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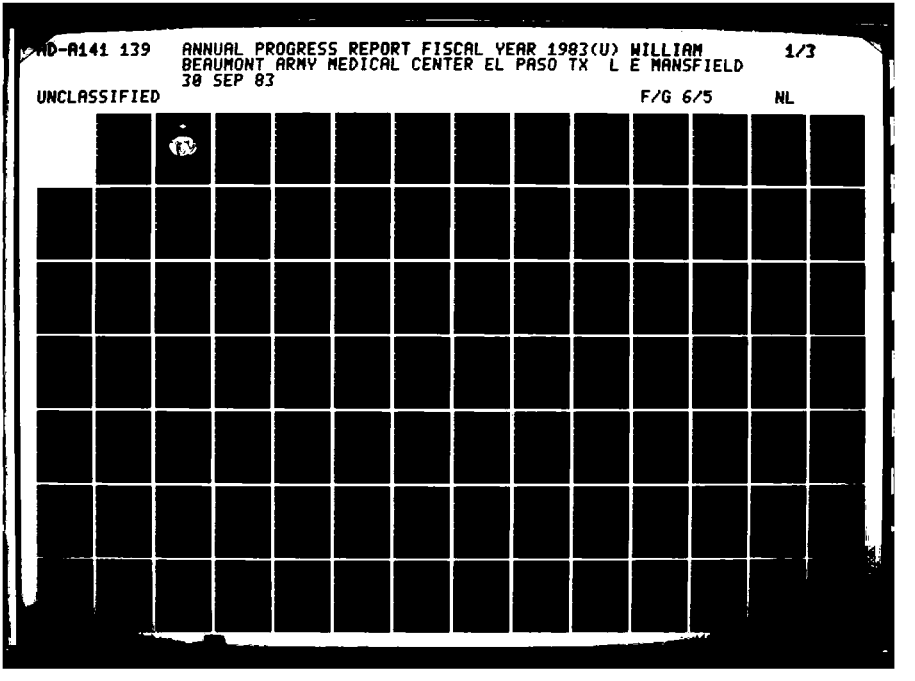

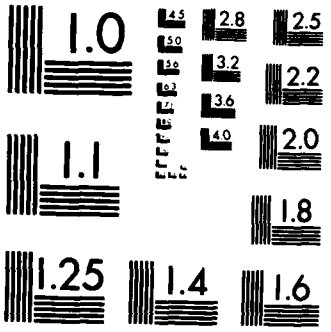

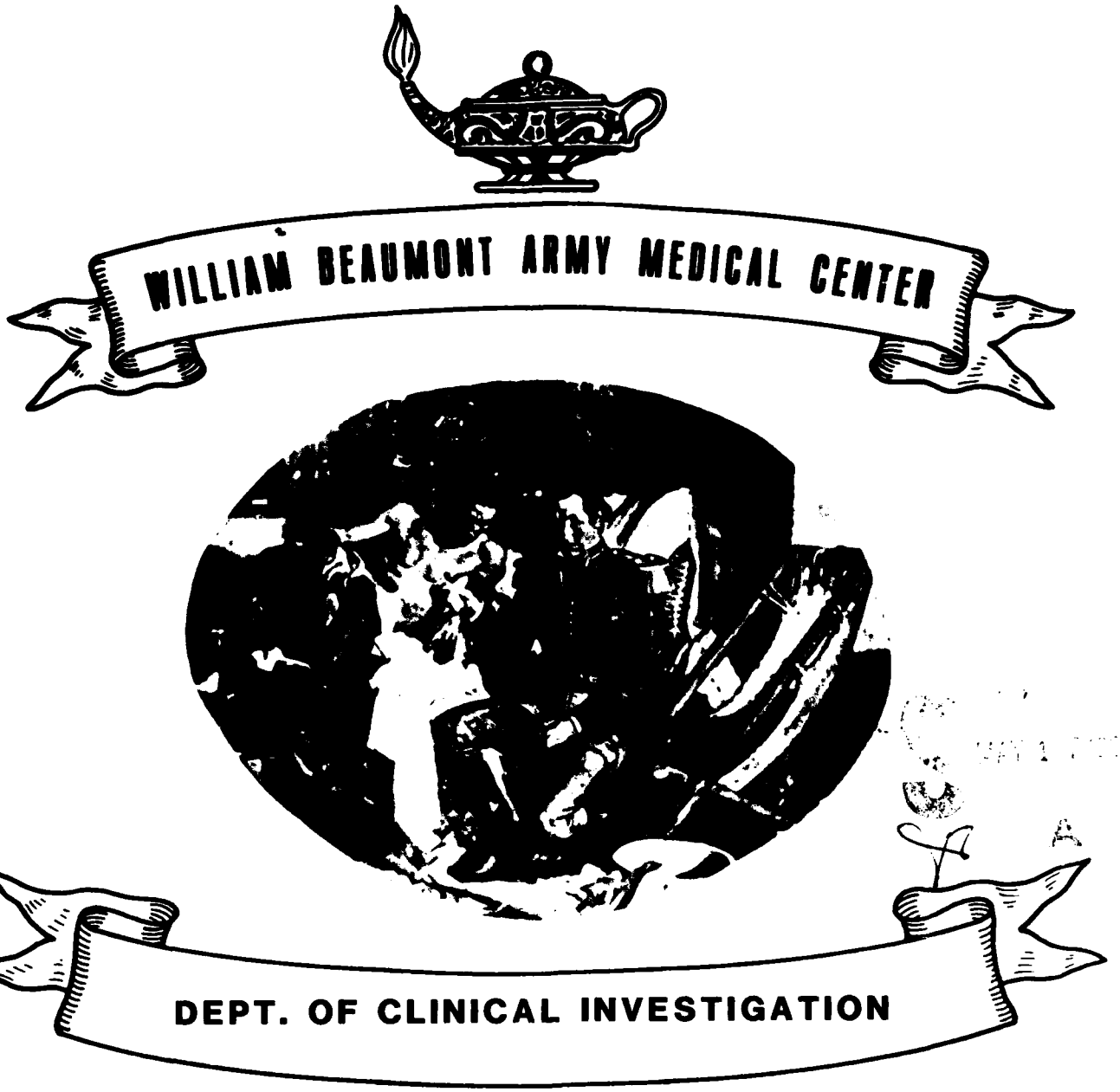




# ANNUAL PROGRESS REPORT
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20. ABSTRACT (Continue on reverse side if necessary and identify by block number)

This report serves to detail the progress, status, and funding of approved projects conducted under protocol by staff members, interns, and residents at William Beaumont Army Medical Center. The varying projects as reported are classified according to the service or department to which the principal investigator belongs. Research conducted at WBAMC is categorized either basic experimental medicine or trials and testing of clinical medicine procedures using the indigenous population for which this medical facility provides support.

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This annual report is dedicated to Dr. L.L. Penney and his staff during the six years he was Chief of the Department of Clinical Investigation.

During those years many changes occurred. The Clinical Investigation Service became a department with all this implies. Significant progress was made in the number of projects which were initiated and completed. In FY78 there were 58 presentations and publications reported from the staff of William Beaumont Army Medical Center. In FY83 this had increased to 161. In FY78 there were 64 ongoing protocols, and in this report 119. This was accomplished despite historical documentation of insufficient personnel and equipment to meet all the demands.

Within the Army there is a salubrious trend to bring more approval authority and responsibility to the local level. Unfortunately the regulatory requirements of outside agencies, such as the FDA and cooperative study groups, has become increasingly stringent. If this trend does not reverse, there is a distinct threat to the spontaneity and creativity of the research process. Investigators will focus on projects that are safe, or sure wins, and limit their horizons.

Informing and protecting human volunteers is of the highest ethical principles of the medical profession. However, the requirement to have distant offices, nameless faces, and long periods of time to judge whether we will do this, can be devastating to a curious mind. It is imperative that the price for human protection does not become impoverishment of the fertile process which has done so much to improve the human condition in our century.

Lyndon E. Mansfield MD.

LYNDON E. MANSFIELD, M.D.
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C, Dept Clinical Investigation

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Reimann B: Operat... [illegible]
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Hamburg, 1982 ...

Roberts WA, Badger VM: [illegible]

Sanders L: Reactive hypoglycemia. [illegible]
Diabetes Care (Sep Oct 82)

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## OBJECTIVES

The Department of Clinical Invesigation, William Beaumont Army Medical Center, was established 2 February 1965 as the Medical Research and Development Service. Following reorganization and official recognition under AR 40-38 (23 Feb 73) the service became the Clinical Investigation Service. Departmental status was achieved in FY80. The mission is to promote, conduct, and coordinate clinical and directed basic research. The policies and objectives are outlined in Department of Defense Directive Number 6000.4 dated 7 April 1971:

> "Clinical investigation is an essential component of optimum medical care and consists of the organized inquiry into clinical health problems, for the following purposes:
>
> 1. To achieve continuous improvement in the quality of patient care.
>
> 2. To provide experience in the mental discipline achieved by participation in such organized inquiries, and to provide experience for personnel who will ultimately be teaching chiefs in military hospitals and medical specialty consultants.
>
> 3. To maintain an atmosphere of inquiry because of the dynamic nature of the health sciences.
>
> 4. To maintain high professional standing and accreditation of advanced health education programs."

Item number 4 continues to be critical in the wake of the GMENAC recommendations and the move to reduce the number of training programs. WBAMC is particularly vulnerable as this institution cannot rely on university affiliations to satisfy basic science requirements and continues to suffer physician and allied scientist understaffing.

The Department supports research and training projects from all MEDCEN departments and from MEDDACs in this medical region. The department furnishes experimental design, statistical, technical, and regulatory expertise; develops and conducts special laboratory procedures; and provides equipment, supplies, and animal resources for research and training protocols. The creative and inspirational environment and the technical knowledge available serve to stimulate the undertaking of basic and clinical research at William Beaumont Army Medical Center by staff members, fellows, residents, and interns. In addition, the department teaches the principles and methods of research.

The Biological Research Service supported training as well as research protocols and organized and directly supported ten training procedures during the past year. Examples of formal training protocols were listed in the FY80 Annual Report. Current projects are available upon request.

The Department of Clinical Investigation has provided scientific and administrative computational support to the Departments of Nursing, Pathology, Medicine, Surgery, and Logistics Division of WBAMC. The department provides this support as it possesses unique skills and equipment necessary to perform the tasks. The tasks may require mathematical modeling, statistical analysis, or graphical representations. In addition, all radioimmunoassay calculations and reports performed by Nuclear Medicine were done utilizing equipment and programs provided by the Department of Clinical Investigation.

TECHNICAL APPROACH

The Department of Clinical Investigation provides support for staff research projects under the guidelines of the Declaration of Helsinki, Clinical Investigation Program (AR 40-38), HSC Reg 40-2, and the Use of Investigational Drugs in Humans and the Use of Schedule I Controlled Drug Substances (AR 40-7). Research is conducted under protocols approved by the Research Committee (WBAMC HR 70-4), the Human Use Committee (WBAMC HR 40-38) and the Radioisotope Committee (WBAMC HR 40-37) where applicable. In those research protocols utilizing laboratory animals, the investigators follow guidelines set forth in "Guide for Laboratory Animal Facilities and Care," published by the National Academy of Sciences-National Research Council, and the criteria established by the American Association for Accreditation of Laboratory Animal Care.

## MANPOWER

| Title | Recognized Requirement (SSI/MOS) | Auth | Assigned | Name |
|---|---|---|---|---|
| OFFICE OF CHIEF | | | | |
| Chief | 60 M9B | 0-6 | 0-5 | Mansfield, L.E. |
| Allied Sci (Biochem) | 68 C9B | 0-3 | 0-4 | Smith, M.L. |
| Editorial Asst | 01087 | GS-7 | GS-7 | Casteel, P.J. |
| Protocol Coord | 01087 | - | - | - |
| Clerk, Supply | 02005 | GS-4 | GS-4 | Turner, L. |
| Internist | 61 F00 | - | - | - |
| CHEMISTRY SERVICE | | | | |
| Supv Res Chem | 01320 | GS-12 | GS-12 | Rauls, D.O. |
| Biochemist | 68 C00 | - | - | - |
| Chemist | 01320 | GS-9 | GS-9 | Sandison, S.W |
| Bio Sci Asst | 01H20 | - | - | - |
| Med Lab Tech | 00645 | GS-7 | GS-7 | Manna, B.S. |
| Med Lab Tech | 00645 | GS-7 | GS-7 | Lund, M. |
| Med Lab Tech | 00645 | - | - | - |
| Med Lab Aide | 00645 | - | - | -- |
| MICROBIOLOGY SERVICE | | | | |
| Supv Microbiol | 00403 | GS-12 | GS-12 | Frederick, R.J. |
| Immunologist | 68 E9B | 0-3 | 0-3 | Serio, C.S. |
| Bio Sci Asst | 01H20 | E-5 | - | - |
| Microbiologist | 00403 | GS-9 | GS-9 | Barren, P |
| Med Lab Tech | 00645 | GS-7 | GS-6 | MacIntyre,S. |
| Med Lab Tech | 00645 | - | - | - |
| Med Lab Tech | 00645 | - | - | - |
| Electron Micr Tech | 00699 | - | - | - |
| BIOLOGICAL RESEARCH SERVICE | | | | |
| C, BioRes Svc | 64C9B | 0-3 | 0-4 | O'Brien,A.W. |
| Vet Anm Sp | 91T20 | E-5 | E-4 | Gleeson, M |
| Animal Care Sp | 91T20 | E-5 | - | - |
| Vet Anm Sp | 91T10 | E-4 | E-4 | Chase,T |
| Vet Anm Sp | 91T10 | E-4 | E-2 | Sedivy,P. |
| Vet Anm Sp | 91T10 | E-3 | E-2 | Rameriz, C |
| Vet Anm Sp | 91T10 | E-3 | - | |
| Hlth Tech | 00699 | GS-7 | GS-7 | Revels, J.E. |
| Anm Caretaker | 05048 | WG-1 | WG-1 | Burton, A.D. |
| Animal Hlth Tech | 00704 | - | - | - |

Seven new recognized requirements were added during FY83. The number of personnel assigned at the end of FY83 was 47% of recognized requirements. Two new positions, Protocol Coordinator and Animal Health Tech, were opened for hiring, and the Chemist position was vacated in February 1983 and remains unfilled.

| EXPENDITURES | FY80 | FY81 | FY82 | FY83 |
|---|---|---|---|---|
| Personnel (Civilian) | 171,444 | 198,298 | 191,190 | 207,914 |
| Consumable Supplies | 60,134 | 86,351 | 122,189 | 120,660 |
| MEDCASE Equipment | 140,836 | 203,884* | 77,965 | 248,000* |
| Capital Equipment | 10,427 | 36,256 | 34,144 | 9,643 |
| TDY | 1,469 | 2,387 | 4,743 | 2,767 |
| Contracts, Services, Printing & Reproduction | 2,494 | 5,905 | 2,982 | 6,242 |
| TOTAL | $386,836 | 531,081 | 433,213 | 595,226 |
| Military Pay | 167,437 | 217,503 | 259,726 | 245,853 |
| | $554,273 | $748,584 | $692,939 | $841,079 |

*The MEDCASE expenditures include year-end supplements. The Dept Clinical Investigation further accounted the supply expenditures into general office $7,204; general laboratory (divided among two or more protocols or for maintenance, standards, etc) $20,920; and general biologic research facility $12,150. The remaining $80,386 was spent on 30 specific protocols and the amount is noted under OMA cost on the appropriate detail sheets. Most equipment is for diverse uses and can not be accounted on individual protocols.

FY83 expenditures of $841,079 were further divided into $672,063 for research and $168,216 for training using estimated fractions of time and resources devoted to each. Research expenditures averaged approximately $5000 per protocol. Administration nearly doubled and the personnel costs to provide this service for the MEDCEN exceeded $1100 per protocol. The avalanche of paperwork increased administration supply costs to $60 per active protocol. This increase raised the fraction of total expenditures dedicated to administration from 7.8% in FY82 to 16.6% in FY83.

TDY for minimal continuing education and mission-essential training was granted. The department was included in the approval process for TDY to present papers from protocols, and the funds available were $25,711 .

The numbers of protocols accepted, the increased number completed, and the increase in publications and presentations continue to attest to the value of DCI staff stabilization as noted in the FY78 report. Stabilization of principal investigators is improving. The MSC corps has increased stabilization tours for research personnel to four years. This will help tremendously in providing continuity in projects involving our allied scientists.

On 1 July 83 COL L.L. Penney, MC, left the DCI to become Chief, Obstetrics-Gynecology and the residency training program. His accomplishments were many and are enumerated in the Foreword. LTC Lyndon E. Mansfield, MC, former Chief of the Allergy/Immunology Service, became the new DCI Chief.

**PROGRESS:** During this fiscal year WBAMC authors had 161 articles accepted for national/regional presentation or publication. This list begins on page 16. Over one-half of these publications and/or presentations resulted directly from protocols. It is important to note the DCI provided editorial and/or statistical assistance on many of the remainder. A tabulation of pertinent workload and dispositions compared to budget (not adjusted for inflation) for the past seven years follows: (FY77 and 7T have been combined, but adjustment to 12 months is shown in parentheses). The final chart is a summary of protocol dispositions per year of origination. The SWOG principal investigator at WBAMC resigned in FY82, forcing termination of many protocols. New SWOG protocols are being conducted under the auspices of Brooke Army Medical Center.

| | Protocols Ongoing 1 Oct | New Protocols Submitted During FY | Total Protocols | Protocols Completed During FY | Protocols Terminated During FY | Publications and Presentations | OMA Budget |
|---|---|---|---|---|---|---|---|
| FY76 | 49 | 32 | 81 | 12 | 16 | 48 | $20,471 |
| FY77 & 77T | 53<br>(42)* | 25<br>(20) | 78<br>(62) | 18<br>(14) | 15<br>(12) | 24<br>(19) | $56,831<br>($45,465) |
| FY78 | 45 | 30 | 75 | 3 | 9 | 28 | $35,923 |
| FY79 | 63 | 43 | 106 | 9 | 14 | 46 | $34,392 |
| FY80 | 83 | 41 | 124 | 25 | 25 | 63 | $60,134 |
| FY81 | 74 | 59 | 133 | 16 | 17 | 80 | $86,351 |
| FY82 | 100 | 58 | 158 | 42 | 45 | 88 | $122,189 |
| FY83 | 71 | 51 | 122 | 24 | 19 | 161 | $120,660 |
| FY84 | 76 | | | | | | |

*Figures in parentheses represent adjustment to a base of 12 months.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 81/33 Status: Ongoing

Title:

Study of the Size and Charge Heterogeneity of Prolactin in Human Seminal Plasma and Spermatozoa

Start Date: April 1981 Est Comp Date: Dec 1982

Principal Investigator: Facility:

MAJ Michael L. Smith, PhD

Dept/Sec: Dept Clinical Invest Assoc Investigators

Key Words:

Prolactin; Seminal fluid; Spermatozoa

Accumulative MEDCASE Cost Est OMA Cost:$184(716) Periodic Review Results

Study Objective:

Prolactin in physiological fluids exists in several forms which differ in molecular weight or molecular charge. Our objective in this study is to identify these forms of prolactin in seminal plasma and spermatozoa and to quantitate them. Identifying and quantitating these forms of prolactin may eventually lead to an understanding of their roles in semen and fertility.

Technical Approach:

Semen samples from males undergoing fertility evaluation will be collected. Those samples with high sperm counts will be saved. Three aliquots of each sample, (1) semen, (2) seminal plasma, and (3) sperm extracts, will be fractionated by sephadex chromatography and the molecular weight distribution of prolactin will be determined by radioimmunoassay of the fractions. The charge heterogeneity will be shown by isoelectric focusing and radioimmunoassay.

Progress:

HPLC work has been discontinued pending the hiring of another laboratory technician. Twelve semen samples which had been discarded from the Department of Pathology were used to investigate the effects of proteolytic enzymes on peptide hormone RIAs. This information was incorporated into a manuscript submitted for publication.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 81/34 Status: Ongoing
Title:

Location of Prolactin, HCG, LH, and FSH in Human Semen: An Immunocytochemical Study

Start Date: Dec 1981 Est Comp Date: Mar 1983
Principal Investigator: Facility:

MAJ M.L. Smith, PhD

Dept/Sec: Dept Clinical Invest Assoc Investigators
Key Words:

Prolactin; Human Chorionic Gonadotropin; Luteinizing Hormone; Follicle-stimulating hormone; Immunocytochemistry

Accumulative MEDCASE Cost Est OMA Cost:$1446(1446) Periodic Review Results-
Study Objective:

The hormones prolactin, HCG, LH, and FSH have been found in semen. HCG and some prolactin is known to be associated with spermatozoa. This study proposes to determine the distribution of these hormones between oval spermatozoa, other morphological cells, and seminal plasma. This will be done by immunofluorescent techniques, light microscopy, and electronmicroscopy.

Technical Approach:

Semen will be collected from volunteers. Sperm will be separated, washed, then subjected to Sternberger's peroxidase antiperoxidase reaction. They will be observed and photographed using light microscopy. If hormone binding is observed, the sperm will also be examined by electron microscopy. Hormone distribution will be determined from electron micrographs.

Progress:

Due to the workload of the Electron Microscope Section and the continued absence of an EM technician in the Department of Clinical Investigation, the electron microscopy and microscopy portion of this protocol was abandoned. The purchased antisera were used for other projects. Samples had been collected from nine vasectomy volunteers. HCG and LH were measured in the seminal plasma and sperm extracts from these samples. The data will be analyzed for prevasectomy/postvasectomy comparison and for distribution of HCG and LH. These results will be used to decide whether or not to continue the project.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 81 46 Status: Ongoing

Title:

Inhibition of the Uterine Vascular Effects of 17β-Estradiol with the H2 Receptor Antagonist Cimetidine; Cortisol; an Adrenergic Blocking Agent, Phentolamine; and Cycloheximide

Start Date: Est Comp Date:

Principal Investigator: Facility:

COL L.L. Penney, MC

Dept/Sec: Dept Clinical Invest Assoc Investigators

Key Words:

17β Estradiol; uterine blood flow; cimetidine; cortisol; phentolamine; cycloheximide

Accumulative MEDCASE Cost Est OMA Cost:$1210(1210) Periodic Review Results

Study Objective:

To quantify uterine blood flow responses two hours after a standard stimulating dose of 17β estradiol given IV to oophorectomized rabbits pretreated with one of the specified agents.

Technical Approach:

The experimental model used in our previous work, Protocol 78/26, and in a current submission for publication, "17β-Estradiol Stimulation of Uterine Blood Flow in Oophorectomized Rabbits with Complete Inhibition of Uterine RNA Synthesis" will be used to determine uterine blood flow with microspheres at time zero and two hours after estradiol, 10 ug/kg IV, in animals pre-treated with cimetidine 10 mg/kg; cortisol 20 mg/kg; phentolamine 10 mg/kg or cycloheximide 4 mg/kg. Twelve animals will be studied in each group and every animal will serve as its own control for comparison by paired t-test within groups.

Progress:

All experiments are completed and manuscript preparation has begun. Details will be published in the FY84 report.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 81/47 Status: Ongoing

Title:

Variability of Estradiol Induced Increases in Uterine Blood Flow as a Function of Time Post-oophorectomy

Start Date: Est Comp Date:

Principal Investigator: Facility:

COL L.L. Penney, MC

Dept/Sec: Dept Clinical Invest Assoc Investigators

Key Words:

17ß estradiol; uterine blood flow

Accumulative MEDCASE Cost Est OMA Cost:$650(650) Periodic Review Results

Study Objective:

To establish the lack of responsiveness of uterine blood flow to estradiol stimulation in rabbits oophorectomized longer than 60 days.

Technical Approach:

We have recently completed a study of the effects of Actinomycin D on estradiol-induced increases of uterine blood flow in oophorectomized rabbits. During that experiment, a delay in shipping labeled microspheres necessitated study of a small group of control animals 60 days post-operatively as opposed to between 1-5 weeks as had been the case. At 60 days an increase in uterine blood flow 2 hours following estradiol, 10 ug/kg, was no longer demonstrable. Such a change with time has not previously been reported. We wish to repeat the study with sufficient numbers of animals to confirm or refute this observation.

Progress:

No animals were studied in FY83. Animals have been ordered to complete the study in FY84.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 81/48 Status: Ongoing

Title:

Variability in Quantifiable Uterine Cytosolic and Nuclear Estrogen Receptors as a Function of Time Following Oophorectomy in Rabbits.

Start Date: Est Comp Date:

Principal Investigator: Facility:

COL L.L. Penney, MC

Dept/Sec: Dept Clinical Invest Assoc Investigators

Key Words:

17ß estradiol; estrogen receptors

Accumulative MEDCASE Cost Est OMA Cost: 0($618) Periodic Review Results

Study Objective:

To correlate the amount of receptor present with the degree of blood flow response to 17ß estradiol.

Technical Approach:

If protocol 81/47 confirms a diminished response of uterine blood flow to 17ß estradiol, as a function of time following operation, this study will be conducted. Since a decreased response is in a sense natural inhibition a quantification for the receptors should aid in elucidating the basic mechanism. In addition to the cytosolic receptor , eosinophilic and a-adrenergic receptors, as well as any others suggested by Protocol 81/46 will be examined by standard techniques detailed in the references. For each receptor 6-8 animals will be studied at 20-40 days following operation and another 6-8 at 60-80 days.

Progress:

No work was done in FY83. The protocol is still considered worthwhile and will be pursued subject to available time from the PI.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/14 Status: Ongoing

Title:
Serum and Urinary Electrolyte and Steroid Concentrations During Danazol Administration

Start Date: Est Comp Date:

Principal Investigator: Facility:

COL L.L. Penney, MC

Dept/Sec: Assoc Investigators

Key Words:

Accumulative MEDCASE Cost Est OMA Cost:$657(647) Periodic Review Results

Study Objective:

To further define electrolyte changes occurring during danazol administration and to examine indirectly potential sites of inhibition in the metabolic pathways involved.

Technical Approach:

Standard methods of testing the mineralocortioid pathway are available. The effects of danazol will be tested on days 6 and 12 to coincide with references in which testing was done on day 6. Our observation has been significant cramps and edema are noted 10 days to 2 weeks after starting therapy. Patients will receive 200 mg of danazol four times a day. Only those patients with documented endometriosis who will be treated as part of this therapy with danazol will be asked to participate. In addition to the battery of tests outlined in the flow chart (see below) patients will be asked to submit a serum sample at 8 a.m. for deoxycorticosterone (DOC), aldosterone (A), plasma renin activity (PRA), Na and K and to collect a 24-hour urine specimen on days 3 and 9. Aliquots of serum will be kept frozen for possible analyses of 18-hydroxycorticosterone (18OHB), corticosterone (B) or other steroids. Na, K, and possibly aldosterone will be determined on each urine collection and aliquots will be frozen for subsequent analyses (by GC-MS) as might be suggested by the serum results. Results will be collated and data analyzed by appropriate t-test after 5-6 patients have been entered to determine the need and direction of further testing.

Study Plan and Flow Chart.

Day (-10): Subjects begin 120 mEq Na and 80 mEq K diets after 24 hour urine Na and K (Day 1 of menstrual cycle).

Day (-5): 24-hour urine Na and K

Day (0) :

A) 24-hour urine Na and K completed by 0700

B) Baseline serum Ca, P, K, DOC, B, 18-OHB, A, PROG, 17OHP, F, DHEA and PRA.

C) Infusion of 25 units (0.25 mg) of ACTH intravenously at 0900. Patient supine from 0700 until 1030.

D) Serum drawn at 0930, 1000 and 1030 from arm opposite the infusion. All serum to be frozen and baseline and 1000 samples to be analyzed; otherwise samples to be studied if needed. Patient starts danazol. at conclusion of sampling.

Day (6): Repeat Day (0). Patient on danazol.

Day (12): Repeat Day (0). Patient on danazol.

Progress:

Four patients have now been entered. Recruiting efforts for one or two more patients continues.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/32 Status: Ongoing

Title:
Effect of Verapamil on Gestational Length in Rabbits

Start Date: Est Comp Date:

Principal Investigator: Facility:
COL L.L. Penney, MC

Dept/Sec: Dept Clin Investigation Assoc Investigators

Key Words:

Verapamil

Accumulative MEDCASE Cost | Est OMA Cost:$1440(1440) | Periodic Review Results

Study Objective:

This is the second in a series of projects designed as preliminary studies to evaluate the potential value of verapamil as a tocolytic agent in the prevention of premature labor.

Technical Approach:

Pregnant rabbits whose time of conception is known within two hours will be used. The rabbits will be randomly divided into two groups and one group will receive oral verapamil in three equally spaced doses beginning on the 22nd day of gestation. The length of gestation will be recorded in all animals. Observations will be made regarding their respiratory status and survival of the pups. The control group will receive placebo in place of verapamil. A second cohort of rabbits will be similarly treated, but will also receive subcutaneous oxytocin 0.5 units every day at 0800, beginning on the 24th day of gestation.

Progress:

Shipping constraints for time-dated pregnant rabbits has hendered this project. Completion is planned in the next FY.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/33 Status: Ongoing

Title:
In vitro Effects of Spironolactone on Gonadotropin Production by the Rat Pituitary and Androgen Formation by the Rat Ovary

Start Date: Est Comp Date:

Principal Investigator: Facility:

COL L.L. Penney, MC

Dept/Sec: Dept Clin Invest Assoc Investigators

Key Words:

Spironolactone; Hormones

Accumulative MEDCASE Cost | Est OMA Cost: $90(90) | Periodic Review Results

Study Objective:

This project is designed as a preliminary study to determine if spironolactone, acting either primarily or secondarily, inhibits gonadotropin production from the pituitary in this animal model.

Technical Approach:

Estrous rats will be sacrificed and the anterior pituitary removed for culture by established techniques. Similarly, the ovaries will be removed and separated into granulosa cell and remaining theca and stroma as published. FSH and LH will be determined by radioimmunoassay with reagents obtained from the NIH. The gonadotropins will be measured in the media of the cultured pituitary glands as a baseline and with spironolactone in concentrations of 0.15, 1.0 and 2.0 X $10^{-6}$M respectively. Glands will also be cultured in physiological concentrations of testosterone, estradiol, and estrone. Once these control levels of gonadotropin release into the media are determined, the experiment will be repeated with spironolactone combined with testosterone, estradiol and estrone individually. The effects of these same concentrations of spironolactone will also be determined on basal and gonadotropin stimulated sex steroid production from the cultured granulosa cells and ovarian stroma.

Progress:

Tissue culture techniques were not perfected until September 1983. The study is commencing at this time.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/39 Status: Ongoing

Title:
Histamine Concentration in Follicular Fluid: Correlation with Follicular Size and Maturation in the Periovulatory Period

Start Date: Est Comp Date: June 1985

Principal Investigator: Facility:
COL L.L. Penney, MC

Dept/Sec: Dept Clin Invest Assoc Investigators

Key Words:
Histamine; Follicular fluid

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To obtain preliminary data regarding a possible role of endogenous histamine in ovulation.

Technical Approach:

Mature, virgin New Zealand white rabbits will be used. Follicular size will be recorded and follicular fluid histamine content measured prior to a standard IM dose of HCG and 2,4,8,12 and 16 hours following HCG in separate groups of animals. Serum estradiol and progesterone will be measured at the time of ovarian sampling in all animals.

Progress:

Preliminary work has been done. It appears the histamine content of whole ovary will need to be correlated. Only one or 2 animals at each time have been studied and more need to be studied.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/48 Status: Completed

Title:
Potentiating Effect of B-Adrenergic Agents on Rat Spleen Cells and Peripheral Blood Lymphocytes in vivo

Start Date: Est Comp Date:

Principal Investigator: Facility:

R.J. Frederick, PhD, DAC

Dept/Sec: Assoc Investigators

Key Words:

Terbutaline; Lymphocytes

**Accumulative MEDCASE Cost** **Est** OMA Cost:(130(130) **Periodic** Review Results

Study Objective:

The objective is to provide experimental evidence that B-adrenergic agents have a direct effect on cells involved in immunological processes.

Technical Approach:

Sprague-Dawley white rats will be used as a model for our experiments. We will first establish a dose response effect by varying the concentration of terbutaline administered and assaying by an in vitro blast transformation assay using $H^3$ thymidine incorporation as a measure of DNA synthesis. Secondly, the time course of the potentiated state will be monitored by injecting a group of rats with the "optimum" dose of terbutaline and taking sequential blood samples over a course of three weeks. Rats given a saline bolus instead of the drug will be used as controls. All in vitro assays will be done using PHA, Con A, and the B-cell specific mitogens Salmonella lipopolysaccharide and protein A. Where appropriate, spleen and thymus cells will also be assayed for response to mitogenic stimulation. Small portions of the sera collected will be reserved for immunoglobulin determinations.

Cells from treated rats will be tested for drug enhanced stimulation of antigen induced DNA synthesis in vitro.

Progress:

Additional trials of terbutaline treatment in rats lacked sufficient reproducibility to continue further study with this animal. Instead, the phenomenon will be explored further in syngenic mice for which a new protocol will be submitted.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/57 Status: Ongoing

Title:
Cardiovascular Effects of Delta-9-Tetrahydrocannabinol in the Pregnant Conscious Sheep

Start Date: 1 Est Comp Date:

Principal Investigator: Facility:

COL L.L. Penney, MC

Dept/Sec: Dept Clinical Investigation Assoc Investigators

Key Words:

Delta-9-THC; Cardiovascular effects

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

To delineate the effects of intravenous delta-9-THC on cardiovascular acid base parameters in the conscious pregnant sheep comparing variable doses and rates of administration.

Technical Approach:

Twelve pregnant sheep at approximately 135 days' gestation will be studied. An indwelling Swan-Ganz catheter and a carotid arterial catheter will be placed under pentobarbital anesthesia. These catheters will be maintained open with a heparin lock and the sheep will be given antibiotics. Utilizing a paired t-test and randomized block (or appropriate variance as per consultation with statistician) design the sheep will be treated 24 hours postoperatively with either 0.25 mg/kg, 0.5 mg/kg, or 1 mg/kg of delta-9-THC injected in the pulmonary artery. Baseline recordings will be obtained prior to injection and cardiac output will be monitored at 3,5,15 and 60 minutes and at hourly intervals thereafter until recovery occurs. CVP will also be monitored at the same times. Continuous monitoring of the heart rate and blood pressure will be conducted and blood gases will be drawn at 5,15 and 60 minutes and thereafter until recovery has occurred. Following rest periods of 48 hours, each sheep will be studied at the next dose in its scheme until all sheep have been studied with each of the three doses. Forty-eight hours after the final study, a continuous infusion of 10 ugm/kg/min for three hours will be conducted and monitoring continued at hourly intervals until recovery occurs. The sheep will be salvaged, if possible. Serum samples will be saved at each blood gas sampling for possible analysis of THC concentration.

Progress:

Over 40 experiments have been performed in 23 sheep, some of which were found to be nonpregnant. Collation of data will be complete in FY84 and a manuscript submitted with details available for the progress report.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/59 Status: Ongoing

Title:
Restriction Enzyme Analyses of E. Coli Bacterial Chromosomes and Their Membrane-Associated Sequence

Start Date: Est Comp Date:

Principal Investigator: Facility:
R.J. Frederick, PhD, DAC

Dept/Sec: Dept Clinical Investigation Assoc Investigators

Key Words:
DNA Membrane bound sequences

| Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results |
|---|---|---|

Study Objective:

The objective will be to analyze membrane associated chromosomal DNA sequences to determine specificity and possible function as a regulatory mechanism in bacterial growth.

Technical Approach:

Bacterial nucleoid isolation and the determination of membrane bound DNA fragments will be done as described previously. A refined quantitation scheme incorporating an improved method for agarose gel electrophoretic analysis of restriction enzyme fragments will be used to estimate the average size of membrane associated DNA. We can then calculate the average number of inherent membrane attachment sites on the bacterial chromosome. These estimates will be compared with results obtained using different restriction enzymes and the techniques reported in the literature. Comparable numbers will add validity to the technique since these should not vary significantly from enzyme to enzyme despite very different average segment size. Isolated membrane associated DNA fragments will be analyzed to determine if they are a unique subset of the entire chromosome by performing rehybridization kinetics and second restriction enzyme analyses. If successful, pulse labeling experiments will be done using E coli mutant strains with temperature sensitive replication mechanisms. Comparative studies of specific DNA fragments can then be done by hybridization assays using labeled probe from temperate phage carrying known sequences of the bacterial DNA.

Progress:

Work on this project was curtailed due to technician transfer and re-prioritization of assignments in the Microbiology Service. If additional technical help can be obtained in FY84, this protocol will be resumed.

Detail Summary Sheet

Date: 01 Oct 83 Prot No: 82/61 Status: Ongoing

Title:

Use of Flow Cytometry to Isolate Novel Revertants of E. coli Partition Deficient Mutants

Start Date: Est Comp Date:

Principal Investigator: Facility:

R.J. Frederick, PhD, DAC

Dept/Sec: Dept Clinical Investigation Assoc Investigators

Key Words:

Flow cytometry; Bacterial mutant enrichment

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

This study is planned to evaluate the use of flow cytometry as an enrichment process in procedures for the isolation of bacterial mutants.

Technical Approach:

Escherichia coli DNA partition (PAR) mutants will be used for the initial screening procedures. At temperatures over 40°C, these mutants stop cell division but continue to replicate their DNA resulting in enlarged cells with four to eight genome equivalents DNA. The first objective will be to establish that the mutant phenotype can be distinguished from wild type cells in the Ortho Cytofluorograph. Cultures will be given at 41°C and 30°C, diluted and mixed with media containing ethidium bromide (DNA stain). The mixed culture will be sorted on the basis of cell size and quantity of DNA (fluorescence intensity) per cell. The efficiency of sorting will be evaluated by microscopic examination under phase and fluorescence illumination. Once the separation conditions are determined revertants may be selected on the basis of their wild type phenotype when grown at 41°C. After sorting, single colony isolates will be screened for temperature sensitivity, i.e., ability to multiply at 41°C. Intragenic or suppressed revertants should grow while extragenic or second site revertants may or may not. Those that did not have the PAR phenotype, but could not grow at 41°C would be the strains of interest initially. Such novel revertants would establish the feasibility (the technique and possibly lead to further insight on the problem of the regulation of bacterial growth.

**Progress:**

**Installation of flow cytometer is now complete. This study has been rescheduled to begin later in FY84 due to priority of other ongoing projects.**

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/62 Status: Ongoing

Title:
Analyses of Copper Complexes in Plasma

Start Date: Est Comp Date:

Principal Investigator: Facility:

David Rauls, PhD, DAC

Dept/Sec: Dept Clinical Investigation Assoc Investigators

Key Words:

Copper salicylates

| Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results |
|---|---|---|

Study Objective:

To develop methodology for the analysis of copper salicylate complexes in plasma and measure blood levels attained upon administration of these complexes to rats.

Technical Approach:

Copper diisopropyl salicylate will be prepared by literature methods. Optimum conditions for analysis of the complex by high performance liquid chromatography will be worked out on the pure substance followed by isolation of the complex from spiked plasma to determine recovery and interferences. Attempts will be made to utilize atomic absorption spectroscopy for quantification of the complex in order to obtain adequate sensitivity. Once the accuracy, precision, and sensitivity of the assay have been established, the copper diisopropyl salicylate will be injected into rats intraperitoneally at doses (100 mg/kg) found to inhibit maximal electroshock seizures in rats. Blood samples will be analyzed at 0.5, 2, and 4 hours post-injection. The existence of the intact copper complex in plasma will be considered proven if a copper containing peak is recovered from injected rat plasma having a HPLC retention time equivalent to that of the pure copper diisopropyl salicylate and such a peak is found to be absent from a plasma sample from a rat injected with vehicle only.

Progress:

Copper diisopropyl salicylate has been synthesized during FY83. Initial attempts at high performance liquid chromatography have failed to induce an adequate assay. Future work will involve development of appropriate analytical conditions for the analysis of the complex in plasma.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/14 Status: Ongoing

Title:
Immunomodulating Effects of Terbutaline in Humans

Start Date: Est Comp Date:

Principal Investigator: Facility:
CPT C.S. Serio, MSC

Dept/Sec: Dept Clin Invest Assoc Investigators

Key Words:
Terbutaline

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To provide experimental evidence that the beta-adrenergic agonist terbutaline may have an effect on cells involved in various immunological processes such as cell mediated and humoral immunity.

Technical Approach:

Forty healthy nonpregnant volunteers will be selected at random from staff and technicians from the various departments of the hospital. The physicians in charge will thoroughly explain the implications of this study and the use/contraindications of terbutaline injections. The voluntters will be divided into four groups of 10 each. All volunteers will have three 10cc tubes of blood drawn on Day 0 for control samples. Group A controls will receive 0.5cc subcutaneous injections of saline (i.e. saline controls). Groups B,C, and D will receive total doses of 250, 500 and 750 ug terbutaline sulfate subcutaneously. At days 4,7,9 and 14 post-terbutaline or saline injection blood samples will be taken and examined.

Progress:

Investigations in a rat model demonstrated an immunomodulating effect of Terbutaline (T) treatment, In this study, these observations were extended to human beings. In 16 adult volunteers (18-39 years), on Day 1, samples were obtained for phytohemagglutinin & conconavalin A (PHA & CON A) lymphocyte blastogenic (LB) measurements. Four subjects received saline injections, and 12 received T (250 ug-750ug). Samples were obtained at 4,7,9 days post-treatment. Responses to CON A and PHA were depressed in the T group at 7 and 9 days post-treatment at the 3 mitogen doses tested. No effects were noted in the saline treated group.

| Maximum Stimulation(X103) | | | | | |
|---|---|---|---|---|---|
| Day | Treatment | 0 | 4 | 7 | [illegible] |
| PHA | Saline | 130 | 132 | 133 | [illegible] |
| | T | 135 | 135 | *114 | *118 |
| CON A | Saline | 119 | 119 | 110 | [illegible] |
| | T | 117 | 111 | *101 | * [illegible] |

The findings suggest that doses of T used routinely in clinical medicine are capable of altering immune function. A dose dependent trend was indicated for the three doses of Terbutaline (250, [illegible], [illegible] ug) used.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/18 Status: Ongoing

Title:
Inhibition of the Uterine Vascular Effects of 17-Beta Estradiol with the Beta Receptor Antagonist Propanolol and with Progesterone

Start Date: Est Comp Date:

Principal Investigator: Facility:
COL L.L. Penney, MC

Dept/Sec: Dept Clin Investigation Assoc Investigators

Key Words:

17-Beta Estradiol, Propanolol, Progesterone

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

To quantify uterine blood flow responses two hours after a standard stimulating dose of 17-beta-estradiol given iv to oophorectomized rabbits pretreated with one of the specified agents.

Technical Approach:

The experimental model used in our previous work will again be utilized. Eight to twelve animals will be studied in each of three groups. The first group will be administered propanolol 0.5 mg/kg intravenously over a 5-10 minutes period, beginning approximately 15 minutes prior to the baseline uterine blood flow study and administration of the 17-beta-estradiol. The second group will consist of animals administered 5 mg/kg of progesterone in oil IM one day prior to the procedure which will then consist of the standard $CE^{141}$ baseline blood flow, administration of 10 ug/kg iv of 17-betaestradiol and a two-hour $Sr^{85}$ blood flow study. the final group will consist of animals treated with 1 mg/kg of progersterone intravenously 30 minutes prior to the remainder of the procedure. A stock solution of progesterone 1 mg/ml in propylene glycol will be utilized. One-half of the animals in the latter group will also receive a continuous infusion of progesterone from a working solution made by stirring 0.96 ml of the stock solution in 8.7 ml of 25% salt-poor albumin and diluting with 0.9% saline to a final progesterone concentration of 16 ug/ml, and infusing at .247 ml/min for the 2 1/2 hour duration of the study.

Each animal will be compared [illegible] baseline utilizing a paired t-test. [illegible] two-hour time period will also be compared [illegible] (already studied) by non-paired two-sample t-test.

Progress:

Data collection on the first two groups is complete. Details will be published in the report in FY84.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/21 Status: Ongoing

Title:
Development of a Simple, Rapid and Reproducible Chemotaxis Assay for Clinical Use

Start Date: Est Comp Date:

Principal Investigator: Facility:
CPT C.S. Serio

Dept/Sec: Dept Clin Investigation Assoc Investigators

Key Words:

Chemotaxis assay

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To provide the clinical laboratory with a chemotaxis assay to measure defects in neutrophil and macrophage function in disease states such as recurrent bacterial infections and tumor insult.

TECHNICAL APPROACH:

Our plan is to develop the methodology and hardware for a chemotaxis assay which will allow for the following:

1. A simple assay that will allow a technician to perform the test with little or no training.
2. A reproducible slide technique in which the quantitation of cell movement can either be made by a scanning spectrophotometer or densitomiter (instruments that are inexpensive and common in most laboratories). In addition, the slides are inexpensive and may be stored as a permanent record or discarded.

3. A slide prepared with the positive and negative chemotactic agents that can be stored in a freezer and utilized immediately upon thawing.

Experimental Design

We will utilize a lab-tek culture dish. As an incubation chamber for both the chemotaxin and the cells to be tested. This chamber consists of eight separate plastic wells (volume .5 ml per well) separated by a nontoxic rubber gasket mounted on a microscope slide. The chemotaxic agent(s) will be combined with agarose (.4% in Hanks balanced salt solution) and placed in each of the four top test chambers at approximately 39°C and allowed to solidify.

The positive chemotaxins to be utilized in this study will be N-formylmethionyl-leucyl-phenylalanine-methylester and human serum derived complement component C5a (These factors once embedded in the agarose will be frozen at -20° and tested for their freezer life). Negative controls will be normal saline in agarose.

Initial studies will be performed with freshly prepared chemotaxins. After the agarose has solidified approximately $2X10^5$ test cells will be placed in opposite wells from the chemotactic factors and the slide placed at a 45° angle for 30 minutes at 37°C to allow for the attachment of neutrophils on the side of the chamber closest to agarose. By doing this, we virtually are lining up the cells on an imaginary starting line. After the initial 30 min incubation, the top plastic wells will be removed off leaving the base rubber gasket in place to act as a border between cells and agarose. The rubber gasket between each set of test wells will then be cut with a scalpel and 100 ul of media (Hanks balanced salt solution) added to the cellular side to allow contact with the agarose embedded chemotactic factor. This contact between media and agarose will result in a gradient formation and the subsequent dispersal of chemotaxins out of the agarose toward the cells. A plastic cover will be placed over the rubber gasket at this time and the slide reincubated in a 5% $CO_2$ incubator at 37°C with 95% humidity. After an incubation period of 2-3 hours, the rubber gasket will be removed, the slides washed in saline, fixed in methanol and stained. The slide will then be mounted on a scanning stage of a Gilford Spectrophotometer and scanned for optical density for the number of cells that have actually migrated toward the chemotactic factor. Preliminary standards for various cell numbers on each slide will be established at different spectrophotometer settings and various slit widths in order to establish maximum sensitiviy. Background readings will be taken with standard microscope slides.

Progress:

No progess due to personnel losses.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/50 Status: Ongoing

Title:
Effects of Terbutaline on Lymphocyte Receptors

Start Date: Est Comp Date:

Principal Investigator: Facility:
MAJ M.J. Smith, MSC

Dept/Sec: Dept Clin Investigation Assoc Investigators

Key Words:

B-adrenergic receptors; lymphocytes

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

OBJECTIVE: To determine the effect of a single dose of terbutaline on beta-adrenergic and concanavalin A (con A) receptors in mouse and human lymphocytes.

Technical Approach:

The project will be approached by (a) developing the needed assays, (b) conducting animal trials, and (c) conducting human trials.

a. Assays

(1) A beta receptor assay developed by Dr. Burman at WRAMC will be established in our laboratory. In brief, the assay is a Scatchard analysis of lymphocyte beta receptors using $^{125}$Iodocyanopindolol. It requires lymphocytes from 16 ml of blood for humans and the spleenocytes from one mouse. The receptors will be measured on the day of sample collection.

(2) Cyclic AMP-RIA kit (New England Nuclear) analysis of lymphocyte cytoplasm will be used.

(3) Cyclic GMP-RIA kit (New England Nuclear) analysis of lymphocyte cytoplasm will also be used. The cyclic AMP (cAMP) and GMP (cGMP) measurements will be important since changes in their concentrations indicate the level of receptor activity prior to collection of the lymphocytes. Samples for analysis will be stored at -20$^{o}$C and run in batch for both cAMP and cGMP.

(4) A concanavalin A(conA) recept[illegible] using a fluorescent activated cell sorter. [illegible] [6] will be bound to the lymphocytes and the [illegible] determined by laser analysis of each sample. Binding affinities of the receptors will be determined by quantitation of bound and free conA using Scatchard analysis. The receptors will be measured on the same day as sample collection.

b. Mouse Study.

Two groups of inbred male mice, 60 mice per group, will be injected ip. Group I, control group, will receive saline. Group II, experimental group, will receive 250 ug/kg of terbutaline sulfate in saline. Twelve mice per group will be anesthetized in the morning at days zero, two, four, seven and fourteen after injection, using Ketamine/xlazine and their spleens removed. They will then be killed by cervical dislocation, and their spleenocytes harvested by established techniques [7]. Spleenocytes from six of the twelve mice will be processed and beta receptor density and binding constants determined [5]. Cyclic AMP and cyclic GMP will be measured in the supernatant of the processed lymphocytes [8].

ConA receptor concentrations and binding constants will be determined for spleenocytes from the other six mice killed on the day of interest using techniques developed in Part A (4).

Lymphocyte transformation using conA [9] will be determined on a portion of the lymphocytes from the twelve mice killed on the day of interest.

c. Human Study.

Two groups of adult male humans, ages 20-49 years, twenty control and twenty experimental, will be studied. They will receive a single subcutaneous injection of 0.2 cc of saline or 250 ug of terbutaline sulfate in 0.2 cc of saline, respectively. In the morning of days zero, two, four, seven, and fourteen, after injection, thirty cc of peripheral blood will be taken and the lymphocytes separated as previously described [9]. These lymphocytes will be divided for beta receptor, cAMP, cGMP, conA receptor, and lymphocyte transformation assays.

d. Statistics

GROUPS

Group I - saline control
Group II - terbutaline treated

VARIABLES OR PARAMETERS

Beta receptor density (number/lymphocyte)
Beta receptor binding strength
Con A receptor density (number/lymphocyte)
Con A receptor binding strength
Lymphocyte transformation (counts/min of incorporated $^{3}H$-thymidine)
cAMP/cGMP concentration ratio.

TIME

Variables measured at 0, 2, 4, 7, 14 days post-injection.

QUESTIONS

Q. 1. Is the control group different from the experimental group for any mean variable value on a given day?
Q.2. Is the control group different from the experimental group for all variable or subsets of the variable?
Q. 3. Which variables are associated?
Q. 4. Is the response of each variable with time different for the control and experimental group?

METHODS

Question one will be answered using a Student's t-test with paired values. Question two will be answered using a multivariate analysis of variance and covariance. Question three will be answered by regression analysis. Question four will be answered using a multivariate analysis with time.

Progress:

This is a newly activated project and there is no progress to report.

Detail Summary Sheet

Date: 1 Oct 82 Prot No: 82/19 Status: Ongoing

Title:
Evaluation of the Mandibular Staple Bone Plate and the Ramus Frame Implant in the Rehabilitation of the Atrophic Edentulous Mandible.

Start Date: Est Comp Date:

Principal Investigator: Facility:
COL F.C. Theisen, DC

Dept/Sec: Assoc Investigators

Key Words:

Mandibular staple

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To evaluate the efficacy of two alloplastic implants in the rehabilitation of the edentulous atrophic mandible. Future application will be evaluated for the reconstruction of avulsive traumatic injuries to the mandible and ablative surgical procedures in treatment of pathology in the mandible. Factors to be evaluated include a) the surgical procedure for insertion, b) stability and retention afforded the denture, c) patient function and comfort, d) complications, e) long term followup stability and overall versatility of both implants.

Technical Approach:

All patients selected will be approved by both the Prosthodontic Service and the Oral Surgery Service, WBAMC. Active duty personnel must have a minimum of 12 months remaining prior to anticipated ETS or PCS. Dependents or retired personnel must be residents of the El Paso area and agree to a minimum of two years followup. The patient will have a minimum of 7mm vertical osseous height for the ramus frame and 9mm for the mandibular staple as measured on a lateral cephalometric radiograph. The oral soft and hard tissues will be free of active disease of pathology. The ramus frame implant will be primarily utilized for those patients who are medically contraindicated for general anesthetic. Patients who are candidates for the mandibular staple will have all pre-implant surgical preparation done a minimum of three months prior to placement of the implant. These include alveoloplasty and vestibuloplasty with skin grafting for lowering of mucosal and muscle attachments. Medical assessment of the patient will be accomplished by the Oral Surgery Svc or by WBAMC medical staff when indicated.

The patient will be counselled on the investigational nature of the procedure, to include expected results and possible complications. The patient will be required tosign an agreement concerning his participation in the study and the required followup.

Patients will complete post-operative questionnaires during the six month postop followup visit.

PROGRESS

The clinical investigation of mandibular implants is progressing smoothly. Currently eight implants are in place and no patients have been lost to followup. Two more are schedule for insertion in the near future. The protocol and followup should continue through April 1985. The clinical comparison of halothane and forane is currently in progress. Approximately 75 of the 100 patients have been completed. The protocol will be completed by April 1985. No manuscripts have been published this year, and no scientific presentations have been made from this department.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/02 Status: Ongoing

Title:
Lidocaine as an Adjunct to General Anesthesia

Start Date: Est Comp Date:

Principal Investigator: Facility:
CPT Kochansky, ANC

Dept/Sec: Dept Nursing Assoc Investigators

Key Words:

Lidocaine

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To evaluate lidocaine as an adjunct to general anesthesia and its hemodynamic and neurological effects.

Technical Approach:

A clinical research design will be used to study the effects of intravenously administered lidocaine in ASA III-IV patients known to have atherosclerotic cardiovascular disease. Control measurements of cardiac indices (myocardial contractility, heart rate, and myocardial wall tension) expressed as left ventricular stroke work index, cardiac output and pulmonary capillary wedge pressure will be taken prior to induction and at induction and incision. Under local anesthesia, a radial artery catheter, central venous pressure catheter, and a Swan-Ganz catheter is routinely placed as part of the anesthetic in ASA III-IV patients who present for aorto-bifemoral bypass grafting, aortic abdominal aneurysmectomy and carotid endarterectomy patients with severe cardioavascular/pulmonary disease. A control group of patients, selected by random entry, will receive fentanyl instead of lidocaine as per standard practice at WBAMC.

Progress:

To date 13 subjects have received fentanyl-nitrous oxide-oxygen anesthesia, six subjects received fentanyl-oxygen anesthesia and eight subjects have received the lidocaine-nitrous oxide-oxygen anesthesia protocol. No morbidity nor mortality have occurred within each of the treatment groups. Preliminary statistical analyses show that lidocaine effects neither the mean arterial pressure nor pulmonary artery pressures in the treatment groups indicating that lidocaine may actually be an excellent adjunct to general anesthesia in the cardiovascularly unstable patient.

Detail Summary Sheet

Date: 1 Oct 82 Prot No: 76/33 Status: Ongoing
Title:

Diagnostic Adrenal Scanning with $^{131}I$ (NP59)

Start Date: Est Comp Date:
Principal Investigator: Facility:

LTC T. Brown, MC

Dept/Sec: Nuclear Medicine Svc Assoc Investigators
Key Words:

Adrenal scanning

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results
Study Objective:

The purpose of this study is to determine the usefulness of $^{131}I$ NP59 in scanning of the adrenal glands. It will be employed for the following purposes: (a) as a screening test for detection of primary aldosterone tumor, Cushing's disease, adrenal cortical adenoma, or pheochromocytoma, (b) imaging of adrenals in patients who require adrenal venography and are allergic to contrast media, (c) detection of unilateral adrenocortical hypofunction: calcification, metastatic carcinoma, post-venography infarction, etc., (d) detection of functioning adrenal remnant after adrenalectomy for Cushing's syndrome, (e) aid in assessment of adrenocortical steroid therapy.

Technical Approach:

Patients with clinical evidence of adrenal disease will be studied upon referral from the Endocrine Service. Adrenal imaging will be performed after injection of the material to assess the presence or absence of visualization of the adrenal glands, their size and response to suppression therapy.

Progress: The annual review of this protocol was conducted 30 Sep 83. No patients have been entered into this study during FY83. Additional patient entry is expected during FY84.

Detail Summary Sheet

Date: 1 Oct 82 Prot No: 81/05 Status: Ongoing

Title:

The Role of Food Allergy in the Pathogenesis of Migraine Headache

Start Date: Est Comp Date:

Principal Investigator: Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Allergy Clinic Assoc Investigators

Key Words:

Food allergy; Migraine headache

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

Assess whether skin testing to a battery of food allergens is of value in defining a diet which will cause a decreased frequency of migraine headaches in affected patients.

Technical Approach:

Subjects will be 18 years or older. They will be selected from the population of the Neurology Clinic, WBAMC. They will be judged by one of the investigators to have migraine syndrome. The nature, the purpose, and proposed benefits of the study will be explained to them. If they are agreeable, the following will be done: (1) Any medications being used for chronic migraine prophylaxis will be discontinued. (2) They will be given a supply of medication for acute migraine attacks. (3) They will report to the Allergy Clinic where the following will be performed:

a. A history regarding possible food provoked migraine.
b. Prick puncture testing on the back to 75 common foods.
c. A diet will be prescribed avoiding those foods which are positive on skin testing (2 mm wheal greater than control).
d. A small blood serum specimen (5 ml) will be collected and frozen for later use if required.

If there are no positive skin tests, the patient will be placed on a corn, egg, milk, wheat free diet. The duration of the diet will be eight weeks. The patients will record symptoms and medications on the diary sheets. Each four weeks the patients will meet with one of the investigators. At the end of eight weeks those who appeared to have had a positive response, that is complete absence of attacks or a greater than 50 percent diminution, will remain on the diet.

Those patients will then undergo a double-blind challenge supervised by one of us. All of the materials for the challenges will be prepared by the other investigator and his staff. The challenge shall be performed in the following manner. Patients will be given a group of opaque capsules containing placebo or freeze-dried foods. The foods chosen will be according to what was eliminated. Interspaced with the foods will be capsules containing placebo (lactose). The maximum amount of challenge food given in one day will be 8 gms. They will take these capsules on a daily basis. This diet challenge period will be individualized for each patient, and may vary in duration. Patients will continue to complete the diary sheets and be seen every four weeks.

Criteria for evaluation of the results will be:

a. Definitely positive: Significant relief of migraine attacks and positive challenges.

b. Possible positive response: One of the challenges positive, one negative, diet trial yields relief.

c. Equivocal placebo effect: Diet trial yields good response in relief of headaches; challenges are negative.

d. Negative: No relief with the diet trial.

Progress:

Forty-seven patients were judged to be adequately evaluated. Thirteen patients had a 2/3 reduction in headache. This was confirmed in six of eight double blind challenged persons.

Detail Summary Sheet

Date: 1 Oct 82 Prot No: 81/10 Status: Terminated

Title:

An Evaluation of the Effects of Beta II Adrenergic Agents on Human Immunoglobulins and Antibody Response

Start Date: Est Comp Date:

Principal Investigator: Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Allergy Clinic Assoc Investigators

Key Words:

Beta II agonists; Immunoglobulins Maj I. Weisman, MC

Accumulative MEDCASF Cost Est OMA Cost: Periodic Review Results

Study Objective:

To determine if the administration of Beta II adrenergic agents affect immunoglobulin levels and the ability to form specific antibodies in the primary and secondary immune response.

Technical Approach:

Forty patients will be selected at random from the Pulmonary Clinic on the basis of a routine therapeutic decision. The pnysician in charge of their case will judge oral beta II adrenergic agents necessary to improve the patient's clinical pulmonary status. Prior to initiating this therapy, the patients will be told the nature of the study and its importance. The patients will have a blood sample drawn which will be used for analysis. Patients will begin on the appropriate oral beta II adrenergic agent and will return to clinic in one month and have a second specimen of blood obtained.

In those patients in whom it is deemed medically advisable, an influenzal and pneumococcal vaccine immunization will be given. These immunizations will be given only to those patients who may be reasonably expected to benefit from their use. A documented history of previous influenzal immunization will be obtained. The results will be analyzed by comparison of the pre-therapy and post-therapy levels of immunoglobulins. The effects on the expected rise of titer of the secondary antibody response will be compared to normal standards. The titer and presence of the primary antibody response

will be compared to reported standards. The serum specimens collected at both times will be analyzed for the following serum immunoglobulins: IgG, A, M, D and E. In all patients, whetner or not they receive immunizations, influenzal and pneumococcal antibody titers will be determined on the pre-therapy and one-month specimens.

Progress:

This study was terminated with data incomplete.

Detail Summary Sheet

Date: 1 Oct 82 Prot No: 81/12 Status: Ongoing

Title:

A Novel Method of Hyposensitization Therapy with Russian Thistle Antigen

Start Date: Est Comp Date:

Principal Investigator: Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Allergy Clinic Assoc Investigators

Key Words:

Hyposensitization; Russian thistle antigen

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

To determine if oral administration of Russian Thistle pollen in a pharmacologically modified release form will be capable of: (a) Demonstrating immunologic changes that are comparable to standard parenteral allergen immunotherapy. (b) Demonstrating in a physiologic test, such as nasal provocation, evidence of lessened reactivity to allergen.

Technical Approach:

Thirty adult allergic patients, who are significantly sensitive to Russian Thistle allergen by history and skin testing, will be the subjects for this protocol. The nature and purpose of this study will be explained to them. The study will be conducted from December to March, when ambient Russian Thistle pollen is not present in El Paso.

The subjects will report to the Allergy Clinic. Prior to the initiation of therapy, the subjects will have:

a. Titrated prick-puncture skin tests performed (3mm wheal end point).

b. 5 ml blood taken to measure specific serum IgG, IgM and IgE antibodies to Russian Thistle allergen.

c. Nasal sensitivity to Russian Thistle allergen determined by nasal provocation (doubling of nasal airway resistance as end point).

The patients will be given capsules containing specifically prepared Russian Thistle allergen. This material will be lacquered to avoid digestion and dissolution in the acid media of the stomach. The schedule on a daily basis: 0.15, 0.30, 0.60, 0.90, 1.20, 1.60, 1.90, 2.0, 2.5, 3.0, 4.0, 5.0, 7.0, 9.0, 12.0, 15.0, 20.0, 25.0, 30.0, 40.0, 50.0 mg.

50 mg will be given weekly as a maintenance dose for four more weeks. After this total schedule, the measurements made prior to therapy will be repeated. The results will be analyzed by paired "t" testing of the mean responses.

Progress:

This study will begin in FY84 during December or January 1984.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 81/36 Status: Ongoing

Title:
Phase II Studies on Ketoconazole (Keto) - Comparison of Two Different Doses of Keto in Treating Coccidiomycosis

Start Date: Est Comp Date:

Principal Investigator: Facility:

CPT Idelle Weismann, MC

Dept/Sec: Dept Medicine Asso. Investigators:

Key Words:
Coccidiomycosis; Ketoconazole MAJ S. Smith, MC

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

To determine the most efficacious dose of Keto for humans with coccidioidomycosis. To evaluate the toxicity of Keto in humans with doses up to 1600 mg per day. To evaluate the CSF penetration of very high doses of Keto.

Technical Approach:

The details are lengthy and specified in the original protocol, which is on file in the Dept Clinical Investigation, WBAMC, and is available upon request.

Progress:

Annual review of this protocol was conducted in September 1983. No patients have been entered into this study during the past year.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 81/38 Status: Ongoing

Title:
The Development of Subsensitivity to Atropine

Start Date: Est Comp Date:

Principal Investigator: Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Dept Medicine, Allergy Cl Assoc Investigators

Key Words:

Atropine; Asthma

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

To determine if repeated use of atropine sulfate as a bronchodilator, by the inhalant routes, leads to development of subsensitivity.

Technical Approach:

Twenty adult asthmatic patients will be selected at random from the Pulmonary and Allergy Clinics at WBAMC. The nature and purpose of the study will be explained. On the first day of the experiment they will be tested at the Pulmonary Function Lab according to the following protocol:

a. 24 hours without oral bronchodilators

b. Baseline pulmonary functions consisting of conventional spirometry, flow volume loops, and plethysmography.

c. Inhalation of atropine sulfate 2 mg by nebulizer.

d. Repeat pulmonary function.

After this the patients will be instructed in the use of a home nebulizer. They will use atropine sulfate 2 mg by nebulizer three times a day for 14 days. At the end of the period, the patients will undergo the same testing as on the initial day. If there is a decrease in response, then ten subjects will be retested after inhalation of 0.5 mg atropine and ten after inhaling 1.0 mg atropine, in addition to the previous 2.0 mg.

Analysis will consist of t-testing of the mean response on each occasion. In the ten subjects of each incremental group, comparison will be made to ascertain which increment, if one is required, to restore responsiveness to the original testing level.

Progress:

The final five patients are being entered into the study. It is hoped to present the data at the Spring 1984 meetings.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 81/39 Status: Ongoing

Title:
The Usefulness of NonAcetylated Salicylates in the Treatment of Inflammatory Disease in Patients with Aspirin Idiosyncratic Asthma.

Start Date: Est Comp Date:

Principal Investigator: Facility:

LTC L.E. Mansfield, MC

Dept/Sec: Dept Medicine, Allergy Cl Assoc Investigators

Key Words:

Salicylates; Asthma

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

To determine if non-acetylated salicylates can be used safely in the treatment of aspirin-idiosyncratic asthmatics with inflammatory disease.

Technical Approach:

Thirty patients with a history of aspirin idiosyncracy will be selected from the Pulmonary and Allergy Clinics of WBAMC. The nature and purpose of the study will be explained to them. They will report to the Pulmonary Function Lab on four occasions. They will be tested according to following protocols. Measured pulmonary functions will be conventional spirometry and flow volume determinations on each occasion.

| DAY 1 | Day 2 | Day 3 | Day 4 |
|---|---|---|---|
| Placebo | Aspirin | Disalcid | Trisilate |
| 1 cap | 32 mg | 250 mg | 250 mg |
| 2 cap | 64 mg | 500 mg | 500 mg |
| 3 cap | 128 mg | 750 mg | 750 mg |
| 4 cap | 325 mg | 1000 mg | 1000 mg |

The patients will not take oral bronchodilators for 24 hours except for corticosteroids. They will be managed by inhaled bronchodilating agents. Each dose will be spaced 30 minutes apart. All medications will be given in identical opaque white capsules, and the patient will be blinded as to the contents of these capsules.

A significant test for each person will be [illegible] forced expiratory volume greater than twenty percent of predicted $FEV_1$, over the fall during the placebo challenge. Any patient who develops clinical symptoms will have their bronchoconstriction reversed. Any subject whose aspirin challenge is negative will be excluded from the study. Each testing will be compared to the placebo day, in terms of possible positive responses.

Specifically, patients will not be entered unless their $FEV_1$ is greater than eighty percent of predicted at the onset of the study, and patients who develop greater than a twenty percent fall in $FEV_1$ will be eliminated from the study at that point.

Progress:

No entry has been made due to inadequate manpower resources.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 81/54 Status: Terminated

Title:
High Resolution Electrophoretic Screening of Body Fluid Proteins

Start Date: Est Comp Date:

Principal Investigator: Facility:

CPT I.L. Levey, MC

Dept/Sec: Dept Medicine Assoc Investigators

Key Words:

Electrophoresis

Accumulative MEDCASE Cost Est OMA Cost: $771(1854) Periodic Review Results

Study Objective:

Study the qualitative and quantitative patterns of proteins in human serum by high resolution two-dimensional electrophoresis. Proteins will be separated in the first dimension according to the net electrical charge of their constituent amino acids by the technique of isoelectric focusing, and in the second dimension according to their molecular weight by electrophoresis in the presence of sodium dodecyl sulfate. This technique can resolve, in theory as well as in practice, a thousand or more individual peptides. Under appropriate conditions, this technique can be expected to depict many of the individual protein components in human serum and other body fluids. If such resolution can be achieved, and a very large number of different peptides be seen, then variations related to disease may be studied, identifications made and the entities of greatest interest isolated.

While the spectrum of serum components in both health as well as disease is of interest, initial studies will be directed toward patients (1) with malignant disease (2) those undergoing chronic hemodialysis, (3) those with hepatic disease, and (4) those with inflammatory/autoimmune diseases.

Technical Approach:

The major objective of the proposed research is to analyze the protein composition of human serum in health and disease. Four specific categories of patients have been selected for initial screening based upon either well-documented abnormalities of routine serum protein electrophoresis or their potential for protein abnormality. These categories include:

a. Patients with malignant disease, including plasma dyscrasias. Alterations of both beta and gamma globulins have been noted, as well as microheterogeneities of serum albumin. Patients will be studied before and during therapy, as well as during progression of disease.

b. Patients with protein-losing nephropathies and those undergoing hemodialysis. Many patients on hemodialysis develop protein electrophorograms resembling type 3 hyperlipoproteinemia. Additionally, those with collagen vascular diseases often experience remission of symptoms and occasionally alteration of serologic status following dialysis.

c. Patients with hepatic disease. The liver is the primary organ for synthesis of most plasma proteins other than the immunoglobulins. However, the Kupffer cells of the liver are involved with the immune system in that they process antigens absorbed from the gut. As a consequence, disorders involving the liver can result in abnormalities of virtually all of the plasma proteins.

d. Patients with inflammatory and/or autoimmune disease. Patients with rheumatic diseases frequently demonstrate plasma protein abnormalities, most commonly associated with the inflammatory response and those resulting from increased antigenic stimulation of the immune system.

Patients will be selected from those with documented abnormalities of routine serum protein electrophoresis as well as those encountered during routine ward activities.

Progress:

Principal Investigator has PCSd and project has been terminated.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 81/56 Status: Terminated

Title:
Ticlopidine Hydrochloride - A Clinical Trial in Patients with Transient Cerebral or Monocular Ischemic Attacks

Start Date: Est Comp Date:

Principal Investigator: Facility:

COL M. Maccario, MC

Dept/Sec: Dept Medicine Assoc Investigators

Key Words:
Ticlopidine; cerebral ischemia

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To determine in a double-blind, randomized, parallel, controlled clinical trial whether ticlopidine hydrochloride can prevent the occurrence of transient or prolonged retinal or cerebral ischemic attacks (CIA), cerebral infarction (CI) as well as occlusive cardiovascular events in patients who are suffering from TIA or amaurosis fugax.

Technical Approach:

Only nonsurgical candidates, or surgical candidates refusing surgical therapy, will be considered eligible for inclusion in this trial. Each qualified subject (to be verified by a neurologically qualified referee) will be randomly allocated to either ticlopidine hydrochloride or identical appearing control medication and in a double-blind fashion. Each participating center will have a separate randomization code for their institution and will essentially operate independent of other institutions enrolled in this trial. All data and case report forms generated by the participating centers will be forwarded to the central data processing center for inspection, handling, coding, correction, etc. Interim planned evaluations of accumulated data will be undertaken to monitor the safety and efficacy of the medications. Any proven or unacceptable side effects or toxicity due to therapy, or any obvious or sustained lack of efficacy of ticlopidine hydrochloride would be reason for premature termination of this clinical trial.

These properties of maintained prostacyclin production by the vessel wall and lack of platelet responsivity to prostaglandin endoperoxide stimulation in ticlopidine hydrochloride treated animals may be two very important therapeutic advantages of ticlopidine hydrochloride over ASA and the other non-steroidal anti-inflammatory compounds.

Ticlopidine hydrochloride at the dose of 250 mg BID for this therapeutic trial is well tolerated and safe in clinical tolerance and therapeutic studies conducted in the USA, Europe, and Japan. We anticipate no intolerance with the possible exception of infrequent, mild initial gastrointestinal discomfort in some patients. A more extensive description of ticlopidine hydrochloride is to be found in the drug monograph.

Purpose of Trial: The short term goal of this study is to investigate the effect of ticlopidine hydrochloride vs controlled therapy (ASA, or placebo) in preventing or reducing the incidence of CIA and/or amaurosis fugaz attacks.

Progress:

Discontinued due to funding and personnel constraints.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 81/58 Status: Ongoing

Title:
The Prevalence of Antibiotic Tolerant Staphylococcus Aureus in Nasal Cultures of Different Adult Population Group

Start Date: Est Comp Date:

Principal Investigator: Facility:

MAJ Frank J Baker, MC

Dept/Sec: Dept Medicine, Infect Dis Assoc Investigators

Key Words:

Staphylococcus

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

To perform an epidemiological survey of Staphylococcus aureus tolerance from isolates not causing clinical infection and determine prevalence rates in different adult population groups.

Technical Approach:

Three population groups consisting of 100 individuals in each group will be studied.

Normals consisting of two subpopulations. Young adults consisting of a defined population, i.e., active duty personnel billeted on post. Older adults consisting of a defined population, i.e., personnel in Health Services Command. This group would be composed of individuals free of chronic disease on no medication or antibiotic therapy.

Outpatients on antibiotics. Young adults from the Dermatology Acne Clinic. Older adults from the Pulmonary Clinic, patients with chronic obstructive pulmonary disease on cyclical antibiotic therapy.

Population with a high prevalence of staph nasal carriage. Renal dialysis and insulin dependent diabetic patients. Hospital personnel. Nasal swabs with culturettes will be obtained from each individual.

(1) All nasal swabs will be streaked on sheep blood agar (SBA). Identification of staph aureus will be by standard methods as per the Manual of Clinical Microbiology, i.e., colonial morphology gram stain.

(2) MIC will be performed in duplicate by standard methods as per the Manual of Clinical Microbiology. After primary inoculation and identification of an organism as staph aureus:

(a) A log phase, four hour growth of the organism will be prepared in Mueller-Hinton Broth (MHB). The inoculum will be standardized to a 0.5 McFarland and a 1/200 dilution prepared. Colony counts will be performed on each inoculum with a desired final concentration 1 or 2 x $10^5$ organisms/ml

Conclusions: If the prevalence rates were significantly different among the study population groups, the contribution of various epidemiological factors could be determined. If the prevalence rates of tolerant organisms were less than those causing clinical infection, the question of increased virulence and microbiological change of the organism from a colonizer to an invasive form would be raised. Conversely, if the prevalence was equal to or greater than those causing clinical infection, the clinical importance might be lessened for this phenomenon.

If in subsequent studies tolerance was found to be therapeutically important, i.e., necessitating higher dosages or different antibiotics not standardly used for staphylococcal infections, this prior identification of epidemiologic factors might aid in initial selection pending further characterization of the organism. By having identified those individuals with high prevalence rates of tolerant organisms and at increased risks for clinical infections with those organisms empiric selection of treatment might be facilitated.

Progress:

Personnel constraints have precluded activation of this protocol to date.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 81/65 Status: Ongoing

Title:
Utility of Furosemide in Early Oliguric Renal Failure. Part of a Multi-center study.

Start Date: Est Comp Date:

Principal Investigator: Facility:

MAJ A. Henry, MC

Dept/Sec: Dept Medicine Assoc Investigators

Key Words:

Furosemide; Renal failure

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

A randomized study of furosemide effect on the outcome of oliguric acute renal failure. Can this diuretic convert a patient with oliguric acute renal failure to non-oliguric acute renal failure

Technical Approach:

Patients with renal oliguria will be considered for this study. Non-oliguric patients will also be included. However, the patients should not have post-renal obstruction, and if obstruction is suspected on clinical grounds, a complete workup will be done. In addition, pre-renal factors contributing to the renal failure, such as hypotension, volume depletion and congestive heart failure, will be corrected. Any patient with diminished hearing as determined clinically by questioning will be excluded from the study. Also any patient that experiences transient hearing loss after the first furosemide dose will be excluded from subsequent doses. Absence of administration of furosemide or other diuretic agents within the previous twelve hours will be a criteria for entry as will serum creatinine greater than 2.0 mg/dl.

There will be two patient groups, furosemide and saline placebo, as determined by the use of a random numbers table. Consecutive patients assigned an even number from the random numbers table will receive furosemide. Patients assigned an odd number will receive saline. The random numbers table will be employed by using horizontal rows.

Progress:

Recommend study be kept open although patient entry has been infrequent.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/01 Status: Terminated

Title:
Comparison of Modalities for Treatment of SLE Nephritis

Start Date: Est Comp Date:

Principal Investigator: Facility:

MAJ M. Nelson, MC

Dept/Sec: Assoc Investigators

Key Words:

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

To evaluate the efficacy and side effects of single daily dose corticosteroids vs split dose steroid therapy. Provide an alternative form of therapy in patients with SLE Nephritis who have not responded to conventional steroids and to evaluate patients' clinical and serologic response to therapy

Technical Approach:

There will be two phases to the protocol with two arms in each phase. Patient selection: All patients above age 12, eligible for care at Army hospitals, with SLE diffuse proliferative nephritis, will be eligible for the study. We hope to have 25-30 patients in three years.

PHASE I: Patients will be randomized to the following therapy:

ARM 1. Single daily a.m. dose of prednisone 1 mg/kg (e.g. 60 mg q.d.)

ARM 2. One mg/kg/day of prednisone in four equal and divided doses every six hours (e.g. 15 mg of Prednisone q 6 hour)

Patients will continue on the above regimen for a minimum of one month. The patient's kidney function will be re-evaluated at the end of this initial treatment interval, and if there is:

a. A decrease in gliomerular filtration rate (GFR) of greater than 25%;

b. A decrease in glomerular filtration rate of less than 25%, but with continued active urinary sediment and heavy proteinuria (greater than 3.5 grams/24 hours);

c. No significant change in the GFR, but remaining at a value less than 30% of normal (serum creatinine greater than 3.0 mg/dl).

Steroid dose would then be doubled (2 mg/kg/day) and continued for a minimum of two weeks, preferably four weeks. If any patient, after two to four weeks of therapy at 2 mg/kg/day (total of 6-8 weeks of steroid therapy) have:

a. Decrease in GFR of greater than 25%*; or

b. Decrease in GFR of less than 25%, but with continued active urinary sediment and heavy proteinuria; or

c. Stabilization of glomerular filtration rate, but at a level less than 30% of normal (serum creatinine greater than 3.0), they would be declared steroid nonresponders and entered into Phase II of the protocol.
*Baseline GFR is that clearance immediately prior to initiation or change in therapy.

Patients would be considered steroid responders if the glomerular filtration rate normalized (Normal GFR - Greater than 90cc/min, creatinine less than 1.8 mg% or 65 cc/min/$m^2$), increased by greater than 50%, or remained stable with serum creatinine values of less than 3.0 mg/dl. Patients will also be considered as responders if their GFR decreases, but less than 25%, and the serum creatinine value is less than 3.0 mg/dl, and there is a clear and consistent improvement in the urinary sediment and the urine protein excretion. These patients should have their steroid dosages continued (e.g. 8-12 weeks), and the dosage thereafter very gradually tapered.

PHASE II: Patients will be randomized to the following therapy:

ARM 1: Pulse solumedrol therapy
ARM 2: Chlorambucil therapy

Pulse therapy would consist of 1 gram of intravenous bolus solumedrol therapy on three consecutive days with a subsequent continuation of steroids at 1 mg/kg/day, given as a split or single dose as on their previous schedule.

Chlorambucil would be administered as follows:

Start at dose of 2 mg/day and continue steroids [illegible] at mg/kg/day. Chlorambucil dose should be increased by 2 mg every two weeks until

a. There is distinct improvement in [illegible]
b. White count falls below 4500 or platelets [illegible]
c. The daily dose reaches 10 mg/day.

In acutely ill patients with rapidly deteriorating renal [illegible] chlorambucil may be initiated at a dose of 10 mg/day for 2- and then tapered to a maintenance dose of 2-5 mg/day. Ther should be continued until:

a. GFR normalizes, or improves by at least 50% for two consecutive months, with minimal urinary sediment and minim proteinuria. At this time chlorambucil can be tapered at 2 and steroid slowly tapered. If patient has a flare of renal during chlorambucil taper, dose would be increased to the l dose that achieved remission with an attempt to taper and discontinue as above after remission is again obtained. So patients could require long-term immunosuppressive therapy.

b. Four consecutive months of therapy that show no clea evidence of benefit toGFR, urinary sediment, or proteinuria

c. GFR deteriorates by 50% from GFR at initiation of t

To enter protocol, patient must:

a. Fulfill ARA criteria for SLE.

b. Have biopsy proven diffuse proliferative glomerulon (DPGN) with active urine sediment and proteinuria. Patient have never been on more than 0.5 mg/kg/day of prednisone or cytotoxic drugs prior to entering Phase I of the protocol. Phase I patient must have had the diagnosis of DPGN nephrit less than three months. Patients could be eligible for Pha the protocol without entering Phase 1, if they had previous on 1 mg/kg/day for one month and 2 mg/kg/day for 2-4 weeks have active disease.

c. On entering the protocol, patient must have CBC wit differential and platelet count, SMA 20, urinalysis, 24-hou for creatinine clearance and protein, DNA% binding, C3, C4, ESR, FANA. At WBAMC Clinic immune complexes will be done.

d. After initiation therapy, patient must have creatin urinalysis, CBC, DNA% binding, C3, C4, and 24-hour urine fo creatinine clearance three days post-therapy, one week post then once weekly for one month. If patient has stabili

above data can then be obtained on a monthly basis. If patients therapy changes by either doubling dose of steroid or entering Phas II of protocol, patient should again have the above data obtained a three days, one week, and weekly times one month, and then on an every month basis.

e. Patient should be seen by physician when laboratory data is being obtained and fill in appropriate flow sheet on clinical signs and symptoms, laboratory and side effects of therapy. Flow sheets will be provided for this data gathering.

f. Consent form must be obtained and physician must counsel patient concerning the randomization of therapy, steroid side effect, and if pertinent, chlorambucil side effects to include possible complication of aplastic anemia, sterility, increased risk of malignancy, and increased susceptibility to infection.

g. Avoid aspirin and other nonsteroidal medication initially a these medications can decrease GFR.

Statistical Analysis: The rate of normalization of creatinine clearance, side effects, morbidity and mortaligy, progression to renal failure will be well studied with the various modes of therapy. Statistical significance of data will be calculated using the Student t-test. Patients clinical and serological data will be evaluated and computed at six months and one year after initiation of protocol.

Randomization: This will be accomplished by a flip of a coin.
Phase I Heads - Single daily dose; Tails - Split dose.
PHASE II Heads - Chlorambucil; Tails - Pulse Medrol Rx

Patients clinical and serologic data will be evaluated and computed at six months and one year after initiation of protocol.

Progress:

Discontinued, not enough patients to enter the study.

Date: 1 Oct 83 Prot No: 82-02 Status: Ongoing
Title:

Comparison of Bone and Joint Scans in Patients with New Onset Polyarthritis or Polyarthralgia.

Start Date: Est Comp Date:
Principal Investigator: Facility:

MAJ Mark W. Nelson, MC

Dept/Sec: Assoc Investigators:
Key Words:

Polyarthritis

Accumulative MEDCASE Cost Est OMA Cost: Period Est Work Start
Study Objective

The detection of inflammation in asymptomatic or arthritic joints is useful for objective documentation of organic disease in medical-legal or Workman's Compensation cases. It is important early in the course of a patient the exact distribution of the involved joints, therefore aiding in diagnosis. Arthritis is usually classified on the basis of joint distribution [illegible] although nonspecific test to detect [illegible] would be useful. We will compare Tc99m MDP bone scan (which reflects metabolic activity of bone with $Tc99mO_4$ which reflects blood pool activity and is cheaper and simpler to obtain.

Technical Approach:

Patient population: New onset polyarthritis or polyarthralgia in adults (symptoms less than six months).

Procedures:

I.a. A rheumatologist will make a clinical joint chart on patients noting joints where objective arthritis is present. This will be done prior to scanning.

b. The patient will then receive both scans, which will be done in the Nuclear Medicine Service under the supervision of Nuclear Medicine staff physicians. The scan will be interpreted without knowledge of the clinical joint chart and independently of each other.

II. a. The number of clinically involved joints will be compared to involved joints on bone and joint scans. A positive bone scan will be considered to be a true-positive of increased metabolic bone activity and a positive joint scan will be considered a true-positive reflecting increased flow to a joint. This applies only to activity in joint area.

b. The previously identified joints on scan will be followed to determine the long-term signficicance of a positive scan.

PROGRESS: Twenty patients have been entered to date.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82-08A Status: Terminated

Title:

Karyology of In Vitro Cultured Human Basal Cell Epithelioma Tissue

Start Date: Est Comp Date:

Principal Investigator: Facility:

LTC J.E. Pryor, MC

Dept/Sec: Assoc Investigators

Key Words:

Karyology

Accumulative MEDCASE Cost: Est OMA Cost: 2555 (2555) Periodic Review Results

Study Objective:

To investigate chromosomal abnormalities in basal cell epithelioma cells and to initiate a cell culture line for this and further studies.

Technical Approach:

The initial efforts will be directd to previously untreated primary skin lesions of BCE. Prospective patients to be included in the study will be presented to the principal investigator for evaluation. Patients with suitable lesions requiring surgical intervention (e.g. curettage and electrodesiccation or excision) will have tissue specimens obtained, cultured, subcultured, and chromosome preparation as described by D.G. Harnden. Data concerning the tumor size, anatomic location, and approximate duration will be documented. While the specimen for tissue culture is being obtained a portion will be submitted in formalin for histologic confirmation of BCE. Once chromosome preparation is completed, coordination for karyotype determination will be made with the Dept Clinical Investigation.

Progress:

Terminated. Investigator is no longer interested.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/06 Status: Terminated
Title:

Effect of Simultaneous Streptokinase Reperfusion with GlK, Nifedipine, or Hyaluronidase on Infarct Size in the Canine Heart

Start Date: Est Comp Date:
Principal Investigator: Facility:

CPT R.D. Latham, MC
Dept/Sec: Assoc Investigators
Key Words:
Streptokinase

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results
Study Objective:

The purpose of this study is to determine if the simultaneous administration of GlK or hyaluronidase, or nifedipine with streptokinase results in a significant reduction in infarct size and increased preservation of left ventricular function as compared with reperfusion alone. This protocol will also assess whether the administration of hyaluronidase or nifedipine prior to reperfusion will salvage ischemic myocardium.

Technical Approach:

Twenty large mongrel dogs will be divided into four groups of five dogs each.

I. Streptokinase alone
II Streptokinase plus GlK
III Streptokinase plus nifedipine
IV Streptokinase plus hyaluronidase

Group II. Five mongrels will receive 15 ng morphine 30 minutes prior to the trial. They will be anesthetized with thiopental and intubated. A mechanical ventilator will be utilized and ABGs monitored to ensure adequate oxygenation. Surface lead II EKG and chest lead will be monitored simultaneously. Dogs will not be heparinized.

a. Pigtail judkins catheter is placed into the left ventricle.
b. MUGA study will be performed and EF compared with LV ventriculogram.
c. An IV of RL will be maintained at TKO rate.

d. Control EKG on LV pressure curve will be taken. A modified judkins catheter will be utilized to cannulate the proximal LAD artery with placement of a guide wire 0.038". The wire is advanced to the apex, the catheter is removed. A copper coil prepared in sulfuric acid and rinsed, is advanced several centimeters into the LAD using a straight cut modified judkins catheter.

e. The ECG will be monitored for development of ischemic injury, which will be allowed to remain about 2 hours.

f. An angiogram will be performed to assess presence of occlusion.

g. A 2F catheter will be advanced to within 1-2mm of the thrombus.

h. A ventriculogram and/or MUGA EF will be obtained.

i. Perfusion of streptokinase by means of a Harvard Pump at a rate of 0.3 ml/min (or 0.4 ml/min)(5000 u/H) will be initiated.

j. ECG continuously monitored. Reperfusion is heralded by arrythmias. VT will be treated by 2-6 mg lidocaine IV bolus via the perfusion catheter. LV pressure will be continuously monitored.

k. An angiogram will be done to assess patency.

l. Infusion will be continued for 60 min.

m. The animal will be heparinized with a dose of 2.0 mg/kg IVP.

n. A ventriculogram will be done to assess EF and wall motion.

o. With catheters removed the animal will remain sedated with SQ MS and receive heparin 10,000 units $q8^{o}$ via heparin lock.

p. After 24 hours the animal will have a repeat MUGA and angiogram. Monastral blue dye may be injected at this time (optional) 0.5 ml/kg over 30 seconds via a catheter in the left atrium.

q. The animal will be sacrificed using concentrated KCl solution.

r. The heart will be removed and immediately placed in ice cold water to remove excess blood. The myocardium will be cut into no greater than 1 cm slabs. Each section is weighed. A clear glass plate is placed over both sides of each slice and inner and outer margins are traced into clear acetate with magnifying lens. Areas not perfused by monastral blue dye will also be traced. Then jthe slices will be incubated in TTC to delineate the infarction. TTC will be made by combination of Trigma HCl (42.56 gm) Trisma base (16.76 gm) and 2,3,5 triphenyl tetrazolium (20 gm) chloride in 2 liters of distilled water. This will be mixed and stored in the dark. Pior to incubation this solution will be warmed on a hot plate to approximately $37^{o}C$. The myocardial slices will be incubated in a pan of the wolution (in the dark) for about 20-30 minutes. At least 1 cm of solution covering the slices is needed. A photographic record will be obtained after placing incubated slices in normal saline solution (made by adding 17.8 gm NaCl to 2.5 1 of 10% formalin).

s. Incubation in JTC at 37C will be done.

t. Estimation of infarct size will be measured from the stained myocardium, using a planimeter and plastic transparencies. Differences in weight of infarct/normal myocardium may be compared. The area at risk $A_r$ = ratio of areas not perfused by monastral blue dye to total area of all slices. Area of necrosis $A_n$ = ratio of areas unstained by TTC to total area of all slices.

Group II

Will repeat above procedure with addition of GlK as solvent for streptokinase. GlK will be made by adding 50 units of insulin and 50 mEqKCl/liter $D_5W$. Nine cc of this solution plus 1 cc streptokinase 150,000 units/cc to be infused at 0.3 cc/min. (5400 units/hr, which is the same for all groups).

Group III

Will undergo same trial as Group I with the addition of nifedipine to the streptokinase solution (to infuse 1 mg/mKg/hr).

Group IV

Same trial as above with the addition of bovine hyaluronidase (to deliver 100 units/kg/hr).

The trials with hyaluronidase and nifedipine may be repeated giving the agents upon thrombosis indicated by segment and continuing them for two hours prior to reperfusion.

The differences in infarct size and EF by MUGA and ventriculogram will be assessed by the unpaired t-test $A_r$ and $A_n$ will be compared between groups as well as An/Ar ratio.

Progress:

Principal investigator has departed. No cardiologist is interested in pursuing this project.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/10 Status: Terminated

Title:

Evaluation of Saline Purge Versus Conventional Barium Enema Preparation in Cleansing the Colon for Air Contrast Barium Enema

Start Date: Est Comp Date:

Principal Investigator: Facility:

CPT Donald R. Johnson, MC

Dept/Sec: Dept Medicine Assoc Investigators

Key Words:

Barium Enema

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

The purpose of this study is to compare the use of saline lavage, which we find to be an effective colonoscopy preparation, to the standard radiological preparation for air contrast barium enema used at William Beaumont Army Medical Center.

Technical Approach:

At the time the barium enema is ordered on any patient in the Gastroenterology Clinic, patient will be asked to participate in this study. Informed consent will be obtained after the study procedure is explained and the patient instruction sheet is discussed. The patient will be randomized into either the saline lavage or standard preparatory method by the GI technicians for x-ray.

Evaluation

1. Radiological

   a. Gas, feces or fluid on the scout film.
   b. Interference of feces, fluid or gas on contrast radiographs.
   c. Clarity of mucosal pattern.

2. Pacing evaluation of procedure

PROGRESS: Principal investigator has departed. No one is interested in assuming this project.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/11 Status: Ongoing

Title:
Serum Gentamicin Levels: Use in a Training Hospital Before and After Institution of an Intensive Educational Program.

Start Date: Est Comp Date:

Principal Investigator: Facility:

MAJ Baker

Dept/Sec: Assoc Investigators

Key Words:

Gentamicin

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

The objectives of this clinical study would be three-fold: (1) To determine when gentamicin levels are ordered by physicians caring for patients receiving this drug and to determine how frequently this information is utilized to adjust dosage and interval. (2) To determine if there is any influence on overall morbidity and mortality in the group of patients in which this information was utilized appropriately compared to the group in which it was not. (3) Having obtained this baseline data, determine any increment of change observed after the institution of an aggressive education program on the use of gentamicin levels.

Technical Approach:
The initial part of the study will be a retrospective review covering a 12 month period. The study population will consist of those patients on medicine wards who received at least three doses of gentamicin and had not received an aminoglycoside antibiotic within two weeks prior to entry into the study. Excluded from the study will be those patients receiving gentamicin from other services, those on hemo- or peritoneal dialysis, and those from whom complete records of hospitalization are unavailable for review.

Patients fitting the above criteria will be identified by a review of pharmacy records. From this review names, SSNs and month of hospitalization will be tabulated and submitted to inpatient records for retrieval. A standardized list of data derived from the records will be completed for each patient included in the study. A review of the radioimmunoassay laboratory records will then be performed and times and results of gentamicin levels will be recorded for each study patient.

From this data, an assessment of percentages of appropriately drawn and utilized serum gentamicin levels will be determined. A comparison of overall morbidity and mortality will be made between the group in which the procedure was used appropriately and the group in which it was not.

The second part of the study will be prospective and 12 months in duration. A list of patients receiving gentamicin will be maintained by the pharmacy. This list will be reviewed daily and those patients meeting the criteria will be entered into the study..

Having obtained baseline data and identified problem areas from the retrospective review, an educational program will be instituted just prior to initiation of the 12 month prospective study. This will consist of lectures on gentamicin pharmacokinetics, toxicity and the appropriate use of gentamicin levels. The results of the retrospective review and problem areas will be included. At two to three month intervals an update of the ongoing prospective study will be reviewed with continuing problem areas emphasized. This will be presented in depth to house staff and staff during one hour lectures, and informally to ward personnel in 30 minute in-services. One to one teaching will occur in those instances where physicians are not using or have inappropriately used gentamicin levels.

At the end of the 12 month study period the data from the retrospective and prospective study will be compared for statistically significant differences.

7. METHODS, DEFINITIONS:

I Patients:

a. The criteria for inclusion/exclusion has been outlined.

b. Patients will be classified into three categories based on the severity of underlying disease by the criteria of McCabe[16].

c. Rapidly fatal disease: to be utilized solely for patients with acute leukemia or blastic relapse of chronic leukemia.

d. Ultimately fatal disease: Arbitrarily based on the severity of the underlying disease rather than the specific diagnosis. The disease is likely to prove fatal within the next five years. Patients with carcinoma, with proved metastases, myeloma, lymphoma, aplastic anemia, severe renal failure and liver disease with spontaneous coma or bleeding esophageal varicies to be included in this group.

e. Non-fatal: The underlying disease is considered unlikely to be fatal within the next five years.

II. Morbidity

a. Nephrotoxicity

A rise in serum creatinine of 0.5 mgm% or greater if initial level is less than 3 mgm%, or a rise in serum creatinine of 1 mgm% if initial creatinine is more than 3 mgm%.

b. Ototoxicity - gross abnormalities, i.e. deafness, ataxia or nystagmus occurring during therapy. Audiometry and aloric testing will not be performed.

c. Length of hospital stay.

III Mortality:

All deaths which occur within 7 days of onset of bacteremia will be considered due to bacteremia unless a 2nd usually lethal event, not associated with or precipitated by bacteremia occurred and there is strong clinical evidence of recovery from the episode of bacteremia. Adapted from McCabes definition[16].

IV Use of gentamicin levels:

a. Defined as:

Therapeutic - peak serum concentration of 4-12 ug/ml
Sub-therapeutic - peak serum concentrations of less than 4 ug/ml
Toxic - Peak serum concentration of more than 12 ug/ml or trough serum concentrations more than 2 ug/ml

b. Time of sampling (correctly drawn)
Peak - drawn 30 minutes after an IV infusion
Trough - drawn just prior (within 30 minutes) of IV infusion

c. Use of levels obtained as correctly drawn peaks/trough pairs will be classified as appropriate if:

(1) The peak and trough is in the therapeutic range and and the dose is not changed.

(2) Peak is more than 12 ug/ml and the dose is decreased.

(3) Peak is less than 4 ug/ml and the dose is increased.

(4) Trough is more than 2 ug/ml and the interval is increased.

(5) Any combination of the last three.

V. Data analysis.

a. At the conclusion of the retrospective study, the percentage of patients having appropriately drawn and utilized levels will be tabulated. Comparisons will be made of these patient categores, defined by severity of underlying disease, who had serum gentamicin levels drawn and utilized appropriately and those who did not. The influence of inappropriately drawn gentamicin levels on overall morbidity and mortality as defined will then be assessed.

b. At the conclusion of the prospective study the percentage of patients who had appropriately drawn and utilized levels will be compared to the retrospective group. If there is a significant difference between the prospective and retrospective group, the influence on overall morbidity and mortality will be assessed. The influence of the education program can then be measured.

Progress:

Data for 40 patients has been tabulated to date.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/13 Status: Terminated

Title:

Infection Induced Kidney Stones: A Multi-Center Clinical Trial of UROSTAT™ (Acetohydroamic Acid)

Start Date: Est Comp Date:

Principal Investigator: Facility:

MAJ A.R. Henry, MC

Dept/Sec: Dept Medicine Assoc Investigators

Key words:

UROSTAT

MAJ S.F. Gouge MAJ JC Norbeck
MAJ JE Crosse MC

Accumulative MEDCASE Cost Est OMA Cost Periodic Review Results

Study Objective:

To ascertain the effectiveness of aceothydroxamic acid (AHA) in the prevention and/or dissolution of infection - induced urinary stones and to study the safety of AHA with respect to side effects.

Technical Approach:

A two year, double-blind study will be conducted in patients with chronic urea-splitting urinary infection that is recalcitrant to effective antimicrobial treatment. The code may be broken and the patient may be placed on the best treatment available, including AHA if there is unequivocal stone growth. Patients will be permitted an ad lib diet, and they may take their usual medications, including antibiotics. Clinical, laboratory, radiographic and compliance data will be recorded.

Patients with recalcitrant urea-splitting urinary infection and/or infected renal calculi are candidates. Patients may have infection-induced stones or they may be surgically stone-free. Patients are ineligible if:

Their urine is infected by an organism that does not make urease (i.e., split urea).

Their urine can be chronically sterilized with culture-specific oral antimicrobial agents.

Their renal function is poor (i.e., serum creatinine greater than 3.0 mg/dl).

AD-A141 139 ANNUAL PROGRESS REPORT FISCAL YEAR 1983(U) WILLIAM BEAUMONT ARMY MEDICAL CENTER EL PASO TX L E MANSFIELD 30 SEP 83 2/3

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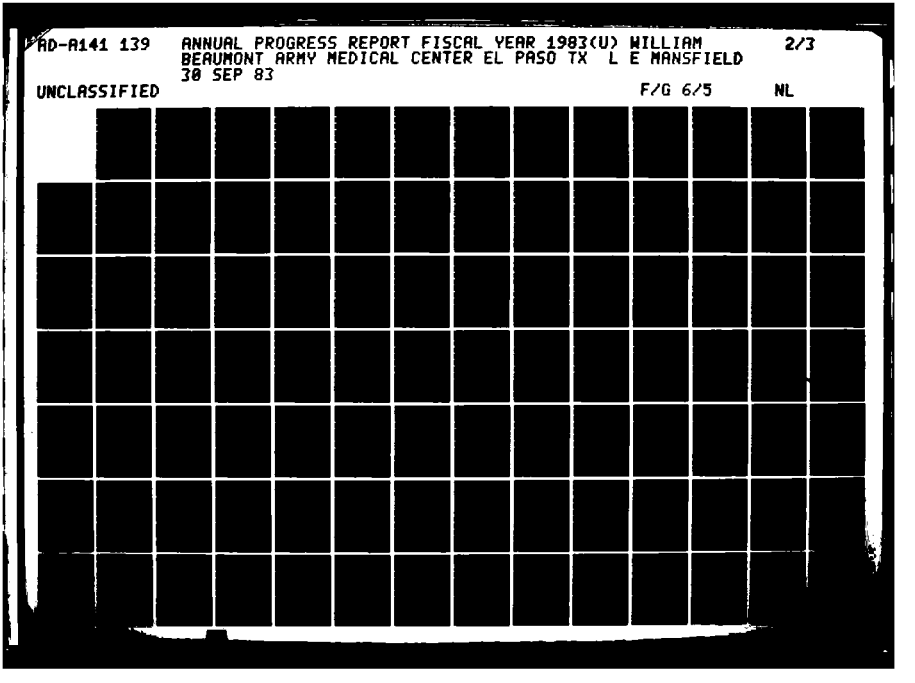

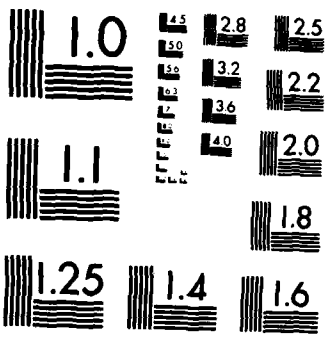

They become pregnant.

Satisfactory effort of contraception is not evidenced by female candidates.

Life-threatening disease involving other organ systems is co-existent.

In the opinion of the attending physicians the risks induced by treatment are likely to outweigh the potential benefits.

Patients may be dropped from participation because of:

Non-compliance (i.e., failure to take medication reliably, failure to return for followup visits and tests, failure to report side effects).

Adverse effects.

Patients may terminate their participation by discontinuing their medication at any time. Such withdrawal will not cause ill will by those providing their care.

Progress:

This drug has been approved by the Food & Drug Administration for general use.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/18 Status: Ongoing

Title:
The Use of a Combination of Isoelectric Focusing, Inhibition Radioautography and Enzyme Labelling to Determine Cross-Reacting Allergens.

Start Date: Est Comp Date:

Principal Investigator: Facility:
LTC L.E. Mansfield, M.D.

Dept/Sec: Dept Medicine Assoc Investigators

Key Words:

Cross-reacting allergens R.F. Frederick, Ph.D

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

To determine if a novel approach using a combination of isoelectric focusing and radioautography and enzyme labelling will be useful in determining cross-reacting allergens of pollen extracts.

Technical Approach:

1. Technical consideration for optimum analytic isoelectric focusing of pollen extracts will be worked out for our laboratory.

2. After this stage has been accomplished, a technique for electroblotting the separated protein bands on paper will be utilized. This procedure will end any significant diffusion of the proteins and make possible Step 3.

3. The paper will be overlayered with human allergic serum specific to the pollens involved. The paper will have been previously treated so that nonspecific binding of serum globulins on the paper cannot occur. After the overlaying and antigen-antibody reaction, the paper will be washed to remove any serum protein not immunochemically bound to the allergen proteins. The next step will be a second overlay with radiolabeled anti-human IgE (FC Specific). This will be followed by another gentle washing. The paper will be dried and placed on an x-ray film for radioactive exposure of the film. Lines of interest should develop where human IgE antibodies have bound to the allergen proteins.

4. In the enzyme labeling technique anti-human IgE chemically bound to horse radish peroxidase will be used as the

marker rather than the radiolabel. The bands will be subjected to a colorimetric reaction catalyzed by enzyme conjugate. The intensity of the reaction will be read by spectrophotometric methods.

5. In this step the human allergic sera will be preincubated with an allergen extract suspected of containing cross-reacting proteins to the allergen extract, electrophoresed and transferred to paper. The incubated sera will be used in the same manner as described in Steps 3 and 4.. Absence or diminution of intensity of the bands on the x-ray film will occur if the allergen extract contains proteins which cross react with allergens in the first extract.

Progress:

The technique is being further developed with a more sensitive horseradish peroxidase method.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/20 Status: Ongoing

Title:
An Investigation Into Possible Bronchoconstrictive Reflexes Arising with Gastric Distention in Asthmatic Subjects

Start Date: Est Comp Date:

Principal Investigator: Facility:
LTC L.E. Mansfield, MC

Dept/Sec: Dept Medicine Assoc Investigators

Key Words:
Gastric Distention

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

To discover if gastric distention causes a bronchoconstrictive response in asthmatic subjects. To determine if pretreatment with atropine ablates this response.

Technical Approach:

Twenty adult asthmatic patients will be selected at random from the allergy immunology clinic population. They will come to the clinic at 0800 (having omitted their morning bronchodilators if tolerated). Total respiratory resistance will be measured by the method of forced oscillations and then conventional spirometric and flow-volume determinations will be performed.

Each subject will drink 20 oz. of water. All pulmonary functions in the same order as at baseline will be repeated. The subject will continue drinking water until he/she experiences the sensation of fullness (as after eating a bit too much). Pulmonary function tests will be repeated.

If the airway response to gastric distention, as measured by pulmonary functions, is compatible with bronchoconstriction, then the five patients in whom this response was most dramatic will be reinvestigated to determine if atropine will inhibit this reaction. These patients will report on a second day at 0800 omitting bronchodilators, if possible. Baseline pulmonary functions will be determined, two mg. atropine sulphate will be delivered to the patient by aerosol nebulization. A post-atropine baseline will be established 15 minutes after this treatment. The same proceudre as outlined above will be followed concerning water ingestion and pulmonary function determinations.

The results will be analyzed by appropriate parametric and nonparametric statistics.

Progress:

Nineteen patients successfully completed this protocol. Statistical analysis revealed evidence of very mild bronchoconstriction upon gastric distention..

Detail Summary Sheet

Date: 1 Oct 82 Prot No: 82/21 Status: Terminated

Title:
The Incidence of Gastroesophageal Reflux and Microaspiration Among Adult Asthmatics.

Start Date: Est Comp Date:

Principal Investigator: Facility:
CPT Gordon D. Graham, M.D.

Dept/Sec: Dept Medicine Assoc Investigators

Key Words:

Asthma; Gastroesophageal reflux

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

To determine, using a new improved capsule technique, the incidence of microaspiration in adult asthmatics.
To determine how frequent gastroesophageal reflux is in a mixed series of adult asthmatics.

Technical Approach:

Two hundred consecutive adult asthmatic patients who require daily bronchodilators will enter the study. The nature and purpose of the study will be explained to them. They will be sent to Nuclear Medicine Service to have a scan for the presence or absence of reflux, as described below. If reflux is demonstrated, they will have a second scan to investigate the possibility of microaspiration, again as described below.

Upon referral from the Allergy Clinic, the patient would be scheduled for a routine gastroesophageal reflux study. A dose of TcSCOL in a gelatin capsule is administered orally and the patient is then given six cups of water to drink. Subsequently a scan is performed in the anterior view while the patient is in a trendelenburg position.

If reflux is demonstrated, a second study would be scheduled in two weeks. The patient would be scheduled for a capsule of Tc SCOL orally at 8 pm after a heavy evening meal. The subsequent morning an anterior and posterior scan would be done of both lung fields.

Progress:

Principal investigator has PCSd. Feasibility of the study has not proven valid.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/22 Status: Ongoing

Title:
Use of Topical Steroid Cordan Tape (Fluorandrenolide) in the Management of Skin Reactions

Start Date: Est Comp Date:

Principal Investigator: Facility:
MAJ S. Ting, MC

Dept/Sec: Dept Medicine Assoc Investigators

Key Words:

Fluorandrenolide

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:
To determine whether locally applied cordan tape suppresses the histamine release, eosinophil migration and ultrastructural changes of mast cells in human allergic skin reaction.

Technical Approach:

Ten volunteers from the Allergy Clinic will be skin tested with ragweed and 48/80. Injections will be 0.02 ml of ragweed 1000 PNU/cc and 48/80. Skin blister technique will be employed and cordan tape placed over both forearms for 24 hours, then skin biopsy to determine measurement of histamine release.

Progress:
Principal investigator has been unable to solicit volunteers during the last reporting period.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/23 Status: Completed

Title:
Use of Hydroxyzine HCL (Atarax) in the Treatment of Allergic Skin Reactions

Start Date: Est Comp Date:

Principal Investigator: Facility:
MAJ S. Ting, MC

Dept/Sec: Dept Medicine Assoc Investigators

Key Words:

Atarax

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

To determine whether orally administered antihistamine (Atarax) blocks the allergen-induced histamine release and ultrastructural changes of mast cells.

Technical Approach:

Ten volunteers from the Allergy Clinic will be skin tested with ragweed and 48/80.

a. Skin testing injections 0.02 ml of ragweed 1000 PNU/cc and 48/80 1000 PNU/cc.

b. Wait 15 minutes.

c. Record the size of the wheals and flares.

d. Proceed to skin blister technique for the measurement of histamine release.

e. Using a skin blister technique -

(1) Charge Chamber A with ragweed 1000 PNU/cc
(2) Charge Chamber B with PBS (phosphate buffered saline).
(3) Charge Chamber C with 48/80.
(4) Charge Chamber D with Ragweed 500 PNU/cc.

f. Place samples in pre-labeled vials on ice and freeze.

g. Remove collecting chambers.

h. Place Metricell (.45uM) filters on the base of each blister, secure with plastic backing and tape.

i. Remove in 2 hours, place in alcohol for future staining and counting of eosinophls.

j. Stain filters using chromotrope 2R stain.
k. Mount and read numbers of eos per $mm^2$
l. Save all mounted filters for future recounts.
m. Volunteer places bandaids coated with antibiotic ointment over all denuded sites and returns home.
n. Atarax 25 mg q.i.d. x 3 days and repeat.
o. Proceed to skin biopsy technique.

**Progress:**
**A total of 10 volunteers entered the study.**

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/24 Status: Terminated

Title:
An Investigation into the Anticholinergic and Local Anesthetic Properties of Cromolyn

Start Date: Est Comp Date:

Principal Investigator: Facility:
LTC L.E. Mansfield, MC

Dept/Sec: Dept Medicine Assoc Investigators

Key Words:

Cromolyn

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To determine if cromolyn sodium has any anticholinergic or local anesthetic properties.

Technical Approach:

Ten normal volunteers will be chosen from the patients and the staff of this hospital. The following studies will be performed.

a. Pure cromolyn powder will be applied to a small patch of the buccal mucosa. A similar area will be treated with placebo powder. The threshold of sensation will be determined by a pain response to a calibrated electric stimulus in both treated and contiguous untreated area.

b. Three cutaneous blisters will be raised by a vacuum blister technique. The blisters will be denuded. Pure cromolyn powder will be applied to one blister site. A second blister site will have placebo powder applied. The threshold response to citric acid will be determined at the treated and untreated sites, using twofold increasing concentrations of citric acid.

c. 0.1 ml of 4% cromolyn solution will be injected subcutaneously into a skin site, 0.1 ml 1% lidocaine, and 0.1 ml placebo solution will be injected into similar sites. Each site and an untreated site will be challenged with 0.1 ml of 0.1 mg per ml methacholine subcutaneously. The size of the methacholine wheal will be measured.

d. This will be the same procedure as in Step 3 except that compound 48/80 will be used to develop the wheal.

e. The forearm sites will be treated as in Step 3, with two additional sites - one injected with 0.1 ml of propanolol 25 mg/ml and one injected with 0.1 ml of a solution combining 4% cromolyn and 25 mg/ml propanolol. The arms will be encased in a plastic bag to induce sweating. Each treated site will be covered with carefully weighed absorbent filter paper disc and a nonporous cover. After sweating has been induced, the filter paper will be removed and weighed to determine the amount of perspiration at each site.

f. These studies will be performed over a period of four weeks.

g. The results will be analyzed to determine if any anticholinergic or local anesthetic effects are seen with the cromolyn treatment.

h. Pure cromolyn powder without lactose will be provided by the Fisons Corp. 4% cromolyn solution will be provided by Fisons Corp.

**Progress:**

**Terminated**

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/35 Status: Terminated

Title:
Skin Response to 48/80 and Codeine in Patients with Atopic Dermatitis

Start Date: Est Comp Date:

Principal Investigator: Facility:
MAJ S. Ting, MC

Dept/Sec: Dept Medicine Assoc Investigators

Key Words:

Atopic dermatitis; Histamine degranulators

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To determine whether locally applied histamine degranulator(s) such as 48/80 and codeine induce increased histamine release in diseased skin versus normal skin.

Technical Approach:

Twenty adult patients will be selected from the allergy clinic. They will undergo skin testing, skin chamber study and skin biopsy.

a. Skin testing will be performed with 48/80 and with codeine.
b. Skin testing procedure: Inject intradermally 0.02 ml of 48/80 mg/ml and intradermally 0.02 ml of codeine 1% on normal skin and on skin with atopic dermatitis.
c. Wait 15 minutes. Record the size of the wheal and flare section.
d. Skin blister technique:

Introduce into chambers A - 48/80
B - control saline
C - codeine 1%
D - control saline

e. Incubate 30 minutes. Remove all chamber fluids for analysis of histamine.
f. Skin biopsy:
Inject intradermally 0.02 ml of 48/80
10 minutes later, using a disposable 3mm punch skin biopsy set, a small amount of skin will be removed under 1% xylocaine. The specimen will be sent to the electronmicroscopy laboratory for electromicroscopic analysis of mast cell changes.

Progress:

Terminated due to lack of patients

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/47 Status: Compl

Title:
Effect of Naloxone on B-Endorphin Response to Exercise

Start Date: Est Comp Date:

Principal Investigator: Facility:
LTC D.M. Suich, MC

Dept/Sec: Dept Medicine Assoc Investigators

Key Words:

B-endorphin; Naloxone; Exercise

Accumulative MEDCASE Cost Est OMA Cost:$400(400) Periodic Review Results

Study Objective:

It has been established that intense exercise induces an incre plasma B-endorphin levels in human beings. The objectives of study are two-fold: (a) to confirm that the levels of exercise obtained in a previous study were indeed sufficient to induce elevation of plasma B-endorphin levels; and (b) to establish elevation of plasma B-endorphin induced by exercise is enhance the presence of a specific opiate antagonist, Naloxone.

Technical Approach:

The plasma specimens to be evaluated were obtained while condu a previous protocol. There are two sets of specimens. The fi group consists of six paired specimens representing plasma obt before exercising six subjects and at the completion of exerci the six subjects. The exercise protocol consisted of a progre graded, multistaged bicycle exercise test lasting approximatel minutes. The second group consists of five paired sets of 3 t specimens obtained from repeat exercise studies in five of the subjects. These specimens were obtained pre-exercise, 25 minu into exercise and at the end of exercise. In all the precedi samples one of the pair was collected when the subject receive naloxone and the other with placebo, saline.

Progress:

Study is completed and in preparation for publication.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/50 Status: Completed

Title:
Effect of Long Term Treatment with Cromolyn Sodium on Nonspecific Bronchial Hyperreactivity

Start Date: Est Comp Date:

Principal Investigator: Facility:
LTC L.E. Mansfield, MC

Dept/Sec: Dept Medicine Assoc Investigators

Key Words:

Cromolyn; Bronchial hypersensitivity

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To investigate whether cromolyn by inhalation will modify histamine induced nonspecific bronchial hyperreactivity.

Technical Approach:

Twenty adult non-pregnant asthmatic patients with the history of seasonal asthma present in the spring and the late summer will be chosen for entry into this study. Each institution will contribute 20 subjects for a grand total of 80 participants. The subjects would not have received any allergen immunotherapy for at least one year prior to entering into the study. To be eligible for the study, they will have 3+, 4+ prick puncture skin test to the relevant spring and fall aeroallergens in the locality of the participating institution. The patients would have had a history of asthma management suggesting that they can be comfortable with "as needed" bronchodilator medication.

The study will commence on or about 1 Jan 83. During the subject's first visit in January 1983, they will undergo a histamine bronchial challenge. This will be considered baseline histamine reactivity. The patient, during this visit will be instructed in the proper use of cromolyn through a spinhaler. They then will return on or about the 1st of February 1983 to receive a spinhaler and a packet which contains either cromolyn or a similar appearing placebo. We will use this on a four-times daily basis and record such usage. They will also record the use of any other "as needed" medication to treat their asthma. The patients will perform three peakflow measurements in the morning, dinner time, and at bedtime. They will record the best peakflow at each of the time frames. At the end of the day, using a daily symptoms score sheet, they will record their

symptoms and medication used on the score sheet. During each week of the study, the subjects will be contacted by a member of the staff of the allergy-immunology service conducting the study. This will be a telephonic conversation to discuss their progress with the medication, their understanding of the symptoms score sheets and data recording, and to maintain their continued compliance with the study. The patients will return to the participating allergy-immunology service at 2 months, 4 months, and 6 months after commencing treatment. During each of these visits, a repeat histamine bronchial challenge will be peformed. During the study period itself, if the subject should have an exacerbation of their asthma, they will be seen as soon as humanly possible by one of the principal investigators from their participating allergy-immunology service. They will be encouraged to utilize this route of care rather than emergency room or primary care unit treatment so that adequate documentation, including pulmonary functions of any acute episode, will be available for future evaluation At the end of the 6 months of treatment, the symptom medication score sheets, the daily peakflow measurements, and the change in bronchial responses to histamine over the course of time will be compared between the placebo and the active treatment group. Statistical analysis will be by both parameteric and nonparametric means as appropriate.

Progress:

This project has been completed. Data is presently being analyzed. Sixteen subjects completed the study successfully.

Detail Summary Sheet

Date: 1 Oct [illegible] No: 82/51 Status: Completed

Title:
The Effect of K[illegible](Zaditen) on Immunologic Pharmacologic Skin Test Reactions

Start Date: Est Comp Date:

Principal Inves[illegible] Facility:
LTC L.E. Mansf[illegible]

Dept/Sec: Depi[illegible] Assoc Investigators

Key Words:

Ketotifen; Skin[illegible]

Accumulative M[illegible]st Periodic
Cost [illegible]MA Cost: Review Results

Study Objective

To investigate [illegible]eally administered Ketotifen (Zaditen) will modify allergen[illegible]kin reactions.

Technical Appro

Twenty adult ma[illegible]lc individuals with a positive skin test to either Russian [illegible]l Bermuda grass will be entered into this study. These p[illegible]tll have highly reactive skin tests; at least a 4+ pric[illegible]nt to one to 20 glycerinated extract of Bermuda grass o[illegible]sthistle pollen. The study will be conducted when [illegible]o to which they are allergic is not present in the atmosphe[illegible]aso. After the initial screening skin test, further s[illegible]eof the subjects will be done with specifically pr[illegible]derial reconstituted from freeze dried extracts on wee[illegible]a All skin testing will be done in the titrated prick [illegible]tmethod on the patient's back. All the pharmacologic a[illegible] be reconstituted likewise each week. The protocol will b[illegible]fd in two phases: Phase I - the subjects will return to t[illegible]l after having been off any antihistamine for five days. [illegible]td skin testing will be performed to include testing to the [illegible]allergen at two-fold dilution from one to twenty to one t[illegible]0utions; doubling dilutions of codeine beginning with [illegible] ml concentration and histamine in two-fold dilutions begin[illegible]one mg [illegible]l concentration. The last dilution that i[illegible]a of eli[illegible]n [illegible]a 3 mm wheal will be considered the [illegible]tponding [illegible]n. The size of the erythema will be measured [illegible]record[illegible] [illegible]ch subject; the subject will then be entered [illegible]er Grou[illegible] [illegible] in a random fashion. The patients in Grou[illegible]receive [illegible]en 1 mg daily for three days with a 1 mg dose [illegible]ourth day when repeat testing will be

performed. Group B will receive 3 days identical looking placebo, but on the fourth day will receive 1 mg of Ketotifen. Skin t: will be repeated in the same fashion as described for the baseline. Then patient will also return at 2, 4, 6, and 8 days while taking no further medication and have this skin testing repeated. The results at each testing time will be compared to the baseline to ascertain: 1) the effects of the varying treatment and 2) the duration of carryover effect if any.

After this information is available, Phase II of the study will begin. In Phase II of the study, the same volunteer subjects, or a similar group, will be chosen. The criteria for entry will be the same, if new volunteers are added to the study. These patients will have titrated prick skin tests performed to establish a baseline. They will take one of the following regimens of Ketotifen in a random blinded fashion. Each patient will receive four capsules twice a day for three days and two capsules on the day of the testing. The capsules in various combinations will contain either 1 mg Ketotifen or placebo. During this three day trial, subjects will receive 1 mg Ketotifen, 2 mg Ketotifen, 3 mg Ketotifen, or 4 mg Ketotifen daily dose. All skin testing will be done at 0800 in the morning in consideration of the recognized circadian variation in skin reactivity. Each volunteer will serve as his own control for analysis in this study. Each volunteer will be tested while on each medication regimen. The skin testing results at varying doses will be compared to see if there is increasing medication effect with greater doses. At the time of the testing, the patient will also be queried as to side effects of the regimen. An IND number has been submitted by the Sandoz Corp for the use of this drug. Skin test responses will also be cellophane tape transferred to paper and measured with a compensating polarized planimeter. Statistical analyses of this skin testing at each time frame will be by parametric and nonparametric methods.

Progress:

This study has been completed. The data is being analyzed for presentation and publication.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/52 Status: Completed

Title:
Usage of Sus-Phrine in Control of Allergic Skin Reaction

Start Date: Est Comp Date:

Principal Investigator: Facility:
MAJ S. Ting, MC

Dept/Sec: Dept Medicine Assoc Investigators

Key Words:

Sus-Phrine; Skin reactions

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To determine duration of action of sus-phrine in inhibiting allergen induced skin reaction.

Technical Approach:

Twenty adult volunteers from the Allergy Clinic with no contraindications to adrenergic therapy.

Skin testing will be performed with an allergen to which a given subject has been shown to be reactive by previous routine skin test, and with 48/80 (mast cell degranulator), codeine, histamine, and sus-phrine.

Skin testing procedure:

Skin prick test with predetermined allergen (e.g., ragweed) 1:20
Skin prick test with 48/80 100 mg/ml
Skin prick test with codeine 1.0%
Skin prick test with histamine 1 mg/ml

After 15 minutes record size of wheal and flare reaction. Subcutaneously inject .15 ml of 1:200 sus-phrine. At fifteen minutes, 1, 2, 4, 6, and 8 hours post sus-phrine injection, repeat.

Progress:

Three subjects were entered into the study. An additional seven are required to complete the study. Limited reactions indicated that Sus-phrine inhibits the allergic reaction only up to two hours.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/53 Status: Completed

Title:
Efficacy Trial Using Cyproheptadine and Cimetidine for Pruritus in Polycythemia Vera PVSG-15

Start Date: Est Comp Date:

Principal Investigator: Facility:
COL Ray O. Lundy, MC

Dept/Sec: Dept Medicine Assoc Investigators

Key Words:

Ha and H2 blocking agents; Pruritus

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

The aim of this study is to determine whether $H_1$ and $H_2$ blocking agents used concomitantly are efficacious in alleviating the pruritus of polycythemia vera. All patients currently on active protocols (PVS-01,05,08) will NOT be eligible. Should usefulness be established, a randomized trial will be considered.

Technical Approach:

The details are lengthy and specified in the Polycythemia Vera Study Group protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress:

Study was completed.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/54 Status: Completed

Title:
Study of the Clinical Features and Natural History of Asymptomatic Patients with Myeloproliferative Disorders PVSG-13

Start Date: Est Comp Date:

Principal Investigator: Facility:
COL Ray O. Lundy, MC

Dept/Sec: Dept Medicine Assoc Investigators

Key Words:

Myeloproliferative disorders

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To obtain a clinical and laboratory data base on patients with myeloproliferative disorders prior to the time they require treatment under other MPD protocols.

To define the natural course of the disease as to the development of: a) splenomegaly; b) progressive fibrosis; c) leukemic conversion; d) thromboembolic complications and e) other neoplasm.

To demonstrate the development of cytogenic and pathologic abnormalities in bone marrow and peripheral blood.

To establish predictors of a more symptomatic stage of the disease.

Technical Approach:

The details are lengthy and specified in the Polycythemia Vera Study Group protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress:

Study was completed.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/55 Status: Completed

Title:
Efficacy Trial Using Hydroxyurea (HU) in Thrombocytosis PVSG-12

Start Date: Est Comp Date:

Principal Investigator: Facility:
COL Ray O. Lundy, MC

Dept/Sec: Assoc Investigators

Key Words:

Hydroxyurea; Thrombocytosis

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

Despite the fact that a number of alkylating agents have been shown to be effective in the treatment of primary thrombocytosis, the known chemogenic and carcinogenic effects of these drugs prohibit their use in young males and females. It is, therefore, of paramount importance to find an agent which will be effective in the treatment of this disease in all age groups, but which might eventually be specifically useful in the treatment of the younger age groups.

The aim of this study is to evaluate the efficacy of HU (a non-mutagenic, noncarcinogenic agent) in preventing and controlling the symptoms of thrombosis and bleeding with 1) the clinical entity primary thrombocythemia, 2) those patients with myelofibrosis-myeloid metaplasia with elevated platelet counts, 3) those patients with unclassified myeloproliferative disease with elevated platelet counts.

Technical Approach:

The details are lengthy and specified in the Polycythemia Vera Study Group protocol. Duplicates are kept on file in the Department of Clinical Investigation and are available upon request.

Progress:

Study has been completed.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/63 Status: Completed

Title:
Effects of Beta-2 Agonist on Codeine 48/80 Induced Skin Reaction

Start Date: Est Comp Date:

Principal Investigator: Facility:
MAJ S. Ting, MC

Dept/Sec: Dept Medicine Assoc Investigators

Key Words:

B-2 agonist; Skin reaction

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To determine whether locally applied $B_2$ agonist suppresses the histamine release induced by codeine and 48/80 in human allergic skin reactions.

Technical Approach:

Ten adult volunteers will be selected from the Allergy Clinic. Skin testing will be performed with codeine 1%, 48/80, 10 mg/ml and terbutaline
Skin testing injections:

0.02 ml of 1% codeine or 1% 48/80
0.02 ml of PBS PNU/cc
0.02 ml of 1% codeine and terbutaline 2 ug/ml
0.02 ml of terbutaline 2 mg/ml (final concentration).

Wait fifteen minutes and record the size of the wheals and flares. Proceed to skin blister technique for measurement of histamine release.

Progress:

Study was completed.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/64 Status: Completed

Title:
Effects of Propanolol on Terbutaline Suppression of Allergic Skin Reaction

Start Date: Est Comp Date:

Principal Investigator: Facility:
MAJ S. Ting, MC

Dept/Sec: Dept Medicine Assoc Investigators

Key Words:

Propranolol; Terbutaline; Skin reactions

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To determine whether locally applied propanolol inhibits terbutaline suppression of histamine release in human allergic skin reactions.

Technical Approach:

Twenty adult patients will be selected on the basis of a 4+ positive prick skin test to ragweed allergen from the Allergy Clinic. Skin testing will be performed with ragweed, terbutaline and propanolol.

Skin testing injections:

0.02 ml of ragweed 1000 PNU/cc
0.02 ml of ragweed 1000 PNU/cc and 0.02 ml of terbutaline 2 ug/ml.
0.02 ml of ragweed 1000 PNU/cc and 0.02 ml of terbutaline and propranolol 2 ug/ml (FC).
0.02 ml of PBS

Wait fifteen minutes and record sizes of the wheals and flares. Proceed to skin blister technique for the measurement of histamine release.

Progress:

This study has been completed.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/01 Status: Ongoing

Title:
A Comparison of Ga-67 Citrate Tc99m MDP and I-111 Labeled White Blood Cells for the Diagnosis of Osteomyelitis

Start Date: Est Comp Date:

Principal Investigator: Facility:
LTC T. Brown, MC

Dept/Sec: Dept Medicine/Nucl Med Assoc Investigators

Key Words:

GA-67 Citrate; Tc99m MDP; I-111 Labeled White Cells

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To compare the sensitivities of Ga-67 citrate, Tc MDP and I-111 WBC in diagnosing osteomyelitis and to determine whether differences in the relative labeling of the radiopharmaceuticals can be used to increase the specificity of the scintigraphic diagnosis of osteomyelitis.

Technical Approach:

New Zealand white rabbits will be anesthetized with 0.8cc of innovar and 0.2cc of atropine. The right hindleg will be shaved and an 18 ga needle introduced into the right femur. One tenth cc of sodium morrhuate and 0.1cc of a suspension of Staphylococcus aureus will be introduced. At the end of four weeks, after appropriate scanning, bacterial culture of bone marrow will substantiate the diagnosis of osteomyelitis. Twenty-one rabbits with presumed osteomyelitis will be divided into groups of three rabbits each. Every two days a group will be imaged with Ga-67 citrate and Tc MDP and then sacrificed. The bone will be cultured to prove the existence of osteomyelitis. Another group of twenty-one rabbits with presumed osteomyelitis will be treated in a like manner except I-111 WBC and Tc MDP will be used for imaging. Images on film will be read by investigators. The first positive image afer initiation with osteomyelitis will be noted for each radiopharmaceutical. A comparison then will be made for sensitivity of each agent for the early states of osteomyelitis. In addition, the images on the computer will be processed to compare relative quantity of each radiopharmaceutical at the site of osteomyelitis.

Progress:

Principal investigator was transferred to Walter Reed and the principal investigator has been changed to LTC T. Brown. Published in the Journal of Nuclear Medicine 24:110-113, 1983.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/06 Status: Completed

Title:

Evaluation and Comparison of the Performance Characteristics of Amerlex and Clinical Assays Free T-4 RIA Kits.

Start Date: Est Comp Date:

Principal Investigator: Facility:

Augustine Solis, DAC

Dept/Sec: Dept Medicine/Nuc Medicine Assoc Investigators

Key Words:

T-4 RIA Kits

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

To determine the relative capability of Free T-r RIA assays by Amersham and Clinical Assay to accurately measure free thyroxine concentrations in human serum.

Technical Approach:

To determine if two new methods for assessing free thyroxine are accurate and reliable, results obtained using these methods will be compared with results obtained using equilibrium dialysis, which has been the standard method for assessing free thyroxine.

The following type and number of samples will be evaluated.

a. Ten euthyroid patients obtained from Blood Bank samples.
b. Ten hypothyroid patients.
c. Ten hyperthyroid patients.
d. Ten pregnant patients.

No subjects to be employed as controls.

Free thyroxine of all samples will be determined using equilibrium dialysis, clinical assays, and Amersham's Free T-4 RIA kit. Correlation of all data and determination of the accuracy and reliability of the two ket methods to assess free T-4 in the four conditions sated above.

Progress:

Both Amersham's and Clinical Assay's Free T-4 RIA Kits were found to be accurate in assessing free thyroxine. There was good correlation between the two kit methods and the free thyroxine index.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/08 Status: Ongoing

Title:
The Evaluation of Two Central Venous Lines Inserted Through One Venipuncture Site

Start Date: Est Comp Date:

Principal Investigator: Facility:
MAJ B.L. Feaster, MC

Dept/Sec: Dept Medicine Assoc Investigators

Key Words:

Venous lines

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

Evaluate the use of the insertion of two central venous lines through one central venipuncture site as a viable alternative to critically ill patient who requires several central venipuncture for central intravenous access. This technique would reduce the number of venipunctures and concomitant morbidity.

Technical Approach:

The study will include 200 patients consecutively admitted to the Medical Intensive Care Unit of WBAMC, requiring central venous lines. They will be randomized on an alternating basis into study group (two central lines through one venipuncture) and control group (one central line through one venipuncture).

Progress:

Principal investigation has PCSd and the new investigator will enter patients into this study in FY84.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/10 Status: Ongoing

Title:
An Investigation of Immunological Reaction to Human Serum Albumin

Start Date: Est Comp Date:

Principal Investigator: Facility:
LTC L.E. Mansfield, MC

Dept/Sec: Allergy/Immunology Svc Assoc Investigators

Key Words:

Immune reaction; HSA

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To determine whether allergy patients receiving injections of allergy extracts containing human serum albumin develop evidence of IgE or igG antibodies directed towards human serum albumin.

Technical Approach:

Evidence of IgE reactivity will be sought by performing intradermal skin tests with the diluent containing 0.03% HSA. These will be performed on consenting individuals who have received injections of allergy extracts from the Army Central Extract Laboratory for a period of one year. Patients will be asked to refrain from antihistamines for 3 days before the skin tests are performed at the same time on the opposite arm. The tests will be placed on the lateral aspect of each upper arm. Wheal and flare for both will be measured and recorded. Any patient who develops a wheal and flare reaction with the injection of the diluent will have blood drawn to perform a RAST and blocking antibody measurement against human serum albumin. In addition, every tenth patient who is skin tested will have blood drawn for specific IgG and IgE antibodies directed towards human serum albumin.

The presence of specific IgG antibodies will be assessed by the performance of a double antibody precipitation test in which the same preparation of human serum albumin employed in the diluent will be radioiodinated, added to a dilution of the patient's serum, to which, after appropriate incubation, will be added an anti-human IgG to precipitate the patient's IgG and any combined radiolabeled human

serum albumin.

RAST: Radioallergosorbent testing will be performed with HSA bond to cellulose disks by the cyanogen bromide technique. Commercial I-125 antihuman IgE will be employed. Positive control will be provided by heterologous antihuman HSA and radiolabeled antisera directed twoards the IgG of that species.

Progress:

Fifty patients have been entered into this study.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/12 Status: Terminated

Title:
Double-Blind Placebo Controlled Clinical Trial of Pseudomonic Acid (BRC 4910A) in the Treatment of Skin Infections

Start Date: Est Comp Date:

Principal Investigator: Facility:
LTC Pryor(Adelman)

Dept/Sec: Dept Medicine Assoc Investigators

Key Words:

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

TECHNICAL APPROACH:

Never started.

PROGRESS:

None. Terminated.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/19 Status: Ongoing

Title:
Characterization of Bronchodilator Activity of Inhaled Dyphlline

Start Date: Est Comp Date:

Principal Investigator: Facility:
LTC L.E. Mansfield, MC

Dept/Sec: Dept Medicine/Allergy Cl Assoc Investigators

Key Words:

Dyphlline

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To determine if dyphylline can be used as an inhaled bronchodilator and to characterize the response for possible clinical application.

Technical Approach:

Ten adult asthmatic, nonpregnant, and not of child bearing potential subjects will be entered into this study. Their asthma will be sufficiently moderate so that they can withhold their usual morning dose of bronchodilators. They will report to the Allergy Clinic at 0800. Baseline pulmonary functions, including conventional spirometry, flow volume curves, and total respiratory resistance will be measured. Serum will be drawn for a theophylline level. The subject will then inhale to completion through a nebulizer (Devilbis 646) with a pulmonaid compressor a solution containing 1 mg/kg of dyphylline (with normal saline added to make a 5 ml total volume). Patients will be observed for any possible adverse reactions such as tachycardia, nausea, or headache. Pulmonary function will be remeasured immediately after finishing the treatment, and at 15, 30, 45, 60, 90, 120, 180, 240 minutes post-treatment. A repeat theophylline level will be obtained at 30 minutes post-treatment. In as many individuals as technically possible, determinations will be continued for 300,360,420, and 480 minutes. Where this will not be possible, a portable peak flow meter will be given to the subject to record PEFR at these time intervals. At any point where the subject notices distress, or in the opinion of the physicians further bronchodilation is indicated, then inhaled albuterol will be used.

In each of the subjects, the same procedure will be repeated at a dose of 3 mg per kg, 5 mg per kg, and 7 mg per kg. Rather than randomize the sequence of doses, it is the investigator's opinion that for the safety and comfort of the volunteers, this progressive dose exposure is more prudent. Therefore, on three other separate individual occasions, the same methodology and parameters will be used to determine the response to these larger doses.

It is estimated that the nebulization system used will deliver between 5-10 percent of actual dose to the patients, so that the effective delivered dose will be 0.1, 0.3, 0.5, 0.7 mg/kg. The usual systemic oral or parenteral doses are between 5-10 mg/kg q6-8h for dyphylline.

During each session subjects will be closely observed for tolerance of the treatment, the side effects and adverse reactions as described above. The unique taste of dyphylline makes the use of a placebo of doubtful value. Data for the expected response of a group of moderate asthmatics to placebo (saline inhalation) is available in the medical literature.

Dose response and durations of effect curves will be plotted.

Progress:

No patients have yet been entered. Technical aspects of this study are complete.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/20 Status: Ongoing

Title:
Tissue Distribution in Pregnant Lactating Sheep of the Six Most Commonly Ued Radiotracers

Start Date: Est Comp Date:

Principal Investigator: Facility:
CPT M.A. Yedinak, DO

Dept/Sec: Dept Medicine/Nuc Med Assoc Investigators

Key Words:

Radiotracers

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To determine tissue distribution patterns of six of the most commonly used radiopharmaceuticals in pregnant sheep. Second, to determine, if possible, the effects of Delta-9-tetrahydrocannabinol (D-9-THC) on tissue distribution and relative perfusion. Third, to calculate the percentage of dose of radiotracer to breast, placenta, and fetal tissue.

TECHNICAL APPROACH:

Twelve pregnant sheep at approximately 131-143 days' gestation will be studied in six sets of two sheep/set. Six different radiopharmaceuticals will be used, one for each set of two sheep. Within each set sheep will be imaged with and without Delta-9-THC. The following is a set by set design.

SET I (99mTc & PYP)

Sheep #1 and 2 will be injected with 99mTc and PYP in a normal resting state and first pass and MUGA studies will be performed. A computer generated first pass and EF (ejection fraction) will be calculated. The breasts, placenta and fetus will be imaged for blood pool activity and a time activity-curve will be obtained. This data should supply relative perfusion to the fetus via the placenta. Specimens will be taken of serum to determine concentrations of radiotracer. The sheep will be studied one day before and one day after catheter placement (see Protocol 82/57) and immediately before and 30 minutes following a 0.5 mg/kg dose of Delta-9-THC. EFs and flows will be compared for drug effects on ejection fraction and placental perfusion.

SET II (99mTc-GLHP)

Sheep #3 and 4 will be injected with GLHP and tissue distribution patterns for brain, breast, renal, placenta and fetal areas will be observed at the same time designated in Set 1.

SET III (99mTc MDP)

Sheep #5 and 6 will be injected during the control periods with MDP (Bone Agent), and two hours later imaged for distribution to breast, placenta and fetus. They will be injected with MDP one hour post-injection with 0.5 mg/kg of D-9-THC and imaged.

SET IV (mmTc DISI)

Sheep #7 and 8 will be injected with DISI (hepatobiliary agent) and breast, placenta, fetus and liver/spleen will be imaged at the control times. They will be injected with DISI 30 minutes following injection with 0.5 mg/kg of D-9-THC and imaged. Blood will be drawn for estrogen and progesterone levels.

SET V (99mTc-Folate)

Sheep #9 and 10 will be injected with tracer-labeled folate to determine normal distribution patterns for this tracer. Particular interest will be focused on breast, placenta and fetus. Depending on control results, they will be injected with radiolabeled folate either before or following injection with D-9-THC and imaged as before

SET VI (Ga-67 Citrate)

Sheep #11 and 12 will be injected with gallium citrate and imaged at 24, 48, and 72 hours post-injection. Areas of interest will be the breast, placenta and fetus. Breast milk samples will be taken at 24, 48 and 72 hours and radiotracer concentrations determined. Upon sacrifice of the experimental animals, specimens will be taken of breast, placenta, cord, and fetus to be used for determination of radiotracer concentrations and autoradiographs will be made to localize tracer accumulations.

If possible, breast milk will be obtained in the other group for radiotracer quantitation. In each group, if resources permit, references at the 0.25 mg and 1.0 mg/kg doses (see protocol 82/57) will be studied.

PROGRESS:

GA 67 study has been eliminated. Remainder of the study will be finished when near-term sheep are available in Spring 84.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/24 Status: Ongoing

Title:
Measurement of Salivary Histamine

Start Date: Est Comp Date:

Principal Investigator: Facility:
MAJ S. Ting, MC

Dept/Sec: Dept Medicine/Allergy Cl Assoc Investigators

Key Words:

Salivary histamine

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To determine whether salivary histamine levels will provide an additional modality for recognition of allergic patients.

Technical Approach:

1. Collect saliva from 100 non-atopic individuals
2. Collect saliva from 100 atopic individuals
3. Collect saliva from 100 atopic individuals on immunotherapy
4. Determine salivary histamine levels.
5. The volunteer will be asked to rinse the mouth with lemon juice, 1 teaspoonful for 1 minute and then spit out the saliva into a container provided.

Progress:

Collection of 40 samples has been completed, awaiting analysis of histamine.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/32 Status: Completed

Title:
Usage of a Non-narcotic Agent (Dexmethorphan) as a Positive Control Skin Testing Reagent in Routine Allergy Skin Testing

Start Date: Est Comp Date:

Principal Investigator: Facility:
MAJ S. Ting, MC

Dept/Sect: Dept Medicine/Allergy Cl Assoc Investigators

Key Words:

Dexmethorphan; allergy

| Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results |
|---|---|---|

Study Objective:

To evaluate whether non-narcotic agent, Dextromethorphan, can replace narcotic agents, such as morphine or codeine, as a positive control skin testing reagent in routine allergy evaluation.

Technical Approach:

Twenty adult volunteers will be tested with a scratch skin testing with dextromethorphan and codeine with wheal and flare skin responses measured in $mm^2$ by electronic planimeter. Intradermal skin testing with dextromethorphan and codeine with measurement of wheal and flare.

Progress:

Completed. Accepted for presentation at the American Academy of Allergy Meeting in 1984.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/35 Status: Completed

Title:

The Effects of Changes in Leisure Time Satisfaction on Work Performance and Job Satisfaction

Start Date: Est Comp Date:

Principal Investigator: Facility:
1LT D.J. Ward, AMSC

Dept/Sec:Dept Medicine/Allergy Cl Assoc Investigators

Key Words:

Job Satisfaction

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To determine if attendance in group sessions designed to increase leisure time satisfaction will lead to improved satisfaction and performance in the work place.

Technical Approach:

Ten members of the Allergy-Immunology Immunization Service staff will participate in this study on a voluntary basis. A questionnaire on job and leisure time satisfaction will be completed prior to the study. Concurrently 400 patients from the Allergy Immunology Service will answer the outpatient questionnaires. Three hundred patients will be from the Allergy-Immunology Section and 300 patients from the Immunization Section. This evaluation of subjects and patients will be repeated at 3,6,9 and 12 months after the study has commenced in the same manner. A grading scale of +2 and +1 for a positive answer, 0 for a neutral answer, and -2 and -1 for a negative answer will be used to grade the questionnaires. A positive group score greater than the previous testing will be indicative of improvement. Scores will be analyzed by analysis of variance. Individual areas, as well as global scores, will be evaluated.

Formal training education sessions of 45 minutes to one hour on eight occasions (on a biweekly basis) will include a) Effects of an imbalanced work/leisure pattern. b) What is a balanced work/leisure pattern? c) Assessment of current leisure usage and satisfaction. d) Future leisure plans. e) Presentation of future leisure plans to group members for feedback. f) Leisure time management group. g) Overcoming barriers/excuses group. h) Conclusions and summation.

Progress:

Completed

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/36 Status: Ongoing

Title:
Prospective Study of Clinical, X-Ray, Histologic, Scintigraphic and Microbiological Characteristics of Diabetic Feet

Start Date: Est Comp Date:

Principal Investigator: Facility:
MAJ John Baker, MC

Dept/Sec:Dept Medicine/Infectious Dis Assoc Investigators

Key Words:

Diabetic feet

| Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results |
|---|---|---|

Study Objective:

To correlate specific x-ray, scintigraphic, clinical and microbiologic characteristics with each other and with the histology of the diseased diabetic foot so that clinicians may better manage their patients.

Technical Approach:

The technical approach is very lengthy and may be reviewed in the Dept Clinical Investigation

Progress:

Personnel constraints preclude activation of this study at the present time.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/37 Status: Ongoing

Title:
Cardiopulmonary Effects of Stressful Exercise at 4,000 feet on SCT Individuals

Start Date: Est Comp Date:

Principal Investigator: Facility:
MAJ I. Weisman, MC

Dept/Sec: Dept Medicine/Pulmonary Cl Assoc Investigators

Key Words:

Sickle cell trait; stress

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

a. To establish baseline pulmonary function data (spirometry, helium dilution lung volumes, Maximum voluntary ventilation L/min (MVV), Arterial blood gas analysis (ABG), single breath diffusing capacity $D_LCO_{SB}$ (ml/min/mmHg) and steady state diffusing capacity $D_LCO_{SS}$ (ml/min/mmHg) (Filley technique) as well as values for the partial pressure of oxygen at 50 saturation (mmHg) ($P_{50}$) in Hgb AS individuals and controls and to determine percent Hgb S and percent Hgb F in individuals heterozygous for sickle cell trait (Hbg AS) at 4000 ft.

b. To carefully document cardiopulmonary response of individuals identified as having Hemoglobin AS during both strenuous incremental and submaximal steady-state exercise at altitude with age, race, sex, smoking, matched non-Hgb AS controls.

c. To correlate observed abnormalities (if any) in parameters of cardiopulmonary performance with levels of Hgb S in individuals with sickle cell trait (i.e. are patients with ≥40 percent of Hgb S more likely than controls to experience abnormalities during vigorous exercise. Also, to determine whether Hgb F levels may be protective as they are in patients with sickle cell disease.

d. To determine whether conditioning (repeat studies after six weeks) is operative in modulating cardiopulmonary performance in both SCT individuals and controls.

e. Conclusive data is not anticipated from this protocol, but a preliminary statement or suggestion may be offered on the important question of occupational restriction of subjects with Hgb AS. This is in keeping with the National Academy of Science - National Research Council's Report of 1973 [1].

Technical Approach:

Phase I (Initial Screening): Approximately 30-35 heterozygous sickle hemoglobin individuals (AS) and a similar number of age, race, smoking, physically conditioned matched normal volunteers (AA) to be used as controls will be studied. Hopefully, the numbers of participants will be screened from incoming recruits at Ft Bliss (four Hgb AS subjects - four normal controls/month). An initial positive screening blood test (modified Sickledex) will be followed up by hemoglobin electrophoresis and Hgb S and Hbg F quantification in order to exclude the possibility of actual SS disease itself and sickling variants other than hemoglobin AS (i.e., Hgb SC, sickle thallasemia, etc). Previous studies have failed to fully characterize the nature and quantity of Hgb S present in patient populations.

Once identified, the Hgb AS individuals as well as subjects to be used as normal controls will be asked to participate in the study acknowledging by signed informed consent.

Phase II. Prior to the initiation of exercise the following will be performed on the Hgb AS and control subjects. a) History and physical exam with chest x-ray. b) Blood work - baseline CBC, peripheral smear (best method to be determined in order to quantify and compare with samples taken during exercise), G-6-PD screens, SMA-20 including CPK and aldolase, and serum osmolality. c) Urine-baseline, urinalysis and urine osmolality, checking specifically for concentrating defects, RBCs in urine, etc. d) Baseline pulmonary function tests to include (1) spirometry (2) MVV (3) helium dilution lung volumes (4) $D_LCO_{SB}$ (1-4 to be performed on pre-existing Collins-DS-520) (5) a resting ABG, 100 $O_2$ ABG study (to determine percent RÔ L shunt) (6) $P_{50}$ value (7) 2,3 DPG level. (8) baseline 12-lead EKG - individuals with abnormal baseline EKG (to be determined by staff cardiologist) and Hgb AS individuals with abnormal EKGs will not be included in this study. They will be referred to Cardiology for appropriate evaluation which may include being exercised in the cardiac cath lab (questionable data to be included in this study).

Individuals with EKGs interpreted as either sinus bradycardia and/or "early repolarization" phenomenon will be exercise-studied according to this protocol.

Individuals with abnormal baseline PFTS and normal EKGs will be exercise-studied.

Phase III. Exercise protocol - preliminary.

a. Preliminary. 1) Informed consent will be obtained from all participants. Both the M.D. and the exercise technician will be blinded as to whether the eight patients being studied monthly (4/4)

are AA or AS respectively).2) Individuals will have an indwelli arterial (either radial or brachial) cannula placed with a three stopcock and slow or intermittent heparin infusion at a concentr tion of 1000 u/100 ml diluent. An arterial line will allow for measurement of $PaO_2$, $PaCO_2$, $SaO_2$, pH, $HCO_3$ as well as allowing for additional blood sampling (i.e. lactate levels) during e cise. 3) A two-lead EKG signal integrated into the exercise sy will be used with continuous oscilloscope display screen as well trip recorders in the event an abnormality is noted on the scree during exercise (A physio-control lifepak with a Hewlett-Packard corder). 4) An ear oximeter will be placed on the ear lobe and held in place with head straps allowing for the monitoring of Sa and trending phenomena in $SaO_2$ appreciated during exercise. 5) Several preliminary exercise studies have been performed on pati with hemoglobin AS who were referred because of exercise induced problems in the last five-six months. These patients were studi using the pre-existing automated exercise system in the pulmonar laboratory. This automated system is the SRL Model 7000 Aerobic Measurement System with Model 7500 Treadmill System. This syste incorporates a mixing chamber for expired gas analyses. As a re the readout from the nonprogrammable computer records only the l 20-30 seconds of data from each minute. It is important to note that the workout characteristics of mixing chambers may give err ous results if mixed expired gas concentrations are rapidly chan (i.e. especially with rapidly incremental work rates which will used in this protocol). An exercise system which allows for bre by breath analysis allows one to follow the changes of rapidly i cremental exercise more accurately than a mixing chamber and wou be preferable for our purposes. The Medical Graphics Corporation (MGC) System 2000B Cardiopulmonary exercise module would satisfy requirements of this protocol design. A $D_LCO_{SS}$ (MGC) apparatus can be interfaced with the breath by breath exercise system with difficulty. With our present system it is not possible to retri data not initially requested because there is no memory bank in present computer. The computer is nonprogrammable and the data file is that which accompanies the system and not necessarily wh the investigator needs.

A treadmill for the purpose of pulmonary exercise, especiall with healthy, otherwise normal individuals, appears to be subopt compared to a bicycle ergometer where the position of the head i more stationary allowing for better control of the ear oximeter the mouthpiece. 6) The patient will be allowed to familiarize self with the equipment - treadmill or cycle ergometer and espec ly breathing through a low resistance, low dead space mouthpiece (Keogh or Lloyd). Exercise will be performed with a technician trained in CPR as well as an M.D. present.

Exercise protocol:

The exercise protocol is a one-minute incremental exercise to exhaustion over a 6' - 10' interval [16]. [illegible] baseline measurements of minute ventilation, heart rate, mixed expired $PO_2$ and $PCO_2$ are established, exercise begins. The individual exercises at workloads increasing by 150 kpm ( equivalent 25 watts ) at one minute intervals. Minute by minute readout of the following parameters will be evaluated: Mixed expired $PO_2$ and $PCO_2$, tidal volume (T.V.), respiratory rate (RR), minute ventilation ($V_E$), $VO_2$ (oxygen consumption), $V_{CO_2}$ ($CO_2$ consumption) RQ = respiratory quotient ($VCO_2/VO_2$), heart rate.

(H.R)., $V_D/V_T$, (dead-space ventilation). At [illegible] anaerobic threshold, ABGs and a lactate level are drawn from the arterial line. When the patient signals exhaustion another sample will be obtained and the test will be discontinued. Factor VIII levels will also be drawn. The highest Minute ventilation($V_E$) (Respiratory rate X tidal volume) oxygen consumption $V_{O_2}$(L/min) and heart rate (H.R.) recorded will be considered the maximal $V_E$, max $VO_2$ and max H.R. With rapid incremental exercise the individual will recover quickly and can be restudied in 30-45 minutes.

Recovery ABGs as well as above parameters will be obtained at that time.

b. After approximately 30-45' from completion of the rapidly incremental exercise test, the individual will perform a resting $D_LCO_{SS}$ maneuver (Filley modification of steady state technique) to be used as baseline. Subsequently the individual will work at a steady state submaximal level (ä 50 of Vo2-max established by incremental study) capacity for another 6' during which an exercise $D_LCO_{SS}$ will be performed. A repeat ABG in order to obtain PaCO2 and enable $V_D/V_T$ determination will be obtained. Minute by minute printout of the PeCO2, PeCO, PACO will be obtained with particular attention to the data generated during the last 1/2 to 1 minute of the steady state exercise. From the above measurements minute by minute $D_LCO_{SS}$ will be computed [18].

c. Repeat incremental exercise test and $D_LCO_{SS}$ at rest and with submaximal exercise after 6 weeks of basic training This aspect of the study is important in terms of establishing whether conditioning may be operative in attenuating the differences if any in the exercise performance of the two groups. In addition, considerable data will be generated in the control population which will enable objective determination of conditioning responses which may be of assistance to the Department of the Army.

Phase IV. Evaluation of data:

a. Consent forms and all other data generated from WBAMC will be maintained along with exercise study reports in the Pulmonary Service of WBAMC. Copies of this data will be available to appropriate individuals through command channels.

b. Evaluation of data: 1) Results of baseline spirometry, MVV, Helium dilution lung volumes and single breath diffusing capacity will be expressed as a percent of published predicted values. Standard descriptive statistical analysis, involving paired Student t-test and analysis of variance will be performed within and between group differences. The data, especially that generated in the control population, may help serve to establish new predicted values for $D_LCO_{SB}$ and spirometry in black individuals. This is badly needed since those presently available are suboptimal [19]. Dr. Ben Burrows has agreed to serve as consultant for this aspect of the project. 2) Exercise - Criteria established by Jones et al. [16], and Wasserman et al [17] will provide predicted values for indices of exercise performance measured during the study. Gas exchange data during rest and exercise (PaCO2, PaO2, (A-a) PO2, $D_LCO_{SS}$ ml/min/mmHg, $V_E$ l/min, VD/VT, $V_{CO_2}$ (L/min), $V_{O2}$ (l/min) and RQ.) in both the Hgb AS subjects and controls will be analyzed using both Student paired t-test and analysis of variance in order to establish differences between rest and exercise and between the two groups.

Next the Hgb AS group will be categorized according to absolute levels of Hgb S. Correlation of individual parameters with levels of Hgb S will be performed by standard regression analysis in order to determine if the levels can be predictive of abnormal cardiopulmonary response. The exercise physiology laboratory, UCLA, Harborview Medical Center, will serve in a consultant capacity for exercise related questions during the study.

Progress:

Funding and personnel difficulties have precluded the start of this project.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/38 Status: Terminated

Title:
Study of Different Modes of Therapies in Chronic/Repeated Middle Ear Infection: Medical vs Surgical

Start Date: Est Comp Date:

Principal Investigator: Facility:
CPT B. Ting, MC

Dept/Sec: Dept Pediatrics Assoc Investigators

Key Words:

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

WITHDRAWN

Technical Approach:

Progress:

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/40 Status: Ongoing

Title:
Use of Protein Infusion to Decrease Absorption of Chemical Moieties from the Serum and to Establish a Working Model for Protein Therapy: A Pilot Study

Start Date: Est Comp Date:

Principal Investigator: Facility:
MAJ G.D. Griffin, MC

Dept/Sec: Assoc Investigators

Key Words:

Protein infusion

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

Use of protein infusion to decrease absorption of chemical moieties from the serum and to establish a working model for protein therapy.

Technical Approach:

In this pilot study dogs will be used as the model. After determining the normal protein levels, dogs will be overdose on ASA to a level of 240 mg/kg. Serum toxic level will be a guide to use as baseline. Determination of ASA and protein level in serum and urine. Levels will be drawn every 15 minutes for four hours to determine baseline and normal progression of the serum ASA and protein levels. Other parameters measured are osmoles SMA-6 ph in urine and serum and respiratory rate, heart rate, and blood gas. After determining base parameters as above the animals will be re-dosed to 240 mg/kg and will be given continuous IV protein infusion of dog albumin. The above serum levels will then be repeated to determine if the exogenous protein changes the concentration of the protein bound drug in the serum, as well as in the tissues. The time interval between baseline determination and redosing depends on the above results - ie., when serum ASA levels are zero redosing occurs. Urine samples will be obtained by catheterization. Sex of the animal should not matter. Each experiment is anticipated to last about 16 hours from beginning to end, and there will be a total of three sixteen hour runs. The three sets of data will then be analyzed and compared.

PROGRESS:

One experiment has been completed

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/42 Status: Ongoing

Title:
The Incidence of Papain and Bromelain Hypersensitivity in an Allergic Population

Start Date: Est Comp Date:

Principal Investigator: Facility:
LTC L.E. Mansfield, MC

Dept/Sec: Dept Medicine/Allergy Cl Assoc Investigators

Key Words:

Papain/Bromelain hypersensitivity

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

To determine the degree of papain and bromelain sensitization in an allergy clinic population; to determine the clinical relevance of such sensitization.

Technical Approach:

Volunteers from the Allergy-Immunology Clinic who have a 3+ or 4+ wheal and flare response to prick/puncture cutaneous allergy testing with 1 mg/ml papain or bromelain will be entered into this study. Patients who believe they have had a life threatening reaction from papain or bromelain ingestion will not be studied. Pregnant patients nor potentially pregnant patients will not be studied. Patients with serious medical problems will be excluded from tne study.

Patients will received a capsule containing papain/or bromelain in an amount used to tenderize an average 8 oz steak, depending on skin test results. If both are positive a second open challenge day will be performed. They will be observed for one hour post-ingestion and given a diary sheet to take home for recording any unusual symptoms over the next 24 hours. If signs or symptoms apper the subject will enter a single blinded phase of the study. They will return on four to six occasions to receive a capsule. This capsule will contain either papain/bromelain or placebo. This procedure will be performed in a single blind fashion. Finally, if any of the symptoms reported are vague, a similar double blind challenge will be instituted instead of single blinding.

Vague symptoms are considered subjective changes such as feeling tired, aching, etc. In general signs and symptoms likely to be observed include urticaria, asthma, rhinitis, headache, nausea, diarrhea and vomiting. Since these subject have not been avoiding tenderizer in their day to day life, it is highly improbable that a more severe previously undetected reaction will occur. The results will be analyzed to gather the following data: Prevalence of sensitization to pain and bromelain in an allergy population; whether people sensitive to one tenderizer are more likely to be sensitive to both; whether this sensitization is clinically meaningful; what is the frequency of clinically meaningful sensitization?

PROGRESS:

Ground work is complete. 412 patients entered into the study. Ten patients had double blind challenges. Three challenges were definitely positive, two were equivocal. Data is now being formulated for an abstract for presentation to the American Academy of Allergy and Immunology. Preliminary work on the manuscript has been performed.

Detail Summary Sheet

Date: 1 Oct 83 Prot No 83/43 Status: Ongoing

Title:

The Incidence of Immediate and Prolonged Bronchoconstriction Following the Use of Metered Dose Inhaler Beta Adrenergic Agents

Start Date: Est Comp Date:

Principal Investigator: Facility:
Ms Josephine Yarbrough, RN

Dept/Sec: Dept Medicine/Allergy Cl Assoc Investigators

Key Words:

Metered dose beta-adrenergic agent

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

To determine how frequently the use of a metered dose inhaler (MDI) bronchodilator is associated with a bronchoconstrictive response. To investigate the nature of the response.

Technical Approach:

Routine bronchodilator responses will be measured in 500 consecutive patients after metaproternol sulfate (MDI) in the Allergy Clinic. A similar testing procedure will involve inhaling the inert ingredients in the MDI by patients who demonstrated a bronchoconstrictive response to either the alkbuterol MDI or metaproternol MDI.

In the second phase it is hoped to obtain special inhalers, if available, where one or more of the inert ingredients have been removed and challenge the responding patients in a more selective fashion. In patients having a bronchoconstriction to albuterol MDI using albuterol through a turbospinhaler device will be used. In patients having a bronchoconstrictive respoonse to MDI-metaproternol, an air driven in nubulizer solution will be used.

Progress:

Routine bronchodilator responses were measured in 560 patients after using metaproternol sulfate (MDI) in the Allergy Clinic. Out of 560 patients 82 experienced a fall in $FEV_1$. Thirty-one our of 82 patients were children ranging in age from 4 to 17 years.

Children's mean Pre $FEV_1$ = 2.22 S.D. = 0.77
Post " = 1.99 S.D. = 0.72
% =12.55 S.D. = 9.93

Adult's mean Pre $FEV_1$ = 2.56 S.D. = 0.68
Post " = 2.26 S.D. = 0.71
% " =12.28 S.D. = 13.05

Presently working on the second phase of this investigation using special inhalers and challenging patients in a more selective manner.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/46 Status: Ongoing

Title:
An Evaluation of Possible Effects of Hepatitis Vaccine on Selected Immune Parameters

Start Date: Est Comp Date:

Principal Investigator: Facility:
LTC L.E. Mansfield, MC

Dept/Sec: Dept Medicine/Allergy Cl Assoc Investigators

Key Words:

Hepatitis vaccine

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To determine whether the administration of hepatitis vaccine is associated with changes in selected immune functions.

Technical Approach:

Approximately 200 patients have partially or completely been immunized against Hepatitis B at our clinic. As many of these patients in the various stages of immunization as possible will be contacted and the nature of the study explained. They will be asked to donate 20 ml of blood from which the following laboratory studies will be done:

1. Hepatitis B antibody titers
2. Total immunoglobulins G, A, M, E
3. Serum protein electrophoresis
4. CBC with WBC
5. Delayed hypersensitivity skin testing to Trichophyton, Candida albicans, tetanus toxoid
6. T-lymphocytes measured by monoclonal antibody OKT3 and the subsets OKT4 and OKT5.
7. B-lymphocytes by surface immunoglobulin markers to include IgM, IgG, IgD.

These results will be compared to known normal values for these measurements which consider age and sex. If there is a suggested abnormality of any parameter, it will be pursued in a Phase II study wherein pre- and post-immunization values will be obtained in the same subject.

Progress:

The FACS machine has been successfully operated. We are awaiting reagents.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/48 Status: Ongoing

Title:
Use of an Enzyme-Linked Immunosorbent Assay (ELISA) for Detection of Microabluminuria

Start Date: Est Comp Date:

Principal Investigator: Facility:
LTC Richard A. Banks, MC

Dept/Sec: Dept Pediatrics Assoc Investigators

Key Words:

ELISA; Serum albumin

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To evaluate the reliability of an ELISA in measuring microalbuminuria in patients with insulin-dependent diabetes mellitus (IDDM), in an effort to detect early changes in renal integrity.

Technical Approach:

There will be several phases in the overall investigation which is proposed. The initial phase will be the development of a reliable and sensitive ELISA for urinary albumin in the range of 10-1000 ng/100 ul. ELISA has been shown to detect antigen concentrations down to 1 ng/ml. Specifically, an attempt will be made to develop both a direct competition and double antibody sandwich assay as described in a standard methods manual for ELISA.

A direct competition ELISA will be performed by attaching anti-human albumin to the microplates with a coupling buffer, and then overlaying these with an unknown amount of unlabelled albumin and a known quantity of horse-radish peroxidase (HRP)-tagged albumin. In the double antibody sandwich technique, goat anti-human albumin is attached to the plates, overlayed with an unknown quantity of albumin. This is washed off after a fixed period and rabbit anti-human albumin antibody added. After incubation, this is removed and goat anti-rabbit immunoglobulin antisera tagged with HRP is added. In both assays a substrate is added and the color change, which occurs, is quantitated. Standard curves are then drawn up.

After the procedures have been established, reproducibility and recovery studies using the scheme outlined by Barnett et al will be performed. This consists of 20 once-a-day analyses of a standard aqueous solution of human albumin, and recovery studies in triplicate at three different levels. A protein determination using the BIORAD Kit will be done at the same time to serve as the reference method. Once sensitivity and reliability have been investigated, one of the techniques will be selected for the next phase.

If the initial phase is successful, urine samples obtained from patients with IDDM will be studied. To ensure the availability of adequate samples, aliquots of 24-hour urine collections will be obtained on pediatric patients with IDDM who are followed by the Pediatric Endocrine Clinic WBAMC and University of Florida, Gainesville. These samples will be submitted ao analysis of microalbuminuria, creatinine, and beta-2-microglobulin. A separate protocol will be submitted prior to initiation of this phase of the study.

Progress:

This is a newly approved project and has not begun as yet.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/49 Status: Ongoing

Title:
Placental Transfer of Radiopharmaceutical and Fetal Radiation Exposure

Start Date: Est Comp Date:

Principal Investigator: Facility:
CPT M. Yedinak, DO

Dept/Sec: Dept Medicine/Nuc Med Assoc Investigators

Key Words:

Placenta: Radiopharmaceuticals

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To determine uteroplacental transfer of selected radiopharmaceuticals in an appropriate animal model (near-term pregnant sheep). The radiopharmaceuticals to be studied include Tc-99m$O_4$, Tc-99m RBC, Tc-99m-EHDP, and In-113mCl. A determination of fetal radiation exposure will be made. The qualitative and quantitative assessment of the radiotracer transfer will be investigated.

Technical Approach:

The placenta and fetus(es) will be externalized after appropriate anesthesia, in this case phenobarbitol. The selected radiopharmaceutical will be injected, via maternal vein. An appropriate dose for the agent will be used. During this time the gamma camera will be placed over the placenta, cord, and fetus. Acquisition of the flow portion of the study will be on an A2 portable computer. Computer generated time activity curves will be created over the placentas. Static images will be obtained to qualitatively evaluate the uterus, placenta, and fetus. The length of time for static image acquisition will be determined by the agent used.

Pretreatment and sequential post-treatment serum will be obtained from the mother and fetus to quantitate the radioactivity. In addition, selected fetal and maternal organs will be obtained when the animal is sacrificed in order to quantitate the radioactivity in these organs. The organs to be studied include blood, kidney, heart, lung, liver, muscle, spleen, thyroid, testes or ovary, urine and bladder, stomach and intestines, and placenta. Sacrificing the sheep will be done with phenobarbitol and T-61. Absorbed fractions for photon dosimetry will be calculated using the methods of Brownell and Loewinger. A comparison between the various determined radiation exposures to the organs of each sheep in a group will be made. A chi-square test can be performed. An analysis of variance can also be performed to compare each radiopharmaceutical group with the other.

Progress:

This is a newly activated protocol and no results have been obtained as yet.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/51 Status: Ongoing

Title:

Biodistribution of Tc-99m-Folic Acid in 30 Normal Rabbits

Start Date: Est Comp Date:

Principal Investigator: Facility:
MAJ Albert J. Moreno, MC

Dept/Sec: Dept Medicine/Nuc Med Assoc Investigators

Key Words:

Tc-99m-Folic Acid

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To radiolabel folic acid (pteroylmonoglutamic acid) with Technetium-99m and to characterize the tag using a physical description and chromatographically; to determine qualitatively and quantitatively the biodistribution of Tc-99m-folic acid in healthy rabbits.

Technical Approach:

An investigation will be conducted to determine the optimum labeling conditions for Tc-99m-folic acid. The major factors to be considered are pH. Past experience has shown that the percent of tagged material which will pass throiugh a 0.22 u millipore filter is pH dependent. Also, folic acid appears to be labeled at either basic pH's or acidic pH's. Imaging of sheep with the apparent Tc-99m-folate demonstrated different biodistribution depending on whether the folate was labeled basic or acidic. Additionally at more physiologic pH, the Tc-99m-folate compound apparently disassociated. To isolate the tagged material at varying pH, paper chromatography will be used. The isolated material will further be characterized by U-V spectroscopy and the HPLC with the help of a chemist. The specific procedures for tagging Tc-99m as sodium pertechnetate to folic acid uses a modified stannous chloride method. After a satisfactory radiolabeled folate is achieved, biodistribution studies will be performed using a rabbit model.

Progress:

This is a newly activated protocol and work has not begun as yet.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/25 Status: Completed

Title:
Fears and Misconception of the Hospitalized Child, Ages 3-8: A Descriptive Study

Start Date: Est Comp Date:

Principal Investigator: Facility:
COL E. Sullivan/Carol L. Roberts

Dept/Sec: Dept Nursing Assoc Investigators

Key Words:

Children's fears

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

An investigation to identify the perceptions and major fears of hospitalized children, ages 3-8, with regard to their environmer (e.g. hospital treatments).

Technical Approach:

Identification of common fears and misperceptions in the specif population. Results will be used to formulate appropriate nurs interventions to prevent such misunderstandings and fears.

The study will include a sample of 15-20 hospitalized children, 3-8, who are being hospitalized for the first time for a diagno that is not life-threatening. Phases of the investigation will include a review of medical records for any data regarding fami history which might influence the childs reactions. Also the medical records will provide a diagnosis, history and physical the present illness. Parental permission will be required. An initial interview with the child will focus on getting acquainte well as establishing the child's cognitive level by administeri assessment of cognitive development test to the child.

Parental interview will establish any preparation for hospitalization the child has received. A second interview wit child will include drawing a picture. This will require the ch to draw a picture to help tell other children what it is like t in a hospital. A play session with dolls and common hospital equipment (e.g. syringe, stethoscope) to assist in identifying child's perception and fears of his hospital invironment. Audio-recording of interviews will be compared with cognitive te

Progress:

Completed.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/31 Status: Completed

Title:

The Effects of Various Teaching Methods on Anxiety Experienced During Cardiac Catheterization: A Pilot Study

Start Date: Est Comp Date:

Principal Investigator: Facility:
COL E. Sullivan(Connie Popper)

Dept/Sec Dept Nursing Assoc Investigators

Key Words:

Anxiety

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

To determine if anxiety can be reduced in patients during cardiac catheterization by manipulating the teaching method prior to procedures.

Technical Approach:

Subjects in this pilot program will require twelve subjects, ages 25-70. A control group of four subjects will receive no experimental intervention. Four subjects will be provided audiovisual presentation of preparatory information. Four subjects will receive the unit protocol for preparation information. All subjects will be asked to take an anxiety inventory test prior to and immediately following the procedure.

Progress:

Completed.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 77/25 Status: Ongoing

Title:
A Comparison of Phospholipid Levels and Choline Phosphotransferase (CPT) Activity in Amniotic Fluid and Newborn Tracheal Fluid

Start Date: Est Comp Date:

Principal Investigator: Facility:

CPT R. Woodruff, MC

Dept/Sec: Obstetrics-Gynecology Assoc Investigators

Key Words:
Phosphatidylglycerol; Amniotic fluid

COL L.L. Penney, MC
David O. Rauls, PhD, DAC

Accumulative MEDCASE Cost | Est OMA Cost:$200(6111) | Periodic Review Results

Study Objective:

To determine if the level of phosphatidyl glycerol (PG) and phosphatidyl inositol (PI) or the activity of choline phosphotransferase could serve as an accurate index of lung maturity.

Technical Approach:

Amniotic fluid, and neonatal gastric and pharyngeal fluids which are normally discarded, will be analyzed for phosphatidyl glycerol, phosphatidyl inositol, choline phosphotransferase, and magnesium. The levels measured will be correlated with the incidence and severity of neonatal respiratory stress and hyaline membrane disease.

Progress:

Data collection on amniotic fluid is now completed. Neonatal data is currently being collected/correlated.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 80/25 Status: Terminated

Title:
Placental Levels of 5a-dihydroprogesterone in Normal Pregnancy and Those Complicated by Pre-eclampsia

Start Date: Est Comp Date:

Principal Investigator: Facility:

David O. Rauls, PhD, DAC

Dept/Sec: Obstetrics-Gynecology Assoc Investigators

Key Words:
Dihydroprogesterone; Pre-eclampsia LTC F. Theard, MC

Accumulative MEDCASE Cost $6,603 Est OMA Cost:$0 (345) Periodic Review Results

Study Objective:

To determine if placentas of pregnancies complicated by pre-eclampsia have a different concentration of 5a-dihydroprogesterone then those of uncomplicated pregnancies.

Technical Approach:

Placentas from normal and pregnancies complicated by pre-eclampsia will be studied for their content of 5a-dihydroprogesterone. After consent has been obtained from patients who are admitted in labor, the placentas obtained at birth will be drained of blood and the membranes excised. They will then be weighed and, using the mass-spectrometer, presence and concentrations of 5a-dihydroprogesterone will be determined. Concentration of 5a-dihydroprogesterone in pregnancies complicated by pre-eclampsia will be compared to that of normal pregnancies. Twenty patients in each group will be studied intially and the mean levels of 5a-dihydroprogesterone will be compared by Student's t-test.

Progress:

Personnel constraints prohibited work on this protocol.

Detail Summary Sheet

Date: 1 Oct 82 Prot No: 81/03 Status: Ongoing

Title:
Serial Measurement of Serum, Zinc, Magnesium, Copper, Lead, Lithium and Arsenic During Pregnancy.

Start Date: Est Comp Date:

Principal Investigator: Facility:

COL L.L. Penney, MC

Dept/Sec: Obstetrics-Gynecology Assoc Investigators

Key Words:

Trace elements

Accumulative MEDCASE Cost Est OMA Cost: $417(1898) Periodic Review Results

Study Objective:

To determine the serum levels of certain trace elements during each trimester of pregnancy in patients from the El Paso area. Specific goals will include: (1) Comparison of the serum levels of trace elements in two populations of patients, first the U.S. Army dependent population; second the native population of Thomason General Hospital. (2) To establish normal mean levels of zinc, magnesium, copper, lead, lithium, and arsenic at various stages of pregnancy. (3) To suggest future studies correlating the findings of serum levels of trace elements with pregnancy outcome.

Technical Approach:

The plan will be to determine the serum levels of copper, zinc, magnesium, lithium, lead and arsenic during the first trimester, again at 20 weeks gestation, and at term. In addition, fetal levels as determined by cord blood at delivery will be obtained. These values will be compared with nonpregnant controls.

Two separate patient populations will be compared, those of William Beaumont Army Medical Center and those of R.E. Thomason General Hospital. The two populations may reflect different levels of environmental exposure to these trace elements, as well as a possible difference in dietary intake.

a. The study would include approximately 50 pregnant patients from the OB Service, WBAMC, and a similar number of patients from the El Paso County population of RETGH.

b. Controls would be nonpregnant females of similar ages.

c. The investigation would include sampling of 10 cc vacutainer at the following intervals during pregnancy: 1st trimester, mid-trimester, time of labor and delivery, and cord blood at delivery.

d. Sampling of controls at one time.

e. A questionnaire stating the historical data pertinent to each patient will be distributed. This will request the information regarding birth place, location of residence, and employment.

f. Additional control - the studied pregnant patients will be tested at six to 12 weeks postpartum.

Progress:

Sampling is completed and trace element analysis is completed. The data analysis is ongoing.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 81/44 Status: Ongoing

Title:
Effect of Intravenous Terbutaline on Phospholipid Content of Adult Dog Lungs

Start Date: Est Comp Date:

Principal Investigator: Facility:

COL L.L. Penney, MC

Dept/Sec: Obstetrics-Gynecology Assoc Investigators

Key Words:

Terbutaline; Surface active phospholipids

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

This study is designed to determine if intravenously administered terbutaline will cause a change in the concentration of phospholipids known to be important in the surfactant system of adult lungs.

Technical Approach:

Two groups of 8 mixed sex adult beagle dogs each will be used in the study. One group will receive 250 ml of 0.9 percent NaCl intravenously over a 30-minute period; these will serve as controls. One-half of these animals will be sacrificed at one hour, and the other half at four hours. The other group will receive 250 ml of 0.9 percent NaCl containing 0.5 mg of terbutaline intravenously over a 30-minute period and will be similarly sacrificed. Portions of lung and alveolar washings from each animal will be freshly obtained and studied for content of total phospholipid, lecithin, sphingomyelin, phosphatidyl inositol and phosphotidyl glycerol. We will then compare the groups to determine any changes in the phospholipid content over the period of time that we investigated.

Progress:

This protocol was not activated until September 1982. The remaining animals will be entered early in FY83 and the samples analysis is ongoing at this time.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/38 Status: Ongoing

Title:
A Comparison of P.O. Vibramycin with IM Kefzol for Prophylaxis in Vaginal Hysterectomy

Start Date: Est Comp Date:

Principal Investigators: Facility:
CPT J.B. Stanley, MC
MAJ K. Kiley, MC

Dept/Sec: Dept Ob-Gyn Assoc Investigators

Key Words:

Vibramycin; Kefzol; Vaginal hysterectomy

| Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results |
|---|---|---|

Study Objective:

To compare the effectiveness of an inexpensive oral antibiotic to a more expensive and painful method of prophylaxis.

Technical Approach:

Each patient to undergo vaginal hysterectomy at WBAMC will be counselled as to the need for antibiotic prophylaxis and the usual routine for administration. The study will be explained to the patient and if not allergic to either drug, they will be asked to give written consent to join the study group. Upon entering the study group, the patient will receive two capsules at 2400 hours the night prior to surgery and an IM injection prior to going to the operating room. The study will be double blinded with all medications being distributed by the pharmacy after they have randomly selected which patients will be in each group. The two capsules taken by the patient will contain a total of 200 mg of vibramycin or a placebo. Those obtaining the vibramycin will receive an IM injection of normal saline diluted with Solu-B complex to match the color of the Kefzol solution, the next day on call from the operating room. The patient receiving the placebo capsules will receive 1 gm Kefzol IM on call from the operating room, prior to surgery. Oral vibramycin has been selected because no oral cephalosporin has ever been available and vibramycin fits all the criteria for an effective prophylactic antibiotic as set forth by Drs. Duff and Park.

The study will commence as soon as the protocol is approved and will end after 100 patients have been entered. To evaluate the study, the definition of febrile morbidity set forth by the Joint Committee on Maternal Welfare will be used: i.e., an oral temperature of 38C on two separate occasions, exclusive of the first 24 postoperative hours. Any patient developing postoperative complications would be treated with the appropriate methods, whetner they are in the study group or not. Groups will be compared by $X^2$ analysis.

PROGRESS

Patient entry is continuing. The code will be broken when the predesignated number of subjects have completed the study. Approximately 85 patients have been entered, with completion projected in early January 1984. No adverse effects have been noted.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/58 Status: Ongoing

Title:
A Longitudinal Study of T-Cells in Pregnancy

Start Date: Est Comp Date:

Principal Investigator: Facility:
CPT Steven Gardner, MC

Dept/Sec: Dept Ob-Gyn Assoc Investigators

Key Words:

T-cells; pregnancy

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To determine in a longitudinal manner concentrations of helper/inducer, suppressor/cytotoxic and all peripheral t-cells during normal pregnancy.

Technical Approach:

Fifteen to twenty volunteers will be solicited from the Family Planning Clinic at the time they discontinued contraceptive measures. If an IUD or oral contraceptive was in use, baseline samples, and repeat samples at three and six week intervals, will be drawn to ascertain the stability of the controls. Those who conceive will be sampled at 6, 12, 18, 24, 30 and 36 weeks of pregnancy and again 6, 12, and 18 weeks postpartum. A single sample will be obtained during the first stage of labor. Twenty mls of heparinized blood will be removed each time so the total during pregnancy will be 140 ml. The t-cell subsets will be counted using the technique described in reference 1, with minor modifications or utilizing fluorescent activated cell sorting should that equipment be functional in our laboratory by the time the experiment is underway. Paired t-test will be used to determine significance. If possible, a cohort of nonpregnant women will be studied in a parallel manner.

Progress:

Cell sorter has arrived, but technique has not been perfected to date.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/04 Status: Completed

Title:
The Use of Vaginal pH in Simplified Treatment of Vaginitis

Start Date: Est Comp Date:

Principal Investigator: Facility:
CPT S.P. Gardner, MC

Dept/Sec: Dept OB-GYN Assoc Investigators

Key Words:

pH; Vaginitis

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To determine if vaginitis can be empirically treated on the basis of the pH of the vagina.

Technical Approach:

Approximately 300 nonpregnant, nonlactating volunteers with symptoms compatible with vaginitis, i.e., vaginal discharge and pruritus will be solicited from the GYN Walk-in Clinic. The patient will be instructed on obtaining the pH of her vagina. She will take a long cotton tipped applicator and insert it into the vagina for ten seconds. After removal she will swab it across the pH paper provided and return for the nurse to interpret the pH value. This pH test will be repeated by the examining physician. He will take an endocervical culture to rule out gonorrhea, observe the appearance of the vagina grossly and the appearance of the discharge microscopically. A culture using Casman's blood agar will be used to assist in verifying Gardnerella vaginalis. If the pH is less than 4.5, she will receive a seven-day course of Clotrimazole vaginally nightly. If the pH is alkaline then Flagyl will be given at the dosage of 500 mg orally two times daily for seven days. Patients who do not have vaginitis by the criteria will not be treated but will be excluded from the study. Monilial vaginitis will be diagnosed if budding hyphae are seen on KOH smear. Trichomonas vaginitis will be noted by the presence of flagellated trichomonads on saline smear. Gardnerella vaginalis vaginitis will be suspected of foul smelling discharge, few to absent PMNs on saline smear, and presence of clue cells. If none of these criteria are noted but an inflammatory appearance of the vaginal mucosa exists, then she will still be included in the study. All treated patients will be asked to return in two weeks for a vaginal exam and further pH study and will be classified as cured or not by

the same criteria. The results of the initial exam will not be available to the physician doing the followup exam. This information will be compared with the followup exam at a later date. Any patient with persistent symptoms will be managed in standard fashion. Efficacy will be judged on the basis of comparison with known standard cure rates with these agents of greater than 90% when examined ten days after therapy.

Progress:

In a busy emergency room or other general medical primary care facility there are often inadequate facilities and gynecologically inexperienced personnel to fully evaluate vaginal discharge. A simple, rapid screening procedure providing guidance for appropriate therapy is desirable. The vaginal pH has previously been shown to correlate with the type of infection, i.e., a pH of 5.0 or greater is associated with Trichomonas or Gardnerella and a pH of 4.5 or less is associated with Candida. Two hundred eighteen nonpregnant patients complaining of vaginal symptoms checked their own vaginal pH. They were further evaluated by examination with appropriate cultures and wet preps; however, therapy was instituted on the basis of the vaginal pH, i.e, metronidazone for pH 5.0 or greater and clotrimazole for pH 4.5 or less. All patients were given two week followup appointments.

One hundred nineteen patients returned for followup. Ninety seven, or 83%, were noted to have negative symptoms, normal pH and negative wet prep; one culture was positive for Neisseria gonorrhea. One hundred ninety five, or 90%, of the initial patients obtained vaginal pH were consistent with the exam and culture results.

Manuscript has been submitted for publication.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/07 Status: Ongoing

Title:
Single Dose Nitrofurantoin in Asymptomatic and Symptomatic Bacteriuria of Pregnancy

Start Date: Est Comp Date:

Principal Investigator: Facility:
CPT Steven P. Gardner,MC

Dept/Sec: Dept OB/GYN Assoc Investigators

Key Words:

Nitrofurantoin; bacteriuria

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To determine the efficacy of a single dose of nitrofurantoin in eradicating bacteriuria of pregnancy.

Technical Approach:

Initially 200 pregnant patients with an initial routine urine culture showing reater than 50,000 colonies of a single organism per ml will be asked to participate in this study. A repeat midstream clean catch specimen of first morning void will be cultured and a positive result of at least 100,000 colonies of a single organism per ml will enable the patient to be included in the protocol. At least two cultures of greater than 100,000 colonies/ml will be required to define significant bacteruria. A history of risk factors, i.e., prior UTIs, prior genitourinary instrumentation, sickle cell disease, diabetes mellitus and renal anomalies, will be obtained. An equal number of patients with such risk factors should be present in the study, as well as control group and the previous publication evaluating single dose therapy did not indicate increased risk, despite these factors, from the single dose therapy. A urinalysis will be done. Patients with symptomatic disease or physical or urine findings suggestive of upper urinary tract disease will be excluded. Patients with known renal parenchymal disease or creatinine clearance less than 40% will be excluded. Black patients will be advised of the potential of hemolytic anemia if they have G6PD deficiency and will be excluded if they are G6PD deficient, but they will be allowed to participate if they choose, without screening. The patient will be given either one dose of 200 mg of nitrofurantoin in the presence of the clinic

nurse or 100 mg every six hours for ten days, based on odd versus even last digit of the social security number. A repeat culture will be obtained three days later in the single dose group. Any immediate failures will be treated by an appropriate antibiotic for ten days. Followup cultures on all patients will be obtained at monthly intervals to allow identification of recurrences. An initial "cure" will be defined as negative urine cultures three days after completing either single or ten-day dosage. A more significant "cure" rate will be based on culture one month after completing either treatment duration. Cultures will be done by the calibrated loop method. The data will be analyzed by 2x2 contingency tables.

Progress:

Forty-five patients have been enrolled so far. Results have been variable. We need to approach our target number of 200 patients before meaningful results can be detailed.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/09 Status: Ongoing

Title:
Antibiotic Irrigation with Cephoxitin Solution at Cesarean Sect
Effects of Febrile Morbidity

Start Date: Est Comp Date:

Principal Investigator: Facility:
CPT R. Woodruff,MC

Dept/Sec: OB/GYN Assoc Investigators

Key Words:

Cephoxitin;

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To determine whether antibiotic irrigation with a cephoxitin solution (2 grams in 1000 cc normal saline) at the time of cesa section, significantly decreases febrile postoperative morbidit use of subsequent therapeutic parenteral antibiotics, severe infectious complications, and length of hospital stay.

Technical Approach:

Two hundred patients will be studied consecutively. Two groups patients of about equal size will be compared - Group 1, Cefox irrigation vs Group 2, Cefamandole irrigation. Selection will randomized with physicians and patients blinded.

Two grams of drug will be mixed in the Operating Room with 100( normal saline. Patients with chorioamnionitis, intrapartum fe anaphylactic type reaction to penicillin, or already on antibi will be excluded from the study. Parenteral therapeutic antib will be used postoperatively whenever appropriate clinically. two groups will be critically analyzed for similarities in percentage of patients with prolonged labor, PROM, number of va exams, repeat c-section, age, race, type of skin and uterine incision, estimated blood loss, parity, and duration of operati The charts will be reviewed shortly after discharge and analyze standard morbidity, positive cultures, need for therapeutic antibiotics, severe morbidity rates (wound infections, septic thrombophlebitis, etc) and length of hospital stay. Statistica analysis of the data will be performed using the chi square met

Progress:

Approximately 175 patients are entered to date. Chart review i process with all but September and October tabulated. Completi the 200 patient series is anticipated by February 1984, with analysis being completed by April 1984.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/11 Status: Completed

Title:
The Use of Progesterone in Decreasing Pelvic Adhesions in the New Zealand White Rabbit

Start Date: Est Comp Date:

Principal Investigator: Facility:
CPT G.R. Patterson,MC

Dept/Sec: Dept OB-GYN Assoc Investigators

Key Words:

Progesterone

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

To evaluate whether progesterone does reduce the number and severity of pelvic adhesions following microsurgery in the New Zealand white rabbit.

Technical Approach:

Mid-portion of both tubes of six New Zealand white rabbits will be transected and then reapproximated using microsurgical technique. These rabbits would receive an oral dose of MPA, 4 mg/kg, the day prior to surgery, the day of surgery, and daily for one week following surgery. These rabbits would then be re-explored two weeks following surgery for evaluation of adhesion formation.

Another six rabbits would be treated in the above fashion except that a solution of MPA, 4 mg/kg in 25cc normal saline, would be left intraperitoneally prior to closure of the abdomen rather than the oral dose of progesterone.

Another six rabbits would be used as a control group and would be irrigated with normal saline prior to closure of the abdomen, but would receive no form of progesterone treatment.

Adhesions would be graded by microscopic assessment of fibroblastic activity and inflammatory reaction. Adhesions would be assessed macroscopically by the following schema. Grade 0 = absence of adhesions; Grade 1 = single, filmy, easily separated adhesions; Grade 2 - more than one filmy adhesion; Grade 3 - single, dense adhesion requiring sharp dissection; and Grade 4 = more than one dense adhesion. The data will be analyzed by nonparametric techniques.

Progress:
A controlled double-blinded prospective study was done to evaluat the effectiveness of medroxyprogesterone acetate (MPA) as an adjuvant in decreasing pelvic adhesions in 31 New Zealand white rabbits following tubal anastamosis.

There were four subgroups: Subgroup I (m=10) received saline; Subgroup II (m-10)received oral MPA; Subgroup III (m=6) received intraperitoneal depo MPA vehicle (IPV); and Subgroup IV (m=5)received depoMPA intraperitoneally (IP).

The results revealed no statistical difference between the treated oral MPA and the saline control subgroups. A marginal difference in reduction of adhesion formation was noted in the depo MPA IP subgroup compared to the IPV Subgroup IPV was inferior to saline as a control ($P<.05$) indicating a causual relationship of the vehicle and adhesion formation. Microscopic assessment of adhesion formation was less discriminating than macroscopic in evaluating treatment results.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/33 Status: Ongoing

Title:

Effect of Breast Stimulation on Cervical Ripening

Start Date: Est Comp Date:

Principal Investigator: Facility:
MAJ K. Kiley, MC

Dept/Sec: Dept OB/GYN Assoc Investigators

Key Words:

Cervical ripening

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To determine the effect of nipple stimulation on cervical ripening in nulliparous patients at term as determined by Bishop score.

Technical Approach:

We propose to compare two groups of nulliparous, uncomplicated, term women by having one group serve as a control and the other group participate in repetitive breast stimulation until delivery and then compare cervical changes, labor and delivery, and outcome.

a. Approximately 200 subjects will be studied. These women will be delivering their first child, with an uncomplicated maternal and obstetrical history (exclusions will include advanced maternal age, hypertension, diabetes mellitus, etc.). Both active duty and civilian dependent women will be included in the study.

b. Approximately 200 controls with the same qualifications will be included.

c. Study subjects who are term by all parameters of dating (FHTs, ultrasonography, LMP) will be counselled and offered inclusion in the study. The cervix will be graded by the modified Bishop's score and the patient will be instructed in nipple rolling for 5-10 minutes with a 2-minute rest, repeating this pattern for 30 minutes four times a day. The patients will be seen weekly and the cervix re-examined. At 42 weeks estimated gestational age, nonstress testing will begin and at 43 weeks, patients will be induced for postdatism. The patient will keep a record at home of nipple stimulation. Control patients will have their cervix examined and the exam recorded; they will be managed in the standard manner for postdates. The Bishop's score is a numerical rating of the cervix based on the degree of cervical dilitation, effacement and station of the presenting part.

d. Post-delivery charts will be reviewed for presenting Bishop's score, incidence of SROM, length of labor, cesarean section rate, and fetal outcome. Comparisons will be made with the unstimulated group utilizing non-paired t-test for measurement data and chi-square testing for contingency data..

Progress:

We have entered approximately 50 patients as controls. No study subjects yet. No adverse effects have been noted.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/44 Status: Ongoing

Title:
Effect of Breast Stimulation on Cervical Ripening in the Multiparous Patient

Start Date: Est Comp Date:

Principal Investigator: Facility:
MAJ Kevin C. Kiley, MC

Dept/Sec: Dept OB-GYN Assoc Investigators

Key Words:
Cervical ripening

| Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results |
|---|---|---|

Study Objective:

To determine the effect of nipple stimulation on cervical ripening in multiparous patients at term as determined by Bishop score.

Technical Approach:

We propose to compare two groups of multiparous uncomplicated, term women by having one group serve as a control and the other group participate in repetitive breast stimulation until delivery and then compare cervical changes, labor and delivery, and outcome.

b. Approximately 200 controls with the same qualifications will be included.

c. Study subjects who are term by all parameters of dating (FHTs, ultrasonography, LMP) will be counselled and offered inclusion in the study. The cervix will be graded by the modified Bishop's score and the patient will be instructed in nipple rolling for 5-10 minutes with a 2-minute rest, repeating this pattern for 30 minutes four times a day. The patients will be seen weekly and the cervix re-examined. At 42 weeks estimated gestational age, nonstress testing will begin and at 43 weeks, patients will be induced for postdatism. The patient will keep a record at home of nipple stimulation. Control patients will have their cervix examined and the exam recorded; they will be managed in the standard manner for postdates. The Bishop's score is a numerical rating of the cervix based on the degree of cervical dilitation, effacement and station of the presenting part.

d. Post-delivery charts will be reviewed for presenting Bishop's score, incidence of SROM, length of labor, cesarean section rate, and fetal outcome. Comparisons will be made with the unstimulated group utilizing non-paired t-test for measurement data and chi-square testing for contingency data..

Progress: Approximately 150 patients entered as controls. We will begin entering study subjects soon with projected completion by June 1984. No adverse complications or reactions.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/60 Status: Ongoing

Title:
Interactions Between Aminoglycoside Antibiotics and Vitamin B6 in vitro and in vivo

Start Date: Est Comp Date:

Principal Investigator: Facility:
MAJ R.C. Keniston, MC

Dept/Sec: Dept Pathology Assoc Investigators

Key Words:

Aminoglycosides; Vitamin $B_6$

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

To develop a method for isolating and quantitating aminoglycosidepyridoxal 5'-phosphate complexes. To isolate these complexes from the urine of patients receiving the aminoglycoside antibiotics. To determine if depletion of vitamin B6 occurs in patients receiving aminoglycoside antibiotics, and if so, how this depletion correlates with morbidity and mortality.

Technical Approach:

Subjects will be patients who are to be given aminoglycoside antibiotics for clinical indications (sepsis, serious gram-negative infections, etc). These patients should also have SMAC 20 chemistry screens and monitoring of their aminglycoside levels (procedures already routinely performed). The blood and urine samples from at least 30 patients will be examined.

Progress:

Progress on this protocol during FY83 has been limited by the difficulty in finding a suitable assay for B6 at the levels required. A fluorescence assay was developed that was suitable for analysis at the 20 ng/ml level. Reagents have been obtained for an attempt at reproducing a recently published literature procedure that is reportedly sensitive enough for this study.

Detail Summary Sheet

Date: 1 Oct 83 Prot No:83/34 Status: Ongoing
Title:

Utilization of Robotics in the Laboratory

Start Date: Est Comp Date:
Principal Investigator: Facility:
CPT P.H. Cordes, MC

Dept/Sec: Dept Pathology Assoc Investigators
Key Words:

Robotics

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results
Study Objective:

To investigate the uses of a simple robot in application to menial and repetitive tasks within the laboratory. To determine whether such applications might be cost effective. To determine what other applications might be feasible and cost effective in the laboratory with more sophisticated robots.

Technical Approach:

a. Purchase robot.
b. Build robot (time frame 1-2 weeks).
c. Begin investigation.

(1) Develop application to routine histological staining. A routine and repetitive task requiring only simple programming sufficient for familiarization with the machine (time frame 2-3 weeks).

(2) Develop application to production of microbiological media. A routine and repetitive task requiring more detailed manipulation of the robot arm and more than one program in order to deal with more than one media type (time frame 1-2 months).

(3) Develop and test application for delivery of laboratory specimens from receipt to the appropriate section. A routine task requiring intensive programming in robot navigation, obstacle avoidance, motion detection and voice output (time frame 3-6 months).

(4) Implement other possible uses that become apparent during utilization of the robot, but which are unforeseen at this time.

d. Evaluation.

(1) Reliability: The ability of the robot to perform a task more than once without reprogramming. Also an estimation of mean time between failures of the hardware.

(2) Suitability: Is this particular robot suitable for this job and/or environment? Would a more sophisticated robot be suitable?

(3) Cost effectiveness: Is the robot cost-effective in each of the above implementations? Would a more sophisticated robot be cost effective?

e. Reporting of results: Writing of an article for publication and/or presentation to laboratorians at a conference.

Progress:

Awaiting purchase of the robot.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 80/2 Status: Completed

Title:
Developmental Analysis of Heavy and Trace Element Hair Content in Normal Children and Childre. with Attention Disorder.

Start Date: Est Comp Date:

Principal Investigator: Facility:

COL P. LoPiccolo, MC

Dept/Sec: Pediatrics Assoc Investigators

Key Words:

Trace elements

Accumulative MEDCASE Cost | Est OMA Cost: $605 (605) | Periodic Review Results

Study Objective:

To investigate developmental changes in the influence of heavy and trace elements on the behavior of normal children and children with attention disorders.

Technical Approach:

Twenty-five normal children and twenty-five children who have been diagnosed as having an attention disorder with excessive activity will be selected from each of the following age groups: Seven-year olds, nine-year-olds, and eleven-year-olds. An additional group of nine-year-old attentional-disordered children will be selected who are currently on medication. One tablespoon of hair will be collected from the nape of the neck. Ten mm of hair nearest the skin will be trimmed to provide the sample. Information will also be solicited regarding such areas as the date of the most recent hair washing, use of medication, and diagnostic status. Achievement information for the normal children will be acquired using the Wide Range Achievement Test (WRAT), while intelligence scores will be computed using the Peabody Picture Vocabulary Test (PPVT). The hair samples will be stored in plastic bags and coded in a manner so that an individual child's name is not associated with the results. Once the required number of hair samples has been acquired, the samples will be analyzed using atomic absorption spectroscopy. Comparisons of each of the element levels for the normal and attention disordered children will be made in order to identify a possible relationship between the levels of certain elements and the performance of certain intellectual activities.

Progress:

The principal investigator has been reassigned.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 81/42 Status: Ongoing

Title:
The Recognition and Frequency of the Polycystic Ovary Syndrome in a General Adolescent Population

Start Date: Est Comp Date:

Principal Investigator: Facility:

CPT W.R. LaForce, MC

Dept/Sec: Pediatrics Assoc Investigators

Key Words:

Polycystic ovary syndrome

Accumulative MEDCASE Cost | Est OMA Cost: $0(2852) | Periodic Review Results

Study Objective:

To establish the frequency of biochemically proven polycystic ovary syndrome (PCOS) in a general adolescent clinic population, and to evaluate parameters of the medical history in its early recognition.

Technical Approach:

Each year in May through August days are set aside for school and sports physical examinations for dependent children at WBAMC. Approximately 350 adolescent girls are examined on these days. Sera will be collected from approximately 200 of these adolescents after patient and parental consent, and a menstrual history will be obtained. Serologic RIA tests will include the gonadotropins LH and FSH, and the androgen testosterone. Aliquots of serum will be kept frozen for possible subsequent hormone analysis to include estrone, estradiol, androstenedione and insulin. Elevated levels of testosterone, and/or elevated LH, with associated low values of FSH, are biochemical evidence of the polycystic ovary syndrome. Patients characterized as cases of this syndrome will be asked to return to the Adolescent Medicine Clinic for further evaluation, including more comprehensive medical history, and pelvic examination. Those cases identified will be counselled regarding future fertility problems, and offered biochemical regulation of their menstrual periods in an effort to offset the symptoms of this disorder.

Progress:

No additional samples have been drawn. The specimens are being analyzed for progesterone to determine the phase of the cycle and the data will be reorganized accordingly for analysis.

Detail Summary

Date: 1 Oct 83 Prot No: 81/66 Status: ongoing

Title: Single Day Therapy with Trimethoprim-Sulfamethoxazole for Lower Urinary Tract Infection

Start Date: Est Comp Date:

Principal Investigator: Facility:

LTC R. Lampe, MC

Dept/Sec: Pediatrics Assoc Investigators

Key Words:

Urinary tract infection

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To determine if a single day of therapy is just as effective as ten days of therapy for lower urinary tract infection. Single day therapy would cut cost, potential development of resistent organisms would be reduced, and patient compliance would be increased.

Technical Approach:

Fifty children, ages 2-12 years will be studied. Children who would not be included: (1) Antibiotic therapy within previous 48 hours. (2) Diabetics. (3) Known anatomic or vascular abnormality of the kidney, or impaired renal function. (4) Any indication of upper urinary tract infection, i.e. flank pain, vomiting, fever greater than 38°C. (5) Known allergy to sulfa drugs.

The diagnosis of lower urinary tract infection will be based upon a) lower abdominal pain, b) frequency of urination, c) urgency or urination, d) dysuria, e) no fever, or fever less than 38°C,) no flank pain or tenderness, g) child does not appear ill (toxic).

Laboratory: One or more of the following: a) unspun urine with bacteria but no casts. b) dipstick-nitrite positive. c) greater than 100,000 colonies on two clean catch urines. d) greater than 10,000-50,000 colonies on a catheterized specimen. e) any growth on a suprapubic aspiration of the bladder.

A complete blood count, ESR, and C-reactive protein will be drawn on all subjects in the study. Selection for single day vs. ten day therapy will be random. Fifty envelopes, twenty-five of which will contain the single day protocol, and twenty-five of which will contain the ten-day protocol, will be utilized for the selection.

The subjects of the study will receive 8 mg per kilogram body weight per dose of trimethoprim-sulfamethoxazole. They will receive one dose at the time they are seen in the clinic and one dose at bedtime that same day. The controls will receive 4 mg per kilkogram body weight per dose of trimethoprim-sulfamethoxazole every twelve hours for a period of ten days.

Each child included in the study will be seen 48 hours after institution of therapy at which time a repeat urine microscopic, dipstick, and culture will be done. At that time children who will be excluded are: (1) initial negative urine culture (2) organism not sensitive to trimethoprim-sulfamethoxazole. (3) Any child who shows signs or symptoms of upper urinary tract infection.

Subsequent to the initial 48 hour followup each patient will be seen two weeks after initiation of therapy, then monthly for six months. All male children will also be studied for urinary tract abnormalities with an intravenous pyelogram and a voiding cystourethrogram.

Progress:

Children continue to be enrolled, but at a very slow rate for reasons not completely evident.

Detail Summary

Date: 1 Oct 82 Prot No: 82/09 Status: Ongoing

Title:
An Evaluation of the Effects of Theophylline and Beta Adrenergic Medication on the Auditory Processing Ability of Children

Start Date: Est Comp Date:

Principal Investigator: Facility:
CPT G.V. Gwinn, MC

Dept/Sec: Dept Pediatrics Assoc Investigators

Key Words:

Theophylline

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

To determine if the use of theophylline or beta adrenergic medications qualitatively or quantitatively affect the auditory processing abilities of children.

Technical Approach:

Twenty asthmatic children currently requiring continuous therapy with theophylline will be entered into the study. Serum theophylline levels will be checked to ensure that they are in the generally accepted therapeutic range of 10-20 micrograms per milliliter.

Each child will be evaluated using the Revised Token Test administered by personnel from the University of Texas at El Paso Speech, Hearing and Language Center. The reliability in the administration of this test is verified to be greater than 98%. The testers will be unaware of which medical regimen the children are on during any of the testing encounters.

Patients will then have their theophylline therapy discontinued and be placed on an inhaled beta-2 agent (Albuterol 180 micrograms) four times daily. Clinical experience suggests that most patients do equally well on this regimen. After one week on this new regimen, the testing will be repeated.

Patients whose clinical condition suggests that their asthma would be adequately controlled on inhaled beta-2 medication taken on an as needed basis will be placed on Albuterol every four to six hours as needed. After one week, they will be retested.

During the fourth week, the subjects will have the inhaled bronchodilators discontinued and once again be placed on their

theophylline regimen. After one week they will be tested once

The patient's pulmonary condition will be monitored by a diary and twice daily Peak Expiratory Flow Rates. Conventional spiro and flow volume determinations will be determined weekly.

After the results are analyzed each child will be placed on the regimen which gave best control of asthma and the least CNS eff

The theophylline preparations used in this study will be whiche preparation the patient is taking on initiation of the study.

Statistical analysis will be done with nonparametric and parame testing as deemed proper by our statistical consultant.

Progress:

Seven patients have been entered into the study. At least thre more need to be entered. Dr. Gold has been transferred t Brool Army Medical Center and Dr. Gwinn is the new principal inv tig

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/28 Status: Completed

Title:
Sleep Patterns of Children and Adolescents

Start Date: Est Comp Date:

Principal Investigator: Facility:
COL P.F. LoPiccolo, MC

Dept/Sec: Dept Pediatrics Assoc Investigators

Key Words:

Sleep patterns

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To determine what are the normal behavior and ritualistic patterns of children/adolescents in regards to sleep. To determine if sleep patterns are predictive of any particular disorder of childhood ex: attentional deficit disorder. To determine what are normal parental behaviors in regards to sleep. To determine the incidence of sleep-walking, night terrors, enuresis and nightmares. To analyze school performance and its possible relationship to sleep patterns.

Technical Approach:

Parents who present to the Pediatric and Child Development Clinic will be asked if they would like to participate in this study. If so, a sleep and behavior questionnaire with a school behavior form will be given to them for completion. Analysis of the data obtained will be statistically analyzed by the Psychology Department at UTEP under the direction of Dr. Terry Allen.

Progress:

Completed.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/43 Status: Ongoing

Title:
Adolescent Immunity to Varicella and Cytomegalovirus

Start Date: Est Comp Date:

Principal Investigator: Facility:
LTC M. Schydlower, MC

Dept/Sec: Dept Pediatrics Assoc Investigators

Key Words:

Varicella; Cytomegalovirus

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To determine the immune status of adolescents age 13-17 years to varicella and cytomegalovirus.

Technical Approach:

Each year, May through August, days are set aside at WBAMC for school and sport physical examinations for military dependent children and adolescents as required by the local schools. Approximately 300 adolescents are examined on these days. Sera will be collected from approximately 150 adolescents and analyzed for seronegativity for varicella by complement fixation and neutralization tests. Sera will also be tested for cytomegalovirus by complement fixation and anticomplement immunofluorescence. The laboratory of Dr. Philip Brunell at the Department of Pediatrics, University of Texas Health Science Center, San Antonio, will test for varicella, and the laboratory of Dr. Martha Yow, Department of Pediatrics, Baylor University in Houston, will test for CMV. Both are experts in the study of these viruses. The data obtained will be correlated with age, sex, ethnic background, rank (as an index of economic background) and history of disease. Approximately 5 cc of blood will be obtained by venipuncture after obtaining appropriate informed consent.

Progress:

During a recent school physical examination day at our medical center, 32 military dependent American adolescents out of 107 gave a negative history for varicella. Twenty-one were female and 11 were male, ranging in age betwen 12 and 19 years (mean 15.9 years). Sera from the negative responders were assayed by the varicella fluorescent antibody to membrane antigen (FAMA) technique. All the samples were varicella-specific antibody positive at screening dilutions of 1:4 and 1:8. Our data suggest that up to 100% seroreactivity is achieved by mid-adolescence in some urban subpopulations. Also, a negative history for chickenpox is not reliable for determination of susceptibility to varicella infection.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/45 Status: Ongoing

Title:
Use of VM-26 in Acute Leukemia

Start Date: Est Comp Date:

Principal Investigator: Facility:
Jerry J. Swaney, M.D., DAC

Dept/Sec: Dept Pediatrics Assoc Investigators

Key Words:

VM-26; Leukemia

| Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results |
|---|---|---|

Study Objective:

VM-26 will be used as remission induction agent and maintenance agent for refractory acute leukemia in children and adolescents. The response rate to VM-26 will be evaluated, as well as its toxicity.

Technical Approach:

Patients to be enrolled for this evaluation will be those children or adolescents with acute leukemia in relapse and refractory to other available chemotherapeutic agents. The number to be enrolled is unknown as this will vary with number of children and adolescents who relapse.

Attempts at induction of remission in refractory acute leukemia in bone marrow relapse will be undertaken with combination chemotherapy of intravenously administered VM-26 and cytosine arabinoside. After determination of hematologic relapse and evaluation of renal and hepatic function with standard laboratory tests chemotherapy will be instituted.

The patients will have prior to beginning therapy a bone marrow aspiration and biopsy, spinal tap, SMA 20, and CBC with platelets. A hemogram will be obtained prior to every course of therapy and an SMA-20 prior to every other course.

Intravenous chemotherapy will be semi-weekly for a total of eight courses. These will be administered on a Monday and Thursday or a Tuesday and Friday schedule for four consecutive weeks. A bone marrow aspiration will be done preceeding the first and fifth courses, and at the time a ninth course would be due.

CHEMOTHERAPY PLAN:

VM-26 will be given in combination with cytosine Arabinoside (Ara-C, Cytosar) for induction and maintenance therapy.

VM-26 165 mg/$m^2$ IV 2 times a week for 4 infusions and cytosine Arabinoside 300 mg/$m^2$ IV just prior to VM-26 2 times a week for four injections. The VM-26 will be mixed at 1 mg/cc in .05 D 1/3 NS to be infused over 30-60 minutes. The Ara-C will be mixed as per package instructions and given IV push.

Bone marrow aspiration and biopsy will be performed Day 15 to determine marrow status and cellularity. Evaluation of peripheral demogram, bone marrow status and patient status will determine if the chemotherapy is to be continued, or modified. Maintenance therapy will consist of the above regimen given every two weeks.

Data will be recorded on the hematology flow sheets currently in use. Copy of consent will be maintained in folder.

Progress:

This IND study is awaiting NCI inclusion.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/23 Status: Ongoing

Title:
Cytomegalovirus Antibody and Serioconversion Among Hospital Personnel

Start Date: Est Comp Date:

Principal Investigator: Facility:
COL R.M. Lampe, MC

Dept/Sec: Dept Pediatrics Assoc Investigators

Key Words:

Cytomegalovirus

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To determine serologic immunity to cytomegalovirus among hospital personnel and the frequency of seroconversion during a nine-month period.

Technical Approach:

Subjects for the study will be hospital personnel who volunteer to have sera drawn initially and nine months later.

Procedure: Period I: Serum drawn from each subject will be stored at -20° in a labeled tube sent from NINCDS, and a form prepared for each subject.

Period II: Nine months later a second serum specimen will be drawn and the form completed. Paried serum specimens will be sent to NINCDS for CMV antibody assay together with the forms. Antibody assays to be performed by ELISA and/or indirect hemagglutination.

Progress:

No work completed due to other commitments by principal investigator related to exess job demands.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/26 Status: Ongoing

Title:
The Efficacy of Oral Electrolyte Solution in Acute Gastroenteritis in Pediatric Inpatients at WBAMC

Start Date: Est Comp Date:

Principal Investigator: Facility:
CPT Mark Crowe, MC

Dept/Sec: Dept Pediatrics Assoc Investigators

Key Words:

Gastroenteritis

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To acquire information and experience in treatent with the World Health Organization's Oral Rehydration Solution in children with acute gastroenteritis and associated dehydration.

Technical Approach:

a. Purpose: To acquire information and experience in treatment with the World Health Organizations - Oral Rehydration Solution in children with acute gastroenteritis and associated dehydration who are admitted to William Beaumont Army Medical Center. This data would be valuable in supporting or refuting other similar studies conducted in this area.

b. Subjects: A minimum of sixty children, age three months to four years of age, who are admitted with a diagnosis of dehydration secondary to diarrhea of less than seven days' duration would be included in the study.

c. Laboratory studies: Laboratory studies: Na, K, Cl, $CO_2$, BUN, Hct on admission and at 6,24, and 48 hours. Stool culture - Shigella, Salmonella and Campylobacter, O&P (every other day, times three), Stool - rotazyme. Record strict input and output. Weight at admission, 24 and 48 hours. This will be accomplished for all patients.

Treatment Group A: (Even social security number) - Standard intravenous therapy: intravenous bolus normal saline (NS) of 10cc per kilogram, then intravenous - $D_5$ 1/3 Normal Saline + 20 milliequivalent potassium per liter to replace dehydration over 24

hours (potassium to be added only after first void, then continue intravenous fluids at maintenance until: 1) two or less diarrhea stools in 24 hours or less than 10cc stool per kilogram per 24 hours, and 2) normal electrolytes, then

12 to 24 hours Pedialyte, then
24 hours 1/2 strength Isomil, then
Full strength Isomil and puree as appropriate for age
Discharge when stable on full strength Isomil greater than 12 hours.

Greater than 10% dry, give 20cc per kilogram normal saline bolus and, if stable, start replacement fluids as above.

Treatment Group B:

(Odd social security number) - oral rehydration solution: If less than 10% dehydrated and not shocky in appearance start WHO - ORS by mouth to replace estimated dehydration losses over 24 hours.

Then continue ORS at maintenance until 1) two or less diarrhea stools in 24 hours or less than 10cc stool per kilogram per 24 hours, and 2) normal electrolytes, then

24 hours 1/2 strength Isomil, then
24 hours full strength Isomil and puree as appropriate for age.
Discharge when stable on full strength Isomil greater than 12 hours.

If greater than 10% dehydrated or shocky, give 20cc per kilogram normal saline (NS) IV bolus - if patient then appears stable, start ORS as noted above.

Significant stool losses will be replaced on a volume for volume basis in both groups.

Criteria for failure: Patients will be considered to have failed on oral rehydration if they will not take oral fluids, if marked signs of initial dehydration persist beyond eight hours, or if evidence of dehydration returns during maintenance therapy. If a patient fails therapy with oral electrolyte solution, he will be treated with standard IV therapy as in Group A.

6. Data analysis: The following items will be compared using Student's t-test analysis:

a. Total number of days hospitalized.
b. Cost of care
c. Change in weight during hospitalization; measured at 6, 12 and 24 hours after beginning of therapy.
d. Changes in laboratory values.

e. Complication rate - Complications reported with IV therapy include infection, overhydration, and skin damage secondary to IV infiltration. Complications reported with oral therapy include failure of therapy as defined above, hypo and hypernatremia, and overhydration. Complications may be better compared using a chi square analysis.

Progress:

A number of patients have been treated. We will continue to accumulate experience and tabulate results.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/45 Status: Completed

Title:

Conservative Management of Minimally Syptomatic Patients with Elevated Blood Levels of Alcohol, Carbamazepine, Theophylline, and thyroxine

Start Date: Est Comp Date:

Principal Investigator: Facility:
CPT Allen F. Kossoy, DO

Dept/Sec: Dept Pediatrics Assoc Investigators

Key Words:

Carbamazepine; Theophylline; thyroxine

| Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results |
|---|---|---|

Study Objective:

To acquire data from previous patients admitted for overdoses with serious toxic symptoms or signs and high blood levels in order to minimize any unnecessary and potentially hazardous therapeutic intervention.

Technical Approach:

Chart review will be done from previously hospitalized pediatric/ adolescent age patients. Future patients admitted with these drug overdoses will be reviewed and results tabulated. Laboratory studies: Na, K, Cl, CO2, BUN, creatinine, toxic levels of urine and serum with particular emphasis on the medication ingested will be tabulated.

Progress:

Completed. The study showed toxic ingestion could be conservatively managed. Manuscript in preparation.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 81/37 Status: Ongoing

Title:
Torque and Its Relationship to Academic Achievement and Behavior in Children

Start Date: Est Comp Date:

Principal Investigator: Facility:

MAJ T.B. Jeffrey, MSC

Dept/Sec: Psychology Svc Assoc Investigators:

Key Words:
Torque

LTC P. Loriccolo, MC
Mr Thomas D. Carter,Jr,M.Ed

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

To evaluate the relationship between torque, academic achievement and behavior in children.

Technical Approach:

One hundred children between the ages of 9 and 13 seen in the Pediatric Outpatient Clinic will be evaluated with the following instruments: Torque Test, Wide Range Achievement Test (Jastok, Bijour, and Jastok, 1963), Connor's Abbreviated Teacher Rating Scale, the Burk's Behavior Rating Scale , the Peabody Picture Vocabulary Test, and selected portions of Reitan's Lateral Dominance Examination.

The Peabody Picture Vocabulary Test correlates at a high level (Range = .63 - .87) with intelligence scales and requires only a few minutes to administer and score. Groups will be matched (torque versus nontorque) for level of intellectual functioning.

The results of the Torque Test will be scored by employing a single blind procedure. Data will be analyzed dichotomously (torque versus nontorque) to determine if a relationship exists between torque, lateral dominance, academic achievement, and behavior through a multivariate analysis of variance paradigm (2x3x2x2 factorial design). It is hypothesized that those with torque will display mixed lateral dominance on Reitan's test. It is also hypothesized that those with torque will do less well as measured by academic

achievement than their torque-free peers. A third hypothesis is that those with torque will have more behavioral problems as perceived by teachers and parents than their torque-free peers.

**Progress:**

Effective 17 October 1983 41 patients have been entered into the study with no untoward occurrences. Recommend the protocol continue through 1 Oct 1984.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82 [illegible] Status: Terminated

Title:
Low Back Pain and Return of Functi[illegible] Medical Intervention

Start Date: Est Comp Date:

Principal Investigator: Facility:
LTC T.B. Jeffrey, MSC

Dept/Sec: Dept Psychiatry Assoc Investigators

Key Words:

Low back pain

| Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results |
|---|---|---|

Study Objective:

To compare selected outcome predictors of medical intervention for relief of low back pain (LBP).

Technical Approach:

A minimum of 200 patients referred to neurosurgery and orthopedic surgery with LBP will be evaluated with a medical history, Cornell Medical Index (CI), A Pain Survey, and the MMPI. Predictions of treatment outcome will be made by the staff neurosurgeon, orthopedic surgeon, and psychologist at the time of the patient's initial presentation to each practitioner. Patients will be provided treatment as is judged appropriate by the staff. Prediction of treatment outcome will be evaluated approximately 60 days after medical intervention through medical review of the patient's response to treatment and a telephone/mail survey in which the patient provides data on relief of pain and/or return of function.

By analysis of covariance, the numerical predictory scales (MMPI, CI, Pain Survey, and Physical Findings) will be evaluated with the criterior variables (Operative/Diagnostic Findings, 60 Day Post Operative Treatment Response Scale) to determine the degree of predictability of any particular scale or combination of scales.

Progress:

This protocol was terminated by the principal investigator.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/17 Status: Completed

Title:
Physiological Correlation of Psychomotor Performance and Decision Making in Medical Officers

Start Date: Est Comp Date:

Principal Investigator: Facility:
CPT M. Hawkins

Dept/Sec: Dept Psychiatry/ARTF Assoc Investigators

Key Words:

Psychomotor performance

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

Due to the extended working hours and special conditions experienced by the medical staff and students in a large teaching hospital, the questions of the effects of sleep-deprivation and other psychophysiological variables become important. The purpose of this proposed study is to measure amounts of sleep-deprivation and other physiological factors such as amount of exercise, alcohol consumption, and time spent in recreational pursuits as they effect ability to perform psychomotor tasks and decision making. The focus of this study is on those departments, and the medical officers comprising them, who experience the largest amount of overnight and on-call working conditions.

Technical Approach:

Functioning was assessed using an abbreviated version of the Raven Progressive Matrices and a timed version of the Trail Making Test (B) from the Halstead-Reitan Neuropsychological Battery. Data were collected on the group described and controls were sampled by administering the tasks to newly arrived interns. Analysis was accomplished using multivariate analysis of covariance. All physical covariates (exercise, alcohol consumption, diet, smoking) were found to be nonsignificant and were excluded from the remaining analysis.

Progress:

Multivariate analysis of variance revealed significant deficits in both primary cognitive functioning tasks involving simple, old-learning skills as well as secondary tasks requiring higher order abstract reasoning and the acquisition of new skills. These deficits only existed for the acutely sleep deprived group, but a startling finding was the appearance of the deficits in individuals who reported five hours or less of sleep, suggesting that current minimum sleep standards of four hours may be insufficient for complex cognitive functioning or even the practice of routine

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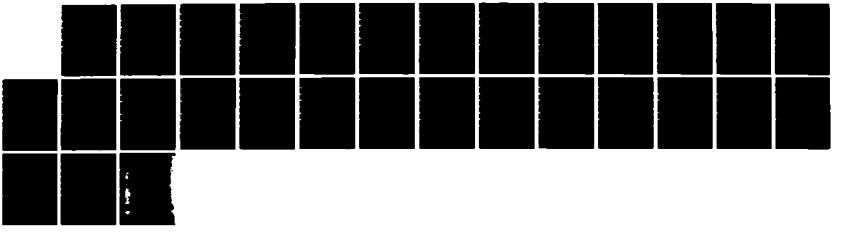

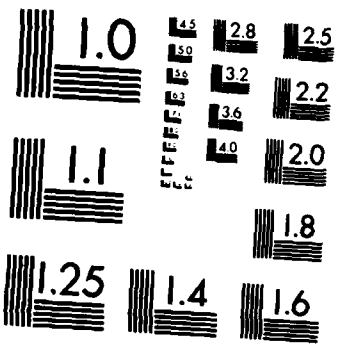

Detail Summary Sheet

Date: 1 Oct 83 | Prot No: 83/27 | Status: Terminated

Title:

Effect of Hypnotizability and Hypnosis on Recovery for Cholecystectomy Patients

Start Date: | Est Comp Date:

Principal Investigator: | Facility:
LTC T.B. Jeffrey, MSC

Dept/Sec: Dept Psychiatry/Psychology | Assoc Investigators

Key Words:

Cholecystectomy; hypnosis

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To evaluate hypnotizability and the effectiveness of hypnotic suggestions for patients undergoing cholecystectomy.

Technical Approach:

Patients scheduled for cholecystectomy will be asked to participate in an investigation on the effects of hypnosis on anesthesia and pain management. Those volunteering will be evaluated via the Stanford Hypnotic Clinical Scale, a Mental Status examination, and an MMPI

Progress:

No patients were entered into the study. Study terminated by the principal investigator.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/28 Status: Completed

Title:
Slosson Intelligence Test and Young Learning Disabled Children: A Comparative Study

Start Date: Est Comp Date:

Principal Investigator: Facility:
LTC T.B. Jeffrey, MSC

Dept/Sec: Dept Psychiatry/Psychology Assoc Investigators

Key Words:

Learning Disability

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To evaluate the effectiveness of the Slosson Intelligence Test (SIT) as a measure of intellectual functioning for young learning disabled (LD) children.

Technical Approach:

Approximately 20 randomly selected first and second grade children scheduled for intellectual evaluation will be assessed with the SIT and Wechsler Intelligence Scale for Children - REvised. The order of test presentation will be reversed for every other child to counterbalance any practice or fatigue effect. Normally these children would be evaluated only with the WISC-R. The SIT will require approximately 20 additional minutes of each child's time. If the SIT proves to be an effective measure of intellectual functioning for LD children, then more widespread use of this instrument by the Psychology Service will permit us to be more responsible to pediatricians and others needing to understand the intellectual functioning of these children.

SIT and WISC-R results will be analyzed by Pearson Product-Mament Coefficient of Correlation to determine the level of correspondence between scores.

Progress:

Twenty-six children were entered into the investigation with no untoward effects. The investigation has been completed and a paper is being prepared for journal submission.

Detail Summary Sheet

Date: 1 Oct 83 | Prot No: 83/29 | Status: Ongoing

Title:
Hypnosis for the Treatment of Smoking Cessation

Start Date: | Est Comp Date:

Principal Investigator: | Facility:
LTC T.B. Jeffrey, MSC | Dept Psychiatry/Psychology Svc

Dept/Sec: Dept Psychiatry/Psychology Sv Assoc Investigators

Key Words:

Smoking cessation; hypnosis

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To evaluate the efficacy of several variables in the treatment of smoking cessation.

Technical Approach:

A number of therapeutic approaches are utilized in the active smoking cessation program in the Psychology Service. Common to all is an underlying reliance on clinical hypnosis. A systematically varying difference among various practitioners providing smoking cessation treatment will be used. These variables are dual versus single induction, group versus individual treatment, exclusion versus nonexclusion therapy, and high versus low anxiety. Support is available in the literature to justify each of the aforementioned variables for the treatment of this problem. Controlled outcome studies on the efficacy of these variables is anticipated.

Progress:

Thirty-five patients were entered into an investigation of dual vs single hypnotic induction with no untoward effects. A paper is being prepared for journal submission on this component of the study.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/30 Status: Terminated
Title:

Effect of Hypnosis on Anesthesia for Abdominal Hysterectomy Patients

Start Date: Est Comp Date:
Principal Investigator: Facility:
LTC T.B. Jeffrey, MSC

Dept/Sec: Dept Psychiatry/Psychology Sv _ Assoc Investigators
Key Words:
Abdominal hysterectomy; hypnosis

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To evaluate the effect of hypnosis on anesthesia for patients undergoing abdominal hysterectomy.

Technical Approach:

Women scheduled for abdominal hysterectomy will be asked to participate in an investigation on the effects of hypnosis on anesthesia. Those volunteering will be evaluated via the Stanford Hypnotic Clinical Scale (SHCS). Subjects will be composed of patients meeting the following criteria: Between 20 and 60 years of age and hospitalized for abdominal hysterectomy. Free of any major psychopathology as determined by Mental Status Examination and MMPI. The three groups will be Group I hypnosis; Group II counselling; Group III control. Dependent variable measures will be: 1) the amount of chemical anesthesia required during surgery; 2) the amount of blood loss during surgery; 3) the amount of narcotics required postoperatively; and 4) the length of hospitalization. One-way analyses of variance will be performed to evaluate treatment effects. Accuracy of statistical conclusions will be made through a multivariate one-way analysis of variance.

Progress:

One patient was entered into the study with no untoward effects. Study was terminated at the request of the principal investigator.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/42 Status: Ongoing

Title:
Clinical and Surgical Correlation Between Computerized Axial Tomography (CT) vs Metrizamide Myelography in the Patient with Low Back Pain.

Start Date: Est Comp Date:

Principal Investigator: Facility:
CPT W.V. McAbee, MC

Dept/Sec: Dept Radiology Assoc Investigators

Key Words:

CAT; Metrizamide Myelography

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To compare which method (CT or metrizamide myelography) has the greatest degree of correlation with surgical and clinical findings in the low back patient and to determine the strengths and weaknesses of both modalities.

Technical Approach:

The study will consist of 100 low back pain patients that would ordinarily receive a metrizamide lumbar myelogram at our institution and who subsequently go to surgery. Initially the patient will receive a lumbar CT scan.

1. Areas to be scanned will coincide with regions of clinical suspicion.

2. IV contrast will be given in bolus form of 100cc (Conray 60).

3. CT cuts at 5 mm thickness spaced at 5 mm distances from the bottom of the superior pedicles to the top of the inferior pedicles of the involved disc space.

4. The doctor performing the study will read the film routinely with available clinical information

5. The film will be read "blindly" by one of the clinical investigators without clinical information filling out the protocol CT form.

Metrizamide myelogram will follow the CT scan.

1. 15cc of 190 mg/cc of metrizamide will be injected into the subarachanoid space.

2. AP, lateral, oblique and cross table lateral decubitus films will be obtained.

3. The doctor performing the study will read out the film with all the clinical information available.

4. The film will be read by one of the clinical investigators without clinical information and he will fill out the protocol myelogram form.

Clinicians will be asked to fill out a clinical information sheet before the performance of any exam. The sheet should include: 1) probable levels of involvement, 2) degree of clinical suspicion, 3) brief history and pertinent physical findings, 4) the surgeon will be asked to comment on the nature of the surgical findings to include:

1. Nerve root impingement and type.

   Hypertrophied facet
   Hypertrophied ligamentum flavum
   Bulging disc
   Free fragment
   Other

2. Amount of saline injected into involved disc.
3. Did he find what he expected on the basis of the CT and myelogram at surgery.

Progress:

No progress reported on this study.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 78/03 Status: Ongoing

Title:
National Intraocular Lens Implantation Study

Start Date: Est Comp Date:

Principal Investigator: Facility:

MAJ Antonio San Martin, MC

Dept/Sec: Surgery, Ophthalmology Assoc Investigators

Key Words:

Intraocular lens

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To participate in the study of clinical results of implantations of intraocular lens organized by the Intraocular Lens Manufacturer's Association in response to directives of the Ophthalmic Classification Panel, FDA.

Technical Approach:

An intraocular lens is a prosthetic replacement for the eye's crystalline lens. It is placed in the eye at the time of cataract surgery, where it is fixated by a variety of means, with the intention that it remain permanently and correct the large refractive error remaining after conventional cataract surgery.

PROGRESS

MAJ Bergin has been transferred from this institution and the new principal investigator of this study will be MAJ Antonio San Martin. Seventy-six intraocular lens were implanted in FY83 with no adverse effects due to implantation.

Detail Summary Sheet

**Date:** 1 Oct 83 **Prot No:** 81/02 **Status:** Termianted

**Title:**
**Replacement of the Infra-Renal Inferior Vena Cava with an Improved Expanded Polyfluorotetraethylene (e-PTFE) Graft and Comparison of Two Graft**

**Start Date:** **Est Comp Date:**

**Principal Investigator:** **Facility:**

**CPT T.E. Gaines, MC**

**Dept/Sec:** Surgery **Assoc Investigators**

**Key Words:**
**Vena cava; PTFE vascular grafts** LTC S. Cabellon, MC

| Accumulative MEDCASE Cost | Est OMA Cost: $750(750) | Periodic Review Results |
|---|---|---|

**Study Objective:**

To evaluate an improved e-PTFA(IMRA) graft in the infra-renal vena cava in dogs. Parameters studied will be those of initial pressure, flow characteristics, and patency. Histologic appearance will also be studied should thrombosis or occlusion occur. The effect of graft diameter is to be compared for two graft sizes, one smaller than, and one approximating, the diameter of the native vessel. Our goal is to work toward development of the reliable grafting procedure and prosthetic material for replacing important veins in humans.

**Technical Approach:**

Dogs will be used as the animal model. It is intended to use the optimum synthetic material and grafting procedure in this study and to test the material and procedure in the most difficult situation. Therefore, an A-V fistula will be employed and anticoagulation will be considered at the time of the procedure. The hemodynamic effect of the A-V fistula will be monitored with blood flow and pressure studies. The graft material will be e-PTFE which has a pore size of approximately 30 microns. The graft will have rigid external support consisting of a spiral of solid teflon. The length of the graft will be 6 cm so as to provide a length that has clinical utility. In addition to the above considerations the effect of velocity of flow will be studied with this experiment. Two graft sizes will be used, one being 8 mm and approximating the native size of the inferior vena cava in the dog, the other, 5 mm, being narrower. Presumably flow does not decrease through the narrower

graft (an assumption to be measured in the study). The velocity of flow would be higher than through the larger graft. The effect of this higher velocity of flow may be to improve patency and this will be monitored.

Progress:

Project terminated by principal investigator.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 81/07 Status: Ongoing

Title:
Comparison of Mortality and Morbidity of Uretero-ileocecosigmoidostomy With Other Urinary Diversions.

Start Date: Est Comp Date:

Principal Investigator: Facility:

COL F.L. Diaz-Ball, MC

Dept/Sec: Surgery Assoc Investigators

Key Words:
Ureteroileocecosigmoidostomy

Accumulative MEDCASE Cost | Est OMA Cost: 1210(1210) | Periodic Review Results

Study Objective:

At present, the urinary diversion methods accepted as effective have been the ones which require an external appliance over a stoma and on occasion ureterosigmoidostomy. Examples among these are: The ileal loop or conduit of Bricker, ileocecal loop, or the colonic loop. All these are prone to complications and are less ideal. In 1972 the senior investigator and associates reported on a study in dogs done at Letterman Army Medical Center in which the feasibility of an internal diversion using a uretero-ileocecosigmoidostomy was established. The anti-reflux action of the ileo-cecal valve can be enhanced with the newly developed Zinman technique. Prior to a wide application in humans, we should prove that the incidence of complications is comparable or preferably less than the accepted methods used at this time. It is projected to perform surgery in control groups of ileal loops, colonic loops, ureterosigmoidostomies and compare incidence of complication with equal numbers of uretero-ileo-cecosigmoidostomies.

Technical Approach:

1. Control Group I - a series of 6-12 dogs will undergo ileal loop diversion.

2. Control Group II - a series of 6-12 dogs will undergo a colonic loop.

3. Control Group III - a series of 6-12 dogs will undergo a ureterosigmoidostomy.

4. Tested Group IV - a series of 6-12 dogs will undergo uretero-ileocecosigmoidostomies.

Data Collection:

Preoperative: Will include serum creatinine, BUN, and CBC. Urine C and S if possible, IVP and R.C. Barium enemas would be performed to establish functional integrity of urinary and bowel tracts including ileocecal valve competence. Kidney biopsy for regular and electron microscopy. Intra-operative: serum creatinine, BUN, urine from renal pelves or ureters for C and S, urine aspirates from bladder for C and S.

Postoperative: Every 1-2 weeks BUN and creatine. Every month an IVP, and every 2 months a cystogram. Will be as in humans with IVs until safe to feed, etc. At least every 1-2 weeks repeat CBC, BUN, creatinine, retrograde cystogram every month times 3 and then every 3 months times 3.

Long Term: Dogs will be kept ideally at least one year alive, facilities permitting. At that time they could be sacrificed, autopsied for detection of changes due to surgery in the urinary system and other systems.

Control groups I and III, and the test group will comprise the initial study. If time and funding permit, control group II, and possibly another group with ileo-cecal cutaneous diversion, may be compared to the tested group.

Progress:

Twelve dogs have undergone stoma type urinary diversion, namely ureteroileocutaneous anastamosis. Three of them are alive one year or more postoperatively and three are alive six months postoperatively. Seven dogs have undergone ureteroileo-cecosigmoidostomy. Three are alive at this time. The mortality (50%) in the ureteroileocutaneous group were mostly related to ileal stoma stricture or ureteral ileal strictures with pyelonephritis and renal failure. The mortality of 57% in the ureteroileoce-cosigmoidostomies have hinged on predisposition to volvulus and other types of intestinal catastrophies while the ureters and kidneys seem to survive as well or better than the ileal loop group. These mortality rates are being reconsidered in terms of the present techniques used with consideration of minor changes which would improve survival of this ureteroileocecosigmoidostomies prior to continuation of the study.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/26 Status: Terminated

Title:
Early or Delayed Surgery for Acute Cholecystitis: A Controlled Randomized Study

Start Date: Est Comp Date:

Principal Investigator: Facility:
LTC S. Cabellon, MC WBAMC

Dept/Sec: Assoc Investigators

Key Words:

Cholecystitis, treatment COL Daniel G. Cavanaugh, MC

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

To compare early and delayed surgery in the management of acute cholecystitis from the standpoint of complications of surgery, duration of the operative procedure, misdiagnosis of the disease and length of hospital stay.

Technical Approach:

Patients with acute cholecystitis diagnosed clinically with the help of ultrasound and cholescintigraphy will be randomly treated surgically either early or delayed. The benefit of each treatment mode will be assessed in terms of the complications of surgery, duration of the operative procedure, misdiagnosis of the disease and length of hospital stay.

Progress:

This study will be discontinued as there are three studies in the literature that have definitely established the superiority of Early Cholecystectomy.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 82/40 Status: Completed

Title:

Prospective Evaluation of the Abdominal Aorta in Peripheral Vascular Patients by Ultrasound

Start Date: 1 June 82 Est Comp Date: FEB 83

Principal Investigator: Facility:

LTC S. Cabellon WBAMC

Dept/Sec:Dept Surgery/Peripheral Vascular Assoc Investigators

Key Words:

Abdominal Aorta, Ultrasound

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

To determine whether the prospective evaluation of the aorta in patients with peripheral vascular disease will uncover a high incidence of undiagnosed abdominal aortic aneurysms. If the incidence is high, then it must be recommended that all patients with peripheral vascular disease should, as part of their routine followup or initial evaluation, undergo an ultrasound examination.

Technical Approach:

Ultrasound examination of the abdominal aorta on patients with atherosclerotic peripheral vascular disease after determining whether their aorta is palpable or nonpalpable.

Progress:

This study is completed with the results published in the November 1983 issue of the American Journal of Surgery.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/03 Status: Ongoing

Title:
The Use of Digital Subtraction Venous Angiographs in Differential Diagnosis of the Traumatically Widened Mediastinum

Start Date: Est Comp Date:

Principal Investigator: Facility:
LTC R.J. Lewis,MC

Dept/Sec: Dept Surgery Assoc Investigators

Key Words:

Digital Subtraction, Venous Angiographs

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:
To assess the accuracy of digital subtraction venous angiography in the diagnoses of injury to vascular structure in the traumatized, widened medadiastinum.

Technical Approach:

All patients who arrive in the Trauma Unit with a history of severe trauma and who are found to have a widened mediastinum by chest x-ray (PA or an upright 6 ft AP film) will undergo, in addition to the usual arteriography, digital subtraction venous angiography in order to assess its accuracy in such instances by comparing it with the known accuracy of the former method. To prevent bias on interpretation, each method will be interpreted by separate "blinded" radiologists.

Progress: No patients were entered into this study before the principal investigator was assigned a long-term TDY OCONUS.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/05 Status: Ongoing

Title:
The Efficacy of Routine Monitoring for Early Occult, Post-Traumatic Deep Venous Thrombosis by Noninvasive Phleborheography

Start Date: Est Comp Date:

Principal Investigator: Facility:

LTC R.J. Lewis, MC,

Dept/Sec: Dept Surgery Assoc Investigators

Key Words:

Thrombosis; phleborheography

Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results

Study Objective:

To assess the efficacy of routine monitoring for early occult post-traumatic deep venous thrombosis.

Technical Approach:

All patients admitted to the Trauma Unit with any and all injuries would be included in the study. The Grass Phleborheography represents a noninvasive method of measuring and recording deep venous flow in the lower extremities. Each patient would be tested twice daily (morning and evening) with recordings of both extremities to determine venous patency. Periodic arterial blood gases would also be followed. Any patient "positive" for suspected deep venous occlusion would be examined by venography to confirm the diagnosis.

Progress:

No patients were entered into this study before the principal investigator as assigned a long-term TDY OCONUS.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/16 Status: Ongoing

Title:
Size of the Abdominal Aorta: In vivo vs Ultrasonic Measurement

Start Date: Est Comp Date:

Principal Investigator: Facility:
LTC Silverio Cabellon,MC

Dept/Sec: Dept Surgery Assoc Investigators

Key Words:

Abdominal aorta

| Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results |
|---|---|---|

Study Objective:

To determine the size of the normal abdominal aorta. To determine the accuracy of ultrasound in measuring the size of the normal abdominal aorta.

Technical Approach:

Measure by caliper the infrarenal aorta at surgery for other abdominal conditions; compare with size determined by ultrasound before or after surgery.

Progress:

Caliper is now available; also personnel are now available to initiate the project.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/22 Status: Ongoing

Title:
Comparison of Cardiovascular Stability with Fentanol and Fentanyl-Nitrous Oxide Induction in Patients Undergoing Peripheral Vascular Surgery

Start Date: Est Comp Date:

Principal Investigator: Facility:
CPT D.D. Gautreaux

Dept/Sec: Dept Surgery Assoc Investigators

Key Words:

Anesthesia, Fentanyl, Periopheral vascular

CPT C. Callender, CPT
CPT J. Martin
CPT D. Hendryx, 1Lt
1LT K. Baethge

Accumulative MEDCASE Cost Est OMA Cost: Periodic Review Results

Study Objective:

To compare the hemodynamic effects of induction of general anesthesia with fentanyl 12 ug/kg with the hemodynamic effects of induction of general anesthesia with a combination of fentanyl 8 ug/kg and a 50% mixture of nitrous oxide and oxygen in patients having carotid endarterectomy of aorto femoral bypass surgical procedures.

Technical Approach:

The sample population will be approximately ten adult patients, both military and civilian, who are electively scheduled for carotid endarterectomy or aortofemoral bypass graft procedures and who are assessed as not having an airway difficult to manage. Each participating subject will sign a voluntary consent form prior to participating in the study. Subjects will be randomly assigned to one of two treatment groups: Group I will receive fentanyl 8 ug/kg and a 50% concentration of $N_2O$ and $O_2$ for induction; Group II will receive fentanyl 12 ug/kg for induction. All patients will be premedicated with morphine 0.1 mg/kg and scopolamine 0.005 mg/kg intramuscularly and preoxygenated with 100% $O_2$ via a Bain(R) anesthesia circuit. Topical application of a 4% solution of lidocaine by laryngoscopy will be given prior to intubation. Each patient will be monitored by electrocardiogram, direct radial artery catheter, and central venous catheter with display via electrical display and waveform monitoring equipment. Data from each of these parameters will be recorded at intervals throughout the induction phase and concluded at the time of surgical incision. Baseline data for each parameter will be recorded prior to the administration of

induction agents. Arterial blood gases will be obtained prior to induction and at fifteen minute intervals through induction to assure steady-state $PaCO_2$ levels. The paired t-test will be used to statistically analyze the data obtained. NOTE: Monitoring techniques and treatment modalities used for this project are accepted as current standard anesthesia practice. No experimental techniques or modalities will be used in the study.

**Progress:**

Data collection for this project was completed on 9 Sep 1983. This data has now been computed and narrative reports of findings are being compiled for initial draft. Expected date of completion is November 1983.

Detail Summary Sheet

Date: 1 Oct 83 Protocol 83/41 Status: Ongoing

Title:
Autonomous Life of Cancer Cells after Host Separation

Start Date: Est Comp Date:

Principal Investigator: Facility:
Dr. Sjord Steunebrink, MD,

Dept/Sec: Dept Surgery Assoc Investigators

Key Words:
Cancer cells

| Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results |
|---|---|---|

Study Objective:

To prove that cancer cells appear viable after 1, 2, or 3 weeks, in contrast to deteriorated other nonmalignant tissue from host.

Technical Approach:

To take a surgical section without preservative, by pathologist, after one and two weeks of any malignant tissue. Tissue should be free from chemotherapy. Tissue should be exposed to normal outside open air. Any successful finding may lead to exposure of cancer tissue to humid air, anerobic air atmosphere and other testing. Further investigative tests, if appropriate, for which another protocol will be written.

Progress:

Lewis lung cancer was inoculated into the thigh of a mouse. For ten days this tumor specimen was exposed to open air. Tissue cultures were done with no apparent viable results. Microscopic tissue examination was also performed with necrotic portions as well as partial preservation of nuclear cytoplasmic details in another area. In consultation a repeat study was suggested. Another sensitive test for viability could be performed. Anaerobic exposure of this malignant tissue can also be done , but another protocol will be written.

Detail Summary Sheet

Date: 1 Oct 83 Prot No: 83/47 Status: Ongoing

Title:

**Levamisole and Vitamin A Therapy in the Prevention of Sepsis in Multi-Traumatic Patients**

Start Date: Est Comp Date:

Principal Investigator: Facility:

**COL Ronald A. Lewis, MC**

Dept/Sec: Assoc Investigators

Key Words:

**Levamisole; Vitamin A**

| Accumulative MEDCASE Cost | Est OMA Cost: | Periodic Review Results |
|---|---|---|

Study Objective:

**To determine the role of levamisole and vitamin A in the prevention of sepsis in multitraumatic patients and to determine the immunopotentiating effects of levamisole and vitamin A as measured by microbial and immunological parameters.**

**Technical Approach:**

**A trial group will be comprised of 60 trauma patients and allocated into four groups of 15 patients each consisting of controls (saline-placebo) levamisole; vitamin A; and levamisole-vitamin A treated. The study will be performed in a double blind fashion with treatment being designated by random fashion derived by random number generation. All drugs will be dispensed in a suitable blinded fashion from the pharmacy. Therapy will begin by injecting immediately after necessary blood samples are taken for routine blood chemistries and removal of an additional 20cc of heparinized blood to be used for the immunological and microbial assays. Additional blood samples (20cc) will be taken on the following days; 3-5, 10-12, and 18-22 in order to monitor the immunological and microbial status of each patient. Only patients between 10 to 65 years of age who are admitted to the Trauma Unit between 2400 and 1200 will be included in this study. The time limitations are imposed due to the time required to perform the various in vitro assays. Blood samples obtained before 0630 will be refrigerated. All testing will be performed on the same day as the blood is drawn. Since this study will be comprised of military, civilian, individuals under the legal age of consent and adults not competent to give informed consent, appropriate consent forms will be accomplished.**

**Progress:**

**Due to long-term TDY OCUNS, principal investigator has not begun this newly approved study.**

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