investigator:  
COL WJ Hennessy, MD

Facility:  
LAMC

Dept/Svc:  
Ambulatory Care

Associate Investigators:  
E Beatrice, MD  
B Stuck, MS

Key Words: argon laser, actinic keratoses

Accumulative MED CASE  
Cost:

Est Accumulative  
OMA Cost:

Periodic Review  
Results:

Study Objective: To determine whether a 3-5 day course of topical 5-FU will photosensitize premalignant skin lesions so that they may be effectively treated with argon laser irradiation.

Technical Approach: A test area of forehead skin with prominent actinic keratoses will be treated for 3-5 days with topical 5-FU. Control site will also be treated with 5-FU. When inflammatory response has occurred, test site will be irradiated with argon laser photocoagulator at predetermined irradiance, exposure duration and irradiance diameter. Test and control site will be examined at 3, 6, and 12 months post treatment. Clinical photos will be obtained. Conclusions will be drawn by comparing the test and control sites utilizing clinical photographs, a clinical rating scheme, total treatment time comparison, healing time comparison, relative incidence of any adverse effects, and patient preference.

Progress: Protocol newly approved. Patients to be accrued.

Detail Summary Sheet

Date: 20 Sep 83

Prot No: Ci-81-01

Status: Ongoing

Title: The role of sex hormone-binding globulin (SHBG) in the pathogenesis of benign prostatic hypertrophy (BPH).

Start Date: 14 Apr 81

Est. Comp. Date: Jun 84

Principal Investigator:  
CE Wade, PhD

Facility:  
L A M C

Dep/Svc:  
Clinical Investigation

Associate Investigators:  
LTC CA Winkel, MD  
LTC G Deshon Jr, MD

Key Words: sex hormone-binding globulin, SHBG, prostatic hypertrophy, BPH

Accumulative MED CASE  
Cost: None

Est Accumulative  
OMA Cost: \$3,000

Periodic Review  
Results:

Study Objective: The etiology of benign prostatic hypertrophy (BPH) remains to be elucidated completely. An important issue in this disease is that of the importance of sex hormones in the pathophysiology of BPH. In this investigation we seek to ascertain whether the percentage of free sex steroid, androgen and estrogen, is different among men with BPH compared to normal males. Moreover, we seek to ascertain differences, either qualitative or quantitative, in SHBG in plasma of men with BPH compared to normal males.

Technical Approach: Samples of plasma are incubated with  $3H$ -steroid and [ $^{14}C$ ] glucose and subjected to centrifugal ultrafiltration through a dialy b are a 37C. The percentage of free estradiol, testosterone, and progesterone in serum are estimated by comparing the ratio of  $3H$ -steroid to [ $^{14}C$ ] glucose in the ultrafiltrate with the corresponding ratio in the serum retained by the dialysis membrane.

Progress: Thirty-two patients have been accrued on this study. Plasma samples have been collected and frozen. Assays for testosterone, estrone, estradiol, androstenediol and SHBG binding capacity will be performed when 50 samples have been obtained. Further age-match controls for some of the subjects will be entered into the study. This protocol hopefully will be completed within the next year.

Detail Summary Sheet

Date: 20 Sep 83

Prot No.: Ci-81-02

Status: Completed

Title: The effect of dietary iron restriction on gastrointestinal metmyoglobin (METMB) reductase activity.

Start Date: 14 Jul 81

Est Comp Date: Completed

Principal Investigators:

LTC CA Winkel, MD

Facility:

L A M C

Dept/Svc:

Clinical Investigation

Associate Investigators:

Key Words: metmyoglobin reductase, dietary iron restriction

Accumulative MED CASE

Cost: None

Est Accumulative

OMA Cost: \$2000

Periodic Review

Results:

Study Objective: To obtain a more thorough understanding of the mechanisms which control gastrointestinal absorption of dietary iron. Therefore, we hope to ascertain (1) the effect of dietary iron restriction on levels of metmyoglobin reductase activity; (2) the function of metmyoglobin reductase in gut mucosa; and (3) the importance of metmyoglobin in iron absorption.

Technical Approach: Male weanling rats were obtained at a weight of 50 g. They were divided into two groups. One group received an iron deficient diet for seven weeks. The other group received an iron replete diet. At the end of this time period the rats were sacrificed and the gut mucosa was isolated. Metmyoglobin reductase activity was determined using spectrophotometric analysis of the reduction of metmyoglobin.

Progress: This protocol has been completed and the data is presently undergoing analysis.

Detail Summary Sheet

Date: 20 Sep 83

Prot No.: Ci-81-03

Status: Terminated

Title: Pharmacokinetics of various cephalosporins employed for treatment of acute pyelonephritis.

Start Date: 18 Aug 81

Est Comp Date: Terminated

Principal Investigators:

LTC CA Winkel, MD

CPT G Boswell, PhD

Facility:

LAMC

Dep/Sec:

Clinical Investigation

Associate Investigators:

Key Words: pharmacokinetics, cephalosporin, pyelonephritis, antibiotics

Accumulative MEDCASE

Cost: None

Est Accumulative

OMA Cost: \$2,000

Periodic Review

Results:

Study Objective: The purpose of this study is to determine the usefulness of a computer modeling approach in selecting the optimum dose of a cephalosporin antibiotic in treating pyelonephritis. In addition, the variations in pharmacokinetics of a number of cephalosporins will be tested employing the computer model.

Technical Approach: Patients admitted to LAMC with a diagnosis of acute pyelonephritis will be entered into the study. They will receive, in a double blinded fashion, a first, second, or third generation cephalosporin antibiotic. Blood and urine samples will be obtained and antibiotic levels determined by standard techniques. These data will be entered into the computer model to determine clinical usefulness in predicting pharmacokinetics in vivo.

Progress: This study has not been commenced at the present time and LTC Winkel has been transferred out of the area. Thus this protocol has been terminated.

Detail Summary Sheet

Date: 5 Jul 83

Prot. No.: Ci-81-04

Status: Completed

Title: Double-blind phase III comparative evaluation of MONISTAT 7 vaginal cream in the treatment of Haemophilus (Gardnerella) vaginalis vaginitis.

Start Date: 3 Sep 81

Est Comp Date: Completed

Principal Investigator:

LTC CA Winkel, MD

LTC J Elliott, MD

Facility:

LAMC

Dept/Svc:

Clinical Investigation

Associate Investigators:

Key Words: MONISTAT 7 vaginal cream, Haemophilus (Gardnerella) vaginalis

Accumulative MEDCASE

Cost:

Est Accumulative

OMA Cost:

Periodic Review

Results:

Study Objective: To determine the efficacy of MONISTAT vaginal cream in treating Gardnerella vaginitis.

Technical Approach: Double blind use of MONISTAT, flagyl and placebo to treat Gardnerella.

Progress: Twenty-two patients have been enrolled in this study which has been completed.

Detail Summary Sheet

Date: 1 Sep 83

Prot. No.: Ci-81-05

Status: Completed

Title: The role of progesterone and metabolism of progesterone in regulation of function of the thymus.

START Date: 8 Dec 81

Est Comp Date: Completed

Principal Investigator:  
LTC CA Winkel, MD

Facility:  
LAMC

Dept/Svc:  
Clinical Investigation

Associate Investigators:  
CPT DL Danley, PhD

Key Words: 21-steroid hydroxylase, deoxycorticosterone

Accumulative MED CASE  
Cost: \$20,000

Est Accumulative  
OMA Cost: \$6000

Periodic Review  
Results:

Study Objective: In previous studies we established that guinea pig spleen has considerable steroid 21-hydroxylase activity and that the activity of this enzyme may be altered significantly by administering steroids or by immunizing the animals prior to assay. The objective of this study is (a) to establish the cellular site of 21-hydroxylase activity within the spleen; (b) to determine whether changes in enzyme activity are related to changes in cell population within the spleen or to enzyme levels within the cells; and (c) to examine the enzyme activity in different strains of guinea pigs to determine if it is linked to the histocompatibility genotype.

Technical Approach: Guinea pigs will be decapitated and then spleens removed for processing. To obtain microsomal preparations containing steroid 21-hydroxylase, spleens will be homogenized and microsomes isolated by ultracentrifugation. Enzyme activity will then be measured by incubating microsomes with 3H-progesterone and an NADPH-generating system. Labeled deoxycorticosterone levels will be measured by purifying this hormone by three successive TLC and three crystallization steps.

Progress: Approximately 80 guinea pigs have been sacrificed and studied for enzyme activity. Our findings show that steroid 21-hydroxylase activity was suppressed by injecting animals with complete Freund adjuvant or killed Mycobacterium tuberculosis but not by incomplete Freund adjuvant. Kinetic studies suggest the suppression is due to a change in enzyme level rather than a change in enzyme

specificity. A comparison of steroid 21-hydroxylase activity in strain 2, strain 13, and C-4 deficient guinea pigs show no consistent variation that might be attributable to histocompatibility differences.

Publications and Presentations:

1. Winkel CA, Casey ML, Wade CE, Danley DL, MacDonald PC: Conversion of progesterone to deoxycorticosterone in guinea pig spleen: an animal model for the study of steroid 21-hydroxylase activity in extraadrenal sites. J Steroid Biochem 18 (in press).
2. Winkel CA, Casey ML, MacDonald PC, Uhr J, and Danley DL: Steroid 21-hydroxylase activity in guinea pig spleen: a potential factor in the regulation of splenic lymphocytic function (abstract). Midwinter Conference of Immunologists.

Detail Summary Sheet

Date: 20 Sep 83

Prot. No.: Ci-81-06

Status: Terminated

Title: Evaluation of cortisol-conjugated polyacrolein microspheres to affect immunocyte function in vitro.

Start Date: 1981

Est Comp Date: Terminated

Principal Investigator:  
CPT DL Danley, PhD

Facility:  
LAMC

Dept/Svc:  
Clinical Investigation

Associate Investigators:  
LTC CA Winkel, MD

Key Words: cortisol-conjugated microspheres, glucocorticoids, immune suppression

Accumulative MED CASE  
Cost:

Est Accumulative  
OMA Cost:

Periodic Review  
Results:

Study Objective: The objective is to determine whether or not cells respond in vitro to the cortisol-conjugated microspheres (CCM) as they do to the unconjugated hormone. Moreover, during this investigation we will also develop and evaluate assays that quantitate the effects of glucocorticoids on different immunocyte populations. We anticipate that these assays will have application in future studies on corticosteroids and immune suppression.

Technical Approach: Polyacrolein microspheres will be produced and conjugated with hydrocortisone 21-hemisuccinate. In-vitro-cell assays will be recovered from 100 congenic mice strain dba/2, and if they differ from normal cells, the cells that demonstrate the greater sensitivity to cortisol will be used. We will examine the T-cell reactivity and examine the PMN reactivity.

Progress: Polyacrolein microspheres were produced by Dr. Richard Yen; however, he was unable to conjugate cortisol hemisuccinate to them. He then prepared another form of microsphere to which cortisol conjugated bovine serum albumin could be attached. This reagent was also unsatisfactory for conjugation experiments. This protocol was terminated.

Detail Summary Sheet

Date: 1 Nov 82

Prot. No.: Ci-82-07

Status: Ongoing

Title: Production of reactive oxygen species by Candida albicans (fungus).

Start Date: 5 Jan 82

Est Comp Date: 1984

Principal Investigator:  
CPT DL Danley, PhD

Facility:  
L A M C

Key Words: C. albicans, polymorphonuclear leukocytes

Dept/Svc:  
Clinical Investigation

Associate Investigators:  
LTC CA Winkel, MD

Accumulative MEDCASE  
Cost: \$48,000

Est Accumulative  
OMA Cost: \$6000

Periodic Review  
Results: N/A

Study Objective: The production by C. albicans may profoundly affect the interaction between the fungus and the host. To examine this possibility, we propose to examine the oxidative metabolism of C. albicans with particular emphasis on determining the biochemical pathway and the physical site(s) for the generation of  $O_2^-/H_2O_2$ ; determine how the generation of  $O_2^-/H_2O_2$  by C. albicans influences the viability and function of host cells in vitro; and to screen a variety of species and strains of Candida for their capacity to release  $O_2^-/H_2O_2$  and test high and low producers for virulence in mice.

Technical Approach: Candida albicans yeast phase cells will be grown overnight at 25C and transferred to fresh medium at 37C for 2 h. Cells initiating log-phase growth appear to produce optional amounts of hydrogen peroxide. These cells will then be examined for their ability to influence the metabolism and viability of polymorphonuclear leukocytes (PMN) in vitro. Yeast cells and PMN will be incubated together at 37C and cell viability will be measured using vital dyes and fluorescence microscopy. Cell metabolism will be evaluated by measuring  $H_2O_2$  production, glucose metabolism, and  $O_2$  consumption.

Progress: Our studies show that low numbers ( $<10^7$  cells/ml) of C. albicans release  $H_2O_2$  in vitro while higher numbers ( $>10^7$  cells/ml) do not. In fact, higher number of fungi release a soluble substance which inhibits  $H_2O_2$  reactivity with peroxidase in

the fixation of radiolabeled iodide or the oxidation of o-dianisidine. Biochemical characterization of this substance is currently being conducted. Preliminary studies on the interaction of C. albicans with PMN indicate that PMN are killed and lysed following phagocytosis of yeast cells. The extent of cytolytic activity by C. albicans appears to be related to viability of the fungus and the temperature at which it is cultivated, i.e., yeast cells grown at 37C are more cytopathic than killed cells or those grown at 5 or 25C.

Publications/Presentations:

1. Danley DL, Winkel CA, Hilger AE: Inhibition of  $H_2O_2$  reactivity by a soluble factor released from Candida albicans. Annual Meeting of the American Society for Microbiology, 1983.
2. Danley DL, Hilger AE, Winkel CA: Generation of hydrogen peroxide by Candida albicans and influence on murine polymorphonuclear leukocyte activity. Infect. and Immun. 40:97-102.

Detail Summary

Date: 15 Sep 83

Prot. No.: C1-82-08

Status: Ongoing

Title: Interaction of plasma osmolality and blood volume in the regulation of plasma vasopressin concentrations.

Start Date: 2 Feb 82

Est Comp Date: 1984

Principal Investigator:  
CE Wade, PhD

Facility:  
LAMC

Key Words: osmoreceptor, plasma osmolality, plasma vasopressin

Dept/Svc:  
Clinical Investigation

Associate Investigators:  
LTC CA Winkel, MD

Accumulative MEDCASE  
Cost: \$6000

Est Accumulative  
OMA Cost: \$3000

Periodic Review  
Results:

Study Objective: To evaluate the osmotic response of the central osmoreceptor regulating plasma vasopressin levels following graded reductions in blood volume produced by hemorrhage.

Technical Approach: Ten dogs will be surgically prepared with carotid loops and allowed 6-8 weeks to recover. This procedure involves isolation of the common carotid arteries which are exteriorized in a piece of skin allowing easy access to vessels. The dogs will be individually housed and maintained on standard laboratory dog chow. The dogs will be trained to stand quietly in a modified Pavlov stand in the laboratory where the experiments will be performed. Each dog will undergo all of the experimental procedures.

Progress: Six animals have been surgically prepared for this protocol and have been evaluated in a series with progressive hemorrhages and an increase in renin activity and plasma vasopressin concentration. Removal of 5 percent of the calculated blood volume did not significantly alter mean arterial pressure or plasma vasopressin levels. Upon an increase of jugular plasma osmolality via bilateral intracarotid infusions of hypertonic saline, elevating osmolality by 15 mOsm/k, a significant increase in plasma vasopressin concentrations was noted in both the control and hemorrhage procedures. There was no significant difference in the increase noted in either sets of these animals.

Publications/Presentations:

1. Wade CE, Keil LC, Ramsay DJ: Role of volume and osmolality in the control of plasma vasopressin in dehydrated dogs. *Neuroendocrinology* (in press).
2. Wade CE, Keil LC, Ramsay DJ: Potentiation of osmotic reactivity of vasopressin release during sodium depletion and intravenous angiotensin II in conscious dogs (submitted).
3. Wade CE, Thrasher TN, Ramsay DJ: Current concepts of osmotic regulation of vasopressin release. In: Factors Influencing Vasopressin Levels in Body Fluids. Presented at the Thirty-fourth Annual Fall Meeting of the American Physiological Society, 21 August 1983, Honolulu, Hawaii (manuscript in preparation).

Detail Summary

Date: 15 Sep 83

Prot. No.: Ci-82-09

Status: Ongoing

Title: Effect of fluid restriction following caval ligation in dogs on the excretion of sodium, and plasma aldosterone concentration.

Start Date: Apr 82

Est Comp Date: 1984

Principal Investigator:

CPT DL Danley, PhD  
CE Wade, PhD

Facility:

LAMC

Dept/Svc:

Clinical Investigation

Associate Investigators:

LTC CA Winkel, MD

Key Words: antidiuretic hormone, thirst, water metabolism, renin angiotensin system, edema, congestive heart failure

Accumulative MEDCASE  
Cost:

Est Accumulative  
OMA Cost: \$3000

Periodic Review  
Results:

Study Objective: Congestive cardiac failure results in polydipsia and the renal conservation of sodium leading to the formation of edema and ascites. Fluid restriction to pre-failure levels of water intake alleviates the ascites and reduces the edema. In a preliminary study this was associated with an increase in the excretion of sodium concurrent to a reduction in plasma aldosterone concentrations. The present study is designed to confirm these preliminary observations and to possibly identify the factors contributing to the reduction in plasma aldosterone levels.

Technical Approach: The animals will be surgically prepared with chronic femoral vein catheters and daily blood samples obtained. Urine will be collected every 24 hr, the animal weighed, fluid intake measured, food consumption measured and a 20 ml blood sample obtained. During surgery a ligature is placed around the cava. After recovery the animal is returned to its metabolic cage and the daily measurement again started. After this period the animal will be followed for one week on fluid once again ad libitum.

Progress: Initial studies in caval-thoracic vena-caval constriction have been completed. Additional studies were performed on the effects on fluid restriction on the initiation of edema following caval constriction. These studies have been completed and are presently undergoing analysis.

Publications/Presentations:

Thrasher TN, Moore-Gillion M, Wade CE, Keil LC, and Ramsay DJ: Naturesis and the regulation of plasma osmolality in response to water deprivation in the dog. American Journal of Physiology 244:R850-R856, 1983.

Detail Summary Sheet

Date: 31 Aug 83

Prot. No.: C1-82-10

Status: Terminated

Title: Hormonal and vasopressor effects of uterine encasement in the pregnant rabbit.

Start Date: April 82

Est Comp Date: Terminated

Principal Investigator:

LTC CA Winkel, MD

CE Wade, PhD

Facility:

LAMC

Dept/Svc:

Clinical Investigation

Associate Investigators:

CPT DL Danley, PhD

Key Words: hormonal, vasopressin

Accumulative MED CASE

Cost: \$27,000

Est Accumulative

OMA Cost: \$5000

Periodic Review

Results:

Study Objective: The purpose of this study is to ascertain the mechanism(s) involved in the elevation of blood pressure in the pregnant rabbit observed following uterine encasement performed at midgestation.

Technical Approach: Animals will have femoral arterial catheters placed on day 14 of gestation. Blood pressure will be recorded daily. On day 19 of gestation, animals will be anesthetized, isparotomy performed and uterine encasement performed. Animals will be returned to metabolic cages and blood pressure, electrolytes, (serum and urine) and weight will be assessed similarly to that performed prior to isparotomy.

Progress: Because of difficulty in obtaining time dated pregnant rabbits the study remains incomplete. New breeding does and bucks have been received and we are planning to breed animals in quarantine in order to obtain pregnant does for study. Because of reassignment, the protocol was terminated.

## Detail Summary

Date: 31 Aug 83

Prot. No.: Ci-82-11

Status: Completed

Title: Conversion of plasma progesterone to deoxycorticosterone in non-pregnant Macaca mulatta.

Start Date: Feb 82

Est Comp Date: Completed

Principal Investigator:

LTC CA Winkel, MD

CE Wade, PhD

Facility:

LAMC

Dept/Svc:

Clinical Investigation

Associate Investigators:

CPT DL Danley, PhD

Key Words: deoxycorticosterone, progesterone, 21-steroid hydroxylase

Accumulative MED CASE

Cost: \$10,000

Est Accumulative

OMA Cost: \$8000

Periodic Review

Results:

Study Objective: To ascertain the fractional conversion of plasma progesterone to deoxycorticosterone in rhesus monkeys from the relationship between the  $^3\text{H}$ : $^{14}\text{C}$  of the infused tracers, [ $^3\text{H}$ ] Progesterone and [ $^{14}\text{C}$ ] DOC, and the  $^3\text{H}$ : $^{14}\text{C}$  of DOC in plasma, and to establish the rhesus monkey as an animal model for studying steroid 21-hydroxylase activity in nonadrenal tissues.

Technical Approach and Progress: To date six nonpregnant female monkeys have been infused with approximately 250  $\mu\text{Ci}$  [ $^3\text{H}$ ] progesterone and approximately 2  $\mu\text{Ci}$  [ $^{14}\text{C}$ ] deoxycorticosterone over a four hour period. Analysis of blood samples obtained after 3 hours and 30 minutes, 3 hours and 45 minutes and 4 hours of infusion, respectively, is complete. In the six primates studied, extraadrenal conversion of radiolabeled progesterone into radiolabeled deoxycorticosterone has been demonstrated. The transfer constant of conversion of progesterone to deoxycorticosterone in these six monkeys is 0.007 to 2.5, values similar to those observed in humans.

### Presentations/Publications:

1. Winkel CA, Brooks D: Conversion of progesterone to deoxycorticosterone (DOC) in Macaca mulatta (abstract). 30th Ann. Mtg. Soc. Gynecol. Invest., March 1983.
2. Winkel CA and Brooks D: Conversion of plasma progesterone to deoxycorticosterone in nonpregnant Macaca mulatta: an animal model for the study of extraadrenal steroid 21-hydroxylase activity. J. Ster. Biochem. (in press).

Detail Summary Sheet

Date: 15 Sep 83

Prot. No.: Ci-82-12

Status: Ongoing

Title: Role of endogenous opioids in dehydrated dogs on the regulation of hormones effecting fluid and electrolyte balance.

Start Date: 8 Apr 82

Est Comp Date: Indefinite

Principal Investigator:  
CE Wade, PhD

Facility:  
L A M C

Dept/Svc:  
Clinical Investigation

Associate Investigators:  
LTC CA Winkel, MD  
CPT DL Danley, PhD

Key Words: endogenous opioids, plasma vasopressin, aldosterone, naloxone, opioid antagonist

Accumulative MEDCASE  
Cost:

Est Accumulative  
OMA Cost: \$4000

Periodic Review  
Results:

Study Objective: The role of endogenous opioids in the regulation of plasma concentrations of vasopressin and aldosterone in dehydrated dogs will be evaluated by the administration of the opioid antagonist naloxone.

Technical Approach: The animals will be weighed, then transferred to the laboratory. The saphenous vein will be cannulated and blood samples obtained (to measure plasma vasopressin and aldosterone concentrations). The blood pressure will be monitored throughout the period. Intravenous injections of saline or saline plus naloxone will be administered. A two-way analysis of variance of repeated measures will be employed and a New man-Keul test used to examine significance.

Progress: The role of endogenous opioids in the regulation of plasma vasopressin concentration during euhydration and dehydration was assessed in seven conscious dogs by the administration of the opioid antagnoist naloxone (1 mg/k). Plasma

osmolality (pOsm) protein concentration and vasopressin concentrations (pAVP) were measured before and after 24 hours of dehydration. Dehydration significantly elevated pOsm ( $16 \pm 2$  mOsm/kg) (protein -  $0.5 \pm 0.1$  g/dl) and pAVP ( $2.7 \pm 0.7$   $\mu$ /ml). Measurement of these parameters as well as blood pressure and heart rate were made prior to and 10, 20, and 30 minutes following the injection of naloxone or normal saline. Naloxone administration to the hydrated animal did not significantly alter pAVP ( $p - 2.1 \pm 0.6$   $\mu$ /ml) at 30 minutes. The injection of normal saline following dehydration did not change pAVP ( $4.6 \pm 1.9$   $\mu$  U) from the pre-injection values. With dehydration, the naloxone injection produces significant increases in pAVP to  $9.4 \pm 3.0$   $\mu$  U/ml at 30 minutes. In the absence of changes in either plasma osmolality or blood volume indicants (plasma protein or blood pressure), the injection of naloxone increased pAVP in the dehydrated dogs.

To evaluate the osmotic reactivity of plasma vasopressin, we performed additional experiments on six euhydrated dogs. Each dog was intravenously infused twice with hypertonic saline (9.8 mg NaCl/kg/min) over 30 minutes. Each dog was injected with an intravenous bolus of naloxone (1 mg/kg) at the start of one infusion and with an intravenous bolus of saline vehicle at the start of the other infusion. Following naloxone infusion, the plasma vasopressin response to intravenous hypertonic saline was significantly increased.

In summary, the blockade of endogenous opioids with the antagonist naloxone increases the plasma vasopressin levels in dehydrated dogs and potentiates the osmotic release of vasopressin during intravenous infusions of hypertonic saline. On the basis of these findings, we suggest that endogenous opioids inhibit the release of vasopressin during dehydration, possibly as a result of the attenuation of osmotic stimulation.

#### Presentations and Publications:

1. Wade CE: Plasma vasopressin response to intravenous naloxone in euhydrated and dehydrated conscious dogs. Federation Proceedings 42(4):738, 1983.
2. Wade CE: Pituitary and adrenal hormone responses to intravenous naloxone in euhydrated and dehydrated conscious dogs (submitted).

Detail Summary Sheet

Date: 10 Sep 83

Prot. No.: Ci-82-13

Status: Ongoing

Title: Environmental survey at LAMC for Legionnaires Disease Bacteria (LDB).

Start Date: Jul 82

Est Comp Date: Apr 84

Principal Investigator:  
SP/5 T Stinnett

Facility:  
LAMC

Key Words: Legionnaires' Disease Bacteria, environmental

Dept/Svc:  
Clinical Investigation

Associate Investigators:  
LT D Craft, MSC

Accumulative MEDCASE  
Cost:

Est Accumulative  
OMA Cost: \$2000

Periodic Review  
Results:

Study Objective: To sample water and ventilation systems within the LAMC facility for the presence of Legionnaires' Disease Bacteria.

Technical Approach: To obtain water and dust samples which will be tested for the presence of LDB according to the Center for Disease Control methods for the detection of the bacteria.

Progress: Samples have been collected from a variety of sources. The investigator is awaiting the availability of Class II containment facilities for testing to begin.

Detail Summary Sheet

Date: 15 Sep 83

Prot. No.: Ci-82-14

Status: Ongoing

Title: Renal function and aldosterone excretion following repeated long distance running during a 20-day road race.

Start Date: 2 June 82

Est Comp Date: Indefinite

Principal Investigator:  
CE Wade, PhD

Facility:  
L A M C

Dept/Svc:  
Clinical Investigation

Associate Investigators:  
Drs C Haddock and L Hill

Key Words: renal function, aldosterone excretion, Na<sup>+</sup> balance

Accumulative MED CASE  
Cost:

Est Accumulative  
OMA Cost: \$3000

Periodic Review  
Results:

Study Objective: In this present study we seek to investigate further the decrease in the urinary excretion rate of aldosterone/creatinine following exercise as well as the alterations in renal function, viz., sodium homeostasis.

Technical Approach: It is proposed to collect blood and urine samples from 18 runners participating in the great Hawaiian Footrace, a 500 km, 20-day road race. Approximately 20-25 ml venous blood samples will be drawn from each subject before and after running on days 1, 10, 13, and 20.

Progress: Resting urinary aldosterone excretion and plasma concentrations were determined in male runners during a 500-km, 20-day road race. We also measured renal responses to changes in aldosterone levels as well as plasma concentrations of sodium cortisol and factors noted to mediate aldosterone secretion. Blood samples were obtained in the morning 20 hours post-exercise on days 1, 11, 13, and 18. The sample obtained on day 13 was collected following 70 hours of rest and overnight urinary collections obtained on days 11 and 13. Plasma aldosterone concentrations were significantly elevated on days 11 and 18 compared to days 1 and 13. The elevation was an increase of 17 ng/dl. Progressively, over the race, there was a

decrease in plasma sodium concentrations (3 mEq/l) with no significant changes in plasma cortisol concentrations noted. Urinary sodium excretions were also significantly reduced on days 11 compared to day 13 following the running. Furthermore, aldosterone excretion, prior to the run, was significantly lower than that observed after running. Over three days of recovery, we observed progressive reduction in aldosterone excretion, in relation to creatinine excretion, respectively. The rate of sodium excretion ( $54 \pm 9$  mEq/min) prior to running increased progressively to a rate of  $138 \pm 15$  mEq/min by the third day of recovery. Potassium excretion, however, was not altered significantly at this time. Aldosterone excretion in the individuals undertaking daily long distance running was elevated following exercise, and remained elevated for 48 hours following cessation of exercise. A similar trend was noted in plasma aldosterone levels. We hypothesize that these alterations in aldosterone and sodium excretion may contribute to the expansion of extracellular fluid volume associated with training.

Presentations and Publications:

1. Wade CE, Hill LC, Dressendorfer RH: Plasma aldosterone regulation and renal function in marathon runners during a 20-day road race. *Medicine and Science in Sports and Exercise* 15:94, 1983.
2. Hill LC, Dressendorfer RH, and Wade CE: Urinary aldosterone excretion during 70-hour recovery period following repeated episodes of prolonged running. *Medicine Science and Sports* 15:94, 1983.

Detail Summary Sheet

Date: 15 Sep 83

Prot. No.: Ci-82-15

Status: Ongoing

Title: Effect of RU 38486, an antiprogesterone, on the hypophysial-adrenal axis.

Start Date: Sept 82

Est Comp Date: 1985

Principal Investigator:

LTC CA Winkel, MD  
CE Wade, PhD

Facility:

LAMC

Key Words: RU 38486, antiprogesterone, hypophysial-adrenal axis

Dept/Svc:

Clinical Investigation

Associate Investigators:

Accumulative MED CASE

Cost:

Est Accumulative

OMA Cost: \$3000

Periodic Review

Results:

Study Objective: The purpose of this study is to ascertain the effect of RU 38486, a potent antiprogestin, on the hypophysial-adrenal axis with special focus on its effects on glucocorticoid and mineralocorticoid secretion as well as action.

Technical Approach: Animals will be injected with a wide range of dosages of RU 38486 and studied for 24 hours following administration of the drug.

Progress: Seven animals have been entered into this protocol. They have received a wide range of doses employing this drug. Following administration of RU 38486, plasma cortisol, ACTH, and aldosterone are significantly elevated. Accompanying the rise in these hormones is an increase in body weight and a reduction in plasma protein concentration in hematocrit. The data collected from these animals is undergoing further reduction at this time. This protocol will hopefully be completed in 1985.

Detail Summary Sheet

Date: 15 Sep 83

Prot. No.: Ci-82-16

Status: Ongoing

Title: The effect of seven consecutive days of two-hour sessions of strenuous exercise in the salt and water balance and associated hormonal control mechanisms.

Start Date: 2 Sept 82

Est Comp Date: 1984

Principal Investigator:

CE Wade, PhD

CPT P Christ, MD

Facility:

LAMC

Dept/Svc:

Clinical Investigation

Associate Investigators:

Key Words: exercise, salt and water balance

Accumulative MED CASE

Cost:

Est Accumulative

OMA Cost: \$4000

Periodic Review

Results:

Study Objective: To assess in 10 healthy, untrained males the effects of daily running on the pituitary-adrenal axis by measuring plasma concentrations of ACTH and cortisol.

Technical Approach: We measured plasma concentrations of ACTH and cortisol in 10 healthy, untrained males before and after two hours of daily running for seven days. The men, aged 21-37 years, underwent one day of control measurements, seven consecutive days of running for two hours, two days of rest and a final day of running for two hours. Running, or the equivalent rest period, was conducted between 0800 and 1030 hours with the fasting samples collected before and within five minutes after running. During these two hours, each man ran the average distance of 18.5 km, which remained constant throughout the study.

Progress: In this cooperative study with Tripler AMC, two projects were carried out. In response to running, concentrations of plasma ACTH and cortisol levels increased significantly. The mean change in levels of plasma cortisol after running progressively decreased from  $16.7 \pm 3.8$  g/dl on day 1, and  $24.3 \pm 3.8$  g/dl on day 7. The mean change in levels of ACTH after running were not significantly altered, ranging from  $30 \pm 10$  kg/mi on day 1, to  $21 \pm 5$  kg/mi on day 7. The relationship

between plasma cortisol and ACTH was demonstrated on day 1, while on day 7, a relationship was noted. Thus, plasma concentration of ACTH and cortisol levels are increased with running. The cortisol response progressively decreases as a result of factors other than ACTH.

After two hours of running, post-exercise serum creatine kinase and aspartic transaminase dehydrogenase activities were elevated along with chronic elevations of the resting levels determined 22 hours later. C-reactive protein levels: over half (n=6) of the subjects showed no detectable rise with haptoglobin concentrations while the haptoglobin concentrations decreased. Findings similar to serum enzymes were noted in serum myoglobin with a peak increase of  $671 \pm 103$  percent after exercise on day 5 with resting levels chronically elevated by  $183 \pm 66$  percent. In the presence of this mild myoglobinemia, no significant changes in renal function were noted.

Publications and Presentations:

Wade CE, Christ P, Hunt MM, Claybaugh JR, Haddick C, Cucinell S, Dressendorfer RH: Changes in plasma concentration of adrenocorticotrophin (ACTH) and cortisol and men in response to daily two-hour runs for seven days. The Physiologist 26:A-17. 1983.

Detail Summary Sheet

Date: 30 Aug 83

Prot. No.: Ci-82-17

Status: Terminated

Title: An evaluation of the mesenchymal-epithelial interactions in human endometrium.

Start Date: 1 Nov 82

Est Comp Date: Terminated

Principal Investigator:

LTC CA Winkel

CPT DL Danley

Facility:

LAMC

Dept/Svc:

Clinical Investigation

Associate Investigators:

Key Words: endometrium, epithelium, mesenchyme

Accumulative MED CASE

Cost: 0

Est Accumulative

OMA Cost: \$500

Periodic Review

Results:

Study Objective: We propose to investigate the interactions between endometrial stroma and endometrial glandular epithelium; specifically, to determine if the response of endometrial cells of one type of the hormonal milieu leads to alteration in the metabolism of the other cell type.

Technical Approach: Human endometrial tissues will be obtained at the time of hysterectomy; the tissue will be minced, digested and filtered to separate stromal cells from glandular epithelium. Both cell types will be plated and maintained in vitro. Conditional media from cultures of one cell type will be harvested and tested for soluble substances that influence the metabolism of the other cell types; specifically, cell proliferation, RNA synthesis, and protein synthesis.

Progress: Endometrial stroma was obtained and passed successfully in vitro; however, attempts to obtain glandular epithelium were not successful.

Detail Summary Sheet

Date: 20 Sep 83

Prot. No.: Ci-82-19 Status: Ongoing

Title: Effects of vasopressin blockade on blood pressure regulation during surgery.

Start Date: Feb 83

Est Comp Date: Indefinite

Principal Investigator:

CPT W Willard, MD

CE Wade, PhD

Facility:

L A M C

Dept/Svc:

Clinical Investigation

Associate Investigators:

Key Words: vasopressin, blood pressure regulation

Accumulative MED CASE

Cost:

Est Accumulative

OMA Cost:

Periodic Review

Results:

Study Objective: To assess the role of endogenous vasopressin via blockade on the regulation of blood pressure during surgery and the compensatory response of other pressor hormones (angiotensin II and catecholamines).

Technical Approach: Thirty-two male rabbits, divided into four groups of eight animals each, will undergo 14 days of quarantine. Each animal will then be subjected to two surgical procedures while under sodium pentobarbital: 1) each will be implanted with Swan-Ganz thermistor-tipped catheters advanced from the femoral artery to the thoracic aorta. The catheter ends will be placed in jackets and maintained by DCI personnel for three days by flushing with sodium heparin; 2) three days after catheter implantation, the animal will again be anesthetized with sodium pentobarbital, followed by an exploratory laparotomy and appendectomy, with pressure monitorings throughout all procedures. Following the surgical procedures, the animal will be injected with vasopressin blocker and arginine-vasopressin solution. A blood sample will be taken, the animal sacrificed with an overdose of sodium pentobarbital, and a thoracotomy performed. Blood sample aliquots will be placed into chilled centrifuge tubes containing heparin or EDTA. Hematocrit, plasma protein,  $\text{Na}^+$ ,  $\text{K}^+$ , and osmolality will be measured. Plasma vasopressin concentrations and plasma renin activity will be measured by radioimmunoassay, while plasma

catecholamine levels will be measured by HPLC. ANOVA will be used to evaluate the data over time and to assess between treatment difference. Significance will be determined at a level of  $< 0.05$ .

Progress: Eighteen rabbits have been entered into the protocol. Data analysis is pending completion.

Detail Summary Sheet

Date: 20 Sep 83

Prot. No.: Ci-82-20 Status: Ongoing

Title: Hormonal and renal responses to angiotensin-converting enzyme inhibition in humans at rest and during exercise.

Start Date: Feb 83

Est Comp Date: Indefinite

Principal Investigator:

CPT CJ White, MD  
CPT W Bowden, MD  
CE Wade, PhD

Facility:

LAMC

Dept/Svc:

Clinical Investigation

Associate Investigators:

Key Words: angiotensin-converting enzyme, exercise

Accumulative MED CASE

Cost:

Est Accumulative

OMA Cost: \$100

Periodic Review

Results:

Study Objective: To assess the role of angiotensin II in the alterations in plasma concentrations of aldosterone and vasopressin, as well as alterations in renal function observed during maximal exercise.

Technical Approach: After voluntarily voiding their bladders, ten 20-40 year-old, physically active, fasting males will undergo body weight and blood pressure measurements. Each will then participate in a preparatory 30-minute period during which the subject will have electrodes placed, and a venous catheter inserted into the antecubital vein. A urine sample and 45 ml venous blood sample will then be obtained prior to experimental manipulations. Each subject will then twice perform to voluntary maximum the supervised treadmill stress test (utilizing a standardized Bruce protocol); once without treatment and acting as his own control, then after ingestion of 50 mg of Captopril (SQ 14225), an angiotensin-converting inhibitor, one hour prior to the exercise procedures. Heart rate, blood pressure, and EKG will be monitored intra- and post-exercise. Venous blood samples will be placed into chilled centrifuge tubes. Hematocrit, colorimetric hemoglobin, and plasma lactate concentration will be measured, and plasma renin activity, aldosterone, cortisol, ACTH, and vasopressin measured by radioimmunoassay. Plasma and urine sodium and

potassium concentrations will be analyzed by flame photometry, and osmolality determined by freezing point depression. Two-way ANOVA will be used to determine significant differences. Correlations will be determined by linear regression analysis using the method of least squares, at a probability significance level of  $< 0.05$ .

Progress: This protocol has yet to be initiated. Patient accrual will begin in November.

Detail Summary Sheet

Date: 1 Sep 83

Prot. No.: Ci-81-21 Status: Ongoing

Title: A study on the interaction of human polymorphonuclear leukocytes with pathogenic microorganisms.

Start Date: 10 Jun 83

Est Comp Date: Sep 84

Principal Investigator:  
CPT DL Danley, PhD

Facility:  
L A M C

Key Words: polymorphonuclear leukocytes, Candida albicans

Dept/Svc:  
Clinical Investigation

Associate Investigators:  
LTC D Haburchak, MD  
MAJ B Fears, MD

Accumulative MEDCASE  
Cost:

Est Accumulative  
OMA Cost: \$5000

Periodic Review  
Results:

Study Objective: This study is designed to utilize procedures developed in DCI to study the microbicidal activity of polymorphonuclear leukocytes (PMN) from normal individuals and patients with recurrent infections or pathological states which might predispose them to infection.

Technical Approach: Blood, obtained by venipuncture, will be processed to recover PMN for assay. To measure the microbicidal activity of PMN, cells will be incubated with Candida albicans blastoconidia and the viability of phagocytosed yeast cells will be measured using acridine orange vital dye and fluorescence microscopy. Furthermore, the oxidative metabolic burst by PMN will be measured using fixation of radiolabeled iodide -125.

Progress: We have observed microscopically that PMN which phagocytose viable C. albicans may be killed and lysed by the fungi. Lysis of PMN has also been confirmed using release of radiolabeled chromium -51. While good quantitation of PMN killing by yeast cells has been achieved, we have had more difficulty demonstrating yeast cell killing by PMN. Finally, we have observed that PMN incubated with zymosan do fix greater amounts of radiolabeled iodide than unstimulated cells. Studies are currently underway comparing the activity of normal leukocytes with those from diabetic patients.

Detail Summary Sheet

Date: 1 Oct 83

Prot. No.: C-77-03    Status: Completed

Title: Evaluation of amiodarone for the therapy of cardiac arrhythmias.

Start Date: Jul 77

Est. Comp. Date: Completed

Principal Investigator:  
COL SM Sobol, MD

Facility:  
LAMC

Dept/Svc:  
Cardiology

Associate Investigators:  
L Rakita, MD

Key Words: amiodarone, life-threatening cardiac arrhythmias

Accumulative MED CASE  
Cost: None

Est Accumulative  
OMA Cost: None

Periodic Review  
Results: Approved

Study Objective: To control life-threatening or severely symptomatic cardiac arrhythmias which have not been responsive to the conventional and accepted forms of treatment or whose control is dependent upon the use of a drug which has been shown to be harmful to or in other ways not tolerated by the individual.

Technical Approach: Unchanged from FY 1982 report except as follows: Rapid reduction in dose to 200 mg qd after successful loading with 1400 mg qd resulted in breakthrough in one patient of a prolonged but self-terminating episode of ventricular tachycardia. Therefore, dosage is gradually adjusted downward, after control is achieved, on a monthly basis.

Progress: This study is now completed, with the initiation of amiodarone for new patients now being carried out through protocol C-82-08 entitled, "Amiodarone treatment for severe, refractory cardiac arrhythmias."

Under the initial protocol and its subsequent modifications, a total of 19 LAMC patients were begun on amiodarone for the control of refractory life-threatening or severely symptomatic arrhythmias. Arrhythmia was successfully controlled in 17 patients. In two instances, the patient died of their arrhythmia before an adequate loading dose of amiodarone could be administered. In all remaining instances, arrhythmias were adequately controlled. Side effects requiring temporary discontinuation or specific therapy occurred in five (26 percent). Side effects requiring permanent discontinuation of the drug occurred in three patients (16 percent). Ten patients died of their underlying cardiac disease or of other medical problems. No patient died as a direct result of amiodarone therapy. Six patients

continue on amiodarone at the time of this report and will, in the future, be carried on C-82-08.

Results of this study demonstrated:

- a) a high (89 percent) success rate in controlling refractory arrhythmias with amiodarone;
- b) a higher than expected incidence of adverse effects, of which some were severe but none were fatal and all were reversible;
- c) the necessity and safety of high initial loading doses to achieve rapid arrhythmia control; and
- d) the delay to maximal effectiveness of a given dose (week to months), and the need for downward dose titration during the last phase of therapy to minimize adverse effects while maintaining arrhythmia control.

Publications and Presentations:

1. Sobol SM, Rakita L: Clinical trial of amiodarone hydrochloride, a new antiarrhythmic drug. Seventh Meeting, Association of Army Cardiology, 4-6 May, 1978.
2. Rakita L, McGee J, Sobol SM, Luria M: Clinical trial of amiodarone hydrochloride for the treatment of refractory arrhythmias. Am J Cardiol 43:358, 1979.
3. Sobol SM, Rakita L, Tri TB, Crone RA: Amiodarone hydrochloride for treatment of severe, refractory arrhythmias: update 1979. Eighth Meeting, Association of Army Cardiology, May 17-19, 1979.
4. Sobol SM, Rakita L: Amiodarone. Circulation 60:1426, 1979.
5. Rakita L, Sobol SM: Dose-response relationship of amiodarone and malignant ventricular arrhythmias. 8th Annual European Congress of Cardiology, Paris, France, June 22-26, 1980.
6. Rakita L, Sobol SM: Amiodarone treatment for refractory arrhythmias: dose-ranging and importance of high initial dosage. Circulation 64 (Suppl IV):IV-263, 1981.
7. Sobol SM, Rakita L: Pneumonitis and pulmonary fibrosis associated with amiodarone treatment: a possible complication of a new antiarrhythmic drug. Circulation 65:819-824, 1982.
8. Sobol SM, Rakita L: Adverse effects of chronic high dose therapy with amiodarone. Proceedings of the IX World Congress of Cardiology, Moscow, June 20-26, 1982.
9. Oetgen WJ, Sobol SM, Tri TB, Heydorn WH, Davia JE, Rakita L: Amiodarone-digoxin interaction: clinical and experimental observations. Circulation 66 (Suppl II):II-382, 1982.
10. Martinez-Arizala A, Sobol SM, McCarty GE, Nicols BR, Rakita L: Amiodarone neuropathy. Neurology 33:643-5, 1983.
11. Rakita L, Sobol SM, Mostow N, Vrobel T: Amiodarone pulmonary toxicity. Amer Heart J 1983 (in press).
12. Rakita L, Sobol SM: Amiodarone in the treatment of refractory arrhythmias: importance and safety of high initial dose therapy. JAMA 1983 (in press).

Detail Summary Sheet

Date: 29 Aug 83

Prot. No: C-77-04

Status: Completed

Title: Effects of experimental ischemic and digitalis toxic arrhythmias of a new antiarrhythmic drug, amiodarone.

Start Date: May 77

Est. Comp. Date: Completed

Principal Investigator:  
COL SM Sobol, MD

Facility:  
L A M C

Dept/Svc:  
Cardiology

Associate Investigators:  
COL WH Heydorn, MD

Key Words: amiodarone, digitalis

Accumulative MED CASE  
Cost: None

Est Accumulative  
OMA Cost: \$7500

Periodic Review  
Results: N/A

Study Objectives: Assessment of the effectiveness of a new antiarrhythmic drug, amiodarone, in the prevention of arrhythmias caused by digitalis toxicity, and assessment of the possible deleterious effect of amiodarone on digitalis toxicity as noted in preliminary phase of this study; assessment of the effect of chronic amiodarone therapy on arrhythmia threshold in chronically digoxin treated animals; and in the prevention of arrhythmias induced by acute ischemia, both in absence and in presence of digoxin therapy.

Technical Approach: Ouabain was infused into pigs at 2 mcg/kg/min until ventricular fibrillation occurred. Two groups were studied: one group was pretreated with oral amiodarone, 20 mg/kg/day for two weeks, while the second group received no amiodarone. Phase III animals were prospectively studied to assess any effect on serum digoxin level in swine when amiodarone was given concomitantly.

Progress: Amiodarone appeared to cause elevation of serum digoxin level. Analysis of arrhythmia data, reviewed by biostatistician, reveals trend toward protection against digitalis- and ischemia-induced arrhythmias by amiodarone, but does not reach statistical significance. Details of method possibly contributing to data scatter include: 1) technique of applying ventricular fibrillation electrodes to epicardium; b) variability among animals in amiodarone absorption, and serum and tissue levels (no method of analysis of serum level was available at time of study); c) variability in proportion of fat/lean body weight among animals, affecting both digoxin and amiodarone tissue distribution.

Detail Summary Sheet

Date: 20 Sep 83

Prot. No.: C-82-06

Status: Ongoing

Title: Effect of longterm vasodilator therapy on natural history of significant aortic regurgitation.

Start Date: Jul 83

Est Comp Date: Indefinite

Principal Investigator:

COL SM Sobol, MD

B Massie, MD

Facility:

LAMC

Dept/Svc:

Cardiology

Associate Investigators:

Key Words: vasodilator therapy, aortic regurgitation

Accumulative MED CASE

Cost:

Est Accumulative

OMA Cost:

Periodic Review

Results:

Study Objective: To determine whether chronic therapy with oral hydralazine will delay the progression or even cause regression of left ventricular dilatation and hypertrophy in patients with chronic aortic insufficiency.

Technical Approach: This is a double blinded, parallel design, placebo controlled study of longterm hydralazine therapy. After the initial examination and randomization, patients will be started on medication (placebo or hydralazine), to be increased at intervals, to achieve ultimately a daily dosage of approximately 3 mg/kg body weight. During this period of medication buildup, patients will be seen or contacted by telephone weekly to assess side effects. If side effects occur, an attempt at t.i.d. or q.i.d dosing or a more gradual increase in dose will be made. Noninvasive diagnostic tests (i.e., Bruce protocol tread mill stress testing to assess exercise tolerance) will be performed for follow-up. The investigators will also provide regular clinical follow-up and manage medication dosing.

Progress: Three patients from LAMC were entered into this protocol, two of whom voluntarily withdrew from the study, one because of adverse effects to hydralazine and the other for unrelated reasons. This protocol is being continued with patients from the Veteran's Administration Hospital, University of California at San Francisco, and the University of Oregon. The anticipated completion date of this study is 1984. No data are available at this time.

Analysis of serum digoxin level data reveals a digoxin-amiodarone interaction, with elevation of the serum digoxin level on concomitant administration of amiodarone. This is of clinical significance and not previously confirmed in an animal model. The mechanism is unclear, and the present study did not include pharmacokinetic investigation into the cause of this interaction.

Publications/Presentations:

1. Sobol SM, Beale GL: Effect of amiodarone hydrochloride on the development of arrhythmias due to digitalis toxicity. Seventh Meeting, Association of Army Cardiology, 4-6 May, 1978.
2. Sobol SM, Heydorn W, Tri TB, Crone RA: Analysis of the interaction of amiodarone and digitalis during acute quabain toxicity and chronic digitalis therapy. Eighth Meeting, Association of Army Cardiology, May 17-19, 1979.
3. Oetgen WJ, Sobol SM, Tri TB, Heydorn WH, Davia JE, Rakita L: Amiodarone-digoxin interaction: clinical and experimental observations. Circulation 66 (Suppl II):II-382, 1982.

Detail Summary Sheet

Date: 20 Sep 83

Prot. No.: C-82-07 Status: Terminated

Title: Intracoronary streptokinase in evolving myocardial infarction.

Start Date: Feb 83

Est Comp Date: Terminated

Principal Investigator:  
MAJ TD Watson, MD

Facility:  
L A M C

Dept/Svc:  
Cardiology

Associate Investigators:  
COL HL Price, MD  
MAJ JD Svinarich, MD  
CPT CJ White, MD

Key Words: streptokinase, myocardial infarction

Accumulative MED CASE  
Cost:

Est Accumulative  
O M A Cost:

Periodic Review  
Results:

Study Objective: To assess the efficacy and safety of intracoronary streptokinase infusions in patients with acute myocardial infarction.

Technical Approach: This is a four-week, open label trial involving 15-30 patients with acute myocardial infarction. Streptokinase will be infused into the obstructed coronary artery through a coronary angiography catheter within 10 hours of onset. The effects of the study drug will be assessed by selective coronary angiography, hemodynamic parameters obtained by right and left heart catheterization. Clinical and laboratory observations for evaluation of safety will be performed prior to, during and at the conclusion of the study.

Progress: Ten patients were entered into this study, with six successful attempts and four unsuccessful attempts to assess efficacy and safety of intracoronary streptokinase infusions with acute myocardial infarction. There was a single death during the course of treatment, probably unrelated to the drug usage. Another patient developed bleeding complications and is still being followed. Because streptokinase was FDA-approved in May 1982, this protocol has been terminated.

Presentations and Publications: Population sample too small to publish data.

Detail Summary Sheet

Date: 1 Oct 83

Prot. No.: C-82-08

Status: Ongoing

Title: Amiodarone treatment for severe, refractory cardiac arrhythmias.

Start Date: Oct 82

Est Comp Date: 1984

Principal Investigator:  
COL SM Sobol, MD

Facility:  
L A M C

Dept/Svc:  
Cardiology

Associate Investigators:  
MAJ TD Watson, MD  
MAJ JT Svinarich, MD

Key Words: amiodarone, cardiac arrhythmias

Accumulative MED CASE  
Cost: N/A

Est Accumulative  
OMA Cost: N/A

Periodic Review  
Results:

Study Objective: To allow use of a potent investigational antiarrhythmic drug, amiodarone, in the treatment with severe life-threatening or symptomatic arrhythmias refractory to standard therapy; and to obtain information on the effectiveness, adverse effects, and most appropriate dosing regimens of this drug.

Technical Approach: Patients are monitored either continuously or with frequent Holter monitors, depending on severity of arrhythmia. Amiodarone is given in large dose (1,400 mg on day 1), followed by 800 or 1,400 mg/day depending on the clinical setting. The eventual, lowest effective maintenance dose is determined by slow titration and frequent Holter monitors. After stabilization, patients are followed bimonthly. Frequent blood chemistries, thyroid function studies, ECGs and chest x-rays are obtained during the first year regarding reported toxicities.

Progress: Six patients have been newly entered to this protocol since its inception. Arrhythmia has been controlled in all patients. Adverse effects requiring therapy or temporary discontinuation of therapy have not occurred in any patient. Adverse effects requiring permanent discontinuation of therapy occurred in one patient.

Detail Summary Sheet

Date: 12 Sep 83

Prot. No.: C-82-09

Status: Ongoing

Title: Nifedipine in the treatment of Raynaud's phenomenon.

Start Date: Mar 83

Est Comp Date: Nov 83

Principal Investigator:  
CPT CJ White, MD

Facility:  
LAMC

Key Words: nifedipine, Raynaud's phenomenon

Dept/Svc:  
Cardiology

Associate Investigators:  
CPT W Phillips, MD  
MAJ TD Watson, MD  
CPT L Abrahams, MD

Accumulative MEDCASE  
Cost: N/A

Est Accumulative  
OMA Cost: \$500

Periodic Review  
Results:

Study Objective: To assess the objective response of patients with Raynaud's phenomenon to nifedipine by measuring skin temperature and recovery time after ice water hand immersion.

Technical Approach: The patient's baseline fingertip temperature is recorded, with hands immersed for 20 seconds in ice water. Time to recovery is then measured. Twenty milligrams of sublingual nifedipine is administered and the test repeated. Finally, a double-blind crossover is sustained for one week of nifedipine administration and one week placebo. The test is again repeated.

Progress: Eleven patients have completed the study. We anticipate four additional patients in the next month.

Detail Summary Sheet

Date: 20 Sep 83

Prot. No.: C-82-10 Status: Completed

Title: Effect of coronary arteriography on parameters of left ventricular systolic and diastolic function.

Start Date: Jan 83

Est Comp Date: Completed

Principal Investigator:  
MAJ TD Watson, MD

Facility:  
L A M C

Dept/Svc:  
Cardiology

Associate Investigators:  
CPT CJ White, MD  
CPT KA Kaplan, MD  
LTC MD Redwine, MD  
COL HL Price, MD

Key Words: coronary arteriography, left ventricular function

Accumulative MED CASE  
Cost:

Est Accumulative  
OMA Cost:

Periodic Review  
Results:

Study Objective: This study is designed to evaluate the effect of coronary angiography on left ventricular end diastolic function and ejection fraction, and on parameters of left ventricular diastolic function obtained from gated equilibrium radionuclide angiograms.

Technical Approach: A pigtail catheter is inserted using standard techniques followed by measurement of aortic and left ventricular pressures and heart rate. A gated equilibrium radionuclide angiogram is obtained. From the time-activity curve generated from the radionuclide angiogram, the left ventricular ejection fraction, peak filling rate and time to peak filling rate will be calculated. Selective right and left coronary angiography will then be performed using standard techniques. Aortic and left ventricular pressures and heart rate will again be measured at the completion of coronary angiography; a second radionuclide angiogram will be performed with the same parameters calculated as previously outlined, due to the presence of residual nuclide material from the first scan. Finally, standard contrast left ventricular angiography will be performed to complete the catheterization. Parameters to be evaluated pre-and post-coronary angiography include heart rate, systolic

pressure, left ventricular end diastolic pressure, left ventricular ejection fraction, peak filling rate and time to peak filling rate. A paired 't' test will be utilized to assess statistical significance of any changes in these parameters. A P value of less than 0.05 will be considered to represent a significant difference.

Progress: Twenty-nine patients were entered into this study, and there were no complications. Results indicate that there was no direct effect of contrast material on either systolic or diastolic left ventricular function. The increase in left ventricular end diastolic pressure appeared to be secondary to volume expansion due to the contrast material.

Presentations and Publications: An abstract has been submitted for publication.

Detail Summary Sheet

Date: 12 Sep 83

Prot. No.: C-82-11 Status: Ongoing

Title: Hemodynamic effects of parenteral nutrition.

Start Date: Apr 83

Est Comp Date: Indefinite

Principal Investigator:

CPT CJ White, MD

Facility:

LAMC

Dept/Svc:

Cardiology

Associate Investigators:

CPT W Bowden, MD

CPT D Boll, MD

CPT S Deppe, MD

CPT J Lindberg, MD

Key Words: parenteral nutrition

Accumulative MEDCASE

Cost: N/A

Est Accumulative

OMA Cost: N/A

Periodic Review

Results:

Study Objective: To assess the hemodynamic effects of parenteral nutrition.

Technical Approach: Radionuclide angiography is performed fasting and on 10 percent dextrose IV, and compared to one performed 72 hours after starting parenteral nutrition. When possible, hemodynamic parameters from Swan-Ganz lines are also compared.

Progress: Three patients have been studied. Acquisition of patients has been slow due to many candidates having alterations of medical therapy (i.e., drugs) which contaminate data.

Detail Summary Sheet

Date: 9 Sep 83

Prot. No.: C-82-12

Status: Ongoing

Title: Assessment of regional wall motion abnormalities by radionuclide angiography: effect of sublingual nitroglycerin.

Start Date: Jul 82

Est Comp Date: 1984

Principal Investigator:  
CPT CJ White, MD

Facility:  
L A M C

Dept/Svc:  
Cardiology

Associate Investigators:  
CPT KA Kaplan, MD

Key Words: wall motion abnormalities, angiography, nitroglycerin

Accumulative MED CASE  
Cost:

Est Accumulative  
OMA Cost:

Periodic Review  
Results:

Study Objective: To assess whether regional wall motion abnormalities of the left ventricle, which improve with nitroglycerin, correlate with improved left ventricular wall motion after coronary artery bypass surgery.

Technical Approach: This will be determined by radionuclide ventriculography before and after surgery.

Progress: This is a joint protocol with FAMC. This study has not yet begun because of a personnel shortage in the nuclear medicine service.

Detail Summary Sheet

Date: 20 June 83

Prot. No.: CCM-83-01 Status: Ongoing

Title: Sterility of Swan-Ganz catheters using guide wire technique versus percutaneous insertion of catheter

Start Date: Mar 82

Est Comp Date: Indefinite

Principal Investigator:  
MAJ A Sado, MD

Facility:  
L A M C

Dept/Svc:  
Critical Care Medicine

Associate Investigators:

Key Words: Swan-Ganz catheters

Accumulative MED CASE  
Cost:

Est Accumulative  
OMA Cost:

Periodic Review  
Results:

Study Objective: To determine if there is a significant difference in intravascular catheter related infection rates utilizing guide wire technique compared to percutaneous reinsertion technique; and to collect data regarding the incidence of Swan-Ganz catheter related infections.

Technical Approach:

Insertion of Swan-Ganz catheter is followed as described in the protocol. Culture technique is a semi-quantitative one as described in protocol.

Progress:

1. There have been three patients enrolled in this study so far: two patients have been in the guide wire group, one in the new insertion group. There have been two catheter-related infections, both in the guide wire group. One patient had greater than 15 organisms on his cordis sheath cultures with positive venous cultures. The other patient had a catheter-related cellulitis with no significant number of microorganisms cultured in his cordis sheath or Swan-Ganz tip. This patient had negative venous blood cultures. Even though both infections occurred within the guide wire group, there are not enough patients in this study yet to make any conclusions about these results.

2. There have been no adverse complications as a result of this investigation.

3. The low number of patients so far enrolled in this study is due to several factors:

a. Many patients in the ICU in the last three months who would have been subjects in this study had contraindications to insertion at a new site because of irreversible coagulopathies.

b. Large number of beds in ICU in the past two months have been occupied by patients requiring chronic care without the necessity for hemodynamic monitoring.

c. The latter has resulted in a reduction in the number of beds open to routine acute care patients who may have required prolonged hemodynamic monitoring.

4. Research data on subjects enrolled in this study has been conducted without any significant alteration in protocol design and without any problem in gathering data.

5. Conclusions: This protocol will be continued cooperatively between LAMC and Madigan AMC, where the investigator has been transferred (as of 1 July 1983).

Detail Summary Sheet

Date: 12 Sep 82

Prot. No.: E-82-08

Status: Ongoing

Title: Timolol effect on thyroid hormones.

Start Date: 3 May 82

Est Comp Date: Jan 84

Principal Investigator:  
CPT C Clark, MD

Facility:  
LAMC

Key Words: timolol, triiodothyronine, reverse triiodothyronine

Dept/Svc:  
Endocrinology

Associate Investigators:  
MAJ R Jones

Accumulative MED CASE  
Cost:

Est Accumulative  
OMA Cost:

Periodic Review  
Results:

Study Objective: To determine whether timolol decreases the level of triiodothyronine while raising reverse triiodothyronine in the blood.

Technical Approach: Patients identified as hypertensive and who are selected by their doctors to start timolol therapy will have blood samples obtained before starting therapy and after one week of timolol. Levels of T<sub>4</sub>, T<sub>3</sub>, and reverse T<sub>3</sub> will be measured.

Progress: Eight patients have been entered into the protocol. Samples are frozen and will be run when 12 to 15 patients have been entered into the protocol.

Detail Summary Sheet

Date: 12 Sep 83

Prot. No.: E-82-09

Status: Ongoing

Title: Effects of topical timolol on thyroid hormones.

Start Date: Sep 82

Est Comp Date: Jun 84

Principal Investigator:  
CPT C Clark, MD

Facility:  
L A M C

Dept/Svc:  
Endocrinology

Associate Investigators:  
MAJ R Jones

Key Words: timolol, thyroid hormones

Accumulative MED CASE  
Cost:

Est Accumulative  
OMA Cost:

Periodic Review  
Results:

Study Objective: To study the effect of applied timolol on thyroid hormones.

Technical Approach: Ten patients, selected to have topical timolol stopped, will have thyroid hormone levels checked while on topical timolol and at the end of two weeks without timolol. Levels of T4, T3, and reverse T3 will be measured. All samples will be frozen and run at the same time.

Progress: Eight patients were entered to this protocol and initial blood samples obtained. Through a misunderstanding, the second sample was not obtained. No further patients have been referred from the Ophthalmology Service.

Detail Summary Sheet

Date: 30 Aug 83

Prot. No.: E-83-10 Status: Ongoing

Title: Bone density in amenorrheic runners.

Start Date: May 83

Est Comp Date: Nov 83

Principal Investigator:

MAJ W Fears, MD  
CPT J Lindberg, MD  
MAJ D Boll, MD

Facility:

LAMC

Dept/Svc:

Endocrinology

Associate Investigators:

Key Words: bone density, exercise, amenorrheic runners

Accumulative MED CASE

Cost: N/A

Est Accumulative

OMA Cost: N/A

Periodic Review

Results:

Study Objective: To determine if low estradiol levels associated with exercise-induced amenorrhea result in a decrease in bone density.

Technical Approach: To measure bone density using a bone mineral analyzer in patients with exercise-induced amenorrhea.

Progress: Seventeen patients with exercise-induced amenorrhea have had their bone mineral measured as well as nine post-menopausal controls and 10 eumenorrheic runners. Currently, we plan to do several more eumenorrheic controls and as many amenorrheic runners as we can get by next month and then analyze the data.

Detail Summary Sheet

Date: 30 Aug 83

Prot. No.: E-83-11 Status: Ongoing

Title: Comparison of white blood cell function in non-insulin dependent diabetes mellitus during improved control after treatment with insulin and after treatment using a modified fasting procedure.

Start Date: Jun 83

Est Comp Date: Dec 83/Jan 84

Principal Investigator:

MAJ W Fears, MD

CPT J Ducey, MD

Facility:

LAMC

Dept/Svc:

Endocrinology

Associate Investigators:

CPT D Danley, PhD

Key Words: white blood cell, noninsulin dependent, diabetes mellitus

Accumulative MFDCASE

Cost: N/A

Est Accumulative

OMA Cost: N/A

Periodic Review

Results:

Study Objective: To assess white blood cell function in non-insulin dependent diabetes mellitus in diabetics who are out of control and rapidly brought under control using IV infusions of insulin; and to then see if improvement of control over several days results in maintaining improved white blood cell function.

Technical Approach: To measure white blood cell phagocytosis in killing capability before and after rapid improvement of blood glucose using IV infusions of insulin. White blood cell functions will be measured by using a measure of iodine uptake with an  $I^{123}$  assay developed by Dr. Dave Danley of Department of Clinical Investigation.

Progress: Four or five patients have been infused with rapid normalization of their blood sugars. It appears in the patients thus far that there is an acute improvement in white blood cell function after rapid normalization of blood sugars which is maintained if blood glucose control is maintained. Currently, we plan to do four-six more patients and then analyze data. In addition, we plan to measure Candida albicans' ability to kill white blood cells in another assay developed by Dr. Danley.

Detail Summary Sheet

Date: 9 Mar 83

Prot. No.: G-82-18

Status: Completed

Title: Evaluation of the effect of weight loss on gastroesophageal reflux.

Start Date: Sep 82

Est Comp Date: Completed

Principal Investigator:

LTC F Goldner, MD

MAJ F Burton, MD

Facility:

LAMC

Key Words: weight loss, gastroesophageal reflux

Dept/Svc:

Gastroenterology

Associate Investigators:

Accumulative MED CASE

Cost: None

Est Accumulative

OMA Cost: \$5000

Periodic Review

Results: N/A

Study Objective: To determine the effect of weight loss on gastroesophageal reflux.

Technical Approach: In patients admitted as part of the weight reduction protocol, 24 hr pH determinations will be performed before and after weight loss. In patients with reflux disease, endoscopy will also be done to determine effect of weight loss on healing.

Progress: Fifteen patients have been entered into this study. The results of the first seven patients suggests that: 1) asymptomatic, obese patients may have a greater degree of GER than published norms; and 2) weight loss may not result in predictable improvement in GER. The eight results of the remaining eight patients have not yet been analyzed.

Detail Summary Sheet

Date: 9 Mar 83

Prot. No.: G-82-19

Status: Completed

Title: Evaluation of Adolph's<sup>TM</sup> Meat Tenderizer (AMT) in the enzymatic digestion of esophageal meat impaction.

Start Date: Sept 82

Est Comp Date: Feb 83

Principal Investigator:  
LTC F Goldner, MD

Facility:  
LAMC/LAIR

Key Words: esophageal meat impaction

Dept/Svc:  
Gastroenterology

Associate Investigators:  
CPT DL Danley  
MAJ W Rodkey, VC

Accumulative MED CASE  
Cost:

Est Accumulative  
OMA Cost: \$1000

Periodic Review  
Results:

Study Objective: To determine the potency, efficacy and safety of a papain solution (Adolph Meat Tenderizer<sup>TM</sup>) in the treatment of esophageal meat impaction.

Technical Approach:

- 1) in vitro determination of papain activity in AMT
- 2) affect of AMT on meat cubes
- 3) utilization of rabbits to determine in vivo effect of AMT on meat impaction as well as esophageal mucosa.

Progress: Data analysis suggests the following: 1) AMT solution has no detectable papain activity in the system tested. Only upon addition of EDTA and cysteine could proteolytic activity be detected (909 µg papain/gm AMT); 2) the papain in AMT solution was not activated by incubation with meat samples; 3) meat digestion - while some softening of texture occurred in AMT samples, there was no change in sample weight or protein released when compared to saline controls; and 4) AMT has no harmful effect on normal esophageal mucosa. Upon contact with inflamed mucosa, however, AMT may cause a significant increase in mucosal damage. Thus, in conclusion, AMT may aid treatment of esophageal meat impaction if an altered meat texture is of value, but decrease in bolus size should not be expected. In addition, AMT is probably safe with normal esophageal mucosa, but increased necrosis may occur if esophagitis is present.

Publications and Presentations: A paper will be presented at the 12th Annual William Beaumont Gastrointestinal Symposium in El Paso, Texas, and at the American Society for Gastrointestinal Endoscopy Meeting, May 1983, Washington, D.C.

Detail Summary Sheet

Date: 9 August 83

Prot. No.: G-82-20

Status: Transferred

Title:  
(MCTD).

Esophageal reflux in patients with mixed connective tissue disease

Start Date: 13 August 82

Est Comp Date: October 1984

Principal Investigator:  
CPT R Peters, MD

Facility:  
LAMC - G.I. Lab

Key Words: reflux, mixed connective tissue disease (MCTD)

Dept/Svc:  
Gastroenterology

Associate Investigators:  
MAJ Keisler, MD  
COL Singleton, MD

Accumulative MEDCASE  
Cost:

Est Accumulative  
OMA Cost: \$500

Periodic Review  
Results:

Study Objective: To determine the incidence and extent of esophageal reflux in patients with MCTD by examining esophageal motility and 24<sup>0</sup> pH monitoring.

Technical Approach: To assess esophageal motility, motility data, i.e., LES pressure, will be compared with Students' 't' test to normals obtained in our laboratory by review of manometry records and 24 hour esophageal pH monitoring.

Progress: An insufficient number of patients (i.e., two patients) have been studied to reach a conclusion. This protocol will be transferred to Eisenhower Medical Center, Augusta, Georgia, for further study.

Detail Summary Sheet

Date: Sep 83

Prot. No.: G-82-21

Status: Ongoing

Title: Comparison of nitrous oxide to carbon dioxide gases for laparoscopy, with special evaluation of intraperitoneal pH and microscopic changes.

Start Date: Apr 83

Est Comp Date: 1984

Principal Investigator:  
MAJ W Murchison, MD  
LTC F Goldner, MD

Facility:  
L A M C

Dept/Svc:  
Gastroenterology

Associate Investigators:  
LTC P Mellick, VC  
MAJ W Rodkey, MD

Key Words: nitrous oxide, carbon dioxide, laparoscopy, intraperitoneal pH

Accumulative MED CASE  
Cost:

Est Accumulative  
OMA Cost:

Periodic Review  
Results:

Study Objective: To determine any significant pH changes in the intraperitoneal fluid following peritoneal insufflation with CO<sub>2</sub> and N<sub>2</sub>O, or evidence of peritoneal serosal damage associated with the use of each gas as manifested by microscopic changes and transerosal potential differences.

Technical Approach: Laparoscopy will be performed.

Progress: No data collected to date. Project will be fully initiated in January 1984.

Detail Summary Sheet

Date: Sep 82

Prot. No.: G-82-22 Status: Ongoing

Title: Esophageal transit of various forms of medication.

Start Date: March 83

Est Comp Date: 1984

Principal Investigator:  
MAJ FV Burton, MD

Facility:  
L A M C

Dept/Svc:  
Gastroenterology

Associate Investigators:  
RF Theoni, MD

Key Words: esophageal transit, oral medication, barium sulfate

Accumulative MED CASE  
Cost:

Est Accumulative  
OMA Cost:

Periodic Review  
Results:

Study Objective: To assess the transit time through the esophagus of various types of medications and to determine where the tablets or capsules may be delayed, and how often this occurs.

Technical Approach: Patients of a control and treatment group (those with a prior history of dysphagia and those asymptomatic of dysphagia) will each receive a gelatin capsule containing barium sulfate, a compacted barium sulfate/sucrose tablet, then an enteric coated tablet containing barium sulfate. Patients will then receive upright PA and lateral chest x-rays to show that the capsule/tablet has passed into the stomach.

Progress: Patient accrual will begin in January 1984.

Detail Summary Sheet

Date: 31 Aug 83      Prot. No.: See below      Status: Ongoing unless otherwise indicated

Hematology/Oncology protocols follow, referenced by LAMC code number and title. Separate code numbers for group cooperatives (i.e., NATIONAL SURGICAL ADJUVANT BREAST PROJECT (\*NSABP), NATIONAL CALIFORNIA ONCOLOGY GROUP (\*\*NCOG), or NATIONAL CANCER INSTITUTE (\*\*NCI) may be found on title line.

Principal Investigator:  
LTC D Gandara, MD

Facility:  
LAMC

Dept/Svc:  
Hematology-Oncology

Associate Investigators:

Key Words: NSABP, NCOG, NCI

Accumulative MED CASE  
Cost: None

Est Accumulative  
OMA Cost: None

Periodic Review  
Results:

### Detail Summary Sheet

Title: H-77-05 (\*B-09). A protocol to compare combined chemotherapy with and without tamoxifen in the management of patients with surgically curable breast cancer.

Progress: This protocol was open for patient entry on 1 January 1977, and by May 1980, sufficient patients had been accrued to answer, eventually, the specific study aims. It was deemed, however, that continued accrual of patients into the L-PAM plus 5-FU plus tamoxifen arm would be desirable to provide further information on the relationship of quantitative estrogen and progesterone receptor to end results in patients who receive tamoxifen. Randomization was subsequently terminated on 16 May 1980, at which time 1800 patients had been randomized. To date, LAMC has entered 21 patients on this protocol, four of which have expired. The remaining 17 patients continue to be actively followed. Analysis is pending.

### Detail Summary Sheet

Title: H-78-08 (\*R-01). The clinical trial to evaluate postoperative radiation and postoperative systemic chemotherapy in the management of resectable rectal cancer.

Technical Approach: Radiation therapy or combination therapy will be administered through the LAMC Radiation Therapy Service of the Hematology Clinic.

Progress: Patient accrual for this protocol began 7 November 1977. As of 31 January 1983, 412 Dukes B and C patients had been randomized to one of the three treatment arms; an additional 170 Dukes A and D patients have been entered for follow-up only. Letterman, to date, has entered 12 patients on this protocol with four having expired. Analysis is pending. The following addendum, dated 29 March 1983, from the National Surgical Adjuvant Project for Breast and Bowel Cancer (NSABP) should be noted: 1) patients previously randomized to chemotherapy arm of R-01 and still receiving drug per protocol must be notified of methyl CCNU leukemogenic effect. A consent form (amendment) must be signed; 2) consent forms for new patients must be modified to include statement that methyl CCNU has been shown to result in a small but increased risk of leukemia when compared to general populations.

### Detail Summary Sheet

Title: H-77-09 (\*C-01). A clinical trial to evaluate postoperative immunotherapy and postoperative systemic chemotherapy in the management of resectable colon carcinoma.

Technical Approach: Combination chemotherapy and immunotherapy are administered through the LAMC Hematology/Oncology Outpatient Clinic.

Progress: Patient accrual began on 7 November 1977, and terminated 28 February 1983. As of 31 January 1983, a total of 1150 Dukes B and C patients have been nationally randomized to one of the three treatment arms. An additional 407 Dukes A and D patients have been entered for follow-up only. To date, LAMC has entered 27 patients on this protocol with seven having expired. Analysis is pending. The following addendum (dated 29 March 1983) from the NSAPB should be noted: 1) as of 1 March 1983, no new Dukes B or C patients will be randomized to C-01; 2) new Dukes B and C untreated patients may be registered to C-01; 3) patients previously randomized to chemotherapy arm of C-01 and still receiving drug per protocol must be notified of methyl CCNU leukemogenic effect. A consent form (amendment) must be signed.

Detail Summary Sheet

Title: H-79-15 (\*\*3P81). Conventional radiotherapy and heavy charged particle radiotherapy in the treatment of local and regional adenocarcinoma of the pancreas.

Technical Approach: Patients with local and regionally advanced adenocarcinoma of the pancreas are treated with heavy, charged particle following surgery.

Progress: LAMC, to date, has entered one patient on this study. The study is now closed with no patients at LAMC surviving. Follow-up is continuing at other institutions. Analysis is pending.

Detail Summary Sheet

Title: H-78-16 (\*\*6G-61). Phase III study of radiotherapy plus hydroxyurea and BCNU versus radiotherapy plus hydroxyurea and procarbazine, CCNU, vincristine (PCV) for the treatment of primary malignant brain tumor.

Technical Approach: Patients were randomized between the two treatment arms.

Progress: LAMC, to date, has entered one patient to this study. The study is now closed with no patients at LAMC surviving. Follow-up is continuing at other institutions. Analysis is pending.

### Detail Summary Sheet

Title: H-78-19 (\*\*3S-62). A phase III study comparing adriamycin in 5-FU (arm C) versus BCNU and adriamycin and Ftorafur (arm N) for patients with mytomyin C and adriamycin and Ftorafur (arm J) with disseminated gastric cancer.

Technical Approach: Patients were randomized between the two treatment arms.

Progress: To date, LAMC has entered three patients to this study. The study is now closed with no patients at LAMC surviving. Follow-up is discontinued at all institutions. Statistical analysis reveals significant KPS (Karnovsky's) for all United States, but only for 90-100 for Japan, possibly reflecting difficulties in assigning KPS. No significant trends are noted for Japanese arm J being better than C or United States arm C being superior to N. Nonmeasurable disease and prior surgery likewise have a better trend (none significant).

Detail Summary Sheet

Title: H-80-28 (\*B-16). A protocol to compare segmental mastectomy and axillary dissection with and without radiation of the breast and total mastectomy and axillary dissection.

Technical Approach: This study is being conducted through General Surgery, Radiation Therapy, and the Hematology-Oncology Clinic.

Progress: Patient accrual began 8 April 1976 for this protocol. As of 31 January 1983, 1742 patients have been randomized nationally among the three treatment groups. LAMC, to date, has entered eight patients in this study, all of which are surviving. Accrual and follow-up continue.

Detail Summary Sheet

Title: H-80-30 (\*\*4P-81). A study of adriamycin versus adriamycin CIS-platinum in patients with unresponsive metastatic prostate cancer.

Technical Approach: Patients with refractory cancer of the prostate were randomly assigned and received adriamycin versus adriamycin and CIS-platinum.

Progress: LAMC, to date, has entered five patients to this study. The study is now closed with no patients at LAMC surviving. Follow-up is continuing at other institutions. Analysis is pending.

Detail Summary Sheet

Title: H-80-33 (\*\*2091). A clinical trial of seven-drug versus nine-drug chemotherapy in extensive disease, and seven-drug with late consolidated radiotherapy and limited disease oat cell lung cancer.

Technical Approach: Patients with extensive oat cell carcinoma are randomly assigned to receive seven versus nine drugs in combination chemotherapy regimens. Patients with limited oat cell carcinoma are treated with a seven drug regimen with late consolidation of therapy.

Progress: This second generation study was activated on 29 May 1980, utilizing the results of NCOG 2061. Extensive disease patients were randomized to one of three chemotherapeutic arms: VAM x 3 → POCC/VAM or alternating POCC/VAM or POCC/VAM/HP. Limited disease patients were to receive alternating POCC/VAM for nine months then be restaged, with patients having a bronchoscopically confirmed, complete response being randomized to receive radiotherapy or no radiotherapy.

To date, LAMC has put 21 patients on this protocol. The three surviving patients are being actively followed. This study is currently open to accrual and to follow-up.

### Detail Summary Sheet

Title: H-81-35 (\*\*4T-82). Combination of chemotherapy for bulky or recurrent germinal cell tumors with and without lithium carbonate.

Technical Approach: Patients with bulky or recurrent germinal cell tumors are randomly assigned to treatment with combination chemotherapy with or without lithium carbonate to evaluate use of this drug to reduce neutropenia.

Progress: This study, which was begun 16 May 1979, is showing excellent results. Patients with advanced pulmonary and/or subdiaphragmatic disease made up the majority of patients (64 percent). Overall, the complete response rate was 82 percent (60/73) and for patients who completed prescribed therapy the rate was 80 percent. To date, LAMC has put nine patients on this protocol, with one having expired. This protocol is open for accrual.

### Detail Summary Sheet

Title: H-81-36 (\*\*4T83J). A randomized comparison of adjuvant versus no adjuvant chemotherapy in testicular cancer. A testicular cancer intergroup study: an intergroup comprehensive protocol for the monitoring of stage I and treatment of stage II non-seminomatous, non-choriocarcinoma testicular germ cell tumors.

Technical Approach: This protocol randomly assigns patients with stage II testicular cancer to close clinical follow-up versus adjuvant chemotherapy following radical lymphadenectomy.

Progress: To date, LAMC has entered four patients on this study. The study is still open to active accrual and follow-up.

### Detail Summary Sheet

Title: H-81-37 (\*\*9M91). A non-randomized trial of combination chemotherapy and sequential hemi-body radiation therapy in high tumor burden multiple myeloma.

Technical Approach:

Progress: Patient accrual began in February 1981. LAMC, to date, has entered three patients to this protocol with one having expired. This study is open for active accrual and follow-up.

Detail Summary Sheet

Title: H-81-39 (\*B14). A clinical trial assessing tamoxifen in primary breast cancer with negative axillary nodes and positive estrogen receptors.

Technical Approach: Tamoxifen will be administered through the Hematology/Oncology Clinic.

Progress: This protocol was open to patient entry on 4 January 1982. Two-hundred and eighty-five patients have been entered nationally as of 31 January 1983. LAMC, to date, has entered four patients to this protocol. This protocol is open to accrual and follow-up.

### Detail Summary Sheet

Title: H-81-40 (\*B13). A clinical trial assessing sequential methotrexate/5-FU in the management of primary breast cancer with negative axillary nodes and estrogen receptors.

Technical Approach: Chemotherapy will be administered through the Hematology/Oncology Clinic.

Progress: This protocol was activated on 1 June 1981. As of 31 January 1983, 118 patients had been randomized nationally. LAMC, to date, has entered one patient to this protocol. This study is open to accrual and follow-up. Changes: previous to 1 February 1982, patient entry had been restricted to node-positive patients whose tumors were kept ER positive. Since 1 February 1982, patient entry has been open to node-positive patients who are age 60-70 regardless of ER or PR. In addition, all patients under 60 who are PR positive are eligible for protocol B-12, except those age 49 or younger with ER negative tumors.

In January 1983, the NSABP executive committee decided to extend the period of tamoxifen administration for those patients currently receiving tamoxifen as part of protocol B-12. The period of tamoxifen administration will be extended one year beyond the normal two-year period of 17 courses of chemotherapy, for a total of three years.

Accrual began 1 June 1981. As of 31 January 1983, 565 patients have been randomized nationally. To date, LAMC has entered four patients to this protocol. This study is open to active accrual and follow-up.

### Detail Summary Sheet

Title: H-81-41 (\*B-12). A clinical trial comparing PF with and without adriamycin in management of primary breast cancer with positive axillary nodes and estrogen receptors positive.

Technical Approach:

Progress: As of 31 March 1983, 565 patients had been randomized nationwide. LAMC, to date, has put four patients on this protocol.

Detail Summary Sheet

Title: H-81-42 (\*B-11). A clinical trial comparing PF with and without adriamycin in management of primary breast cancer with positive axillary nodes and estrogen receptors negative.

Technical Approach:

Progress: Accrual began 1 June 1981. As of 31 January 1983, 379 patients have been randomized nationally. To date, LAMC has entered two patients to this protocol. This protocol is open for active accrual and follow-up.

Detail Summary Sheet

Title: H-81-43 (\*\*I80-12). Delta 9 tetra hydrocannabinol for nausea and vomiting induced by antineoplastic chemotherapy.

Technical Approach: To reduce nausea and vomiting induced by antineoplastic agents in patients refractory to conventional treatment.

Progress: The purpose of this NCI study is to only follow the adverse reactions that are reported from various institutions participating in this study. To date, LAMC has put 14 patients on this protocol. As of August 1983, one patient continues to participate in this study. This study is open to active accrual and follow-up.

### Detail Summary Sheet

Title: H-82-43 (\*\*1B-80-1). A phase II randomized study comparing effective non-cross resistant, alternating combinations (CMF/FOAM) with sequential use of the same combinations for metastatic breast cancer.

Technical Approach: To determine the efficacy of alternating versus sequential use of CMF and FOAM in this class of patients, in terms of response, toxicity and survival.

Progress: To date, overall accrual for the NCOG protocol has been 52 patients. LAMC has put one patient on this protocol. An insufficient number of patients makes drawing meaningful conclusions from the two groups difficult. Toxicity is acceptable and patient tolerance of the multidrug combination is good. This study is open to accrual and follow-up.

Detail Summary Sheet

Title: H-82-44 (\*\*13L-80-2). A phase II study of intermittent prednimustine in the treatment of refractory non-Hodgkins lymphoma.

Technical Approach: To determine the efficacy of prednimustine in this class of patients in terms of response, toxicity and survival.

Progress: This study began in September 1981. To date, LAMC has entered four patients to this protocol with one having expired. This protocol is currently open to accrual and follow-up.

Detail Summary Sheet

Title: H-82-45 (\*\*9L80-3). A phase II study of intermittent prednimustine treatment of refractory, chronic, lymphocytic leukemia.

Technical Approach: Prednimustine is administered to patients with refractory chronic lymphocytic leukemia.

Progress: Protocol accrual began in May 1981, and 20 patients had been registered as of 31 December 1982. LAMC has entered eight patients to this protocol, three of whom have expired. This protocol is currently open for active accrual and for follow-up.

### Detail Summary Sheet

Title: H-82-46 (\*\*6G81). A randomized study of irradiation, irradiation plus misonidazole, and irradiation plus BCNU for the treatment of metastases to the brain.

Technical Approach: This protocol involves the application of irradiation to three treatment groups.

Progress: As of 1 December 1981, 23 patients had been entered to this randomized study to evaluate three treatments for brain metastases. Accrual has been disappointingly low. Misonidazole became available for this protocol in October 1980, but even with this fact, patient accrual rate is about 1.5 patients per month. At this rate of entry or at a substantially increased rate of entry (doubling), the study will require seven to fifteen years of additional accrual. As a result of the lack of patient entry and apparent lack of interest, this protocol was closed as of 23 March 1982, after consideration of the possible amendments by the study chair and the NCOG Executive Committee. LAMC had entered five patients to this protocol, all of whom expired. This protocol is closed to accrual and follow-up is discontinued.

Detail Summary Sheet

Title: H-82-47 (\*\*1B81-1). A phase II study to determine the effectiveness of medroxyprogesterone acetate (Provera) in refractory breast cancer in postmenopausal women.

Technical Approach: This protocol involves the administration of Provera to postmenopausal women with refractory breast cancer.

Progress: This study was opened on 12 February 1982, and as of 31 December 1982, there were 16 patients registered for the Northern California Oncology Group. LAMC, to date, has entered three patients to this protocol, one of whom has expired. This protocol is currently open for active accrual and follow-up.

### Detail Summary Sheet

Title: H-82-48 (\*\*6G91). A study of 5-FU and CCNU before radiotherapy and HU and before radiotherapy and HU and misonidazole followed by alternating courses of procarbazine and vincristine and BCNU and 5-FU for treatment of primary malignant brain tumor.

Technical Approach: This protocol involves the application of different modalities of treatment to patients with primary malignant brain tumors.

Progress: Between 21 November 1980 and 31 December 1982, this phase II protocol accrued 101 patients from all institutions participating in the NCOG. LAMC entered five patients to this protocol with four patients having expired. This protocol is currently closed to accrual with only active follow-up continuing. Results, to date, show median survival was 47 weeks for all patients and 58 weeks for those receiving post-XRT chemotherapy. Further analysis is pending.

Detail Summary Sheet

Title: H-82-49 (\*\*1B81). Evaluation of cardiotoxicity of weekly adriamycin.

Technical Approach: This protocol involves the weekly administration of adriamycin to chemotherapy patients.

Progress: This protocol was open for accrual 28 October 1981. To date, LAMC has entered eight patients on this protocol with five having expired. This study is currently closed for accrual. Active follow-up continues. Analysis is pending.

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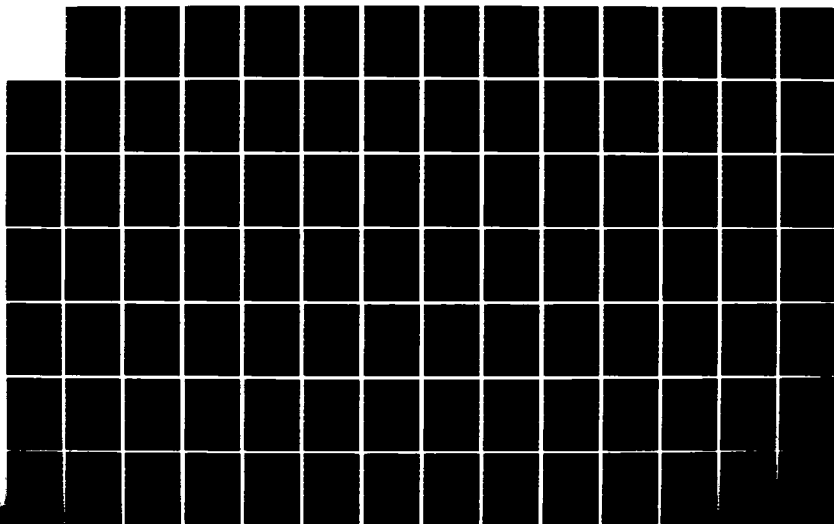
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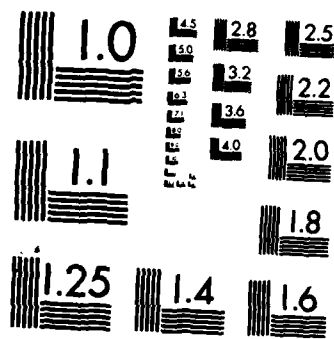
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### Detail Summary Sheet

Title: H-82-50 (\*\*6G80-1). A phase II study of PCNU for recurrent primary malignant brain tumor.

Technical Approach:

Progress: This study was open for accrual 16 December 1980. It was designed to evaluate the effectiveness of PCNU for recurrent primary brain tumors. Early results were most promising in the subset of NGM patients who had not been previously chemotherapeutically treated. Forty-six patients were accrued for all of NCOG, 26 of whom were NGM with no prior chemotherapy. LAMC entered two patients to this study, one of whom has expired. The main conclusion is as follows: the observed activity of PCNU in this study (27% response rate in median time to progression of 28 weeks) is comparable with other nitrosoureas. However, BCNU and CCNU are clinically available and widely used. There appears to be no reason to make available yet another nitrosourea for clinical trials. This study is currently closed with registered patients in active follow-up only.

Detail Summary Sheet

Title: H-82-51 (\*\*5091). Chemotherapy of advanced ovarian cancer: adriamycin - cyclophosphamide versus platinum-adriamycin-cyclophosphamide.

Technical Approach:

Progress: This study was activated on 15 August 1980, and was closed to accrual on 16 March 1983. LAMC entered two patients to this study, one of which expired. Active follow-up on registered patients continues. Analysis is pending.

### Detail Summary Sheet

Title: H-82-52 (\*\*7H81). A randomized phase II study of platinum with or without methotrexate for recurrent metastatic squamous cell carcinoma of the head and neck.

Technical Approach:

Progress: This study was activated on 13 June 1979, and closed 30 September 1981. LAMC had put two patients on this study, both of whom have expired. This study is closed for accrual and follow-up. This study has been submitted for publication with the following results: this study shows that methotrexate with leucovorin can safely be added to CIS-platin without increased nephrotoxicity. Only 10 percent of patients had a creatinine elevation less than 2 mg percent, and those were reversible. Hematologic and oral toxicity were more severe in the combination group, although this resulted in only one possible chemotherapy-related death. In conclusion, the combination of two of the best single agents for head and neck cancer, CIS-platin and methotrexate, did not improve results for treatment of recurrent disease. Combinations which appear to have improved results should be compared to single agents.

Detail Summary Sheet

Date: 21 Aug 83

Prot. No.: H-82-53

Status: Terminated

Title: The prophylactic use of intravenous immunoglobulin in adult neutropenic patients with acute hematologic malignancies.

Start Date: May 82

Est Comp Date: Terminated

Principal Investigator:

LTC J Redmond, MD

MAJ H Wold, MD

Facility:

LAMC

Dept/Svc:

Hematology/Oncology

Associate Investigators:

Key Words: intravenous immunoglobulin, neutropenia

Accumulative MEDCASE

Cost:

Est Accumulative

OMA Cost:

Periodic Review

Study Objective: To evaluate the efficacy of immunoglobulin in preventing hospital acquired infection in terms of patients with hematologic malignancies and therapy-induced neutropenia.

Technical Approach: Patients were randomized to placebo or intravenous immunoglobulin on a regular schedule. Clinical and documented infections were then tabulated. Measurements of baseline immunoglobulins and immunoglobulin levels after drug administration were measured. It was anticipated that immunoglobulin specificity for the bacteria recovered from infections could be analyzed. This information would be compared to the activity of the preparation delivered as prophylaxis.

Progress: This study was terminated by the principal investigator at Walter Reed Army Medical Center, Dr. Barbara Alving. This was because of lack of accrual in that institution.

### Detail Summary Sheet

Title: H-82-54 (\*\*3E81). The phase II protocol of heavy charged particle radiotherapy for localized esophageal squamous cell carcinoma.

Technical Approach:

Progress: This is a phase II, non-randomized study for helium and heavy ion irradiation of localized carcinoma of the esophagus. The tumor dose was initially 60.0 Gray-equivalence given at 2.0 Gray-equivalence protraction over a period of seven to eight weeks, but has been raised in increments to the present level of 69.75 Gye given at 2.25 Gye protraction in 7.5-9 weeks. Of the initial 22 patients treated with helium, only four had local control of their tumor (18 percent). The mean and median survival was nine months in helium-treated patients.

As these results did not appear different than those obtained with low LET megavoltage radiotherapy, we have started a phase II trial using neon ion irradiation. The superior biological potential of this beam over helium ions may afford an improvement in local control. If there is a significant improvement in results, a prospective randomized study may be needed. To date, LAMC has entered no patients to this study. This study is open for active accrual and follow-up.

### Detail Summary Sheet

Title: H-82-55 (\*\*3S91). A phase I-II study evaluating the toxicity and effectiveness of charged particle radiotherapy for patients with unresectable localized gastric cancer.

Technical Approach:

Progress: This NCOG protocol, activated on 13 July 1981, was closed 25 May 1982 due to lack of accrual. LAMC did not enter any patients to this protocol. Because of insufficient data, and a low accrual rate of three patients, the information from this study will not be analyzed. It should be noted that the inclusion of these patients in a broader disease category of upper abdominal cancer is being considered in a developing protocol using a multimodal approach, randomizing the radiotherapy portion. This protocol is closed for accrual and for follow-up.

### Detail Summary Sheet

Title: H-82-56 (\*\*3S81J). A phase III study comparing adriamycin and Ftorafur versus radiation and adriamycin and Ftorafur versus mitomycin C and Ftorafur for patients with disseminated gastric cancer.

Technical Approach:

Progress: This protocol was activated 16 April 1981, and closed as of 25 May 1982. LAMC entered 0 patients to this study. This protocol is closed to accrual and follow-up. No analysis is pending.

### Detail Summary Sheet

Title: H-82-57 (\*\*4B81-2). A phase II trial of CIS-platin, methotrexate and vinblastine in metastatic carcinoma of the urinary bladder, ureters or renal pelvis.

Technical Approach:

Progress: To date, LAMC has entered two patients to this protocol with one having expired. This study is currently open for active accrual and follow-up. Projected completion of this study is 1983.

### Detail Summary Sheet

Title: H-82-58 (\*\*0C-81-1). A phase II study of 4<sup>1</sup> epi-doxorubicin (4<sup>1</sup> epi-adriamycin) in the treatment of metastatic melanoma in carcinoma of the breast or colorectum and an evaluation of cardiotoxicity.

Technical Approach:

Progress: This study was activated 12 July 1982, and closed 16 March 1983. LAMC had entered four patients to this protocol, one of whom has expired. This study is closed to accrual. The patients are being actively followed. It was concluded in this study that 4<sup>1</sup>-epi-adriamycin is a well tolerated drug with little activity in colorectal carcinoma.

### Detail Summary Sheet

Title: H-82-59 (\*\*2N-81-1). A phase II study of advanced lung cancer: master protocol. Arm A: a phase II study of 4<sup>1</sup> epi-doxorubicin in the treatment of advanced lung cancer and an evaluation of cardiotoxicity.

Technical Approach:

Progress: This study was activated 12 July 1982, and closed as of 16 March 1983, to adeno and squamous histologic types. It remains open for large types. To date, LAMC has entered three patients to this study, two of which have expired. This study remains open to all patients with large cell histology and all patients who are registered for this study are in active follow-up.

Detail Summary Sheet

Date: 31 Aug 83

Prot. No.: H-82-60

Status: Terminated

Title: Platelet-specific antibody in thrombocytopenic disorders.

Start Date:

Est Comp Date:

Principal Investigator:  
MAJ GS Chapman, MD

Facility:  
L A M C

Dept/Svc:  
Hematology/Oncology

Associate Investigators:

Accumulative MED CASE  
Cost:

Est Accumulative  
OMA Cost:

Periodic Review  
Results:

Study Objective: To develop and test an assay for measuring platelet bound IgG, IgM, and complement (C<sub>1</sub>Q). The assay will then be used to evaluate patients with thrombocytopenia of diverse etiologies.

Technical Approach: This study will be performed in conjunction with a protocol utilizing <sup>111</sup>Indium oxine as a radiolabel to measure in vivo platelet survival. Seventy-five patients will be evaluated. The assay procedure will include the following: white blood will be drawn from the subject into EDTA by antecubital fossa venipuncture using standard aseptic technique. Platelet-rich plasma will be prepared by centrifugation. The platelets will be pelleted, resuspended in autologous platelet poor plasma, and then washed over a Sepharose 2-B column using isotonic buffer. Platelet aliquots will then be incubated separately with appropriate amounts of <sup>125</sup>I labeled molecular probes. The platelet suspension will then be washed over a millipore filter, and the specific activity of the platelets adherent to the filter determined using a gamma scintillation counter. The quantity of immunoglobulin or complement bound to the platelets will be calculated according to the specific activity of the <sup>125</sup>I labeled molecular probe used in the assay. An elevated level will be defined as that greater than two SD above the normal range determined from non-thrombocytopenic volunteers.

Progress: This protocol was never activated and there are no plans to activate it.

Detail Summary Sheet

Date: 31 Aug 83

Prot. No.: H-82-61

Status: Ongoing

Title: Effect of mezlocillin on platelet function.

Start Date: Feb 83

Est Comp Date: Indefinite

Principal Investigator:

LTC D Gandara, MD  
MAJ HG Wold, MD  
CPT RP Mansour, MD  
CPT R Ulirsch, MD  
LTC DR Haburchak, MD

Facility:

L A M C

Dept/Svc:

Hematology/Oncology

Associate Investigators:

Key Words: mezlocillin, platelet function

Accumulative MEDCASE

Cost:

Est Accumulative

OMA Cost:

Periodic Review

Results:

Study Objective: To evaluate the effects of mezlocillin on platelet function in terms of toxicity.

Technical Approach: A total of five patients were treated for clinical sepsis, receiving a loading dose of 2 mg/kg, then 1.5 mg/kg every eight hours, of Tobramycin, and 250 kg/day of mezlocillin in six divided doses with a maximum of 18 grams for 24 hours. Laboratory tests (i.e., baseline PT, APTT, platelet counts, template bleeding times, and platelet aggregation studies) were performed on each patient.

Progress: The preliminary results in the initial five patients show no thrombocytopenia, no prolongation of PT or APTT, no abnormalities of platelet aggregation, normal template bleeding times, and no clinical bleeding. However, it is too early to assess the clinical significance of the preliminary findings. Further patient studies will have to be performed for adequate evaluation of platelet function of this drug regimen.

### Detail Summary Sheet

Title: H-82-62 (\*\*3082-1). Phase II study of continuous infusion FUDR: intravenous versus intra-arterial in patients with colon cancer metastatic to liver.

Technical Approach:

Progress: This protocol was activated 5 April 1983. To date, LAMC has entered 0 patients to this protocol. This protocol is open to active accrual and follow-up. Anticipated completion date of this protocol is 1986.

Detail Summary Sheet

Date: 30 Aug 83

Prot. No.: H-83-63

Status: Ongoing

Title: Double-blind, randomized, parallel comparison of two different dosage regimens of naproxen sodium in patients with bone pain due to metastatic cancer.

Start Date: May 83

Est Comp Date: Indefinite

Principal Investigator:

LTC D Gandara, MD

CPT R Mansour, MD

Facility:

L A M C

Dept/Svc:

Hematology-Oncology

Associate Investigators:

Key Words: naproxen sodium, metastatic cancer

Accumulative MED CASE

Cost:

Est Accumulative

OMA Cost:

Periodic Review

Results:

Objective: To compare the relative efficacy and safety of a higher total daily dose of naproxen sodium (1650 mg/day for three days) to a lower total daily dose (1100 mg on day 1 followed by 825 mg on days 2 and 3) in patients with moderate to severe, persistent bone pain due to metastatic cancer.

Technical Approach: This is a double-blind, randomized parallel comparison study of three days duration in a minimum of 20-25 (per investigator) hospitalized patients or in suitable outpatients.

Progress: The total number of subjects randomly assigned to this study during the report period was two. Both patients completed the study and attained good pain relief from the drug regimen received. No adverse effects were noted in these patients. The accrual for this study has been very slow. Thus, additional patients need to be entered to this study during the next study period.

Detail Summary Sheet

Date: 31 Aug 83

Prot. No.: H-83-64

Status: Ongoing

Title: Droperidol and dexamethasone for the control of chemotherapy-induced nausea and vomiting.

Start Date: April 83

Est Comp Date: Indefinite

Principal Investigator:

CPT L Geier, MD

LTC D Gandara, MD

Facility:

LAMC

Dept/Svc:

Hematology/Oncology

Associate Investigators:

Key Words: droperidol, dexamethasone, chemotherapy-induced nausea and vomiting

Accumulative MED CASE

Cost:

Est Accumulative

OMA Cost:

Periodic Review

Results:

Study Objective: To evaluate the combination of high-dose droperidol and high-dose dexamethasone, given in intermittent intravenous injections, for its effectiveness in preventing or controlling nausea and vomiting related to strongly emetogenic cancer chemotherapy drugs.

Technical Approach: One half of the patients will receive droperidol/dexamethasone with their first course and crossover to metoclopramide with the second course of chemotherapy; the other half will receive the reverse of this. In this way, each patient serves as his own control. Patients will randomly be assigned to either group, which will be similar with respect to patient age, underlying malignancy, and type of chemotherapy received.

Progress: A total of seven patients were entered into this protocol, one of whom died in the course of the study. Six patients were treated for chemotherapy-induced nausea and vomiting by administration of dexamethasone, droperidol, and metoclopramide. Preliminary results show comparable effectiveness between metoclopramide and the combination of droperidol and dexamethasone in controlling chemotherapy-induced nausea and vomiting. However, it is too early to assess the clinical significance of the preliminary findings. Further patient studies will have to be performed for adequate evaluation of this drug combination in controlling chemotherapy-induced nausea and vomiting.

Detail Summary Sheet

Date: 30 Aug 83

Prot. No.: H-83-65

Status: Ongoing

Title: Incidence of asymptomatic von Willebrand syndromes in patients with mitral valve prolapse.

Start Date: June 83

Est Comp Date: Indefinite

Principal Investigator:

CPT R Mansour, MD

CPT C White, MD

LTC D Gandara, MD

CPT R Ulirsch, MD

H Palkuti, BS

Facility:

L A M C

Dept/Svc:

Hematology/Oncology

Associate Investigators:

Key Words: von Willebrand syndromes, mitral valve prolapse

Accumulative MEDCASE

Cost:

Est Accumulative

OMA Cost:

Periodic Review

Results:

Study Objective: To determine the incidence of von Willebrand's disease in patients with mitral valve prolapse.

Technical Approach: The plasma of patients with mitral valve prolapse will be studied via laboratory evaluation to determine if a relationship exists between mitral valve prolapse and asymptomatic von Willebrand disease.

Progress: The total number of subjects involved in this study during the report study was nine. Blood was obtained from nine subjects and bleeding times were done. All bleeding times have been normal. All plasma samples were frozen for further testing. All initial mechanisms for patient referral and data control have been set up. No patient have suffered ill effects as a result of this study. Additional patients will have to be entered and plasma samples collected during the coming year. It is anticipated study will be completed in the spring of 1984.

Detail Summary Sheet

Date: 30 Aug 83

Prot. No.: H-83-66

Status: Ongoing

Title: National intergroup protocol for intermediate thickness melanomas 1.0 to 4.0 mm: evaluation of optimal surgical margins (2 vs 4 cm) around the primary melanoma and evaluation of elective regional lymph node dissection.

Start Date: August 83

Est Comp Date: Indefinite

Principal Investigator:  
COL J Homann, MD

Facility:

Dept/Svc:  
Hematology/Oncology and General  
Surgery

Associate Investigators:

Key Words:

Accumulative MEDCASE  
Cost:

Est Accumulative  
OMA Cost:

Periodic Review  
Results:

Study Objective:

Technical Approach:

Progress: See S-83-07, same title, for complete annual report.

### Detail Summary Sheet

Title: H-83-67 (\*\*6G82-1). Phase I-II study of radiotherapy plus BUdR and procarbazine, CCNU, vincristine (PCV) for the treatment of primary malignant brain tumors.

Technical Approach:

Progress: This protocol was activated 3 January 1983. LAMC, to date, has entered 0 patients to this protocol. This protocol is open for active accrual and follow-up. Anticipated completion date is 1986.

Detail Summary Sheet

Title: H-83-68 (\*\*4P-82-1). A phase II trial of single agent thymosin fraction 5 for inoperable extensive renal or prostate carcinoma.

Progress: This protocol was activated 4 March 1983. To date, LAMC has entered one patient to this protocol. This protocol is open for active accrual and follow-up. Anticipated completion date is 1986.

Detail Summary Sheet

Date: 20 Sep 83

Prot. No.: ID-83-03 Status: Completed

Title: An investigation of the bacterial colonization of physicians' stethoscopes at Letterman Army Medical Center.

Start Date: Apr 83

Est Comp Date: Completed

Principal Investigator:  
CPT D Weldon, MD

Facility:  
LAMC

Dept/Svc:  
Infectious Disease

Associate Investigators:  
LTC DR Haburchak, MD  
M Stevenson, MPH  
SP4 P Black

Key Words: bacterial colonization

Accumulative MED CASE  
Cost:

Est Accumulative  
OMA Cost:

Periodic Review  
Results:

Study Objective: To attempt to determine what role the stethoscopes of physicians, nurses, and other health care personnel may have as a vehicle for spread of common hospital pathogenic bacteria, the longevity of pathogenic bacteria on stethoscopes, and the effectiveness of readily available cleansing procedures.

Technical Approach: Medical personnel will complete a standard form with physician and patient information, as well as frequency of stethoscope cleaning. A swabbing will be obtained of the diaphragm, bell and sides of the stethoscope, and cultures quantitatively evaluated for pathogens (i.e., immersion of four autoclaved military issue stethoscopes into saline dilutions of  $10^5$  organisms/ml of S. Aureus, K. Pneumoniae, and P. Aeruginosa, with subsequent air-drying and sampling at one, six and 24 hours). Stethoscopes are then washed with alcohol prep-pads, and two days later, cultures are repeated on all stethoscopes. Survey forms are recompleted.

Progress: Staphylococcus epidermidis was found to be a major colonizer, and there were no apparent gram negative rod contaminants. Abstract has been submitted.

Detail Summary Sheet

Date: 12 Aug 83

Prot. No.: Ns-82-03 Status: Ongoing

Title: Social-psychiatric patient and nursing.

Start Date: Oct 82

Est Comp Date: Indefinite

Principal Investigator:

LTC JPG Moskovites, ANC

MAJ R Fetter, ANC

CPT R Billingsly, MC

V Peterson-Tilden, DNS

Facility:

LAMC

Dept/Svc:

Nursing

Associate Investigators:

Key Words: psychiatric patient, nursing

Accumulative MED CASE

Cost:

Est Accumulative

OMA Cost:

Periodic Review

Results:

Study Objective: To determine social-psychiatric variables related to use of restraints on psychiatric patients by nursing staff, and to measure staff perception of ward atmosphere as a variable in the incidence of the use of restraint. This is a preliminary study to ultimately assess under multiple conditions restraint-related intervention by nursing staff.

Technical Approach: In this descriptive study, the investigators will correlate social-psychiatric patient profile and milieu, and the use of restraint by nursing and physician staff. Retrospective and prospective demographic and diagnostic data and milieu factors will be collected, utilizing patient files of both restrained and non-restrained patients. The nurse-initiator of restraint will code the incidence. Ward atmosphere will be measured by the Moos Ward Atmosphere Scale. Data will be comparatively analyzed for trends, using Chi-square analysis for nominal data, analysis of variance for unequal groups, and multiple regression for interval data.

Progress: Data presently being collected.

Detail Summary Sheet

Date: 1 Nov 82

Prot. No.: OB-78-01

Status: Ongoing

Title: Large animal surgery: an important addition to residency training in obstetrics and gynecology.

Start Date: Aug 78

Est Comp Date: Indefinite

Principal Investigator:  
LTC CA Winkel, MD

Facility:  
L A M C

Dept/Svc:  
Obstetrics/Gynecology

Associate Investigators:  
OB-GYN staff

Key Words: large animal, surgery, obstetrics, gynecology

Accumulative MED CASE  
Cost: None

Est Accumulative  
OMA Cost: \$2000

Periodic Review  
Results: Approved

Study Objective: The purpose of this project is to augment residency education in Obstetrics and Gynecology by providing hands-on experience in bowel, genitourinary tract, and vascular surgery. The project is set up in a fashion to allow junior residents an opportunity to learn surgical techniques, develop proficiency in instrument handling, and develop self confidence while doing surgery under a no-pressure situation.

Technical Approach: At the present time, residents are performing surgery on laboratory dogs. The techniques taught include small-bowel resection and re-anastomosis, large bowel resection, re-anastomosis of ureters, and repair of vena caval injuries.

Progress: Large animal surgery, which was stopped prior to July 1982 because of an insufficient number of staff members, has been resumed as a result of an increase in personnel.

Detail Summary Sheet

Date: 20 Sep 83

Prot. No.: OB-80-11

Status: Terminated

Title: The role of extraadrenal 21-hydroxylation of plasma progesterone as a source of deoxycorticosterone (DOC) in the development of hypertension in pregnant and nonpregnant subjects: establishment of an animal model.

Start Date: 14 Oct 80

Est Comp Date: Terminated

Principal Investigator:  
LTC CA Winkel, MD

Facility:  
L A M C

Dept/Svc:  
Obstetrics/Gynecology

Associate Investigators:

Key Words: deoxycorticosterone, pregnant, hypertension, animal model

Accumulative MED CASE  
Cost:

Est Accumulative  
OMA Cost: \$5000

Periodic Review  
Results:

Study Objective: The extraadrenal formation of deoxycorticosterone (DOC) from circulating progesterone has been demonstrated in pregnant and nonpregnant women, adrenalectomized women, and men. To study the role of extraadrenal 21-hydroxylase activity in the development of pregnancy-induced hypertension, it is necessary to have an animal model. The objective of this study is to determine if extraadrenal DOC formation from progesterone will lead to the development of hypertension in the rabbit.

Technical Approach: Five rabbits were surgically prepared with femoral artery catheters. Following recovery from surgery, the animals were placed in metabolic cages for a five-day control period. On the sixth day, a subdermal osmotic mini pump containing progesterone was implanted and the animals returned to the cages for 14 days of observation. Blood pressure, heart rate, plasma hormones and electrolyte as well as 24-hour balances were taken prior to and 4, 9, and 14 days after the implantation of the pump.

Progress: The animals showed a progressive increase in body weight of 220 grams associated with an increase in food and water intake in the absence of changes in urinary excretion. Blood pressure and heart rate were not altered. Plasma electrolytes, osmolality, protein and hematocrit were not significantly changed. Plasma progesterone was elevated but the values obtained were well below those desired, i.e., similar to levels during pregnancy. Plasma aldosterone was increased, while ACTH tended to fall. This study was discontinued due to the inability to develop chronically elevated progesterone levels of the magnitude desired.

Detail Summary Sheet

Date: 5 Jul 83

Prot. No.: OB-81-15

Status: Ongoing

Title: A comparison of in vivo tissue levels of cefoxitin following IM section and post surgical irrigation in the guinea pig genital tract.

Start Date: 18 Aug 80

Est Comp Date: 1 Sep 83

Principal Investigator:  
CPT E Oortman, MD

Facility:  
L A M C

Dept/Svc:  
Obstetrics/Gynecology

Associate Investigators:  
LTC JP Elliot, MD  
LTC CA Winkel, MD

Key Words: cefoxitin, IM injection, irrigation, guinea pig

Accumulative MED CASE  
Cost: None

Est Accumulative  
OMA Cost: \$4000

Periodic Review  
Results: N/A

Study Objective: To determine the mechanism of action of antibiotics used in irrigation at time of C-section.

Technical Approach: Serum and tissue levels of cefoxitin were obtained at timed intervals following IM injection and uterine irrigation in pregnant guinea pigs.

Progress: All in vivo testing completed. Final runs of HPLC to determine levels now being done.

Publications/Presentations: Abstract of paper accepted for presentation at the Armed Forces District meeting of ACOG and at the meeting of the Infectious Disease Society for Obstetrics and Gynecology. The paper will also be submitted for publication.

Detail Summary Sheet

Date: 5 Jul 83

Prot. No.: 0B-81-17

Status: Completed

Title: Evaluation of modes of administration of prophylactic cefoxitin for cesarean section.

Start Date: Oct 81

Est Comp Date: Completed

Principal Investigator:  
LTC JP Elliott, MD

Facility:  
L A M C

Dept/Svc:  
Obstetrics/Gynecology

Associate Investigators:  
CPT J Flaherty, MD

Key Words: cefoxitin, cesarean section, prophylaxis

Accumulative MED CASE  
Cost: None

Est Accumulative  
OMA Cost: \$4000

Periodic Review  
Results: N/A

Study Objective: To determine if the clinical outcome in patients having C-sections is similar with different methods of administering prophylactic antibiotics.

Technical Approach: Four treatment groups were defined: Group A (control) received no antibiotics. Group B (IV) was administered 2 g Cefoxitin IV after cord was clamped, then every six hours IV x 8 doses. Group C (irrigation) received 2 g cefoxitin to irrigate the uterus and peritoneum. Group D (IV plus irrigation) received a combination of B and C.

Progress: Data on 103 patients have been collected and analyzed. No significant statistical differences were found between the three treatment groups, but each treatment group approaches statistical significance when compared to the control group. Thus it would seem clinically appropriate and cost effective to administer one dose of antibiotic by uterine lavage at the time of C-section.

Publications/Presentations: A paper has been accepted for presentation at the AFD ACOG meeting in Las Vegas in October 1983.

Detail Summary Sheet

Date: 5 Jul 83

Prot. No.: OB-82-19

Status: Completed

Title: A prospective randomized study of breast stimulation to prevent postdates pregnancy.

Start Date: May 82

Est Comp Date: Completed

Principal Investigator:  
LTC JP Elliott, MD

Facility:  
L A M C

Key Words: breast stimulation, postterm pregnancy

Dept/Svc:  
Obstetrics/Gynecology

Associate Investigators:

Accumulative MED CASE  
Cost:

Est Accumulative  
OMA Cost:

Periodic Review  
Results:

Study Objective: To determine the effect of self-breast stimulation at home on the incidence of postdates pregnancy.

Technical Approach: One hundred patients were randomly assigned to a control group and 100 to the breast stimulation group at 39 weeks. Patients were analyzed for the total number reaching 42 weeks with an unripe cervix.

Progress: In the control group, 15/100 patients reached 42 weeks with a Bishop score of 8 or less compared to 5/100 in the group that breast stimulated. This difference is significant at the  $p < .01$  level. There were no antepartum or intrapartum complications associated with breast stimulation. In the low risk patient at term, breast stimulation will decrease the number of patients that will become post dates with the attendant risks of prolongation of pregnancy.

Publications and Presentations: A manuscript has been accepted for presentation at the AFD ACOG meeting in October 1983, in Las Vegas, and, in addition, has been submitted to the American Journal of Obstetrics and Gynecology.

Detail Summary Sheet

Date: 1 Nov 82

Prot. No.: OB-82-20

Status: Terminated

Title: Serum levels of oxytocin, prostaglandin F2 and PGFM, and arginine vasopressin associated with oxytocin challenge test and breast stimulation stress test.

Start Date: Oct 82

Est Comp Date: March 83

Principal Investigator:  
LTC JP Elliot, MD

Facility:  
L A M C

Key Words: oxytocin, prostaglandin, arginine vasopressin, stress test

Dept/Svc:  
Obstetrics/Gynecology

Associate Investigators:  
LTC CA Winkel, MD  
CE Wade, PhD

Accumulative MED CASE  
Cost: None

Est Accumulative  
OMA Cost: \$3000

Periodic Review  
Results: N/A

Study Objective: This study is designed to compare the standard oxytocin challenge test to a new method of causing contractions by breast stimulation. We want to determine if the contractions produced by each method are comparable.

Technical Approach: Forty patients will be assigned randomly to two treatment groups; group A will receive an OCT, Group B a BSST. Oxytocin, AVP, PCF<sub>2</sub> and PGFM baseline levels will be determined once, then subsequently reestablished when a readable test is achieved (3 contractions in a 10 minute period).

Progress: Terminated due to departure of principal investigator.

Detail Summary Sheet

Date: 9 Jun 83

Prot. No.: OB-82-21

Status: Completed

Title: Anaerobic bacteremia at parturition.

Start Date: 1 Nov 82

Est Comp Date: Completed

Principal Investigator:  
CPT J Zimmerman, MD

Facility:  
L A M C

Key Words: bacteremia, anaerobe, parturition

Dept/Svc:  
Obstetrics/Gynecology

Associate Investigators:  
R Leanza, PhD  
LTC JP Elliott, MD

Accumulative MED CASE  
Cost: None

Est Accumulative  
OMA Cost: None

Periodic Review  
Results: N/A

Study Objective: To establish the incidence of anaerobic bacteremia, following an uncomplicated vaginal delivery, in normal, term pregnant patients.

Technical Approach: Blood cultures were drawn from the patient 15 minutes postdelivery of the infant, and immediately following delivery of the placenta, cultures from the endometrium were acquired through triple-lumen catheters.

Progress: Blood and endometrial cultures were performed in fifty-four women who had uncomplicated vaginal delivery at term. The organisms recovered from the endometrial cultures were Lactobacillus, Hemophilus, Influenza, and Bacteroides (non-fragilis). One anaerobe was isolated. The organism was sensitive to penicillin, so current recommendations (i.e., penicillin G and gentamycin) appear to be adequate. Further investigation is needed to reveal the presence of other anaerobes not sensitive to penicillin.

Presentations and Publications: A paper will be presented at ACOG Armed Forces District Meeting in Las Vegas, Nevada, in October 1983, and submitted for publication to Obstetrics and Gynecology.

Detail Summary Sheet

Date: 5 Jul 83

Prot. No.: OB-82-22 Status: Terminated

Title: Neonatal effects of magnesium sulfate administered as a tocolytic agent.

Start Date: February 83

Est Comp Date: Terminated

Principal Investigator:

LTC JP Elliott, MD

LTC H Kilbride, MD

Facility:

LAMC

Dept/Svc:

Pediatrics

Associate Investigators:

Key Words: neonatal, magnesium sulfate, tocolytic agent

Accumulative MED CASE

Cost:

Est Accumulative

OMA Cost:

Periodic Review

Results:

Study Objective: To determine if magnesium sulfate administered to pregnant mothers in premature labor has any adverse effect on the neonate.

Technical Approach: Twenty-five patients with a diagnosis of premature labor or preterm premature rupture of membranes with or without labor will be studied. Gestational age must be between 26-36 weeks and magnesium sulfate must have been administered to the mother within 24 hours preceding delivery for candidacy. Maternal magnesium levels will be determined at delivery. Cord blood levels of magnesium and calcium and total protein will be determined. Apgar scores at birth, modified Prechtl neurological score, serial blood chemistries (magnesium, calcium, total protein, and bilirubin), and serial dextro stix will be assessed. Values obtained for magnesium, calcium, protein and bilirubin will be compared to published normal values in premature infants by  $X^2$  analysis.

Progress: No patients were accrued to this study. The protocol has been withdrawn because of reassignment of the principal investigator.

Detail Summary Sheet

Date: 20 Sep 83

Prot. No.: OB-83-23 Status: Ongoing

Title: Hormone and gonadotropin levels pre- and post-operatively in patients undergoing tubal ligation.

Start Date: Feb 83

Est Comp Date: 1984

Principal Investigator:  
LTC JR Caughron, MD

Facility:  
L A M C

Dept/Svc:  
Obstetrics/Gynecology

Associate Investigators:  
LTC CA Winkel, MD  
CE Wade, PhD

Key Words: gonadotropin, tubal sterilization

Accumulative MED CASE  
Cost:

Est Accumulative  
OMA Cost:

Periodic Review  
Results:

Study Objective: To evaluate hormonal and gonadotropic changes before and after tubal sterilization in healthy women of reproductive age.

Technical Approach: Fifty healthy, 20-40 year-old women, who request elective tubal sterilization, will be selected and undergo a physical examination and history. Selected patients will have a thyroid profile and fasting blood sugar drawn and assayed when the first control samples are collected, followed by basal body temperature graphs for the duration of the study. Serial samples for E2, Prog, LH, and FSH assay will be drawn on cycle days 5, 10, and on the fourth and eighth days after the thermal nadir and/or subsequent temperature rise. The blood samples will be labeled, the serum decanted and divided into four separate aliquots for storage, then frozen and stored at -75C in the Department of Clinical Investigation for processing at a later time. The pre-operative samples will be drawn the month preceding surgery. No blood will be drawn during the cycle month of surgery. All studies will be repeated during the second and sixth menstrual cycles following surgery and all of the serum samples processed. When all of the patient specimens have been collected they will be assayed to minimize possible laboratory error. Statistical evaluation will include ANOVA, regression analysis, chi-square and the Student's 't' test.

Progress: Patient accrual is expected to begin within the next month.

Detail Summary Sheet

Date: 8 Sep 83

Prot. No.: Path-83-01

Status: Ongoing

Title: Utilization of guinea pig RBCs for the detection of paramyxoviruses by the HAd procedure.

Start Date: Jul 83

Est Comp Date: Indefinite

Principal Investigator:  
COL CD Smith, MD

Facility:  
L A M C

Dept/Svc:  
Pathology

Associate Investigators:  
R Shiromoto

Key Words: hemadsorption, myxo-paramyxoviruses

Accumulative MED CASE  
Cost: N/A

Est Accumulative  
OMA Cost: N/A

Periodic Review  
Results:

Study Objective: To maintain a colony of 6-9 guinea pigs for the purpose of obtaining fresh RBCs. The GP RBCs are used in the standard hemadsorption procedure to detect the presence of myxo-paramyxoviruses in clinical specimens.

Technical Approach: Each week a guinea pig will be anesthetized and blood removed by cardiac puncture. The guinea pigs will be rotated on a regular basis to allow animals to recuperate from the trauma.

Progress: This process is an ongoing activity which is a standard and recognized method for detecting the presence of myxo-paramyxovirus. The methods used and data generated for routine clinical diagnosis of viruses are not applicable for presentation or publication.

Detail Summary Sheet

Date: 16 Sep 83

Prot. No.: Peds-81-01

Status: Ongoing

Title: Model for neonatal intubation and thoracostomy.

Start Date: 14 Jul 81

Est. Comp. Date: Indefinite

Principal Investigators:  
MAJ JH Jirka, MD

Facility:  
LAMC

Key Words: neonatal, intubation, thoracostomy

Dept/Svc:  
Pediatrics

Associate Investigators:

Accumulative MED CASE  
Cost: None

Est Accumulative  
OMA Cost: \*

Periodic Review  
Results: N/A

Study Objective: To provide a live model for neonatal intubation and thoracostomy for teaching these procedures to pediatricians, obstetricians, anesthesiologists and nursing personnel.

Technical Approach: Using sodium thiopental, cats are used for practice in placing endotracheal tubes and thoracostomy tubes.

Progress: Laboratory sessions were conducted (in 1982) to provide neonatal intubation practice to personnel from Pediatrics, Obstetrics, Anesthesia and Nursing. Laboratory sessions will be scheduled on a recurring basis.

\* Animals belong to MAJ Turner.

Detail Summary Sheet

Date: 14 Nov 82

Prot. No.: Peds-82-02

Status: Ongoing

Title: Comprehensive care of the child with neuroblastoma: a stage and age oriented study, phase III.

Start Date: 12 Aug 82

Est Comp Date: Indefinite

Principal Investigator:  
LTC Thomas, MD

Facility:  
L A M C

Key Words: childhood, neuroblastoma

Dept/Svc:  
Pediatrics

Associate Investigators:

Accumulative MED CASE  
Cost: None

Est Accumulative  
OMA Cost: None

Periodic Review  
Results: Approved

Study Objective: This Pediatric Oncology Group (POG) study is part of a large National Study to evaluate new chemotherapy and staging regimens in neuroblastoma.

Technical Approach: All patients to be entered in this study are patients with a diagnosis of neuroblastoma. Upon entry into the study, each patient will have his/her disease staged clinically according to the POG criteria. Thereafter, patients will be treated with surgery, surgery and shortterm chemotherapy, chemotherapy, or chemotherapy and radiotherapy. Chemotherapeutic agents to be employed include cytoxan, adriamycin, RM-26, and CIS-platinum. In addition, a number of nontherapeutic studies, including assays of serum, catecholamines, IgG, VMA/HVA ration, LDH and/or ESR, will be performed. Survival data will be collected, as well as data on toxicity and complications.

Progress: Current patient accrual is approximately 100 patients/year in the national study. Study to remain open for 2-3 years. The L A M C patient on this protocol remains in complete remission.

Detail Summary Sheet

Date: 16 Sep 83

Prot. No.: Peds-82-03

Status: Ongoing

Title: Newborn bathing techniques: effect on colonization in the nursery and at home.

Start Date: 1 Aug 82

Est Comp Date: 1 Feb 84

Principal Investigator:  
MAJ JH Jirka, MD

Facility:  
L A M C

Key Words: newborn, bathing, colonization, nursery, home

Dept/Svc:  
Pediatrics

Associate Investigators:  
MAJ Mitchell, MD

Accumulative MED CASE  
Cost: None

Est Accumulative  
O M A Cost: None

Periodic Review  
Results:

Study Objective: To determine whether infants bathed by the tub method prior to healing of the umbilicus and circumcision site will have a rate of infectious complications or bacterial colonization significantly different from that of infants bathed by the sponge method, and to assess any differences in parental attitudes toward bathing methods.

Technical Approach: One-hundred well, term infants are randomly assigned to a tub or sponge bathing group. Prior to the first bath, axillary temperatures are measured and the nose and umbilical cord stump are cultured. Temperatures are repeated following bathing. Prior to discharge, cultures are repeated. Parents are to continue the same bathing method after discharge. Cultures are repeated weekly for three weeks. Parents are asked to complete a questionnaire regarding bathing techniques, problems, and satisfaction with the method employed.

Progress: Seventy-five infants have completed the study to date. Twenty-five more infants need to complete the study.

Detail Summary Sheet

Date: 20 Sep 83

Prot. No.: Peds-82-04 Status: Completed

Title: Birth weight and gestational age: a retrospective study of the patient population at LAMC.

Start Date: Feb 83

Est Comp Date: Completed

Principal Investigator:

LTC H Kilbride, MD

CE Wade, PhD

Facility:

LAMC

Dept/Svc:

Pediatrics

Associate Investigators:

Key Words: birth weight, gestational age

Accumulative MED CASE

Cost:

Est Accumulative

OMA Cost:

Periodic Review

Results:

Study Objective: To construct a relationship between gestational age and birth weight utilizing data obtained over the last 15 years.

Technical Approach: The data for gestational age and birth weight over the last 15 years will be obtained from LAMC nursery records. The data will be stored in the computer in the Department of Clinical Investigation. A nomogram, generated for gestational age and body weight, will be derived from this data and comparisons made between years.

Progress: Gestation age and birthweights were obtained on 4774 births at LAMC from 1975 to 1981. A growth curve was generated and compared to establish curves. The LAMC data demonstrated significantly greater birth weight at gestational ages of 38 to 42 weeks.

Presentations and Publications: This work is in preparation for presentation.

Detail Summary Sheet

Date: 30 Aug 83

Prot. No.: Peds-83-05

Status: Ongoing

Title: Effects of continuous versus intermittent suction during endotracheal suctioning in intubated infants on transcutaneous oxygen tension, removal of secretions, and incidence of bacteremia.

Start Date: Jun 83

Est Comp Date: Jun 84

Principal Investigator:  
MAJ BS Turner, ANC

Facility:  
LAMC

Dept/Svc:  
Pediatrics (Newborn)

Associate Investigators:  
LTC H Kilbride, MD  
COL F Bruhn, MD  
CPT R Leanza

Key Words: endotracheal suctioning, transcutaneous oxygen tension, bacteremia, secretion recovery

Accumulative MEDCASE  
Cost: N/A

Est Accumulative  
OMA Cost: N/A

Periodic Review  
Results:

Study Objective: To determine whether intermittent suction used during endotracheal suctioning recovers more secretions, causes less hypoxemia and tissue damage than continuous suction used during endotracheal suctioning.

Technical Approach: Intubated infants with indwelling arterial lines whose parents have given written consent serve as their own controls for two endotracheal suctioning procedures within a four-hour period. The endotracheal suction procedure differs only in respect to the application of continuous or intermittent negative pressure used during the procedure. Oxygenation levels are measured by transcutaneous skin oxygen tension ( $tcPO_2$ ). Secretion recovery is measured by weighing the secretions removed from the trachea with suctioning. Tissue damage is estimated by serial blood specimens drawn before and up to five minutes after suctioning. Organisms found in blood specimens are indicative of disturbances to tracheal epithelium.

Progress: Seven infants in gestational age from 30 to 40 weeks with post-natal ages of three to fifteen days were admitted to the study. All infants were classified as being appropriate-for-gestational age. Secretion recovery using continuous suction was over two times greater than that obtained with intermittent suction, but the amounts recovered were so small that the differences were insignificant. No pathogenic organisms were identified in any blood or tracheal aspirate cultures. Levels of oxygenation dropped with the use of both types of negative pressure. There were no significant differences in the drops during suctioning between the two types of negative pressure used; however, there were clear post-suction differences. In infants suctioned using continuous suction, there was a rapid climb in oxygenation over control levels of 50 torr as compared to 20 torr with the use of intermittent negative pressure. The plan is to continue data collection until 20 subjects have been admitted to the study.

Detail Summary Sheet

Date: 23 Aug 83

Prot. No.: Pharm-82-01 Status: Terminated

Title: Post-marketing medication monitoring program—surveillance of anti-acne medications.

Start Date: Feb 83

Est Comp Date: Terminated

Principal Investigator:  
LTC RW Severson, MS •

Facility:  
L A M C

Dept/Svc:  
Pharmacy

Associate Investigators:

Key Words: post-marketing monitoring, anti-acne medications

Accumulative MED CASE  
Cost:

Est Accumulative  
OMA Cost:

Periodic Review  
Results:

Study Objective: To observe the use and effects of anti-acne medications in a usual use situation.

Technical Approach: Patients will be accrued during the presentation of a prescription to a cooperating pharmacist. Participants will be registered by the pharmacist and a registry form, containing patient-identifying data, will be mailed to the Medication Monitoring Program along with signed consent. Patient follow-up will include a telephone-administered Modular Questionnaire, which covers drug use habits, health events, and perception of the effectiveness of the acne medication. An abbreviated questionnaire will be administered eight weeks following the first questionnaire, and additional follow-up made on those patients bothered by diarrhea as reported in the questionnaire. Data analysis will consist of descriptive statistics and comparisons of data related to perceived adverse and beneficial effects of various regimens, as well as associated health events. Continuation rates will be measured using survival analysis techniques. Where applicable, incidence density methods will be used to assess frequency of event by length of exposure to drug.

Progress: Because an insufficient number of patients fit the category, this study was discontinued.

Detail Summary Sheet

Date: 29 Aug 83

Prot. No.: PhM-82-01

Status: Ongoing

Title: Evaluation of the multi-Frecodyn device as a modality in the treatment of chronic low back pain of musculoskeletal origin.

Start Date: Jan 83

Est Comp Date: Indefinite

Principal Investigator:

COL A Scavarda, MD

Facility:

L A M C

Dept/Svc:

Physical Medicine

Associate Investigators:

LTC E Bautista, MD

Key Words: muti-Frecodyn device, chronic low back pain

Accumulative MED CASE

Cost:

Est Accumulative

OMA Cost:

Periodic Review

Results:

Study Objective: To compare the effectiveness of the multi-Frecodyn device with conventional physical therapy (i.e., ultrasound) for treatment of chronic low back pain.

Technical Approach: Patients with chronic low back pain will undergo an evaluative examination, including x-ray, physical, and history. A control and treatment group will be utilized; multi-Frecodyn versus ultrasound.

Progress: Necessary equipment unavailable for utilization to date. Thus, protocol has not been activated. The investigator expects the device to arrive within the next month.

Detail Summary Sheet

Date: 9 Aug 83

Prot. No.: P-81-09

Status: Completed

Title: Childhood depression in a tri-service population.

Start Date: 12 May 81

Est. Comp. Date: Completed

Principal Investigators:  
CPT P Jensen

Facility:  
LAMC

Dept/Svc:  
Psychiatry

Associate Investigators:

Key Words: childhood depression, father absence

Accumulative MED CASE  
Cost: None

Est Accumulative  
OMA Cost:

Periodic Review  
Results: Approved

Study Objective: To determine the effects of father absence (due to military assignments) on children, using various questionnaires designed to measure depression in children; and to determine in children the effects and/or correlation of depression and high life changes in parents with high depression scores.

Technical Approach: Invitations to participate in the study were sent to 110 parents (i.e., Army, Navy, and Coast Guard populations) whose children attend Hamilton School; 25 families agreed to participate in the study. Each father and mother independently completed the following tests: 1) Beck Depression Inventory, 2) Child Behavior Checklist, 3) Coddington's Life Change Scale for Children. To measure the child's attributions of responsibility for school success or failure, each child completed: 1) Childhood Depression Inventory, 2) KASTAN (test to measure certain internal, stable, and global self-attributions) and 3) IAR (test designed to measure child's attributions of responsibility for school success and failure). Parents also completed a questionnaire measuring the number and length of father absences from home over the last 12 months.

Progress: Twenty-five families (parents) have completed all of the above questionnaires, as have 33 children (some families have two children participating). Prior to further testing and data collection, a preliminary computer analysis and one-way ANOVA have been performed to determine interparent reliability. Results suggest only modest interparent reliability (i.e., agreement in rating their children's behavior and emotions).

Detail Summary Sheet

Date: Aug 83

Prot. No.: P-82-12

Status: Ongoing

Title: Efficacy of progressive muscle relaxation and spousal participation in reducing adverse reactions to cancer chemotherapy.

Start Date: Mar 83

Est Comp Date: Indefinite

Principal Investigator:  
CPT D Ruck, MD

Facility:  
L A M C

Dept/Svc:  
Psychiatry

Associate Investigators:  
MAJ G Laskow, PhD  
CPT P O'Rourke, A N C  
Ms M Scott, MS

Key Words: muscle relaxation, cancer chemotherapy

Accumulative MEDCASE  
Cost: 0

Est Accumulative  
OMA Cost: 0

Periodic Review  
Results:

Study Objective: To establish efficacy of progressive muscle relaxation (PMR) in controlling anticipatory nausea and vomiting associated with cancer chemotherapy; and to evaluate the role of spousal participation in learning PMR and home practice.

Technical Approach: Outpatients will be assigned to spousal participation or non-spousal participation groups. Each group will receive training in PMR and efficacy of control of anticipatory nausea and vomiting will be measured in the clinic (via clinic rating scale) and at home (home rating scale).

Progress: Two patients were enrolled in the study. One decided not to participate after one week and the other was hospitalized, which disqualified her from the study. LTC R McAuley has transferred to WRAMC and has been replaced by Ms Scott, who will conduct the PMR training. CPT O'Rourke remains the liaison for patient accrual between the Hematology/Oncology Service and Psychiatry. Research will continue now that sufficient staff is available.

Detail Summary Sheet

Date: 15 Jun 83

Prot. No.: P-83-15

Status: Ongoing

Title: Stress, social assets, and outpatient clinic utilization

Start Date: 15 May 83

Est Comp Date: 15 May 84

Principal Investigator:  
CPT P Jensen

Facility:  
L A M C

Dept/Svc:  
Psychiatry

Associate Investigators:  
CPT J Algeo, MD  
CPT R Saum, RN, MA

Key Words: life events, social supports, stress, social assets

Accumulative MED CASE  
Cost:

Est Accumulative  
OMA Cost:

Periodic Review  
Results:

Study Objective: To assess the impact of stressful life events, presence or absence of social supports, and "person-environment fit" on outpatient clinic utilization.

Technical Approach: One hundred and twenty retired and retired dependent patients, 60 active duty and 60 active duty dependent patients will fill out questionnaires to assess their life stress and social supports. After six months, medical records will be screened to determine which of these factors best predict clinic utilization. Ninety subjects from the ID card section will also complete the questionnaires to allow comparison with the patient group.

Progress: Because the principal investigator is being reassigned, the protocol has been transferred to CPT Robert Saum, ANC, L A M C, as principal investigator, along with CPT James Algeo, MD, L A M C.

Detail Summary Sheet

Date: 18 Aug 83

Prot. No.: R-82-01

Status: Ongoing

Title: Evaluation of the role of nuclear magnetic resonance (NMR) in the diagnosis and staging of prostatic carcinoma: a preliminary study.

Start Date: Mar 82

Est Comp Date: 1983

Principal Investigator:  
DB Spring, MD

Facility:  
L A M C

Dept/Svc:  
Radiology

Associate Investigators:  
COL RA Watson, MD

Key Words: nuclear magnetic resonance, prostate, carcinoma

Accumulative MED CASE  
Cost: None

Est Accumulative  
OMA Cost: None

Periodic Review  
Results: N/A

Study Objective: To evaluate, for the first time, the NMR characteristics of the normal and abnormal male pelvis; in particular, to characterize normal and abnormal pelvic tissue in individuals with proven prostatic carcinoma.

Technical Approach: Patients to be admitted to this study include adult males with prostatic disease. Patients will be grouped according to clinical stage of prostatic carcinoma. Each patient will undergo NMR scanning. Thereafter, correlations between results of NMR and CT scans will be made, as well as comparisons between NMR and surgical findings.

Progress: Initial results have been extremely encouraging. We have scanned nine patients to date. NMR imaging of the male pelvis and pathology were found to relate to prostatic disease. The greatest potential of NMR appears to be its ability to detect pathology confined to the gland. However, it is not known if a neoplastic nodule can be differentiated from chronic prostatitis. Unlike x-ray or CT, metallic clips produce no streaking artifacts, giving NMR a definite advantage in the evaluation of patients following radical surgery. If the results are confirmed with a larger number of patients, NMR will assume a prominent role in the clinical evaluation of bladder and prostate cancer.

A clinical patient NMR scanner has been installed at UCSF Medical Center. There has been EPA-site approval.

Presentations and Publications: An abstract has been submitted to the American Journal of Radiology.

Detail Summary Sheet

Date: 9 Aug 83

Prot. No.: R-82-02

Status: Terminated

Title: Effect of glucagon injection on diagnostic accuracy of double-contrast and barium examinations of the upper and lower gastrointestinal tract.

Start Date: May 82

Est Comp Date: 1983

Principal Investigator:  
RF Thoeni, MD

Facility:  
L A M C

Dept/Svc:  
Radiology

Associate Investigators:  
CPT FN Vandeman, MD  
SP4 E Quintana

Key Words: glucagon, double-contrast, barium examinations, gastrointestinal tract

Accumulative MED CASE  
Cost:

Est Accumulative  
OMA Cost:

Periodic Review  
Results:

Study Objective: To determine the effect of glucagon-induced hypotonicity on the diagnostic accuracy of double-contrast barium enema examinations.

Technical Approach: This effect was determined in 133 consecutive patients in a double-blinded, cross-over study. All patients underwent colonoscopy and served as their own controls by undergoing a double-contrast study after intravenous injection of 1 mg of glucagon and another after intravenous injection of 1 ml of saline placebo, in randomized order.

Progress: One hundred and fifty patients were accrued for the upper GI series study over a six-month period. With the glucagon added there are more true positives, fewer false positives and false negatives, and fewer equivocal results than with saline. Sensitivity, specificity and accuracy are all significantly better with glucagon. Seventy percent of the glucagon images are good to excellent, compared with 57 percent for saline images. Superficial lesions are also seen better with the glucagon added. This portion of the study was completed in November.

For the lower GI series, 115 patients had been accrued, but a large percentage of these have been normal individuals. Until the present films have been read, it is uncertain whether additional subjects will be necessary, as the investigators wish to have a certain number of individuals presenting with disease.

With the glucagon barium enema, not much difference is seen in comparison with the saline barium enema. Superficial and inflammatory lesions show a trend of better resolution with glucagon, but nothing was statistically significant. There are also trends of improved sensitivity, specificity and accuracy, but again, not of statistical significance. From these findings the investigators recommend the procedure for select diagnoses.

Detail Summary

Date: 18 Aug 83

Prot. No.: R-82-03

Status: Ongoing

Title: CT (computerized tomography) evaluation of retroperitoneal gas resorption after abdominal aortic surgery: a prospective study.

Start Date: May 82

Est Comp Date: 1984

Principal Investigator:  
DB Spring, MD

Facility:  
LAMC

Dept/Svc:  
Radiology

Associate Investigators:  
T McDonald, MD  
K Kumar, MD  
CPT W Marx, DO

Key Words: retroperitoneal gas, CT

Accumulative MEDCASE  
Cost:

Est Accumulative  
OMA Cost:

Periodic Review  
Results:

Study Objective: To determine the normal rate of disappearance of non-pathological post-operative gas after routine abdominal aortic surgery by CT scan.

Technical Approach: Patients will undergo imaging of the aorta and retroperitoneal prior to undergoing abdominal aortic surgery during the next 12 months of study. Limited CT scans at 1-2 cm increments in the region of the aorta will be obtained. Intravenous contrast material will be injected, as is customary, for better visualization of the vascular structures, and dilute oral contrast material will be given to delineate overlying bowel loops. CT scans will be obtained pre-operatively at 5-7 days post-operatively and every 5-7 days until the disappearance of retroperitoneal gas is confirmed by CT. The presence or absence of retroperitoneal gas is confirmed by CT. The presence or absence of retroperitoneal gas will be determined from each study. If there is a rapid fall-off of the presence of retroperitoneal gas, this shall be noted; if disappearance is slow, an actual rate of disappearance shall be determined. The results will be evaluated utilizing Fisher's exact chi-square in conjunction with the Department of Information Services computer assistance.

Progress: Fifteen patients have been entered into this study. No data has been analyzed to date.

Presentations and Publications: Dr J Sumfest, L A M C, presented some of our initial results in a presentation entitled, "Prosthetic Graft Infections, L A M C, 1977-1982," at the Gary Wratten Symposium at Eisenhower Medical Center in Augusta, Georgia, during May 1983.

Detail Summary Sheet

Date: 18 Aug 83

Prot. No.: R-82-04

Status: Ongoing

Title: Effect of respiratory phase on the CT evaluation of the retroperitoneal region—particularly in the evaluation of retroperitoneal adenopathy.

Start Date: May 83

Est Comp Date: 83

Principal Investigator:  
DB Spring, MD

Facility:  
L A M C

Dept/Svc:  
Radiology

Associate Investigators:

Key Words: CT, retroperitoneal adenopathy

Accumulative MED CASE  
Cost:

Est Accumulative  
OMA Cost:

Periodic Review  
Results:

Study Objective: To compare scans of the high retroperitoneum in the region of the diaphragmatic crura in full expiration and full inspiration.

Technical Approach: Subjects in this study will include those with known or strongly suspected neoplasms who are being investigated with CT scanning of the upper abdomen. After scanning in the usual manner, additional scans in the high abdomen during full expiration shall be obtained. No additional contrast medium shall be given. A localized expiratory scout-view scan will be obtained. The investigator shall subjectively review each case and grade the degree of diagnostic certainty in identification of pericrural adenopathy for every study. Inspiratory and expiratory studies shall then be compared for each patient, noting if one respiratory phase is preferable in demonstrating pericrural adenopathy. Statistical analysis will be made.

Progress: With the dynamic scanning capability of our CT scanner, patients are routinely being scanned during quiet respiration, and evaluation is selectively being limited to those patients with equivocal adenopathy.

Detail Summary Sheet

Date: 12 Jul 83

Prot. No.: R-82-05

Status: Terminated

Title: Identification of tubular ectasia and medullary sponge kidney on radionuclide scan.

Start Date: Jun 82

Est Comp Date: Terminated

Principal Investigator:  
CPT DA Boll, MD

Facility:  
L A M C

Dept/Svc:  
Radiology

Associate Investigators:  
DB Spring, MD

Key Words: tubular ectasia, medullary sponge kidney, radionuclide scan

Accumulative MED CASE  
Cost:

Est Accumulative  
OMA Cost:

Periodic Review  
Results:

Study Objective: To examine the role of  $^{99m}\text{TcDTPA}$  renal scanning detection of medullary sponge kidney in the absence of infection and obstruction.

Technical Approach: All excretory urograms will be screened for the presence of medullary sponge kidney. Ten patients with medullary sponge kidney or tubular ectasia will also undergo  $^{99m}\text{Tc}$  technetium renal scanning. An additional 10 patients without tubular ectasia or medullary sponge kidney will also undergo renal scanning as controls. Statistical analysis of the frequency of photon deficiency in medullary changes will then be assessed.

Progress: This study was terminated before any patients had been accrued. Several patients with medullary sponge kidney or tubular ectasia had been identified prior to submission of the protocol but they either refused to participate or were unreachable. A subsequent paucity of eligible patients led to the termination of the study before it actually began.

Detail Summary Sheet

Date: 12 Sep 83

Prot. No.: R-82-06

Status: Completed

Title: IV barium for liver/spleen CT scanning

Start Date: 5 Feb 83

Est Comp Date: Completed

Principal Investigator:

CPT S Munderloh, MD

Facility:

LAMC/LAIR

Dept/Svc:

Radiology

Associate Investigators:

J Barkovich

Key Words: IV barium, liver/spleen scanning

Accumulative MEDCASE

Cost:

Est Accumulative

OMA Cost:

Periodic Review

Results:

Study Objective: To determine if IV barium sulfate is effective as a liver/spleen CT contrast agent.

Technical Approach: One hundred rats were used to determine dosage and efficacy of IV barium sulfate by injecting intravenously with barium sulfate/saline solution. After approximately 20 minutes, a liver CT scan was performed to see if the barium increased the density of these organs. To determine harmful effects of IV barium, an experimental group received a previously determined optimal dosage of barium sulfate while a control group received only saline. Full necropsies were then performed and results analyzed.

Progress: The study is complete. Results suggest excellent liver/spleen opacification, with necropsies showing no damage. This method was also used with a rhesus monkey with equal success. The only side effect was a decrease in platelets and white blood cells which returned to normal by 48 hours. We conclude that IV barium sulfate is effective for liver/spleen CT scanning. Further work is necessary to determine any other side effects.

Detail Summary Sheet

Date: 29 Aug 83

Prot. No.: NuM-78-05    Status: Ongoing

Title: Intravenous administration of  $^{131}\text{I}$ -6-B iodo-methyl-nor-cholesterol (NP-59) for adrenal evaluation and imaging.

Start Date: Mar 78

Est Comp Date: Indefinite

Principal Investigator:  
COL RJ Lull, MD

Facility:  
L A M C

Key Words: NP-59, adrenal imaging, iodo methyl-nor-cholesterol

Dept/Svc:  
Nuclear Medicine

Associate Investigators:  
MAJ DA Boll, MD  
CPT(P) KA Kaplan, MD

Accumulative MED CASE  
Cost: None

Est Accumulative  
OMA Cost:

Periodic Review  
Results:

Study Objective: Clinical evaluation of NP-59 as a diagnostic agent for the detection of adrenal-cortical disorders and as a potential scanning agent for detecting structural abnormalities of the adrenal medulla.

Technical Approach: Radioiodinated cholesterol has been used successfully in over 200 patients throughout the U.S. for diagnosing both functional and structural abnormalities of the adrenal. NP-59 is a second generation radiopharmaceutical for adrenal imaging and is considered the agent of choice, since it achieves 5 to 10 times the adrenal concentration of the earlier adrenal radiopharmaceutical,  $^{131}\text{I}$ -19-Iodocholesterol. NP-59 is currently in Phase III clinical investigation at a number of medical centers.

Progress: NP-59 has proven useful in the evaluation and diagnosis of adrenal disease. Due to its limited commercial value, NP-59 will probably not become an NDA drug. In order to provide this diagnostic tool to our patient population, it is necessary to maintain this protocol.

During the period between 1 October 1982 and 31 August 1983, only one patient was studied under this protocol. There were no reported adverse reactions to the drug and acceptable static images of the adrenal glands were obtained in this case.

Detail Summary Sheet

Date: 19 Sep 83

Prot. No.: NuM-79-07

Status: Ongoing

Title: Comparative sensitivity of tomographic and planar scintigraphy in myocardial perfusion and small organ imaging.

Start Date: 25 Sep 78

Est Comp Date: Indefinite

Principal Investigator:  
COL RJ Lull

Facility:  
LAMC

Key Words: tomographic and planar, scintigraphy, myocardial, imaging

Dept/Svc:  
Nuclear Medicine

Associate Investigators:  
MAJ D Boll, MD  
CPT(P) K Kaplan, MD

Accumulative MED CASE  
Cost: None

Est Accumulative  
OMA Cost:

Periodic Review  
Results: Approved

Study Objective: This protocol is designed to evaluate a form of limited angle tomography (seven-pinhole collimator) imaging of the heart and other small organs compared to standard planar scintigraphic imaging. The results of both tomographic and planar imaging will be evaluated for improvement in sensitivity or specificity of disease detection.

Technical Approach: Following administration of the radiopharmaceutical, the patient is imaged by both the standard planar and tomographic imaging system. Only when necessary for thallium-201 myocardial perfusion studies will a second dose of radiopharmaceutical be administered to allow reversal of the imaging sequence in an attempt to eliminate temporal redistribution bias. Study results are compared to final diagnosis to determine sensitivity and specificity.

Progress: This study remains inactive due to the lack of needed software for the clinic's upgraded computer system, which no longer runs the original software that is now obsolete. During the period that this protocol has remained inactive due to inadequate software, several other investigators at other institutions have reported the presence of imaging abnormalities induced artifactually by the limited sampling angle of the seven-pinhole tomographic system. These observations are similar to those seen in our cases that were studied prior to the computer upgrade. The delay in completion of this study may eliminate its potential value, since other investigators will have already reported and confirmed the objectives of this protocol. If software is not obtained soon, this project may need to be cancelled.

Detail Summary Sheet

Date: 19 Sep 83

Prot. No.: NuM-79-09

Status: Ongoing

Title: The natural history of the technetium 99MTC MDP bone scan after elective joint replacement.

Start Date: Oct 79

Est Comp Date: Indefinite

Principal Investigator:  
COL RJ Lull

Facility:  
L A M C

Key Words: technetium, bone scan, joint replacement

Dept/Svc:  
Nuclear Medicine

Associate Investigators:  
LTC E Galvin, MD

Accumulative MED CASE  
Cost: None

Est Accumulative  
OMA Cost: None

Periodic Review  
Results:

Study Objective: To obtain in a prospective manner serial bone scans at defined intervals for two years after insertion of total joint prostheses in the hips or knees. The changes in scintigraphy at each time interval will be assessed and correlated with clinical status and outcome to define the normal changes in asymptomatic patients and those with complications, such as loosening or infection.

Technical Approach: Bone scintigraphy is performed at one- to six-month intervals during the first two years after total joint replacement. Image results will be quantified by a 1+ to 4+ scale relating various regions of peri-prosthetic bone activity to normal bone activity of the iliac crest.

Progress: At present, no patients have been entered into this prospective protocol. The protocol entry point for informed consent is the Orthopaedic Service. However, a retrospective analysis of arthroplasty patients in whom serial bone scintigraphy has been performed for clinical indications has been completed.

Publications and Presentations: This retrospective data has been reported at several national nuclear medicine meetings in both verbal presentation format and exhibit format. The exhibit at the annual Society of Nuclear Medicine in June 1983 was awarded the Silver Medal for excellence.

Detail Summary Sheet

Date: 30 Aug 83

Prot. No.: NuM-80-11

Status: Ongoing

Title: Evaluation of indium oxine In-111 labeled cellular blood components.

Start Date: 1 Dec 82

Est Comp Date: May 84

Principal Investigator:  
COL RJ Lull, MD

Facility:  
LAMC

Key Words: indium oxine In-111, labelled blood components, leukocytes, platelets

Dept/Svc:  
Nuclear Medicine

Associate Investigators:  
MAJ DA Boll, MD  
CPT(P) KA Kaplan, MD

Accumulative MED CASE  
Cost: None

Est Accumulative  
OMA Cost: None

Periodic Review  
Results:

Study Objective: To evaluate the clinical efficacy of indium In-111 oxine labeled cellular blood components.

Technical Approach: Platelets will be injected with a maximum of 0.5 mCi of indium In-111 oxine tagged to autologous cellular blood components (either white blood cells or platelets). Spot views and/or whole-body scans will be carried out with a Picker gamma camera at appropriate time intervals.

Progress: During the period between 1 October 1982 to 31 August 1983, a total of 12 patients were studied with indium In-111 oxine white blood cells and two patients with In-111 oxine platelets. In all cases, acceptable images were obtained and useful information for the patients' immediate clinical condition was reported. No adverse reactions were noted.

Detail Summary Sheet

Date: 29 Aug 83

Prot. No.: NuM-82-14

Status: Completed

Title: Reverse redistribution on 201-thallium chloride stress and redistribution images--reproducible?

Start Date: Jul 82

Est Comp Date: Completed

Principal Investigator:

MAJ D Boll, MD

Facility:

LAMC

Dept/Svc:

Nuclear Medicine/Cardiology

Associate Investigators:

MAJ CJ White, MD

Key Words: 201-thallium, redistribution images

Accumulative MEDCASE

Cost:

Est Accumulative

OMA Cost:

Periodic Review

Results:

Study Objective: To determine if reverse redistribution on 201-thallium chloride stress test is reversible.

Technical Approach: Patients with previous diagnosis of reverse redistribution by prior 201-thallium chloride stress test were restudied in an identical fashion as if there had been no change in functional therapeutic class in the interim between the two tests.

Progress: Seven patients (6 male, 1 female) were restudied in a range of 1-18 months following the original exam. Simliar levels of exercise were achieved by all patients except one who markedly increased his level of exercise. None of the seven patients had evidence of reverse redistribution on their second 210-thallium chloride exams. This study has been completed.

Presentations and Publications: Publication of results is pending.

Detail Summary Sheet

Date: 7 Sep 83

Prot. No.: NuM-82-15

Status: Ongoing

Title: The non-invasive assessment of coronary artery disease (CAD) using parameters of left ventricular diastolic function.

Start Date: 1 Sep 82

Est Comp Date: 1 Sep 84

Principal Investigator:  
CPT K Kaplan, MD

Facility:  
L A M C

Dept/Svc:  
Nuclear Medicine/Cardiology

Associate Investigators:  
MAJ CJ White, MD  
MAJ TD Watson, MD  
COL RJ Lull, MD

Key Words: coronary artery disease, left ventricular function, radionuclide angiography

Accumulative MED CASE  
Cost: N/A

Est Accumulative  
OMA Cost: N/A

Periodic Review  
Results: N/A

Study Objective: To study patients with high pre-test probability of having CAD with a non-invasive method of MUGA imaging prior to planned coronary catheterization; to look for abnormal function of the left ventricle during diastole in patients with normal systolic function; and to compare sensitivity of diastolic function with abnormalities seen during catheterization.

Technical Approach: To perform standard MUGA scans (at rest) on patients with suspected CAD; determine systolic and diastolic function parameters; perform coronary catheterization on all patients; and determine systolic diastolic sensitivities albeit without "gold standard" catheterization data.

Progress: Approximately 75-80 patients have been analyzed to date. Many have been included in the group that were having the MUGA scan for a separate clinical indication and who subsequently underwent catheterization. Data, to date, shows diastolic function to be normal in 91 percent of patients with prior myocardial infarction (MI) and CAD; 77 percent of patients with CAD and no prior MI versus only approximately 14 percent of patients with CAD/no MI who have abnormal systolic function.

A complete computer analysis of the entire group is pending.

Presentations and Publications: CPT Kaplan presented early data at Western Regional Society of Nuclear Medicine in San Diego, California, during October 1982 (abstract in Clinical Nuclear Medicine, Sep 82). CPT White presented updated data at the Army Cardiology Meeting in Augusta, Georgia, during May 1982.

Detail Summary Sheet

Date: 22 Aug 83

Prot. No.: S-81-02

Status: Completed

Title: Human beta endorphin levels during surgery.

Start Date: Jun 82

Est Comp Date: Jun 83

Principal Investigator:  
WH Heydorn, COL, MC

Facility:  
LAMC

Key Words: beta endorphin, surgery

Dept/Svc:  
Surgery

Associate Investigators:  
JD O'Benar, PhD  
COL RF Bellamy, MD  
LTC WY Moores, MD

Accumulative MEDCASE  
Cost: None

Est Accumulative  
OMA Cost: \$2000

Periodic Review  
Results: N/A

Study Objective: To determine the blood levels of beta endorphin in human beings who are undergoing either routine abdominal surgery or coronary artery bypass surgery, using cardiopulmonary by-pass.

Technical Approach: Five patients about to undergo cholecystectomy and five patients about to undergo coronary artery bypass were studied. Patients had blood samples obtained prior to surgery, after induction of anesthesia but prior to surgical incision, after incision, and in the recovery room. All samples were assayed for beta-endorphin, ACTH, and cortisol.

Progress: The levels of plasma beta-endorphin immunoreactivity, adrenocorticotrophin, and cortisol in the blood of 10 patients were measured. Five patients underwent coronary artery surgery using cardiopulmonary bypass and five patients underwent cholecystectomy. Arterial and venous samples were analyzed for existing differences. Similar anesthetic techniques were used in both groups, with fentanyl common to both. There were no differences between arterial and venous samples in levels of beta-endorphin immunoreactivity, ACTH, or cortisol at any time. Neither surgical stress nor anesthesia induction stimulated the hypothalamic-pituitary-adrenal axis to increase blood levels of these substances. A significant rise in all three substances was noted one hour after surgery in group I, the cardiopulmonary bypass group. A rise in all three was also found in group II, which was significant for cortisol.

Publications and Presentations: Results were presented at the annual meeting of the Association of Army Cardiology and at Dwight David Eisenhower Medical Center in May 1983. The data has been submitted for publication, but thus far has not been accepted.

Detail Summary Sheet

Date: 22 Aug 83

Prot. No.: S-82-03

Status: Completed

Title: Arterial venous pressure flow relations in porcine coronary circulation.

Start Date: Jan 83

Est Comp Date: Completed

Principal Investigator:  
COL WH Heydorn, MD

Facility:  
L A M C

Dept/Svc:  
Surgery

Associate Investigators:  
COL RF Bellamy, MD  
JS O'Benar, PhD

Key Words: coronary circulation, pressure flow relations

Accumulative MEDCASE  
Cost: N/A

Est Accumulative  
OMA Cost: N/A

Periodic Review  
Results: N/A

Study Objective: The object of this experiment was to develop a model in which coronary artery in-flow and coronary sinus out-flow could be measured directly and simultaneously. The purpose of this would be to test the hypothesis that cessation of coronary artery in-flow during diastole would indicate cessation of coronary sinus outflow rather than the concept that coronary capacitance is so large that pressure flow relationships observed in epicardial arteries would not be indicative of the entire coronary bed.

Technical Approach: Ten swine were utilized in an attempt to measure coronary artery in-flow and coronary sinus out-flow simultaneously during prolonged diastole. After appropriate premedication and anesthetic induction, a mid-line incision was made in the neck, and the carotid artery and vagus nerves were identified. A fluid-filled catheter was placed through the carotid artery into the aortic root. This was for arterial pressure measurement. Electrocardiographical electrodes were sutured into the vagus and connected to a simulator. The heart was to be arrested by stimulating the vagus with a Grass stimulator. A left thoracotomy was made and electromagnetic flow probe was placed around the left main coronary artery. A cannulation flow probe was placed into the hemizygous vein and the coronary sinus ligated. Flows and pressure in the coronary artery and coronary vagus system were to be measured during periods of diastole.

Progress: In the original preparation that was described, it was impossible to obtain pressure flow relationships as desired because of the inability to sustain prolonged diastole by the techniques described under technical approach. However, by modifying the approach, a satisfactory preparation was developed. In this case, after appropriate medication and anesthetic induction, a mediastinotomy was performed. The right atrium was cannulated with a large catheter. The animal was exsanguinated through this catheter in the reservoir of a bubble oxygenator. The aortic root was then transected and a catheter inserted into the left coronary artery through the aortic root. This catheter was equipped with in-line pressure and flow transducers so as to be able to measure pressure in the coronary arterial system, flow through the coronary artery system, and thirdly to induce pharmacological agents. The coronary sinus is then cannulated with an in-line flow probe to measure venous out-flow from the heart. A small bore intracath is inserted in a large epicardial vein to measure coronary venous pressure. A Millar microtransducer is inserted in the myocardium to monitor intramyocardial pressure. Utilizing this approach, it was possible in four experiments to demonstrate coronary arterial venous pressure flow relationships. These findings validated the vascular water fall hypothesis which had been proposed by Dr. Bellamy as an operative factor in determining coronary flow and represented the first demonstration that the magnitude of the water fall could be increased by vasospastic response and suggested that this may be a factor in the development of Prinzmetal's variant angina. For these reasons, a new protocol has been submitted to characterize acetylcholine-induced vasal constriction in the isolated pig heart, the modulating influence of parasympathetic tone on the constrictor response by stimulating the vagus nerve, and finally, the effect of nitroglycerin infusions in this coronary vasospasm model.

Detail Summary Sheet

Date: 22 Aug 83

Prot. No.: S-83-04

Status: Ongoing

Title: Longterm evaluation of pericardial substitutes.

Start Date: Jun 83

Est Comp Date: Jan 85

Principal Investigator:  
COL WH Heydorn, MD

Facility:  
L A M C

Dept/Svc:  
Surgery

Associate Investigators:  
MAJ WR Berry, MD  
CPT JJ Daniels, MD

Key Words: pericardial substitutes

Accumulative MED CASE  
Cost: None

Est Accumulative  
OMA Cost: \$54,700

Periodic Review  
Results: N/A

Study Objective: To evaluate four materials as pericardial substitute.

Technical Approach: Twenty-four mongrel dogs will be anesthetized. A 10 x 5 cm section of pericardium will be excised through a right thoracotomy and replaced with a pericardial patch of one of four materials. Two dogs from each of the four groups will be sacrificed at three months, eight and nine months. At the time of sacrifice, the development of lesions and epicardial reaction will be graded. Histological studies of the prosthetic material will be performed.

Progress: At the present time, 11 dogs have been operated upon. The initial group of eight dogs, which includes two with each of the pericardial substitutes, has been completed. With an 18-month follow-up on this group, the time of completion of the experiment would be in January or February of 1984. It is anticipated that all patches will be in the experimental animals by October of this year.

Detail Summary Sheet

Date: 22 Aug 82

Prot. No.: S-83-05

Status: Ongoing

Title: Advanced trauma life support (ATLS) training course.

Start Date: Apr 83

Est Comp Date: Ongoing

Principal Investigator:  
COL WH Heydorn, MD

Facility:  
L A M C

Dept/Svc:  
Surgery

Associate Investigators:

Key Words: trauma, training course, department, surgery

Accumulative MED CASE  
Cost: None

Est Accumulative  
OMA Cost: N/A

Periodic Review  
Results: N/A

Study Objective: To provide training in advanced trauma life support to physicians.

Technical Approach: This protocol covers the necessity of utilizing four animals for the purpose of teaching techniques in advanced trauma life support.

Progress: Three or four courses of this type are taught annually. The next course is an instructor course scheduled for September 1983. It is contemplated that this will be an ongoing project with no completion date.

Detail Summary Sheet

Date: 7 Sep 83

Prot. No.: S-83-06

Status: Ongoing

Title: Impact of various volume expansion regimens in aortic surgery patients: a pilot study.

Start Date: 8 Sep 82

Est Comp Date: Sep 85

Principal Investigator:

CPT M Morgan, MD

CPT S Deppe, MD

Facility:

LAMC

Dept/Svc:

General Surgery

Associate Investigators:

COL PT McDonald, MD

COL N Ninos, MD

MAJ A Ross, MD

CPT R Dallas, MD

CPT W Willard, MD

Key Words: volume expansion, fluid therapy, aortic surgery

Accumulative MED CASE

Cost: \*Indeterminate to date

Est Accumulative

OMA Cost: \*

Periodic Review

Results:

Study Objective: To compare effects of various fluid resuscitative agents on the pre-operative and post-operative management of patients undergoing abdominal aortic surgery; perform multiple physiological profile analysis on the above patients with comparisons thereof; and to separate fluid analysis with regard to above, namely: a) lactated Ringers; b) 5 percent albumin solution; and c) Hetastand's solution.

Technical Approach: Patients are randomized to one of three separate fluid regimens. Routine invasive hemodynamic monitoring under close supervision is performed on each patient. Extensive biochemical analysis of multiple physiologic systems are then performed. Systemic computer analysis of exhaustive data is performed for both storage and to significance differences in above mentioned data, both within each fluid group and between fluid groups.

Progress: Two patients, one lactated Ringers group and one albumin group, have been evaluated hemodynamically and biochemically, with systematic methods for obtaining information developed. Computerization process has not yet been finalized.

Detail Summary Sheet

Date: 6 Sep 83

Prot. No.: S-83-07

Status: Ongoing

Title: National intergroup study for intermediate thickness melanoma.

Start Date: Jul 83

Est Comp Date: Indeterminate

Principal Investigator:  
COL J Homann, MD

Facility:  
L A M C

Dept/Svc:  
General Surgery/  
Hematology-Oncology

Associate Investigators:

Key Words: melanoma

Accumulative MED CASE  
Cost:

Est Accumulative  
OMA Cost:

Periodic Review  
Results:

Study Objective: This is an intergroup study to evaluate optimal treatment for intermediate thickness melanoma, i.e., whether it is necessary to perform a wide local excision for local control of primary melanomas measuring from 1 to 4 cm in thickness, for their relative value in predicting the patient's clinical course and the risk of local recurrence.

Technical Approach: Eligible patients with melanomas on the trunk or proximal extremity will be prospectively randomized into two groups: 1) those with a standard wide excision of at least 4 cm of healthy tissue from the margin of the primary or the scar resulting from excisional biopsy of the primary lesion; or 2) those with an excision with margins 2 cm from the edge of the primary lesion or the biopsy scar. Eligible patients with melanomas on the head, neck and distal extremity will all have a definitive excision with a 2 cm margin of skin. Additionally, to determine whether the timing of surgical lymphadenectomy for regional node metastatic disease influences survival rates in those patients deemed at-risk for micrometastases confined to their lymph nodes, eligible patients will be randomized into two groups, either that of immediate (elective) lymphadenectomy or of observation of the regional nodes with delayed (therapeutic) lymphadenectomy if indicated for clinically suspicious nodal metastases.

Progress: This protocol was approved one month ago. Thus, patients have not yet been accrued.

Detail Summary Sheet

Date: 24 June 83

Prot. No.: A-82-06

Status: Terminated

Title: Inhibition of increased intraocular pressure by motor paralysis of orbicularis oculi muscle.

Start Date: April 82

Est Comp Date: Terminated

Principal Investigator:  
CPT S Foutz, MD  
MAJ T Moore, MD

Facility:  
L A M C

Dept/Svc:  
Anesthesia

Associate Investigators:  
MAJ H Hicks, MD  
CPT D Jacobs, MD

Key Words: intraocular pressure, orbicularis oculi muscle

Accumulative MED CASE  
Cost:

Est Accumulative  
O M A Cost:

Periodic Review  
Results:

Study Objective: To determine in human volunteers whether intraocular pressure which rises after IV administration of succinylcholine is the result of contraction of the orbicularis oculi muscle.

Technical Approach: We will ascertain the nature of increased intraocular pressure to perform a nerve block. On the day of surgery, no premedication is to be given. Upon arrival to the operating room a peripheral intravenous line, precordial stethoscope, blood pressure cuff, EKG and twitch monitor will be placed. Intraocular pressure will be measured in both eyes. A right facial nerve block will be performed. The patient will be anesthetized with sodium pentathol and succinylcholine and intraocular pressure.

Progress: At the present time, only four have been entered into this study. No complications were noted and no difference noted after block of orbicularis oculi muscle. Patients will no longer be entered into the study, since both investigators have been transferred. The protocol will not be continued and is thus terminated. Data analysis is pending.

Detail Summary Sheet

Date: 18 Sep 83

Prot. No.: Neusg-82-01

Status: Ongoing

Title: Microvascular surgery technique.

Start Date: Feb 83

Est Comp Date: Indefinite

Principal Investigator:  
MAJ SC Lange, MD

Facility:  
LAIR

Dept/Svc:  
Neurosurgery

Associate Investigators:  
MAJ WC Bergman, MD  
LTC T Dela Cruz, MD

Key Words: microvascular surgery, anastomosis, rat

Accumulative MED CASE  
Cost:

Est Accumulative  
OMA Cost:

Periodic Review  
Results:

Study Objective: To enhance operative skills of fine vessel anastomosis at the microscope.

Technical Approach: Under pentobarbitol anesthesia, the hair is shaved over the carotid arteries in rats. Linear incision is performed and dissection is carried to both carotids. The carotids are then distally ligated and under microscopic observation microvascular suture technique is practiced.

Progress: The Neurosurgery Service staff members at LAMC have performed anastomosis at LAIR at an approximate rate of one per week. During these procedures, microvascular suture technique has been practiced. Initial results in the first few animals were disappointing. The suture had either failed to competently prevent blood loss or, in the extreme, had completely ligated the transposed vessel. Both of these would have resulted in disaster had they been performed on human brain. Subsequent attempts at the anastomosis are progressing quite satisfactorily. Using 10-0 suture to anastomose the end of a 1.5 mm carotid artery to the side of the contralateral carotid artery has met with success in a recent series of approximately seven animals. Using interrupted or running suture technique, the vessels have remained open without leakage of blood from the suture site. Following exposure of the carotid artery, the time for anastomosis was originally 2.5 to 3 hours in duration. Most recent anastomosis was accomplished in 1.5 hours. As mentioned in the original protocol, the project should be ongoing. The dexterity gained can easily be lost with disuse.

Detail Summary Sheet

Date: 6 Sep 83

Prot. No.: OPH-78-01

Status: Ongoing

Title: Investigative plan for FDA regulations for intraocular lens implantation.

Start Date: Mar 78

Est. Comp. Date: Indefinite

Principal Investigators:  
COL SM Jackson, MD

Facility:  
LAMC

Key words: intraocular lens

Dept/Svc:  
Ophthalmology

Associate Investigators:  
CPT KY Gleitsmann  
CPT RG Smith

Accumulative MEDCASE  
Cost: N/A

Est Accumulative  
OMA Cost: N/A

Periodic Review  
Results:

Study Objective: The lens is surgically placed after surgery. Since 1982, all lens used at LAMC have been placed in either the posterior chamber or anterior chamber. Posterior chamber lenses are placed primarily, i.e., during the cataract operation. Anterior chamber lenses may be placed primarily or secondarily, i.e. by a second operation later than the cataract extraction.

Technical Approach: The lenses are placed in the eye after either intra- or extracapsular cataract extraction. Their fixation and placement vary with the particular lens type selected.

Progress: IOL records are kept by the calendar year; last year's report was submitted in December 1982. This report is for calendar year 1983, and includes implantations through August 1983. As of this date, 63 implantations have been done, 44 posterior chambers and 19 anterior chambers. One reportable adverse reaction occurred: a case of post-operative endophthalmitis in a patient with a posterior chamber implant. The infection resolved and at last visit (25 August 1983) the eye was stable with 20/20 vision. A question of adequate safety with the Azar anterior chamber lens has recently been raised by the FDA. A complete report is scheduled for the Human Use Committee (all anterior chamber implants were done with the Azar lens). The posterior chamber lens of Precision-Cosmet, used in all LAMC posterior chamber implants, has been approved by the FDA, and may be removed from this study.

Detail Summary Sheet

Date: 7 Sep 83

Prot. No.: OPH-82-03

Status: Ongoing

Title: Intraocular liquid silicone for retinal detachment.

Start Date: 12 Jan 82

Est Comp Date: Indefinite

Principal Investigator:

COL H Cohen, MD

Facility:

LAMC

Key Words: intraocular, silicone, retinal detachment

Dept/Svc:

Ophthalmology

Associate Investigators:

W Stern, MD

Accumulative MED CASE

Cost: None

Est Accumulative

OMA Cost:

Periodic Review

Results: Approved

Study Objective: To study the effectiveness of silicone oil in seven retinal detachment cases.

Technical Approach: Initial surgical procedures consists of vitrectomy, or removal of the vitreous body. Eye fluid is then replaced with silicone and subretinal fluid internally and externally drained. Silicone oil will then be injected until the retina is either flat or almost completely flat. Any membranes or wrinkles on the retinal surface that remain following silicone oil dissection will be dissected beneath the silicone oil. In cases involving treatment of retinal detachment, scleral buckling techniques will be utilized.

Progress: One LAMC patient has been entered to date. In this case, the silicone oil was partially effective; however, longterm prognosis is poor.

Detail Summary Sheet

Date: 7 Sep 83

Prot. No.: OPH-82-05

Status: Ongoing

Title: A double masked study to determine the long-term safety and ocular hypotensive effect of L-bunolol 0.5 percent b.i.d. and L-bunolol 1.0 percent in open angle glaucoma and ocular hypertensive subjects.

Start Date: 15 May 82

Est Comp Date: Indefinite

Principal Investigator:  
COL HB Cohen, MD

Facility:  
L A M C

Key Words: L-bunolol, hypotension, glaucoma

Dept/Svc:  
Ophthalmology

Associate Investigators:  
COL SM Jackson, MD

Accumulative MED CASE  
Cost: None

Est Accumulative  
OMA Cost: None

Periodic Review  
Results: Approved

Study Objective: To study effectiveness of L-bunolol in the treatment of glaucoma and ocular hypertensea.

Technical Approach: The study will be double-masked with subjects randomized into three parallel groups so that both eyes of each subject will receive b.i.d. treatment with solutions of either 0.5 percent bunolol, 1.0 percent bunolol, or 0.5 percent timolol as a positive control. The subjects will undergo treatment for 24 weeks. At this time, the data will be reviewed and a decision will be made as to whether the study may be continued for an additional 24 weeks. Thus, the protocol is designed for 24 weeks, with a possible extension to 48 weeks.

Progress: Twenty-nine patients have been entered in the study. To present date, all have been controlled adequately on medication. One patient was dropped from the study due to allergic reaction.

Detail Summary Sheet

Date: 9 Jun 83                      Prot. No.: Ortho-81-03                      Status: Completed  
Title: 67 Gallium and 99<sup>m</sup> Technetium bone imaging in experimental osteomyelitis  
Start Date: 10 Feb 81                      Est. Comp. Date: Completed  
Principal Investigators:                      Facility:  
CPT M LaGrone, MD                      LAMC

Key Words: osteomyelitis, nuclear imaging

Dept/Svc:                      Associate Investigators:  
Orthopaedics                      COL R Lull, MD  
   COL J Fitzwater, MD  
   BE Van Dam  
   V Coppes  
   D Brooks  
   B Fay

<u>Accumulative MED CASE</u>	<u>Est Accumulative</u>	<u>Periodic Review</u>
<u>Cost:</u> \$2666	<u>OMA Cost:</u> \$2,000	<u>Results:</u> N/A

Study Objective: To determine which scanning agent, 99<sup>m</sup>-Technetium or 67-Gallium, was more sensitive for the early detection of acute experimental osteomyelitis.

Technical Approach: Thirty-four New Zealand white rabbits were used for the study with 30 rabbits infected with Staphylococcus aureus and four rabbits plus the contralateral tibia serving as controls. Nuclear imaging was performed using 99<sup>m</sup>-technetium and 67-Gallium periodically over a three-week period. After completion of nuclear imaging, the animals were sacrificed and histologic examination of the infected and controlled tibias performed.

Progress: Twenty-five of 30 injected rabbits developed unequivocal osteomyelitis on histologic examination for an infection rate of 83.3 percent. The sensitivities of 99<sup>m</sup>-Technetium and 67-Gallium were compared at 7, 14, and 21 days post infection in rabbits with proven osteomyelitis. Although 67-Gallium was slightly more sensitive in the detection of osteomyelitis with fewer false negative results, the differences were not statistically significant. The most significant finding statistically was the fact that 28 percent of the 99<sup>m</sup>-Technetium scans and 20 percent of the 67-Gallium scans were falsely negative one week after infection.

Since all rabbits with false negative 67-Gallium scans also had false negative 99-<sup>m</sup> Technetium scans, 20 percent of rabbits with proven osteomyelitis had negative bone scans with both agents at one week after infection. It was concluded that there was no significant difference in sensitivities between 99-<sup>m</sup> Technetium and 67-Gallium in the early detection of acute experimental osteomyelitis and that there is a significant chance of getting false negative scans with both 99-<sup>m</sup> Technetium and 67-Gallium in the face of known acute osteomyelitis.

Presentations and Publications: This work has been submitted for presentation to the American Academy of Orthopaedic Surgeons 1984 Annual Meeting and will be submitted to the Journal of Bone and Joint Surgery for publication.

Detail Summary Sheet

Date: 7 Sep 83

Prot. No.: Orth-83-04

Status: Ongoing

Title: Retropatellar pain syndrome study.

Start Date: 1 Apr 83

Est Comp Date: 1 Apr 85

Principal Investigator:

MAJ SF Dye, MD

MAJ DA Boll, MD

Facility:

L A M C

Dept/Svc:

Orthopaedic

Associate Investigators:

Key Words: retropatellar pain

Accumulative MED CASE

Cost: N/A

Est Accumulative

OMA Cost: \$2000

Periodic Review

Results: N/A

Study Objective: To define the relationship between symptoms of retropatellar pain and to the diagnostic modalities of physical examination, radiographs, radionuclide imaging and arthroscopic examination of the involved knees. The ultimate objective is to define the etiology, pathology, and natural history of the clinical entity of retropatellar pain syndrome through comparative analysis of subjective complaints with objective measurements.

Technical Approach: Individuals with complaints of retropatellar pain between the ages of 18 and 45 are referred by an orthopaedic surgeon to the RPPS clinic at which time they undergo a thorough physical examination, have plain radiographs obtained and Technetium-99 radionuclide imaging of their knees performed. Selected individuals who have symptoms of retropatellar pain associated with a positive bone scan in the absence of radiographic abnormalities have, in addition, an arthroscopic examination in the involved knee to document the condition of the interior of the knee joint. All individuals are placed on a similar treatment regimen which involves profile restriction against running as well as restriction of straight leg raising exercises and an appropriate anti-inflammatory agent such as enteric-coated aspirin. Patients are scheduled for re-examination every two months and are scheduled for repeat radionuclide imaging of their knees performed at three months and six months after the initial scan.

Progress: The RPPS clinic has been established and patients are being referred to this clinic from the Orthopaedic Surgery Service both at Letterman and Fort Ord.

To date, 53 individuals are being followed in the RPPS Clinic. The percentages of those individuals with increased radionuclide uptake of their patellae are running roughly in the 70 percent range for males and 50 percent range for females.

We have performed arthroscopy on six of these individuals and have found significant chondromalacic changes of the patellar facets in three out of six individuals.

This protocol investigation is still in its early stages and, to date, has correlated well with the initial findings as presented in the manuscript entitled, "Radionuclide Imaging in Retropatellar Pain Syndrome," by Dye, Boll, and Dunigan.

We hope, within the next six to nine months, to be able to better define by means of repeat physical examination and radionuclide imaging the metabolic activity of the patellae of individuals with retropatellar pain syndrome.

The Hospital for Special Surgery in New York City is proceeding with a joint study of this topic utilizing our protocol. MAJ Dye will spend several weeks at the Hospital for Special Surgery in early Spring 1984 to further coordinate the joint research efforts on this project.

We are considering requesting additional approval from the Clinical Investigation Committee and the Human Use Committee to obtain intraosseous pressure measurements of patellae of those individuals who undergo arthroscopy as well as obtaining a small core of patellar bone for microscopic examination.

Publications and Presentations: MAJ Scott F Dye will present an initial summary of the results of the preliminary study and the initial results of the current study to the Society of Orthopaedic Surgeons Annual Meeting to be held in Colorado Springs, Colorado, November 13-17, 1983.

Detail Summary Sheet

Date: 9 Sep 83

Prot. No.: Ts-80-01

Status: Terminated

Title: Human implantation of the St. Jude cardiac valvular prosthesis.

Start Date: 8 Jul 80

Est. Comp. Date: Terminated

Principal Investigators:

COL T Bowen, MD

LTC R Albus, MD

Facility:

LAMC

Key Words: St. Jude cardiac prosthesis

Dept/Svc:

Cardio-Thoracic Surgery

Associate Investigators:

COL M Barry, MD

COL JS Clarke, MD

Accumulative MED CASE

Cost: None

Est Accumulative

OMA Cost: None

Periodic Review

Results: Approved

Study Objective: To assess the efficacy of the St. Jude medical cardiac valve prosthesis in patients with a small aortic annulus.

Technical Approach: Patients with a size #19 or #21 aortic, or a size #21 or #23 mitral annulus, as measured at valve replacement, are selected to receive a St. Jude medical prosthesis rather than undergo annulus enlarging procedures. Postoperative routine followup will include evaluation for hemolysis, thrombosis and cardiac function.

Progress: The St. Jude prosthesis has been released by the FDA for clinical use and the present Thoracic Surgery staff has no plans for further investigation of this subject. Thus, this protocol has been terminated.

Detail Summary Sheet

Date: 6 Sep 83

Prot. No.: Ts-82-01A

Status: Ongoing

Title: Advanced cardiopulmonary surgery techniques.

Start Date: Jan 83

Est Comp Date: Indefinite

Principal Investigator:

COL JS Clarke, MD

COL M Barry, MD

MAJ JD Rumisek, MD

Facility:

LAMC

Dept/Svc:

Cardio-Thoracic Surgery

Associate Investigators:

MAJ W Berry, MD

LTC V Farraris, MD

Key Words: cardiopulmonary surgery

Accumulative MED CASE

Cost:

Est Accumulative

OMA Cost:

Periodic Review

Results:

Study Objective: To enable thoracic and cardiovascular residents and teaching staff to gain experience in complicated, uncommon, or unusual surgical techniques in the animal lab prior to human utilization for treatment of clinical disease.

Technical Approach: Fifty to 100 kg pigs are placed on cardiopulmonary bypass and the cardiac procedure chosen is performed. Weaning from the bypass to observe hemostatic security and hemodynamic function is performed prior to sacrifice, while still fully anesthetized.

Progress: Animals used thus far have proven extremely valuable in gaining insight and surgical expertise, particularly on the resident level. Scheduling difficulties resulted in excess growth to pigs such that their utilization was not possible. This should be avoidable in the future. There is no completion date for this ongoing teaching tool.

Detail Summary Sheet

Date: 6 Sep 82

Prot. No.: Ts-82-02

Status: Ongoing

Title: Thrombogenicity and longterm fate of albumin-coated vascular prostheses.

Start Date: Aug 83

Est Comp Date: Indefinite

Principal Investigator:

MAJ JD Rumisek, MD

CPT K Kaplan, MD

COL JS Clarke, MD

Facility:

LATR

Dept/Svc:

Cardio-Thoracic Surgery

Associate Investigators:

D Brooks

CE Wade, PhD

Key Words: thrombogenicity, vascular prostheses, albumin-coated

Accumulative MED CASE

Cost:

Est Accumulative

OMA Cost:

Periodic Review

Results:

Study Objective: To determine if heat denatured albumin, impregnated in the interstices of vascular prostheses, results in a hemostatic, nonthrombogenic surface; to determine the longterm patency of such grafts in comparison to currently available porous textile grafts.

Technical Approach: 1. A Wesoloski column is used to determine the porosity of untreated, preclotted, and denatured albumin impregnated prosthetic grafts. A burst strength apparatus is used to determine the stability of the albumin impregnation in maintenance of a low porosity.

Thrombogenicity of the graft surface is analyzed in vivo by the timed appearance/disappearance of <sup>131</sup>I-labeled fibrinogen, <sup>111</sup>IN-labeled platelets, and <sup>51</sup>Cr-labeled red blood cells in paired external graft blood flow circuits using well gamma-counting of unit area graft samples. Acute morphologic changes of the graft surface is analyzed using light and scanning electron microscopy.

2. Two different graft preparations are implanted into canine iliofemoral arterial segments, one in each side, for short-term and long-term harvesting. Timed appearance of <sup>111</sup>IN-labeled platelets by imaging is used to calculate relative thrombogenicity indices of the implants. Specimens of short-term, long-term, as well as unexpected thrombosed grafts are analyzed with light and scanning electron microscopy for graft surface and surrounding tissue morphology.

3. Comparative long-term (12-month) patency of each graft preparation is analyzed for statistical significance.

Progress: Investigation has just begun with the Wesoloski apparatus and with implantation portions of the study. Radionuclear thrombogenicity studies should begin within two weeks. The burst strength apparatus has not yet been constructed. Grafts have been implanted in two dogs as pilot study animals. One graft, albumin coated, has thrombosed. Sacrifice of the animal is pending to reveal the failure mode, suspected to be technical. The main cohort of study animals has just been released from quarantine with initiation of the long-term implantation portion of the study to commence shortly.

Detail Summary Sheet

Date: 5 Apr 82

Prot. No.: Ts-82-03

Status: Ongoing

Title: Replacement of canine femoral veins with albumin-autoclaved vascular prostheses.

Start Date: Mar 83

Est Comp Date: 1984

Principal Investigator:

COL WH Heydorn, MD

COL MJ Barry, MD

COL JS Clarke, MD

CPT K Kaplan, MD

LTC MA Oddi, MD

Facility:

LAMC

Dept/Svc:

Cardio-Thoracic Surgery

Associate Investigators:

MAJ JD Rumisek, MD

MAJ WR Berry, MD

Key Words: thrombogenicity, vascular prostheses, dacron, albumin-autoclaved

Accumulative MED CASE

Cost:

Est Accumulative

OMA Cost:

Periodic Review

Results:

Study Objective: To compare long and shortterm patency grafts in the replacement of canine femoral veins with autologous reimplanted femoral veins with woven dacron prostheses that have been autoclaved after soaking in albumin.

Technical Approach: In 10 mongrel dogs blood will be removed in heparin for platelet labelling with Indium <sup>111</sup> Oxine. After segments of femoral veins are excised aseptically, the left femoral vein will be reimplanted as an operative control and the right femoral vein replaced with a segment of dacron graft soaked in albumin and autoclaved. No anticoagulants will be used to perform anastomoses. The previously labelled blood will be injected following graft hemostasis. Images and counts will be performed by Nuclear Medicine. Platelet labelling, injection, imaging and counts will be performed successively postop and patency confirmed by venogram. Animals will be sacrificed at six months and grafts inspected grossly and microscopically.

Progress: Data to be collected in January 1984.

Detail Summary Sheet

Date: 6 Sep 83

Prot. No.: Ts-83-04

Status: Ongoing

Title: Infection resistance of antibiotic impregnated albumin coated vascular prostheses.

Start Date: Sep 83

Est Comp Date: Indefinite

Principal Investigator:

MAJ JD Rumisek  
LTC D Haburchak  
COL JS Clarke

Facility:

LAIR

Dept/Svc:

Cardio-Thoracic Surgery  
Internal Medicine  
Clinical Investigation

Associate Investigators:

CPT G Boswell, PhD  
CPT T Hamel  
CE Wade, PhD

Key Words: vascular prostheses

Accumulative MEDCASE

Cost:

Est Accumulative

OMA Cost:

Periodic Review

Results:

Study Objective: To develop a reliable animal model to determine the susceptibility of intravascular material to infection; utilize this model to determine the effectiveness of various types of graft pretreatment with antibiotic agents in decreasing incidence of vascular prosthetic infections; and specifically analyze availability, concentration, and disappearance of antibiotics impregnated in heat-denatured albumin coated vascular prostheses.

Technical Approach: 1. 3 mm x 20 mm strips of textile is fixed inside the right atrium of large rats. Control of animals are followed to rule out a significantly high rate of endogenous bacterial seeding of the intraatrial foreign body. Sensitivity of the model will be assayed by intravenous injection of Staph aureus strain ATCC 25923.

2. The functional stability of various antibiotics in 25 percent albumin solution following heat denaturation will be assayed using the Kirby-Bauer disc technique. Combinations of heat stable antibiotics will then be mixed in albumin solution and heat denatured onto textiles by autoclaving. 3 mm x 20 mm strips of the textile will be implanted in the right atria of the model, with

albumin solution and heat denatured onto textiles by autoclaving. 3 mm x 20 mm strips of the textile will be implanted in the right atria of the model, with antibiotic levels followed by using HPLC or radionuclide labeling of each antibiotic at timed harvests of the implants.

3. Staph aureus strain ATCC25923 will then be injected intravenously into completed models, with or without antibiotic impregnation, to compare susceptibilities to bacteremic seeding of implanted grafts.

Progress: Cephalosporin, vanomycin, and gentamicin have been found to be relatively heat stable and suitable for further study. Rats have been found unsuitable for use as the model base because of their small right atrial size as well as common pleural cavity resulting in lethal pneumothorax. Rabbits are being investigated now for model suitability.

Detail Summary Sheet

Date: 20 Sep 83

Prot. No.: U-79-03

Status: Ongoing

Title: Large animal surgery: an important addition to residency training in urology.

Start Date: Mar 79

Est. Comp. Date: Indefinite

Principal Investigator:  
LTC RA Watson, MD

Facility:  
LA MC

Key Words: large animal surgery, urology, residency training

Dept/Svc:  
Urology

Associate Investigators:  
COL R Agee, MD  
LTC G Deshon Jr, MD

Accumulative MEDCASE  
Cost: None

Est Accumulative  
OMA Cost: \$2000

Periodic Review  
Results: N/A

Study Objective: To broaden the skills of urologic residents.

Technical Approach: Each resident is invited to perform selective surgical procedures on an animal model to complement his educational and technical training in Urology. As outlined in the protocol, carefully planned, supervised, and postoperatively monitored series of new procedures are performed by each resident during the second year of his training as a supplement to his clinical experience.

Progress: Over the past year five surgical procedures have been performed utilizing two animals, providing surgical experience for two urologic residents. Dr W Traverso, CCC, LAIR, has provided invaluable input in terms of bowel surgery and surgical techniques in general. The program continues to provide an important and welcome supplement to urologic training for residents.

Publications/Presentations: Watson RA, Deshon GE, Agee RE: Surgical experience with large animals, important adjunct to residency training in urology. Urology 20: 154-156, (August) 1982.

Detail Summary Sheet

Date: 20 Sep 83

Prot. No.: U-81-05

Status: Ongoing

Title: Human prostate grafts in nude mice.

Start Date: May 81

Est. Comp. Date: Oct 83

Principal Investigators:  
CPT Tu-Hi Hong, MD

Facility:  
LAIR

Key Words: prostate, nude mice

Dept/Svc:  
Urology

Associate Investigators:  
CPT W Jederberg, MD  
COL RE Agee, MD  
LTC GE Deshon Jr, MD

Accumulative MED CASE  
Cost: None

Est Accumulative  
OMA Cost: \$4000

Periodic Review  
Results: N/A

Study Objective: The main objective is to examine the feasibility of growing human prostatic tissue in nude mice. This involves the investigation of various factors that might influence the outcome of such a heterotransplantation. These factors are: (1) age and sex of the recipient animal; (2) hormonal manipulation; (3) the distinct method by which the tissue was harvested and implanted; (4) the period of incubation of tissue prior to transplantation; and (5) the duration of graft.

Technical Approach: Human prostatic tissues were obtained, with informed consent, during diagnostic and therapeutic procedures. The tissue was incubated in the Roswell Park Memorial Institute medium 1640 until time of transplantation. Cell suspensions were injected into the dorsal subcutaneous space, with negative results (i.e., no graft survived). Subsequently, a piece of tissue was placed in the dorsal subcutaneous space. The tissues were then harvested at the predetermined time, and recovered tissues examined histologically and compared with original histology.

Progress: Data being compiled.

Detail Summary Sheet

Date: 20 Sep 83

Prot. No.: J-81-06

Status: Ongoing

Title: A phase II prospective controlled study to determine the role of thio-tepa versus mitomycin C prophylaxis in the treatment of superficial, low-grade bladder tumors.

Start Date: Nov 81

Est. Comp. Date: Indefinite

Principal Investigators:  
COL RA Watson, MD

Facility:  
LAIR

Key Words: thio-tepa, mitomycin C prophylaxis, low-grade bladder tumors

Dept/Svc:  
Urology

Associate Investigators:  
CPT W Jederberg  
COL RE Agee  
LTC GE Deshon Jr, MD

Accumulative MEDCASE  
Cost: None

Est Accumulative  
OMA Cost: \$4000

Periodic Review  
Results: N/A

Study Objective: To evaluate and compare the effectiveness of thio-tepa and/or mitomycin C intravesical chemotherapy in preventing recurrences in patients with superficial bladder tumors; to study the effectiveness of intravesical thio-tepa and/or mitomycin C in preventing higher grade-stage tumor recurrences; to compare the side effects (i.e., morbidity of intravesical mitomycin C versus thio-tepa) in similar groups of patients.

Technical Approach: Patients will be randomly assigned to either drug treatment group. The treatment courses will be repeated for four weeks then monthly for 24 months. Any patient who develops a progressive disease will be considered a treatment failure and will be removed from protocol-assigned prescription but will be followed in the study for survival; subsequent drug (e.g., mitomycin C, cystectomy) will be recorded. Any patient who develops a recurrence without evidence of progressive disease will have the tumor resected, have preselected mucosal biopsies performed, and will go on to complete the 24-month course of treatment.

Progress: This protocol has received wide acclaim for its high caliber of science. This study involves a highly specified group of patients in a randomized and prospective fashion. Regrettably, the specific definition of the patient population resulted in a very slow accrual rate. More specifically, since most patients with recurrent bladder tumors have already received a course of thio-tepa some time in

the past, they are excluded. An ongoing campaign is aimed at promoting more rapid accrual. Presently, some 28 patients have been placed on study. The National Cancer Institute is now providing the mytomyacin-C free of charge to patients who are randomized to that treatment arm. The availability of mytomyacin-C without cost to the patient will, hopefully, encourage more rapid accrual.

Detail Summary Sheet

Date: 20 Sep 83      Prot. No.: U-82-08      Status: Completed

Title: The biopsy-cucumber unit.

Start Date: Sep 82      Est. Comp. Date: Completed

Principal Investigators:      Facility:  
COL RA Watson, MD      LAIR

Key Words: cold-cup biopsy, bladder tumors, carcinoma

Dept/Svc:      Associate Investigators:  
Urology      LTC J Fitzwater, MD

<u>Accumulative MED CASE</u>	<u>Est Accumulative</u>	<u>Periodic Review</u>
<u>Cost:</u> None	<u>OMA Cost:</u> \$4000	<u>Results:</u> N/A

Study Objective: To determine whether processed cucumber slices provide an advantageous vehicle for cold-cup bladder biopsy specimens.

Technical Approach: Slices of cucumber will be dehydrated through sequential passage in absolute alcohol. When processed, these 3-4 mm thick slices will be utilized on a test specimen. From the mucosa of the bladder of a sacrificed animal, utilized in an unrelated LAIR experiment, cold-cup biopsy bites from the mucosa will be obtained. One bite will be placed on a single cucumber slice, mucosa face down. (The slice will be first dried, then coated with egg albumen.) A second specimen will be placed "sandwich style" between two slices of cucumber and a third slice will be placed in the same specimen cup with no cucumber vehicle. The process will be repeated in three separate cups. Each of the nine specimens will then be processed routinely and inspected by the principal and assistant investigators to determine whether there is any apparent advantage in using the cucumber as a one-or two-layer vehicle. If the initial study proves inconclusive, additional specimens may be obtained and so processed.

Progress: This study has been completed. Specially processed cucumber slices have proven effective mounts for biopsy tissue.

Publications and Presentations: The findings of this study were reported at the 1982 Kimbrough Urologic Seminar in New Orleans, and were subsequently highlighted in the June 1983 issue of Urology Times. The report has since been accepted for publication in Urology.

Detail Summary Sheet

Date: 9 Aug 83

Prot. No.: LAIR-81-05

Status: Completed

Title: Evaluation of amniotic wound dressings.

Start Date: 10 Feb 81

Est Comp Date: Completed

Principal Investigator:  
SFC J Surinchak

Facility:  
LAMC/LAIR

Key Words: wound healing, amnion, physiology, wound dressings

Dept/Svc:  
Combat Casualty Care, LAIR

Associate Investigators:  
COL Bellamy, LTC Winkel

Accumulative MED CASE  
Cost: None

Est Accumulative  
OMA Cost: None

Periodic Review  
Results: N/A

Study Objective: Amnion has been used extensively in burn and indolent ulcer cases. In these situations it has been found to speed wound closure, alleviate pain and suppress bacterial growth. It has not been evaluated as a dressing for full thickness, mechanically induced skin wounds such as those received from bullets, mine blast or artillery rounds. The primary purpose of this investigation is to evaluate the possible use of amnion as a dressing for full thickness skin wounds.

Technical Approach: Ten rabbits will have a 4 cm<sup>2</sup> skin wound created on their backs and have the amniotic dressing applied (changed every other day). Ten additional rabbits, wounded in the same manner, will have the wound site covered with a conventional dressing (Telfa pads). Wound areas will be measured daily to determine rate of healing.

Progress: This investigation is completed. Results indicate that amniotic dressings accelerate healing approximately 30 percent over the controls. No significant difference in the bacterial populations has been observed.

Detail Summary Sheet

Date: 9 Aug 83

Prot. No.: CH-81-01

Status: Ongoing

Title: Human skin for purposes of research concerning penetration of chemicals and for studies of function.

Start Date: Mar 81

Est Comp Date: Indefinite

Principal Investigator:

LTC K Black, MD

MAJ J Jackson, MD

Facility:

LAIR

Dept/Svc:

Cutaneous Hazard, LAIR

Associate Investigators:

CPT Jederberg

Dr W Reifenrath

Key Words: human skin graft, nude mice

Accumulative MEDCASE

Cost: N/A

Est Accumulative

OMA Cost: N/A

Periodic Review

Results:

Study Objective: To establish self-sustaining colonies of nude (nu/nu) mice at LAIR; establish and become proficient in the procedure for grafting human skin and pig skin on nude mice; and to compare the permeabilities of skin on normal humans and on pigs with the permeabilities of xenografts of cadaver skin and excised pig skin on nude mice.

Technical Approach: The skin is taken to LAIR after surgery at LAMC. The skin is trimmed and full or split thicknesses are prepared. The skin is kept at 37C. in Roswell Park Memorial Institute (RPMI) media No. 1640, containing gentamycin until it is used.

Progress: The Plastic Surgery Service at LAMC supplied the Division of Cutaneous Hazards at LAIR with 53 specimens of non-diagnostic human skin obtained under informed consent at surgery and donated for research purposes. Three-hundred and ninety-nine nude mice were grafted with pieces of the skin.

Twenty-one of the grafted mice were used in metabolic studies for in vivo measurements of the penetration of fluocinolone acetonide, caffeine, lindane,

parathion, DDT, progesterone and testosterone. The human skin grafted nude mouse shows promise as a model which ranks the permeability of compounds in the above chemicals similar in the human and pig skin grafted nude mice.

Four specimens of skin were used in in vitro studies to compare the permeabilities of human and pig skin. Penetrations of DEET, benzoic acid, caffeine and lindane were similar through each type of skin.

Thirteen human skin grafted mice were used to study the effects of applications of various dosages of phenyl dichloroarsine. Nineteen were used in a similar manner for study of the effects of application of nitrogen mustard. The former caused epidermal vacuolization leading to necrosis. The latter caused degeneration of actively proliferating areas of the epidermis and the hair follicles.

Forty-eight of the human skin grafted nude mice were sent to the Aberdeen Proving Ground for study of the effect of blistering agents on the skin. Histological studies are underway.

Fourteen human skin grafted nude mice were used to study the effect of the bite of the sandfly. Results are pending.

Effort is being made to establish a murine hepatitis-free nude mouse colony. It is expected that losses of the animals due to wasting will decrease. There is no fixed completion date for this investigation project.

Publications/Presentations:

CPT WW Jederberg presented a summary of the results of this study to the Second Annual Chemical Defense Bioscience Review, US Army Medical Research Institute of Chemical Defense, Aberdeen Proving Ground, on 13-14 May 1982.

Detail Summary Sheet

Date: 19 Aug 83

Prot. No.: SBH AH-83-01

Status: Ongoing

Title: The influence of stress and social support on physical well being.

Start Date: Apr 84

Est Comp Date: Jul 84

Principal Investigator:  
MAJ J Zarinczuk, MD

Facility:  
Silas B Hays Army Hospital (SBH AH),  
Fort Ord

Dept/Svc:  
Family Practice

Associate Investigators:

Key Words: social support, stress, health behavior

Accumulative MED CASE  
Cost:

Est Accumulative  
OMA Cost:

Periodic Review  
Results:

Study Objective: To describe the relationship between stressors, social support, and health behavior.

Technical Approach: A questionnaire will be mailed to subjects to determine stressors and social support. Health behavior will be determined by review of medical charts. Data will be computer stored and analyzed.

Progress: No patients to date have been entered into this study. As of this date, MAJ Zarinczuk has been assigned on TDY and will resume this study in six months, upon his return to SBH AH.

## Presentations

### Department of Clinical Investigation

Danley DL, Casey ML, Brooks DE, Winkel CA: Conversion of progesterone to deoxycorticosterone (DOC) in guinea-pig spleen - an animal model for the study of steroid 21-hydroxylase activity in extraadrenal sites. Federation Proceedings 42(7):1836, 1983. (CI-81-05)

Hill LC, Dressendorfer RH, Wade CE: Urinary aldosterone excretion during a 70 hour recovery period following repeated episodes of prolonged running. Medicine and Science in Sports and Exercise 15(2):94, 1983. (U-83-14)

Thrasher TH, Moore-Gillion MJ, Wade CE, Keil LC, Ramsay DJ: Effect of water restriction in dogs with chronic constriction of the thoracic vena-cava. Federation Proceedings 42(4):738, 1983.

Wade CE: Plasma vasopressin response to intravenous naloxone in euhydrated and dehydrated conscious dogs. Federation Proceedings 42(4):1116, 1983. (CI-82-12)

Wade CE, Hill LC, Dressendorfer RH: Plasma-aldosterone regulation and renal function in marathon runners during a 20-day road race. Medicine and Science in Sports and Exercise 15(2):94, 1983. (CI-82-14)

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#### Cardiology Service

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#### Gastroenterology Service

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#### Hematology-Oncology

Geier LJ, Volk SA, Weldon D, Redmond J: Late relapse in testicular cancer after chemotherapy. Lancet 1(8332):1049, 1983.

#### Neurology Service

Chang GY: Vascular headache. Hospital Practice 18(4):178, 1983.

Department of Surgery

Heydorn WH and Moores WY: Naloxone - ineffective in improving cardiac performance after shock in swine. Journal of Trauma 23(7):642, 1983.

Otolaryngology Service

Wong RT: Methylene-blue stained temporalis fascia graft in tympanoplasty. Laryngoscope 93(2):241, 1983.

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### Department of Obstetrics-Gynecology

Flaherty JF, Boswell GW, Winkel CA, Elliott JP: Pharmaco-kinetics of cefoxitin in patients at term gestation: lavage versus intravenous administration. American Journal of Obstetrics and Gynecology 146(7):760-766, 1983.

Woods JR, Coppes V, Brooks DE, Freeman M, Knowles PJ, Parisi V, Omara P, McCarty GE: Measurement of visual evoked potential in the asphyctic fetus and during neonatal survival. American Journal of Obstetrics and Gynecology 143(8):944-951, 1982.

### Department of Surgery

#### Urology Service

Watson RA, Sanders NZ: Social and sexual adjustment of men operated for hypospadias during childhood - a controlled study. Journal of Urology 127(5):995, 1982.

### Department of Psychiatry

Hales RE, Borus JF: Teaching psycho-social issues to medical house staff - a liaison program on an oncology service. General Hospital Psychiatry 4(1):1-6, 1982.

Hales RE, Fink PJ: A modest proposal for consultation for liaison psychiatry in the 1980s. American Journal of Psychiatry 139(8):1015-1021, 1982.

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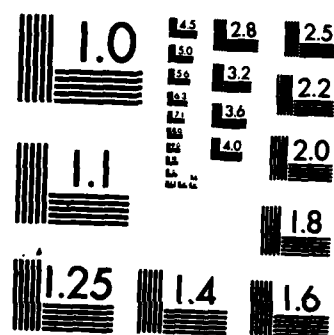
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