

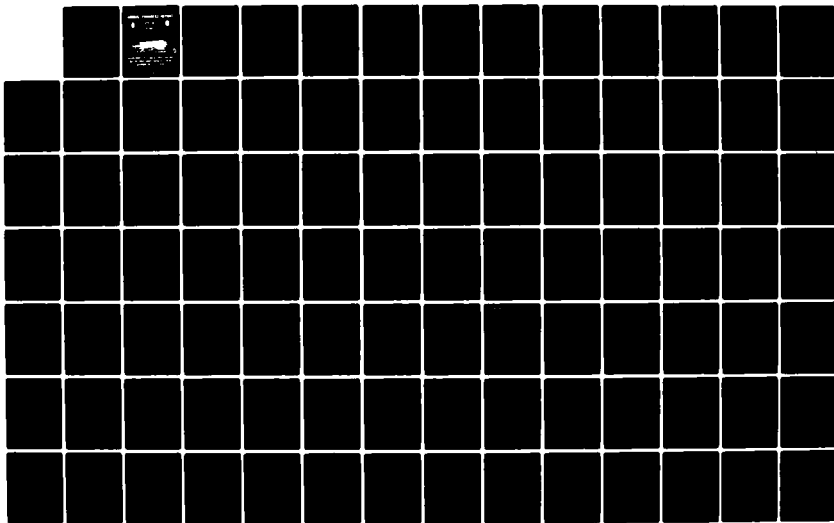
AD-A129 243 ANNUAL PROGRESS REPORT FY-82 VOLUME II(U) WALTER REED
ARMY MEDICAL CENTER WASHINGTON DC 1982

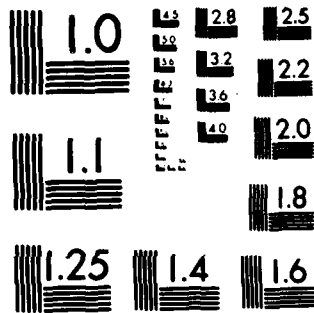
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ANNUAL PROGRESS REPORT

FY-82

VOLUME II



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WALTER REED ARMY MEDICAL CENTER
WASHINGTON, D. C. 20307**

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DATE: 30 Sep 82 WORK UNIT NO.: 2534 STATUS: INTERIM X FINAL

STARTING DATE: October 1980 DATE OF COMPLETION: September 1983

KEY WORDS: hearing aids, subjective judgments, binaural amplification

TITLE OF PROJECT: Subjective Comparisons of Binaural vs. Monaural Amplification

PRINCIPAL INVESTIGATOR(S): Sue A. Erdman, Roy K. Sedge

ASSOCIATE INVESTIGATOR(S):

FACILITY: WRAMC DEPT/SVC: Dept. of Surgery/Otolaryngology Service

ACCUMULATIVE MEDCASE COST: _____ ACCUMULATIVE CONTRACT COST: _____ ACCUMULATIVE SUPPLY COST: \$162.95

FY-83 MEDCASE: _____ CONTRACT COST: _____ SUPPLY COST: _____ DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: The purpose of this study is to determine (1) the consistency of subjective differences noted between binaural and monaural hearing aid fittings, and (2) the stability of preferences for either fitting over time.

TECHNICAL APPROACH: Records of new and former hearing aid candidates seen at WRAMC have been reviewed to determine rationale for preferences of monaural vs. binaural amplification. Comparisons are being made of preferences of first time fittings and fittings following extended use of monaural hearing aids. Results of auditory training exercises completed during patients' rehabilitation program while aided monaurally and binaurally are also being compared. A comparison of monaural vs. binaural fittings utilizing the present protocol will be conducted with a dependent population purchasing their own aids. The data will be compared to present data to determine to what extent cost is a factor in successful binaural hearing aid fittings.

PROGRESS DURING FY-82: Two papers were presented and are being prepared for publication.

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 TOTAL (TO DATE): 90 BEFORE COMPLETION OF STUDY: 120

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Annual Progress Report (cont.) - Work Unit #2534

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): None.

CONCLUSIONS: Not applicable at this time.

PUBLICATIONS OR ABSTRACTS, FY-82: Two papers were presented at the annual meeting of the American Speech-Language-Hearing Association, Los Angeles, California, Nov 1981.

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DATE: 30 Sep 82 WORK UNIT NO.: 2535 STATUS: INTERIM X FINAL

STARTING DATE: February 1981 DATE OF COMPLETION: December 1982

KEY WORDS: aural rehabilitation, automation, hearing loss

TITLE OF PROJECT: Development of a Method for Generating Individualized Aural Rehabilitation Materials and Evaluation Data for Hard-of-Hearing Patients (A Materials-Generating Algorithm)

PRINCIPAL INVESTIGATOR(S): Allen A. Montgomery

ASSOCIATE INVESTIGATOR(S): Brian E. Walden, Daniel M. Schwartz, Robert A. Prosek, Donald Wittich

FACILITY: WRAMC DEPT/SVC: Dept. of Surgery/Otolaryngology Service

ACCUMULATIVE MEDCASE COST: _____ ACCUMULATIVE CONTRACT COST: _____ ACCUMULATIVE SUPPLY COST: _____

FY-83 MEDCASE: _____ CONTRACT COST: _____ SUPPLY COST: _____ DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT
FEB 25 1983

STUDY OBJECTIVE: This project is aimed at developing an interactive procedure (implemented on a computer-graphics system) which will record and analyze a hearing-impaired patient's diagnostic test scores and then generate an individualized therapeutic plan and rehabilitation materials for use in that patient's treatment program.

TECHNICAL APPROACH: The project is proceeding in three stages:
First, the records of approximately 50 recent patients will be analyzed to determine the general nature and specific details of the algorithm needed to generate training materials. That is, the procedures needed to analyze the tests and generate the materials by hand will be abstracted and translated into steps and logic amenable to computer implementation.
Second, the computer and graphics system will be programmed and debugged to yield a functioning program capable of generating the clinical materials.
Third, the initial version of the program will be made available to therapists in the Aural Rehabilitation Section for use and evaluation on the job. A set of 30 patients will be processed and the resulting lessons will be used and evaluated by the therapists on the basis of their experience and knowledge, and modifications in the program will be made as needed.

Annual Progress Report (cont.) - Work Unit #2535

PROGRESS DURING FY-82: The materials-generating algorithm (MGA) has been revised to reflect clinical experience gained during the year. The current version is being evaluated by comparing lessons generated by the MGA with those developed by clinicians for a representative set of 30 aural rehabilitation patients.

NUMBER OF SUBJECTS STUDIED:

FY-82: 10 TOTAL (TO DATE): 10 BEFORE COMPLETION OF STUDY: 20

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): None.

CONCLUSIONS: Data collection is still in progress, so no final conclusions can be drawn. To date the output of the revised MGA seems to be quite similar to the clinicians' work, and it appears unlikely that further revisions will be required.

PUBLICATIONS OR ABSTRACTS, FY-82: A manuscript presenting the general principles of the automated generation of clinical materials is in preparation.

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| DATE: 30 Sep 82 | WORK UNIT NO.: 2536 | STATUS: INTERIM <u>X</u> FINAL <u> </u> |
| STARTING DATE: March 1981 | | DATE OF COMPLETION: January 1983 |
| KEY WORDS: lipreading, aural rehabilitation, perception, hearing loss | | |
| TITLE OF PROJECT: Effects of Consonantal Context on Vowel Lipreading | | |
| PRINCIPAL INVESTIGATOR(S): Allen A. Montgomery | | |
| ASSOCIATE INVESTIGATOR(S): Brian E. Walden, Robert A. Prosek, Daniel M. Schwartz, Donald Wittich | | |
| FACILITY: WRAMC | DEPT/SVC: Dept. of Surgery/Otolaryngology Service | |
| ACCUMULATIVE MEDCASE COST: _____ | ACCUMULATIVE CONTRACT COST: _____ | ACCUMULATIVE SUPPLY COST: \$70.00 |
| FY-83 MEDCASE: _____ | CONTRACT COST: _____ | SUPPLY COST: _____ |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: The purpose of this investigation is to study the effects of consonantal context on vowel lip configurations and lip readability.

TECHNICAL APPROACH: A videotape of five speakers will be prepared containing consonant-vowel-consonant (CVC) words selected to contain a full range of consonantal contexts and vowels. This videotape will be shown individually to a set of 30 hearing-impaired patients for lipreading, and confusion matrices will be generated. In addition, the videotape will be analyzed frame-by-frame to yield a set of physical measurements for each vowel sound in each utterance. The resulting physical and perceptual data sets will be examined with univariate and multivariate statistical techniques to test specific hypotheses about the influence of consonants on the visual intelligibility and lip configurations of vowels.

PROGRESS DURING FY-82: The first of two phases of the project has been completed. To evaluate the relationship between physical characteristics of the lips during vowel production and vowel lipreading confusions, four female talkers were videotaped speaking/producing 15 American English vowels and diphthongs in /h/-V-/g/ context. Ten normal-hearing adults in three repetitions of the task identified the stimuli through lipreading, guessing where necessary. Three analyses were performed. First, using the confusion matrices for the individual and pooled talkers, the stimuli were displayed

in two dimensional space using multidimensional scaling. The ten monophthongs revealed a clear lip spread-lip rounded dimension and a tongue height dimension and, while diphthongs showed influence of lip rounding, more variability on the tongue height dimension was apparent, depending on whether N_1 or N_2 received more visible emphasis. Second, vowel duration data were obtained and tracings were made of the talker's lips on a single videotape field representing the vowel maximum for each of the 40 monophthong tokens (10 vowels x 4 talkers), and relationships among six physical measurements of the token were examined. Third, difference scores and other measures of physical pairwise similarity were used as predictors of two ways of representing the vowel lipreading confusions in a multiple regression paradigm.

NUMBER OF SUBJECTS STUDIED:

FY-82: 10 TOTAL (TO DATE): 20 BEFORE COMPLETION OF STUDY: 30

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): None.

CONCLUSIONS: Overall, we can conclude that the physical measurements, especially height, width, and height-width distance which describe the general size of the lip opening, explain over half the variance in multi-dimensional distance and perhaps 40% of the variance in the confusions. While it is encouraging to find that an extremely simple set of measurements made on a single representative videotape frame per vowel accounts for a significant portion of the lipreading behavior, it is also true that much of the viewers' perception remains to be explained. We speculate that at least four types of physical measurements would be necessary for a full explanation of confusions arising in vowel lip reading: 1) the basic dimensions of the lip opening at the vowel maximum, as employed in the present study, 2) measures of the temporal aspects of visible vowel production, such as rate of opening and change in area of opening across time, 3) better estimates of differences between vowels in shape of opening (and surrounding tissue), and 4) a single measurement or composite that is sensitive to the complex changes in appearance including mandible-lip discrepancies that signify degrees of lip rounding/protrusion.

PUBLICATIONS OR ABSTRACTS, FY-82:

Montgomery, A., and Jackson, P. Physical characteristics of the lip underlying vowel lipreading performance. Submitted to Journal of the Acoustical Society of America.

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| DATE: 7 Sept 82 | WORK UNIT No.: 2537 | STATUS: INTERIM <input checked="" type="checkbox"/> FINAL |
| STARTING DATE: May, 1981 | DATE OF COMPLETION: | |
| KEY WORDS: CO ₂ Laser excision, laryngeal anatomy | | |
| TITLE OF PROJECT: | | |
| The Anatomy of CO ₂ Laser Cordectomy | | |
| PRINCIPAL INVESTIGATOR(S): Roy K. Davis, MAJ, MC | | |
| ASSOCIATE INVESTIGATOR(S): Hyams, CPT, USN | | |
| FACILITY: WRAVC | DEPT/SVC: Otolaryngology | |
| ACCUMULATIVE FEDCASE COST: None | ACCUMULATIVE CONTRACT COST: None | ACCUMULATIVE SUPPLY COST: None |
| FY-83 FEDCASE: None | CONTRACT COST: None | SUPPLY COST: None |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT JAN 26, 1982 |

STUDY OBJECTIVE: To determine how effectively CO₂ laser transoral excision will encompass T2 and selected T3 supraglottic + endolaryngeal lesions.

TECHNICAL APPROACH:

See protocol - no changes

PROGRESS DURING FY-82: No patients enrolled secondary to: (1) Lack of new Coherent Laser 450 until May, 1982; (2) lack of appropriate patients after May, 1982

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 TOTAL (TO DATE): 0 BEFORE COMPLETION OF STUDY: 5

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS:

N.A. Study yet to be done

PUBLICATIONS OR ABSTRACTS, FY-82:

None

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| DATE: 30 Sep 82 | WORK UNIT NO.: 2538 | STATUS: INTERIM <u>X</u> FINAL |
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STARTING DATE: 27 January 1981 DATE OF COMPLETION: June 1983

KEY WORDS: phoneme boundaries, hearing loss, acoustic filtering,
categorical perception

TITLE OF PROJECT: Phoneme Boundaries of Hearing Impaired Listeners

PRINCIPAL INVESTIGATOR(S): Brian E. Walden

ASSOCIATE INVESTIGATOR(S): Allen A. Montgomery, Daniel M. Schwartz, Robert
A. Prosek, Rodney K. Jamison

FACILITY: WRAMC DEPT/SVC: Dept. of Surgery/Otolaryngology Service

ACCUMULATIVE MEDCASE
COST: _____

ACCUMULATIVE CONTRACT
COST: _____

ACCUMULATIVE SUPPLY
COST: \$5,209.00

FY-83 MEDCASE: _____ CONTRACT COST: _____ SUPPLY COST: _____

DATE OF COMMITTEE APPROVAL
OF ANNUAL PROGRESS REPORT
FEB 25 1983

STUDY OBJECTIVE: The purpose of this research is to observe the possible effects of peripheral hearing impairment on phoneme boundaries. Included will be an effort to determine the extent to which these possible effects can be simulated by acoustic filtering.

TECHNICAL APPROACH: Fourteen computer-generated five-formant synthetic consonant-vowel stimuli are produced via Klatt's cascade formant synthesizer (Klatt, 1980). The loci of the F₂ and F₃ transitions are varied systematically across the fourteen stimuli. (Detailed descriptions of the stimuli are provided in the Application for Clinical Investigation Project.) The resulting synthetic stimuli vary along a voiced stop consonant continuum from /ba/ to /da/ to /ga/.

The subjects of this investigation are adults with unilateral sensorineural hearing losses, with sufficient residual hearing in the impaired ear to respond to synthetic consonant-vowel syllables.

The participation of a subject in the experiment proceeds in five steps: (1) Initially, the subject is trained to respond to the synthetic CV syllables presented to the normal ear. The best exemplars of /ba/, /da/ and /ga/ are used for this purpose. (2) Next, phoneme boundaries are obtained for the normal ear (unfiltered) using the full array of fourteen stimuli. (3) Following this, the "suprathreshold audiometric configuration" of the impaired ear is simulated on a spectrum shaper in the manner described by Walden et al. (1980). Next, phoneme boundaries are obtained

Annual Progress Report (cont.) - Work Unit #2538

for the normal ear listening through the multifilter set to simulate the spectrum shaping imposed by the hearing impairment. (5) Finally, phoneme boundaries are obtained for the impaired ear.

The phoneme boundary estimates for each of the three syllable recognition conditions (i.e., normal ear, unfiltered; normal ear, filtered; hearing-impaired ear) are statistically compared for each subject. Of particular interest is determining if the location and slopes of the phonemes boundaries differ among the test conditions.

PROGRESS DURING FY-82: The Bruel & Kjaer spectrum shaper, which malfunctioned during FY-81, was returned by the factory. Following some minor adjustment, it has functioned relatively well. To date, data for twelve unilaterally hearing-impaired patients have been obtained. Analysis of these data has not begun. Identifying patients with the appropriate audiometric configuration for this experiment has proved to be more difficult than was anticipated and, therefore, the data acquisition phase of this project has been extended.

Additional pilot data were obtained to determine the effects of adding noise burst to the synthetic stop consonant stimuli. The data revealed that the effect of adding the plosive burst was relatively small. Specifically, there was a slight shift of the b/d boundary to the right along the abscissa and recognition of the /d/ exemplar was slightly improved by the addition of the noise burst.

NUMBER OF SUBJECTS STUDIED:

FY-82: 12 TOTAL (TO DATE): 32 BEFORE COMPLETION OF STUDY: 50
(including pilot studies)

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): None.

CONCLUSIONS: Not applicable.

PUBLICATIONS OR ABSTRACTS, FY-82: Paper based on pilot data accepted for presentation to the 1982 Annual Convention of the American Speech-Language-Hearing Association, Toronto, Canada, November 1982 - ("Identification of Synthetic Stop Consonant Stimuli by Hearing-Impaired Listeners").

DATE: 30 Sep 82 WORK UNIT NO.: 2540 STATUS: INTERIM ___ FINAL X

STARTING DATE: February 1981 DATE OF COMPLETION: 30 Sep 82

KEY WORDS: acoustic reflex latency, auditory brainstem response

TITLE OF PROJECT: Relationship Between Acoustic Reflex Latency Test and Auditory Brainstem Response in Patients with High Frequency Sensorineural Hearing Loss

PRINCIPAL INVESTIGATOR(S): Daniel M. Schwartz and H. Gustav Mueller

ASSOCIATE INVESTIGATOR(S): Bahman Jabbari, Brian E. Walden, Robert A. Prosek, Allen A. Montgomery, Donald Wittich

FACILITY: WRAMC DEPT/SVC: Dept. of Surgery/Otolaryngology Service

ACCUMULATIVE MEDCASE
COST: _____

ACCUMULATIVE CONTRACT
COST: _____

ACCUMULATIVE SUPPLY
COST: \$650.00

FY-83 MEDCASE: _____ CONTRACT COST: _____ SUPPLY COST: _____

DATE OF COMMITTEE APPROVAL
OF ANNUAL PROGRESS REPORT
FEB 25 1983

STUDY OBJECTIVE: To examine the relationship between the latency of the acoustic reflex and ABR responses in patients with high frequency hearing loss.

TECHNICAL APPROACH: None.

PROGRESS DURING FY-82: None -- recent research has shown that the acoustic reflex latency is an artifact of the measuring device, thus precluding continuation of this study.

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 TOTAL (TO DATE): 0 BEFORE COMPLETION OF STUDY: 0

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): None.

CONCLUSIONS: None -- Investigator has resigned his position at WRAMC.

PUBLICATIONS: NONE

NOTE: The Principal Investigator on this protocol has resigned his position effective 1 October 1982.

DATE: 30 Sep 82 WORK UNIT NO.: 2541 STATUS: INTERIM _____ FINAL X

STARTING DATE: 8 May 1981 DATE OF COMPLETION: 23 July 1982

KEY WORDS: audiometric configuration, pure tone threshold, speech band threshold

TITLE OF PROJECT: Influence of Audiometric Configuration on Pure Tone Versus Speech Band Thresholds in Adults with Sensori-neural Hearing Losses

PRINCIPAL INVESTIGATOR(S): Rauna K. Surr

ASSOCIATE INVESTIGATOR(S): Daniel M. Schwartz, Joyce H. Seidman, H. Gustav Mueller

FACILITY: WRAMC DEPT/SVC: Dept. of Surgery/Otolaryngology Service

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| FY-83 MEDCASE: _____ | CONTRACT COST: _____ | SUPPLY COST: _____ | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT <u>FEB 25 1983</u> |
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STUDY OBJECTIVE: To evaluate the efficacy of speech band stimuli developed by Franklin (1980) as an alternative to pure tone audiometry for hearing threshold measurements. A secondary purpose was to examine the test retest and inter-tester reliability of speech band thresholds.

TECHNICAL APPROACH: Hearing threshold was determined using conventional pure tone signals at octave frequencies from 250-8000 Hz and again using tapes of filtered speech bands having center frequencies analogous to those of pure tone signals. For comparative analysis, the 100 audiograms selected from the 60 listeners (some unilateral, some bilateral hearing losses) were divided into five groups of equal size on the basis of audiometric roll-off frequency. For one-half of the audiograms the threshold measurements were done twice to obtain estimates of test-retest reliability.

PROGRESS DURING FY-82: A paper was presented at the Annual Convention of the American Speech-Language-Hearing Association in Los Angeles in Nov 81 based on the data collected that calendar year. Spectrographic and 1/3-octave band analyses of the speech band tapes were performed and the results compared to the clinical threshold measurements. A manuscript was submitted and accepted for publication in Ear and Hearing.

Annual Progress Report (cont.) - Work Unit #2541

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 TOTAL (TO DATE): 60 BEFORE COMPLETION OF STUDY: 60

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): None.

CONCLUSIONS: In contrast to the findings of Franklin (1980) who reported excellent agreement between speech band and pure tone thresholds, the present data showed acceptable agreement between the two sets of stimuli only for listeners with flat hearing loss pattern. For patients with sloping audiometric configurations, speech band audiometry seriously underestimated the degree of high frequency loss. The 1/3-octave band analysis supported the clinical threshold results. They showed that the peak energy was not centered at the audiometric test frequency as stated by Franklin, particularly in the high frequency speech band tapes. In addition, a considerable amount of energy was measured at lower frequency regions below the stated limits of the bands, suggesting that Franklin did not achieve a 48 dB per octave filter slope as was indicated in the test manual. Based on our clinical test results and the analyses of the speech band stimuli, we strongly recommended continued investigation and refinement of the stimulus tapes before further clinical use.

PUBLICATIONS OR ABSTRACTS, FY-82:

The Effects of Audiometric Configuration on Speech Band Thresholds in Sensorineural Hearing Loss Subjects, Ear and Hearing (in press).

(NOTE: Projected date of publication is Sep-Oct 82. Reprint will be forwarded to DCI as soon as available.)

DATE: 30 Sep 82 WORK UNIT NO.: 2542 STATUS: INTERIM FINAL X

STARTING DATE: April 1981 DATE OF COMPLETION: December 1982

KEY WORDS: hearing aid, amplification, perceived benefit, questionnaire

TITLE OF PROJECT: An Assessment of the Benefit Derived from Hearing Aid Use

PRINCIPAL INVESTIGATOR(S): Brian E. Walden

ASSOCIATE INVESTIGATOR(S): Ernest L. Hepler, Marilyn E. Demorest, Roy K. Sedge, Robert L. Henderson

FACILITY: WRAMC

DEPT/SVC: Dept. of Surgery/Otolaryngology Service

ACCUMULATIVE MEDCASE COST: _____

ACCUMULATIVE CONTRACT COST: _____

ACCUMULATIVE SUPPLY COST: _____

FY-83 MEDCASE: _____ CONTRACT COST: _____ SUPPLY COST: _____

DATE OF COMMITTEE APPROVAL
OF ANNUAL PROGRESS REPORT
FEB 25 1983

STUDY OBJECTIVE: The objective of this research is to determine the relative benefit of amplification in a variety of common listening situations. The specific purposes are:

a. To detect significant differences in the benefit of hearing aid use as the following vary:

- (1) Setting - familiar vs. unfamiliar
- (2) Speaker - familiar vs. unfamiliar
- (3) Environment - noisy vs. quiet
- (4) Distractions (without masking) - present or not
- (5) Distance - close vs. far
- (6) Signal - soft vs. loud
- (7) Stimulus - speech vs. nonspeech
- (8) Masker - soft vs. loud
- (9) Masker - intermittent vs. steady
- (10) Location - indoor vs. outdoor
- (11) Visual Cues - present or not
- (12) Speech - live vs. reproduced
- (13) Acoustics - reverberant vs. non-reverberant
- (14) Patient age
- (15) Years of experience in hearing aid use
- (16) Formal aural rehabilitation training
- (17) Monaural vs. binaural hearing aid fitting
- (18) Hearing aid gain - mild, moderate, strong

- (19) Type of hearing aid - in-the-ear, ear-level, eyeglass, body aid
- (20) Education level of patient
 - b. To provide an indication of the overall long-term success of hearing aid use by hearing-impaired soldiers.
 - c. To provide data to be used in patient counselling regarding realistic expectations from amplification.
 - d. To assess the content validity of present hearing aid evaluation procedures.

TECHNICAL APPROACH: A self-assessment questionnaire is used to assess the perceived benefit of amplification in various environmental situations. The subject sample consists of experienced hearing aid users returning to the Army Audiology and Speech Center for periodic follow-up or other services, and experienced hearing aid users seen in the Hearing Clinic, Purdue University. The questionnaire uses a 5-point rating scale to quantify perceived benefit, with one being "very helpful" and five being "hinders performance." Subject ratings on the inventory are subjected to computer analysis.

PROGRESS DURING FY-82: A preliminary analysis of the data revealed that the twelve bipolar features were highly redundant and probably reflected fewer independent features. A factor analysis of the data, therefore, was performed. The results revealed that a quiet and a noise feature were dominant. Additionally, a "reduced stimulus input" factor and a "nonspeech/reproduced speech" factor also emerged. These four features were subjected to a reliability analysis which revealed relatively high coefficient alphas (i.e., .94 to .81). Analysis of variance and regression techniques were used to relate these factors to background variables.

NUMBER OF SUBJECTS STUDIED:
FY-82: _____ TOTAL (TO DATE): 129 BEFORE COMPLETION OF STUDY: 129

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): None.

CONCLUSIONS: The results revealed, among other significant effects, that (1) in-the-ear hearing aids are perceived as providing significantly less benefit in quiet situations and for nonspeech stimuli than ear-level or eyeglass aids, (2) aural rehabilitation experience produces significantly more perceived benefit in quiet listening situations, (3) the more hours of hearing aid use per day, the greater the perceived benefit, and (4) the effects of reduced sensory input is greater for older hearing aid users.

PUBLICATIONS OR ABSTRACTS, FY-82: A manuscript is currently being prepared for submission to the Journal of Speech and Hearing Disorders.

DATE: 30 Sep 82 | WORK UNIT NO.: 2544 | STATUS: INTERIM ___ FINAL X

STARTING DATE: 1 August 1981 | DATE OF COMPLETION: 26 August 1982

KEY WORDS: stuttering, rate, treated speech, temporal alterations

TITLE OF PROJECT: The Effects of Time Domain Manipulation of Speech on the Identification of Treated Stutterers

PRINCIPAL INVESTIGATOR(S): Robert A. Prosek

ASSOCIATE INVESTIGATOR(S): Charles M. Runyan, Allen A. Montgomery, Brian E. Walden, Daniel M. Schwartz, Susan P. Abernathy

FACILITY: WRAMC | DEPT/SVC: Dept. of Surgery/Otolaryngology Service

ACCUMULATIVE MEDCASE COST: _____ | ACCUMULATIVE CONTRACT COST: _____ | ACCUMULATIVE SUPPLY COST: \$600.00

FY-83 MEDCASE: _____ CONTRACT COST: _____ SUPPLY COST: _____ | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT
FEB 25 1983

STUDY OBJECTIVE: To determine whether changes in the segment and pause durations of the speech samples of treated stutterers affect the ability of listeners to discriminate these samples from those of nonstutterers.

TECHNICAL APPROACH: Both the stimulus tape and the listener judgments of previous studies were used to obtain the speech material that was manipulated in the present study. The tape recording consisted of 140 paired speech samples, four separate samples from 35 stutterers and 35 nonstutterers matched only for age and sex. Twenty-nine of the stutterers had successfully completed one of six stuttering treatment programs, and the selection procedures were confined to the 116 pairs produced by these talkers and their nonstuttering counterparts.

The listener responses obtained in previous investigations were examined in order to select stimulus pairs in which the treated stutterer and the nonstutterer had been readily discriminated by the judges, and in which the talkers had been reading the same material. The process yielded two groups of samples which met these criteria. In the first group, 20 pairs of stimuli were found in which the treated stutterer had been correctly identified 82% of the time or more, and these samples are referred to as the Easily Identified Treated Stutterers. The reading rates used by the treated stutterers in this group varied from 2.71 syllables per second (SS) to 4.67 SS (mean reading rate, 3.36 SS), whereas the nonstutterers in this group used reading rates which varied from 4.52 SS to 7.10 SS (mean reading

rate, 5.55 SS). In each pair of samples in this group, the nonstutterer had produced the sample using a faster reading rate than the treated stutterer with whom he had been paired.

In the second group of stimuli, 12 pairs were found in which the treated stutterer had been correctly identified only 35% of the time or less, and these samples are referred to as the Poorly Identified Treated Stutterers. The samples in this group were discriminable, but the nonstutterers were more likely to be labelled as the treated stutterers than the treated stutterers themselves. The reading rates used by the treated stutterers in this group varied from 3.60 SS to 6.01 SS (mean reading rate, 4.80 SS), while the rates used by the nonstutterers varied from 2.96 SS to 5.25 SS (mean reading rate, 4.16 SS). For these Poorly Identified samples, the treated stutterer in each pair had produced the sample using a faster reading rate than the normally fluent talker with whom he had been paired.

Reading rate was manipulated by altering the pause and segment durations produced by the treated stutterer to match those of the nonstutterer in each pair. Since reading rate is determined by phone and pause durations, equating these durations would have the effect of matching the reading rates. It was expected that once the reading rates had been matched, listeners would no longer be able to distinguish between the treated stutterers and the normally fluent talkers.

The 64 speech samples were lowpass filtered at 4.8 kHz, sampled at 10 kHz using a 12-bit A/D converter, and stored as disk files on the laboratory computer of the Army Audiology and Speech Center. The duration of each vowel, consonant and pause for every sample was measured using the waveform measurement program developed as part of the current study. Then each treated stutterer's file was edited in order to match his segment and pause durations to those of the nonstutterer with whom he had been paired, as closely as possible. This was accomplished by selecting a portion from the middle of a segment or pause and either replicating it until the desired duration was obtained or deleting it so that the remainder of the segment equalled the desired duration. Table 1 presents averaged duration and rate data for the nonstutterers and the unedited and edited versions of the treated stutterers' samples. A comparison of the reading rates of the nonstutterers and the edited samples of the stutterers reveals that excellent rate matches were obtained due to the editing.

A test tape was constructed from the disk files representing the original and edited samples. The tape consisted of the 32 original pairs, 32 pairs in which the sample produced by the treated stutterer had been edited, and 64 pairs of foils. The foils were randomly chosen from the pairs on the original stimulus tape which had not been selected for manipulation in the current study. The tape was judged by a group of 10 speech-language pathologists who had considerable experience with stutterers and stuttering therapy. Judgments were obtained individually from each therapist who was told that she would hear pairs of speech samples in which one sample was produced by a nonstutterer and one sample was produced by a treated stutterer. She was to indicate on a response sheet which member of each pair was the treated stutterer.

Since it is possible that a single subcomponent of rate, such as vowel or pause duration, may be responsible for the listener judgments, additional test tapes were prepared using the same materials and procedures described above. In the preparation of the second test tape, however, only the vowels produced by the treated stutterers were edited so that their durations

matched those of the corresponding nonstutterer; for the third tape, only the treated stutterers' consonants were edited; and for the fourth tape, only the pauses were edited. Each of these test tapes were judged by a separate group of 10 listeners who were graduate students in speech-language pathology. Again, the judges were required to indicate which member of each pair was the treated stutterer.

PROGRESS DURING FY-82: The listener responses obtained from the judgments of the first test tape, in which the durations of segments and pauses had been altered, were examined to determine if the listeners' labelling behavior had been affected. Of the 200 responses obtained for the unedited samples of the Easily Identified Treated Stutterers, 182 (91%) were correct, indicating that, as expected, listeners readily distinguished the speech of the treated stutterers in this group from that of the nonstutterers. In contrast, of the 200 responses obtained for the edited samples of this group, only 127 (64%) were correct. Thus when the difference in reading rate between pairs of talkers is reduced, listeners can no longer readily distinguish between them. Similar results were obtained for the Poorly Identified Treated Stutterers. Of the 120 responses obtained for the unedited samples of this group, only 32 (27%) were correct. That is, as expected the treated stutterers of this group were not likely to be labelled as the treated stutterer, but their samples were distinguishable from those of the normally fluent talkers. For the edited samples of the Poorly Identified Treated Stutterers, 73 of the 120 responses (61%) were correct. Again, when the difference in reading rate between pairs of talkers is minimized, listeners' responses are altered. The significance of the change in correct responses was assessed using McNemar's Exact Test for Correlated Proportions under the null hypothesis that minimizing the differences in reading rate had no effect on the listeners' ability to correctly identify the treated stutterers. The data for this test condition are arranged in Table 2 as separate contingency tables for the Easily Identified and Poorly Identified Treated Stutterers. For the Easily Identified group, McNemar's Test yielded a probability of 2.379×10^{-11} , while for the Poorly Identified group, the probability was 1.673×10^{-7} , both of which are significant. Thus, reading rate has a substantial influence on the correct identification of treated stutterers in paired comparison tests.

The listener responses obtained when only the vowel durations of the treated stutterers are edited to match those of the nonstutterers are presented in Table 3. For the unedited samples of the Easily Identified Treated Stutterers, 82.5% of the responses were correct, while for the edited samples, 76% of the responses were correct. Although the listeners' ability to distinguish the samples in this group is reduced, the change in labelling behavior due to minimization of vowel duration differences clearly is not as great as when all phone and pause durations are matched. For the original, unedited samples of the Poorly Identified Treated Stutterers, 35% of the responses were correct, while 44% were correct for the edited versions of the stimuli. Again, the ability to distinguish between talkers is reduced, but the magnitude of the change is less than when all durations are manipulated. The data in Table 3 were tested using McNemar's Test, and probabilities of 0.096 and 0.177 were obtained for the Easily Identified and Poorly Identified groups, respectively. These values indicate that the

change in labelling behavior due to alterations in vowel durations is not significant.

The contingency tables formed from the listener responses obtained when only the consonant durations of the treated stutterers were altered are presented in Table 4. These results are similar to those presented in Table 3 in that the ability to distinguish between pairs of talkers is reduced, but the magnitude of the change in correct responses is less than that obtained when all segment and pause durations are edited. The probabilities calculated by McNemar's Test were 0.203 and 0.143 for the Easily Identified and Poorly Identified groups, respectively.

Finally, the listener responses obtained for the test condition in which only the pauses of the treated stutterers were edited to match those of the nonstutterers are presented in Table 5. Unlike previous test conditions, the ability to distinguish between talkers was increased, rather than reduced, due to the pause alterations. For the unedited productions of the Easily Identified Treated Stutterers, 83% of the responses were correct, while 86% of the responses were correct for the edited versions of these samples. For the unedited versions produced by the Poorly Identified Treated Stutterers, 33% of the responses were correct, and this dropped to 29% for the edited samples. Although the change in number of correct responses in this condition was not in the direction anticipated, the results of McNemar's Test were not significant. The probability obtained for the Easily Identified Treated Stutterers was 0.392 and that for the Poorly Identified Treated Stutterers was 0.500.

NUMBER OF SUBJECTS STUDIED: Not applicable.

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): None.

CONCLUSIONS: The major finding of the current study is that the labelling behavior of listeners is affected by the reading rate used in the pairs of samples they are asked to judge. Further, when the durations of the individual subcomponents of rate (vowels, consonants and pauses) are manipulated, listeners' ability to distinguish between pairs of talkers is not altered significantly. Thus, reading rate in its entirety is a major factor influencing the perception of the speech of treated stutterers. An important implication of this result for both the experimental and clinical evaluation of the speech of treated stutterers is that the reading or speaking rates used by the patients should be measured. Since research involving normally fluent talkers indicates that they can be expected to produce speech which varies in rate from 4.4 to 5.9 syllables per second, this range appears to be a reasonable goal for treated stutterers to attain. In addition, the rates used by control talkers will need to be measured to insure that they are not biased toward either extreme of the rate continuum.

If the goal of a stuttering treatment program is the production of speech by the stutterer which is as close to normal as possible, then the rate used by the patient at the termination of therapy must be evaluated critically. Speech which is produced too slowly at the end of treatment very likely will not be judged as "normal" even though behaviors traditionally associated with stuttering have been eliminated. The rate used by a treated stutterer will have an effect in everyday situations as well as in

the clinic or laboratory. Research concerning impression formation indicates that when any talker uses a relatively slow rate and/or pauses frequently, listeners tend to form an unfavorable impression of that talker. Thus, a treated stutterer who increases fluency by decreasing speech rate may bias his listeners simply by his manner of speech production. Since speech rate is not difficult to measure, its use in the evaluation of treated stutterers should be readily implemented.

PUBLICATIONS OR ABSTRACTS, FY-82:

Prosek, R. A. and Runyan, C. M. Temporal characteristics related to the discrimination of stutterers' and nonstutterers' speech samples. Journal of Speech and Hearing Research, 1982, 25, 29-33.

A second manuscript entitled "The Effects of Segment and Pause Manipulations on the Identification of Treated Stutterers" currently is being prepared for submission to the Journal of Speech and Hearing Research.

Table 1. Averaged durations (in msec) and reading rate (in syllables per second) for the treated stutters and their non-stuttering counterparts. "Unedited Stutterers" refers to the original speech samples produced by the treated stutters, while "Edited Stutterers" refers to the samples after the durations had been altered.

| | <u>Easily Identified Treated Stutterers</u> | | | | | | | | |
|------------|---|-------------|----------------------------|----------|--------------------------|-------------------|----------|-------------|-------------------|
| | <u>NONSTUTTERERS</u> | | <u>UNEDITED STUTTERERS</u> | | <u>EDITED STUTTERERS</u> | | | | |
| | <u>n</u> | <u>MEAN</u> | <u>STAN. DEV.</u> | <u>n</u> | <u>MEAN</u> | <u>STAN. DEV.</u> | <u>n</u> | <u>MEAN</u> | <u>STAN. DEV.</u> |
| VOWELS | 263 | 111.65 | 25.53 | 264 | 161.27 | 31.55 | 264 | 112.89 | 21.01 |
| CONSONANTS | 414 | 58.41 | 19.40 | 427 | 87.81 | 24.07 | 427 | 58.36 | 12.80 |
| PAUSES | 4 | 307.10 | 149.08 | 31 | 345.40 | 138.06 | 4 | 229.30 | 134.50 |
| RATE | | 5.55 | .687 | | 3.36 | .528 | | 5.56 | .725 |
| | | | | | | | | | |
| | <u>Poorly Identified Treated Stutterers</u> | | | | | | | | |
| | <u>NONSTUTTERERS</u> | | <u>UNEDITED STUTTERERS</u> | | <u>EDITED STUTTERERS</u> | | | | |
| | <u>n</u> | <u>MEAN</u> | <u>STAN. DEV.</u> | <u>n</u> | <u>MEAN</u> | <u>STAN. DEV.</u> | <u>n</u> | <u>MEAN</u> | <u>STAN. DEV.</u> |
| VOWELS | 145 | 148.17 | 26.49 | 145 | 136.81 | 22.98 | 145 | 162.05 | 30.58 |
| CONSONANTS | 211 | 72.48 | 27.67 | 216 | 66.48 | 32.34 | 216 | 78.41 | 27.70 |
| PAUSES | 12 | 376.07 | 76.14 | 4 | 333.05 | 15.85 | 12 | 354.08 | 116.74 |
| RATE | | 4.16 | .728 | | 4.80 | .791 | | 4.06 | .815 |

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Table 2. Number of correct and incorrect responses obtained for the unaltered stimulus pairs and the pairs in which the durations of the segments and pauses of the treated stutterers had been altered.

Easily Identified Treated Stutterers

| | | UNEDITED SAMPLES | | |
|-------------------|-----------|------------------|------------------|--------------|
| | | <u>CORRECT</u> | <u>INCORRECT</u> | <u>TOTAL</u> |
| EDITED SAMPLES | CORRECT | 118 | 9 | 127 |
| | INCORRECT | 64 | 9 | 73 |
| | TOTAL | 182 | 18 | 200 |

Poorly Identified Treated Stutterers

| | | UNEDITED SAMPLES | | |
|-------------------|-----------|------------------|------------------|--------------|
| | | <u>CORRECT</u> | <u>INCORRECT</u> | <u>TOTAL</u> |
| EDITED SAMPLES | CORRECT | 21 | 52 | 73 |
| | INCORRECT | 11 | 36 | 47 |
| | TOTAL | 32 | 88 | 120 |

Table 3. Number of correct and incorrect responses obtained for the unedited pairs and the pairs in which the vowel durations of the treated stutterer had been edited to match those of the nonstutterer in each pair of stimuli.

Easily Identified Treated Stutterers

| | | UNEDITED SAMPLES | | |
|-------------------|-----------|------------------|------------------|--------------|
| | | <u>CORRECT</u> | <u>INCORRECT</u> | <u>TOTAL</u> |
| EDITED SAMPLES | CORRECT | 137 | 16 | 153 |
| | INCORRECT | 28 | 19 | 47 |
| | TOTAL | 165 | 35 | 200 |

Poorly Identified Treated Stutterers

| | | UNEDITED SAMPLES | | |
|-------------------|-----------|------------------|------------------|--------------|
| | | <u>CORRECT</u> | <u>INCORRECT</u> | <u>TOTAL</u> |
| EDITED SAMPLES | CORRECT | 20 | 33 | 53 |
| | INCORRECT | 22 | 45 | 67 |
| | TOTAL | 42 | 78 | 120 |

Table 4. Number of correct and incorrect responses obtained for the unedited stimulus pairs, and the edited pairs in which the consonant durations of the treated stutterer in each pair had been altered to match those of the nonstutterer.

Easily Identified Treated Stutterers

| | | UNEDITED SAMPLES | | |
|-------------------|-----------|------------------|------------------|--------------|
| | | <u>CORRECT</u> | <u>INCORRECT</u> | <u>TOTAL</u> |
| EDITED SAMPLES | CORRECT | 134 | 20 | 154 |
| | INCORRECT | <u>30</u> | <u>16</u> | <u>46</u> |
| | TOTAL | 164 | 36 | 200 |

Poorly Identified Treated Stutterers

| | | UNEDITED SAMPLES | | |
|-------------------|-----------|------------------|------------------|--------------|
| | | <u>CORRECT</u> | <u>INCORRECT</u> | <u>TOTAL</u> |
| EDITED SAMPLES | CORRECT | 20 | 24 | 44 |
| | INCORRECT | <u>14</u> | <u>62</u> | <u>76</u> |
| | TOTAL | 34 | 86 | 120 |

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Table 5. Number of correct and incorrect responses obtained for the unedited stimulus pairs and for the pairs in which the number of pauses and pause durations of the treated stutterer in each pair had been altered to match those of the nonstutterers.

| | | UNEDITED SAMPLES | | |
|-------------------|-----------|------------------|-----------|-------|
| | | CORRECT | INCORRECT | TOTAL |
| EDITED SAMPLES | CORRECT | 152 | 20 | 172 |
| | INCORRECT | 14 | 14 | 28 |
| | TOTAL | 166 | 34 | 200 |
| | | | | |
| | | UNEDITED SAMPLES | | |
| | | CORRECT | INCORRECT | TOTAL |
| EDITED SAMPLES | CORRECT | 20 | 15 | 35 |
| | INCORRECT | 20 | 65 | 85 |
| | TOTAL | 40 | 80 | 120 |

DATE: 30 Sep 82 | WORK UNIT NO.: 2546 | STATUS: INTERIM ___ FINAL X

STARTING DATE: April 1982 | DATE OF COMPLETION: September 1982

KEY WORDS: hearing loss, hearing aids, aural rehabilitation, adult, follow-up survey

TITLE OF PROJECT: Follow-up Survey of New Hearing Aid Users

PRINCIPAL INVESTIGATOR(S): Charlene K. Scherr

ASSOCIATE INVESTIGATOR(S): Daniel M. Schwartz, Gregory A. Antoine

FACILITY: WRAMC | DEPT/SVC: Dept. of Surgery/Otolaryngology Service

ACCUMULATIVE MEDCASE COST: _____ | ACCUMULATIVE CONTRACT COST: _____ | ACCUMULATIVE SUPPLY COST: _____

FY-83 MEDCASE: _____ CONTRACT COST: _____ SUPPLY COST: _____ | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT
FEB 25 1983

STUDY OBJECTIVE: To describe the patient acceptability ratings and frequency of use patterns of new hearing aid users who received a brief 1½ hour hearing aid orientation at the Army Audiology and Speech Center.

TECHNICAL APPROACH: This study was an evaluation of the results of a follow-up survey of patients seen at the Army Audiology and Speech Center for a brief hearing aid orientation following hearing aid fitting.

PROGRESS DURING FY-82: Follow-up questionnaires were obtained from 377 patients and subjected to statistical analysis. Additional audiometric data were obtained from a subsample of 194 patients' records. The audiometric data were then employed as a basis to examine the relationship between hearing loss and hearing aid usage patterns. These results were reported at a professional meeting, and a manuscript was prepared.

NUMBER OF SUBJECTS STUDIED:
FY-82: 377 | TOTAL (TO DATE): 377 | BEFORE COMPLETION OF STUDY: 377

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): None.

CONCLUSIONS: The results indicate that the patients surveyed use their post-auricular hearing aids extensively in a variety of listening environments and that they report few problems with aid use in general. They continue to have their greatest difficulty listening in noisy and group situations but are basically well satisfied with their fittings.

PUBLICATIONS OR ABSTRACTS, FY-82:

Scherr, C., and Schwartz, D. Follow-up Survey of New Hearing Aid Users. Presented at Summer Institute of the Academy of Rehabilitative Audiology, Big Canoe, Georgia, June 1982.

Scherr, C., Schwartz, D., and Montgomery, A. Follow-up Survey of New Hearing Aid Users. Manuscript submitted for publication in the Journal of the Academy of Rehabilitative Audiology.

| | | |
|--|---|--|
| DATE: 30 Sep 82 | WORK UNIT NO.: 2547 | STATUS: INTERIM <u>X</u> FINAL <u> </u> |
| STARTING DATE: 1 September 1982 | | DATE OF COMPLETION: 1 September 1983 |
| KEY WORDS: voice disorders, acoustical analysis, voice quality | | |
| TITLE OF PROJECT: Acoustic Correlates of Voice Quality Judgments | | |
| PRINCIPAL INVESTIGATOR(S): Robert A. Prosek | | |
| ASSOCIATE INVESTIGATOR(S): Allen A. Montgomery, Brian E. Walden, John M. Dobrowski | | |
| FACILITY: WRAMC | DEPT/SVC: Dept. of Surgery/Otolaryngology Service | |
| ACCUMULATIVE MEDCASE COST: <u> </u> | ACCUMULATIVE CONTRACT COST: <u> </u> | ACCUMULATIVE SUPPLY COST: <u> \$574.00 </u> |
| FY-83 MEDCASE: <u> \$17,000 </u> | CONTRACT COST: <u> </u> | SUPPLY COST: <u> </u> |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT <u> FEB 25 1983 </u> |

STUDY OBJECTIVE: To determine if the perceptual properties of voice quality can be related to acoustic features.

TECHNICAL APPROACH: Vowel samples produced by 44 patients diagnosed as unilateral vocal fold paralysis, vocal nodules and vocal polyps are the speech material to be used in the study. These vowels will be mixed with those produced by 16 normal talkers and 8 talkers with laryngitis and presented to a panel of 10 speech-language pathologists for judgments of voice quality. The listeners will rate each voice sample on eleven scales: 1) adequacy, 2) pitch breaks, 3) voice tremor, 4) excess loudness variation, 5) loudness decay, 6) harshness, 7) hoarseness, 8) breathiness, 9) strained-strangled voice, 10) voice stoppages, and 11) pitch variations. The "pitch variations" scale was added to the perceptual variables in order to assess slow changes in pitch which occur during the production of the vowel. The scale had been inadvertently omitted from the original protocol. Each vowel sample will be classified according to the perceptual scales having the highest index of agreement among the judges. Acoustical analysis of the voice samples will consist of computer-based measurements of the spectral flatness of the inverse filter, spectral flatness of the residue signal, pitch perturbation quotient, amplitude perturbation quotient, pitch amplitude, coefficient of excess, slope of the pitch amplitude function, change-over frequency, weighted spectral energy and fundamental vocal frequency. The acoustical and perceptual data will be analyzed using profile analysis

Annual Progress Report (cont.) - Work Unit #2547

techniques in order to determine if different patterns of acoustical variables are strongly associated with different voice quality labels.

PROGRESS DURING FY-82: The stimulus tape consisting of the vowel samples in a random order was prepared and listener judgments are being obtained at the present time. Complete acoustical analysis will begin when funds are available for the real time, narrow-band analyzer.

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 TOTAL (TO DATE): 0 BEFORE COMPLETION OF STUDY: 44
(recorded voice samples)

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): None.

CONCLUSIONS: Not applicable at the present time.

PUBLICATIONS OR ABSTRACTS, FY-82: Not applicable at the present time.

| | | | |
|--|-----------------------------|---|--|
| DATE: 22 Oct 82 | WORK UNIT NO.: 2610 | STATUS: INTERIM XX | FINAL |
| STARTING DATE: | | DATE OF COMPLETION: 1983 | |
| KEY WORDS: ALG - Transplant Rejection | | | |
| TITLE OF PROJECT: Use of Antilymphocyte Preparation in Renal Transplantation | | | |
| PRINCIPAL INVESTIGATOR(S): J.A. Light, COL, MC | | | |
| ASSOCIATE INVESTIGATOR(S): J.A. Biggers, K. Oddenino, B. Reinmuth, S. Metz | | | |
| FACILITY: WRANC | | DEPT/SVC: Dept of Surgery, Organ Transplant Svc | |
| ACCUMULATIVE MEDICASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: | |
| FY-83 MEDICASE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT |
| | | \$380.40 | FEB 25 1983 |

STUDY OBJECTIVE: 1. To improve allograft and patient survival in recipients of renal transplants. 2. To determine whether ALG used as primary treatment for rejection is superior to ALG used as prophylaxis in the early post transplant TECHNICAL APPROACH: /period to prevent rejection.

Cadaver transplant recipients were randomized to receive ALG either as prophylaxis or therapy for allograft rejection. Lymphocyte enumeration and classification (over)

PROGRESS DURING FY-82: Twenty-two additional patients have been treated in accordance with this protocol in the past year (14-prophylaxis, 8-rejection reversal). To date, 52 patients have been treated with ALG (31-prophylaxis, 21-rejection reversal

NUMBER OF SUBJECTS STUDIED: (over)

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: 28

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

The risk of ALG reaction is 8%/course of ALG, although 20% of patients with repeated courses may experience a significant reaction.

CONCLUSIONS: ALG reverses 93% of acute rejection episodes compared with 50% for steroids. The use of ALG is associated with 25% improvement in one year graft survival. It appears that ALG when used primarily for rejection reversal is as effective as when used in the traditional prophylactic manner, although definitive conclusions are still premature. Adequate numbers of patients and adequate followup should be available after one more year of study. The dose (over)

PUBLICATIONS OR ABSTRACTS, FY-82:

Sequential Antilymphocyte Globulin (ALG) Therapy (Rx) Improves Graft and Patient Survival. Presented August 1982, IXth International Congress, Transplantation Society. To be published in Transpl Proc 15, 1983.

TECHNICAL APPROACH: (Cont) and biopsies were routinely performed. Rejected grafts were removed and examined microscopically, and eluted. Eluates were analyzed for immunoglobulins and HLA specificity.

PROGRESS DURING FY82: (Cont) 84% of patients experienced at least one rejection episode. Twenty-one of the 31 patients in the prophylaxis group have functioning grafts (68%). These 31 patients experienced a total of 46 rejection episodes (1.5/patient) of which 35 were treated with ALG, all but 3 successfully. 40% of this group experienced allograft rejection while receiving ALG prophylaxis suggesting the dose utilized for prophylaxis was suboptimal. Sixteen of 21 patients in the rejection reversal group are still functioning (76%). There have been 42 rejection episodes (2.0/pt), 31 of which were treated with ALG, all but 3 successfully. Serum creatinines are similar in both groups. Two patients in the prophylaxis group and 1 patient in the rejection reversal group are chronically rejecting. One prophylaxis patient died 6 months post transplant from an MI (SCr - 1.6 mg/dl).

CONCLUSIONS: of ALG has been increased to 30 mg/kg/qd x 14 days in the prophylaxis group from 20 mg/kg/qd x 10 days and 20 mg/kg/qod x 10 days. Groups using larger dose have about 45% acute rejection.

DATE: 18 Oct 82 | WORK UNIT NO.: 2615 | STATUS: INTERIM XX FINAL

STARTING DATE: _____ DATE OF COMPLETION: _____

KEY WORDS: _____

TITLE OF PROJECT: Serum Beta 2 Microglobulin (B₂M): An Adjunctive Monitoring Test in Renal Transplantation

PRINCIPAL INVESTIGATOR(S): J.A. Light, COL, MC

ASSOCIATE INVESTIGATOR(S): J.A. Biggers, W. Hayes, B. Reinmuth

FACILITY: WRMC | DEPT/SVC: Dept of Surgery, Organ Transplant Svc

ACCUMULATIVE FEDCASE COST: _____ ACCUMULATIVE CONTRACT COST: _____ ACCUMULATIVE SUPPLY COST: _____

FY-83 FEDCASE: \$8,000 | CONTRACT COST: _____ | SUPPLY COST: \$51,935.01 | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983

STUDY OBJECTIVE: Assess the value of B₂M in monitoring renal function, allograft rejection activity, impact of immunosuppression, and infection on the transplanted kidney.

TECHNICAL APPROACH: Serum is collected and analyzed daily and compared with other standard clinical parameters.

PROGRESS DURING FY-82: Approximately 1500 analyses were performed on 43 additional patients in FY82 (all together 5200 analyses on 146 patients). B₂M tests have been run every day that a Serum Creatinine determination was made. (over)

NUMBER OF SUBJECTS STUDIED:

FY-82: 43 | TOTAL (TO DATE): 146 | BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): _____

CONCLUSIONS: B₂M is a sensitive, reliable, reproducible test that is a better indicator of allograft rejection activity than other available parameters. It aids significantly the differential diagnosis of infection, obstruction, ATN and rejection. The reasons for BMV elevation in viremia is intriguing and will be further investigated. B₂M elevations after therapy appear to signal ongoing allograft rejection and suggest that further antirejection (over)

PUBLICATIONS OR ABSTRACTS, FY-82:

Serum Beta-2-Microglobulin: An Adjunctive Monitoring Test in Renal Transplantation, J.A. Light, J.A. Biggers, M.R. Alijani, M. Smith, & K. Oddenino, Proc Clin Dial Transpl Forum 10:67-72, 1980 (published July 82)

Progress During FY82: (Cont) Eighty-one patients having 111 identifiable rejection episodes were analyzed in depth. The B₂M predicted the rejection episode before the SCr in 73% of cases (49/67) by a mean of 4 days, and confirmed the diagnosis in the remainder. There were no false negative tests. In 7 identifiable cases of isolated CMV infection, the B₂M/SCr ratio increased to 8.0 (normal 2.5-3.0, rejection 4-5). In 3 cases of ureteral obstruction the B₂M remained unchanged while the SCr doubled. In 7 rejection episodes the B₂M did not return to normal levels (the SCr did). Six of 7 had subsequent rejection within 2 weeks. In 55 rejection episodes where both parameters returned to normal levels, only 29 had subsequent rejection occurring after 1 month.

Conclusions: (Cont) treatment should be employed. B₂M levels also correlate with graft survival. Further research is needed to improve test automation and to develop better correlation with other assays for the differential diagnosis of rejection and viral infection.

DATE: 22 Oct 82 | WORK UNIT No.: 2617 | STATUS: INTERIM XX FINAL

STARTING DATE: | DATE OF COMPLETION:

KEY WORDS:

TITLE OF PROJECT: Lymphocyte depletion: Immunosuppression for Renal Transplantation

PRINCIPAL INVESTIGATOR(S): J.A. Light, COL, MC - J.A. Biggers, MAJ, MC

ASSOCIATE INVESTIGATOR(S): D.M. Strong, S. Metz, K. Oddenino

FACILITY: WRANC | DEPT/SVC: Dept of Surg, Organ Transplant Svc

ACCUMULATIVE MEDICASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST:

FY-83 MEDICASE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT
\$1,441.85 | FEB 25 1983

STUDY OBJECTIVE: Alter immune system's response to sensitized transplant antigens by lymphocyte depletion.

TECHNICAL APPROACH: Cannulation of thoracic duct and drainage of whole lymph for 6 weeks. Lymph is cell depleted by centrifugation or freeze thaw killing and reinfused daily.

PROGRESS DURING FY-82: Three additional patients have had successful thoracic duct drainage. One patient transplanted with a positive crossmatch failed at 2 months due to rejection. Two patients transplanted with negative (over)

NUMBER OF SUBJECTS STUDIED:

FY-82: 3 | TOTAL (TO DATE): 11 | BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
None

CONCLUSIONS: One year graft survival in patients with positive crossmatch kidneys is 50% with pre transplant preparation by lymphocyte depletion. Overall actual graft success in all patients transplanted after lymphocyte depletion is 56%. TDD is the only accepted method of preparation for highly sensitized patients, but the mechanism remains elusive despite substantial investigation. New technology is expected in FY83 to further investigate the basic immunological events.

PUBLICATIONS OR ABSTRACTS, FY-82:
Successful Renal Transplantation (Tx) Despite Positive T Cell Crossmatch with Pre Transplant Lymphocyte Depletion (LD), Biggers, J.A., Light, J.A., Strong, D.M. Metz, S., Detrick-Hooks, B. Submitted to IXth International Congress, Transplantation Society, Mar 1982. (not accepted)

| | | |
|---|--|--|
| DATE: 22 Oct 82 | Work UNIT No.: 2617 | STATUS: INTERIM XX FINAL |
| STARTING DATE: | | DATE OF COMPLETION: |
| KEY WORDS: | | |
| TITLE OF PROJECT: Lymphocyte depletion: Immunosuppression for Renal Transplantation | | |
| PRINCIPAL INVESTIGATOR(S): J.A. Light, COL, MC - J.A. Biggers, MAJ, MC | | |
| ASSOCIATE INVESTIGATOR(S): D.M. Strong, S. Metz, K. Oddenino | | |
| FACILITY: WRAHC | DEPT/SVC: Dept of Surg, Organ Transplant Svc | |
| ACCUMULATIVE WEDCARE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
| FY-83 WEDCARE: | CONTRACT COST: | SUPPLY COST: |
| | | \$1,441.85 |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: Alter immune system's response to sensitized transplant antigens by lymphocyte depletion.

TECHNICAL APPROACH: Cannulation of thoracic duct and drainage of whole lymph for 6 weeks. Lymph is cell depleted by centrifugation or freeze thaw killing and reinfused daily.

PROGRESS DURING FY-82: Three additional patients have had successful thoracic duct drainage. One patient transplanted with a positive crossmatch failed at 2 months due to rejection. Two patients transplanted with negative (over)

NUMBER OF SUBJECTS STUDIED:

FY-82: 3 TOTAL (TO DATE): 11 BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS: One year graft survival in patients with positive crossmatch kidneys is 50% with pre transplant preparation by lymphocyte depletion. Overall actual graft success in all patients transplanted after lymphocyte depletion is 56%. TDD is the only accepted method of preparation for highly sensitized patients, but the mechanism remains elusive despite substantial investigation. New technology is expected in FY83 to further investigate the basic immunological events.

PUBLICATIONS OR ABSTRACTS, FY-82:

Successful Renal Transplantation (Tx) Despite Positive T Cell Crossmatch with Pre Transplant Lymphocyte Depletion (LD), Biggers, J.A., Light, J.A., Strong, D.M. Metz, S., Detrick-Hooks, B. Submitted to IXth International Congress, Transplantation Society, Mar 1982. (not accepted)

PROGRESS DURING FY82: (Cont) crossmatches have functioning kidneys one month and 4 months post op.

Overall Progress: Eleven patients have had attempted thoracic duct drainage. Two had no major thoracic duct which could be cannulated. Three patients were transplanted with negative crossmatch kidneys (2 of 3 successful, all successful at 6 months). Six patients were transplanted with positive crossmatch kidneys. Two had hyperacute rejection and loss of their grafts. One had acute rejection and loss of her kidney at 2 months. The remaining 3 patients have functioning kidneys 14 months, 19 months and 24 months post transplant. The project also supplies lymph for WU #2621 and WU#1327-81. The cells are also used to supply IL-Z for long term cell culture studies at NCI, NMRI and USUHS.

| | | |
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| DATE: 25 Oct 82 | Work Unit No.: 2618 | STATUS: INTERIM XX FINAL |
| STARTING DATE: August 1980 | DATE OF COMPLETION: | |
| KEY WORDS: | | |
| TITLE OF PROJECT: Intentional Donor Specific Pretransplant Transfusion | | |
| PRINCIPAL INVESTIGATOR(S): J.A. Light, J. Kumar | | |
| ASSOCIATE INVESTIGATOR(S): J.A. Biggers, S. Metz, K. Oddenino | | |
| FACILITY: HRMC | DEPT/SVC: Dept of Surgery, Organ Transplant Svc | |
| ACCUMULATIVE MEDICASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
| FY-83 MEDICASE: | CONTRACT COST: \$1,830.66 | SUPPLY COST: |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: 1. Decrease incidence of rejection & improve long term results of transplantation. 2. Determine which type of blood is most efficient. 3. Determine antibody production to T & B lymphocytes & red cell antigens with the types of ~~TECHNICAL APPROACH:~~ /transfusion. 4. Measure MLC & CML responses before & after trans- fusion./

TECHNICAL MODIFICATION: (over)

PROGRESS DURING FY-82: Fifteen additional donor-recipient pairs have been trans- fused according to the stored DST protocol. Thirteen have been transplanted, 11 successfully. One kidney was lost to hyperacute rejection and 1 to acute (over)

NUMBER OF SUBJECTS STUDIED:

FY-82: 15 TOTAL (TO DATE): 27 BEFORE COMPLETION OF STUDY: 10

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS: Sensitization is a severe risk when fresh DST are used. Four of 7 patients on the protocol were sensitized. Stored DST on the other hand, offers a minimal risk of sensitization. Although the incidence of acute graft rejection has been comparable to previous haploidentical living related transplants (13/16 as opposed to 18/24), the severity of the rejection episodes have been mild and the long term survival results excellent (88% vs 68% at 1 year). Studies

PUBLICATIONS OR ABSTRACTS. FY-82: /are underway to identify underlying mechanisms.

1. Fresh Vs Stored Blood in Donor Specific Transfusion, Presented 1st Inter- national Transfusion/Transplant Conference, Los Angeles, Feb 1982. Published Transpl Proc, Vol XIV, No.2 (June), 296-301, 1982.
2. Donor Specific Transfusion without Sensitization. Presented to Amer Society of Transplant Surgeons, Chicago, IL, June 1982. Transplantation, in press, Dec 1982.
3. Donor Specific Transfusion with Minimal Sensitization. Presented to IX Inter- national Congress, Transplantation Society, Brighton, England Aug, 1982. To be published Transpl Proc 15, 1983.

(over)

TECHNICAL MODIFICATION: (Cont) The question of which blood product to use seems to be relatively clear from the data collected on the patients treated under this protocol as it currently exists. A modification to address different aspects of DST has been written and approved.

In order to address the need for recipient exposure to donor antigen, the recipient population will be divided into two groups: 1. one group will receive blood from the intended kidney donor and 2. the other group will be transfused with blood from an unrelated donor who shares the HLA antigens shared by the donor and recipient but lacks the antigens that the donor does not share with the recipient. All transfusions will be collected, stored, crossmatched and administered as before.

In order to address the mechanism of the transfusion effect, suppressor cell assays will be performed on recipients who will be transfused locally. Blood samples will be collected between transfusions and pretransplantation and tested for the presence of suppressor cell subpopulations. Functional suppressor cell assay will be done in conjunction with the mixed lymphocyte culture. Suppressor cell surface markers will be assessed using the FACS.

At the time of each transfusion, an aliquot of the transfused blood will be saved for FACS analysis (only when FACS is available) in an effort to assess the cellular components of the stored unit.

The patients to be included in this study will be expanded to include HLA identicals as well as haploidenticals. At the University of Alabama, a similar protocol has yielded similar results in the haploidentical group. In addition, they have used stored DST's in HLA identical recipients. Only 1/15 experienced rejection post transplant. In our HLA identical series, where the recipients receive deliberately 3 units of random blood prior to transplantation, 10/16 have experienced acute rejection episodes. We have elected to extend to our HLA identical patients the same protocol as is used for haploidentical recipients, and to delete random donor transfusions, except where medically indicated.

PROGRESS DURING FY82: rejection (ruptured kidney) 6 weeks post op. Two patients developed a positive T cell crossmatch post stored DST and could not be transplanted with their intended DST donor. (One additional patient (TC) was entered on the fresh DST protocol. This patient developed a strong T cell positive crossmatch after the first transfusion.)

No patients developed RBC antibodies. This aspect of the study is discontinued. MLC and CML responses changed in an unpredictable manner. Lymphocytes are still collected and frozen, but run now in retrospect in a single matrix in selected patients.

Pilot studies on the effects of storage on cellular constituents of blood from normal donors have been performed and suggest selective loss of T cells as blood ages. Further studies are in progress.

PUBLICATIONS OR ABSTRACTS: (Cont)

Poster Presentations

1. Antibody Formation in Fresh Vs. Stored Donor Specific Transfusion. Presented Feb 1982 to the American Association of Clinical Histocompatibility Testing, San Francisco, CA.
2. Cellular Characteristics of Stored Blood Used for Transfusion. Presented Feb 1982 to the American Association of Clinical Histocompatibility Testing, San Francisco, CA.

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| DATE: 27 Oct 82 | WORK UNIT NO.: 2620 | STATUS: INTERIM X FINAL |
| STARTING DATE: | DATE OF COMPLETION: | |
| KEY WORDS: | | |
| TITLE OF PROJECT: Use of Steroids for Transplantation Rejection | | |
| PRINCIPAL INVESTIGATOR(S): J.A. Light, COL, MC | | |
| ASSOCIATE INVESTIGATOR(S): J.A. Biggers, K. Oddenino | | |
| FACILITY: WRAMC | DEPT/SVC: Dept of Surgery, Organ Transplant Svc | |
| ACCUMULATIVE MEDICASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
| FY-83 MEDICASE: None | CONTRACT COST: None | SUPPLY COST: None |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: 1. To determine the most effective means of administering high dose steroids for the treatment of acute allograft rejection. 2. To quantitate ~~changes in lymphocyte subsets following steroid administration.~~

TECHNICAL APPROACH: Patients who were rejecting their transplants were to be randomized to receive Solumedrol either 5 mg/kg IV BID or 10 mg/kg IV QD and to have serial lymphocyte subset analysis by monoclonal antibody determinations using the FACS.

PROGRESS DURING FY-82: No patients were entered into this protocol. The ability to measure lymphocyte subsets failed to materialize again in 1982. We still feel the question is worth addressing and recommend continuing the protocol in inactive status/

NUMBER OF SUBJECTS STUDIED:

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

N/A

CONCLUSIONS: Presumably the project will be activated, probably in modified format sometime this year. A protocol addendum will be submitted.

PUBLICATIONS OR ABSTRACTS, FY-82:

None

DATE: 27 Oct 82 ~~Work Unit No.:~~ 2621 (Addendum to 2617) STATUS: INTERIM FINAL
STARTING DATE: February 1981 DATE OF COMPLETION: February 1984

Key Words: Lipoproteins - Thoracic Duct Drainage

TITLE OF PROJECT: The Metabolism of Lymph Lipoproteins in patients undergoing Thoracic Duct Drainage, Addendum to WU #2617

PRINCIPAL INVESTIGATOR(S): Jimmy A. Light, MD

ASSOCIATE INVESTIGATOR(S): E. J. Schaefer, MD, B. Brewer, MD, & Jeffrey Hoen, MD

FACILITY: ~~WARD~~ Ward 48 DEPT/SVC: Dept of Surg, Transplant Svc

ACCUMULATIVE MEDICARE COST: None ACCUMULATIVE CONTRACT COST: None ACCUMULATIVE SUPPLY COST: None

FY-83 MEDICARE: None CONTRACT COST: None SUPPLY COST: None DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: Jan. 26, 1982

STUDY OBJECTIVE: To study the metabolism of lymph lipoproteins in vivo and in vitro. Lymph lipoproteins and their precursors are isolated following various dietary manipulations. Radiiodinated and reinfused in selected situations. The isolated TECHNICAL APPROACH: lipoproteins are extensively studied in vitro with a variety of sophisticated biochemical techniques at the NIH.

PROGRESS DURING FY-82: Lymph lipoproteins from 5 additional patients undergoing thoracic duct drainage have been studied. Tremendous progress has been made. A new isoform of A-1 apoprotein has been isolated from lymph following fat (over) NUMBER OF SUBJECTS STUDIED:

FY-82: 5 TOTAL (TO DATE): 8 BEFORE COMPLETION OF STUDY: # of pts under-going thoracic duct drainage

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
None

CONCLUSIONS: The study of lymph lipoproteins precursors is contributing significantly to the understanding of lipoprotein metabolism which, in due course, will have direct impact on our understanding of arteriosclerotic cardiovascular disease.

PUBLICATIONS OR ABSTRACTS, FY-82:

Publication: Apolipoprotein A-1 Isoforms in Human Lymph; Effect of Fat Absorption, Ghaselli, G., Schaefer, E., Light, J.A., Brewer, B. Jour Clin Invest (in press) 1982.

Abstract: Apolipoprotein A-1 Polymorphism in Human Lymph; Effect of Fat Feeding. Ghaselli, G., Schaefer, E., Zech, L., Light, J.A., Brewer, B. Arteriosclerosis (in press) 1982.

PROGRESS DURING FY82: feeding. This isoform is the precursor for A-1 apoprotein which is a major constituent for high density lipoproteins. This new isoform has only been found previously in Tangiers disease patients and has an extremely short half life in the serum. It is dependent upon a specific kind of diet and has not been previously studied extensively. The plans are to continue the study of this protein which has an extremely short half life, to isolate it, determine its amino acid sequence, and to study its regulation of apoprotein metabolism in HTL levels. In addition, chylomicron remnants isolated from the lymph will be studied in vitro with a liver membrane system to further examine the metabolism of these lipoproteins.

DATE: 22 Oct 83 WORK UNIT NO.: 2622 STATUS: INTERIM FISCAL: XX

STARTING DATE: DATE OF COMPLETION:

KEY WORDS:

TITLE OF PROJECT: Immunological Monitoring: Whole Blood Blastogenesis Levels and Relationship to Graft Rejection Episodes in Renal Allograft Recipients

PRINCIPAL INVESTIGATOR(S): J.A. Light, COL, MC

ASSOCIATE INVESTIGATOR(S):

FACILITY: WRMC DEPT/SVC: Dept of Surg, Organ Transplant Svc

ACCUMULATIVE FEDCASE COST: ACCUMULATIVE CONTRACT COST: ACCUMULATIVE SUPPLY COST:

FY-83 FEDCASE: CONTRACT COST: SUPPLY COST: \$270.00 DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To ascertain spontaneous blastogenesis levels in the whole blood of renal allograft recipients and determine whether or not the variation of these levels can predict or signify onset or ending of rejection.

TECHNICAL APPROACH: This 2 hour test using unseparated blood sample measures the "turned on" state of absolute numbers of lymphocytes - as found in peripheral circulation during the post transplant period. Blastogenesis is measured by tritiated thymidine uptake.

PROGRESS DURING FY-82: / No experimental work has been performed on this protocol in FY82 for the following reasons: insufficient technical staff combined with low probability

NUMBER OF SUBJECTS STUDIED: /of yielding significant new information. Recommend termination. FY-82: TOTAL (TO DATE): BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT(IF NONE SO STATE):

CONCLUSIONS:

PUBLICATIONS OR ABSTRACTS, FY-82:

DATE: 4 Feb 83 (21) UNIT No.: 2623 STATUS: INTERIM XX Final

STARTING DATE: DATE OF COMPLETION:

KEY WORDS:

TITLE OF PROJECT: Immunological Monitoring: Determination of C-Reactive Protein (CRP) Levels in Serum of Post Transplant Patients & Correlation of those levels with Allograft Rejection

PRINCIPAL INVESTIGATOR(S): J.A. Light, COL, MC

ASSOCIATE INVESTIGATOR(S): W. Hayes

FACILITY: WRMC DEPT/SVC: Dept of Surgery, Organ Transplant Service

ACCUMULATIVE MEDICASE COST: ACCUMULATIVE CONTRACT COST: ACCUMULATIVE SUPPLY COST:

FY-83 MEDICASE: CONTRACT COST: SUPPLY COST: DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1993

STUDY OBJECTIVE: To establish a productive test to aid in early recognition of rejection of allograft and permit more appropriate and effective treatment of post transplant patients.

TECHNICAL APPROACH: A kit for testing C-reactive protein using the radial immuno diffusion technique has been standardized for use. The sera are added to the plate and the diameters of the resulting precipitin rings are measured. Daily serum samples are tested. PROGRESS DURING FY-82: 21 patients were studied serially during a variety of infection and/or rejection syndromes following renal transplantation. See the attached abstract submitted & accepted by the 3rd International Immunological Monitoring Symposium. See below.

NUMBER OF SUBJECTS STUDIED: FY-82: 21 TOTAL (TO DATE): 49 BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS: CRP assays have not been particularly useful monitoring tests in this institution. A particular series of patients with viremia are an interesting subset for further study during this year. There is a newer technique, both simpler and faster, called rate nephelometry which we intend to investigate.

PUBLICATIONS OR ABSTRACTS, FY-82:

Poster presentation at 3rd Int Imm Monitoring Symposium 21-24 November 1981, Miami - Nonspecific Monitoring for Transplant Rejection: Beta 2 Microglobulin and C-Reactive Protein. Light, J. et al. A manuscript is being created.

DATE: 22 Oct 82 | WORK UNIT No.: 2624 | STATUS: INTERIM XX FINAL

STARTING DATE: | DATE OF COMPLETION:

KEY WORDS:

TITLE OF PROJECT: Immunological Monitoring: A mini Micro Technique for In Vitro Culture Assays

PRINCIPAL INVESTIGATOR(S): J.A. Light, COI, MC

ASSOCIATE INVESTIGATOR(S): D.M. Strong, F. May

FACILITY: IRAMC | DEPT/SVC: Dept of Surg. Organ Transplant Svc

ACCUMULATIVE FEEDCASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST:

FY-83 FEEDCASE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To adapt the Terasaki microplate culture system of O'Brien, Knight, et al, 1979, for use in assessing immune response in transplant patient population.

TECHNICAL APPROACH: Terasaki microplates are used in place of the more commonly used Lindbro microtiter plates for performance of such lymphocyte culture assays as mitogens, MLC, CML and PLT. About one tenth the number of cells (over) ~~PROGRESS DURING FY-82:~~ We have found that this method is well suited to the primed lymphocyte assay. One tenth the number of cells used in the conventional assay is adequate for discrimination response (no response in primed cells). (over) NUMBER OF SUBJECTS STUDIED:

FY-82: | TOTAL (TO DATE): | BEFORE COMPLETION OF STUDY: 20

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS: This technique is being very successfully used for all the blastogenic assays. Additional tests are necessary for statistical calculation.

PUBLICATIONS OR ABSTRACTS, FY-82:

Primed Lymphocyte Testing Using Mini Microculture Technique. Metz, S., Simonis, T., May, F., Light, J.A., Strong, D.M. Poster session at AACHT, San Francisco, May 1982.

TECHNICAL APPROACH: (Cont) are used in this technique as compared to the larger system. Incubation, pulsing and harvesting are done in a fashion comparable to the more common system.

PROGRESS DURING FY82: (Cont) Additional numbers of donor-recipient pairs need to be tested for MLC using this method and the conventional method in order to establish stimulation index and relative response ranges that correlate with graft survival.

DATE: 22 Oct 82 | WORK UNIT NO.: 2625 | STATUS: INTERIM XX FINAL

STARTING DATE: | DATE OF COMPLETION:

KEY WORDS:

TITLE OF PROJECT: Immunological Monitoring: Determination of Histocompatibility between Renal Transplant Donors and Recipients Using Primed Lymphocyte Typing (PLT)

PRINCIPAL INVESTIGATOR(S): J.A. Light, COL, MC

ASSOCIATE INVESTIGATOR(S): D.M. Strong, S. Metz, F. May

FACILITY: WRAVC | DEPT/SVC: Dept of Surg, Organ Transplant Svc

ACCUMULATIVE MEDICASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST:

FY-83 MEDICASE: CONTRACT COST: SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983
\$4,000.00 | \$1,400.72

STUDY OBJECTIVE: To determine the role of HLA-D related antigen specificities in renal allograft survival using primed lymphocyte testing as a means of detecting histocompatibility.

TECHNICAL APPROACH: All donor-recipient pairs are B cell typed using the nylon column separation technique and microcytotoxicity test. Cells on these pairs are frozen for retrospective testing. Lymphocytes primed to the various HLA-D(over)

PROGRESS DURING FY-82: Freezing of lymphocytes on donor-recipient pairs has continued with 25 additional pairs stored (total 50 pairs). Expansion of primed typing cells began in Nov-Dec 1981 but ceased when tech resigned. Expansion (over)

NUMBER OF SUBJECTS STUDIED:

FY-82: 25 | TOTAL (TO DATE): 50 | BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS: None at this time

PUBLICATIONS OR ABSTRACTS, FY-82:

TECHNICAL APPROACH: (Cont) region specificities are expanded in culture using T cell growth factor. These primed cells are mixed in culture for 2 days; tritiated thymidine uptake measures blastogenesis. Serologically defined DR antigens are compared with PLT assignments and these are correlated with graft survival.

PROGRESS DURING FY82: (Cont) of cells with TCGF began again in May using a tech borrowed from USUHS. Fifteen pairs are ready for typing.

DATE: 22 Oct 82 Work Unit No.: 2626 STATUS: INTERIM XX FINAL

STARTING DATE: Not yet begun DATE OF COMPLETION:

KEY WORDS: Leukapheresis - Transplantation

TITLE OF PROJECT: Intensive Pretransplant Leukapheresis

PRINCIPAL INVESTIGATOR(S): J.A. Light, J. Kumar, D. Wright

ASSOCIATE INVESTIGATOR(S): J.A. Biggers, K. Oddenino, S. Metz

FACILITY: WRAIC DEPT/SVC: Dept of Surg, Transplant Svc; Dept of Pathology

ACCUMULATIVE FEDCASE COST: ACCUMULATIVE CONTRACT COST: ACCUMULATIVE SUPPLY COST:

FY-83 FEDCASE: CONTRACT COST: SUPPLY COST: DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983

STUDY OBJECTIVE: Preparation of sensitized recipients for transplantation by selective lymphocyte depletion using pheresis.

TECHNICAL APPROACH: Patients are connected to the cell separator TIW for 6-8 weeks until T cells are depleted as indicated by FACS analysis.

PROGRESS DURING FY-82: None. Project cannot begin until personnel hiring action can occur

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 TOTAL (TO DATE): 0 BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): None

CONCLUSIONS: Very exciting project already being done at other transplant centers. Potentially could replace TDD as method of preparation for sensitized transplant recipients.

PUBLICATIONS OR ABSTRACTS, FY-82: None

DATE: 3 Nov 82 | WORK UNIT No.: 2627 | STATUS: INTERIM XX FINAL

STARTING DATE: Not yet begun | DATE OF COMPLETION:

KEY WORDS: Allograft rejection - Plasmaleukapheresis

TITLE OF PROJECT: Plasma Leukapheresis for Acute Allograft Rejection

PRINCIPAL INVESTIGATOR(S): J.A. Light, J. Kumar, D. Wright

ASSOCIATE INVESTIGATOR(S): K. Oddenino, S. Metz, J.A. Biggers

FACILITY: WRMC | DEPT/SVC: Dept of Surg, Transpl Svc, Dept of Path

ACCUMULATIVE MEDICASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST:

FY-83 MEDICASE: | CONTRACT COST: | SUPPLY COST: None | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To investigate the effects of PLP on the rejection process as compared with ALG. To rescue rejection episodes resistant to other parameters.

TECHNICAL APPROACH: Patients experiencing 2nd rejection episodes will receive either 10 PLP or 10 ALG treatments. Crossover and rescue is allowed for graft salvage, but will be judged as ineffective therapy.

PROGRESS DURING FY-82: None. Project cannot be activated until hiring freeze is lifted. 11 patients have received PLP as rescue therapy for 12 intractable rejection episodes with 50% response.

NUMBER OF SUBJECTS STUDIED: No protocol patients; 11 random patients

FY-82: | TOTAL (TO DATE): | BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
Two patients have experienced allograft rupture during PLP for severe rejection. The relationship remains under scrutiny.

CONCLUSIONS: PLP subtracts lymphokines, mediators, lymphocytes and platelets, while other anti-rejection measures add substances. The proposed study is original and has a reasonable chance of comparing favorably with the present standard - ALG.

PUBLICATIONS OR ABSTRACTS, FY-82: None

DATE: 15 NOV 82 | WORK UNIT NO.: 2809 | STATUS: INTERIM | FINAL

STARTING DATE: 1979 | DATE OF COMPLETION: 1984

KEY WORDS: PROSTATE CANCER AND NON-ESTERIFIED CHOLESTEROL

TITLE OF PROJECT: RELATIONSHIP BETWEEN PROSTATIC CANCER AND EXCRETION OF URINARY CHOLESTEROL

PRINCIPAL INVESTIGATOR(S): HARRY Y.C. WONG, Ph.D

ASSOCIATE INVESTIGATOR(S): DAVID G. MCLEOD, MD - EUSTUS NELSON, MD

FACILITY: WRAHC | DEPT/SVC: UROLOGY

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| ACCUMULATIVE MEDICASE COST: 0 | ACCUMULATIVE CONTRACT COST: 0 | ACCUMULATIVE SUPPLY COST: 0 |
|----------------------------------|----------------------------------|--------------------------------|

FY-83 MEDICASE: 0 | CONTRACT COST: 0 | SUPPLY COST: 0 | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: TO DETERMINE URINARY LEVELS OF NON-ESTRIFIED CHOLESTEROL IN PATIENTS WITH CARCINOMA OF THE PROSTATE; ATTEMPT TO ESTABLISH A CORRELATION BETWEEN ELEVATED URINARY LEVELS OF N.E.C. IN VARIOUS STAGES OF PROSTATIC CANCER AND TECHNICAL APPROACH: HOPEFULLY UTILIZE THIS METHOD AS A MEANS TO EARLY DIAGNOSIS OF THE DISEASE, AND AS A PROGNOSTIC INDICATION

24 HOUR URINE SPECIMENS ARE OBTAINED ON PATIENTS WITH CARCINOMA OF THE PROSTATE

PROGRESS DURING FY-82: None - The Chromagography Equipment has not been in operation the entire year. We are awaiting new equipment.

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 | TOTAL (TO DATE): | BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
None

CONCLUSIONS:

In black males there is a correlation between urinary levels of non-estrified cholesterol to prostatic cancer.

PUBLICATIONS OR ABSTRACTS, FY-82:

None

DATE: 15 Nov 82 Work Unit No.: 2810 STATUS: INTERIM \ FINAL

STARTING DATE: DATE OF COMPLETION:

KEY WORDS: CANCER OF BLADDER, IRRADIATION

TITLE OF PROJECT: COMPARATIVE STUDY OF HIGH DOSE VERSUS LOW DOSE PRE-OPERATIVE RADIATION TO RADICAL CYSTECTOMY FOR CONTROL OF TRANSITIONAL CELL CARCINOMA OF THE BLADDER

PRINCIPAL INVESTIGATOR(S): DAVID G. MCLEOD, MD

ASSOCIATE INVESTIGATOR(S): RONALD DORN, MD

FACILITY: IRAMC DEPT/SVC: UROLOGY & RADIATION THERAPY

ACCUMULATIVE MEDICAL CASE COST: 0 ACCUMULATIVE CONTRACT COST: 0 ACCUMULATIVE SUPPLY COST: 0

FY-83 MEDICAL CASE: CONTRACT COST: SUPPLY COST: DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: TO COMPARE SHORT COURSES VERSUS LONG COURSES OF PRE-OPERATIVE RADIATION THERAPY IN THE TREATMENT OF INVASIVE CANCER OF THE BLADDER

TECHNICAL APPROACH: NO DEVIATION FROM PROTOCOL. THERE ARE NO INCREASED SIDE EFFECTS OR INCREASED INCIDENCE OF EXPECTED UNDESIRABLE SIDE EFFECTS.

PROGRESS DURING FY-82:

See Below

NUMBER OF SUBJECTS STUDIED:

FY-82: 6 TOTAL (TO DATE): 22 BEFORE COMPLETION OF STUDY: 30

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS:

We are now trying to collect data with anticipation of closing out this study in the next 18 months.

PUBLICATIONS OR ABSTRACTS, FY-82:

None

| | | | |
|---|-----------------------------|--|--|
| DATE: 15 Nov 82 | WORK UNIT No.: 2812 | STATUS: INTERIM | FINAL |
| STARTING DATE: 25 March 1980 | | DATE OF COMPLETION: | |
| KEY WORDS: TESTIS TUMOR (SEMINOMA) | | | |
| TITLE OF PROJECT: HUMAN CHORIONIC GONADOTROPIN (HCG) PRODUCING CELLS IN SEMINOMATOUS GERM CELL TUMORS OF THE TESTIS: A PROSPECTIVE AND RETROSPECTIVE CORRELATION WITH TUMOR HISTOLOGY AND RESPONSE TO THERAPY | | | |
| PRINCIPAL INVESTIGATOR(S): DAVID G. MCLEOD, MD, COL, MC | | | |
| ASSOCIATE INVESTIGATOR(S): CHARLES DAVIS, COL, MC SUSAN KERN, CPT, MC | | | |
| FACILITY: WRANC | | DEPT/SVC: UROLOGY/PATHOLOGY/AFIP GENITO-URINARY BRANCH | |
| ACCUMULATIVE MEDICAL CASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: | |
| 0 | 0 | 0 | |
| FY-83 MEDICAL CASE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
| | | | |

STUDY OBJECTIVE: TO SEE IF THERE IS ANY CORRELATION BETWEEN HCG PRODUCING TUMORS AND DEGREE OF MALIGNANCY IN SEMINOMAS.

TECHNICAL APPROACH: WE ARE TRYING TO COLLECT, FOR EXAMINATION, TISSUE BLOCKS AS OUTLINED IN THE PROTOCOL. NO FUNDS ASKED AND NO FUNDS NEEDED.

PROGRESS DURING FY-82:

No Progress

NUMBER OF SUBJECTS STUDIED:

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None
CONCLUSIONS:

None

PUBLICATIONS OR ABSTRACTS, FY-82:

DATE: 15 Nov 82 | Work Unit No.: 28148 | STATUS: INTERIM FINAL
STARTING DATE: 1 June 1980 | DATE OF COMPLETION: 30 April 1982

KEY WORDS: PROSTATE CANCER

TITLE OF PROJECT: A COMPARISON OF COMBINATION CHEMOTHERAPY-HORMONAL THERAPY WITH HORMONAL THERAPY ALONE IN PATIENTS WITH CLINICAL STAGE D PROSTATE CARCINOMA

PRINCIPAL INVESTIGATOR(S): DAVID G. MCLEOD, MD

ASSOCIATE INVESTIGATOR(S): H. GRANT TAYLOR, MD, STEVEN J. SKOOG, MD

FACILITY: HRAVC

DEPT/SVC: UROLOGY/HEMATOLOGY-ONCOLOGY

ACCUMULATIVE MEDICASE COST:
0

ACCUMULATIVE CONTRACT COST:
0

ACCUMULATIVE SUPPLY COST:
0

FY-83 MEDICASE: 0 CONTRACT COST: 0 SUPPLY COST: 0

DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE:

CHEMOTHERAPY & HORMONAL THERAPY IN PROSTATE CANCER

TECHNICAL APPROACH:

MULTI-INSTITUTIONAL STUDY OF PROSTATE CANCER PATIENTS

PROGRESS DURING FY-82: The National Prostatic Cancer Project closed out this Protocol as the number of patients from all institutions met criteria for completion.

NUMBER OF SUBJECTS STUDIED:

FY-82: See Attached Sheet TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

See Protocol

CONCLUSIONS:

Statistical data being collected for publication in the next year or so.

PUBLICATIONS OR ABSTRACTS, FY-82:

NPCP CHEMOTHERAPY PROTOCOL - 600
 TABLE 2
 DISTRIBUTION OF PATIENTS BY INSTITUTION

| INSTITUTION | RECEIVING TREATMENT | DEAD OR OFF TREATMENT | NOT EVALUABLE | TOTAL |
|--------------------|------------------------|--------------------------|------------------|------------|
| UNIV. OF IOWA | 7 | 18 | 5 | 30 |
| MASON CLINIC | 2 | 5 | 1 | 8 |
| MASS. GENERAL | 0 | 6 | 2 | 8 |
| JOHNS HOPKINS | 5 | 14 | 5 | 24 |
| UNIV. OF TENNESSEE | 11 | 41 | 5 | 57 |
| SAN DIEGO | 1 | 12 | -- | 13 |
| TULANE MED. SCHOOL | 6 | 7 | 2 | 15 |
| WAYNE STATE | 1 | 6 | 2 | 9 |
| RPMI | 5 | 4 | -- | 9 |
| BAYLOR | 4 | -- | -- | 4 |
| WALTER REED | 1 | 1 | -- | 2 |
| UCLA | 1 | 7 | 1 | 9 |
| TOTAL | <u>44</u> | <u>121</u> | <u>23</u> | <u>188</u> |

DATE: 15 Nov 82 | WORK UNIT NO.: 2814 C | STATUS: INTERIM / FINAL

STARTING DATE: 1 June 1980 | DATE OF COMPLETION: OPEN

KEY WORDS: PROSTATE CANCER

TITLE OF PROJECT: A COMPARISON OF LONG-TERM ADJUVANT CHEMOTHERAPY WITH CYCLOPHOSPHAMIDE (NSC 26271), ESTRACYT (NSC 89199), OR NO-ADDITIONAL TREATMENT IN PATIENTS WITH DEFINITIVE SURGICAL TREATMENT FOR ADENOCARCINOMA OF THE PROSTATE 0400

PRINCIPAL INVESTIGATOR(S): DAVID G. MCLEOD, MD

ASSOCIATE INVESTIGATOR(S): H. GRANT TAYLOR, MD, STEVEN J. SKOOG, MD

FACILITY: IRANC

DEPT/SVC:

ACCUMULATIVE MEDICASE COST:
0

ACCUMULATIVE CONTRACT COST:
0

ACCUMULATIVE SUPPLY COST:
0

FY-83 MEDICASE: 0 | CONTRACT COST: 0 | SUPPLY COST: 0

DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: CHEMOTHERAPY AND HORMONAL THERAPY IN PROSTATE CANCER

TECHNICAL APPROACH: MULTI-INSTITUTIONAL STUDY OF PROSTATE CANCER PATIENTS

PROGRESS DURING FY-82:

NUMBER OF SUBJECTS STUDIED:

FY-82: See Attached Total (to date): _____ BEFORE COMPLETION OF STUDY: _____
Sheet

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

CONCLUSIONS:

On-going study

PUBLICATIONS OR ABSTRACTS, FY-82:

NPCP ADJUVANT CHEMOTHERAPY PROTOCOL 900
 TABLE 3
 DISTRIBUTION OF PATHOLOGICAL STAGES BY TREATMENT
 FOR ELIGIBLE PATIENTS

| PATHOLOGICAL STAGE | ADJUVANT TREATMENT | | | | | | TOTAL | |
|-----------------------|--------------------|----|---------|----|----------|----|-------|----|
| | NONE | | CYTOXAN | | ESTRACYT | | NO. | % |
| | NO. | % | NO. | % | NO. | % | | |
| B ₂ | 7 | 32 | 10 | 34 | 12 | 39 | 29 | 35 |
| C | 7 | 32 | 9 | 31 | 9 | 29 | 25 | 30 |
| D ₁ | 3 | 36 | 10 | 34 | 10 | 32 | 28 | 34 |
| TOTAL | 22 | | 29 | | 31 | | 82 | |

DATE: 15 Nov 82 Work Unit No.: 2814D STATUS: INTERIM XX FINAL

STARTING DATE: 1 June 1980 DATE OF COMPLETION: Open

KEY WORDS: Prostate Cancer

TITLE OF PROJECT: A COMPARISON OF LONG-TERM ADJUVANT CHEMOTHERAPY WITH CYCLOPHOSPHAMIDE (NSC26271), ESTRACYT (NSC 89199) OR NO-ADDITIONAL-TREATMENT IN PATIENTS WHO HAVE HAD DEFINITIVE RADIOTHERAPY FOR ADENOCARCINOMA OF THE PROSTATE 120-0

PRINCIPAL INVESTIGATOR(S): DAVID G. MCLEOD, MD

ASSOCIATE INVESTIGATOR(S): H. GRANT TAYLOR, MD, STEVEN J. SKOOG, MD

FACILITY: WRNYC DEPT/SVC: UROLOGY/HEMATOLOGY-ONCOLOGY

| | | |
|----------------------------------|----------------------------------|--------------------------------|
| ACCUMULATIVE MEDICASE COST: 0 | ACCUMULATIVE CONTRACT COST: 0 | ACCUMULATIVE SUPPLY COST: 0 |
|----------------------------------|----------------------------------|--------------------------------|

| | | | |
|----------------------|---------------------|-------------------|--|
| FY-83 MEDICASE: 0 | CONTRACT COST: 0 | SUPPLY COST: 0 | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT |
|----------------------|---------------------|-------------------|--|

STUDY OBJECTIVE: CHEMOTHERAPY AND HORMONAL THERAPY IN PROSTATE CANCER

TECHNICAL APPROACH: MULTI-INSTITUTIONAL STUDY OF PROSTATE CANCER PATIENTS

PROGRESS DURING FY-82:

NUMBER OF SUBJECTS STUDIED:

FY-82: See Attached TOTAL (TO DATE): BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

CONCLUSIONS:

On-going study

PUBLICATIONS OR ABSTRACTS, FY-82:

NPCP ADJUVANT CHEMOTHERAPY PROTOCOL - 1000

TABLE 3
DISTRIBUTION OF PATHOLOGICAL STAGES BY TREATMENT
FOR ELIGIBLE PATIENTS

| PATHOLOGICAL STAGE | ADJUVANT TREATMENT | | | | | | TOTAL | |
|-----------------------|--------------------|----|---------|----|----------|----|-------|----|
| | NONE | | CYTOXAN | | ESTRACYT | | NO. | % |
| | NO. | % | NO. | % | NO. | % | | |
| B ₂ | 6 | 15 | 4 | 11 | 1 | 3 | 11 | 10 |
| C | 4 | 10 | 5 | 14 | 6 | 17 | 15 | 13 |
| D ₁ | 30 | 75 | 28 | 75 | 28 | 80 | 86 | 76 |
| TOTAL | 40 | | 37 | | 35 | | 113 | |

DATE: 15 Nov 82 ~~Work~~ UNIT No.: 2814E STATUS: INTERIM X FINAL

STARTING DATE: 1 June 1980 DATE OF COMPLETION: 31 December 1981

KEY WORDS: Prostate Cancer

TITLE OF PROJECT: A COMPARISON OF METHOTREXATE (NSC-740), CIS-DIAMMINEDICHLORO-PLATINUM (II NSC-119875), AND ESTRACYT (NSC-89199) IN PATIENTS WITH ADVANCED CARCINOMA OF THE PROSTATE (11ccc)

PRINCIPAL INVESTIGATOR(S): DAVID G. MCLEOD, MD

ASSOCIATE INVESTIGATOR(S): H. GRANT TAYLOR, MD, STEVEN J. SKOOG, MD

FACILITY: WRAIC DEPT/SVC: UROLOGY/HEMATOLOGY-ONCOLOGY

ACCUMULATIVE MEDICASE COST: 0 ACCUMULATIVE CONTRACT COST: 0 ACCUMULATIVE SUPPLY COST: 0

FY-83 MEDICASE: 0 CONTRACT COST: 0 SUPPLY COST: 0 DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE:

CHEMOTHERAPY AND HORMONAL THERAPY IN PROSTATE CANCER

TECHNICAL APPROACH:

MULTI-INSTITUTIONAL STUDY OF PROSTATE CANCER PATIENTS

PROGRESS DURING FY-82: The National Prostatic Cancer Project closed out this Protocol as the number of patients from all institutions met criteria needed for completion.

NUMBER OF SUBJECTS STUDIED:

FY-82: See attached Total (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____
Sheet

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
SEE PROTOCOL

CONCLUSIONS:

Statistical data being collected for publication in the next year or so.

PUBLICATIONS OR ABSTRACTS, FY-82:

NPCP CHEMOTHERAPY PROTOCOL - 1100
 TABLE 2
 DISTRIBUTION OF PATIENTS BY INSTITUTION

| INSTITUTION | RECEIVING TREATMENT | DEAD OR OFF TREATMENT | EXCLUDED | TOTAL |
|--------------------|------------------------|--------------------------|-----------|------------|
| UNIV. OF IOWA | 3 | 16 | 1 | 20 |
| MASON CLINIC | 7 | 16 | 3 | 26 |
| MASS. GENERAL | -- | -- | 1 | 1 |
| JOHNS HOPKINS | 4 | 21 | 3 | 28 |
| UNIV. OF TENNESSEE | 8 | 24 | 3 | 35 |
| SAN DIEGO | 5 | 5 | 1 | 11 |
| TULANE MED. SCHOOL | 7 | 5 | 6 | 18 |
| WAYNE STATE | 2 | 6 | 1 | 9 |
| ROSWELL PARK | 2 | 13 | 2 | 17 |
| BAYLOR MED. SCHOOL | -- | 2 | 2 | 4 |
| WALTER REED | 3 | 6 | 1 | 10 |
| RUSH-PRESBYTERIAN | 3 | -- | -- | 3 |
| UCLA | 2 | 4 | 1 | 7 |
| TOTAL | <u>46</u> | <u>118</u> | <u>25</u> | <u>189</u> |

| | | |
|---|---------------------------------------|---|
| DATE: 15 Nov 82 | WORK UNIT No.: 2814F | STATUS: INTERIM <input checked="" type="checkbox"/> FINAL |
| STARTING DATE: 1 June 1980 | DATE OF COMPLETION: 31 January 1982 | |
| KEY WORDS: PROSTATE CANCER | | |
| TITLE OF PROJECT: A COMPARISON OF ESTRACYT (NSC 89199) VERSUS CIS-DIAMMINEDICHLORO-PLATINUM (DDP) (II NSC 119875) VERSUS ESTRACYT PLUS DDP IN PATIENTS WITH ADVANCED CARCINOMA OF THE PROSTATE WHO HAVE HAD EXTENSIVE IRRADIATION TO THE PELVIS OR LUMBOSACRAL AREA 7/20/82 | | |
| PRINCIPAL INVESTIGATOR(S): DAVID G. McLEOD, MD | | |
| ASSOCIATE INVESTIGATOR(S): H GRANT TAYLOR, MD, STEVEN J. SKOOG, MD | | |
| FACILITY: WRAVC | DEPT/SVC: UROLOGY/HEMATOLOGY-ONCOLOGY | |
| ACCUMULATIVE MEDICASE COST: 0 | ACCUMULATIVE CONTRACT COST: 0 | ACCUMULATIVE SUPPLY COST: |
| FY-83 MEDICASE: 0 | CONTRACT COST: 0 | SUPPLY COST: 0 |
| DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1982 | | |

STUDY OBJECTIVE: CHEMOTHERAPY AND HORMONAL THERAPY IN PROSTATE CANCER

TECHNICAL APPROACH: MULTI-INSTITUTIONAL STUDY OF PROSTATE CANCER PATIENTS

PROGRESS DURING FY-82: The National Prostatic Cancer Project closed out this Protocol as number of patients from all institutions met criteria needed for completion.

NUMBER OF SUBJECTS STUDIED:
 FY-82: See Attached Total (to date): _____ BEFORE COMPLETION OF STUDY: _____
 Sheet

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
 SEE PROTOCOL

CONCLUSIONS:
 Statistical data being collected for publication in the next year or so.

PUBLICATIONS OR ABSTRACTS, FY-82:

NPCP CHEMOTHERAPY PROTOCOL - 1200
 TABLE 2
 DISTRIBUTION OF PATIENTS BY INSTITUTION

| INSTITUTION | RECEIVING TREATMENT | DEAD OR OFF TREATMENT | NOT EVALUABLE | TOTAL |
|--------------------|------------------------|--------------------------|------------------|-----------|
| UNIV. OF IOWA | -- | 7 | 1 | 8 |
| MASON CLINIC | 10 | 32 | 4 | 46 |
| MASS. GENERAL | 2 | -- | 2 | 4 |
| JOHNS HOPKINS | 4 | 18 | 2 | 24 |
| UNIV. OF TENNESSEE | 2 | 10 | 3 | 15 |
| SAN DIEGO | 2 | 5 | 2 | 9 |
| TULANE MED. SCHOOL | -- | 1 | 1 | 2 |
| WAYNE STATE | 2 | -- | 1 | 3 |
| RPMI | 2 | 6 | 1 | 9 |
| BAYLOR | 1 | 5 | 2 | 8 |
| WALTER REED | 1 | 8 | -- | 9 |
| RUSH-PRESBYTERIAN | 2 | -- | -- | 2 |
| UCLA | <u>1</u> | <u>6</u> | <u>3</u> | <u>10</u> |
| TOTAL | 29 | 98 | 22 | 149 |


DISPOSITION FORM

For use of this form, see AR 340-15; the proponent agency is TAGO.

| REFERENCE OR OFFICE SYMBOL | SUBJECT |
|----------------------------|---|
| HSWP-QCR | Termination of Protocol, Work Unit #2815. |

TO Ray E. Stutzman, COL MC FROM C, Dept of Clin Inv DATE 28 Dec 81 CMT 1
C, Urology Svc DrBoehm/ee/61390

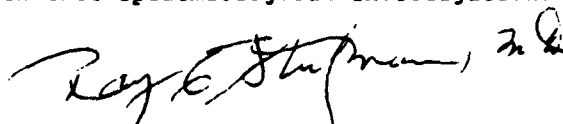
1. Despite repeated requests for your annual progress report for FY-81, you have not complied with this legal and Army regulation requirement so that an annual review of your research can be accomplished.
2. Effective immediately you are to terminate all work on your project entitled, "An Epidemiologic Investigation of Testicular Cancer".
3. Your situation will be considered at the 23 February 1982 Clinical Investigation and Human Use Committee meeting.
4. Notification will be made to the FDA/drug manufacturers of your noncompliance with research regulations.


TIMOTHY M. BOEHM
LTC, MC
Chief, Department of Clinical
Investigation

HSWP-SGU

TO: C, Dept of Clin Inv. FROM: Ray E. Stutzman, COL MC DATE: 4 Jan 82 CMT 2

1. The Epidemiological Investigation of Testicular Cancer in conjunction with Bethesda Naval Hospital and the National Cancer Institute is near completion of the active data collection. At the current time, the data is being processed with no patients to be added but those already within the study may yet be contacted for completion of pertinent data.
2. No medications or drugs were utilized in this epidemiological investigation.


RAY E. STUTZMAN, M.D.
COL MC USA
Chief, Urology Service

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| | | | |
|---|-------------------------------|---------------------------------------|--|
| DATE: 15 Nov 82 | Work Unit No.: 2816 | STATUS: INTERIM | FISCAL |
| STARTING DATE: 1 Sept 82 | DATE OF COMPLETION: OPEN | | |
| KEY WORDS: PROSTATE CANCER | | | |
| TITLE OF PROJECT: A COMPARISON OF DIETHYLSTILBESTROL (DES) OR ORCHIECTOMY VS CYCLOPHOSPHAMIDE + 5-FLUOROURACIL (5-FU) + DES OR ORCHIECTOMY VS ESTRACYT ALONE IN NEWLY DIAGNOSED PATIENTS WITH CLINICAL STAGE D CANCER OF THE PROSTATE WHO HAVE NOT HAD PRIOR HORMONAL TREATMENT OR CHEMOTHERAPY (13 cc) | | | |
| PRINCIPAL INVESTIGATOR(S): DAVID G. McLEOD, MD | | | |
| ASSOCIATE INVESTIGATOR(S): H. GRANT TAYLOR, MD, STEVEN J. SKOOG, MD | | | |
| FACILITY: WRAVC | | DEPT/SVC: UROLOGY/HEMATOLOGY-ONCOLOGY | |
| ACCUMULATIVE MEDICASE COST: 0 | ACCUMULATIVE CONTRACT COST: 0 | ACCUMULATIVE SUPPLY COST: | |
| FY-83 MEDICASE: 0 | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE:

CHEMOTHERAPY AND HORMONAL THERAPY IN PROSTATE CANCER

TECHNICAL APPROACH:

MULTI-INSTITUTIONAL STUDY OF PROSTATE CANCER PATIENTS

PROGRESS DURING FY-82:

NUMBER OF SUBJECTS STUDIED:

FY-82: See Attached Sheet TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
SEE PROTOCOL

CONCLUSIONS:

On-going study

PUBLICATIONS OR ABSTRACTS, FY-82:

NPCP CHEMOTHERAPY PROTOCOL - 1300
 TABLE 2
 DISTRIBUTION OF PATIENTS BY INSTITUTION

| INSTITUTION | RECEIVING TREATMENT | DEAD OR OFF TREATMENT | NOT EVALUABLE | TOTAL |
|--------------------|------------------------|--------------------------|------------------|------------|
| UNIV. OF IOWA | 21 | 3 | 1 | 25 |
| MASON CLINIC | 2 | 2 | -- | 4 |
| MASS. GENERAL | 15 | 5 | 3 | 23 |
| JOHNS HOPKINS | 4 | 1 | -- | 5 |
| UNIV. OF TENNESSEE | 21 | 4 | -- | 25 |
| SAN DIEGO | 4 | -- | 1 | 5 |
| TULANE MED. SCHOOL | 8 | 1 | 1 | 10 |
| WAYNE STATE | 18 | 1 | 2 | 21 |
| RPMI | 13 | 3 | -- | 16 |
| BAYLOR | 30 | 6 | 1 | 37 |
| WALTER REED | 20 | 2 | -- | 22 |
| RUSH-PRESBYTERIAN | 8 | 1 | -- | 9 |
| UCLA | 5 | 6 | 2 | 13 |
| TOTAL | <u>169</u> | <u>35</u> | <u>11</u> | <u>215</u> |

| | | | |
|--|-----------------------------|---------------------------|--|
| DATE: 15 Nov 82 | WORK UNIT No.: 2817 | STATUS: INTERIM | FINAL |
| STARTING DATE: 1 May 1981 | | DATE OF COMPLETION: | |
| KEY WORDS: CEFsulODIN SODIUM; AMINOGLYCOSIDE; PSEUDOMONAS AEROGINOSA | | | |
| TITLE OF PROJECT: A COMPARISON STUDY OF CEFsulODIN SODIUM (ABBOTT 46811, M81-009) WITH AN AMINOGLYCOSIDE IN PATIENTS WITH URINARY TRACT INFECTIONS DUE TO PSEUDOMONAS AEROGINOSA | | | |
| PRINCIPAL INVESTIGATOR(S): | | DAVID G. McLEOD, MD | |
| ASSOCIATE INVESTIGATOR(S): | | BRIAN J. MILES, MD | |
| FACILITY: WRAVC | | DEPT/SVC: UROLOGY | |
| ACCUMULATIVE MEDCARE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: | |
| FY-83 MEDCARE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: STAGE 3 STUDY OF A NEW CEPHALOSPORIN

TECHNICAL APPROACH: SEE PROTOCOL

PROGRESS DURING FY-82:

3 Patients were placed on protocol. This study has been superseded by a new study comparing different dosages of Cefsulodin.

NUMBER OF SUBJECTS STUDIED:

FY-82: 3 TOTAL (TO DATE): 3 BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
None

CONCLUSIONS:

Data to be collaborated by Abbott Laboratory

PUBLICATIONS OR ABSTRACTS, FY-82:

DATE: 15 NOV 82 Work Unit No.: 2818 STATUS: INTERIM FINAL
STARTING DATE: 1 JUNE 1981 DATE OF COMPLETION: 1 July 1982
KEY WORDS: RENAL CELL CARCINOMA, POLYNOSTIA; ACCESSORY NIPPLES
TITLE OF PROJECT: ASSOCIATION OF ACCESSORY NIPPLES WITH RENAL CELL CARCINOMA

PRINCIPAL INVESTIGATOR(S): STEPHEN A. SIHELNIK, MD, CPT, MC, USA

ASSOCIATE INVESTIGATOR(S):

FACILITY: WRMC

DEPT/SVC: UROLOGY

ACCUMULATIVE FEDCASE COST:

ACCUMULATIVE CONTRACT COST:

ACCUMULATIVE SUPPLY COST:

0

0

0

FY-83 FEDCASE:

CONTRACT COST:

SUPPLY COST:

DATE OF COMMITTEE APPROVAL OF

ANNUAL PROGRESS REPORT FEB 25 1983

0

0

0

STUDY OBJECTIVE: INVESTIGATE ASSOCIATION OF RENAL CARCINOMA WITH IDENTIFIABLE SKIN LESIONS

TECHNICAL APPROACH:

SEE PROTOCOL

PROGRESS DURING FY-82:

NONE

NUMBER OF SUBJECTS STUDIED:

FY-82: 0

TOTAL (TO DATE): -

BEFORE COMPLETION OF STUDY: -

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

NONE

CONCLUSIONS:

All data has been turned into the NIH Collaborators

PUBLICATIONS OR ABSTRACTS, FY-82:

| | | |
|--|-----------------------------------|--|
| DATE: 30.12.82 | WORK UNIT No.: 2901 | STATUS: INTERIM X FINAL |
| STARTING DATE: 1 Aug. 1980 | DATE OF COMPLETION: 15.1.1984 | |
| KEY WORDS: Microvascular free flaps. Reconstructive Microvascular Surgery. | | |
| TITLE OF PROJECT: Neovascularization study of Microvascular free flaps in dogs. | | |
| PRINCIPAL INVESTIGATOR(S): LTC Jimmy A. Chow, MC | | |
| ASSOCIATE INVESTIGATOR(S): COL H.D. Peterson, MC, SP5 J.M. Callahan, SP5 R Wolf. | | |
| FACILITY: WRAHC | DEPT/SVC: Plastic Surgery Service | |
| ACCUMULATIVE MEDICASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
| FY-83 MEDICASE: | CONTRACT COST: | SUPPLY COST: |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: To study the specific time interval in the post-operative period necessary for adequate neovascularization of successfully performed (refer to Continuation sheet)

TECHNICAL APPROACH: Microvascular free-flaps based on the inferior epigastric vessels are used for the canine model of this study. Investigation also performed on control non-microvascular island flaps based on inferior epigastric vessels.

PROGRESS DURING FY-82: Research data obtained with 26 dogs. Projection from present data suggests that microvascular free hypogastric flaps in dogs may survive following ligation of the nutrient vessels at about 2 weeks post-operative.

NUMBER OF SUBJECTS STUDIED:

FY-82: 12 TOTAL (TO DATE): 26 BEFORE COMPLETION OF STUDY: 60

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
NONE

CONCLUSIONS: Satisfactory progress and results obtained with the study so far. Further work need to be performed in order to complete the total number of flaps designated so that the conclusions may be of statistic significance.

PUBLICATIONS OR ABSTRACTS, FY-82:

CONTINUATION

Project Work Unit No. 2901

Principal Investigator: LTC Jimmy A. Chow, MC

Title : Neovascularization Study of Microvascular Free Flaps in dogs.

Study Objective (Continued)

microvascular free flaps, so as the flap will continue to survive despite occlusion (ligation) of the feeding vessels of the flap. The study is mission-essential because the information so obtained will indicate when secondary bone grafts, nerve grafts or tendon transfers may be safely performed on patients following successful free-flap coverage for traumatic gun-shot wounds, blast injuries or open fractures of the lower extremities.

HSHL-SP (2 Aug 82)

SUBJECT: Annual Progress Report: FY-82, Clinical Investigation Program. Work Unit #2902, Neuropathies of the Upper Extremity following Surgery Employing a Median Sternotomy

TO C, Dept Clin Invest FROM Alan E. Seyfer, LTC MC DATE 6 Oct 82 CMT 2
Plastic Surgery Service

The following are the elements of the Annual Progress Report requested:

- a. 1 Oct 82
- b. #2902
- c. Interim
- d. March, 1982
- e. April, 1983
- f. Neuropathies, Upper Extremity
- g. Neuropathies of the Upper Extremity following Surgery Employing a Median Sternotomy
- h. Alan E. Seyfer, LTC, MC, Asst C, Plastic Surgery and Hand Section.
Usha Chaundry, MAJ, MC, Physical Medicine
Russ Zajtchuk, COL, MC, Thoracic Surgery
Peter Napoli, 2LT, MSC
- i. Plastic Surgery and Hand Surgery
- j. None
- k. None
- l. To study nerve injuries secondary to surgery employing a median sternotomy
- m. No modifications
- n. 12 subjects studied to date; the study is progressing well in spite of the busy schedules of the investigators
- o. Total: 50
- p. No serious/unexpected side effects
- q. None

This investigation of neuropathies secondary to sternotomy procedures is proceeding as planned. The goal is to study 50 patients preoperatively and postoperatively and to document any neuropathy accrued to the patient after surgery.

It is too early to tell the number of patients which become symptomatic after this type of surgery, but several patients have demonstrated ulnar nerve abnormalities.

Alan E. Seyfer, MD

ALAN E. SEYFER, MD
LTC, MC
Asst Chief, Plastic Surgery Svc
Asst Chief, Hand Surgery Section
Orthopaedic Surgery Svc

DATE: 8 Oct 82 Work Unit No.: 3144 STATUS: INTERIM X FISCAL
STARTING DATE: 8 March 1977 DATE OF COMPLETION: October 1981

KEY WORDS:

TITLE OF PROJECT: Neurophysiologic, Immunologic and Biochemical Aspects of Bronchial Asthma

PRINCIPAL INVESTIGATOR(S): Laurie J. Smith, M.D.

ASSOCIATE INVESTIGATOR(S): Richard Evans III, COL MC; Richard J. Summers, COL MC

FACILITY: WRAVC DEPT/SVC: Allergy-Clinical Immunology Service

ACCUMULATIVE MEDICAL CASE COST: ACCUMULATIVE CONTRACT COST: ACCUMULATIVE SUPPLY COST:

FY-83 MEDICAL CASE: CONTRACT COST: SUPPLY COST: DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT **FEB 25 1983**

STUDY OBJECTIVE: To characterize a group of atopic asthmatics by their alpha and beta adrenergic as well as cholinergic responses, looking in particular for a cholinergic imbalance

TECHNICAL APPROACH:

See attached sheet

PROGRESS DURING FY-82: No work was done on this protocol this year.

NUMBER OF SUBJECTS STUDIED: N/A

FY-82: TOTAL (TO DATE): BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
N/A

CONCLUSIONS: We would like to keep this protocol active. However, because of other commitments, we did not do any patients under this study this year. We feel the study is still important.

PUBLICATIONS OR ABSTRACTS, FY-82:

| | | | |
|---|---------------------|---------------------|-------|
| DATE: 8 Oct 82 | WORK UNIT No.: 3146 | STATUS: INTERIM X | FINAL |
| STARTING DATE: 26 April 1977 | | DATE OF COMPLETION: | |
| KEY WORDS: Immunotherapy; Potency; Persistence; RAST Inhibition | | | |
| TITLE OF PROJECT: Immunotherapy Kit Potency Persistence | | | |

PRINCIPAL INVESTIGATOR(S): Richard J. Summers, COL MC

ASSOCIATE INVESTIGATOR(S): Richard Evans III, COL MC Michael S. Edwards, CPT MSC

FACILITY: WRAMC DEPT/S/C: Allergy-Clinical Immunology Service

| | | |
|-----------------------------|-----------------------------|---|
| ACCUMULATIVE MEDICASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: \$2,000.00 |
| FY-83 MEDICASE: | CONTRACT COST: \$3,700 | SUPPLY COST: \$2,000 |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983 |

STUDY OBJECTIVE: Determine persistence of biological potency of allergy extracts during shipment and use.

TECHNICAL APPROACH: RAST (Radioallergosorbent Test) will be performed to determine potency persistence.

PROGRESS DURING FY-82: Six patients studied and abstract (see below) presented.

NUMBER OF SUBJECTS STUDIED:

FY-82: 6 TOTAL (TO DATE): 6 BEFORE COMPLETION OF STUDY: 10

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
None

CONCLUSIONS: Immunotherapy kit potency is effected by multiple environmental variables.

PUBLICATIONS OR ABSTRACTS, FY-82: Standardization of Allergen Extracts: A Comparison of RAST Inhibition, Isoelectric Focusing, and Skin Test Titration. M. Edwards, PharmD, R. Evans III, MD, H. Baer, PhD, M. Anderson, MS, and P. Turkeltaub, MD. The J. of Allergy and Cl. Immun. Vol. 69, No. 1, Part 2, Jan 1982.

DATE: 1 OCT 82 WORK UNIT NO.: 3160-R STATUS: INTERIM FUND:
STARTING DATE: Fall 1979 DATE OF COMPLETION: Fall 1984
Sm, RNP
KEY WORDS: Sjogren's Syndrome, Rheumatic diseases, SS-A, SS-B, rheumatoid factor,
TITLE OF PROJECT: Study of Rheumatoid Arthritis and Sjogren's Syndrome precipitins
in Rheumatic Diseases

PRINCIPAL INVESTIGATOR(S): Joseph T. Tesar, MD, Bernard H. Berne, MD, Ph.D.

ASSOCIATE INVESTIGATOR(S): Richard C. Welton, MD; James H. Armstrong, BS

FACILITY: IRANC DEPT/SVC: Medicine/Rheumatology Service

ACCUMULATIVE MEDICASE COST: ACCUMULATIVE CONTRACT COST: ACCUMULATIVE SUPPLY COST:

FY-83 MEDICASE: CONTRACT COST: SUPPLY COST: DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: The study was designed to evaluate the diagnostic value and biological properties of several autoantibodies in major rheumatic diseases. These antibodies are: SS-A, SS-B, Sm, RNP precipitins, and rheumatoid factors.

TECHNICAL APPROACH:

SEE REVERSE SIDE.

PROGRESS DURING FY-82:

SEE REVERSE SIDE.

NUMBER OF SUBJECTS STUDIED:

FY-82: TOTAL (TO DATE): BEFORE COMPLETION OF STUDY: Additional 25-30 pt

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS: 20 MCTD, 38 Sjogren's Syndrome, 25 Scleroderma, 62 SLE and 45 RA sera were examined for the SS-A, SS-B, RNP, Sm precipitins. Many sera were examined sequentially. The frequency of these autoantibodies in connective tissue diseases was established. A paper summarizing these data is being prepared for publication.

PUBLICATIONS OR ABSTRACTS, FY-82:

Berne B, Lawless OJ: Immune Complexes in Sjogren's Syndrome. Protids in Biol Fluids, 1979.

Floyd M, Tesar JT: The Role of IgM Rheumatoid Factor in Experimental Vasculitis. Clin. Exp. Imm. 36:165, 1979.

Tesar JT, Schmid FR: Complement Fixation by IgM-Rheumatoid Factor. Eur. Congr. Rheum. 1979, Wiesbaden, W. Germany (Abstract)

TECHNICAL APPROACH: 3 sets of reference sera were obtained with monospecific precipitating antibodies against SS-A(Ro), SS-B(LA) Sm, RNP antigens. The antigens used in the study were prepared by extraction of calf thymus nuclei and human spleen. The antibodies were further purified by ultracentrifugation and sequential ammonium sulfate precipitation. The precipitin reactions were performed using the Ouchterlony Technique. Immune complexes were assayed by the Clq binding assay.

PROGRESS DURING FY-82: During the past year an additional 85 sera of rheumatic disease patient's and controls were examined for Sm, RNP, SS-A(Ro) RF and SS-B(LA) precipitating antibodies.

Since the initiation of study 421 patient and control sera were examined. These data will enable us now to answer many clinically important questions: The value of SS-A, SS-B antibody assays in detection of clinically latent Sjogren Syndrome, association SS-B, SS-A antigen with seronegative systemic lupus erythematosus, also the value of RNP antibody assay in lupus and mixed connective tissue disease.

The practical immediate benefit of this study is that we have developed methods for determinations of the above autoantibodies, some of which are useful in clinical diagnosis. Previously these tests could be done only at great expense through commercial immunology laboratories.

DATE: 1 OCT 82 WORK UNIT NO.: 3162-R STATUS: Final

STUDY OBJECTIVE:

TECHNICAL APPROACH:

PROGRESS DURING FY-82: As part of this project, we evaluated the FIAX fluorometric immunoassay for antibodies to DNA and compared it with the Farr assay which we had used previously for this study. Commercial kits are available for the FIAX method. In this assay, sticks containing absorbed DNA are provided by the manufacturer. These are dipped in patient serum, washed, and then immersed in fluoresceinated antibodies to human immunoglobulin. The resultant fluorescence is read in a fluorometer and converted into anti-DNA units by a computer.

We found the FIAX method to be faster and simpler than the Farr assay. We could process 200 tests per day with FIAX, but only 50 with Farr. Results of the FIAX assay were available within 2 hours, while the Farr assay could not produce results until the day following the start of the test. Further, the Farr assay uses radioactively labelled DNA, while the FIAX assay avoids the use of radioactivity.

In an extensive study, we found that the two assays correlated well ($r=0.87$), and that both were equally specific for SLE. With rare exceptions, only those patients with clinically documented SLE had significantly elevated levels with both assays. The two assays detected similar numbers of SLE patients with significantly elevated anti-DNA antibodies and both showed the same changes in levels during disease therapy.

We found neither assay to be highly reproducible. Coefficients of variation exceeded 10% in within-run and between-run tests with both assays. Most clinical immunoassays produce smaller coefficients than this. Most likely, the variation is partially due to the instability of double-stranded DNA during preparation, storage and testing.

Because of its simplicity, speed and avoidance of radioactivity, we found the FIAX method to be the preferable one. Its cost in consumable materials is twice as high as that of the Farr assay, but its savings in technician time and assay time more than compensate for this.

We evaluated the FIAX fluorometric immunoassay for measuring antibodies to DNA in SLE and other diseases. WE found that it gave similar results to the Farr radioimmunoassay, which had been used previously in the study. Neither assay showed good reproducibility. It is thus necessary to conduct extensive quality control studies when performing these assays.

WORK UNIT NO.: 3162-R

CONCLUSIONS: (CONTINUATION)

The FIAX assay was faster and simpler than the Farr assay, and avoided the use of radioactivity. Although the consumable supply cost of the FIAX assay is higher than that of the Farr assay, its savings in technician time and assay time more than compensate for this. We plan to use the FIAX method for future measurement of anti-DNA antibodies for patient care on the Rheumatology Service, as well as in further research studies on SLE and related disease. We recommend its use in other Army installations as the most cost-effective current method of measuring anti-DNA antibodies in the rheumatic diseases. When the volume of samples assayed is sufficient to justify the \$14,000.00 cost of the FIAX equipment, or when this equipment is on hand to perform other immunological assays.

Work on this protocol has been terminated as of June 1982.

PUBLICATIONS OR ABSTRACTS, FY-82:

Several abstracts have been presented to the regional and national meetings of the Arthritis and Rheumatism Association, and one paper published.

(a) Measurement of Anti-DNA Antibody Levels by the FIAX Fluorometric Immunoassay and the Farr Technique.

1. Southeastern Rheumatism Association, December 1981 (abstract).
2. Northeastern Rheumatism Association, October 1982 (abstract).
3. National Arthritis and Rheumatism Association Meeting, June 1982 (abstract).
4. "Clinical Chemistry", Volume 28, #7, page 1596, 1982 (abstract).
5. Arthritis and Rheumatism, Volume 25(8), page 997, August 1982, (paper).

(b) Serologic and Urinary Course of Treated SLE Glomerulonephritis.

1. National Arthritis and Rheumatism Association Meeting, June 1982 (abstract).

DATE: 1 OCT 82 Work Unit No.: 3163-R STATUS: INTERIM FUND:
 STARTING DATE: FY 80 DATE OF COMPLETION: 1983
 KEY WORDS: Acute anterior uveitis, B-7 CREG, Cw2, HLA B27
 TITLE OF PROJECT: Histocompatibility Antigens in Acute Anterior Uveitis (AAU)

PRINCIPAL INVESTIGATOR(S): Joseph T. Tesar, MD, Paul Killian MD, Michael Strong, Ph.D.

ASSOCIATE INVESTIGATOR(S): Susan Metz, B.S.

FACILITY: IRANC

DEPT/SVC: Medicine/Rheumatology Service

ACCUMULATIVE FEBCASE COST:

ACCUMULATIVE CONTRACT COST:

ACCUMULATIVE SUPPLY COST:

FY-83 FEBCASE: CONTRACT COST: SUPPLY COST:

DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE:

ON REVERSE SIDE.

TECHNICAL APPROACH:

ON REVERSE SIDE.

PROGRESS DURING FY-82: An additional 14 patients with acute anterior uveitis were typed for HLA B-7 CREG, HLA A,B,C antigens

NUMBER OF SUBJECTS STUDIED:

FY-82: 14

TOTAL (TO DATE): 66

BEFORE COMPLETION OF STUDY: 10

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None.

CONCLUSIONS: New HLA antigen associations discovered in patients with acute anterior uveitis in the course of this study were:

HLA-B7-CREG (HLA B7, B27, Bw22, B40, B-42) = 68%

HLA Cw2 = 58%

Frequency of above antigens in normal controls were 42% (B7-CREG) and 10% (Cw2)

Frequency of B-27 antigen was found to be 40% in AAU (NL=9%).

PUBLICATIONS OR ABSTRACTS, FY-82:

NONE.

STUDY OBJECTIVE: Purpose of the study is Two fold: (I.) To improve the diagnostic value of histocompatibility antigen determinations in acute anterior uveitis; (II.) To define new HLA-antigen associations of acute anterior uveitis and characterize the genetic background and factors of susceptibility to the disease.

TECHNICAL APPROACH: A total number of 40-50 patients with idiopathic acute anterior uveitis will be examined by an ophthalmologist and rheumatologist. Each patients blood (1 green top tube) is submitted to histocompatibility testing (HLA A,B,C and B-7 CREG).

DATE: 23 Nov 82 WORK UNIT No.: 3164 STATUS: INTERIM FISCAL XX

STARTING DATE: 18 January 1980 DATE OF COMPLETION: July 1982

KEY WORDS: Prophylactic Therapy in Asthma: Ketotifen

TITLE OF PROJECT: The Comparison of Zaditen[®] and Theophylline in the Prophylaxis of Bronchial Asthma.

PRINCIPAL INVESTIGATOR(S): Anthony J. Deutsch, MAJ MC COL, MC

ASSOCIATE INVESTIGATOR(S): Richard J. Summers, COL MC, Richard Evans III, Michael S. Edwards,

FACILITY: WRAYC DEPT/SVC: Allergy-Clinical Immunology^{CPT MSC} Svc

ACCUMULATIVE MEDICASE COST: ACCUMULATIVE CONTRACT COST: ACCUMULATIVE SUPPLY COST:

FY-83 MEDICASE: CONTRACT COST: SUPPLY COST: DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE:

TECHNICAL APPROACH:

PROGRESS DURING FY-82:

Completed 12-month study on 17 patients.

NUMBER OF SUBJECTS STUDIED:

FY-82: 17 TOTAL (TO DATE): 17 BEFORE COMPLETION OF STUDY: Complete

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
No complications.

CONCLUSIONS:

Study concluded and data submitted to Sandoz for inclusion in multicenter study.

PUBLICATIONS OR ABSTRACTS, FY-82:

Abstract submitted to American Academy of Allergy for the March 1983 meeting.

DATE: 8 Oct 82 | WORK UNIT No.: 3165 | STATUS: INTERIM X FINAL
STARTING DATE: June 1980 | DATE OF COMPLETION: July 1982

KEY WORDS: Penicillin; Allergy; Skin Testing

TITLE OF PROJECT: Clinical Trial of Skin Testing with Major and Minor Penicillin Determinants in Hospitalized Patients

PRINCIPAL INVESTIGATOR(S): Richard J. Summers, COL MC

ASSOCIATE INVESTIGATOR(S): James R. Baker, Jr., CPT MC

FACILITY: MRAHC

DEPT/SVC: Allergy-Clinical Immunology Service

ACCUMULATIVE MEDICASE COST:

0

ACCUMULATIVE CONTRACT COST:

ACCUMULATIVE SUPPLY COST:

FY-83 MEDICASE: CONTRACT COST: SUPPLY COST:

DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983

STUDY OBJECTIVE: To determine adequacy of current penicillin skin test determinants for predicting the patient's response to penicillin and related compounds.

TECHNICAL APPROACH: Skin test history positive patients who will be given penicillin and record reactions.

PROGRESS DURING FY-82: To date 26 patients have been skin tested: 23 history positive and 3 history negative. Of the patients tested 6 had + skin tests and were not given penicillin. The remainder were given penicillin without reaction.

NUMBER OF SUBJECTS STUDIED:

FY-82: _____

TOTAL (TO DATE): 26

BEFORE COMPLETION OF STUDY: 200

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
None

CONCLUSIONS: None can be drawn at this time

PUBLICATIONS OR ABSTRACTS, FY-82: None

| | | |
|--|---|---|
| DATE: 22 Aug 82 | Work Unit No.: 3166 | STATUS: INTERIM X FINAL |
| STARTING DATE: 2 March 1980 | DATE OF COMPLETION: Fall 1983 | |
| KEY WORDS: Local anesthetic; skin tests; challenge; adverse reaction | | |
| TITLE OF PROJECT: An Evaluation of Local Anesthetic Skin Testing and Progressive Challenge in Patients with a History of an Adverse Reaction to Local Anesthetics. | | |
| PRINCIPAL INVESTIGATOR(S): Richard J. Summers, MD, COL MC; Michael Schatz, MD N. S. Nelson, COL MC | | |
| ASSOCIATE INVESTIGATOR(S): Richard Evans III, COL, MC; Richard Weber, LTC, MC Bonnie Baswell, MAJ MC | | |
| FACILITY: WRAMC | DEPT/SVC: Allergy-Clinical Immunology Service | |
| ACCUMULATIVE MEDCASE COST: N/A | ACCUMULATIVE CONTRACT COST: N/A | ACCUMULATIVE SUPPLY COST: N/A |
| FY-83 MEDCASE: N/A | CONTRACT COST: _____ | SUPPLY COST: _____ |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983 |

STUDY OBJECTIVE: Evaluation of local anesthetic skin testing and progressive challenge in patients with previous adverse reaction to local anesthetic.

TECHNICAL APPROACH: Skin testing to local anesthetic to which the patient has reacted (by history) is performed at low concentrations. The concentration is gradually increased until either a positive skin test occurs or full strength local anesthetic has been tolerated.

PROGRESS DURING FY-82: To date 15 patients have been completely skin tested and found to be negative at full strength.

NUMBER OF SUBJECTS STUDIED:

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

CONCLUSIONS:

PUBLICATIONS OR ABSTRACTS, FY-82:

DATE: 8 Oct 82 WORK UNIT NO.: 3167 STATUS: INTERIM FINAL X

STARTING DATE: DATE OF COMPLETION:

KEY WORDS:

TITLE OF PROJECT: The Effect of Hypnosis and Strategic Psychological Intervention on the Bronchial Response to Mecholy1

PRINCIPAL INVESTIGATOR(S): Laurie J. Smith, M.D.

ASSOCIATE INVESTIGATOR(S): Richard Evans III, COL MC; Harold J. Wain, PhD

FACILITY: MRMC

DEPT/SVC: Allergy-Clinical Immunology Service

ACCUMULATIVE MEDCASE COST:

ACCUMULATIVE CONTRACT COST:

ACCUMULATIVE SUPPLY COST:

FY-83 MEDCASE: CONTRACT COST: SUPPLY COST:

DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To determine effect of hypnosis on bronchial reactivity

TECHNICAL APPROACH: Using methacholine challenge test pre and post hypnosis to detect if hypnosis alters bronchial reactivity.

PROGRESS DURING FY-82: No work was performed on this study. Currently, the paper is being written.

NUMBER OF SUBJECTS STUDIED:

FY-82: TOTAL (TO DATE): BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

CONCLUSIONS: Hypnosis had a significant effect on bronchial response to methacholine.

PUBLICATIONS OR ABSTRACTS, FY-82:

DATE: 1 OCT 82 | WORK UNIT NO.: 3168-R | STATUS: INTERIM | FILE:
STARTING DATE: | DATE OF COMPLETION:

KEY WORDS:
TITLE OF PROJECT: Comparison of Modalities for Treatment of SLE Nephritis.
Phase I and Phase II.

PRINCIPAL INVESTIGATOR(S): Richard C. Welton, MD, WRAMC
ASSOCIATE INVESTIGATOR(S): Mark Nelson, MD; WBAMC ; Daniel Nash, MD, WRAMC
Sterling West, MD; FAMC

FACILITY: WRAMC | DEPT/SVC: Medicine/Rheumatology Service

ACCUMULATIVE NEDCASH COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST:

FY-83 NEDCASH: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983

STUDY OBJECTIVE: SEE REVERSE SIDE.

TECHNICAL APPROACH: SEE REVERSE SIDE

PROGRESS DURING FY-82: SEE REVERSE SIDE

NUMBER OF SUBJECTS STUDIED:
FY-82: | TOTAL (TO DATE): | BEFORE COMPLETION OF STUDY: 25

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
None

CONCLUSIONS:
ON REVERSE SIDE

PUBLICATIONS OR ABSTRACTS, FY-82:
None.

STUDY OBJECTIVE: (1) To evaluate the efficacy and side effects of single daily dose corticosteroids vs split dose steroid therapy. (2) 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: The majority of patients with diffuse proliferative SLE Nephritis appear to respond to high (1-2 mg/kg day) prednisone or equivalent. It has been suggested by many that because of the lymphocytopenic effect which peaks in 4-6 hours after a dose of steroids, that steroids should be given in split doses q 6-8 hours during active disease.

It is well known that splitting the steroid dose causes more adrenal suppression and cushingoid side effects. However, to date there is no data comparing the efficacy of split dose vs single dose steroid therapy in SLE Nephritis.

Although steroid therapy appears to be effective in a majority of patients, there are a subset of patients who fail to respond to steroids or develop intolerable side effects on the dose of steroid required for disease suppression. It is this subset of patients in whom we feel that a trial of cytotoxic therapy is indicated.

PROGRESS DURING FY-82: This treatment protocol is the first of several proposed multi-Army MEDCEN protocols organized and accepted by the newly established Association of Army Rheumatologist with representatives at each Army MEDCEN. This same protocol is ongoing at William Beaumont AMC under the direction of Major Mark Nelson, MD and at Fitzsimons AMC under Major Sterling West, MD.

Because of early and temporary administrative difficulties, only a few patients have been entered on this protocol. Because of the National disagreement and lack of uniformity as a standard of medical care in Lupus Nephritis that exists among Rheumatologists and Nephrologists, treatment protocols of this nature are required as a prospective controlled attempt to gather meaningful data in order to compare efficacy of treatment regimens. Depending upon the progression of this protocol expansion of the number of patients required for the completion of this study may be required to improve statistical comparison of treatment subgroups.

DATE: 1 OCT 82 | MON. UNIT NO.: 3169-R | STATUS: INTERIM | FUND:
 STARTING DATE: 1981 | DATE OF COMPLETION: 1983
 KEY WORDS: B-7 CREG, "X" - HLA Antigen, Acute Anterior Uveitis
 TITLE OF PROJECT: Study of Cross-Reactive "X" HLA Antigen in Uveitis

PRINCIPAL INVESTIGATOR(S): Joseph T. Tesar, MD; Sterling West, MD; John Hobbs, MD;
 Associate Investigator(s): Michael Strong Ph.D.; Benjamin Schwartz

FACILITY: IRANC | Dept/Svc: Medicine, Rheumatology Service
 ACCUMULATIVE MEDICASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST:
 FY-83 MEDICASE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983

STUDY OBJECTIVE: SEE ATTACHED PAGE.

TECHNICAL APPROACH: SEE ATTACHED PAGE.

PROGRESS DURING FY-82: SEE ATTACHED PAGE.

NUMBER OF SUBJECTS STUDIED:
 FY-82: 25 | TOTAL (TO DATE): 66 | BEFORE COMPLETION OF STUDY: 80

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
 None

CONCLUSIONS: The HLA Typing Data confirms usefulness of HLA-"X" typing in acute anterior uveitis showing a prevalence of 68% in this population.

PUBLICATIONS OR ABSTRACTS, FY-82:
 West ST, Tesar JT and Schwartz B: Increased prevalence of HLA-X Antigen in Acute Anterior Uveitis. Arthritis and Rheumatism, June 1982 (Abstract)

WORK UNIT #: 3169-R

STUDY OBJECTIVE: Previous studies of HLA antigens defined a distinct association of HLA B-7 CREG with acute anterior uveitis. This HLA antigen group contains a public antigenic determinant, the "X" HLA-Antigen. Using a monospecific antibody to this determinant we proposed to study the incidence of this HLA antigen in a population of patients with acute anterior uveitis. The hypothesis on which this study is based is: The factor which determines a genetic susceptibility to acute anterior uveitis, and to spondyloarthropathies is not the HLA B27 antigen itself, but the "X" antigenic determinant which is present on HLA B-7, B-27, Bw22, B-40, and B-42.

TECHNICAL APPROACH: The plan of this study is examination of minimally 45 subjects with diagnosis of acute idiopathic uveitis, 25 subjects with spondyloarthropathy and associated acute anterior uveitis, 25 patients with secondary uveitis, and a large number of normal control subjects (date already available from grant studies). The study subjects are examined by a rheumatologist and an ophthalmologist, then a small sample of blood from each patient and control is HLA typed using an "X" HLA-antigen specific antiserum.

PROGRESS DURING FY-82: An additional 25 patients with acute anterior uveitis were examined during the past year. A total of 66 patients were examined to this date. All patients were typed with antibodies to HLA-A, B,C antigen specificities 25 with X-antiserum. The frequency of "X" antigen in uveitis was 68%. HLA typing data (HLA-A,B,C determinations) for a random population of 189 white and 92 black control individuals are available from the Tissue Typing Laboratory.

DATE: 1 OCT 82 WORK UNIT No.: 3170-R STATUS: INTERIM FISCAL

STARTING DATE: DATE OF COMPLETION:

KEY WORDS:

TITLE OF PROJECT: Reiter's Syndrome in the United States Army

PRINCIPAL INVESTIGATOR(s): Richard C. Welton (Oliver Lawless & Sterling West)

ASSOCIATE INVESTIGATOR(s): Robert Claypool, Peter T. Singleton

FACILITY: WRANC DEPT/SVC: Dept Medicine/Rheumatology Svc

ACCUMULATIVE MEDICASE COST: ACCUMULATIVE CONTRACT COST: ACCUMULATIVE SUPPLY COST:

FY-83 MEDICASE: CONTRACT COST: SUPPLY COST: DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: (a) To establish the clinical, laboratory, and radiologic characteristics of Reiter's Syndrome in the U.S. Army; b) To define any prognostic factors as well as the prognosis of Reiter's Syndrome in this population.

TECHNICAL APPROACH:

PROGRESS DURING FY-82:

NUMBER OF SUBJECTS STUDIED:

FY-82: TOTAL (TO DATE): BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

CONCLUSIONS: As discussed and noted on last year's annual progress report this protocol has been terminated as of June 1981. The abstract submitted and presented at the annual meeting of the Arthritis and Rheumatism Association June 1981 was submitted with last years progress report. Lack of supporting personnel has prevented any further work on this project.

PUBLICATIONS OR ABSTRACTS, FY-82:

DATE: 8 Oct 82 Work Unit No.: 3171 STATUS: Interim Final

STARTING DATE: February 1981 DATE OF COMPLETION:

KEY WORDS:

TITLE OF PROJECT: Immunoregulation of Human IgE Biosynthesis

PRINCIPAL INVESTIGATOR(S): Thomas A. Fleisher, LTC MC

ASSOCIATE INVESTIGATOR(S): Richard Evans III, COL MC

FACILITY: WRMC DEPT/SYC: Allergy-Clinical Immunology Service

ACCUMULATIVE FEDCASE COST: ACCUMULATIVE CONTRACT COST: ACCUMULATIVE SUPPLY COST:

FY-83 FEDCASE: CONTRACT COST: SUPPLY COST: DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: Evaluate in vitro human IgE production - conditions and cellular requirements.

TECHNICAL APPROACH: Culture human peripheral blood mononuclear cells under varying culture conditions, additives and times, then evaluate supernatant for IgE content using highly specific low level IgE RIA.

PROGRESS DURING FY-82:

See attached sheet

NUMBER OF SUBJECTS STUDIED:

FY-82: 14 TOTAL (TO DATE): 22 BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS: To date we are unable to generate an in vitro culture system for human IgE synthesis that results in de novo IgE production by lymphocytes such that immunoregulatory questions can be satisfactorily answered. Because of a variety of major technical difficulties at this juncture in vito IgE in man awaits further clarification.

PUBLICATIONS OR ABSTRACTS, FY-82:

Regulation of Human IgE Synthesis
1st Carl W. Tempel Symposium

Annual Progress Report: FY-82
Work Unit No.: 3171, Immunoregulation of Human IgE biosynthesis
(continued)

Progress During FY-82:

We have continued to find that hydrocortisone in the dose range of $10^{-6}M$ to $10^{-8}M$ induces in vitro IgE by atopic patients in relatively small quantities (i.e., nanogram amounts from 2×10^6 lymphocytes). We have also been unable to demonstrate any de novo IgE synthesis by non atopic patients. The IgE production by atopic patients does not appear to directly correlate with the serum IgE concentration.

DATE: 8 Oct 82 WORK UNIT No.: 3172 STATUS: INTERIM X FINAL

STARTING DATE: February 1981 DATE OF COMPLETION:

KEY WORDS:

TITLE OF PROJECT: Microplate Enzyme-Linked Immunosorbent Assay (ELISA) for the Immunodiagnosis of Cat Antigen Specific IgE

PRINCIPAL INVESTIGATOR(S): Thomas A. Fleisher, LTC MC

ASSOCIATE INVESTIGATOR(S): Richard Evans III, COL MC

FACILITY: WRAHC DEPT/SVC: Allergy-Clinical Immunology Service

ACCUMULATIVE MEDCARE COST: ACCUMULATIVE CONTRACT COST: ACCUMULATIVE SUPPLY COST:

FY-83 MEDCARE: CONTRACT COST: SUPPLY COST: DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To develop an ELISA system for antigen specific IgE

TECHNICAL APPROACH: Work out antigen specific ELISA for IgE including defining absolutely specific antisera to IgE and evaluate antigen specific IgG

PROGRESS DURING FY-82:

See attached sheet

NUMBER OF SUBJECTS STUDIED:

FY-82: TOTAL (TO DATE): BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS: Methodology is well worked out and project is in the process of being expanded.

PUBLICATIONS OR ABSTRACTS, FY-82: None

Annual Progress Report FY-82
Work Unit No.: 3172
(continued)

Progress During FY-82

The antigen specific ELISA for IgE appears to be a very useful test that ultimately could be considered an alternative method to the RAST method. We have expanded our modification of the system to amplify the sensitivity and are currently exploring using biotinylated anti IgE and avidin bound enzyme. We are in the process of submitting an addendum to this protocol to expand the antigens we examine with the ELISA system as well as looking for IgE contained within circulating immune complexes.

DATE: 1 OCT 82 | Work Unit No.: 3173-R | STATUS: INTERIM FINAL

STARTING DATE: _____ DATE OF COMPLETION: _____

KEY WORDS:

TITLE OF PROJECT: Evaluation of Histocompatibility Antigens in SLE Patients

PRINCIPAL INVESTIGATOR(S): Richard C. Welton, MD

ASSOCIATE INVESTIGATOR(S): Frank Scott, MD; Walter Moore, MD

FACILITY: MR/MC | DEPT/SVC: Medicine/Rheumatology Service

ACCUMULATIVE MEDICASE COST: _____ ACCUMULATIVE CONTRACT COST: _____ ACCUMULATIVE SUPPLY COST: _____

FY-83 MEDICASE: _____ CONTRACT COST: _____ SUPPLY COST: _____ DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT **FEB 25 1983**

STUDY OBJECTIVE: To determine whether a statistical association exists for HLA B cell and non-B cell alloantigens with circulating serum autoantibodies and clinical manifestations in SLE.

TECHNICAL APPROACH:
SEE REVERSE SIDE.

PROGRESS DURING FY-82:
SEE REVERSE SIDE.

NUMBER OF SUBJECTS STUDIED:
FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
None

CONCLUSIONS:
SEE REVERSE SIDE

PUBLICATIONS OR ABSTRACTS, FY-82:
None

TECHNICAL APPROACH: Histocompatibility typing will be performed on peripheral blood lymphocytes obtained from patients with SLE. Data on HLA haplotypes of 200 normal individual blood donors are already available and will serve as controls. The patients eligible and consenting to this protocol will be typed for HLA-A,B,C and DRW locuses using the microcytotoxicity method of Mittal and Terasaki. Well defined and mono-specific typing antisera obtained from the National Institutes of Health or from the International Histocompatibility Workshop pool of antisera will be used.

PROGRESS DURING FY-82: We have examined the frequency of B lymphocyte (HLA-DRw) alloantigens in 35 patients who fulfilled the American Rheumatism Association criteria for Systemic Lupus Erythematosus (SLE). We separated these patients into three clinical subsets: With nephritis (13), without nephritis (15), and with mixed connective tissue disease (MCTD) (7). Twenty-nine were females, 6 were males. The frequency of HLA-DRw3 (46%) and DRw2 (46%) was increased for the SLE patients as a group compared to the controls (25%) and (27%) respectively. DRw3 was further increased to 92% ($P= 0.001$) in the subset with Nephritis. Anti-native DNA (dsDNA) antibodies were positive in 55% of the total SLE group but in 92% of the subset with Nephritis. These data show a significant association between DRw3, anti dsDNA antibodies and nephritis in SLE ($p 0.001$). This association supports the concept of a human immune response gene linked to a specific HLA complex which codes for the production of anti dsDNA antibodies as one of the etiological factors in the pathogenesis of the nephritis of SLE. Our findings provide the first evidence of an effect of an immune response gene in the pathogenesis of a clinical manifestation of SLE. A tendency for DR-7 association with MCTD was also noted.

These initial findings supporting the concept of genetic predisposition for subgroups of clinical SLE are being confirmed through increased typing of SLE patients that have been categorized into clinically recognized subgroups. Recent articles suggest however that the HLA DR3 and DR7 gene may also be closely associated with other forms of arthritis including the spondyloarthropathies and Sjogren's Syndrome. Therefore in order to prove a specific association the HLA complex B cell alloantigens with SLE, other arthritis syndromes must be investigated for DR antigen association. Addenda to this protocol are being written at this time to properly define the DR antigen associations in SLE through expansion of disease categories studies in the same manner.

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| DATE: 18 Nov 82 | WORK UNIT No.: 3174 | STATUS: INTERIM X FINAL |
| STARTING DATE: 27 July 1981 | | DATE OF COMPLETION: 1984 |
| KEY WORDS: Asthma specific antibody responses | | |
| TITLE OF PROJECT: Quantitative Immunoglobulin Levels and Other Parameters of In Vivo Immune Function in Steroid-Dependent and Non-Steroid Dependent Asthmatics | | |
| PRINCIPAL INVESTIGATOR(S): Renata J. M. Engler, LCDR, MC, USNR | | |
| ASSOCIATE INVESTIGATOR(S): Cheryl D. C. Rosenblatt, CDR, MC, USN; Richard J. Summers, COL, MC | | |
| FACILITY: WRAAC and NMMC | | DEPT/SVC: Allergy-Clinical Immunology Service |
| ACCUMULATIVE PECCASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
| FY-83 PECCASE: | CONTRACT COST: | SUPPLY COST: |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: To determine whether or not steroids do interfere with specific antibody responses. Preliminary data has suggested that in contrast to what is in the literature certain patients have markedly attenuated specific antibody response to booster immunization with diphtheria, tetanus and Pneumovac.

TECHNICAL APPROACH: We would like to continue the study to increase our patient numbers & improve statistical analyses.

Procedure and workup as outlined in the original protocol.

PROGRESS DURING FY-82: Abstract was accepted at XI International Congress of Allergology and Clinical Immunology, London, England, October 1982. Data is being compiled and statistically analyzed for paper.

NUMBER OF SUBJECTS STUDIED:

81: Approx. 30
 FY-82: 16 or 18 TOTAL (TO DATE): 38 BEFORE COMPLETION OF STUDY: 80

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

No significant adverse effects have resulted throughout the study.

CONCLUSIONS: We would like to continue the present study with expanded number of enrolled patients in order to clarify the question of whether or not steroids have a primary effect on specific antibody response in certain asthmatic patients or if this is unique to certain patients because of an underlying immune deficiency.

PUBLICATIONS OR ABSTRACTS, FY-82:

Abstract presented at American Academy of Allergy meeting, Montreal, Canada, March 1982.

Abstract accepted at XI International Congress of Allergology and Clinical Immunology, London, England, October 1982.

DATE: 1 OCT 82 | WORK UNIT NO.: 3175-R | STATUS: INTERIM FINAL

STARTING DATE: _____ DATE OF COMPLETION: _____

KEY WORDS:

TITLE OF PROJECT: Identification of dsDNA Binding Cells in SLE Patients

PRINCIPAL INVESTIGATOR(S): Richard C. Welton, MAJ, MC

ASSOCIATE INVESTIGATOR(S): _____

FACILITY: WRAMC | DEPT/S/C: Medicine/Rheumatology Service

ACCUMULATIVE MEDICASE COST: _____ ACCUMULATIVE CONTRACT COST: _____ ACCUMULATIVE SUPPLY COST: _____

FY-83 MEDICASE: _____ CONTRACT COST: _____ SUPPLY COST: _____ DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT **FEB 25 1983**

STUDY OBJECTIVE:

TECHNICAL APPROACH:

PROGRESS DURING FY-82:

NUMBER OF SUBJECTS STUDIED:

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

CONCLUSIONS: Lack of personnel support to perform the laboratory procedures of this protocol as well as other protocols, and because of other more pressing protocol priorities no progress has been made on this protocol to date. Because of no apparent foreseeable change in the above situation, I have to recommend termination of this protocol at this time.

PUBLICATIONS OR ABSTRACTS, FY-82:

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| DATE: 1 OCT 82 | Work Unit No.: 3176-R | STATUS: <u>INTERIM</u> | FINAL |
| STARTING DATE: | | DATE OF COMPLETION: | |
| KEY WORDS: | | | |
| TITLE OF PROJECT: Measurement of Immune Complexes in Systemic Lupus Erythematosus. | | | |
| PRINCIPAL INVESTIGATOR(S): Charles S. Via, MAJ, MC | | | |
| ASSOCIATE INVESTIGATOR(S): Richard C. Welton, MAJ(P), MC | | | |
| FACILITY: WRAMC | | DEPT/SVC: Medicine/Rheumatology Service | |
| ACCUMULATIVE MEDICARE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: | |
| FY-83 MEDICARE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT <u>FEB 25 1983</u> |

STUDY OBJECTIVE:

TECHNICAL APPROACH:

PROGRESS DURING FY-82:

NUMBER OF SUBJECTS STUDIED:

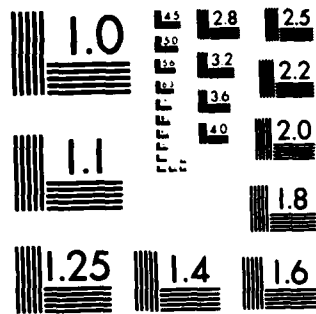
FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

CONCLUSIONS: Work was completed on this protocol in June 1982. The abstract generated by the data was submitted to the Annual Meeting of the Arthritis and Rheumatism Association in June 1982. Please see attached.

No further work will be applied to this protocol in the upcoming year. I consider this protocol terminated.

PUBLICATIONS OR ABSTRACTS, FY-82:
See attached.



MICROCOPY RESOLUTION TEST CHART
NATIONAL BUREAU OF STANDARDS 1963-A

Annual Progress Report

Work Unit No.: 3177

Status: Interim

Estimated Completion Date: 30 September 1982

Key Words: Complement Receptor, Binding, C3b, Leukocyte

Title of Project: Binding of C3b Oligomers to Human C3b Receptors

Investigators:

Principal: Melvin Berger, MAJ MC
Allergy-Clinical Immunology Service
Walter Reed Army Medical Center

Technical Approach:

1. Avidin was used to link biotinyl C3b into oligomers which were then isolated by gel filtration. Relative affinities of oligomers for polymorphonuclear leukocyte complement receptors were determined using a rosette inhibition assay.
2. Complement receptors on B-lymphocytes were also studied using the rosette inhibition assay.
3. Effects of lymphokines on polymorphonuclear leukocyte complement receptors were also studied by rosette formation assays as well as by direct binding studies of ^{125}I -C3b.

Progress during FY-82:

1. Reproducible oligomer formation has been achieved and oligomers have been characterized and purified by sequential gel filtration steps. Dimers may be obtained in good yield but the yield of tetramers has been disappointingly low. Results of rosette inhibition studies show that dimers, whether formed by avidin-biotin linkage or spontaneously during the cleavage of C3 to C3b, bind about 5 times better than monomeric C3b. (5.81 ± 0.80 for spontaneous dimers, 4.61 ± 1.47 for avidin-linked). Large oligomers bind 6.9 ± 2.0 fold more effectively than monomers. Experiments are currently underway to determine if these oligomers activate neutrophils by cross-linking C3b receptors.
2. The B-lymphocyte C3b receptor has been found to be similar to the C3b receptor of neutrophils and red cells in that it is not blocked by native C3 at physiologic concentrations but is effectively inhibited by monomeric C3b at 5-6 $\mu\text{g}/\text{ml}$.
3. A lymphocyte culture supernatant factor has been shown to specifically increase neutrophil C3b receptors while having little or no effect on Fc receptors for IgG. Effects of this material on metabolic processes of the cell have been described previously. These findings suggest an additional mechanism which may be important in vivo.

Annual Progress Report
Work Unit No.: 3177
(continued)

Number of Subjects: N/A

Side Effects: "No serious or unexpected side effects occurred"

Conclusions: See above under progress

Abstract: Neutrophil activating factor from a continuous lymphoid cell line mediates increased number of neutrophil C3b receptors and increased functional activity. Submitted to 15th Int. Leukocyte Culture Conf. A. Cross, M. Berger, G. Lowell, J. Sadoff.

Publication:

Characterization of Ligand Binding to Human B-Lymphocyte Complement (CR1) Receptor
M. Berger, T. Fleisher, manuscript in preparation.

Funding Requirements: Unchanged

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| DATE: 1 OCT 82 | WORK UNIT NO.: 3178-R | STATUS: <u>INTERIM</u> | FINAL |
| STARTING DATE: 1982 | DATE OF COMPLETION: | | 1984 |
| KEY WORDS: Seronegative Arthritis, B-7 CREG, X-antigens | | | |
| TITLE OF PROJECT: Study of Cross Reactive B-7 CREG and B-lymphocyte antibodies in Seronegative Rheumatoid Arthritis Patients | | | |
| PRINCIPAL INVESTIGATOR(S): Joseph T. Tesar, MD; Frank Wellborne, MD | | | |
| ASSOCIATE INVESTIGATOR(S): Arthur Kunath, MD; Richard C. Welton, MD | | | |
| FACILITY: <u>WRAVE</u> | | DEPT/SVC: Medicine/Rheumatology Service | |
| ACCUMULATIVE FEBCASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: | |
| FY-83 FEBCASE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
| STUDY OBJECTIVE: To determine the frequency of HLA-X, A,B,C antigens in seronegative Rheumatoid Arthritis patients. | | | |
| TECHNICAL APPROACH: HLA-X, A,B,C typing using the NIH microlymacytotoxicity technique. Patients examined according to standardized protocol. | | | |
| PROGRESS DURING FY-82: A total of 23 seronegative rheumatoid arthritis patients were examined and HLA typed. | | | |
| NUMBER OF SUBJECTS STUDIED: | | | |
| FY-82: 23 | TOTAL (TO DATE): 23 | BEFORE COMPLETION OF STUDY: 48-50 | |
| SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): None, preliminary | | | |
| CONCLUSIONS: 72% of 23 patients with seronegative rheumatoid arthritis had a B-7 CREG antigen, as determined by HLA A,B,C typing. Control individuals had a 47% incidence of this antigen complex. | | | |
| PUBLICATIONS OR ABSTRACTS, FY-82: | | | |
| Abstract in preparations for 1982 (study in progress for 5-6 months only). | | | |

DATE: _____ Max Unit No.: 3179-R STATUS: INTERIM FISCAL
STARTING DATE: _____ DATE OF COMPLETION: _____

KEY WORDS:

TITLE OF PROJECT: Fluorescent Antinuclear Antibody Detection in Polymyositis, Dermatomyositis, Scleroderma and CREST Syndrome, Using a KB cultured

PRINCIPAL INVESTIGATOR(S): Robert Ehrhart, CPT, MC

ASSOCIATE INVESTIGATOR(S): _____

FACILITY: WRMC DEPT/SVC: Medicine/Rheumatology & Clinical Immun.

ACCUMULATIVE PEDCASE COST: _____ ACCUMULATIVE CONTRACT COST: _____ ACCUMULATIVE SUPPLY COST: _____

FY-83 PEDCASE: _____ CONTRACT COST: _____ SUPPLY COST: _____ DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE:

TECHNICAL APPROACH:

PROGRESS DURING FY-82:

NUMBER OF SUBJECTS STUDIED:

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): _____

CONCLUSIONS: Lack of personnel support to perform the laboratory procedures of this protocol as well as other protocols, and because of other more pressing protocol priorities no progress has been made on this protocol to date. Because of no apparent foreseeable change in the above situation, I have to recommend termination of this protocol at this time.

PUBLICATIONS OR ABSTRACTS, FY-82:

DATE: 6 Oct 82 WORK UNIT No.: 3180 STATUS: INTERIM XX FINAL

STARTING DATE: Dec 1981 DATE OF COMPLETION: June 1983

KEY WORDS: Immediate Skin Tests Uremia Transplant

TITLE OF PROJECT: EVALUATION OF IMMEDIATE HYPERSENSITIVITY IN PATIENTS WITH RENAL INSUFFICIENCY.

PRINCIPAL INVESTIGATOR(S): James R. Baker, Jr., MD CPT MC

ASSOCIATE INVESTIGATOR(S): Harrison Hassell, Jack Moore

FACILITY: WRAHC DEPT/SVC: Allergy/Renal

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| ACCUMULATIVE FEEDCASE COST: .00 | ACCUMULATIVE CONTRACT COST: .00 | ACCUMULATIVE SUPPLY COST: .00 |
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| FY-83 FEEDCASE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
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STUDY OBJECTIVE: Study to see if skin tests are reliable in renal failure.

TECHNICAL APPROACH: Skin testing, serum rast determinations, serum IgE determinations.

PROGRESS DURING FY-82: Fifteen patients were tested, 12 of which had positive skin tests. No statistical difference in allergen skin (below)

NUMBER OF SUBJECTS STUDIED:

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| FY-82: 15 | TOTAL (TO DATE): 15 | BEFORE COMPLETION OF STUDY: 30 |
|-----------|---------------------|--------------------------------|

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): NONE

CONCLUSIONS: There may be an increase in the threshold for now. Specific histamine release in uremia.

PUBLICATIONS OR ABSTRACTS, FY-82: NONE

Progress continued from above: tests were noted. A decrease in the threshold of non-specific histamine release was noted (p < .05). None of the in vitro tests done -- blood has been collected.

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|------------------------------|--------------------------|---|
| DATE: 12 Oct 82 | MOX UNIT No.: 3181 | STATUS: INTERIM <input checked="" type="checkbox"/> FINAL |
| STARTING DATE: February 1982 | DATE OF COMPLETION: 1984 | |

KEY WORDS:

TITLE OF PROJECT: Lymphoid Responsiveness to Human Interferon in Systemic Lupus Erythematosus

PRINCIPAL INVESTIGATOR(S): Thomas A. Fleisher, LTC MC

ASSOCIATE INVESTIGATOR(S): Richard Welton, MAJ MC

FACILITY: WRAVC DEPT/SVC: Allergy-Clinical Immunology Service

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| ACCUMULATIVE MEDICASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
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| FY-83 MEDICASE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
|-----------------|----------------|--------------|--|

STUDY OBJECTIVE: Evaluate the responsiveness of in vitro B cell Ig production by patients with systemic lupus erythematosus to human lymphoblastoid interferon.

TECHNICAL APPROACH: Set up in vitro cultures for polyclonal immunoglobulin using normal and patient lymphoid cells and compare the effect of varying concentrations of human lymphoblastoid IFN on Ig production.

PROGRESS DURING FY-82: There appears to be a small subgroup of SLE patients that do NOT demonstrate IFN mediated suppression of polyclonal Ig production in contrast to normals and the other SLE patients.

NUMBER OF SUBJECTS STUDIED:

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| FY-82: 24 | TOTAL (TO DATE): 24 | BEFORE COMPLETION OF STUDY: 50 |
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SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
None

CONCLUSIONS: Study continuing to identify common features in abnormal responding group and to further characterize the level of the defect (i.e., if it is at the B cell level); also suggestion of possible therapy with IFN in those SLE patients that are suppressed by IFN.

PUBLICATIONS OR ABSTRACTS. FY-82:

1. Fleisher, TA, AM Attallah, J Misiti, G Tosato and WC Greene. 1982. Interferon mediated regulation of human immunoglobulin synthesis. Clinical Res 2:348A.
2. Fleisher, TA, AM Attallah, G Tosato, RM Blaese, and WC Greene. 1982. Interferon-mediated inhibition of human polyclonal immunoglobulin synthesis. J. Immunol 129:1099.

DATE: 8 Oct 82 Work Unit No.: 3182 STATUS: INTERIM Final X

STARTING DATE: DATE OF COMPLETION: 23 Sep 82

KEY WORDS: Silicone; Patch Testing

TITLE OF PROJECT: Silicone Patch Testing

PRINCIPAL INVESTIGATOR(S): Artie L. Shelton, LTC MC

ASSOCIATE INVESTIGATOR(S): Renata Engler, LCDR, MC Richard J. Summers, COL MC

FACILITY: HRAHC DEPT/SYC: Allergy-Clinical Immunology Service

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| ACCUMULATIVE MEDICASE COST: 0 | ACCUMULATIVE CONTRACT COST: 0 | ACCUMULATIVE SUPPLY COST: 0 |
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| FY-83 MEDICASE: 0 | CONTRACT COST: 0 | SUPPLY COST: 0 | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
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STUDY OBJECTIVE: To determine propensity of silicone causing delayed hypersensitivity or type IV reaction.

TECHNICAL APPROACH: Patch testing and anergy skin

PROGRESS DURING FY-82: Continuing research data. Presented at Fitzsimons Army Med Ctr. Assembling findings for presentation and publication of paper for the American Academy of Allergy Journal of Allergy and Clinical Immunology.

NUMBER OF SUBJECTS STUDIED:

FY-82: 20 TOTAL (TO DATE): 20 BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS:

One patient with positive reaction to silicone

PUBLICATIONS OR ABSTRACTS, FY-82: None

Paper in process for presentation and publication for Journal of Allergy and Clinical Immunology.

Annual Progress Report

Work Unit No.: 3183

Status: Interim

Estimated Completion Date: 30 September 1983

Key Words: Complement, Antibody, Bacteria, Avidin-Biotin, Affinity Chromatography

Title of Project: Isolation of Acceptors for Acylation by C3 during Complement Activation

Investigators:

Principal: Melvin Berger, MAJ MC
Allergy-Clinical Immunology Service
Walter Reed Army Medical Center

Study Objective: Development of methods to isolate and characterize the constituents to which C3 becomes attached during activation and to study the physiology of the C3 molecule.

Technical Approach: Biotinylated C3 was allowed to become activated by addition to serum or with purified complement components, with or without antibody, in the presence of sheep erythrocytes or pneumococci as targets. In addition, a model of C3 activation using trypsin cleavage in the presence of radio labelled small molecules as acceptors was also employed. Avidin conjugates were then used to localize the sites of C3 deposition by electron microscopy and avidin-Sepharose was used for isolation of acyl acceptors by affinity chromatography.

Progress During FY-82:

1. Use of biotinyl C3 and avidin-ferritin to localize sites of C3 deposition or pneumococci-electron micrographs demonstrated that anti-cell wall antibody localized C3 to the bacterial cell wall and that anti-capsular antibody localized C3 to the capsule. C3 fixed by the alternative pathway of complement activation was quantitatively similar for encapsulated and rough organisms but could only be identified by avidin-ferritin staining with rough organisms presumably due to interference by the capsule with the large ferritin moieties. Although it has not yet been possible to isolate the bacterial constituent to which C3b becomes attached per se, use of ^{125}I -labelled antibody allowed recovery of both IgG and IgM on avidin-Sepharose columns indicating that covalent linkages between C3b and these antibodies had been formed during activation. These complexes were only partly released by hydroxylamine treatment suggesting that amide as well as ester linkages were formed.
2. Trypsin cleaved biotinyl C3 formed covalent linkages with both ^3H -raffinose and ^3H -lysine. These radiolabelled small molecules were then retained on avidin-Sepharose, as predicted. Following treatment with hydroxylamine, all of the ^3H -raffinose was released, as expected since this complex sugar can form only ester linkages. With ^3H -lysine however, similar release was also obtained with hydroxylamine although in this case, hydroxylamine-resistant peptide bonds were expected. Further analysis by SDS-polyacrylamide gel electrophoresis revealed extensive proteolysis had taken place probably accounting for the release. These experiments are continuing.

Annual Progress Report
Work Unit No.: 3183
(continued)

3. Attempts to identify acyl acceptors from sheep erythrocytes have, as yet, been unsuccessful regardless of whether ^{125}I was bound to IgG or IgM antibody or to the surface of the red cell. This may be due to problems with the specificity of uptake of ^{125}I onto exposed molecules which are not the true targets for acylation. In each case, only non-specific binding (not prevented by excess biotin) to avidin-Sepharose was obtained.

Number of Subjects: N/A

Serious/Unexpected Side Effects in Subjects Participating in Projects: "No serious or unexpected side effects"

Conclusions:

1. Approach basically sound but problems with non-specific binding to avidin-Sepharose limits general applicability of this system.
2. When specific acceptors (or putative acceptors) can be labelled, appropriate controls for non-specific binding can be performed and this system can be used.
3. In particular, these methods have been used for localization of C3b and antibody or pneumococci and isolation of C3b-antibody complexes from organisms.

Publications and Abstracts

Abstracts:

Use of biotinylated reagents to localize antibody and complement on pneumococci. M. Berger, E. Brown, R. Cole and M. M. Frank. Fed. Proc. 41:829 (1982). Presented at 66th Annual FASEB meeting, New Orleans, LA, April 1982.

Publications:

1. Localization of C3 on streptococcus pneumoniae: Anticapsular antibody causes C3 deposition on the pneumococcal capsule. E. J. Brown, K. A. Joiner, R. M. Cole and M. Berger. Infection and Immunity, in press.
2. Classical complement pathway activation by anti-pneumococcal antibodies leads to covalent binding of C3b to antibody molecules. E. J. Brown, M. Berger, K. A. Joiner, M. M. Frank. Submitted for publication. Science.

Funding Requirements for FY-83: Unchanged

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|--|-----------------------------|---|--|
| DATE: 1 OCT 82 | WORK UNIT NO.: 3184-R | STATUS: <u>INTERIM</u> | TYPE: |
| STARTING DATE: | | DATE OF COMPLETION: | |
| KEY WORDS: | | | |
| TITLE OF PROJECT: Nifedipine in the Treatment of Raynaud's Disease and Scleroderma-associated Raynaud's Syndrome | | | |
| PRINCIPAL INVESTIGATOR(S): John L. Luetkemeyer, MD ; Joseph T. Tesar, MD | | | |
| ASSOCIATE INVESTIGATOR(S): Richard C. Welton, MD | | | |
| FACILITY: IMANC | | DEPT/SVC: Medicine/Rheumatology Service | |
| ACCUMULATIVE PEDCASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: | |
| FY-85 PEDCASE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE:

TECHNICAL APPROACH:

PROGRESS DURING FY-82:

NUMBER OF SUBJECTS STUDIED:

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

CONCLUSIONS:

This protocol was only recently approved. Therefore progress on this protocol has just begun. A report on the progress of this protocol would therefore be most appropriate at a later date.

PUBLICATIONS OR ABSTRACTS, FY-82:

DATE: 8 Oct 82 WORK UNIT No.: 3185 STATUS: INTERIM X FISCAL
STARTING DATE: September 1981 DATE OF COMPLETION: January 1983
KEY WORDS: Urine; Histamine; Assay
TITLE OF PROJECT: Urine Histamine Assay Study

PRINCIPAL INVESTIGATOR(S): Artie L. Shelton, LTC, MC

ASSOCIATE INVESTIGATOR(S): Michael A. Kaliner, MD, Head, Allergic Disease Section, NIAID

FACILITY: WRANC DEPT/SVC: Allergy-Clinical Immunology Service

ACCUMULATIVE PECCASE COST: ACCUMULATIVE CONTRACT COST: ACCUMULATIVE SUPPLY COST:

FY-83 PECCASE: CONTRACT COST: SUPPLY COST: DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT **FEB 25 1983**

STUDY OBJECTIVE: To analyze differences in urinary histamine levels between patients having systemic reactions and those without a reaction related to intravenous pyelogram (IVP) studies.

TECHNICAL APPROACH: The specimens obtained will be the post void urine which is a routine part of the intravenous pyelogram study. These samples will be analyzed for histamine release.

PROGRESS DURING FY-82: All data collected. It is being correlated for publication now.

NUMBER OF SUBJECTS STUDIED:

FY-82: 100 TOTAL (TO DATE): 100 BEFORE COMPLETION OF STUDY: 100

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
None

CONCLUSIONS:

Histamine seems to be released into urine during anaphylaxis.

PUBLICATIONS OR ABSTRACTS, FY-82:
None

DATE: 6 Oct 82 | WORK UNIT No.: 3186 | STATUS: INTERIM XX FINAL

STARTING DATE: Aug 1982 | DATE OF COMPLETION: June 1984

KEY WORDS:

TITLE OF PROJECT: In Vivo and In Vitro Analysis of the Large Local Reaction to Hymenoptera Venom.

PRINCIPAL INVESTIGATOR(S): J.R. Baker, Jr., MD

ASSOCIATE INVESTIGATOR(S): Drs. Fleischer and Summers

FACILITY: WRMC

DEPT/SVC: Allergy Immunology

ACCUMULATIVE MEDCASE COST:

ACCUMULATIVE CONTRACT COST:

ACCUMULATIVE SUPPLY COST:

\$432.70

FY-83 MEDCASE: CONTRACT COST: SUPPLY COST:

DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT

FEB 25 1983

STUDY OBJECTIVE: Determine what causes the reaction to venom.

TECHNICAL APPROACH:

Lymphocyte stimulation and skin biopsies.

PROGRESS DURING FY-82: We had difficulty obtaining patients who fit the protocol. Two patients were found, but the results were not conclusive.

NUMBER OF SUBJECTS STUDIED:

FY-82: 2 | TOTAL (TO DATE): 2 | BEFORE COMPLETION OF STUDY: 20

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS:

None at present. The cause of this reaction is still unknown.

PUBLICATIONS OR ABSTRACTS, FY-82:

None

| | | |
|---|------------------------------------|--|
| DATE: 6 Oct 82 | Work Unit No.: 3187 | STATUS: INTERIM xx FINAL |
| STARTING DATE: 2 August 1982 | DATE OF COMPLETION: 1 June 1983 | |
| KEY WORDS: Heart Antibodies Elisa | | |
| TITLE OF PROJECT: DEVELOPMENT OF AN ELISA ASSAY FOR ANTIHEART ANTIBODIES. | | |
| PRINCIPAL INVESTIGATOR(S): J.R. Baker, Jr., MD, CPT, MC | | |
| ASSOCIATE INVESTIGATOR(S): Drs. Burger, Summers and Fleischer | | |
| FACILITY: WRAAC | | DEPT/SVC: Allergy Immunology |
| ACCUMULATIVE MEDICASE COST: .00 | ACCUMULATIVE CONTRACT COST: .00 | ACCUMULATIVE SUPPLY COST: \$1,610.55 |
| FY-83 MEDICASE: | CONTRACT COST: | SUPPLY COST: |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: Develop an assay for antiheart antibodies which was practical.

TECHNICAL APPROACH: Use an Elisa system.

PROGRESS DURING FY-82: An assay has been developed. Statistical results have been shown between normals and Dresslers' syndrome. Refinements of the assay are now being done to make (below)

NUMBER OF SUBJECTS STUDIED:

FY-82: 75 TOTAL (TO DATE): 75 BEFORE COMPLETION OF STUDY: 150

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
None

CONCLUSIONS: The assay does measure antiheart antibodies, and probably will be very practical to perform on a large scale.

PUBLICATIONS OR ABSTRACTS, FY-82: None. Will be done in FY-83.

DATE: 1 OCT 82 Max Unit No.: 3188-R STATUS: MINIMUM FIRM
 STARTING DATE: 1 April 1982 DATE OF COMPLETION: 30 March 1984
 KEY WORDS: Anti-DNA Antibodies; systemic lupus erythematosus
 TITLE OF PROJECT: Comparison of the FIAX and Crithidia luciliae methods for measuring anti-DNA antibodies in systemic lupus erythematosus.

PRINCIPAL INVESTIGATOR(S): Bernard H. Berne, M.D., Ph.D.; Richard C. Welton, MAJ, MC

ASSOCIATE INVESTIGATOR(S):

FACILITY: WRANC DEPT/SVC: Medicine/Rheumatology & Clin. Imm. Svc

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| ACCUMULATIVE MEDICASE COST: 0 | ACCUMULATIVE CONTRACT COST: 0 | ACCUMULATIVE SUPPLY COST: \$2,640.00 |
| FY-83 MEDICASE: | CONTRACT COST: | SUPPLY COST: |
| | \$7,000.00 | |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983 |

STUDY OBJECTIVE: SEE ATTACHED SHEET.

TECHNICAL APPROACH:

PROGRESS DURING FY 82:

NUMBER OF SUBJECTS STUDIED:

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

CONCLUSIONS:

PUBLICATIONS OR ABSTRACTS, FY-82:

DATE: 1 OCT 82

WORK UNIT NO.: 3188-R

Status: Interim

STUDY OBJECTIVE: Compare the reproducibilities, specificities, sensitivities and other parameters of the FIAX fluorometric immunoassay and the Crithidia luciliae microscopic immunofluorescence assay for anti-DNA antibodies. Determine the preferable method for use in the diagnosis and management of systemic lupus erythematosus (SLE).

TECHNICAL APPROACH: Commercial anti-DNA kits using Crithidia luciliae and the FIAX assay are being tested for specificity, reproducibility, sensitivity, cost and reliability in the diagnosis and management of SLE.

PROGRESS DURING FY-82: The project started in the middle of FY-82. We have performed over 1000 tests using the Crithidia method for reproducibility studies. We have established a correlation between the units used in the FIAX assay and the antibody titers in the Crithidia assay. We find the reproducibility of the Crithidia assay to be generally good, except when antibodies are in low titer. This may cause difficulties in distinguishing between positive and negative tests.

NUMBER OF SUBJECTS STUDIED:

FY 82: 15 TOTAL (TO DATE): 15 BEFORE COMPLETION OF STUDY: 200

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT: None

CONCLUSIONS: Although the reproducibility of the Crithidia assay seems fairly good at high titers of anti-DNA antibodies, background fluorescence causes difficulties in measuring these antibodies when they are in low titer. We plan to determine whether this is clinically relevant, and whether the assay is less reproducible than FIAX at low levels. In addition, we have found the Crithidia assay to be significantly more expensive and time consuming than FIAX because it appears to require duplicate tests at four different dilutions to establish an accurate titer, while a similar accuracy appears obtainable by FIAX with only two tests.

PUBLICATIONS OR ABSTRACTS, FY-82: None.

Date: 1 OCT 82 | MAX. INFL. NO.: 3189-R | STATE: INDIAN | FY: FY82
Starting Date: 1 April 1982 | Date of Completion: 30 March 1985

Key Words:
TITLE OF PROJECT: Development of FIAX assays for circulating immune complexes (CIC) in rheumatic diseases

PRINCIPAL INVESTIGATOR(S): Bernard H. Berne, MD, Ph.D.; Richard C. Welton, MAJ, MC

ASSOCIATE INVESTIGATOR(S):

FACILITY: IRANC | DEPT/SVC: Medicine/Rheumatology & Clin. Immun. Svc

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| ACCUMULATIVE MEDICINE COST: 0 | ACCUMULATIVE CONTRACT COST: 0 | ACCUMULATIVE SUPPLY COST: \$1,264.11 |
|----------------------------------|----------------------------------|---|

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|---------------------------|---------------------|----------------------------|--|
| FY-83 MEDICINE COST: 0 | CONTRACT COST: 0 | SUPPLY COST: \$5,000.00 | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983 |
|---------------------------|---------------------|----------------------------|--|

STUDY OBJECTIVE: SEE ATTACHED SHEET.....

TECHNICAL APPROACH:

PROGRESS DURING FY-82:

NUMBER OF SUBJECTS STUDIED:
FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

CONCLUSIONS:

PUBLICATIONS OR ABSTRACTS, FY-82:

DATE: 1 OCT 82

WORK UNIT NO.: 3189-R

Status: Interim

STUDY OBJECTIVE: Develop assays for CIC using the FIAX fluorometric immunoassay system. Assess the value of these assays for monitoring and diagnosing rheumatic diseases.

TECHNICAL APPROACH: We are trying to develop several quantitative assays for CIC using the FIAX method. These include the solid-phase Clq binding method, the anti-C³ method, the conglutinin binding method, and the monoclonal rheumatoid factor method. Levels of CIC will be correlated with disease activities in systemic lupus erythematosus and other diseases.

PROGRESS DURING FY-82: This project started in the middle of FY-82. We attempted to develop the anti-C³ method by absorbing anti-C³ antibody to an immunoadsorbent FIAX stick, incubating with serum containing CIC, and reacting with a fluoresceinated antibody to human immunoglobulin. Initial results showed no specific binding of CIC. We are investigating the cause of the lack of activity.

NUMBER OF SUBJECTS STUDIED:

FY 82: 5 TOTAL (TO DATE): 5 BEFORE COMPLETION OF STUDY: 200

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT: None

CONCLUSIONS: The anti-C³ assay for CIC requires the attachment of a large amount of purified antibody fraction to a surface. It appears that the amount of antibody attaching is presently too low. Because of the high cost of this antibody fraction, it may not be cost-effective to develop this assay. We are now preparing to develop an assay using Clq attached to the surface. This can bind CIC and can be isolated from plasma in large quantities without great expense. We should therefore not encounter the same problem with this assay.

PUBLICATIONS OR ABSTRACTS, FY-82:

DATE: 1 OCT 82 Work Unit No.: 3190-R STATUS: INTERIM FISCAL
STARTING DATE: Mid September 1982 DATE OF COMPLETION:

KEY WORDS:

TITLE OF PROJECT: A Six Week Double-Blind Study of the Efficacy, Safety, and Tolerance of Pirazolac B.I.D. Compared with Placebo in Patients with Ankylosing Spondylitis.

PRINCIPAL INVESTIGATOR(S): Richard C. Welton, MAJ, MC; Michele Wineland, RN, M.S.N.

ASSOCIATE INVESTIGATOR(S):

FACILITY: WRAVC

DEPT/SVC: Medicine/Rheumatology Service

ACCUMULATIVE FEDCASE COST:

ACCUMULATIVE CONTRACT COST:

ACCUMULATIVE SUPPLY COST:

FY-83 FEDCASE: CONTRACT COST: SUPPLY COST:

DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE:

TECHNICAL APPROACH:

PROGRESS DURING FY-82:

NUMBER OF SUBJECTS STUDIED:

FY-82: TOTAL (TO DATE): BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

CONCLUSIONS: This protocol was just recently approved (mid September 1982) by the Surgeon General's Office. Therefore progress on this protocol has just begun. A report on the progress of this protocol would therefore be most appropriate at a later date.

PUBLICATIONS OR ABSTRACTS, FY-82:

DATE: 30 Nov 82 | WORK UNIT No.: 4113 | STATUS: INTERIM XX FINAL

STARTING DATE: NA | DATE OF COMPLETION: NA

KEY WORDS:

TITLE OF PROJECT:

Cooperative Gynecologic Oncology Group

PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC, USA

ASSOCIATE INVESTIGATOR(S): LTC Paul Heller, MC, USA - MAJ Ronald V. Dorn, MC,

FACILITY: WRAMC | DEPT/SVC: OB-GYN Oncology Service
MAJ Hiroo Advani, MC

ACCUMULATIVE MEDICASE COST:
NA

ACCUMULATIVE CONTRACT COST:
NA

ACCUMULATIVE SUPPLY COST:
NA

FY-83 MEDICASE:
NA

CONTRACT COST:
NA

SUPPLY COST:
NA

DATE OF COMMITTEE APPROVAL OF
ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: The Walter Reed section of Gynecologic Oncology is involved with the nationally organized Gynecologic Oncology Group which consist of 35 major medical centers in the country which are interested in the area of gynecologic tumors and treatment. The GOG is recognized and funded through the national cancer institute.

See below:

PROGRESS DURING FY-82: About 433 patients have been placed on GOG protocols from Walter Reed. There have been about 21 patients entered since the last reporting period.

NUMBER OF SUBJECTS STUDIED: Unknown

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

Detailed in reports.

CONCLUSIONS:

Detailed in previous reports.

PUBLICATIONS OR ABSTRACTS, FY-82: Detailed in individual progress reports.

Technical Approach: Walter Reed is active in approximately 32 GOG protocols. Presently there are 32 protocols either continuing to collect data or active. These protocols involve treatment of ovarian carcinoma, cervical carcinoma, adenocarcinoma of the endometrium, uterine sarcoma and vulvar carcinoma, and gestational trophoblastic disease. About 433 patients from Walter Reed had been placed in specific protocol studies.

DATE: 25 Jan 83 | WORK UNIT No.: 4116 | STATUS: INTERIM X FINAL

STARTING DATE: 1975 | DATE OF COMPLETION:

KEY WORDS:

TITLE OF PROJECT: Evaluation of Fetal Systolic Time Intervals and Beat-to-Beat Intervals in FHR As Early Indicators of Fetal Maturity and Fetal Distress

PRINCIPAL INVESTIGATOR(S): LTC James Haddock

ASSOCIATE INVESTIGATOR(S): H. Skiba-Powell

FACILITY: WRAVC | DEPT/SVC: OB

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| <u>ACCUMULATIVE MEDICASE COST:</u> 0 | <u>ACCUMULATIVE CONTRACT COST:</u> 0 | <u>ACCUMULATIVE SUPPLY COST:</u> 0 |
|---|---|---------------------------------------|

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|-----------------------------|----------------------------|--------------------------|---|
| <u>FY-83 MEDICASE:</u> 0 | <u>CONTRACT COST:</u> 0 | <u>SUPPLY COST:</u> 0 | <u>DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT</u> FEB 25 1983 |
|-----------------------------|----------------------------|--------------------------|---|

STUDY OBJECTIVE: To determine fetal condition by evaluating cardiac function by fetal systolic time intervals.

TECHNICAL APPROACH: Determinations made by EKG and phono cardiography

PROGRESS DURING FY-82: Project has been waitive while we have been developing Unit # 4151. We are now testing this with entry of data into computer. All equipment is now delivered and functioning.

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 | TOTAL (TO DATE): 0 | BEFORE COMPLETION OF STUDY: 60

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
None

CONCLUSIONS:

Pending application of this protocol to patients when 4151 is running satisfactorily.

PUBLICATIONS OR ABSTRACTS, FY-82:

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| DATE: 25Jan83 | Work Unit No.: 4124 | STATUS: INTERIM X FINAL |
| STARTING DATE: 1973 | DATE OF COMPLETION: | |
| KEY WORDS: | | |
| TITLE OF PROJECT: Fetal Intensive Care Monitoring in a Long-range Continuing Project | | |
| PRINCIPAL INVESTIGATOR(S): LTC James Haddock | | |
| ASSOCIATE INVESTIGATOR(S): T. Frank, A. Presbylick, H. Skiba-Powell | | |
| FACILITY: IRANC | DEPT/SYC: OB | |
| ACCUMULATIVE MEDICASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
| FY-83 MEDICASE: _____ | CONTRACT COST: _____ | SUPPLY COST: _____ |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: To accumulate a data based on perinatal outcome in relation to fetal heart rate and labor curve abnormalities.

TECHNICAL APPROACH: Each fetal tracing and labor curve has been classified and catalogued. We have not entered these on disks as our computer support has been used on other projects.

PROGRESS DURING FY-82:
As Above.

NUMBER OF SUBJECTS STUDIED:

FY-82: 1,562 TOTAL (TO DATE): 9,500 BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS:

PUBLICATIONS OR ABSTRACTS, FY-82:

DATE: 25Jan83 WORK UNIT No.: 4129 STATUS: INTERIM X FINAL
STARTING DATE: 1976 DATE OF COMPLETION:

KEY WORDS:

TITLE OF PROJECT: Antepartum Fetal Evaluation of Noise Evoked Heart Rate Response
as an Indicator of Fetal Well-being

PRINCIPAL INVESTIGATOR(S): LTC James Haddock

ASSOCIATE INVESTIGATOR(S): T. Frank, A. Presbylic, H. Skiba-Powell

FACILITY: WRAHC

DEPT/SYC: OB

ACCUMULATIVE MEDICASE COST:

ACCUMULATIVE CONTRACT COST:

ACCUMULATIVE SUPPLY COST:

0

0

0

FY-83 MEDICASE: CONTRACT COST: SUPPLY COST:

0

0

0

DATE OF COMMITTEE APPROVAL OF
ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To compare FHR accelerations spontaneously derived and evoked as indicators of fetal well being through spectral frequency analysis of the evoked response. The approach involves obtaining a fetal EKG signal from the maternal abdomen
TECHNICAL APPROACH: which is now being done.

PROGRESS DURING FY-82:

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 TOTAL (TO DATE): 0 BEFORE COMPLETION OF STUDY: 100

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

CONCLUSIONS:

Pending application of this new technique.

PUBLICATIONS OR ABSTRACTS, FY-82:

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|---|-----------------------------------|-----------------------------------|---|
| DATE: 19 Nov 82 | WORK UNIT NO.: 4134 | STATUS: INTERIM | FINAL XXX |
| STARTING DATE: NA | DATE OF COMPLETION: 15 June 1981 | | |
| KEY WORDS: Cervical Cancer, Radiotherapy, C-Parvum | | | |
| TITLE OF PROJECT: Treatment of Women with Cervical Cancer, Stage IIB, IIIB, IVA, Confined to the Pelvis and/or Para-Aortic Nodes with Radiotherapy, alone versus Radiotherapy plus immunotherapy (Intravenous C-Parvum) (Phase III) GOG #24 | | | |
| PRINCIPAL INVESTIGATOR(S): COL. ROBERT C. PARK, MC, USA | | | |
| ASSOCIATE INVESTIGATOR(S): LTC HELLER, ADVANI, DORN | | | |
| FACILITY: WRAHC | | DEPT/SVC: Ob-GYN Oncology Service | |
| ACCUMULATIVE MEDICASE COST: NA | ACCUMULATIVE CONTRACT COST: NA | ACCUMULATIVE SUPPLY COST: NA | |
| FY-83 MEDICASE: NA | CONTRACT COST: NA | SUPPLY COST: NA | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: Radiotherapy is the standard treatment for patients with advanced cervical carcinoma. The goal of this project is determined if the addition of immunotherapy will enhance the radiation response rate.

TECHNICAL APPROACH: - The patients are randomized to one of two treatment regimens: 1) Radiotherapy alone, or 2) Radiotherapy plus C-Parvum. Amendment to the protocol states that patients who have clinical Stage IB found to have disease extending out to the pelvic side walls at surgery are eligible. An additional optional method of para-aortic node assessment (fine needle biopsy) has been added to the study.

NUMBER OF SUBJECTS STUDIED: 322

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE, SO STATE): 6 patients, bone marrow depression, 2 patients, fistula (bladder or bowel) 4 patients, radiation fibrosis, 12 patients. Other complications not listed, 28 patients.

CONCLUSIONS:

PUBLICATIONS OR ABSTRACTS, FY-82:

PROGRESS DURING FY-82 - 322 patients have been entered to the protocol from the entire group. 19 patients have been entered from Walter Reed.

PUBLICATIONS OR ABSTRACTS, FY-81 - Presented at 2nd International Meeting on Immunotherapy of Cancer at the NCI, 28-30 Apr 80. To be published in Proceedings of Immunotherapy Meetings.

DATE: 19 Nov 82 | WORK UNIT No.: 4139 | STATUS: INTERIM FISCAL X X

STARTING DATE: 4 January 77 | DATE OF COMPLETION: 15 October 1979

KEY WORDS: Endometrial carcinoma, Stage III and IV, treated with chemotherapy.

TITLE OF PROJECT: A Randomized Comparison of Melphalan, 5FU, and Megace Versus Adriamycin, Cytosan, 5FU and Megace in the Treatment of Patients with Primary Stage III or IV Recurrent or Residual Endometrial Carcinoma (Phase III) GOG 28.

PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC, USA

ASSOCIATE INVESTIGATOR(S): Heller, Advanti, Dorn

FACILITY: WRMC

DEPT/SVC: OB-GYN Oncology Service

ACCUMULATIVE MEDICAL CASE COST:
NA

ACCUMULATIVE CONTRACT COST:
NA

ACCUMULATIVE SUPPLY COST:
NA

FY-83 MEDICAL CASE COST: CONTRACT COST: SUPPLY COST:
NA NA NA

DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To determine the efficacy of multi-drug preparations and to see if one of two programs previously shown to be effective by pilot studies is superior.

TECHNICAL APPROACH: Patients with advanced or recurrent endometrial carcinoma are randomized to one of two treatment regimens: 1) Melphalan, 5FU, and Megace, and 2) Adriamycin, Cytosan, 5 FU and Megace.

PROGRESS DURING FY-82: 358 patients were entered into this protocol. For the entire group 309 patients were valuable. Two patients were entered from Walter Reed. One was valuable.

NUMBER OF SUBJECTS STUDIED: 358

FY-82: TOTAL (TO DATE): BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

There were some hemotologic toxicities in 10 patients and 3 drug-related deaths.

CONCLUSIONS: The overall objective response rate was 36.8%. The activity of Melphalan and 5FU for the first time the treatment of this disease has been established. There is suggestion that there is a better response to combination chemotherapy in patients with poor prognosis endometrial carcinoma in comparison to a single agent therapy. The study is closed. Patients already on study will continue treatment for followup.

PUBLICATIONS OR ABSTRACTS, FY-82: Manuscript has been prepared and will be submitted shortly

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|---|-----------------------------|--------------------|-------|
| DATE: 19 Nov 82 | WORK UNIT No.: 4140 | STATUS: INTERIM XX | FINAL |
| STARTING DATE: 25 Nov 80 | DATE OF COMPLETION: Unknown | | |
| KEY WORDS: Endometrial carcinoma, Stage I and II, surgical investigation | | | |
| TITLE OF PROJECT: A Clinical-Pathologic Study of Stage I and II Carcinoma of the endometrium" GOG #33 | | | |

PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC

ASSOCIATE INVESTIGATOR(S): Heller, Advani

FACILITY: IRANC DEPT/SVC: OB-GYN/GYN Oncology Service

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| ACCUMULATIVE MEDICASE COST: NA | ACCUMULATIVE CONTRACT COST: NA | ACCUMULATIVE SUPPLY COST: NA |
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| FY-83 MEDICASE: NA | CONTRACT COST: NA | SUPPLY COST: NA | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
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STUDY OBJECTIVE: To determine the incidence of pelvic and aortic lymph node metastasis and the relationship of these node metastasis to other prognostic factors in Stage I and II carcinoma of the endometrium. All patients with Stage I and II endometrial carcinoma to be admitted to this protocol which will involve a surgical procedure and pathologic followup.

See below **

PROGRESS DURING FY-82: 1/10/81- amendment to the protocol was the fact that a discharge summary is required as part of the patient forms submitted. Total number of entries to this protocol were 1,052, total number of evaluable patients were 671. Walter Reed has

NUMBER OF SUBJECTS STUDIED: entered 68 patients of which 49 were evaluable.

FY-82: Unknown

TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): 530 patients experienced no complications. GI injury or obstruction noted in 15 patients. GU

CONCLUSIONS: injury or fistula was noted in 3 patients. Pulmonary emboli was noted in 8 patients. Evisceration was noted in 3 patients. Death was noted in 2 patients. Hemorrhage greater than or equal to 1000 cc's was noted in 18 patients.

PUBLICATIONS OR ABSTRACTS, FY-82: A limited preliminary report presented to the American Cancer Society National Conference of Gynecologic Cancer, Los Angeles, 9-11- Oct 80. Cancer, 2, 48: 568-574, 15 July 1981. Manuscript In Press In the Journal of Cancer.

TECHNICAL APPROACH: The patient will have a total AH, BSO, selective pelvic and para-aortic lymphadenectomy and peritoneal cytology sampling. Thereafter, the patient will be followed up or entered onto an additional GOG protocol. Patients with Stage I, Grade I disease are not eligible for this protocol. All patients are to be entered to the protocol after the surgery has been performed.

CONCLUSIONS: Preliminary evaluation would tend to indicate that this larger study verifies the findings of a previous pilot study. It would appear that this study could define the surgical procedure required for optimal evaluation in endometrial cancer.

DATE: 19 Nov 82 | WORK UNIT No. 4141 | STATUS: INTERIM XX FINAL

STARTING DATE: 22 Aug 78 | DATE OF COMPLETION: Unknown

KEY WORDS: Stage I and Occult Stage II endometrial carcinoma treated by Adriamycin
TITLE OF PROJECT: A Randomized Study of Adriamycin as an Adjuvant after Surgery and Radiation Therapy in Patients with High-Risk Endometrial Carcinoma, Stage I and Occult Stage II, GOG 34.

PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC

ASSOCIATE INVESTIGATOR(S): Heller

FACILITY: WRAHC | DEPT/SVC: OB-GYN/GYN Oncology Service

| ACCUMULATIVE PEOCASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
|----------------------------|-----------------------------|---------------------------|
| NA | NA | NA |

| FY-83 PEOCASE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT |
|----------------|----------------|--------------|--|
| NA | NA | NA | FEB 25 1983 |

STUDY OBJECTIVE: To study the differences in morbidity in patient's survival as functions of various tumor growth patterns in a patient with poor risk endometrial cancer.

TECHNICAL APPROACH: patients are selected for this protocol by extent of disease determined at surgery. Those who have greater than 1/2 myometrial invasion or pelvic or para-aortic node involvement or microscopic evidence of cervical involvement will receive ~~radiation~~ therapy. Following this, there will be randomization to Adriamycin or no further treatment.

NUMBER OF SUBJECTS STUDIED: Approx 75/yr for four years.

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): There have been no complications noted in 52 patients. There has been a bowel obstruction noted

CONCLUSIONS: in 2 cases Adverse radiotherapy effects in 2 or more incidences have been noted in 7 patients. For those patients who have received Adriamycin for too early to draw conc. at least one course, there has been 7 incidences of grade III, WBC toxicity.

PUBLICATIONS OR ABSTRACTS, FY-82: None

PROGRESS FY-82 Amendments-Discharge summary was required as part of the patient forms to be submitted after January 1981. Correction of cumulative dose of Adriamycin has been changed to 500 mg/M². To date 142 patients have been entered into the protocol of whom 81 are evaluable. Walter Reed has entered 7 patients of whom 3 are evaluable.

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|---|-----------------------------------|---------------------------------|---|
| DATE: 19 Nov 82 | WORK UNIT No. 4142 | STATUS: INTERIM XX | FINAL |
| STARTING DATE: 27 Sep 78 | DATE OF COMPLETION: Unknown | | |
| KEY WORDS: ICRF-159 in advanced pelvic malignancies. | | | |
| TITLE OF PROJECT: A Phase II Trial of ICRF in Patients with Advanced Pelvic Malignancies - GOG 26-G | | | |
| PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC, USA | | | |
| ASSOCIATE INVESTIGATOR(S): Heller | | | |
| FACILITY: WRAHC | | DEPT/SVC: OB-GYN/GYN Oncology | |
| ACCUMULATIVE MEDICASE COST: NA | ACCUMULATIVE CONTRACT COST: NA | ACCUMULATIVE SUPPLY COST: NA | |
| FY-83 MEDICASE: NA | CONTRACT COST: NA | SUPPLY COST: NA | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983 |

STUDY OBJECTIVE: To determine the efficacy of ICRF-159 in the treatment of advanced pelvic malignancies.

TECHNICAL APPROACH: Patients with histologically advanced and recurrent and persistent metastatic or local gynecologic cancer with documented disease progression will be entered into this treatment.

PROGRESS DURING FY-82: A total of 69 patients have been entered in the entire GOG. 6 patients have been entered from Walter Reed. As of November 80 patients with squamous cell carcinoma of the cervix are not eligible for entry. Patients with epithelial carcinoma of the ovary as of June 80 are no longer eligible for entry.

NUMBER OF SUBJECTS STUDIED: 25
 FY-82: 25 TOTAL (TO DATE): BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
 There have been no serious unexpected side effects.

CONCLUSIONS: ICRF appears to have moder activity in squamous cell carcinoma of the cervix and no significant activity in epithelial tumors of the ovary at the dose and schedule tested.

PUBLICATIONS OR ABSTRACTS, FY-82:
 Abstract-C-414-ASCO-May 80
 Manuscript - Cervix- Submitted 4/22/81 to Cancer Treatment Reports
 A manuscript for epithelial tumors of the ovary will be prepared.

| | | | |
|--|-----------------------------|---------------------------------------|--|
| DATE: 19 Nov 82 | WORK UNIT No.: 4143 | STATUS: INTERIM | FINAL XX |
| STARTING DATE: 1 November 1978 | | DATE OF COMPLETION: 3 August 1981 | |
| KEY WORDS: Local excision, cryotherapy, CIN-1, 2, 3. | | | |
| TITLE OF PROJECT: A Randomized Comparison of Local Excision Versus Cryosurgery in Patients with Limited Grade 1, 2 or 3 Cervical Intraepithelial Neoplasia-GOG 31. | | | |
| PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC, USA | | | |
| ASSOCIATE INVESTIGATOR(S): Heller, Advanti | | | |
| FACILITY: WRAMC | | DEPT/SVC: OB-GYN/GYN-Oncology Service | |
| ACCUMULATIVE MEDICARE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: | |
| NA | NA | NA | |
| FY-83 MEDICARE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT |
| NA | NA | NA | FEB 25 1983 |

STUDY OBJECTIVE: To evaluate and compare the immediate and long-term effectiveness of outpatient cryosurgery and outpatient local excision in the treatment of limited cervical intraepithelial neoplasia (CIN) Grade 1, 2 or 3. Patients are then TECHNICAL APPROACH: randomized to prospective studies.

Patients are randomized to one of two treatment arms: 1) Outpatient cryosurgery or 2) Outpatient surgical excision.

PROGRESS DURING FY-82: To date there have been 500 patients entered into this protocol, 198 of them are evaluable. From Walter Reed 48 patients were entered into the protocol. 12 of these were evaluable.

NUMBER OF SUBJECTS STUDIED: 500

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
None

CONCLUSIONS: None (Because of inability to follow patients after initial treatment, This protocol has been closed. This protocol was terminated on 29 October 1981.

PUBLICATIONS OR ABSTRACTS, FY-82: Manuscript published in Gynecologic Oncology October 1981, pages S302-S305.

DATE: 19 Nov 82 | WORK UNIT No.: 4144 | STATUS: INTERIM | FUND: XX

STARTING DATE: September 78 | DATE OF COMPLETION: 1981

KEY WORDS: Surgical conization, cryosurgery, CIN-3

TITLE OF PROJECT: A Randomized Comparison of Surgical Conization versus Cryosurgery in patients with extensive Grade 3 Cervical Intraepithelial Neoplasia (CIN) GOG 32.

PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC

ASSOCIATE INVESTIGATOR(S): Heller, Advanti

FACILITY: WRAHC

DEPT/SVC: OB-GYN/GYN Oncology Service

ACCUMULATIVE MEDICASE COST:
NA

ACCUMULATIVE CONTRACT COST:
NA

ACCUMULATIVE SUPPLY COST:
NA

FY-83 MEDICASE: NA | CONTRACT COST: NA | SUPPLY COST: NA

DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: Standard treatment of patients with cervical intraepithelial neoplasia Grade 3 would be in-hospital conization or in-hospital surgical hysterectomy. The purpose of this study is to evaluate and compare the immediate and long-term effectiveness of outpatient cryosurgery to the standard cold-knife conization in the treatment of extensive surgical intraepithelial neoplasia (CIN) Grade 3 in a randomized prospective study.

PROGRESS DURING FY-82: A total of 118 patients were entered into the protocol from the entire group of which 36 were evaluable. 10 patients were entered from Walter Reed of which 4 were evaluable.

NUMBER OF SUBJECTS STUDIED: 118

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS: This study was terminated early because of the inability to obtain adequate followup of the majority of the patients. No useful information is likely to be forthcoming. Protocol was terminated 29 October 1981.

PUBLICATIONS OR ABSTRACTS, FY-82: Gynecologic Oncology Part II, S302-205 October 1981.

TECHNICAL APPROACH: The patient is randomized to one of two treatment arms. 1) Out-patient cryosurgery, or 2) Inpatient surgical conization.

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|---|---------------------------------------|--|
| DATE: 19 Nov 82 | WORK UNIT NO.: 4145 | STATUS: INTERIM XX FINAL |
| STARTING DATE: 22 August 78 | DATE OF COMPLETION: 1983 | |
| KEY WORDS: Early ovarian carcinoma, Melphalan versus no treatment | | |
| TITLE OF PROJECT: A Randomized Comparison of Melphalan Versus No Treatment in the Treatment of patients with selected Stage IAi, II, IIBi Ovarian Cancer (Well to Moderately differentiated). NCI Protocol 7601 | | |
| PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC, USA | | |
| ASSOCIATE INVESTIGATOR(S): LTC Paul B. Heller, Advani | | |
| FACILITY: MRANC | DEPT/SVC: OB-GYN/GYN Oncology Service | |
| ACCUMULATIVE MEDICASE COST: NA | ACCUMULATIVE CONTRACT COST: NA | ACCUMULATIVE SUPPLY COST: NA |
| FY-83 MEDICASE: NA | CONTRACT COST: NA | SUPPLY COST: NA |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: Scattered non-randomized studies employing alkylating agents, chemotherapy have reported 5-year survivals as high as 90% in patients with Stage I ovarian carcinoma. Unfortunately, the non-randomized nature, the small numbers, and TECHNICAL APPROACH: the unavailability of detailed pathologic information make the definitive conclusions of these studies impossible. It is the purpose of the present study to determine the value of chemotherapeutic prophylactic therapy after surgery in definitive staging in patients with Stage IAi and IBI ovarian adenocarcinoma.

NUMBER OF SUBJECTS STUDIED: Approximately 110.

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): There has been one death. This patient possibly had pulmonary emboli. She had no evidence of disease at the time of death. No relapses have been reported however several patients have CONCLUSIONS: been lost to followup or refused 2nd look surgery.

None

PUBLICATIONS OR ABSTRACTS, FY-82:
None

TECHNICAL APPROACH: Staging laparotomy and TAH, BSO is performed after which the patients are randomized to one of two schema 1) Observation or 2) Melphalan.

PROGRESS DURING FY-82: A total of 39 patients have been entered to the protocol from the entire GOG, Walter Reed has entered 3.

DATE: 19 Nov 82 | WORK UNIT No.: 4146 | STATUS: INTERIM XX Final

STARTING DATE: 22 Aug 1978 | DATE OF COMPLETION: 1982 or 1983

KEY WORDS: Melphalan versus radio-isotopes in selected early ovarian cancer

TITLE OF PROJECT: A Randomized Comparison of Melphalan versus Radio-Isotopes in the treatment of patients with no microscopic residual disease, having all stages IC and II (A, B and C), and of selected Stages IAii, and IBii ovarian cancer. NCI Protocol 7602

PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC

ASSOCIATE INVESTIGATOR(S): LTC Paul B. Heller, MC, Advani

FACILITY: WRMC | DEPT/SVC: OB-GYN/GYN Oncology Service

ACCUMULATIVE MEDCASE COST: NA | ACCUMULATIVE CONTRACT COST: NA | ACCUMULATIVE SUPPLY COST: NA

FY-83 MEDCASE: NA | CONTRACT COST: NA | SUPPLY COST: NA | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983

STUDY OBJECTIVE: Mean 5-year survival of 39% with operation plus radiation. 24% survival for those treated with operation alone in Stage II and poor prognosis Stage I patients with minimal residual disease. In some successful series, 30-40% of the patients die of recurrent ovarian carcinoma despite surgery and subsequent radiotherapy. The purpose of this study is to compare the usefulness of Melphalan chemotherapy in intra-abdominal radio-active phosphorus in resectable stage II and poor prognosis Stage I patient

PROGRESS DURING FY-82: There have been 60 cases entered to the protocol through the GOG.

NUMBER OF SUBJECTS STUDIED: Approximately 200-400

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): There have been 8 deaths reported. One patient died with no evidence of disease with a CVA. 1 patient was randomized to P32 and received Melphalan because the isotope could not be injected. This patient relapsed and died. 13 relapses have been reported.

None

PUBLICATIONS OR ABSTRACTS, FY-82: None

TECHNICAL APPROACH: Patients who have had staging laparotomy including total AH and BSO if there is no microscopic residual disease, randomization will be to 1) Melphalan or 2) Radiotope. In the case of residual disease in Stage IIB and IIC lesions, the patients will be randomized to 1) Pelvic radiotherapy and Melphalan or 2) Melphalan alone.

DATE: 19 Nov 82 WORK UNIT No.: 4147 STATUS: INTERIM XX FINAL

STARTING DATE: 15 Nov 78 DATE OF COMPLETION: 1983

KEY WORDS: Surgical pathologic study, squamous cell carcinoma of vulva

TITLE OF PROJECT: Surgical Pathological Study of Women with squamous cell carcinoma of the vulva GOG #36

PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC

ASSOCIATE INVESTIGATOR(S): Heller, Advani

FACILITY: WRAHC DEPT/SVC: OB-GYN/GYN Oncology Service

ACCUMULATIVE MEDICASE COST: NA ACCUMULATIVE CONTRACT COST: NA ACCUMULATIVE SUPPLY COST: NA

FY-83 MEDICASE: NA CONTRACT COST: NA SUPPLY COST: NA DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

See below*

STUDY OBJECTIVE: To determine the validity of current FIGO staging to the pathologic prognosis factors of size of lesion, location of lesion, depth of invasion of tumor in mm, histologic rate, site, and number of positive lymph nodes in Stage I-IV carcinoma of the vulva. To rapidly accumulate prospective surgical pathologic data for development of further protocol. To determine the morbidity of primary radical surger: vulvar carcinoma.

PROGRESS DURING FY-82: There have been 429 patients entered from the entire GOG of whom 284 are evaluable. Walter Reed has entered 1 patient to this protocol.

NUMBER OF SUBJECTS STUDIED: N/A

FY-82: TOTAL (TO DATE): BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): Severe lymphadema was noted in 2 patients. Death was noted in 5 patients. Myocardial infarction was noted in one patient. Pneumonia noted in 2 patients. Pulmonary emboli noted in 1 patient.

CONCLUSION: Too early for conclusions;

PUBLICATIONS OR ABSTRACTS, FY-82: None

TECHNICAL APPROACH: All patients with primary previously untreated histologically confirmed invasive squamous cell carcinoma of the vulva, clinically determined to be Stage I-IV, that radical vulvectomy suffices to remove all of the lesion. Patients will have radical vulvectomy plus bilateral groin node dissection and will be randomized depending upon whether they have negative groin nodes to followup alone or positive groin nodes to more advanced protocol involving radiotherapy.

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| DATE: 19 Nov 82 | Work UNIT No. 4148 | STATUS: INTERIM | FINAL |
| STARTING DATE: 15 November 1978 | DATE OF COMPLETION: 1983 | | |
| KEY WORDS: Randomized study, squamous cell, vulva carcinoma, positive groin nodes. | | | |
| TITLE OF PROJECT: A Randomized Study of Radiation Therapy Versus Pelvic Node Resection for patients with invasive squamous cell carcinoma of the vulva having positive groin nodes. GOG #37 | | | |
| PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC | | | |
| ASSOCIATE INVESTIGATOR(S): Heller, Advani, Dorn | | | |
| FACILITY: WRAVC | | DEPT/SVC: OB-GYN/GYN Oncology Service | |
| ACCUMULATIVE MEDICAL CASE COST: NA | ACCUMULATIVE CONTRACT COST: NA | ACCUMULATIVE SUPPLY COST: NA | |
| FY-83 MEDICAL CASE COST: NA | CONTRACT COST: NA | SUPPLY COST: NA | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: To determine the benefit and morbidity of adding adjunctive radiotherapy to pelvis and groin in patients with positive groin nodes at radical vulvectomy and bilateral groin dissection.

TECHNICAL APPROACH: - All patients with primary previously untreated histologically confirmed invasive squamous cell carcinoma of the vulva, such that radical vulvectomy suffices to remove all the local lesion and whose surgery revealed nodes in the groin on one or both sides containing metastatic carcinoma. Patients will be randomized after a radical vulvectomy plus bilateral groin nodes dissection to one of two regimens. Negative nodes the patient will be taken off study. Positive nodes the patient is to be randomized to two regimens. 1 including pelvic node dissection or regimen, 2 including bilateral groin and pelvic node irradiation.

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): In those patients completing radiotherapy 1 fistula (bladder or bowel) has been noted. Also 1 incidence of bowel obstruction in a pt completing radiotherapy has been noted. There had been 20 wound infections noted. There has been 1 incidence of moderate lymphadema.

CONCLUSIONS: Too early for definitive conclusions

PUBLICATIONS OR ABSTRACTS, FY-82: None

PROGRESS DURING FY-82 A total of 65 patients have been entered into the protocol. To date none have been entered from Walter Reed.

NO. OF PATIENTS TO BE STUDIED: Approximately 200

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| DATE: 25 Jan 83 | Work Unit No.: 4149 | STATUS: INTERIM X FINAL |
| STARTING DATE: 1979 | DATE OF COMPLETION: | |
| KEY WORDS: | | |
| TITLE OF PROJECT: Automated Detection of Fetal Heart Pattern Abnormalities | | |
| PRINCIPAL INVESTIGATOR(S): LTC James Haddock | | |
| ASSOCIATE INVESTIGATOR(S): Presblyll, A.; Frank, P.; Skiba-Powell, H. | | |
| FACILITY: IRANC | DEPT/SVC: OB | |
| ACCUMULATIVE FEDCASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
| FY-83 FEDCASE: | CONTRACT COST: | SUPPLY COST: |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE:

To develop a computer program to recognize fetal heart rate pattern anomalies and flag them for medical staff.

TECHNICAL APPROACH:

Same As above.

PROGRESS DURING FY-82: This has been a low priority item since we hired a part-time consultant last year because (1) other items have been more important (2) connection to this research computer still has not been made (3) others have these at a sophisticated level. Modifications of existing technology of these techniques are still potentially important.

NUMBER OF SUBJECTS STUDIED: FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: 1400/yr

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS: The technology to read FHR traces is still in its infancy. Any application here would involve further development and modification. I believe this can be done with local personnel following the delivery and installation of our cable which Mr. Thurman promises will be accomplished before the end of Mar 83.

PUBLICATIONS OR ABSTRACTS, FY-82:

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| DATE: 25Jan83 | Work Unit No.: 4150 | STATUS: INTERIM X Final |
| STARTING DATE: Sep 81 | DATE OF COMPLETION: | |
| KEY WORDS: | | |
| TITLE OF PROJECT: On-Line Interpretation of Labor Curve Abnormalities | | |
| PRINCIPAL INVESTIGATOR(S): LTC James Haddock | | |
| ASSOCIATE INVESTIGATOR(S): Presbylick, A.; Frank, T.; Skiba-Powell, H. | | |
| FACILITY: IRVAC | DEPT/SVC: OB | |
| ACCUMULATIVE PEDCASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
| FY-83 PEDCASE: | CONTRACT COST: | SUPPLY COST: |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: To correlate labor curve abnormalities with uterine activity and to investigate the effect of therapy where uterine activity has been normal or abnormal.

TECHNICAL APPROACH: Uterine activity, pelvic exams, and therapies are entered automatically and by hand on line to the CB Research Computer. The computer is to be programmed to perform the above functions.

PROGRESS DURING FY-82: The development of the program has been the chief task of Mr. Presbylick. We have encountered considerable difficulty in cabling our monitors to the computer room but understand the contract to do this has finally been signed.

NUMBER OF SUBJECTS STUDIED:

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: 700

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
None

CONCLUSIONS:

PUBLICATIONS OR ABSTRACTS, FY-82:

| | | |
|---|----------------------------------|--|
| DATE: 25 Jan 83 | WOS UNIT NO.: 4151 | STATUS: INTERIM <input checked="" type="checkbox"/> FINAL |
| STARTING DATE: Jan 81 | DATE OF COMPLETION: | |
| KEY WORDS: | | |
| TITLE OF PROJECT: Early Reliable Detection of FHR Variability by Adoptive Digital Filtering | | |
| PRINCIPAL INVESTIGATOR(S): LTC James Haddock | | |
| ASSOCIATE INVESTIGATOR(S): Frank, T.; Presblyick, A.; Skiba-Powell, H. | | |
| FACILITY: IRANC | DEPT/SVC: OB | |
| ACCUMULATIVE PECCASE COST: 0 | ACCUMULATIVE CONTRACT COST: 0 | ACCUMULATIVE SUPPLY COST: 0 |
| FY-83 PECCASE: 0 | CONTRACT COST: 0 | SUPPLY COST: 0 |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: To derive FHR variability from a non-invasive maternal abdominal EKG leads:

TECHNICAL APPROACH: The above signal is computer processed by adoptive digital filtering.

PROGRESS DURING FY-82: The computer is programmed, the equipment delivered and functioning. We still need cabling to the computer put in place through Mr. Thurman's office but we have tested amplifiers on the program on ourselves.

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 TOTAL (TO DATE): 0 BEFORE COMPLETION OF STUDY: 25

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

CONCLUSIONS: This progress has applicability to several other protocols and we are hopeful this will now bear fruit.

PUBLICATIONS OR ABSTRACTS, FY-82:

DATE: 19 Nov 82 WORK UNIT No.: 4152 STATUS: INTERIM XX FINAL
 STARTING DATE: 21 Nov 78 DATE OF COMPLETION: Unknown
 KEY WORDS: Phase II, Maytansine, pelvic malignancies
 TITLE OF PROJECT: A Phase II Trial of Maytansine in Patients with Advanced Pelvic Malignancies - GOG #26-H

PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC, USA
 ASSOCIATE INVESTIGATOR(S): Heller
 FACILITY: WRAHC DEPT/SVC: OB-GYN/GYN Oncology Service
 ACCUMULATIVE MEDICASE COST: NA ACCUMULATIVE CONTRACT COST: NA ACCUMULATIVE SUPPLY COST: NA
 FY-83 MEDICASE: NA CONTRACT COST: NA SUPPLY COST: NA DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To determine the efficiency of chemotherapy agents in patients whose advanced malignancies have been resistant to high priority methods of treatment. A rejection type of design will be used involving a fixed sample size of 25 evaluable TECHNICAL APPROACH: patient per disease site per drug studied. The design allows replacement of ineffective regimens by newer agents or combinations.
 (See below)

PROGRESS DURING FY-82: A total of 69 patients have been entered into the protocol from the entire GOG. This study is closed to squamous cell carcinoma of the cervix and epithelial tumors of the ovary. Accrued continues in other categories.
 NUMBER OF SUBJECTS STUDIED: 25 Patients in each category of disease.

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
 None

CONCLUSIONS: Maytansine has insignificant activity against squamous cell carcinoma of the cervix and epithelial tumors of the ovary. Too few cases have accrued in other categories to comment. The study is closed to squamous cell carcinoma of the cervix and epithelial tumors of the ovary and no further evaluation of the drug is planned in these neoplasms.

PUBLICATIONS OR ABSTRACTS, FY-82:

Abstract - ASCO, C-420-May, 1980 (Cervix)
 Manuscript - (Ovary) American Journal of Clinical Oncology, In Press.
 Manuscript - (Cervix) American Journal of Clinical Oncology, In Press.
 TECHNICAL APPROACH: Maytansine appears to be similar to the vinca alkaloids, affecting DNA synthesis in arresting cells in metaphase of mitosis by inhibition of tubulin polymerization. Maytansine has shown activity against many animal tumor models. Three schedules have been studied in Phase trials. Single bolus every 3 weeks is convenient dose for patients. Only 1 gynecologic malignancy was included in the 20 patients. This was an ovarian carcinoma in which one response was seen in 5 patients. Other responses were confined to non-gynecologic malignancies.

DATE: 19 Nov 82 | WORK UNIT No.: 4153 | STATUS: INTERIMXX FINAL

STARTING DATE: 21 Nov 1978 | DATE OF COMPLETION: Unknown

KEY WORDS: Phase II, Baker's antifol, advanced pelvic malignancy

TITLE OF PROJECT: A Phase II Trial of Baker's Antifol in Patients with Advanced Pelvic Malignancies - GOG #26-F

PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC

ASSOCIATE INVESTIGATOR(S): Heller

FACILITY: WRAHC | DEPT/SVC: OB-GYN/GYN Oncology

ACCUMULATIVE MEDCARE COST: NA | ACCUMULATIVE CONTRACT COST: NA | ACCUMULATIVE SUPPLY COST: NA

FY-83 MEDCARE: NA | CONTRACT COST: NA | SUPPLY COST: NA | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To determine the efficacy of Baker's Antifol in patients whose advanced malignancies have been resistant to high priority methods of treatment. A rejection type of design will be used involving 6 sample size of 25 evaluable
TECHNICAL APPROACH: patients per disease site per drug.

See below

PROGRESS DURING FY-82: A total of 68 patients have been entered into this protocol from the entire GOG. None have been entered from Walter Reed. This protocol has been closed to squamous cell carcinoma of the cervix and epithelial carcinoma of the

NUMBER OF SUBJECTS STUDIED: ovaries.

25 patients per disease site.

FY-82: TOTAL (TO DATE): BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

Some Grade 3 mucocytis has been observed in two of the patients.

CONCLUSIONS: Although limited activity is noted, this drug is not as useful as more conventional drugs and probably will not add to our current therapeutic regimens.

PUBLICATIONS OR ABSTRACTS, FY-82: Abstract-ASCO-C417, May 80
Manuscript-Squamous cell carcinoma of the cervix, submitted to Cancer Treatment Report, August 29, 1980

TECHNICAL APPROACH: Baker's antifol, also known as triazinate, is an antagonist of folate metabolism which acts by blocking dihyd. folate reductase. This drug is believed to diffuse passively into the cells by active transport mechanism. The drug is able to penetrate the CNS levels of 1-5% of blood levels following IV administration. It is excreted mainly by the liver and much less extent by the kidney. Toxicities include myocutaneous and gastrointestinal effects. Moderate myelosuppression has been observed.

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|---|-----------------------------------|---------------------------------------|---|
| DATE: 19 Nov 82 | WORK UNIT NO.: 4154 | STATUS: INTERIM | FINAL: XX |
| STARTING DATE: 9 Feb 1979 | | DATE OF COMPLETION: 1 April 1982 | |
| KEY WORDS: Cis-Platinum in advanced carcinoma of cervix, Stage III | | | |
| TITLE OF PROJECT: A Randomized Comparison of Cis-Platinum 50 mg/M ² every 3 weeks versus Cis-Platinum 100 mg/M ² versus Cis-Platinum 20 mg/M ² Day X Five in the Treatment of patients with advanced carcinoma of the cervix (Phase III). GOG #43. | | | |
| PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC, USA | | | |
| ASSOCIATE INVESTIGATOR(S): LTC Paul B. Heller, MC, USA | | | |
| FACILITY: WRAMC | | DEPT/SVC: OB-GYN/GYN Oncology Service | |
| ACCUMULATIVE MEDICASE COST: NA | ACCUMULATIVE CONTRACT COST: NA | ACCUMULATIVE SUPPLY COST: NA | |
| FY-83 MEDICASE: NA | CONTRACT COST: NA | SUPPLY COST: NA | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983 |

STUDY OBJECTIVE: To Confirm the effectiveness of Cis-platinum in advanced and recurrent therapy or surgery. To compare the frequency and duration of response, and adverse effect of DDP therapy using three different doses and treatment schedules. To

See below *** TECHNICAL APPROACH: evaluate the roles of serial determination of serum carcinoembryoni antigen (CEA) Levels and determining extent of disease, response of treatment, and in predicting treatment failure.

PROGRESS DURING FY-82: There have been 581 patients assessed to this protocol from the entire GOG, 476 of them are evaluable. Walter Reed has assessed 20 patients to this protocol.

NUMBER OF SUBJECTS STUDIED: Approximately 175/yr

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): There have been 19 Grade III WBC toxicities. There have been 4 Grade III, and 6 Grade IV platelet toxicities. There have been 43 Grade III, GI toxicities and there have been CONCLUSIONS: 3 Grade IV Renal toxicities. There were 3 Grade III neurotoxicities.

There is no difference in the efficacy of the three regimens. There is less toxicity with the lower dose. The efficacy of continuous versus bolus infusion of Cis-Platinum will be explored in another protocol.

PUBLICATIONS OR ABSTRACTS, FY-82: (Abstract) C-425, April 1982

TECHNICAL APPROACH: Patients who have histologically confirmed local, advanced recurrent, persistent or metastatic disease of the cervix which is resistant to curative treatment with surgery or radiotherapy are eligible. All patients must have lesions which are measurable or evaluable by a physical exam.

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|---|-----------------------------|---------------------------------------|--|
| DATE: 19 Nov 82 | WORK UNIT No.: 4155 | STATUS: INTERIM XX | FINAL |
| STARTING DATE: 9 Feb 1979 | DATE OF COMPLETION: Unknown | | |
| KEY WORDS: Vincristine, Actinomycin-D, Cyclophosphamide, germ cell tumors of ovary | | | |
| TITLE OF PROJECT: Evaluation of Adjuvant Vincristine, Dactinomycin, and Cyclophosphamide therapy in Malignant Germ Cell Tumors of the Ovary after Resection of all Gross Tumor (Phase III). | | | |
| PRINCIPAL INVESTIGATOR(S): | | COL Robert C. Park, MC, USA | |
| ASSOCIATE INVESTIGATOR(S): | | LTC Paul B. Heller, MC, USA | |
| FACILITY: WRAAC | | DEPT/SVC: OB-GYN/GYN Oncology Service | |
| ACCUMULATIVE MEDICINE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: | |
| NA | NA | NA | |
| FY-83 MEDICINE COST: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT |
| NA | NA | NA | FEB 25 1983 |

STUDY OBJECTIVE: To evaluate the effect of combined prophylactic Vincristine, Dactinomycin and Cyclophosphamide (VAC) chemotherapy in patients with endodermal sinus tumor ~~embryonal carcinoma, immature teratoma (Grade 2 and 3), choriocarcinoma, and malignant~~

TECHNICAL APPROACH: mixed germ cell tumors of the ovary, Stages I and II after removal of all gross tumor. To evaluate the role of serum markers, especially alphafetoprotein (AFP) and human chorionic gonadotrophin (beta HCG) when these are present in

PROGRESS DURING FY-82: predicting response and relapse.

There have been 59 entries to the protocol in the entire GOG. 46 of them are present. ~~evaluable 3 patients have been entered from Walter Reed of which 2 are evaluable.~~ 17

NUMBER OF SUBJECTS STUDIED: patients with immature teratoma have been entered 15 of these have had pathology review. 11 of these are clinically free of disease with a followup

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

CONCLUSIONS: It is too early to draw conclusions.

PUBLICATIONS OR ABSTRACTS, FY-82: (Abstract) ASCO, C-214, March 1981

PROGRESS DURING FY-82 Continued from above.

Six of these were Grade III. Of these, 4 had second look procedures and three were negative. 29 cases of epidermal sinus tumor were entered. Second look has been performed at 21 instances, 18 being negative.

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| DATE: 19 Nov 82 | WORK UNIT NO.: 4156 | STATUS: INTERIM XX FINAL |
| STARTING DATE: 29 June 1979 | DATE OF COMPLETION: Unknown | |
| KEY WORDS: Advanced germ cell tumors of the ovary treated with Cinblastine, Bleomycin and Cis-Platinum. | | |
| TITLE OF PROJECT: Evaluation of Vinblastine, Bleomycin and Cis-Platinum in Stage III and IV and Recurrent Malignant Germ Cell Tumors of the Ovary (Phase III) GOG #45. | | |
| PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC, USA | | |
| ASSOCIATE INVESTIGATOR(S): LTC Paul B. Heller, MC, USA | | |
| FACILITY: WRAVC | DEPT/SVC: OB-GYN/GYN Oncology Service | |
| ACCUMULATIVE MEDICASE COST: NA | ACCUMULATIVE CONTRACT COST: NA | ACCUMULATIVE SUPPLY COST: NA |
| FY-83 MEDICASE: NA | CONTRACT COST: NA | SUPPLY COST: NA |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: To evaluate the effect of 4 cycles of combined Vinblastine, Bleomycin and Cis-Platinum (VBP) chemotherapy in the management of patients with endodermal sinus tumor, embryonal carcinoma, immature teratoma (all grades), choriocarcinoma, and TECHNICAL APPROACH: malignant mixed germ cell tumors of the ovary with advanced or recurrent disease, incompletely resected. To evaluate the role of serum markers, especially alphafetoprotein and human chorionic gonadotrophin when these are present ~~Progress During FY-82~~ response and relapse.

Below**

See below

NUMBER OF SUBJECTS STUDIED: Approximately 15/yr
 FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): There have been 28 patients who have had moderate or severe WBC toxicity. There have been 4 patients with moderate to severe platelet toxicity. There have been 7 patients with moderate or severe GI toxicity, and one patient with moderate neuro toxicity. There has been one Grade IV pulmonary toxicity. 3 Deaths are believed related to therapy.
 Toxicities are considerable but generally manageable. Early results are encouraging.

PUBLICATIONS OR ABSTRACTS, FY-82: (Abstract) ASCO, C-430, April 1982

TECHNICAL APPROACH: Histologically confirmed malignant germ cell tumors of the ovary with advanced (Stage II of IV) or recurrent disease, incompletely resected, excluding patients with pure dysgerminoma (mature anaplastic) are eligible. Patients with incompletely resected Stage II disease are eligible. Patients previously treated with VAC are eligible. After surgery, the patients are placed on 4 course of Velban, Bleomycin and Cis-Platinum. Vinblastine maintenance portion of the study is discontinued 1981. The concept of markers as evidence of recurrent disease in all germ cell tumors as approved.

PROGRESS DURING FY-82 There have been 47 patients entered into this protocol from the entire GOG, 37 of which are evaluable. one patient has been entered from

Walter Reed. Of point 2 second look operations performed, 12 were negative. There have been 8 recurrences in patients who did not have second look operations.

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| DATE: 19 Nov 82 | WORK UNIT No.: 4159 | STATUS: INTERIM | FINAL XX |
| STARTING DATE: 6 Apr 1979 | | DATE OF COMPLETION: 16 Jan 1982 | |
| KEY WORDS: Chemotherapy for recurrent or advanced uterine sarcoma. | | | |
| TITLE OF PROJECT: Treatment of Recurrent or Advanced Uterine Sarcoma. A Randomized Comparison of Adriamycin Versus Adriamycin and Cyclophosphamide (Phase III) GOG #42. | | | |
| PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC | | | |
| ASSOCIATE INVESTIGATOR(S): LTC Paul B. Heller, MC | | | |
| FACILITY: WRAMC | | DEPT/SVC: OB-GYN/GYN Oncology Service | |
| ACCUMULATIVE MEDICASE COST: NA | | ACCUMULATIVE CONTRACT COST: NA | |
| | | ACCUMULATIVE SUPPLY COST: NA | |
| FY-83 MEDICASE: NA | CONTRACT COST: NA | SUPPLY COST: NA | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: To determine if Adriamycin alone is more effective than ADriamycin and Cyclophosphamide in producing responses in advanced or recurrent uterine sarcoma. The second objective is to determine if the duration of response for each treatment arm

TECHNIQUE APPROACH: Patients with primary Stage III, primary Stage IV, or recurrent uteri sarcoma are eligible. Both patients with non-measurable and measurable disease are eligible but they may be analyzed separately. Patients with all cell types of uterine sarcoma are eligible. Patients previously treated with Radiotherapy to the pelvic bed are eligible but they must have completed this radiation more than 3 months prior to entry on

PROGRESS DURING FY-82: uterine sarcoma are eligible. Patients previously treated with Radiotherapy to the pelvic bed are eligible but they must have completed this radiation more than 3 months prior to entry on

NUMBER OF SUBJECTS STUDIED: study. The patients will have an exploratory laparotomy, TAH/BSO, omentectomy if feasible.

FY-82: 50 per/yr TOTAL (TO DATE): BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): There has been 4 Grade 4 WBC toxicities. There have been no Grade 3 or 4 Platelet toxicities. There has been 2 Grade 2 toxicities related to nausea and vomiting. There has been 1 Grade 4 cardiac toxicity. There has been 1 Grade III, stomatitis. There have been 5 Grade III, granulocytotoxicities. There has been one patient who had Grade 4 toxicity associated with BUN, Creatinine and alkaline phosphatase.

PUBLICATIONS OR ABSTRACTS, FY-82: Manuscript in progress. Protocol has been closed.

PROGRESS DURING FY-82: There have been 132 patients assessed to this protocol, 108 of them are evaluable. Walter Reed has placed two patients into this protocol.

CONCLUSIONS: Regimens have been well tolerated. Response has been low. Although the response rate in patients with measurable disease has approached 20%, it is doubtful that these responses are of clinical benefit.

DATE: 19 Nov 82 WORK UNIT No.: 4160 STATUS: INTERIM XX FINAL
 STARTING DATE: c August 79 DATE OF COMPLETION: Unknown
 KEY WORDS: Clinical pathologic study, Stage I and II, uterine sarcoma
 TITLE OF PROJECT: A Clinical Pathologic Study of Stage I and II Uterine Sarcomas
 GOG #40

PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC
 ASSOCIATE INVESTIGATOR(S): Heller
 FACILITY: WRAVC DEPT/SVC: OB-GYN/GYN Oncology Service
 ACCUMULATIVE MEDICASE COST: NA ACCUMULATIVE CONTRACT COST: NA ACCUMULATIVE SUPPLY COST: NA
 FY-83 MEDICASE: NA CONTRACT COST: NA SUPPLY COST: NA DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: The purpose of this study is to determine the incidence of pelvic and aortic lymph node metastasis associated with Stage I and II uterine sarcomas. The relationship of these node metastasis to other important prognostic factors such as TECHNICAL APPROACH: mytotic indexes, tumor and the complication rate of the procedures. All patients with histologically proven uterine sarcoma, clinical Stage I and II who are medically suitable for hysterectomy and lymphadenectomy are eligible PROGRESS DURING FY-82: for this study. All patients will undergo, at a minimum, a simple extrafascial abdominal hysterectomy, BSO, selective pelvic and para aortic lymphadenectomy. Peritoneal cytology will be obtained. Omental biopsy is recommended as an optional procedure. All histologic types of uterine sarcomas are acceptable. Studies amended 15 Apr. 82 to NUMBER OF SUBJECTS STUDIED: Unknown TOTAL (TO DATE): allow entry BEFORE COMPLETION OF STUDY: of patients with prior gynecologic glucoency evidence or coma diag-
SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): nosed more than None .5 years per recurrent sarcoma.
CONCLUSIONS: The distribution of cell type shows up dominance of mixed mesodermal tumors as found in earlier sarcoma protocols. There is a trantowards tumor size being a significant factor. No significant serous adverse effects have been encountered.

PUBLICATIONS OR ABSTRACTS, FY-82: None

PROGRESS DURING FY-82 A total of 138 patients have been entered to the study for the entire GOG of which 68 patients are evaluable. Walter Reed has entered 7 patients.

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| DATE: 19 Nov 82 | WORK UNIT NO.: 4161 | STATUS: INTERIM XX | FISCAL |
| STARTING DATE: 6 April 79 | DATE OF COMPLETION: Unknown | | |
| KEY WORDS: Surgical staging, ovarian carcinoma | | | |
| TITLE OF PROJECT: Surgical Staging of Ovarian Carcinoma GOG#41 | | | |

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| PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC, USA | | |
| ASSOCIATE INVESTIGATOR(S): LTC Paul B. Heller, MC USA | | |
| FACILITY: WRAHC | DEPT/SVC: OB-GYN/GYN Oncology Service | |
| ACCUMULATIVE MEDCASE COST: NA | ACCUMULATIVE CONTRACT COST: NA | ACCUMULATIVE SUPPLY COST: NA |
| FY-83 MEDCASE: NA | CONTRACT COST: NA | SUPPLY COST: NA |
| DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 | | |

STUDY OBJECTIVE: To determine the spread of ovarian carcinoma to intraperitoneal structures and retroperitoneal lymph nodes by direct examination, cytologic sampling and biopsy. To establish a surgical protocol for patients entered into GOG ovarian TECHNICAL APPROACH: cancer treatment protocol. To determine the complication rate of (See below) procedures outlined.

PROGRESS DURING FY-82: There have been 184 patients entered into the study from the entire GOG from which 96 are presently evaluable. Walter Reed has entered 19 patients into this study.

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| NUMBER OF SUBJECTS STUDIED: Unknown |
| FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____ |

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS: Too early for conclusions at this time.

PUBLICATIONS OR ABSTRACTS, FY-82: None

TECHNICAL APPROACH: All patients explored in the investigator's institution and found to have Stages I, II or III (optimal) ovarian carcinoma are eligible. All histologic types of ovarian carcinoma and differentiation are acceptable for entry into this protocol. Patients whose procedures were performed at referral institutions are eligible for entry provided that the eligibility criteria are met. Borderline lesions to the ovary are acceptable for entry into this study.

DATE: 19 Nov 82 WORK UNIT No.: 4162 STATUS: INTERIM XX FINAL

STARTING DATE: 21 August 1979 DATE OF COMPLETION: December 1983

KEY WORDS: Melphalan, ICP-32, Epithelial carcinoma of ovary

TITLE OF PROJECT: A Randomized Comparison of Melphalan Versus intraperitoneal chronic phosphate in the treatment of Women with Stage I (Exclusive of Stage IAi, GI; and IBi GI) Epithelial carcinoma of the ovary (Phase III).

PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC, USA

ASSOCIATE INVESTIGATOR(S): LTC Paul B. Heller, MC, USA

FACILITY: WRANC

DEPT/SVC: OB-GYN/GYN Oncology Service

ACCUMULATIVE MEDCARE COST:
NA

ACCUMULATIVE CONTRACT COST:
NA

ACCUMULATIVE SUPPLY COST:
NA

FY-83 MEDCARE:
NA

CONTRACT COST:
NA

SUPPLY COST:
NA

DATE OF COMMITTEE APPROVAL OF
ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: The purpose of this study is to evaluate the relative effectiveness of Melphalan versus peritoneal radioactive chronic phosphate as adjuvant therapy in ~~Stage I exclusive of IAi, GI and IBi, GI epithelial cancers of the ovary~~ in a randomized prospective study. Patients who are eligible are those with surgical Stage IA i, Ga G3; IAii, IBi, Ga, G3, IBii; and IC epithelial cancer of the ~~ovary, FIGO classification who have undergone optimal staging~~.

PROGRESS DURING FY-82: To date there have been 11 entries to the protocol.

NUMBER OF SUBJECTS STUDIED: 93 to each treatment arm.

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
None

CONCLUSIONS: Too early to draw any conclusions.

PUBLICATIONS OR ABSTRACTS, FY-82:
None

TECHNICAL APPROACH: Patients with Stage IAi, G2, G3, IAii, IBi, G2, G3, or IBii or IC epithelial cancer of the ovary are eligible for this protocol and those who have undergone optimal staging. As of March 1981, patients with Stage IB subgroup 1, G1, epithelial cancer will be eligible.

DATE: 19 Nov 82 Work Unit No.: 4163 STATUS: INTERIM XX FINAL

STARTING DATE: 6 Apr 79 DATE OF COMPLETION: Unknown

KEY WORDS: Phase II, Cis-Platinum, advanced gynecologic malignancy

TITLE OF PROJECT: A Phase II Trial of Cis-Platinum in the Treatment of Advanced Gynecologic Cancer GOG #26-C

PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC

ASSOCIATE INVESTIGATOR(S): LTC Paul B. Heller, MC

FACILITY: WRAVC DEPT/SVC: OB-GYN/GYN Oncology Service

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| ACCUMULATIVE PEDCASE COST: NA | ACCUMULATIVE CONTRACT COST: NA | ACCUMULATIVE SUPPLY COST: NA |
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| FY-83 PEDCASE: NA | CONTRACT COST: NA | SUPPLY COST: NA | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
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See below

STUDY OBJECTIVE: To determine the efficacy of Cis-Platinum in the treatment of advanced or recurrent gynecologic cancers. A rejection type design will be used involving a fixed sample size of 25 evaluable patients per disease site per day or a combination of drug studies. The design allows replacement of ineffective regimens by newer agents or combinations.

PROGRESS DURING FY-82: A total of 258 patients have been entered into this protocol to the entire GOG. Walter Reed has entered 2. Combinations of Cis-Platinum and other regimens are in the process of being tested. The protocol is closed to squamous cell carcinoma of the cervix, non-squamous cell carcinoma of the cervix, epithelial carcinoma's of the ovary, and endometrial carcinomas and uterine sarcomas.

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): There have been some Grade III GI and Grade III hypokalemia noted. There have been 4 patients with Grade III or IV renal toxicity noted.

CONCLUSIONS: Cis-Platinum has marked activities as first-line chemotherapeutic in squamous cell carcinoma of the cervix and is active as a second-line therapy for advanced adenocarcinoma of the ovary and mixed mesodermal sarcoma of the uterus. The drug appears to be inactive against endometrial carcinoma and leiomyosarcoma of the uterus, but may have limited activity in therapy of cervical adenocarcinomas.

PUBLICATIONS OR ABSTRACTS, FY-82: Chemotherapy in the management of advanced or recurrent cervical and endometrial carcinoma. Cancer, 48:658-665, 15 July 1981(cont below)

TECHNICAL APPROACH: Cis-Platinum appears to exert its cytotoxic action by cross linking DNA and thus acting in a manner similar to the bifunctional alkylating agents. Cis-Platinum has demonstrated activity in animal studies against transitional cell carcinoma in mice. Toxicity trials in animals reveals myelosuppression, lymphoid atrophy, hemorrhagic enterocolitis, renal tubular necrosis, and cocclear damage, as well as some degree of immunosuppression.

NO. OF SUBJECTS TO BE STUDIED: 25 per disease site

PUBLICATIONS OR ABSTRACTS, FY-82: Cis-Platinum in the treatment of advanced or recurrent adenocarcinoma of the ovary: A Phase II study of the Gynecologic Oncology Group. American Journal of Clinical Oncology; Cancer Clinical Trials- In Press.

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|--|-----------------------------------|---------------------------------------|---|
| DATE: 19 Nov 82 | WORK UNIT NO.: 4165 | STATUS: INTERIM XX FINAL | |
| STARTING DATE: 21 Aug 79 | | DATE OF COMPLETION: Unknown | |
| KEY WORDS: Phase II, AMSA, advanced pelvic malignancies | | | |
| TITLE OF PROJECT: A Phase II Trial of AMSA in Patients with Advanced Pelvic Malignancies - GOG 26-I. | | | |
| PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC, USA | | | |
| ASSOCIATE INVESTIGATOR(S): Heller | | | |
| FACILITY: MRAHC | | DEPT/SVC: OB-GYN/GYN Oncology Service | |
| ACCUMULATIVE MEDICASE COST: NA | ACCUMULATIVE CONTRACT COST: NA | ACCUMULATIVE SUPPLY COST: NA | |
| FY-83 MEDICASE: NA | CONTRACT COST: NA | SUPPLY COST: NA | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: To determine the efficacy of AMSA in patients whose advanced malignancies have been resistant to high priority methods of treatment. A rejection type design will be used involving a fixed sample size of 25 evaluable patients per disease site

TECHNICAL APPROACH: - AMSA is acridine derivative with significant activity per drug. in several animal tumors. The drug inhibits DNA synthesis but has little effect upon RNA synthesis. It binds the DNA through intercalation and external binding.

see below- *PROGRESS DURING FY-82: It has particular affinity for adenin-thyamine pairs. In a Phase I trial responders were observed in a case of lymphangiosarcoma and in a case of ovarian carcinoma. AMSA is attractive because its activity is about the same as

NUMBER OF SUBJECTS STUDIED: Adriamycin but it has less larger producing effects. 25 Patients who have received previous Adriamycin are ineligible for this protocol.

FY-82: TOTAL (TO DATE): BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
Essentially none

CONCLUSIONS: It is too early for any definitive conclusions.

PUBLICATIONS OR ABSTRACTS, FY-82: None

PROGRESS DURING FY-82 A total of 36 patients have been entered to this protocol to date.

DATE: 19 Nov 82 WORK UNIT No.: 4166 STATUS: INTERIM XX FINAL

STARTING DATE: 21 Aug 79 DATE OF COMPLETION: Unknown

KEY WORDS: A Phase II Trial of Yoshi-864 in patients with advanced pelvic malignancy

TITLE OF PROJECT: - A Phase II Trial of Yoshi-864 in patients with advanced pelvic malignancies GOG-26J

PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC, USA

ASSOCIATE INVESTIGATOR(S): Heller

FACILITY: WRAMC DEPT/SVC: OB-GYN/GYN Oncology Service

ACCUMULATIVE FEDCASE COST: NA ACCUMULATIVE CONTRACT COST: NA ACCUMULATIVE SUPPLY COST: NA

FY-83 FEDCASE: CONTRACT COST: SUPPLY COST: DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To determine the efficacy of Yoshi-864 in patients whose advanced malignancies have been resistant to high priority methods of treatment. A rejection type design will be used involving a fixed sample size of 25 evaluable patients

TECHNICAL APPROACH: Yoshi-864 is a sulfonic acid ester of amino-glycol synthesized by Elmerzabinisakurai as an alkylating agent active against experimental tumors resistant to nitrogen mustard derivatives. Structurally it is

see below **PROGRESS DURING FY-82: similar to busulfan but is active against the LI210 system in mice where busulfan is not active. Exact mechanism of action has yet been elucidated. It may have alkylating activity. The initial dose

NUMBER OF SUBJECTS STUDIED: of Yoshi-864 has been reduced to 1.5 mg/kg/day. Patients with abnormal liver functions test secondary to metastatic tumor are ineligible.

FY-82: 25 TOTAL (TO DATE): BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): There has been a Grade IV neurologic toxicity noted in one patient. There has been some Grade IV Neurologic toxicity noted in one patient. There has been some Grade III & IV thrombocytopenias noted. There has been one Grade III parasthesia observed. One Grade III red blood cell count depression observed.

CONCLUSIONS: It is too early to draw any conclusions.

PUBLICATIONS OR ABSTRACTS, FY-82: Manuscript (ovary) submitted to cancer treatment reports In Press.

PROGRESS DURING FY-82 Total of 64 patients have been entered into this protocol.

DATE: 19 Nov 82 WORK UNIT No.: 4167 STATUS: INTERIM FINAL XX

STARTING DATE: 21 August 1979 DATE OF COMPLETION: 1 March 1982

KEY WORDS: Adriamycin, Cytosan, Cis-Platinum treatment in advanced adenocarcinoma of
OF the ovary.

TITLE OF PROJECT: A Phase II Randomized Study of Adriamycin Plus Cyclophosphamide versus
Adriamycin plus Cyclophosphamide plus Cis-Platinum in patients with Advanced Ovarian
Adenocarcinoma, suboptimal Stage III, Stage IV and recurrent. GOG #47

PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC

ASSOCIATE INVESTIGATOR(S): LTC Paul B. Heller, MC

FACILITY: WRAMC DEPT/SVC: OB-GYN/GYN Oncology Service

ACCUMULATIVE FEDCASE COST: ACCUMULATIVE CONTRACT COST: ACCUMULATIVE SUPPLY COST:
NA NA NA

FY-83 FEDCASE: CONTRACT COST: SUPPLY COST: DATE OF COMMITTEE APPROVAL OF
NA NA NA ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To determine if the addition of Cis-Platinum to Adriamycin, plus cyclo-
phosphamide improves remission rate, remission duration, or survival in Stage IV,
suboptimal Stage III and recurrent ovarian adenocarcinoma. To determine the frequency
and duration of true complete remission using these regimens as judged at a second
look laparotomy.

PROGRESS DURING FY-82:

NUMBER OF SUBJECTS STUDIED:

FY-82: TOTAL (TO DATE): BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): Renal toxicity
was observed in 36.2 patients who received Cis-Platinum and were evaluable for toxicity.
None were Grade I except 4. There are 190 cases of WBC toxicity.
There is no survival difference in either arm. The addition of Cis-Platinum appears
to significantly influence the response and progression free interval.

PUBLICATIONS OR ABSTRACTS, FY-82: (Abstract) ASCO, C-403, April 1982

TECHNICAL APPROACH: Patients who have been diagnosed as Stage IV and suboptimal Stage
III primary cases or recurrent cases are eligible. Suboptimal Stage III is defined as
those Stage III patients with at least one residual lesion at the time of surgery
equal to or greater than 3 cm. in the largest diameter in the abdomen or pelvis.
Histologic types eligible are serious adenocarcinoma, mucinous adenocarcinoma, clear
cell adenocarcinoma, endometrioid adenocarcinoma undifferentiated carcinoma un-
differentiated carcinoma or mixed epithelial carcinoma. There have been 515 pts.
entered from the entire GOG. Walter Reed has entered 27 patients to this protocol.
There has been moderate to severe WBC toxicity in 190 patients. There has been
moderate or severe platelet toxicity in 19 patients. There has been moderate
GI toxicity in 44 patients. Renal toxicity was observed in 33.4% of the cases
who received Cis-Platinum and were evaluable for toxicity. All were Grade I except
for 4 cases which were Grade II, III and IV.

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| DATE: 19 Nov 82 | | WORK UNIT NO.: 4171 | STATUS: INTERIM XX FINAL | |
| STARTING DATE: 10 July 1980 | | DATE OF COMPLETION: 1983 | | |
| KEY WORDS: Advanced endometrial carcinoma, hormonal failure, Adriamycin, Cytosan | | | | |
| TITLE OF PROJECT: A Study of Pregestin Therapy in a Randomized Comparison of Adriamycin versus Adriamycin plus Cyclophosphamide in Patients with Advanced Endometrial Carcinoma after Hormonal Failure GOG #48 | | | | |
| PRINCIPAL INVESTIGATOR(S): | | COL Robert C. Park, MC | | |
| ASSOCIATE INVESTIGATOR(S): | | LTC Paul B. Heller, MC | | |
| FACILITY: WRMC | | DEPT/SVC: OB-GYN/GYN Oncology Service | | |
| ACCUMULATIVE MEDCARE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: | | |
| NA | NA | NA | | |
| FY-83 MEDCARE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT | |
| NA | NA | NA | FEB 25 1983 | |

See Below **

STUDY OBJECTIVE: To evaluate the response of advanced or recurrent endometrial carcinoma to oral progestins in patients who have received no prior hormonal therapy. To compare a combination of Adriamycin and Cyclophosphamide or Adriamycin alone as therapy.

TECHNICAL APPROACH: for advanced or recurrent endometrial carcinoma which no longer responds to or has failed to respond to progestines in patients who have received no prior cytotoxic drug.

PROGRESS DURING FY-82: 319 Patients have been entered into the protocol from the entire GOG; 243 are evaluable at present. Protocols amended to allow entry of patients with rapid progression of disease on hormonal therapy on to the chemotherapy.

NUMBER OF SUBJECTS STUDIED: arm of the study without the necessity of three week period. (9 Jan 1981). Of 183 evaluable cases 175 are evaluable for FY-82: 100 Per/yr TOTAL (TO DATE): BEFORE COMPLETION OF STUDY: response. Cont. below.

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): There have been 37 patients with Grade III or IV WBC toxicity. There has been one patient with Grade Platelet toxicity and 1 patient with Grade III GI toxicity.

CONCLUSIONS: Too early for conclusions.

PUBLICATIONS OR ABSTRACTS, FY-82: None

TECHNICAL APPROACH: Patients must have documented primary Stage III, primary Stage IV recurrent or residual endometrial adenocarcinoma, adenocanthoma, or adeno-squamous carcinoma. Those patients with positive cytology as evidence of spread are eligible as non-measurable disease cases. Those patients with prior hormonal therapy will be entered directly. Those patients with prior hormonal therapy will be entered directly. Those patients with no prior hormonal therapy will receive Provera, 50 mg tid until progression of disease.

PROGRESS DURING FY-82 95 of these have non-measurable disease, 3 had complete response, 7 had partial response, 40 had stable disease and 30 had increasing disease.

DATE: 9 Oct 82 | WORK UNIT NO.: 4172 | STATUS: INTERIM XX FINAL
STARTING DATE: 1 Jan 80 | DATE OF COMPLETION: /unknown

KEY WORDS: Dextran; adhesions

TITLE OF PROJECT: Efficacy of 32% Dextran 70 in the Prevention of Adhesions Following Tubal Surgery

PRINCIPAL INVESTIGATOR(S): Thomas A. Klein, COL, MC

ASSOCIATE INVESTIGATOR(S):

FACILITY: WRAHC

DEPT/SVC: OB-GYN/GYN Endocrinology Infert. Service

ACCUMULATIVE MEDCASE COST:
NA

ACCUMULATIVE CONTRACT COST:
NA

ACCUMULATIVE SUPPLY COST:
NA

FY-83 MEDCASE:
NA

CONTRACT COST:
NA

SUPPLY COST:
NA

DATE OF COMMITTEE APPROVAL OF
ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To establish the efficacy (or lack thereof) of 32 % Dextran 70 in the prevention of pelvic adhesions following tubal surgery.

TECHNICAL APPROACH: Randomized double-blind placebo-controlled protocol in which a solution of drug or placebo is poured into the abdominal cavity prior to closure. "second-look" laparoscopy to assess results.

PROGRESS DURING FY-82: No patients were enrolled due to unwillingness of patients to undergo second-look laparoscopy. Recruitment efforts will continue.

NUMBER OF SUBJECTS STUDIED:

FY-82: None TOTAL (TO DATE): None BEFORE COMPLETION OF STUDY: 10

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS:

None

PUBLICATIONS OR ABSTRACTS, FY-82:

None

| | | | |
|---|-----------------------------------|---------------------------------|--|
| DATE: 19 Nov 81 | WORK UNIT No.: 4174 | STATUS: INTERIM | FINAL X |
| STARTING DATE: NA | DATE OF COMPLETION: NA | | |
| KEY WORDS: | | | |
| TITLE OF PROJECT: Transplantation of Female Genital Cancer to Nude Mice | | | |
| PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC | | | |
| ASSOCIATE INVESTIGATOR(S): LTC Paul B. Heller, MC | | | |
| FACILITY: WRAHC | | DEPT/SVC: OB-GYN Oncology Svc. | |
| ACCUMULATIVE MEDICASE COST: NA | ACCUMULATIVE CONTRACT COST: NA | ACCUMULATIVE SUPPLY COST: NA | |
| FY-83 MEDICASE: NA | CONTRACT COST: NA | SUPPLY COST: NA | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: The purpose of this study is to establish hereotransplanted human endometrial and ovarian carcinomas in nude athymic mice for the purpose of evaluating estrogen receptors.

TECHNICAL APPROACH: Protocol is designed to establish transplanted human endometrial and ovarian carcinomas in nude mice so that by serial transplantation, adequate volumes of tumors of the same type will be available for study. This particular PROGRESS DURING FY-82: protocol will have 2 arms.

No patients have been entered into this protocol

NUMBER OF SUBJECTS STUDIED:
 FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

CONCLUSIONS: This protocol was discontinued because of failure of the nude mouse colony. No patients were entered and the project was closed until after further investigation.

PUBLICATIONS OR ABSTRACTS, FY-82:

DATE: 19 Nov 81, WORK UNIT No.: 4175 STATUS: INTERIM FINAL XX

STARTING DATE: DATE OF COMPLETION:

KEY WORDS:

TITLE OF PROJECT: Estrogen Receptors in Human Endometrium

PRINCIPAL INVESTIGATOR(S): COL. Robert C. Park, MC

ASSOCIATE INVESTIGATOR(S): LTC Paul B. Heller, MC

FACILITY: WRANC DEPT/SVC: OB-GYN Oncology Service

ACCUMULATIVE MEDICASE COST: NA ACCUMULATIVE CONTRACT COST: NA ACCUMULATIVE SUPPLY COST: NA

FY-83 MEDICASE: NA CONTRACT COST: NA SUPPLY COST: NA DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: The purpose of this study is to determine if there are profiles of estrogen receptors, cytosol and/or nuclear, that can be correlated with various histologic patterns of human endometrium.

TECHNICAL APPROACH: Determine the estrogen receptor concentrations in normal proliferative and secretory endometrium obtained from the same and different individuals at various times during the ovulatory cycle; determine the estrogen receptor concentrations associate with benign pathologic tissue patterns; determine the estrogen receptor concentrations associated with the pre-malignant endometrial histologic patterns of atypical adenomatous hyperplasia and carcinoma insitu.

PROGRESS DURING FY-82: No patients have been entered into this protocol.
NUMBER OF SUBJECTS STUDIED: _____

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

CONCLUSIONS:

PUBLICATIONS OR ABSTRACTS, FY-82:

DATE: 19 Nov 82 WORK UNIT NO.: 4176 STATUS: INTERIM XX FINAL

STARTING DATE: 1 May 81 DATE OF COMPLETION: 1988

KEY WORDS: Stage IB Cervix, Radical hysterectomy, node positivity, radiation therapy
TITLE OF PROJECT: versus no radiation therapy.

A Surgical Pathologic Study of Women with Invasive Carcinoma of the
cervix, Stage IB and Randomly Assigned Radiation Therapy versus no further therapy
in selected patients GOG #49

PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC

ASSOCIATE INVESTIGATOR(S): LTC Paul B. Heller, MC

FACILITY: MRA-1C DEPT/SVC: OB-GYN/GYN Oncology Service

| | | |
|-----------------------------|-----------------------------|---------------------------|
| ACCUMULATIVE MEDICASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
| NA | NA | NA |

| | | | |
|-----------------|----------------|--------------|--|
| FY-83 MEDICASE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT |
| NA | NA | NA | FEB 25 1983 |

see Below*

STUDY OBJECTIVE: To determine by observation of the 5-year survival and disease-free interval, the validity of current FIGO staging to the histopathologic prognostic factors of size of lesion, location of lesion, depth of invasion of tumor millimeters, ~~lymph node grade~~, growth pattern and site and number of positive lymph nodes in Stage IB carcinoma of the cervix. To determine if radiation therapy will improve survival of selected patients with positive nodes.

PROGRESS DURING FY-82: To date 339 patients have been assigned to the protocol from the entire GOG of which 218 are evaluable. Walter Reed has accessed 10 patients.

NUMBER OF SUBJECTS STUDIED: 250-400 patients annually
FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): There have been 4 patients with Grade III, or IV hematologic toxicity. There have been 2 patients with Grade III or IV GI toxicity. There have been 1 patient with Grade III cardiovascular toxicity.

CONCLUSIONS: Too early for conclusions.

PUBLICATIONS OR ABSTRACTS, FY-82:
None

TECHNICAL APPROACH: Eligible patients with invasive carcinoma of the cervix, Stage IB treated by radical hysterectomy plus pelvic and para-aortic node dissection will be eligible if after examination of the tissue pathologically 3 or less positive nodes are found unilaterally. These patients will be randomized to receive radiotherapy to the pelvis versus no radiotherapy. The total dose will be 5000 rads to the pelvis.

TOXICITY

| | Grade | | | | | Total |
|----------------|-------|----|---|---|---|-------|
| | 0 | 1 | 2 | 3 | 4 | |
| Hematologic | 200 | 9 | 5 | 3 | 1 | 218 |
| GU | 200 | 17 | 1 | 0 | 0 | 218 |
| GI | 211 | 1 | 4 | 1 | 1 | 218 |
| Pulmonary | 217 | 1 | 0 | 0 | 0 | 218 |
| Fever | 208 | 7 | 1 | 2 | 0 | 218 |
| Cardiovascular | 216 | 1 | 0 | 1 | 0 | 218 |
| Cutaneous | 217 | 0 | 1 | 0 | 0 | 218 |

Other Toxicity

Pelvic cellulitis (Grade 2). 1
Hepatitis (Grade 2). 1

Recurrence and Survival

Too early.

Conclusion: Too early.

Future Plans: To be determined.

Publication: None.

180
 180
 180

DATE: 19 Nov 82 | WORK UNIT NO.: 4177 | STATUS: INTERIM X X FINAL

STARTING DATE: 2 Oct. 1980 | DATE OF COMPLETION: 1984

KEY WORDS: Ovarian sarcoma, Adriamycin, postoperative therapy.

TITLE OF PROJECT: A Study of Adriamycin as postoperative therapy for Ovarian sarcoma, Primary or recurrent, with no prior chemotherapy. GOG #50

PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC

ASSOCIATE INVESTIGATOR(S): LTC Paul B. Heller, MC

FACILITY: WRAVC | DEPT/SVC: OB-GYN/GYN Oncology Service

| | | |
|-----------------------------------|-----------------------------------|---------------------------------|
| ACCUMULATIVE MEDICASE COST: NA | ACCUMULATIVE CONTRACT COST: NA | ACCUMULATIVE SUPPLY COST: NA |
|-----------------------------------|-----------------------------------|---------------------------------|

| | | | |
|-----------------------|----------------------|--------------------|---|
| FY-83 MEDICASE: NA | CONTRACT COST: NA | SUPPLY COST: NA | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
|-----------------------|----------------------|--------------------|---|

STUDY OBJECTIVE: To evaluate the efficacy of Adriamycin in treatment of ovarian sarcomas primary or recurrent to restore controls. To accumulate additional surgical pathological data relevant to ovarian sarcomas.

TECHNICAL APPROACH: Patients with ovarian sarcoma, Stage I-IV, primary or recurrent, measurable or non-measurable, with nor prior chemotherapy will be eligible for the protocol. Laparotomy if surgically indicated will be performed. The patient will receive Adriamycin 75 mg/M² every 3 weeks to a maximum cumulative dose of 550 mg/M² or until progression or adverse effects prohibit further therapy. Second lool laparotomy will be performed if there is complete response or detectable disease

See below **

NUMBER OF SUBJECTS STUDIED: thought to be resectable.
FY-82: 5-8 per/yr for entire group.
TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): There have been 3 Grade IV granulocytotoxicity, 1 Grade IV alopecia, 1 Grade III mucocytes
CONCLUSIONS: and 1 Grade III cardiac toxicity noted.

Too early for conclusions.

PUBLICATIONS OR ABSTRACTS. FY-82: None

PROGRESS DURING FY-82 There have been 21 entries to the protocol by the entire GOG. 2 patients have been excluded. Walter Reed has not entered any patients to this protocol.

| | | | |
|--|-----------------------------------|---------------------------------------|---|
| DATE: 19 Nov 82 | WORK UNIT NO.: 4178 | STATUS: INTERIM XX | FISCAL |
| STARTING DATE: Jan 1981 | DATE OF COMPLETION: 1984 | | |
| KEY WORDS: Hydatidiform Mole, Hormonal Contraception | | | |
| TITLE OF PROJECT: Hormonal Contraception and Trophoblastic Sequelae after Hydatidiform Mole, Phase III GOG #55 | | | |
| PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC | | | |
| ASSOCIATE INVESTIGATOR(S): LTC Paul B. Heller, MC | | | |
| FACILITY: WRAVC | | DEPT/SVC: OB-GYN/GYN Oncology Service | |
| ACCUMULATIVE MEDICASE COST: NA | ACCUMULATIVE CONTRACT COST: NA | ACCUMULATIVE SUPPLY COST: NA | |
| FY-83 MEDICASE: NA | CONTRACT COST: NA | SUPPLY COST: NA | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: To determine whether administration of estrogen/progesterone oral contraceptives following the evacuation of hydatidiform mole and prior to its HCG titer reaching undetectable levels affects the incidence of trophoblastic sequelae.

TECHNICAL APPROACH: requiring chemotherapy.

PROGRESS DURING FY-82: There have been 39 patient entries from the entire GOG with no exclusions.

NUMBER OF SUBJECTS STUDIED:
 FY-82: 85/yr TOTAL (TO DATE): BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
 None

CONCLUSIONS:
 NONE

PUBLICATIONS OR ABSTRACTS, FY-82:
 None

TECHNICAL APPROACH: After mole evacuation the patient will be randomized to hormonal contraception versus mechanical contraception. The patient will be followed by evaluation of the HCG assay. The patient will be judged to have no sequelae if the titer has reached normal range by 12 weeks post evacuation, and the patient has no clinical evidence of persistent disease.

| | | |
|--|---------------------------------------|--|
| DATE: 20 Nov 82 | WORK UNIT NO.: 4179 | STATUS: INTERIM XX FINAL |
| STARTING DATE: January 1981 | DATE OF COMPLETION: Unknown | |
| KEY WORDS: PALA in advanced pelvic malignancies | | |
| TITLE OF PROJECT: A Phase II Trial of PALA in patients with advanced pelvic malignancies GOG #26-M | | |
| PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC | | |
| ASSOCIATE INVESTIGATOR(S): Heller | | |
| FACILITY: WRAHC | DEPT/SVC: OB-GYN/GYN Oncology Service | |
| ACCUMULATIVE MEDICASE COST: NA | ACCUMULATIVE CONTRACT COST: NA | ACCUMULATIVE SUPPLY COST: NA |
| FY-83 MEDICASE: NA | CONTRACT COST: NA | SUPPLY COST: NA |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: To determine the efficacy of PALA in treatment of advanced pelvic malignancies.

TECHNICAL APPROACH: Patients with histologically advanced and recurrent and persistent metastatic or local gynecologic cancer with documented disease progression will be entered into this treatment. Patients with abnormal liver function test secondary to metastatic tumor are eligible for protocol. This protocol is closed to epithelial tumors of the ovaries as of 8 Sept 1981.

NUMBER OF SUBJECTS STUDIED: 25 patients per site

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): There has been one Grade III WBC toxicity, one Grade III platelet toxicity. There have been 2 Grade III GI toxicities and 5 Grade III dermatologic toxicities. There has been a Grade III mucocites and Grade III paresthesias.

CONCLUSION: There is no activity with this drug in ovarian cancer in previously treated patients.

PUBLICATIONS OR ABSTRACTS, FY-82: In Preparation

PROGRESS DURING FY-82 18 Patients have been entered into this protocol to date

DATE: 19 Nov 82 MON Unit No.: 4180 STATUS: INTERIM XX FINAL

STARTING DATE: 26 January 1981 DATE OF COMPLETION: 5 February 1982

KEY WORDS: Tamoxifen, advanced endometrial cancer

TITLE OF PROJECT: A Phase II Trial of Tamoxifen in patients with advanced endometrial cancer. GOG # 26-L

PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC

ASSOCIATE INVESTIGATOR(S): Heller

FACILITY: WRAVC

DEPT/SVC: OB-GYN/GYN Oncology Service

ACCUMULATIVE PEDICASE COST:
NA

ACCUMULATIVE CONTRACT COST:
NA

ACCUMULATIVE SUPPLY COST:
NA

FY-83 PEDICASE: CONTRACT COST: SUPPLY COST:
NA NA NA

DATE OF COMMITTEE APPROVAL OF
ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To determine the efficacy of Tamoxifen in patients with advanced endometrial cancer.

TECHNICAL APPROACH: Patients with histologically advanced and recurrent or persistent endometrial cancer with documented disease progression will be entered into this treatment. Patients with performance Grade III in GOG scale and eligible for entry.

PROGRESS DURING FY-82: Patients with abnormal liver function test secondary to metastatic tumor are eligible for entry.

See Below

NUMBER OF SUBJECTS STUDIED: 25 patients

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS:

PUBLICATIONS OR ABSTRACTS, FY-82: None

PROGRESS DURING FY-82 28 Patients have been entered into this protocol.

| | | | |
|---|-----------------------------------|---------------------------------------|---|
| DATE: 19 Nov 82 | WORK UNIT No.: 4181 | STATUS: INTERIM XX | FINAL |
| STARTING DATE: 5 Feb 1981 | DATE OF COMPLETION: 1990 | | |
| CAP Ovarian Adenocarcinoma, Stage III | | | |
| TITLE OF PROJECT: A Phase III Randomized Study of Cyclophosphamide plus Adriamycin plus Platinol (CAP) versus Cyclophosphamide plus Platinol (CP) in patients with optimal Stage III Ovarian Adenocarcinoma GOG #52 | | | |
| PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC | | | |
| ASSOCIATE INVESTIGATOR(S): LTC Paul B. Heller, MC | | | |
| FACILITY: MRAVC | | DEPT/SVC: OB-GYN/GYN Oncology Service | |
| ACCUMULATIVE MEDICASE COST: NA | ACCUMULATIVE CONTRACT COST: NA | ACCUMULATIVE SUPPLY COST: NA | |
| FY-83 MEDICASE: NA | CONTRACT COST: NA | SUPPLY COST: NA | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: To determine inoptimal Stage III adenocarcinoma (ovarian), if the addition of Adriamycin to Cyclophosphamide plus Cis-Platinum improves progression free interval, frequency of negative second look laparotomy and survival.

TECHNICAL APPROACH: After debulking surgery for Stage III ovarian adenocarcinoma, the patient if noted to have optimal disease less than 1 cm. lesion in any one area, will be given every 2 weeks for 8 courses. After 8 courses the patient will have 2nd look laparotomy if response has occurred. If the patient has less than clinical response, the patient will be followed. If there is less than complete response, the patient will be off study and followed either on or off chemotherapy as determined by the investigator.

NUMBER OF SUBJECTS STUDIED: gator.

FY-82: Approx 100/yr TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): There have been 29 Grade III or IV WBC toxicities noted. There have been 39 Granulocytes Grade III or IV toxicity noted. There have been 5 patients with Grade III GI toxicity.

CONCLUSIONS: toxicity.

Too early for conclusions.

PUBLICATIONS OR ABSTRACTS. FY-82:

None

PROGRESS DURING FY-82: There have been 101 patients entered into the protocol in the entire GOG of which 68 are presently evaluable. Walter Reed has entered 5 patients to the protocol.

| | | |
|---|---------------------------------------|---------------------------------|
| DATE: 19 Nov 82 | WORK UNIT No.: 4182 | STATUS: INTERIM XX FINAL |
| STARTING DATE: February 1981 | DATE OF COMPLETION: 1988 | |
| KEY WORDS: Malignant Ovarian stromal tumors, VAC, Adriamycin | | |
| TITLE OF PROJECT: The treatment of Women with malignant tumors of the ovarian stroma with combination of Vincristine, Dactinomycin and Cyclophosphamide, Phase III, and a Phase II evaluation of Adriamycin in malignant tumors of the ovarian stroma refractory to Primary chemotherapy. | | |
| PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC | | |
| ASSOCIATE INVESTIGATOR(S): LTC Paul B. Heller, MC | | |
| FACILITY: WRAVC | DEPT/SVC: OB-GYN/GYN Oncology Service | |
| ACCUMULATIVE MEDCARE COST: NA | ACCUMULATIVE CONTRACT COST: NA | ACCUMULATIVE SUPPLY COST: NA |
| FY-83 MEDCARE: NA | CONTRACT COST: NA | SUPPLY COST: NA |
| DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 | | |

STUDY OBJECTIVE: To evaluate the effectiveness of Vincristine, Actinomycin and Cyclophosphamide in the treatment of malignant tumors of the ovarian stroma. To confirm completeness of response to VAC treatment with restaging laparotomy. To evaluate the response to Actinomycin in patients who fail on primary treatment with VAC.

TECHNICAL APPROACH:

PROGRESS DURING FY-82: There have been 6 entries to this protocol from the entire GOG. No entries from Walter Reed at present.

NUMBER OF SUBJECTS STUDIED:

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
None of note

CONCLUSIONS: Too early for conclusions

PUBLICATIONS OR ABSTRACTS, FY-82: None

TECHNICAL APPROACH: Patients with Stage II, III, IV and recurrent disease completely resected would be eligible. Patients will receive 3 cycles of VAC. If there is progression the patient will be placed on Adriamycin. If there is response the patient will continue with VAC for a total of 10 cycles. Complete partial response or resectable disease will be treated by restaging laparotomy. If there is progression at 10 courses Adriamycin will be instituted. If there is residual disease at restaging laparotomy, Adriamycin will be instituted. Patients with prior concomitant endometrial carcinoma will be permitted in the study. An additional objective has been added to learn more about hormonal effects and stromal tumors. (24 July 1981)

| | | | |
|--|-----------------------------------|---------------------------------------|--|
| DATE: 82 | WORK UNIT NO.: 4183 | STATUS: INTERIM XX | FINAL |
| STARTING DATE: February 1981 | DATE OF COMPLETION: 1986 | | |
| KEY WORDS: Radiation Enhancers, radiation therapy, stage IIB, III and IVA cervical carcinoma, negative para-aortic nodes | | | |
| TITLE OF PROJECT: A Randomized Comparison of Hydroxyurea versus Misonidazole as an adjunct to Radiation therapy in patients with Stages IIB, III and IVA Carcinoma of the Cervix and Negative para-aortic nodes, Phase III GOG #56 | | | |
| PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC | | | |
| ASSOCIATE INVESTIGATOR(S): LTC Paul B. Heller, MC | | | |
| FACILITY: WRAHC | | DEPT/SVC: OB-GYN/GYN Oncology Service | |
| ACCUMULATIVE MEDICASE COST: NA | ACCUMULATIVE CONTRACT COST: NA | ACCUMULATIVE SUPPLY COST: NA | |
| FY-83 MEDICASE: NA | CONTRACT COST: NA | SUPPLY COST: NA | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: To determine whether Hydroxyurea or Misonidazole is superior as a potentiator of radiation therapy in advanced cervical cancer.

TECHNICAL APPROACH: Patients with Stage IIB, III and IVA cervical carcinoma confined to the pelvis who have noninvasive staging by CAT scan, sonography or lymphangiogram. Histological evaluation of nodes will either be done by surgical staging or percutaneous biopsy. Patients with negative nodes will have randomization to either Misonidazole and pelvic radiation therapy or Hydroxyurea and pelvic radiation therapy.

NUMBER OF SUBJECTS STUDIED: Approximately 55/yr

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): There has been one Grade III and one Grade IV toxicity.

CONCLUSIONS:

Too early for conclusions

PUBLICATIONS OR ABSTRACTS, FY-82: None

PROGRESS DURING FY-82: 30 Patients have been entered into the protocol from the entire GOG.

| | | |
|---|--------------------------|--------------------------|
| DATE: 19 Nov 81 | Work Unit No.: 4185 | STATUS: INTERIM XX FINAL |
| STARTING DATE: 1981 | DATE OF COMPLETION: 1986 | |
| KEY WORDS: Cervical cancer, positive para-aortic nodes, adjuvant chemotherapy | | |
| TITLE OF PROJECT: Adjuvant Chemotherapy for Cervical Cancer with Para-aortic lymph Node Disease | | |

PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC

ASSOCIATE INVESTIGATOR(S): LTC Paul B. Heller, MC

FACILITY: WRANVC DEPT/SVC: OB-GYN Oncology Svc.

| | | |
|----------------------------|-----------------------------|---------------------------|
| ACCUMULATIVE FEDCASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
| NA | NA | NA |

| | | | |
|----------------|----------------|--------------|--|
| FY-83 FEDCASE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT |
| NA | NA | NA | FEB 25 1983 |

STUDY OBJECTIVE: To determine the efficacy of chemotherapy in the overall survival of FIGO stage IIB and IIIB cervical cancer patients with positive para-aortic nodes. To determine colony forming assay of cervical cancer stem cells and prediction of TECHNICAL APPROACH: results in the status of para-aortic nodes.

Biopsy proven cervical cancer stages IIB & IIIB will be verified. Para-aortic lymph node involvement will be verified by surgical staging. Patients with positive lymph

PROGRESS DURING FY-82: nodes will have pelvic radiation with adjuvant chemotherapy to include Cis-Platinum, Mitamicence and Bleomycin. Those with negativ pelvic nodes will not be on protocol.

See below

NUMBER OF SUBJECTS STUDIED: 25

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
None

CONCLUSIONS:

None

PUBLICATIONS OR ABSTRACTS, FY-82:
None

PROGRESS DURING FY-82. A total of 7 patients have been eligible for staging laparotomy. Only two of these patients have been entered to protocol because of node positivity.

| | | | |
|--|-----------------------------------|---------------------------------------|--|
| DATE: 9 Nov 82 | WORK UNIT No.: 4186 | STATUS: INTERIM XX | FINAL |
| STARTING DATE: May 1981 | DATE OF COMPLETION: 1987 | | |
| KEY WORDS: Poor prognosis GTD, MAC, Bagshawe Protocol | | | |
| TITLE OF PROJECT: A Randomized Comparison of Multiple Agent Chemotherapy with Methotrexate, Actinomycin-D, and Chlorambucil versus the Modified Bagshawe Protocol in the Treatment of "Poor Prognosis" Metastatic Gestational Trophoblastic Disease GOG #57. | | | |
| PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC | | | |
| ASSOCIATE INVESTIGATOR(S): LTC Paul B. Heller | | | |
| FACILITY: WRAVC | | DEPT/SVC: OB-GYN/GYN Oncology Service | |
| ACCUMULATIVE MEDCARE COST: NA | ACCUMULATIVE CONTRACT COST: NA | ACCUMULATIVE SUPPLY COST: NA | |
| FY-83 MEDCARE: NA | CONTRACT COST: NA | SUPPLY COST: NA | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: To evaluate the effectiveness and toxicity of the modified Bagshawe Protocol in patients with poor prognosis metastatic gestational trophoblastic disease. To compare the effectiveness and toxicity of the modified Bagshawe Protocol with TECHNICAL APPROACH: standard triple agent chemotherapy (MAC) See Below

PROGRESS DURING FY-82: 3 patients have been entered into the protocol to date from the entire GOG. None have been entered from Walter Reed.

NUMBER OF SUBJECTS STUDIED: 12-20 annually
 FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
 None of note

CONCLUSIONS:
 Too early for conclusions.

PUBLICATIONS OR ABSTRACTS, FY-82: None

TECHNICAL APPROACH: Metastatic gestational trophoblastic disease will be randomized to MAC versus modified Bagshawe Protocol. Patients with brain and liver metastases will receive respective radiation to these areas. The patients will be followed with Beta subunit HCG titers. Patients will continue as long as the Beta HCG is decreasing at an appropriate rate.

| | | | |
|---|-----------------------------------|---------------------------------------|--|
| DATE: 19 Nov 82 | WORK UNIT No.: 4187 | STATUS: INTERIM XX | FINAL |
| STARTING DATE: 8 September 1981 | DATE OF COMPLETION: Unknown | | |
| KEY WORDS: DAHAD, Advanced pelvic malignancies | | | |
| TITLE OF PROJECT: A Phase II Trial of Dihydroxyanthracenedione ((DHAD) in GOG #26-N | | | |
| PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC | | | |
| ASSOCIATE INVESTIGATOR(S): Heller | | | |
| FACILITY: VRMC | | DEPT/SVC: OB-GYN/GYN Oncology Service | |
| ACCUMULATIVE FEDCASE COST: NA | ACCUMULATIVE CONTRACT COST: NA | ACCUMULATIVE SUPPLY COST: N A | |
| FY-83 FEDCASE: NA | CONTRACT COST: NA | SUPPLY COST: NA | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: Determine the efficacy of chemotherapeutic agents in patients whose advanced malignancies have been resistant to higher priority methods of treatment.

TECHNICAL APPROACH: Patients who respond or demonstrate stable disease will continue to receive the agent until progression has occurred. The minimum treatment period will be one cycle with survival measured to the beginning of the next cycle.

See below **PROGRESS DURING FY-82: Cardiac monitoring is required before each course of the AJD in patients previously treated to a total dose of 350 mg/M² of Doxorubicin.

NUMBER OF SUBJECTS STUDIED: 25 per disease site

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
None of note.

CONCLUSIONS: Too Early

PUBLICATIONS OR ABSTRACTS, FY-82: None

PROGRESS DURING FY-82- A total of 10 patients in the entire GOG have been entered into this protocol.

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|---|-----------------------------------|---------------------------------------|--|--|
| DATE: 19 Nov 82 | | WORK UNIT NO.: 4188 | STATUS: INTERIM XX FINAL | |
| STARTING DATE: June 1981 | | DATE OF COMPLETION: 1985 | | |
| KEY WORDS: Cytoplasmic Progesterone and Estradiol Receptors, Endometrial Adenocarcinoma | | | | |
| TITLE OF PROJECT: A study of cytoplasmic progesterone and estradiol receptors as Markers of Progestin Endometrial Adenocarcinomas GOG #58 | | | | |
| PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC | | | | |
| ASSOCIATE INVESTIGATOR(S): LTC Paul B. Heller, MC | | | | |
| FACILITY: WRANC | | DEPT/SVC: OB-GYN/GYN Oncology Service | | |
| ACCUMULATIVE MEDICASE COST: NA | ACCUMULATIVE CONTRACT COST: NA | ACCUMULATIVE SUPPLY COST: N A. | | |
| FY-83 MEDICASE: NA | CONTRACT COST: NA | SUPPLY COST: NA | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 | |

STUDY OBJECTIVE: To determine if Cytoplasmic Progesterone and/or Estradiol receptors can identify progestin response in recurrent or advanced endometrial adenocarcinoma.

TECHNICAL APPROACH: Tissue obtained by excisional biopsy depending upon amount of tissue available for studies progesterone and estradiol receptors will be performed on various priorities as described by the protocol.

PROGRESS DURING FY-82: 12 Patients have been entered into the study from the entire GOG. None have been entered from Walter Reed.

NUMBER OF SUBJECTS STUDIED: 60/per year

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
None of note

CONCLUSIONS: None

PUBLICATIONS OR ABSTRACTS, FY-82:
None

DATE: 19 Nov 82 Work Unit No.: 4189 STATUS: INTERIM FINAL XX

STARTING DATE: NA DATE OF COMPLETION: NA

KEY WORDS:

TITLE OF PROJECT: A Randomized double blind clinical trial evaluating cholestyramine prophylaxis for radiation induced diarrhea (Phase II) GOG #53

PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC

ASSOCIATE INVESTIGATOR(S): LTC Paul B. Heller, MC

FACILITY: WRAMC DEPT/SVC: OB-GYN/GYN Oncology Service

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| ACCUMULATIVE MEDICAL CASE COST: NA | ACCUMULATIVE CONTRACT COST: NA | ACCUMULATIVE SUPPLY COST: NA |
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| FY-83 MEDICAL CASE: NA | CONTRACT COST: NA | SUPPLY COST: NA | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
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STUDY OBJECTIVE: Assess the therapeutic effectiveness of cholestyramine administered prophylactically to patients during pelvic irradiation. The effectiveness of cholestyramine will be assessed in a randomized double-blind study in which radiotherapy plus cholestyramine will be compared with radiotherapy plus placebo.
TECHNICAL APPROACH: See below

PROGRESS DURING FY-82: This protocol has been withdrawn. The protocol was never implemented.

NUMBER OF SUBJECTS STUDIED:

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

CONCLUSIONS:

PUBLICATIONS OR ABSTRACTS, FY-82:

TECHNICAL APPROACH: The effectiveness of cholestyramine in preventing radiation-induced diarrhea will be determined in a clinical trial in which patients who are to undergo pelvic irradiation for malignancy will be randomized in a double-blind fashion to receive either prophylactic oral cholestyramine during radiotherapy or only placebo.

DATE: 19 Nov 82 Work Unit No.: 4190 STATUS: INTERIM XX FINAL

STARTING DATE: 9 February 1982 DATE OF COMPLETION:

KEY WORDS: Advanced Ovarian adenocarcinoma, CAP versus CAP BCG

TITLE OF PROJECT: A Phase II Randomized Study of Doxorubin plus cyclophosphamide plus Cisplatinum versus Doxorubicin plus cyclophosphamide plus Cisplatinum BCG in patients with Advanced Suboptimal Ovarian Adenocarcinoma GOG #60

PRINCIPAL INVESTIGATOR(S): COL Robert C. Park, MC

ASSOCIATE INVESTIGATOR(S): LTC Paul B. Heller, MC

FACILITY: WRAVC DEPT/SVC: OB-GYN/GYN Oncology Service

ACCUMULATIVE MEDICASE COST:
NA

ACCUMULATIVE CONTRACT COST:
NA

ACCUMULATIVE SUPPLY COST:
N A

FY-83 MEDICASE:
NA

CONTRACT COST:
NA

SUPPLY COST:
NA

DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To determine if the addition of BCG to Doxorubicin plus cyclophosphamid plus Cisplatinum improves remission rate, remission duration, or survival in sub-optimal Stage III and IV ovarian adenocarcinoma. To determine the frequency and TECHNICAL APPROACH: duration of true complete remission using these regimens as judged SEE BELOW at 2nd look laparotomy.

PROGRESS DURING FY-82: 36 Patients have been entered into this protocol from the entire GOG.

NUMBER OF SUBJECTS STUDIED: 150/per year

FY-82: TOTAL (TO DATE): BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None of note

CONCLUSIONS:

None

PUBLICATIONS OR ABSTRACTS, FY-82:

None

TECHNICAL APPROACH: To determine if the addition of BCG improves the results of treatment. The total duration will be 8 courses. After that treatment will be stopped. At the completion of 8 courses of treatment, the physician may not be able to detect any left over cancer by routine exam. The physician will propose surgery to determine the completeness of the response to chemotherapy or to provide removal of residual cancer.

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| DATE: 1/24/83 | WORK UNIT No.: 4191 | STATUS: INTERIM X FINAL |
| STARTING DATE: 21 Sept 1981 | DATE OF COMPLETION: | |
| KEY WORDS: | | |
| TITLE OF PROJECT: THE RELATIONSHIP BETWEEN OVARIAN STEROIDOGENIC ENZYME ACTIVITIES AND OVULATION. | | |
| PRINCIPAL INVESTIGATOR(S): Munabi, A. | | |
| ASSOCIATE INVESTIGATOR(S): Klein, T.A. | | |
| FACILITY: WRAVC | DEPT/SVC: OB-Gyn | |
| ACCUMULATIVE PECASE COST: 0 | ACCUMULATIVE CONTRACT COST: 0 | ACCUMULATIVE SUPPLY COST: 0 |
| FY-83 PECASE: 0 | CONTRACT COST: 0 | SUPPLY COST: 0 |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: To determine if follicular estrogen production can regulate ovarian thecal androgen production by modulating ~~steroid biosynthetic enzymes.~~

TECHNICAL APPROACH: Measurement of steroid biosynthetic enzymes in human ovarian tissue, correlation with intrafollicular E₂ levels.

PROGRESS DURING FY-82: Technical problems have been encountered in tissue enzyme measurement.

NUMBER OF SUBJECTS STUDIED:

FY-82: 2 TOTAL (TO DATE): 2 BEFORE COMPLETION OF STUDY: 100

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS: Efforts are underway to resolve problems above. No further patient accrual at present.

PUBLICATIONS OR ABSTRACTS, FY-82:

NONE

DATE: 2 Mar 83 | Proj. ID# 4192 | STATUS: INTERIM - FHS

START DATE: 2 November 1981 | DATE OF COMPLETION: April 1989

KEY WORDS: Squamous Cervical Cancer, Metastatic to common iliac and para aortic nodes.

TITLE OF PROJECT: Extended Field Radiation Therapy and Hydroxyurea followed by randomized comparison of Cis-Platinum or no further therapy in patients with cervical squamous cell carcinoma metastatic to high common iliac and/or para aortic nodes. GOG Protocol #59

PRINCIPAL INVESTIGATOR(S): ROBERT C. PARK, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): PAUL B. HELLER, MD, LTC, MC | Hiru Advani, MAJ, MC

FACILITY: WAFB | Dept/Sec: OB-GYN/GYN-Oncology

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| ACCUMULATIVE RELEASE COST: N/A | ACCUMULATIVE CONTRACT COST: N/A | ACCUMULATIVE SUPPLY COST: N/A |
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|-----------------------|-----------------------|---------------------|--|
| FY-85 RELEASE: N/A | CONTRACT COST: N/A | SUPPLY COST: N/A | DATE OF COMPLETION REPORT: FHS/MS Progress Report |
|-----------------------|-----------------------|---------------------|--|

STUDY OBJECTIVE: To understand significance of surgical and pathologic factors involved in staging cervical cancer. To understand addition of chemotherapy in combination with positive nodes.

TECHNIQUES/METHODS: Patients with squamous cell cancer of the cervix with positive high common or para-aortic nodes will receive pelvic and para-aortic irradiation therapy plus Hydroxyurea. They will be then randomized to adjuvant Cis-platinum or Placebo. Phase IY 82: no further therapy.

There have been 26 patients entered into the protocol. None have been entered from Ft. Her. Recd.

NUMBER OF SUBJECTS STUDIED: 26

FY-82: TOTAL (TO DATE): 26 BEFORE COMPLETION OF STUDY: 20-25 per/yr

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): None

CONCLUSIONS: None

PUBLICATIONS OR ABSTRACTS, FY 82: None

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DATE: 2 Mar 83 | P & O# 4193 | STATUS: Interim xx | Line

START DATE: 15 Dec 1981 | DATE OF COMPLETION: December 1987

KEY WORDS: Second Line Cis-Platinum, Cytosin versus Hexamethylmelamine
TITLE OF PROJECT: After "positive" second look, ovarian cancer.

Phase III Randomized Study of Cis-Platinum plus Cyclophosphamide versus Hexamethylmelamine after second look surgery in non-measurable stage III & IV ovarian adenocarcinoma, partially responsive to previous regimens containing Cis-Platinum and

PRINCIPAL INVESTIGATOR(S): ROBERT C. PARK, MD, MC | Cyclophosphamide, COG
ASSOCIATE INVESTIGATOR(S): PAUL B. HELLER, MD, MC | Protocol #61

FACILITY: WAFB | Dept/Svc: OB-GYN/CYN-Oncology

ACCUMULATIVE PHASEASE COST: N/A | REOPERATIVE CONTRACT COST: N/A | ACCUMULATIVE SUPPLY COST: N/A

FY-83 PHASEASE: N/A | CONTRACT COST: N/A | STUDY COST: N/A | DATE OF COMMITTEE APPROVAL OF LEADUM PROGRESS REPORT

STUDY OBJECTIVE: To determine in non-measurable but residual stage III ovarian adenocarcinoma partially responsive after treatment with radiation containing Cis-Platinum and Cyclophosphamide, if progression free interval and survival rate are improved by continuing Cyclophosphamide plus Cis-Platinum or by changing treatment of Hexamethylmelamine. Those patients who have residual non-measurable disease after second look laparotomy for stage III adenocarcinoma of ovary are eligible for randomization to treatment with Cytosin and Cis-Platinum versus Hexamethylmelamine.

There have been 27 entries to this protocol, two have been entered from Walter Reed.

NUMBER OF SUBJECTS STUDIED:

FY-82: 27 | Total (to date): 27 | PERCENT COMPLETION OF STUDY: 35 per/yr for the entire COG.

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): N/A

CONCLUSIONS: Too Early

PUBLICATIONS OR ABSTRACTS, FY 82: None

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479B

DATE: 2 Mar 83 | WORK UNIT NO.: 4194 | STATUS: Initial XX Final

START DATE: 1 December 1981 | DATE OF TERMINATION: December 1986

KEY ISSUES: Advanced pelvic malignancies, AZQ

TITLE OF PROJECT: A Phase II Trial of Aziridinylbenzoquinone (AZQ) in patients with advanced pelvic malignancies. GOG Protocol #26-0

PRINCIPAL INVESTIGATOR(S): ROBERT C. PARK, COL, MC

ASSOCIATE INVESTIGATOR(S): PAUL B. HEMLER, LTC, MC

FACILITY: WRAFC | DEPT/SVC: OB-GYN/GYN-Oncology

ACCUMULATIVE FEBCASE COST: N/A | ACCUMULATIVE CONTRACT COST: N/A | ACCUMULATIVE SUPPLY COST: N/A

FY-83 FEBCASE: N/A | CONTRACT COST: N/A | SUPPLY COST: N/A | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT

STUDY OBJECTIVE: To determine the efficacy of AZQ in the treatment of advanced pelvic malignancies.

TECHNICAL APPROACH: Patients with histologically confirmed advanced recurrent persistent metastatic or local gynecologic cancer with documented disease progression not amenable to higher priority protocol or standard regimens of therapy.

PROGRESS DURING FY 82: There have been 5 patients accession to the protocol for the entire group. None have been accession from Walter Reed.

NUMBER OF SUBJECTS STUDIED: 5

FY-82: 5 | TOTAL (TO DATE): 5 | BEFORE COMPLETION OF STUDY: 25 per disease site per year.

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF MORE SO STATE): None Noted

CONCLUSIONS: Too Early

PUBLICATIONS OR ABSTRACTS, FY-82:

None

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DATE: 2 Mar 83 | Book Entry No.: 4196 | STATUS: Interim XX Final
START Date: 15 October 1982 | Date of Completion: January 1988

Key Words: Cervical Carcinoma, clinical pathologic study.
TITLE OF PROJECT: Clinical pathologic study of stages IIB, III and IVA carcinoma of the Cervix. GOC Protocol #63

PRINCIPAL INVESTIGATOR(S): ROBERT C. PARK, COL, MC

ASSOCIATE INVESTIGATOR(S): PAUL B. HELLER, LTC, MC | HIRU ADVANI, MAJ, MC

FACILITY: WRAFC | Dept/Svc: OB GYN/CYN-Oncology

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| ACCUMULATIVE FEE/LEASE COST: N/A | ACCUMULATIVE CONTRACT COST: N/A | ACCUMULATIVE SUPPLY COST: N/A |
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| FY-83 FEE/LEASE: N/A | CONTRACT COST: N/A | SUPPLY COST: N/A | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT |
|-------------------------|-----------------------|---------------------|---|

STUDY OBJECTIVE: To evaluate the sensitivity and specificity of non-invasive procedures such as sonograms, CAT scans and lymphangiography to detect metastasis to the lymph nodes in cervical cancer as compared to surgical staging.
TECHNICAL APPROACH: Patients will undergo non-invasive staging procedures mentioned. CAT, Sonogram, Lymphangiogram and be evaluated by fine needle para-aortic biopsy or para-aortic lymphadenectomy and intra-peritoneal exploration.
PROGRESS DURING FY-82: None

NUMBER OF SUBJECTS STUDIED: No patients entered. Protocol not activated until 15 October 1982. 75 per/yr 1983
FY-82: 0 | TOTAL (TO DATE): 0 | BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF TRUE, SO STATE):
N/A

CONCLUSIONS:
None

PUBLICATIONS OR ABSTRACTS, FY-82:
None

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DATE: 2 of 83 | EXECUTIVE NO.: 4197 | STATUS: INTERIM XX FINAL

STARTING DATE: 12 April 1982 | DATE OF COMPLETION: April 1985

KEY WORDS: Cis-Platinum, Advanced Cervical Cancer

TITLE OF PROJECT: Randomized comparison of rapid versus prolong (24 hr) infusion of Cis-Platinum and therapy of squamous cell carcinoma of the cervix (Phase III) GOG Protocol #64

PRINCIPAL INVESTIGATOR(S): ROBERT C. PARK, COL, MC

ASSOCIATE INVESTIGATOR(S): PAUL B. HELLER, LTC, MC

FACILITY: PRMC | DEPT/SYS: OB-GYN/ GYN-Oncology

ACCUMULATIVE MEDICINE COST: N/A | ACCUMULATIVE CONTRACT COST: N/A | ACCUMULATIVE SUPPLY COST: N/A

FY-85 RESEARCH: N/A | COMPANY COST: N/A | SUPPLY COST: N/A | DATE OF COMPLETION: Journal Of Gynecological Progress Report

STUDY OBJECTIVE: To determine if the duration of response in squamous cell carcinoma of the cervix is altered by prolonging the infusion of Cis-Platinum. To determine if prolonging the infusion of Cis-Platinum reduces the side-effects related to TECHNICAL PROBLEM: its administration.

Those patients with advanced recurrent squamous cell carcinoma with measurable disease will be eligible to randomization of Cis-Platinum IV 50 mg/m² 1 mg/min PROGRESS PERIOD: FY 82: every three weeks or Cis-Platinum 50 mg/m² over 24 hrs every 3 wks

There have been 9 entries into the protocol. None of these have been from Walter Reed.

NUMBER OF SUBJECTS STUDIED: 9
FY-82: | TOTAL (to date): 9 | RARE COMPLETION OF STUDY: 140/yr

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF ANY SO STATE):
None

CONCLUSIONS:
Too early

PUBLICATIONS OR ABSTRACTS: FY 82:
None

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DATE: _____ WORK UNIT NO.: 4198 STATUS: INTERIM FIRM: XX
STARTING DATE: N/A DATE OF COMPLETION: N/A

KEY WORDS: Vindesine, Recurrent Cervical Cancer
TITLE OF PROJECT: Phase II Trial of Vindesine for recurrence cervical carcinoma.

PRINCIPAL INVESTIGATOR(S): ROBERT C. PARK, MD COL, MC

ASSOCIATE INVESTIGATOR(S): PAUL B. HELLER, MD LTC, MC

FACILITY: ABAME Dept/Svc: OB-GYN/CYR-Oncology

ACCUMULATIVE MEDICINE COST: ACCUMULATIVE CONTRACT COST: ACCUMULATIVE SUPPLY COST:
N/A N/A N/A

FY-83 FISCAL YEAR: CONTRACT COST: SUPPLY COST: DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT
N/A N/A N/A

STUDY OBJECTIVE: To determine if patients who have histologically documented carcinoma of the cervix not amenable to radiation or surgery will respond to the chemotherapy of Vindesine.

EXCLUSION CRITERIA: Patients who have failed higher priority treatment or standard therapy will be eligible if they have a recurrent or advanced cervical carcinoma.

PROGRESS DURING FY 82: None - Protocol was never initiated because Principal Investigator from the associated institution left that institution and the project was discontinued.

NUMBER OF SUBJECTS STUDIED: 0

FY-82: TOTAL (TO DATE): BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

N/A

COMMENTS: N/A

PUBLICATIONS OR ABSTRACTS, FY 82:

N/A

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479F

DATE: 2 Mar 83 | Work Unit No.: 4199 | STATUS: INTERIM X FINAL

STARTING DATE: 15 July 1982 | Date of Completion: July 1985

KEY WORDS: Ultra-structural consideration, small cell carcinoma of cervix.

TITLE OF PROJECT: Ultra-structural, Staging and Therapeutic consideration in small cell carcinoma of the cervix. (Phase II) GOG Protocol #66

PRINCIPAL INVESTIGATOR(S): ROBERT C. PARK, COL, MC

ASSOCIATE INVESTIGATOR(S): PAUL B. HELLER, LTC, MC | HIRU ADVANI, MAJ, MC

FACILITY: ABNMC | Dept/Sec: OB GYN/GYN-Oncology

ACCUMULATIVE FEDERAL COST: N/A | ACCUMULATIVE CONTRACT COST: N/A | ACCUMULATIVE SUPPLY COST: N/A

FY-83 FEDERAL COST: N/A | CONTRACT COST: N/A | SUPPLY COST: N/A | DATE OF COMPLETION APPROVAL OF FORMAL PROGRESS REPORT

SUBJECTIVE: To determine if the incidence of neuro-endocrine carcinoma of the cervix in cases which are histologically classified as small cell carcinoma. To determine the response rate to combination chemotherapy in pts. with stage IVB

TECHNICAL APPROACH: small cell carcinoma of the cervix and progressive local disease after radiation therapy.

Staging studies having been completed micron-microscopy studies will be performed of this disease. Staging T1/T2 will be treated with standard

PROGRESS DURING FY 82: (See below) therapy. Stages IVB where those with recurrence after radiation therapy will be treated with combinations of Vincristine,

NUMBER OF SUBJECTS STUDIED: Doxyrubicin and Cyclophosphamide. Those who fail on this regimen will be offered VT 16.

FY-82: None | TOTAL (TO DATE): None | BUDGET COMPLETION OF STUDY: 10 per yr for the entire group.

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF MORE SO STATE): None

CONCLUSIONS: Too Early

PUBLICATIONS OR ABSTRACTS, FY-82: None

PROGRESS DURING FY-82- None

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DATE: _____ WORK UNIT NO.: 4200 STAGE: INTERIMX IIRX

STARTING DATE: 11 Aug. 82 DATE OF COMPLETION: 1985

KEY WORDS: Prostaglandin-Invasive Genital Cancer

TITLE OF PROJECT: Plasma Prostaglandin F₂ Levels in Patients with Invasive and Preinvasive Genital Cancer.

PRINCIPAL INVESTIGATOR(S): ROBERT C. PARK MD COL MC

ASSOCIATE INVESTIGATOR(S): PAUL B. HELLER MD LTC MC

FACILITY: WRMC Dept/Spec: OB-GYN-GYN/Oncology

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| ACCUMULATIVE MEDICINE COST: N/A | ACCUMULATIVE CONTRACT COST: N/A | ACCUMULATIVE SUPPLY COST: N/A |
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| FY-83 MEDICINE: N/A | CONTRACT COST: N/A | SUPPLY COST: N/A | DATE OF COMPLETION: 1985 FROM PROGRESS REPORT |
|------------------------|-----------------------|---------------------|--|

STUDY OBJECTIVE: To determine the correlation between elevation of prostaglandin F₂ (PGF₂) and presence of female genital cancer. Patients with preinvasive or invasive genital cancer will have two blood test drawn for Prostaglandin F₂ prior to treatment and after completion of therapy for the disease.

PROGRESS DURING FY-82:
N/A

NUMBER OF SUBJECTS STUDIED: None

FY-82: Total (to date): N/A Before Completion of Study: 140 patients are to be accrued to this study.

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF ANY SO STATE):
None

CONCLUSIONS: None

PUBLICATIONS OR ABSTRACTS, FY-82:
None

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470 H

DATE: 27 Apr 82 WORK UNIT NO.: 4514 STATUS: INTERIM _____ FINAL xxx

STARTING DATE: 25 June 1974 DATE OF COMPLETION: 23 Feb 1982

KEY WORDS: Indium In-111 DTPA, Cisternogram, CSF Leak, Hydrocephalus

TITLE OF PROJECT: Clinical Evaluation of Indium-111 DTPA

PRINCIPAL INVESTIGATOR(S): DOUGLAS VAN NOSTRAND, M.D. LTC, MC, Asaf Durakovic, M.D. MAJ, MC

ASSOCIATE INVESTIGATOR(S): Richard E. Stotler, LTC MSC, James H. Corley, MAJ, MSC

FACILITY: WRAMC DEPT/SVC: Nuclear Medicine Service

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| ACCUMULATIVE MEDCASE COST: \$0 | ACCUMULATIVE CONTRACT COST: \$0 | ACCUMULATIVE SUPPLY COST: \$0 |
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| FY-81: MEDCASE: \$0 | CONTRACT COST: \$0 | SUPPLY COST: \$0 | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983 |
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STUDY OBJECTIVE: The purpose of this study was to evaluate the efficacy and safety of the radiopharmaceutical In-111 DTPA in the evaluation of cerebral spinal fluid flow.

TECHNICAL APPROACH:
No modifications have been made to the original protocol.

PROGRESS DURING FY-81-82: During the period 1 Oct 81 thru 23 Feb 82, a total of 7 patients were studied.

NUMBER OF SUBJECTS TO BE STUDIED BEFORE COMPLETION OF STUDY: NONE

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT:
NONE

CONCLUSIONS: of the 7 patients studied there were 2 Normals, 2 with Communicating Hydrocephalus, 2 with Normal Pressure Hydrocephalus, and 1 with a blockage of CSF flow. The reason the project is terminated is that Indium-111 DTPA has been approved

PUBLICATIONS OR ABSTRACTS, FY-81: by the U.S. Food and Drug for routine use in cisternography. Effective 24 Feb 82.
None

DISPOSITION FORM

For use of this form, see AR 340-15; the proponent agency is TAGO.

REFERENCE OR OFFICE SYMBOL

HSWP-XN

SUBJECT

Termination of Clinical Investigational Projects

TO C, Clinical Investigation
ATTN: LTC Boehm
WRAMC

FROM C, Nuclear Medicine Svc
WRAMC

DATE 27 April 1982

LTC Stotler/msm/61186

CMT 1

1. The Clinical Investigational Service is notified of termination of three investigational projects.

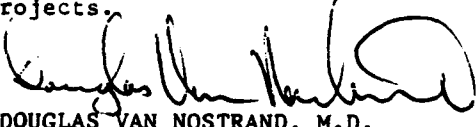
- a. Work unit #4524 - Technetium 99m HIDA for Hepatobiliary Scintigraphy
- b. Work unit #4528 - Technetium 99m Labeled Di-isopropyl-ida (DISIDA) for Hepatobiliary Scintigraphy

Reason: A better IDA analog Tc99m DISIDA (Hepatolite NEN) has received U.S. FDA approval for routine use in diagnosis of hepatobiliary disease.

- c. Work Unit #4514 - Clinical Evaluation of Indium 111 DTPA

Reason: Medi-physics NDA for Indium 111 DTPA received U.S. FDA approval 24 February 1982 for routine use in cisternography.

2. Attached are final reports for all three projects.



DOUGLAS VAN NOSTRAND, M.D.

LTC, MC

C, NUCLEAR MEDICINE SERVICE

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|--|--|-----------------------------|--|
| DATE: FEB 83 | WORK UNIT No.: 4523 | STATUS: INTERIM | FINAL X |
| STARTING DATE: | DATE OF COMPLETION: | | |
| KEY WORDS: | Glomerular Filtration Rate | | |
| TITLE OF PROJECT: | Determination of Glomerular Filtration Rate Using Radiotracer Techniques | | |
| PRINCIPAL INVESTIGATOR(S): | Frank Atkins, Ph.D. | | |
| ASSOCIATE INVESTIGATOR(S): | Douglas Van Nostrand, M.D., LTC, MC | | |
| FACILITY: WRAHC | DEPT/SVC: Nuclear Medicine Service | | |
| ACCUMULATIVE MEDICASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: | |
| FY-83 MEDICASE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
| STUDY OBJECTIVE: | | | |
| NA | | | |
| TECHNICAL APPROACH: | | | |
| NA | | | |
| PROGRESS DURING FY-82: | | | |
| NA | | | |
| NUMBER OF SUBJECTS STUDIED: | | | |
| FY-82: | TOTAL (TO DATE): | BEFORE COMPLETION OF STUDY: | |
| SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): | | | |
| NA | | | |
| CONCLUSIONS: | | | |
| Study terminated without action. | | | |
| PUBLICATIONS OR ABSTRACTS, FY-82: | | | |
| NA | | | |

DATE: 27 April 1982 | WORK UNIT No.: 4524 | STATUS: INTERIM___ FINAL xxx

STARTING DATE: 5 March 1981 | DATE OF COMPLETION: 6 April 1982

KEY WORDS: Technetium Tc-99m HIDA (Hepato-Scan) (Lidofenin) Hepatobiliary Scanning.

TITLE OF PROJECT: Technetium 99m HIDA (N-2,6-Dimethylphenyl Carbamoylmethyl iminodiacetic acid) for Hepatobiliary Scintigraphy.

PRINCIPAL INVESTIGATOR(S): DOUGLAS VAN NOSTRAND, M.D. LTC MC, Asaf Durakovic, M.D. MAJ, MC

ASSOCIATE INVESTIGATOR(S): Richard E. Stotler, LTC, MSC, James H. Corley, MAJ, MSC

FACILITY: WRAMC | DEPT/SVC: NUCLEAR MEDICINE SERVICE

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|-----------------------------------|------------------------------------|----------------------------------|
| ACCUMULATIVE MEDCASE COST: \$0 | ACCUMULATIVE CONTRACT COST: \$0 | ACCUMULATIVE SUPPLY COST: \$0 |
|-----------------------------------|------------------------------------|----------------------------------|

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|---------------------|--------------------|------------------|---|
| FY-82: MEDCASE: \$0 | CONTRACT COST: \$0 | SUPPLY COST: \$0 | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
|---------------------|--------------------|------------------|---|

STUDY OBJECTIVE: clinical evaluation of Tc-99m HIDA as a diagnostic tool in hepatobiliary disease.

TECHNICAL APPROACH: No Modifications were made to the original protocol.

PROGRESS DURING FY-82: 82 During the period 1 Oct 81 thru 6 April 82 a total of 38 patients were studied.

NUMBER OF SUBJECTS TO BE STUDIED BEFORE COMPLETION OF STUDY: NONE

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT: NONE

CONCLUSIONS: Of the 38 patients referred to Nuclear Medicine for this study there were 19 Normals, 5 Hepatocellular Dysfunctions, 4 Chronic Cholecystitis, 3 Acute Cholecystitis, 2 Cystic Duct Obstructions, 1 Indeterminate, 1 Duodenal/Gastric Reflux, and 1 patient refused the study. Project terminated because a better IDA analog

PUBLICATIONS OR ABSTRACTS, FY-82: NONE
Tc-99m DISIDA (Hepatolite NEN) has received U.S. FDA approval for routine use in diagnosis of hepatobiliary disease.

DATE: 6 Oct 82 WORK UNIT NO.: 4525 STATUS: INTERIMXX FINAL
STARTING DATE: 17 Mar 81 DATE OF COMPLETION: 1 Sept 83
KEY WORDS: I 131 6-B Iodomethylnorcholesterol (NP-59, Adrenal Imaging)
TITLE OF PROJECT: Intravenous Administration of 131 I-6-B Iodomethylnorcholesterol (NP-59) for Adrenal Evaluation and Imaging.

PRINCIPAL INVESTIGATOR(S): Douglas Van Nostrand M.D. LTC MC

ASSOCIATE INVESTIGATOR(S): Richard E. Stotler LTC, MSC

FACILITY: WRMC

DEPT/SVC: Nuclear Medicine Service

ACCUMULATIVE MEDICASE COST:
-0-

ACCUMULATIVE CONTRACT COST:
\$ 0

ACCUMULATIVE SUPPLY COST:
\$ 0

FY-83 MEDICASE:
\$ 0

CONTRACT COST:
\$ 0

SUPPLY COST:
\$ 0

DATE OF COMMITTEE APPROVAL OF
ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: Clinical evaluation of NP-59 as a diagnostic agent for the detection of adrenal-cortical disorders.

TECHNICAL APPROACH: As approved by C.I.C. study is now open to patients under the age of 18.

PROGRESS DURING FY-82: 3 patients were studied.

NUMBER OF SUBJECTS STUDIED:

FY-82: 3

TOTAL (TO DATE): 4

BEFORE COMPLETION OF STUDY: 46

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
NONE

CONCLUSIONS: Of the 3 patients studied there was one normal and 2 positives consistent with bilateral adrenal hyperplasia.
The agent is proving to be a useful diagnostic tool.

PUBLICATIONS OR ABSTRACTS, FY-82:
NONE

DATE: 6 Oct 82 | Work UNIT No.: 4527 | STATUS: INTERIM^{XY} FINAL

STARTING DATE: 1 Dec 81 | DATE OF COMPLETION: 1 Dec 84

KEY WORDS: Lymphoscintigraphy, Tc99m Antimony Trisulfide Colloid

TITLE OF PROJECT: Technetium (Tc99m) Antimony Trisulfide Colloid - A Lymphoscintigraphic Agent.

PRINCIPAL INVESTIGATOR(S): R.B. Shaw, MAJ MC

ASSOCIATE INVESTIGATOR(S): Richard E. Stotler LTC, MSC

FACILITY: WRMC

DEPT/SVC: Nuclear Medicine Service

ACCUMULATIVE MEDICASE COST:
\$0

ACCUMULATIVE CONTRACT COST:
\$0

ACCUMULATIVE SUPPLY COST:
\$0

FY-83 MEDICASE: \$0 | CONTRACT COST: \$0 | SUPPLY COST: \$0

DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: Clinical evaluation of Tc99m Antimony Trisulfide Colloid in the anatomical location of the internal mammary lymph nodes in patients with

~~Breast cancer.~~
TECHNICAL APPROACH: One-time exception to perform antimony trisulfide colloid scan to investigate lymphatic drainage from melanoma in the region of the left scapula. (10Aug82)

PROGRESS DURING FY-82: Studied one patient during this period.

NUMBER OF SUBJECTS STUDIED:

FY-82: 1 | TOTAL (TO DATE): 1 | BEFORE COMPLETION OF STUDY: 99

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
NONE

CONCLUSIONS: Agent proved useful in evaluation of lymphatic drainage.

PUBLICATIONS OR ABSTRACTS, FY-82:
NONE

DISPOSITION FORM

For use of this form, see AR 340-15; the proponent agency is TAGO.

REFERENCE OR OFFICE SYMBOL

HSHL-XN

SUBJECT

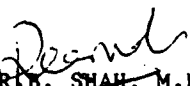
Annual Progress Report - Work Unit #4528

TO Clinical Investigation

FROM Asst C, Nuclear Med Svc DATE 17 SEP 82
MAJ Shah/msm/61186

CMT 1

1. No investigative procedures have been performed under protocol work unit #4528.
2. As of March 1982, this protocol has not been followed as FDA approved the same investigational drug for general use.
3. The protocol work unit #4528 is effectively terminated as of March 1982 following FDA approval for DISIDA in general population.


R.B. SHAH, M.D.

MAJ, MC

Asst C, Nuclear Medicine Service

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DATE: 27 April 82 | WORK UNIT NO.: 4528 | STATUS: INTERIM | FINALXXX

STARTING DATE: | DATE OF COMPLETION: 26 April 1982

KEY WORDS:

TITLE OF PROJECT: Technetium 99m Labeled Di-isopropyl-ida (DISIDA) for Hepatobiliary Scintigraphy

PRINCIPAL INVESTIGATOR(S): R.B. SHAH, MAJ, MC

ASSOCIATE INVESTIGATOR(S):

FACILITY: WRAMC | DEPT/SVC: Nuclear Medicine Service

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|------------------------------|-------------------------------|-----------------------------|
| ACCUMULATIVE MEDCASE COST: 0 | ACCUMULATIVE CONTRACT COST: 0 | ACCUMULATIVE SUPPLY COST: 0 |
|------------------------------|-------------------------------|-----------------------------|

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|-------------------|------------------|----------------|---|
| FY-81: MEDCASE: 0 | CONTRACT COST: 0 | SUPPLY COST: 0 | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983 |
|-------------------|------------------|----------------|---|

STUDY OBJECTIVE: Clinical evaluation of Tc99m DISIDA as a diagnostic tool in hepatobiliary disease.

TECHNICAL APPROACH:

PROGRESS DURING FY-82: The study was never instituted as Tc99m DISIDA (Hepatolite NEN) has received U.S. FDA approval for routine use in diagnosis of hepatobiliary disease.

NUMBER OF SUBJECTS TO BE STUDIED BEFORE COMPLETION OF STUDY: NA

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT: NA

CONCLUSIONS: The study was never instituted as Tc99m DISIDA (Hepatolite NEN) has received U.S. FDA approval for routine use in diagnosis of hepatobiliary disease.

PUBLICATIONS OR ABSTRACTS, FY-82: None

DATE: 6 Oct 82 | WORK UNIT No.: 4529 | STATUS: INTERIM XX Fina:

STARTING DATE: 1 May 82 | DATE OF COMPLETION: 1 May 85

KEY WORDS: Spleen Scintigraphy, Splenic Trauma, Heat damaged Tc RBCs.

TITLE OF PROJECT: Comparison of liver/spleen scintigraphy, selective spleen scintigraphy computer tomography, and ultrasound in the diagnosis of splenic trauma.

PRINCIPAL INVESTIGATOR(S): Douglas Van Nostrand, M.D. LTC MC.

ASSOCIATE INVESTIGATOR(S): Richard E. Stotler LTC, MSC, Ralph Kyle, John Sherman MAJ, MC

FACILITY: WRAVC

DEPT/SVC: Nuclear Medicine Service

Jon M'ellstrup MAJ, MC

ACCUMULATIVE PEDCASE COST:
\$0

ACCUMULATIVE CONTRACT COST:
\$0

ACCUMULATIVE SUPPLY COST:
\$0

FY-83 PEDCASE:
\$0

CONTRACT COST:
\$0

SUPPLY COST:
\$0

DATE OF COMMITTEE APPROVAL OF
ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To determine the sensitivity and specificity of Tc Sulfur Colloid Liver Spleen Scan (LS), Computer tomography (CT), 99mTc heat damaged red blood cell spleen scan (SSS), and ultraasonography (US) in the diagnosis of splenic trauma.

TECHNICAL APPROACH: No changes to original protocol.

PROGRESS DURING FY-82: This is a new protocol and no patients have been studied under it during FY-82.

NUMBER OF SUBJECTS STUDIED:

FY-82: 0

TOTAL (TO DATE): 0

BEFORE COMPLETION OF STUDY: 30

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

N/A None

CONCLUSIONS:

None

PUBLICATIONS OR ABSTRACTS, FY-82:

N/A

| | | | |
|---|----------------------------------|---|--|
| DATE: 1/21/83 | WORK UNIT No.: 4601 | STATUS: INTERIM <input checked="" type="checkbox"/> FINAL | |
| STARTING DATE: 1967 | DATE OF COMPLETION: 1985 | | |
| KEY WORDS: Clinical trial, Hodgkin's, radiotherapy | | | |
| TITLE OF PROJECT: Participation in the National Cooperative Study of Early Hodgkin's Disease | | | |
| PRINCIPAL INVESTIGATOR(S): George B. Hutchison, M. D. Harvard, Boston | | | |
| ASSOCIATE INVESTIGATOR(S): Raymond B. Weiss, M. D. Walter Reed | | | |
| FACILITY: NRCAC | | DEPT/SYC: Hematology-Oncology | |
| ACCUMULATIVE MEDICASE COST: 0 | ACCUMULATIVE CONTRACT COST: 0 | ACCUMULATIVE SUPPLY COST: | |
| FY-83 MEDICASE: 0 | CONTRACT COST: 0 | SUPPLY COST: 0 | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: To determine the effects on survival, disease extension, and complications of therapy of differing irradiation volumes in ~~treatment of early staged Hodgkin's disease.~~

TECHNICAL APPROACH: This clinical trial was randomized and prospective, comparing localized irradiation to clinically involved region with extended field irradiation to clinically involved region plus regions suspected of being sites of sub-clinical

PROGRESS DURING FY-82: Interim report submitted for publication in 1982, undergoing revision in response to reviewers. Paper submitted at meeting of NCI, September, 1981, and published 1982. Extended follow-up to 15 years shows no reduction in mortality.

NUMBER OF SUBJECTS STUDIED: 460

FY-82: no new accessions TOTAL (TO DATE): 460 BEFORE COMPLETION OF STUDY: 460

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): None in current follow-up year.

CONCLUSIONS: To date comparison of localized fields with extended fields of therapy of early Hodgkin's disease has not shown a clear superiority of either technique within 15 years of follow-up.

PUBLICATIONS OR ABSTRACTS. FY-82: Survival and Extension-free survival following involved and extended field therapy of Hodgkin's disease, stages I and II. In preparation.

Fuller, L.M. and Hutchison, G. B. Collaborative clinical trial for Stage I and II Hodgkin's disease: Significance of mediastinal and nonmediastinal disease in laparotomy- and non-laparotomy-staged patients. Cancer Treatment Reports 66: 775-787. 1982.

DATE 29-9-82 | WORK UNIT No.: #4703 | STATUS: INTERIM X FISCAL
STARTING DATE: 1 July 1981 | DATE OF COMPLETION: 1 April 1983
KEY WORDS: Pharynx, swallowing, fluoroscopy, videorecording
TITLE OF PROJECT: Pharyngeal Swallow: Prospective Incidence of Disease

PRINCIPAL INVESTIGATOR(S): David J. Curtis, M.D., Arnold Friedman, M.D.

ASSOCIATE INVESTIGATOR(S): Abraham Dachman, M.D., Eugene Maso, M.D.

FACILITY: IRAMC | DEPT/SVC: Diagnostic Radiology/WRAMC TV

ACCUMULATIVE MEDICARE COST: N.A. | ACCUMULATIVE CONTRACT COST: N.A. | ACCUMULATIVE SUPPLY COST: N.A.

FY-83 MEDICARE: N.A. | CONTRACT COST: N.A. | SUPPLY COST: N.A. | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE:

Determine criteria of normal pharyngeal swallowing by prospective ~~selection~~ of population.

TECHNICAL APPROACH:

Questionnaire of thirty-eight questions filled out prior to ~~videorecording~~ of pharyngeal swallow. Review of swallows.

PROGRESS DURING FY-82:

Computer entry of questionnaires. Review of 200 of 1000 swallows.

NUMBER OF SUBJECTS STUDIED: 819 swallows performed; 227 questionnaires filled out.

FY-82: 87 | TOTAL (TO DATE): 227 | BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
None

CONCLUSIONS: No conclusions have been made in that all data must be generated prior to matching by computer to maintain the prospective nature of the study.

PUBLICATIONS OR ABSTRACTS. FY-82: Laryngeal dynamics, CRC Critical Reviews in Diagnostic Imaging, 18:29-30, May 1982.

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|--|-----------------------------|-----------------------------|--|
| DATE: | WORK UNIT No.: 4704 | STATUS: INTERIM | FINAL XX |
| STARTING DATE: | | DATE OF COMPLETION: | |
| KEY WORDS: | | | |
| TITLE OF PROJECT: ULTRASOUND SCROTAL SCANNING. | | | |
| PRINCIPAL INVESTIGATOR(S): Lynne Blei, MD | | | |
| ASSOCIATE INVESTIGATOR(S): | | | |
| FACILITY: WRAMC | | DEPT/SVC: Dept of Radiology | |
| ACCUMULATIVE MEDICASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: | |
| FY-83 MEDICASE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE:

TECHNICAL APPROACH:

PROGRESS DURING FY-82:

NUMBER OF SUBJECTS STUDIED:

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

CONCLUSIONS:

Dr. Blei is no longer assigned to Dept of Radiology.
She has left WRAMC.

PUBLICATIONS OR ABSTRACTS, FY-82:

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|--|-----------------------------|--------------------------------|--|--|
| DATE: 1 Oct 82 | | WORK UNIT No.: 6021 A | STATUS: INTERIM X FINAL | |
| STARTING DATE: 1 September 1982 | | DATE OF COMPLETION: Sept 1985 | | |
| KEY WORDS: LHRH in Children | | | | |
| TITLE OF PROJECT: Gonadotropin response to LHRH in Children and Adolescents | | | | |
| PRINCIPAL INVESTIGATOR(S): Chandra M. Tiwary, MD, LTC, MC | | | | |
| ASSOCIATE INVESTIGATOR(S): | | | | |
| FACILITY: WRAHC | | DEPT/SVC: Pediatrics | | |
| ACCUMULATIVE MEDICASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: | | |
| Nil | Nil | Nil | | |
| FY-83 MEDICASE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT | |
| \$1,300.00 | \$2,300.00 | | FEB 25 1983 | |
| <u>STUDY OBJECTIVE:</u> To use LHRH as a diagnostic agent in evaluating hypothalamic hypophyseal gonadal axis | | | | |
| <u>TECHNICAL APPROACH:</u> Same as in the protocol | | | | |
| <u>PROGRESS DURING FY-82:</u> Approval to use the LHRH from HSG was not received till the end of August 1982. We used LHRH in two children in September 1982, the lab data is available on one patient | | | | |
| NUMBER OF SUBJECTS STUDIED: | | | | |
| FY-82: 25 | TOTAL (TO DATE): 2 | BEFORE COMPLETION OF STUDY: 75 | | |
| <u>SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):</u> | | | | |
| none | | | | |
| <u>CONCLUSIONS:</u> No conclusion can be drawn, only two patients have been studied and the serum gonadotropin results are available only in one patient. I would like to continue the study. | | | | |
| <u>PUBLICATIONS OR ABSTRACTS, FY-82:</u> NIL | | | | |

DATE: _____ WORK UNIT No.: 6025 STATUS: INTERIM X FINAL

STARTING DATE: _____ DATE OF COMPLETION: _____

KEY WORDS:

TITLE OF PROJECT: Role of surface tension measurement of amniotic fluid lipid extract in prediction of development of RDS in neonates

PRINCIPAL INVESTIGATOR(S): Chandra M. Tiwary, M.D., LTC, MC

ASSOCIATE INVESTIGATOR(S): Richard Landes, M.D., COL, MC

James B. Haddock, M.D., LTC, MC

FACILITY: WRMC

DEPT/SVC: Pediatrics

ACCUMULATIVE MEDCASE COST:

ACCUMULATIVE CONTRACT COST:

ACCUMULATIVE SUPPLY COST:

FY-83 MEDCASE: _____ CONTRACT COST: _____ SUPPLY COST: _____

DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To measure surface tension of amniotic fluid lipid extract prior to and during labor, and to correlate it with the subsequent development of RDS in newborns.

TECHNICAL APPROACH: No Modification

PROGRESS DURING FY-82: Fifteen amniotic fluid specimens have been analyzed. The total number of specimen analyzed to date has been 105.

NUMBER OF SUBJECTS STUDIED:

FY-82: 15 TOTAL (TO DATE): 105 BEFORE COMPLETION OF STUDY: 125

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS: Surface tension of amniotic fluid is useful in predicting the occurrence of RDS in the neonate.

A low ST of the amniotic fluid suggest possible occurrence of a complication in the neonatal period and that infant child should be observed carefully during the first few days.

PUBLICATIONS OR ABSTRACTS, FY-82: NIL

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|---|-----------------------------|--|
| DATE: | WORK UNIT No.: 6026 | STATUS: INTERIM X FISCAL |
| STARTING DATE: | | DATE OF COMPLETION: |
| KEY WORDS: | | |
| TITLE OF PROJECT: Tracheal aspirate surface tension as a prognostic indicator in infants with respiratory distress syndrome (RDS) | | |
| PRINCIPAL INVESTIGATOR(s): Chandra M. Tiwary, M.D., LTC, MC | | |
| ASSOCIATE INVESTIGATOR(s): Richard D. Landes, M.D., COL, MC Doris Burgess, Medical Technologist | | |
| FACILITY: WRAVC | | DEPT/SVC: Pediatrics |
| ACCUMULATIVE FEDCASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
| FY-83 FEDCASE: | CONTRACT COST: | SUPPLY COST: |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE:

TECHNICAL APPROACH:

PROGRESS DURING FY-82: No tracheal aspirate samples were submitted because very few babies required intubation, we have not measured surface tension on any specimen since submission of the last report.

NUMBER OF SUBJECTS STUDIED: 30

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
none

CONCLUSIONS: Our preliminary results were encouraging and we would like to continue the study

PUBLICATIONS OR ABSTRACTS, FY-82:

DATE: NOV 82 WORK UNIT No.: 6030 STATUS: INTERIM FINAL X
STARTING DATE: 22 OCT 79 DATE OF COMPLETION: NOV 82
KEY WORDS: Neutrophil chemotaxis, agarose
TITLE OF PROJECT: Studies of adult and newborn neutrophils under agarose.

PRINCIPAL INVESTIGATOR(S): Paul J. Thomas, MD, LTC MC

ASSOCIATE INVESTIGATOR(S): Doris Burgess, et al

FACILITY: WRAVC

DEPT/SVC: Pediatric Hematology-Oncology

ACCUMULATIVE FECCASE COST:

ACCUMULATIVE CONTRACT COST:

ACCUMULATIVE SUPPLY COST:

FY-83 FECCASE: CONTRACT COST: SUPPLY COST:

DATE OF COMMITTEE APPROVAL OF
ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To study the chemotaxis of adult and newborn neutrophils under agarose according to the technique of Quie, et al and to roughly compare results with the Boyden chamber chemotaxis.

TECHNICAL APPROACH: Chemotaxis using agarose plates and varying the types of chemoattractants and the concentration of neutrophils with electron micrography of the cells undergoing chemotaxis.

PROGRESS DURING FY-82: Additional attempts to get reproducibly reliable results using this technique have been unsuccessful. The technique, has, therefore, been a disappointment.

NUMBER OF SUBJECTS STUDIED: Newborn: 6; Adult: 22

FY-82: NB:1;AD:2 TOTAL (TO DATE): NB:6;AD:22 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT(IF NONE SO STATE): NONE

CONCLUSIONS: This technique, although potentially useful because of the relatively small amount of blood required for the test, has been too unreliable for us to draw any conclusions about it. Our work with other projects has relegated this to low priority and there does not appear to be any good reason to pursue this technique any further. Our recommendation is the closure of this protocol.

PUBLICATIONS OR ABSTRACTS, FY-82: NONE

DATE: 3 JAN 83 WORK UNIT No.: 6032 STATUS: Annual Progress Report
INTERIM 7, FINAL

STARTING DATE: Undetermined DATE OF COMPLETION: 30 June 84

KEY WORDS: Gavage Feeding, Transcutaneous Oxygen, Nasogastric, Orogastric

TITLE OF PROJECT:

Effect of Nasogastric Feeding Tubes on Oxygenation

PRINCIPAL INVESTIGATOR(S): Richard D. Landes, M.D., COL, MC, USA

ASSOCIATE INVESTIGATOR(S): John Nading, M.D., LCDR, MC, USN

FACILITY: WRANIC

DEPT/SVC: Pediatrics

ACCUMULATIVE MEDICASE COST:

ACCUMULATIVE CONTRACT COST:

ACCUMULATIVE SUPPLY COST:

FY-83 MEDICASE: \$18,500.00

CONTRACT COST: 0

SUPPLY COST: \$1,000.00

DATE OF COMMITTEE APPROVAL OF
ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To determine if there is a clinically significant difference in oxygenation during the use of nasogastric versus orogastric gavage tubes.

TECHNICAL APPROACH: Approach is to continuously measure transcutaneous PO₂ to compare the effects on oxygenation of neonates while being fed via nasogastric versus orogastric tubes. Differences in oxygenation between the two feeding methods will be analyzed.

PROGRESS DURING FY-82: The study has not been started to date due to the lack of appropriate hardware to record and analyze continuously recorded data. A request for funding and purchase of the necessary equipment was submitted to Clinical Investigation Service on 4 May 1982.

NUMBER OF SUBJECTS STUDIED:

FY-82: -0-

TOTAL (TO DATE): -0-

BEFORE COMPLETION OF STUDY: Approximately 30

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS: Request John Nading, M.D., LCDR, USN, be added as Co-investigator and that funding be approved so that this study may be completed.

PUBLICATIONS OR ABSTRACTS, FY-82:

None

DATE: 25 Jan 83 | WORK UNIT NO.: 6034 | STATUS: INTERIM XXX FINAL

STARTING DATE: 15 January 1982 | DATE OF COMPLETION: 1 April 1982

KEY WORDS: oral decongestants; oral decongestant-antihistamine mixtures

TITLE OF PROJECT: The effectiveness of Oral Decongestants and Decongestant-antihistamine mixtures in the treatment and prevention of otitis media and secretory otitis media.

PRINCIPAL INVESTIGATOR(S): Peter M. Zawadsky, M.D. LTC(P), MC
Pediatric Infectious Disease Fellow

ASSOCIATE INVESTIGATOR(S):

FACILITY: HRMC | DEPT/SVC: Pediatrics

ACCUMULATIVE FEEDBACK COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST:

FY-83 FEEDBACK: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To determine how widely oral decongestants and decongestant-antihistamine mixtures are used in children with otitis media and secretory otitis media.

TECHNICAL APPROACH: 600 physicians (200 ENT, 200 gen. pediatricians, and 200 family practitioners) were polled by questionnaire to determine how often they use oral decongestants and decongestant-antihistamine mixtures.

PROGRESS DURING FY-82: Questionnaires were mailed. Over three months a total of questionnaires were returned fully answered. Tabulations of results are now being completed.

NUMBER OF SUBJECTS STUDIED:
FY-82: 600 | TOTAL (TO DATE): 600 | BEFORE COMPLETION OF STUDY: ----

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

CONCLUSIONS: A preliminary summary of results indicate a significant number of physicians in each specialty employ decongestants and decongestant-antihistamine mixtures. A prospective clinical research project on the efficacy of these medications is being designed. The preliminary results of the questionnaire will be submitted for publication.

PUBLICATIONS OR ABSTRACTS, FY-82:

AD-A129 243

ANNUAL PROGRESS REPORT FY-82 VOLUME II(U) WALTER REED
ARMY MEDICAL CENTER WASHINGTON DC 1982

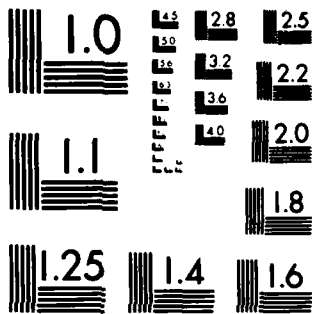
3/4

UNCLASSIFIED

F/G 6/5.

NL

A large grid of 13 columns and 10 rows of blacked-out cells, representing redacted content. The grid is composed of 130 individual cells, all of which are completely blacked out, obscuring any text or data that might have been present. The grid is positioned in the lower two-thirds of the page, below the header information.



MICROCOPY RESOLUTION TEST CHART
NATIONAL BUREAU OF STANDARDS-1963-A

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| DATE: Oct. 82 | WORK UNIT NO.: 6035 | STATUS: INTERIM ^x FINAL |
| STARTING DATE: Oct. 82 | DATE OF COMPLETION: Sept. 83 | |
| KEY WORDS: Group B streptococcal antigen, newborn neutrophil aggregation | | |
| TITLE OF PROJECT: Does Group B Streptococcal Extract Cause Neutrophil Aggregation and Chemotaxis in Adults. | | |
| PRINCIPAL INVESTIGATOR(S): Dr. Thomas Olson | | |
| ASSOCIATE INVESTIGATOR(S): Dr. Paul J. Thomas | | |
| FACILITY: IRAC | DEPT/SVC: Pediatric Hematology/Oncology | |
| ACCUMULATIVE PEDCASE COST: N/A | ACCUMULATIVE CONTRACT COST: N/A | ACCUMULATIVE SUPPLY COST: N/A |
| FY-83 PEDCASE: | CONTRACT COST: | SUPPLY COST: |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: To demonstrate adult neutrophil aggregation and chemotaxis in the presence of a recently isolated extract of group B streptococci

TECHNICAL APPROACH:

See attached page

PROGRESS DURING FY-82:

See attached page

NUMBER OF SUBJECTS STUDIED:

FY-82: 6 TOTAL (TO DATE): 6 BEFORE COMPLETION OF STUDY: 30

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
none

CONCLUSIONS: 1). Group streptococcal extract (from USUHS) can cause chemotaxis of adult PMN'S (further documentation needed), and possible aggregation of adult PMN'S. 2) Further technical time needed.

PUBLICATIONS OR ABSTRACTS, FY-82:

TECHNICAL APPROACH: Group B strepococcal extract is isolated and supplied to us by Dr. Val Hemming from USUHS. Standard concentrations of cells are studied after addition of this agent, in a Sienco Dual Chamber aggregator. Chemotaxis will be done using Boylen chambers and adult PMN'S treated with, and without Group B strepococcal extract.

PROGRESS DURING FY 82: This extract has not been soluble in water / solution. Presently, USUHS is supplying us with a more purified product. There is some evidence that this extract may act as an aggregating agent. It also appears to have chemotactic properties. Further studies with recent purified extract has been seriously limited by lack of technician time (they are involved in other investigational projects). These early results need to be confirmed, as they will add greatly to the significance of this substance, as described by researchers at USUHS. We need further technician time to complete and possibly extend the newborn PMN study.

DATE: OCT 82 WORK UNIT NO.: 6036 STATUS: INTERIM x FIRM:

STARTING DATE: Nov 81 DATE OF COMPLETION: Oct 84

KEY WORDS: Newborn neutrophil, aggregation, chemotaxis

TITLE OF PROJECT: Effects of Lactoferrin on Aggregation and chemotaxis of Newborn Neutrophils.

PRINCIPAL INVESTIGATOR(S): Bruce A. Cook Maj, MC (until 7/82)
Thomas A. Olson, MD, Cpt, MC (after 7/82)
ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: IRVAC Dept/Svc: Pediatric Hematology/Oncology

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| ACCUMULATIVE PECCASE COST: N/A | ACCUMULATIVE CONTRACT COST: N/A | ACCUMULATIVE SUPPLY COST: N/A |
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| FY-83 PECCASE: N/A | CONTRACT COST: N/A | SUPPLY COST: N/A | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983 |
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STUDY OBJECTIVE: To study the effects of Lactoferrin on the chemotactic and aggregating abilities of newborn neutrophils.

TECHNICAL APPROACH: See next page

PROGRESS DURING FY-82: See next page

NUMBER OF SUBJECTS STUDIED:
FY-82: 6 TOTAL (TO DATE): 6 BEFORE COMPLETION OF STUDY: 30

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF ANY, SO STATE):
none

CONCLUSIONS: 1) minimal work has been done due to other protocols and technician
2) Preliminary data indicates that further studies should be done to determine the observed effects on irreversible newborn aggregates 3) study should continue until Oct 84, as one year has been insufficient time to collect data.

PUBLICATIONS OR ABSTRACTS: FY-82:
none

Technical Approach: Using approximately 1×10^7 cells/ml normal adult and newborn neutrophil aggregation will be studied with a Sienco dual channel aggregometer. Lactoferrin will be used at various counterrotations to determine if it will induce aggregation. This will be compared with standard agents such as ZAS and FNLP. In a slight modification, lactoferrin will be added after known aggregating to determine its effect on the irrevversible nature of newborn neutrophil aggregation. Chemotaxis will be studied with lactoferrin using adult and newborn cells in Boyden chamber and difference compared using counts/minutes. Transmission and scanning EM's will be done on the aggregate, also increase number to 30 to do adequate aggregation, 10 to do chemotaxis.

Progress During FY 82:

We have only studied three newborns and adults to date. We do know lactoferrin is in high concentration in neutrophils, and breast milk. Other studies have shown that lactoferrin has a role in augmenting the bacteriacidal effect in conjunction with rabbit PMN'S, but its effect on human neutriphils is not known. In our preliminary results, we do not see lactoferrin as an aggregating agent, but it was able to cause deaggregation^{of} previously unpermeable aggregated newborn P MN'S. This is a phenomenon we have not seen before. As further study, this response is essential because of the need to find agents which will cause the newborn PMN to deaggreate.

Our studies have been seriously delayed because of the lack of technician time. We have to compete with other investigators for her time. Also newborn cells are not readily available. For this reason, we had to delay studying the phenomemenon and we have been unable to do chemotaxis. We will be able to spend more time with this study during FY 83. It would be helpful if we could get authorization for our manpower justification.

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| DATE: 1 Oct 82 | WORK UNIT No.: 6037 | STATUS: INTERIM X | FUND: |
| STARTING DATE: March 1982 | | DATE OF COMPLETION: | |
| KEY WORDS: Diet Obesity Insulin Glucagon | | | |
| TITLE OF PROJECT: Effect of Dietary Modifications on Weight Change in obese Children with Different Insulin Responses to Glucose and Leucine Challenges. | | | |
| PRINCIPAL INVESTIGATOR(S): Chandra M. Tiwary, M.D., LTC, D. Roberts R.N. | | | |
| ASSOCIATE INVESTIGATOR(S): Mary L. Maras RD; Wolfe J. Rinke PhD, RD | | | |
| FACILITY: WRANC X | | DEPT/SVC: Pediatrics | |
| ACCUMULATIVE MEDICARE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: | |
| -0- | 16,625.00 | 600:00 | |
| FY-83 MEDICARE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT |
| -0- | 7000 | 150 | FEB 25 1983 |

Technical Approach: Red cell Nas/K P&T Pase has not been determined because the laboratory technician at the USUHS left. We will try to measure this at the pediatric research laboratory Walter Reed Army Medical Center.

Study Objective: To determine if specific dietary modifications can result in improved weight reduction in certain categories of obese children. To ~~develop a profile for these children by tolerance testing.~~ identifying common characteristics

PROGRESS DURING FY-82: Six patient were tested, two were hyperinsulinemic to both glucose and leucine load, one was hyperinsulinemic to glucose only. Two were on control diet. Two on low sugar, one on low protein diet and ~~remaining one is waiting to be put on a dietary regimen. One girl on low~~

NUMBER OF SUBJECTS STUDIED: sugar diet has completed the study. She lost weight.

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): _____

CONCLUSIONS:

No conclusion can be drawn because of small number of subjects studied.

PUBLICATIONS OR ABSTRACTS, FY-82: _____

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| DATE: OCT 82 | WORK UNIT NO.: 6101 | STATUS: INTERIM X FINAL |
| STARTING DATE: 2 MAY 80 | DATE OF COMPLETION: 83 | |
| KEY WORDS: Acute Lymphocytic Leukemia, Relapse, Extramedullary Sites | | |
| TITLE OF PROJECT: POG #7834, Second Induction and Maintenance in Acute Lymphocytic Leukemia, Phase III (Amended) | | |

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRAMC DEPT/SVC: Pediatric Hematology/Oncology

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| ACCUMULATIVE MEDCARE COST: N/A | ACCUMULATIVE CONTRACT COST: N/A | ACCUMULATIVE SUPPLY COST: N/A |
|-----------------------------------|------------------------------------|----------------------------------|

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| FY-83 MEDCARE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
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STUDY OBJECTIVE: Investigate the effectiveness of multidrug conditions in the re-induction and maintenance of remission in acute lymphocytic leukemia relapses in extramedullary sites.

TECHNICAL APPROACH: Randomized study between two maintenance arms after induction with vincristine, prednisone, and adriamycin. This protocol is used in conjunction with appropriate CNS or extramedullary site radiotherapy protocol.

No WRAMC patients were entered on this protocol.

NUMBER OF SUBJECTS STUDIED:

FY-82: N/A TOTAL (TO DATE): N/A BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS:

Study remains open for extramedullary disease

PUBLICATIONS OR ABSTRACTS, FY-82: None

DATE: OCT 82 WORK UNIT NO.: 6103 STATUS: INTERIM X FUND:

STARTING DATE: 3 MAY 80 DATE OF COMPLETION: 83

KEY WORDS: m-AMSA, acute leukemia (relapse), non-Hodgkin's lymphoma.

TITLE OF PROJECT: POG #7919 Evaluation of m-AMSA in Children with Acute Leukemia and Non-Hodgkin's Lymphoma in Relapse, Phase II.

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRAMC DEPT/SVC: Pediatric Hematology/Oncology

ACCUMULATIVE MEDICASE COST: N/A ACCUMULATIVE CONTRACT COST: N/A ACCUMULATIVE SUPPLY COST: N/A

FY-83 MEDICASE: N/A CONTRACT COST: N/A SUPPLY COST: N/A DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To study the effectiveness of m-AMSA as an inducing agent for acute leukemia and non-Hodgkin's lymphoma in relapse.

TECHNICAL APPROACH: Non-randomized study for non-Hodgkin's lymphoma and for acute non-lymphocytic leukemia; randomized between two different dosage schedules for acute lymphocytic leukemia.

PROGRESS DURING FY-82: One patient entered in FY-81 (one entered in FY 80 also) with transient response of the peripheral counts but no apparent effect on the marrow.

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 TOTAL (TO DATE): 2 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE, SO STATE): None at WRAMC however, reports nationally of severe cardiac arrhythmias with several deaths attributed to this side effect.

CONCLUSIONS: Study remains open with the precaution of cardiac monitoring continually during the administration of the drug and for two hours thereafter along with careful watching of electrolytes, since the arrhythmias may be related to low serum potassium. No patients from WRAMC were entered on this study in FY 82.

PUBLICATIONS OR ABSTRACTS, FY 82: NONE

DATE: OCT 82 WORK UNIT NO.: 6104 STATUS: INTERIM X Final

STARTING DATE: 14 JUL 80 DATE OF COMPLETION: 83

KEY WORDS: Rubidazone, recurrent acute leukemia

TITLE OF PROJECT: POG # 7818 Evaluation of Rubidazone in Children with Acute Lymphoblastic and Acute Myelogenous Leukemia, Phase II

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruyman, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: IRANC DEPT/SVC: Pediatric Hematology/Oncology

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| ACCUMULATIVE MEDICASE COST: N/A | ACCUMULATIVE CONTRACT COST: N/A | ACCUMULATIVE SUPPLY COST: N/A |
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| FY-83 MEDICASE: N/A | CONTRACT COST: N/A | SUPPLY COST: N/A | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
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STUDY OBJECTIVE: To study the effectiveness of Rubidazone in inducing remissions in children with recurrent leukemia.

TECHNICAL APPROACH: Randomized study of two dosage schedules of Rubidazone.

PROGRESS DURING FY-82: One additional patient entered in FY 81 (one in FY 80) with a transient marrow response (acute lymphoblastic leukemia).

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 TOTAL (TO DATE): 2 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE, SO STATE):
NONE

CONCLUSIONS: The study remains open; more patient accrual is needed. Group wide, the drug appears to be effective.

PUBLICATIONS OR ABSTRACTS, FY-82: NONE

DATE: OCT 82 WORK UNIT NO.: 6107 STATUS: INTERIM FUND: X
STARTING DATE: 14 July 80 DATE OF COMPLETION: Nov 81

KEY WORDS: Anguidine, acute leukemia in relapse
TITLE OF PROJECT: POG # 7810 Evaluation of Anguidine in Children with Acute Lymphoblastic and Non-Lymphoblastic Leukemia in Relapse, Phase II.

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: MRANC DEPT/SVC: Pediatric Hematology/Oncology

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| ACCUMULATIVE MEDICARE COST: N/A | ACCUMULATIVE CONTRACT COST: N/A | ACCUMULATIVE SUPPLY COST: N/A |
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| FY-83 MEDICARE: N/A | CONTRACT COST: N/A | SUPPLY COST: N/A | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983 |
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STUDY OBJECTIVE: To study the effectiveness of anguidine in inducing remissions in children with acute leukemia in relapse.

TECHNICAL APPROACH: Non-randomized study of anguidine with dosage modification depending on degree of toxicity.

PROGRESS DURING FY-82: No new patients entered in 1982 (one patient entered in FY 80 with transient response).

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 TOTAL (TO DATE): 1 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
NONE

CONCLUSIONS: The study is closed. Anguidine made no apparent contribution to overall disease-free survival. It may have some use in monocytic leukemia, but the number of patients studied was minimal.

PUBLICATIONS OR ABSTRACTS, FY-82:

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| DATE: OCT 82 | WORK UNIT NO.: 6108 | STATUS: INTERIM | FUND: X |
| STARTING DATE: 24 MAR 80 | DATE OF COMPLETION: 10/21/81 | | |
| KEY WORDS: MOPP, OPP, brain tumors | | | |
| TITLE OF PROJECT: POG # 7621 MOPP versus OPP in the Treatment of Children with Recurrent Brain Tumors, Phase III. | | | |
| PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC | | | |
| ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al | | | |
| FACILITY: WRAMC | | DEPT/SVC: Pediatric Hematology/Oncology | |
| ACCUMULATIVE MEDICASE COST: N/A | ACCUMULATIVE CONTRACT COST: N/A | ACCUMULATIVE SUPPLY COST: N/A | |
| FY-83 MEDICASE: N/A | CONTRACT COST: N/A | SUPPLY COST: N/A | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983 |

STUDY OBJECTIVE: To study the effect of vincristine, prednisone, and procarbazine with or without nitrogen mustard in the treatment of children with recurrent brain tumors.

TECHNICAL APPROACH: Randomized study stratified by tumor type.

PROGRESS DURING FY-82: No WRAMC patients were entered on this study.

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 TOTAL (TO DATE): 0 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
NONE

CONCLUSIONS: The study was closed 10/21/81. The final analysis of data has not been completed.

PUBLICATIONS OR ABSTRACTS, FY-82: Med & Ped. Onc. 4:253, 1978

DATE: OCT 82 Work Unit No.: 6111 STATUS: Interim Final

STARTING DATE: 3 MAR 80 DATE OF COMPLETION: 1983

KEY WORDS: Anguidine, recurrent brain tumors

TITLE OF PROJECT: POG # 7812 Evaluation of Anguidine in the treatment of Central Nervous system Tumors, Phase II.

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRAMC DEPT/SVC: Pediatric Hematology/Oncology

ACCUMULATIVE MEDICASE COST: N/A ACCUMULATIVE CONTRACT COST: N/A ACCUMULATIVE SUPPLY COST: N/A

FY-83 MEDICASE: N/A CONTRACT COST: N/A SUPPLY COST: N/A DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983

STUDY OBJECTIVE: To study the effect of intravenous anguidine given weekly in children with recurrent brain tumors.

TECHNICAL APPROACH: Non-randomized study with dosage adjustments for impaired liver, kidney, and bone marrow function at the time of starting therapy.

PROGRESS DURING FY-82: No WRAMC patients have been entered on this study to date.

NUMBER OF SUBJECTS STUDIED: NA

FY-82: 0 TOTAL (TO DATE): 0 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): NONE

CONCLUSIONS: Study remains open for non-astrocytomas.

PUBLICATIONS OR ABSTRACTS, FY-82: Abstract submitted to ASCO.

DATE: OCT 82 WORK UNIT NO.: 6112 STATUS: INTERIM FUND: X

STARTING DATE: 14 JULY 80 DATE OF COMPLETION: 1982

KEY WORDS: Rubidazone, recurrent solid tumors

TITLE OF PROJECT: POG # 7843 Evaluation of Rubidazone in the Treatment of Children with Solid Tumors, Phase III

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRAMC

DEPT/SVC: Pediatric Hematology/Oncology

ACCUMULATIVE FEDCASE COST:
N/A

ACCUMULATIVE CONTRACT COST:
N/A

ACCUMULATIVE SUPPLY COST:
N/A

FY-83 FEDCASE: N/A CONTRACT COST: N/A SUPPLY COST: N/A

DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT **FEB 25 1983**

STUDY OBJECTIVE: To study the effect of rubidazone on recurrent solid tumors and brain tumors in children.

TECHNICAL APPROACH: Non-randomized study with dosage and adjustments for impaired liver, kidney, and bone marrow function at the time of beginning therapy.

PROGRESS DURING FY-82: No WRAMC patients have been entered on this study.

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 TOTAL (TO DATE): 0 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
NONE

CONCLUSIONS: The study is closed. There was no response to the drug in 15 evaluable patients.

PUBLICATIONS OR ABSTRACTS, FY-82:

NONE

DATE: OCT 82 WORK UNIT NO.: 6115 STATUS: INTERIM X FUND: open ended
STARTING DATE: 21 March 81 DATE OF COMPLETION:

KEY WORDS: Histiocytosis X

TITLE OF PROJECT: POG # 7376 Evaluation of the Natural History of Histiocytosis X.

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRAMC

DEPT/SYC: Pediatric Hematology/Oncology

ACCUMULATIVE MEDICAL COST:
N/A

ACCUMULATIVE CONTRACT COST:
N/A

ACCUMULATIVE SUPPLY COST:
N/A

FY-83 MEDICAL COST:
N/A

CONTRACT COST:
N/A

SUPPLY COST:
N/A

DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To characterize the course of Histiocytosis X in children who have not been previously treated.

TECHNICAL APPROACH: Studies of extent of disease, immunologic competence, effect of disease, and effect of therapy at yearly intervals.

PROGRESS DURING FY-82: No WRAMC patients have been entered on this study.

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 TOTAL (TO DATE): 0 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
NONE

CONCLUSIONS: The study is being revised, in order to collect more data concerning the pathophysiology of the disease.

PUBLICATIONS OR ABSTRACTS, FY-82: Abstract: ASCO C-65, 1976; SPR 1976; SSPR, 1977
ASCO C-335, 1978
Publication: Med. Pediatric Oncology, 8:35-40, 1980, accepted in Cancer 3/17/80, submitted to J. Pediatr. 2/14/80.

DATE: OCT 82 WORK UNIT NO.: 6116 STATUS: INTERIM x FINAL

STARTING DATE: 2 MAR 80 DATE OF COMPLETION: 1983

KEY WORDS: Hodgkin's Disease, Stage III

TITLE OF PROJECT: POG # 7612 MOPP plus Bleomycin and A-COPP with involved Field Radiation Therapy in Stage III Hodgkin's Disease in Children, Phase III.

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRAVC DEPT/SVC: Pediatric Hematology/Oncology

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| ACCUMULATIVE MEDICASE COST: N/A | ACCUMULATIVE CONTRACT COST: N/A | ACCUMULATIVE SUPPLY COST: N/A |
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| FY-83 MEDICASE: N/A | CONTRACT COST: N/A | SUPPLY COST: N/A | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983 |
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STUDY OBJECTIVE: To study the effectiveness of radiation therapy (involved field) after chemotherapy with either MOPP+Bleomycin or A-COPP.

TECHNICAL APPROACH: Randomized study between two chemotherapy regimen MOPP+Bleo (nitrogen mustard, vincristine, prednisone, procarbazine and bleomycin) and A-COPP (Adriamycin, cyclophosphamide, vincristine, prednisone, and procarbazine), followed by standardized radiation therapy, followed by more chemotherapy with the same drugs.

No additional patients have been placed on the study. The two on study remain well.

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 TOTAL (TO DATE): 2 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

NONE

CONCLUSIONS: Study remains open. Group-wide, there does not appear to be any significant differences in the two regimens.

PUBLICATIONS OR ABSTRACTS, FY 82:

NONE

DATE: OCT 82 Work Unit No.: 6117 STATUS: Interim Final

STARTING DATE: 14 July 81 DATE OF COMPLETION: 1983

KEY WORDS: CNS leukemia
TITLE OF PROJECT: POG # 7712 Comparison of Treatment regimens for the First CNS Relapse in Children with Acute Lymphocytic Leukemia, Phase III.

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRMC DEPT/SVC: Pediatric Hematology/Oncology

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| ACCUMULATIVE MEDICINE COST: N/A | ACCUMULATIVE CONTRACT COST: N/A | ACCUMULATIVE SUPPLY COST: N/A |
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| FY-83 MEDICINE: N/A | CONTRACT COST: N/A | SUPPLY COST: N/A | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983 |
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STUDY OBJECTIVE: To study the effectiveness of radiation therapy and intrathecal therapy in the treatment of CNS leukemia; to study the effect of maintenance intrathecal therapy vs. no maintenance in the duration of response.

TECHNICAL APPROACH: After successful therapy with radiation therapy to the skull and intrathecal therapy (methotrexate, hydrocortisone, ARA-C), randomization between: ~~no further therapy~~ vs intrathecal therapy every 8 weeks. Requires systemic re-induction protocol in addition to the CNS therapy.

NO WRMC patients were entered on this study.

NUMBER OF SUBJECTS STUDIED:
FY-82: 0 Total (to date): 0 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
NONE

CONCLUSIONS: Study remains open.

PUBLICATIONS OR ABSTRACTS, FY-82: NONE

DATE: OCT 82 WORK UNIT NO.: 6118 STATUS: INTERIM X FUND:

STARTING DATE: 14 July 80 DATE OF COMPLETION: 83

KEY WORDS: Non-hodgkin's lymphoma

TITLE OF PROJECT: POG #7905 ACOP-plus for Non-Hodgkin's Lymphoma in Children, Phase III.

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRAVC

DEPT/SVC: Pediatric Hematology/Oncology

ACCUMULATIVE MEDICINE COST:
N/A

ACCUMULATIVE CONTRACT COST:
N/A

ACCUMULATIVE SUPPLY COST:
N/A

FY-83 MEDICINE COST: N/A

CONTRACT COST: N/A

SUPPLY COST: N/A

DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To study the effectiveness of radiation therapy plus ACOP-plus chemotherapy vs radiation therapy plus LSA₂-L₂ chemotherapy in inducing and maintaining remissions in childhood non-Hodgkin's lymphomas.

TECHNICAL APPROACH:

Randomized study between the two chemotherapy arms.

PROGRESS DURING FY-82: One patient was entered in FY 82 and is still in induction therapy. The two patients entered in FY 80 are still in remission. The patient entered in FY 82 has since died.

NUMBER OF SUBJECTS STUDIED:

FY-82: 1 TOTAL (TO DATE): 4 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

NONE

CONCLUSIONS: Study remains open

PUBLICATIONS OR ABSTRACTS, FY 82:

NONE

DATE: OCT 82 MONS UNIT NO.: 6119 STATUS: INTERIM X FIRM:
STARTING DATE: 14 July 80 DATE OF COMPLETION: 11 March 81

KEY WORDS: Retinoblastoma, Unilateral

TITLE OF PROJECT: POG # 7796. Adjuvant Chemotherapy for Localized Unilateral Retinoblastoma, Reese-Ellsworth Group 5, Phase III.

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: IRAC

DEPT/SVC: Pediatric Hematology/Oncology

ACCUMULATIVE MEDICINE COST:
N/A

ACCUMULATIVE CONTRACT COST:
N/A

ACCUMULATIVE SUPPLY COST:
N/A

FY-83 MEDICINE COST:
N/A

CONTRACT COST:
N/A

SUPPLY COST:
N/A

DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983

STUDY OBJECTIVE: To study the effectiveness of chemotherapy vs no chemotherapy after enucleation of unilateral retinoblastoma, Reese-Ellsworth Group 5.

TECHNICAL APPROACH: Randomized study between chemotherapy with vincristine and cyclophosphamide vs. no chemotherapy.

PROGRESS DURING FY-82: There have been no new patients on this study. The patient entered in FY 81 has had no sign of the retinoblastoma with the chemotherapy.

NUMBER OF SUBJECTS STUDIED:

FY-82: 0

TOTAL (TO DATE): 1

BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

NONE

CONCLUSIONS: Study was closed by the group because of slow accrual from two groups (approximately 120 treating institutions).

PUBLICATIONS OR ABSTRACTS, FY 82:
NONE

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| DATE: OCT 82 | WORK UNIT NO.: 6120 | STATUS: INTERIM X | FINAL |
| STARTING DATE: 14 July 80 | | DATE OF COMPLETION: 1983 | |
| KEY WORDS: T-cell ALL | | | |
| TITLE OF PROJECT: POG #7837 Evaluation of systemic Therapy for Children with T-cell Acute Lymphocytic Leukemia, Phase III. | | | |
| PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC | | | |
| ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al | | | |
| FACILITY: WRAMC | | DEPT/SYC: Pediatric Hematology/Oncology | |
| ACCUMULATIVE FEDCASE COST: N/A | ACCUMULATIVE CONTRACT COST: N/A | ACCUMULATIVE SUPPLY COST: N/A | |
| FY-83 FEDCASE: N/A | CONTRACT COST: N/A | SUPPLY COST: N/A | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: To evaluate two different methods of chemotherapy for the treatment of T-cell leukemia.

TECHNICAL APPROACH: Randomized study between the "Duke" regimen and POG-modified LSA₂-L₂ regimen. Basically, the "Duke" protocol is a more intense modification of the usual ALL protocol; the LSA₂-L₂ a modified version of Sloan-Kettering's Progress During FY-82: lymphoma protocol.

There have been no patients entered on this study at WRAMC in FY 82. Four ~~patients have been entered in the past. One failed induction and was taken off study.~~
NUMBER OF SUBJECTS STUDIED: Three patients remain in remission.

FY-82: 0 TOTAL (TO DATE): 4 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE, SA STATE):
 The "Duke" arm of the study was closed in FY 81, due to the high rate of testicular relapses.

CONCLUSIONS: Study remains open as a non-randomized study using the L₂ arm only with modification to include cranial radiation because of the higher number of CNS relapses on this arm.

PUBLICATIONS OR ABSTRACTS, FY-82:

Pilot Data: Clinical Res. Vol. 27 #5. Abstract A 815, 1979, Clin. Res.

DATE: OCT 82 WORK UNIT NO.: 6121 STATUS: INTERIM X FID#
STARTING DATE: 4 Feb 80 DATE OF COMPLETION: On-going register
KEY WORDS: Rare Tumors, Childhood
TITLE OF PROJECT: POG # 7799 Rare Tumor Registry

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRAMC DEPT/SVC: Pediatric Hematology/Oncology

ACCUMULATIVE MEDICARE COST: N/A ACCUMULATIVE CONTRACT COST: N/A ACCUMULATIVE SUPPLY COST: N/A

FY-83 MEDICARE: N/A CONTRACT COST: N/A SUPPLY COST: N/A DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983

STUDY OBJECTIVE: To accumulate data on unusual, uncommon, infrequent, and rare tumors of childhood.

TECHNICAL APPROACH: Registry with pathology review of patients with rare tumors with annual reporting on status of patient.

PROGRESS DURING FY-82: One patient with synovial cell sarcoma was entered on this protocol in FY 81. There were no new patients at WRAMC in FY 82.

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 TOTAL (TO DATE): 1 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

NONE

CONCLUSIONS: Registry remains open, studies of certain tumors are being planned using data from the registry.

PUBLICATIONS OR ABSTRACTS, FY-82: NONE

DATE: OCT 82 WORK UNIT NO.: 6122 STATUS: INTERIM FUND: X

STARTING DATE: 14 July 80 DATE OF COMPLETION: 1982

KEY WORDS: CNS Leukemia

TITLE OF PROJECT: POC # 7829 A Comparison of Two Dose Regimens of Intrathecal Methotrexate for Treatment of CNS Leukemia, Phase II.

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRAMC Dept/Svc: Pediatric Hematology/Oncology

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| ACCUMULATIVE MEDICASE COST: N/A | ACCUMULATIVE CONTRACT COST: N/A | ACCUMULATIVE SUPPLY COST: N/A |
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| FY-83 MEDICASE: N/A | CONTRACT COST: N/A | SUPPLY COST: N/A | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
|------------------------|-----------------------|---------------------|---|

STUDY OBJECTIVE: To evaluate the effectiveness and toxicity of two dose methotrexate dosages given intrathecally for the treatment of CNS leukemia.

TECHNICAL APPROACH: Randomized study between standard dose methotrexate and low dose methotrexate given intrathecally for the treatment of CNS leukemia.

PROGRESS DURING FY-82: No WRAMC patients were entered on this study in FY 81.

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 TOTAL (TO DATE): 0 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
NONE

CONCLUSIONS: The study is closed. The accrual rate for patients was very small. The induction rate on low dose vs high dose methotrexate is fairly equal. More research will be done in this area.

PUBLICATIONS OR ABSTRACTS, FY-82:

NONE

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|----------------------------|--------------------------|-------------------|-------|
| DATE: OCT 82 | WORK UNIT No.: 6123 | STATUS: INTERIM X | FIND: |
| STARTING DATE: 24 March 80 | DATE OF COMPLETION: 1981 | | |

KEY WORDS: Acute Lymphocytic Leukemia

TITLE OF PROJECT: POG # 7623 Evaluation of Systemic Regimens in the Treatment of Acute Leukemia of Childhood (ALinC 12)

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRAMC

DEPT/SVC: Pediatric Hematology/Oncology

ACCUMULATIVE MEDICINE COST:
N/A

ACCUMULATIVE CONTRACT COST:
N/A

ACCUMULATIVE SUPPLY COST:
N/A

FY-83 MEDICINE COST:
N/A

CONTRACT COST:
N/A

SUPPLY COST:
N/A

DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To investigate more intensive therapy vs less intensive therapy in the treatment of standard risk and high risk acute lymphocytic leukemia, non-T, non-B.

TECHNICAL APPROACH: Randomized study between three treatment regimens with variation in the intensiveness of therapy in the maintenance.

PROGRESS DURING FY-82:

There were no patients from WRAMC put on this study in FY 82. There have been eight patients put on this study in the past three years. One of the patients relapsed, the others achieved a satisfactory remission.

FY-82: 0

TOTAL (TO DATE): 8

BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
NONE

CONCLUSIONS: Study closed in 1981 with the activation of the next generation protocol (ALinC 13). Patients will continue to be followed on this protocol.

PUBLICATIONS OR ABSTRACTS, FY 82:

Monographs in Pediatric Hematology-Oncology (in press)

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| DATE: OCT 82 | WORK UNIT NO.: 6124 | STATUS: INTERIM X Final |
| STARTING DATE: 24 March 80 | DATE OF COMPLETION: 1983 | |
| KEY WORDS: Wilm's Tumor | | |
| TITLE OF PROJECT: POG #8000 The National Wilm's Tumor Study | | |
| PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC | | |
| ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al | | |
| FACILITY: MAFIC | DEPT/SVC: Pediatric Hematology/Oncology | |
| ACCUMULATIVE MEDICARE COST: N/A | ACCUMULATIVE CONTRACT COST: N/A | ACCUMULATIVE SUPPLY COST: N/A |
| FY-83 MEDICARE: N/A | CONTRACT COST: N/A | SUPPLY COST: N/A |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983 |

STUDY OBJECTIVE: To study the therapy of different stage and histology of Wilm's Tumor using surgery, radiation therapy, and chemotherapy.

TECHNICAL APPROACH: Randomized study by stage (I-IV) and histology (favorable or unfavorable). Randomization between two chemotherapy regimens and two radiation therapy dosages except for Stage IV and all stages of unfavorable histology, all of which

PROGRESS DURING FY-82: are treated with maximal radiation therapy and chemotherapy. Four new patients were treated in FY 82. Four are in remission, and the fifth is still in induction therapy. Five patients treated earlier remain disease free.

NUMBER OF SUBJECTS STUDIED:

FY-82: 5 TOTAL (TO DATE): 10 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
NONE

CONCLUSIONS:

The study remains open.

ABSTRACT: or Abstracts, FY 82:

Epidemiologic features of Wilm's tumor. JNCI, March 1982, Breslow and Beckwith
PUBLICATION:
 "Biology and Management of Wilm's Tumor". Cancer in the Young, Levine.

DATE: OCT 82 MON. UNIT NO.: 6125 STATUS: INTERIM FINAL

STARTING DATE: 18 Sept 80 DATE OF COMPLETION: 1983

KEY WORDS: Medulloblastoma, Ependymoma

TITLE OF PROJECT: POG # 7909 Evaluation of MOPP Adjuvant Chemotherapy in the Treatment of Localized Medulloblastoma and Ependymoma, Phase III.

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, NC et al

FACILITY: WRAMC DEPT/SVC: Pediatric Hematology/Oncology

ACCUMULATIVE MEDICINE COST: N/A ACCUMULATIVE CONTRACT COST: N/A ACCUMULATIVE SUPPLY COST: N/A

FY-83 MEDICINE: N/A CONTRACT COST: N/A SUPPLY COST: N/A DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983

STUDY OBJECTIVE: To evaluate radiation therapy alone versus radiation therapy plus chemotherapy with 4 drugs (MOPP) in the treatment of localized medulloblastoma and ependymoma.

TECHNICAL APPROACH: Randomized study between radiation therapy with, and radiation therapy without chemotherapy with MOPP. A non randomized arm has been closed.

PROGRESS DURING FY-82: One patient from WRAMC was entered on this study in FY 82. Patient had a severe reaction to Procarbazine, and was removed from study at the parents request.

NUMBER OF SUBJECTS STUDIED:

FY-82: 1 TOTAL (TO DATE): 1 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

The MOPP courses occasionally result in moderate myelosuppression. This has been reduced by dropping the dose of nitrogen mustard from 6 mg/m² to 3 mg/m²

CONCLUSIONS:

The study remains open.

PUBLICATIONS OR ABSTRACTS, FY 82:

NONE

DATE: OCT 82 WORK UNIT NO.: 6126 STATUS: INTERIM X FINAL
STARTING DATE: 14 July 80 DATE OF COMPLETION: March 1981
KEY WORDS: Retinoblastoma, extra-ocular
TITLE OF PROJECT: POG # 7994 Therapy for Extra-ocular retinoblastoma with Cyclophosphamide, Vincristine, Adriamycin, and irradiation. Phase III.

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: IRANC DEPT/SVC: Pediatric Hematology/Oncology

ACCUMULATIVE PEDCASE COST: N/A ACCUMULATIVE CONTRACT COST: N/A ACCUMULATIVE SUPPLY COST: N/A

FY-83 PEDCASE: N/A CONTRACT COST: N/A SUPPLY COST: N/A DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To study the effect of chemotherapy and irradiation in the treatment of extra-ocular retinoblastoma by class and degree and type of spread.

TECHNICAL APPROACH: Non-randomized study with treatment specified for each class of extra-ocular retinoblastoma.

PROGRESS DURING FY-82: The patient entered in FY 80 continues to be disease free. No new patients have been entered on this study. The study is closed because of inadequate accrual of patients (group wide).

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 TOTAL (TO DATE): 1 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
NONE

CONCLUSIONS: Study is closed; however, the patient will be continued to be followed for long term follow-up.

PUBLICATIONS OR ABSTRACTS, FY-82:

NONE

DATE: OCT 82 WORK UNIT NO.: 6128 STATUS: INTERIM X FINAL

STARTING DATE: 16 May 80 DATE OF COMPLETION: 1983

KEY WORDS: Extra-medullary Leukemia

TITLE OF PROJECT: POG # 7901 Rescue Therapy for Non-CNS Extra-medullary Disease in Children with Acute Lymphoblastic Leukemia. Phase III.

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: MRFMC DEPT/SVC: Pediatric Hematology/Oncology

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| ACCUMULATIVE MEDICASE COST: N/A | ACCUMULATIVE CONTRACT COST: N/A | ACCUMULATIVE SUPPLY COST: N/A |
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| FY-83 MEDICASE: N/A | CONTRACT COST: N/A | SUPPLY COST: N/A | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
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STUDY OBJECTIVE: To determine the effectiveness of radiation therapy to local areas of extra-medullary, non-CNS leukemia.

TECHNICAL APPROACH: Non-randomized study using specified amounts of radiation therapy for extra-medullary sites of leukemia relapse. Requires concurrent systemic chemotherapy.

PROGRESS DURING FY-82: One patient previously entered in FY80. No new patients entered on this study in FY 82.

NUMBER OF SUBJECTS STUDIED:
FY-82: 0 TOTAL (TO DATE): 1 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
NONE

CONCLUSIONS: Study remains open with apparent reasonable success of therapy reported by the group.

PUBLICATIONS OR ABSTRACTS, FY-82:
none

DATE: OCT 82 WORK UNIT No.: 6130 STATUS: INTERIM FINAL X
STARTING DATE: 22 Oct 80 DATE OF COMPLETION: 1981

KEY WORDS: Neuroblastoma

TITLE OF PROJECT: POG # 8002 Combination Chemotherapy with Adriamycin Cis-diamminedichloroplatinum, Vincristine, and Cytosin in Children with Metastatic Neuroblastoma, Stage IV.

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRAMC

DEPT/SVC: Pediatric Hematology/Oncology

ACCUMULATIVE MEDICAL COST:
N/A

ACCUMULATIVE CONTRACT COST:
N/A

ACCUMULATIVE SUPPLY COST:
N/A

FY-83 MEDICAL COST:
N/A

CONTRACT COST:
N/A

SUPPLY COST:
N/A

DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To study the effectiveness of intensive multidrug chemotherapy on stage IV neuroblastoma.

TECHNICAL APPROACH: Non-randomized study using four drug chemotherapy regimen devised by investigators at Washington University, St. Louis, MO.

PROGRESS DURING FY-82: No WRAMC patients were entered on this study in FY 82.

NUMBER OF SUBJECTS STUDIED:

FY-82: 0

TOTAL (TO DATE): 0

BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
NONE

CONCLUSIONS: The study has been closed due to an adequate accrual of patients.

PUBLICATIONS OR ABSTRACTS, FY-82:

Manuscript submitted to Cancer Treatment Reports 5/19/82.

DATE: OCT 82 WORK UNIT NO.: 6131 STATUS: INTERIM FISCAL

STARTING DATE: 1 OCT 80 DATE OF COMPLETION: 1983

KEY WORDS: Immune Complexes, circulating

TITLE OF PROJECT: POG # 8075 Circulating immune Complexes in Pediatric Malignancies.

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruyman, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRAMC DEPT/SVC: Pediatric Hematology/Oncology

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| ACCUMULATIVE MEDICASE COST: N/A | ACCUMULATIVE CONTRACT COST: N/A | ACCUMULATIVE SUPPLY COST: N/A |
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| FY-83 MEDICASE: N/A | CONTRACT COST: N/A | SUPPLY COST: N/A | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
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STUDY OBJECTIVE: To measure the levels of circulating immune complexes in the serum of patients with leukemia, neuroblastoma, and osteosarcoma, before, during, and after therapy.

TECHNICAL APPROACH: Serum from patients sent to reference laboratory for detection of circulating immune complexes. Levels of the circulating immune complexes will be correlated with the course of the disease.

PROGRESS DURING FY-82: No WRAMC patients have been entered on this study.

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 TOTAL (TO DATE): 0 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
NONE

CONCLUSIONS: Adequate accrual has been achieved with caucasians with acute lymphocytic leukemia. The study remains open for all others. Note: It has been shown that 60% of stage IV (D) NB patients exhibited significant elevation of CIC.

PUBLICATIONS OR ABSTRACTS, FY-82:

NONE

DATE: OCT 82 WORK UNIT No.: 6132 STATUS: INTERIM FISCAL X

STARTING DATE: 81 DATE OF COMPLETION: 2/17/82

KEY WORDS: Medulloblastoma, Ependymoma

TITLE OF PROJECT: POG # 8016 PCNU in Recurrent Childhood Medulloblastoma and Ependymoma

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruyman, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRAMC

DEPT/SVC: Pediatric Hematology/Oncology

ACCUMULATIVE RECOURSE COST:
N/A

ACCUMULATIVE CONTRACT COST:
N/A

ACCUMULATIVE SUPPLY COST:
N/A

FY-83 RECOURSE: N/A CONTRACT COST: N/A SUPPLY COST: N/A

DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To study the effectiveness of the investigational agent PCNU on childhood medulloblastomas and ependymomas.

TECHNICAL APPROACH: Phase II drug study of PCNU with provisions for dosage modification or escalation depending on response/toxicity.

PROGRESS DURING FY-82: No new WRAMC patients were entered on this study in FY 82.

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 TOTAL (TO DATE): 0 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
None reported by Group.

CONCLUSIONS: The study is closed. There have been no documented responses to PCNU. Of the 12 evaluable patients on this study, none showed any decrease in the size of the tumor. All 12 patients evaluated for toxicity developed thrombocytopenia. In 8 patients the platlet count dropped below 50, 000/mm³. A final report has not been completed on this study.

PUBLICATIONS OR ABSTRACTS, FY-82:

NONE

DATE: OCT 82 WORK UNIT No.: 6133 STATUS: INTERIM X FINAL

STARTING DATE: 1981 DATE OF COMPLETION: 1983

KEY WORDS: Pediatric Tumors, m-AMSA

TITLE OF PROJECT: POG # 8018 Evaluation of m-AMSA in Children with Solid Tumors, Phase II.

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRAMC DEPT/SVC: Pediatric Hematology/Oncology

ACCUMULATIVE MEDICASE COST: N/A ACCUMULATIVE CONTRACT COST: N/A ACCUMULATIVE SUPPLY COST: N/A

FY-83 MEDICASE: N/A CONTRACT COST: N/A SUPPLY COST: N/A DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To study the effectiveness of the investigational agent m-AMSA in recurrent solid tumors of childhood which are resistant to standard forms of therapy.

TECHNICAL APPROACH: Non-randomized phase II study of the drug m-AMSA in recurrent childhood tumors with stratification by tumor type, and with provisions for dose modification.

PROGRESS DURING FY-82: No WRAMC patients were entered on this study in FY 82. In FY 81, the dosage was escalated because of evidence of easy tolerability and greater effectivity of higher dosages.

NUMBER OF SUBJECTS STUDIED:
FY-82: 0 TOTAL (TO DATE): 0 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): The significant toxicity has been cardiac arrhythmias which necessitate cardiac monitoring during and after the administration of the drug.

CONCLUSIONS: The study will be closed shortly. All available data indicates that m-AMSA has some activity in neuroblastoma, but no complete responses were achieved at a severely myelotoxic dose. The drug may also be active in Histiocytosis X. Final analysis will be done after the study is closed.

PUBLICATIONS OR ABSTRACTS, FY-82: ABSTRACT: Civin C.I., Land V.J., Nitschke R., Kamen B.A., and Vats I.S.: m-AMSA Methanesulfon-m-Anisidine, 4-(9-Acridinylamino) 24992 Activity in Pediatric Solid Tumors. Proc. Am. Soc. Clin. Oncol. 1: 178, 1982.

DATE: OCT 82 WORK UNIT NO.: 6134 STATUS: INTERIM X FINAL

STARTING DATE: 1981 DATE OF COMPLETION: 1983

KEY WORDS: Methyl-GAG, Acute Leukemia, Lymphoma

TITLE OF PROJECT: POG # 8021 Evaluation of Methyl-GAG in Children with ANLL Lymphoma, and ALL in Relapse, Phase II

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: IRANC DEPT/SVC: Pediatric Hematology/Oncology

ACCUMULATIVE MEDICASE COST:
N/A

ACCUMULATIVE CONTRACT COST:
N/A

ACCUMULATIVE SUPPLY COST:
N/A

FY-83 MEDICASE: N/A CONTRACT COST: N/A SUPPLY COST: N/A

DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To study the effectiveness of the investigational drug Methyl-GAG in the treatment of recurrent acute non-lymphocytic leukemia, lymphoma, and acute lymphocytic leukemia unresponsive to standard therapy.

TECHNICAL APPROACH: Non-randomized phase II drug study of methyl-GAG with provisions for dosage modification depending on response or toxicity.

PROGRESS DURING FY-82: One patient was placed on the study in FY 81, but there was no response to the treatment. There have been no new patients placed on the study in FY 82.

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 TOTAL (TO DATE): 1 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): NONE

CONCLUSIONS: The study remains open.

PUBLICATIONS OR ABSTRACTS, FY-82:

NONE

DATE: OCT 82 WORK UNIT No.: 6135 STATUS: INTERIM X FISCAL

STARTING DATE: 1981 DATE OF COMPLETION: 1983

KEY WORDS: Vindesine, Lymphoid Malignancies

TITLE OF PROJECT: POG # 8022 Evaluation of 1,2,4,6 Desacetyl Vinblastine (Vindesine) Twice weekly plus Prednisone and a Cross Over Study of Vindesine-Prednisone vs. Vincristine-Prednisone in Children with Lymphoid Malignancies, Phase II and III.

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruyman, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRANC

DEPT/SVC: Pediatric Hematology/Oncology

ACCUMULATIVE MEDICASE COST:
N/A

ACCUMULATIVE CONTRACT COST:
N/A

ACCUMULATIVE SUPPLY COST:
N/A

FY-83 MEDICASE:
N/A

CONTRACT COST:
N/A

SUPPLY COST:
N/A

DATE OF COMMITTEE APPROVAL OF
ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: Study of the effectiveness of vindesine in the reinduction of remission in lymphoid malignancies and comparison of vindesine with vincristine in inducing such a remission.

TECHNICAL APPROACH: Randomized study between vindesine-prednisone and vincristine-prednisone in treating relapse lymphoid malignancies with built in cross-over if induction fails.

PROGRESS DURING FY-82: There were no patients entered on this study in FY 82

NUMBER OF SUBJECTS STUDIED:

FY-82: 0

TOTAL (TO DATE): 1

BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
NONE

CONCLUSIONS: The response to vindesine and vincristine in the non-vincristine resistant group seems to be identical. Vincristine resistant group demonstrates about 33% response (CR+PR) to vincristine/prednisone. Enough patients have been accrued in this arm and therefore the patient entry in this treatment has been closed by the Group.

PUBLICATIONS OR ABSTRACTS. FY-82:

Cancer 47(12):2789-2792, 1981

DATE: OCT 82 WORK UNIT No.: 6136 STATUS: INTERIM FINAL

STARTING DATE: 1981 DATE OF COMPLETION: 1983

KEY WORDS: HLA typing, Malignancy

TITLE OF PROJECT: POG # 8079 HLA Antigen Phenotype

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRAMC DEPT/SVC: Pediatric Hematology/Oncology

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| ACCUMULATIVE MEDICASE COST: N/A | ACCUMULATIVE CONTRACT COST: N/A | ACCUMULATIVE SUPPLY COST: N/A |
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|------------------------|-----------------------|---------------------|---|
| FY-83 MEDICASE: N/A | CONTRACT COST: N/A | SUPPLY COST: N/A | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
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STUDY OBJECTIVE: To study the HLA phenotypes of pediatric patients with acute leukemia and neuroblastoma in order to establish a correlation if any, between HLA type and malignancy.

TECHNICAL APPROACH: Study of HLA types of patients with malignancies. Abcillary study.

PROGRESS DURING FY-82:
No WRAMC patients were entered on this study in FY 82.

NUMBER OF SUBJECTS STUDIED:
FY-82: 0 TOTAL (TO DATE): 0 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

NONE

CONCLUSIONS: Adequate accrual of caucasian patients with ALL, the rest are still eligible for entry on study. Black children with certain factor B and C4 phenotypes appear to be genetically predisposed to ALL, according to the preliminary results of this study. Preliminary analysis for white ALL disclosed an excess of HLA A₂. The coordinators are awaiting further follow-up before analyzing clinical characteristics and disease outcome data.

PUBLICATIONS OR ABSTRACTS, FY-82:

Abstract: Black Children With Certain Factor B and C4 Phenotypes are genetically Predisposed to ALL. B. Budowle, J. Dearth, P. Bowman, R. Go, W. Crist, R. Acton. The University of Alabama in Birmingham, St. Jude Children's Research Hospital and the Pediatric Oncology Group, Birmingham, AL, Memphis, TN, St. Louis, MO.

DATE: OCT 82 WORK UNIT NO.: 6137 STATUS: INTERIM X FINAL

STARTING DATE: 1981 DATE OF COMPLETION: 1983

KEY WORDS: Ewing's Sarcoma, Metastatic

TITLE OF PROJECT: POG # 8095 Intergroup Metastatic Ewing's Sarcoma

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRAMC

DEPT/SVC: Pediatric Hematology/Oncology

ACCUMULATIVE MEDICARE COST:
N/A

ACCUMULATIVE CONTRACT COST:
N/A

ACCUMULATIVE SUPPLY COST:
N/A

FY-83 MEDICARE: N/A CONTRACT COST: N/A SUPPLY COST: N/A

DATE OF COMMITTEE APPROVAL OF
ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To study the effectiveness of uniform approach of surgery, radiation therapy, and five drug intensive chemotherapy on metastatic Ewing's sarcoma.

TECHNICAL APPROACH: Non-randomized study of intensive approach to metastatic Ewing's sarcoma.

PROGRESS DURING FY-82:

No patients from WRAMC were entered on this study in FY 82.

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 TOTAL (TO DATE): 0 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
NONE

CONCLUSIONS:

Study remains open.

PUBLICATIONS OR ABSTRACTS, FY-82:

NONE

DATE: OCT 82 WORK UNIT NO.: 6139 STATUS: INTERIM X FINAL

STARTING DATE: Oct 81 DATE OF COMPLETION: 1984

KEY WORDS: Acute Lymphoid Leukemia

TITLE OF PROJECT: POG # 8035/36 Laboratory Subclassification and Evaluation of Treatment Regimens in Acute Lymphoid Leukemia of Childhood

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRAMC DEPT/SVC: Pediatric Hematology/Oncology

ACCUMULATIVE MEDICARE COST: N/A ACCUMULATIVE CONTRACT COST: N/A ACCUMULATIVE SUPPLY COST: N/A

FY-83 MEDICARE: N/A CONTRACT COST: N/A SUPPLY COST: N/A DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: The study is divided into two parts. Part I attempts to organize a subgroup classification of ALL at the time of diagnosis. Part II is the treatment portion of the protocol; utilizes 3 regimens. Results are compared, and ~~Technical Approach~~ related to subgroup classification in Part I (T-ALL, B-ALL not eligible). Various laboratory methods used in Part I. 3 regimens used in Part II. The first 8 weeks of treatment are the same in all regimens. Beginning on ~~week 9, the chemotherapy agent changes.~~

PROGRESS DURING FY-82:

One patient was entered on this study from WRAMC in FY 82, and remains in remission.

NUMBER OF SUBJECTS STUDIED:

FY-82: 1 TOTAL (TO DATE): 1 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
NONE

CONCLUSIONS:

The study remains open.

PUBLICATIONS OR ABSTRACTS, FY-82:

NONE

DATE: OCT 82 WORK UNIT NO.: 6140 STATUS: Interim x Final
STARTING DATE: OCT 81 DATE OF COMPLETION: 1985
KEY WORDS: Histiocytosis X, bone
TITLE OF PROJECT: POG # 8047. Histiocytosis X in Bone

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRAMC Dept/Svc: Pediatric Hematology/Oncology

ACCUMULATIVE MEDICASE COST: N/A ACCUMULATIVE CONTRACT COST: N/A ACCUMULATIVE SUPPLY COST: N/A

FY-83 MEDICASE: N/A CONTRACT COST: N/A SUPPLY COST: N/A DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983

STUDY OBJECTIVE: To determine incidence of complete resolution after surgical excision or biopsy; to determine role of radiation therapy, and to determine natural history of the disease.

TECHNICAL APPROACH: Surgery to remove as much of the histiocytosis as possible; randomized dose of radiation therapy. (This is a two arm study during the radiation phase only)

PROGRESS DURING FY-82:

There have been no patients from WRAMC entered on this study in FY 82

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 TOTAL (TO DATE): 0 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

NONE

CONCLUSIONS:

The study is still open.

PUBLICATIONS OR ABSTRACTS: 1984:

NONE

DATE: OCT 82 WORK UNIT NO.: 6141 STATUS: INTERIM X FINAL

STARTING DATE: Dec 81 DATE OF COMPLETION: 1985

KEY WORDS: Acute nonlymphocytic leukemia (ANLL)

TITLE OF PROJECT: POG # 8101 Acute Nonlymphocytic Leukemia (ANLL) in Children Phase III.

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRAMC

DEPT/SVC: Pediatric Hematology/Oncology

ACCUMULATIVE MEDICARE COST:
N/A

ACCUMULATIVE CONTRACT COST:
N/A

ACCUMULATIVE SUPPLY COST:
N/A

FY-83 MEDICARE: N/A CONTRACT COST: N/A SUPPLY COST: N/A

DATE OF COMMITTEE APPROVAL OF
ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To determine the effect of remission rate and duration and toxicity, with an intensive 3-drug regimen + an anthracycline free induction regimen. To accumulate clinical and laboratory data; gain more information on ANLL.

TECHNICAL APPROACH: This is a randomized study in two parts, with the induction chemotherapy being randomized, and later the maintenance chemotherapy is randomized.

PROGRESS DURING FY-82:

One patient from WRAMC was entered on this study in FY 82. She is now on maintenance chemotherapy, and remains disease free.

NUMBER OF SUBJECTS STUDIED:

FY-82: 1 TOTAL (TO DATE): 1 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

NONE

CONCLUSIONS:

The study remains open.

PUBLICATIONS OR ABSTRACTS, FY-82:

NONE

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| DATE: Oct 82 | WORK UNIT No.: 6142 | STATUS: INTERIM X FISCAL |
| STARTING DATE: 1981 | DATE OF COMPLETION: March 1983 | |
| KEY WORDS: Neutrophil aggregation, amphotericin-B | | |
| TITLE OF PROJECT: Studies of Neutrophil Aggregation by Amphotericin-B | | |

PRINCIPAL INVESTIGATOR(S): Cook, Bruce A. et al

ASSOCIATE INVESTIGATOR(S): Thomas, Olson, Ruymann

FACILITY: WRANC DEPT/SVC: Pediatric Hematology/Oncology

ACCUMULATIVE MEDICARE COST: ACCUMULATIVE CONTRACT COST: ACCUMULATIVE SUPPLY COST:

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| FY-83 MEDICARE: N/A | CONTRACT COST: N/A | SUPPLY COST: N/A | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983 |
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STUDY OBJECTIVE: To study the aggregation-production ability of Amphotericin-B using adult volunteer neutrophils

TECHNICAL APPROACH: Using our current method of investigation of neutrophil aggregation (aggregometer), study the effect of amphotericin-B on neutrophil aggregation.

PROGRESS DURING FY-82: Using our technique of centrifugal separation of the neutrophils from blood, adult neutrophils from 20 healthy adults were exposed to amphotericin-B as an aggregating agent. (see conclusions)

NUMBER OF SUBJECTS STUDIED:

FY-82: 20 TOTAL (TO DATE): 20 BEFORE COMPLETION OF STUDY: 0-5

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

NONE

CONCLUSIONS: Amphotericin-B in our testing situation was not found to be an aggregating agent. However, it was discovered that by pre-incubating the neutrophils with amphotericin-B, subsequent aggregation using our standard aggregating agents produced irreversible aggregation of the neutrophils. Several more aggregation experiments may need to be run in order to have the results ready for publication.

PUBLICATIONS OR ABSTRACTS, FY-82: Cook BA, Olson TA, Burgess DP, Bailey WR, Thomas PJ, Ruymann FB: In-vitro irreversible aggregation of Amphotericin-B pretreated polymorphonuclear leukocytes: a possible mechanism for pulmonary toxicity. Presented as an Ogden Bruton Award Finalist paper at the Uniformed Services Pediatric Seminar, March, 1982.

DATE: OCT 82 WORK UNIT No.: 6143 STATUS: INTERIM X FINAL

STARTING DATE: Feb 82 DATE OF COMPLETION: 1983

KEY WORDS: Rhabdomyosarcoma

TITLE OF PROJECT: POG # 8157 Multi-agent Chemotherapy with Adjuvant Whole Body Irradiation in Half-body Increments in Patients with Clinical Group IV Rhabdomyosarcoma.

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRAMC DEPT/SVC: Pediatric Hematology/Oncology

ACCUMULATIVE MEDICASE COST: N/A ACCUMULATIVE CONTRACT COST: N/A ACCUMULATIVE SUPPLY COST: N/A

FY-83 MEDICASE: N/A CONTRACT COST: N/A SUPPLY COST: N/A DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983

STUDY OBJECTIVE: To establish the efficacy and safety of integrated systemic irradiation and multi-agent chemotherapy in patients with advanced rhabdomyosarcoma.

TECHNICAL APPROACH: Autologous bone marrow re-infusions are done on patients after chemotherapy.

PROGRESS DURING FY-82: One patient was entered on the study from WRAMC in FY 82. He is in remissions having completed HBI and autologous bone marrow infusion 4/1/82. WRAMC, Johns Hopkins, Emory Medical College of VA, WA university, M.D. Anderson Hospital, are participants.
NUMBER OF SUBJECTS STUDIED:

FY-82: 1 TOTAL (TO DATE): 1 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): NONE

CONCLUSIONS:

Improved accrual of patients is needed to complete observations. The study is still open.

PUBLICATIONS OR ABSTRACTS, FY-82:

NONE

DATE: OCT 82 Work Unit No.: 6144 STATUS: INTERIM X FINAL
STARTING DATE: Jan 26, 1982 DATE OF COMPLETION: 1986
KEY WORDS: Wilm's Tumor
TITLE OF PROJECT: POG # 8158, NWTs Long Term Follow-up Study

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: IRAMC DEPT/SVC: Pediatric Hematology/Oncology

ACCUMULATIVE MEDICARE COST: N/A ACCUMULATIVE CONTRACT COST: N/A ACCUMULATIVE SUPPLY COST: N/A

FY-83 MEDICARE: N/A CONTRACT COST: N/A SUPPLY COST: N/A DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983

STUDY OBJECTIVE: To gather epidemiological and late effects data on Wilm's tumor patients.

TECHNICAL APPROACH: Data on patients sent to coordinator in order to evaluate effects of therapy.

PROGRESS DURING FY-82:

No patients were entered on this study in FY 82

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 TOTAL (TO DATE): 0 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
NONE

CONCLUSIONS:

The study remains open.

PUBLICATIONS OR ABSTRACTS, FY-82:

NONE

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| DATE: OCT 82 | WORK UNIT No.: 6145 | STATUS: <u>INTERIM</u> <u>FINAL</u> |
| STARTING DATE: Jan 26, 1982 | DATE OF COMPLETION: 1984 | |

KEY WORDS: Advanced, acute lymphocytic Leukemia

TITLE OF PROJECT: POG # 8155 Determination of Qualitative and Quantitative Toxicity of L-Alanosine in Children with Solid Tumors and Acute Leukemia; Phase I, Evaluation of Response and Further Determination of Toxicity in Children with Advanced Acute Lymphocytic Leukemia, Phase II.

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRAMC

DEPT/SVC: Pediatric Hematology/Oncology

ACCUMULATIVE MEDICASE COST:
N/A

ACCUMULATIVE CONTRACT COST:
N/A

ACCUMULATIVE SUPPLY COST:
N/A

FY-83 MEDICASE:
N/A

CONTRACT COST:
N/A

SUPPLY COST:
N/A

DATE OF COMMITTEE APPROVAL OF
ANNUAL PROGRESS REPORT **FEB 25 1983**

STUDY OBJECTIVE: To determine the maximum tolerated doses, and toxicity of L-Alanosine in patients with acute lymphocytic leukemia, in relapse.

TECHNICAL APPROACH: Investigate dose levels of L-ALANOSINE in order to evaluate the optimum level of chemotherapy to be administered, and it's effectiveness against the tumor. This is a Phase I and Phase II study.

PROGRESS DURING FY-82: No WRAMC patients were entered on this study in FY 82.

NUMBER OF SUBJECTS STUDIED:

FY-82: 0

TOTAL (TO DATE): 0

BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
NONE

CONCLUSIONS:

Study remains open. Patient accession is very slow.

PUBLICATIONS OR ABSTRACTS, FY-82:

NONE

DATE: OCT 82 WORK UNIT No.: 6146 STATUS: INTERIM X FINAL

STARTING DATE: Feb 1982 DATE OF COMPLETION: 1984

KEY WORDS: Solid tumors, mitoxatrone

TITLE OF PROJECT: POG 8139 Evaluation of Response and Toxicity of Dihydroxyanthracenedione (Mitoxantrone) in Children with Solid Tumors unresponsive to Standard Therapy (Phase II).

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRAMC DEPT/SVC: Pediatric Hematology/Oncology

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| ACCUMULATIVE MEDICASE COST: N/A | ACCUMULATIVE CONTRACT COST: N/A | ACCUMULATIVE SUPPLY COST: N/A |
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| FY-83 MEDICASE: N/A | CONTRACT COST: N/A | SUPPLY COST: N/A | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
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STUDY OBJECTIVE: To determine the toxicity, response rate and duration of response of dihydroxyanthracenedione in children with advanced malignant disease.

TECHNICAL APPROACH: Non randomized study of the effectiveness of a relatively new drug.

PROGRESS DURING FY-82:
No WRAMC were entered on this study in FY 82

NUMBER OF SUBJECTS STUDIED:
FY-82: 0 TOTAL (TO DATE): 0 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
NONE

CONCLUSIONS:
The study remains open.

PUBLICATIONS OR ABSTRACTS, FY-82:
NONE

DATE: OCT 82 Work Unit No.: 6147 STATUS: INTERIM ^X FINAL

STARTING DATE: Feb 82 DATE OF COMPLETION: 1985

KEY WORDS: Advanced, Acute Leukemia, mitoxantrone
TITLE OF PROJECT: POG #8067 Evaluation of Response and Toxicity of Mitoxantrone
in Children with Advanced Acute Leukemia Resistant to Standard Therapy.

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRAMC DEPT/SVC: Pediatric Hematology/Oncology

ACCUMULATIVE MEDICASE COST: N/A ACCUMULATIVE CONTRACT COST: N/A ACCUMULATIVE SUPPLY COST: N/A

FY-83 MEDICASE: N/A CONTRACT COST: N/A SUPPLY COST: N/A DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To determine response rate, duration of response, and toxicity of two different regimens of mitoxantrone in children with acute leukemia.

TECHNICAL APPROACH: Randomized study between two treatment regimens.

PROGRESS DURING FY-82:

No WRAMC patients were entered on this study in FY 1982

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 TOTAL (TO DATE): 0 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

CONCLUSIONS:

The study is still open. The protocol has been amended so that there would be no randomization for patients with ANLL.

PUBLICATIONS OR ABSTRACTS, FY-82:

NONE

DATE: OCT 82 WORK UNIT NO.: 6148 STATUS: INTERIM X FINAL

STARTING DATE: May 1982 DATE OF COMPLETION: 1984

KEY WORDS: Neuroblastoma, age and stage

TITLE OF PROJECT: POG # 8104 Comprehensive Care of the Child with Neuro-blastoma:
A Stage and Age Oriented Study, Phase III

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRAMC

DEPT/SVC: Pediatric Hematology/Oncology

ACCUMULATIVE MEDICASE COST:
N/A

ACCUMULATIVE CONTRACT COST:
N/A

ACCUMULATIVE SUPPLY COST:
N/A

FY-83 MEDICASE:
N/A

CONTRACT COST:
N/A

SUPPLY COST:
N/A

DATE OF COMMITTEE APPROVAL OF
ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To prospectively evaluate the prognostic impact of stage, using a surgical, pathological staging system.

TECHNICAL APPROACH: Patients are treated with a variety of therapies, according to their age, and the stage of the disease.

PROGRESS DURING FY-82: One patient from WRAMC was placed on the study in FY 82. He is now in remission, and feeling well.

NUMBER OF SUBJECTS STUDIED:

FY-82: 1

TOTAL (TO DATE): 0

BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
NONE

CONCLUSIONS:

Study is still open.

PUBLICATIONS OR ABSTRACTS, FY-82:

NONE

DATE: OCT 82 MOOS COST NO.: 6149 STATUS: INTERIM X FUND:
STARTING DATE: April/May 1982 DATE OF COMPLETION: 1985
KEY WORDS: Cis-platinum, Recurrent brain tumor
TITLE OF PROJECT: POG # 8140 Cis-platinum in Recurrent Brain Tumors, Phase II

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRAMC

DEPT/SVC: Pediatric Hematology/Oncology

ACCUMULATIVE MEDICINE COST:
N/A

ACCUMULATIVE CONTRACT COST:
N/A

ACCUMULATIVE SUPPLY COST:
N/A

FY-83 MEDICINE COST: N/A

CONTRACT COST: N/A

SUPPLY COST: N/A

DATE OF COMMITTEE APPROVAL OF
ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To study anti-tumor activity and establish toxicity of Cis-platinum in recurrent and advanced brain tumor patients.

TECHNICAL APPROACH: Non randomized study using Cis-platinum in the treatment of recurrent brain tumor; developed by Oklahoma Children's Memorial Hospital.

PROGRESS DURING FY-82: One patient was entered on this study from WRAMC in FY 1982. Patient developed a severe reaction, and was removed from the study.

NUMBER OF SUBJECTS STUDIED:

FY-82: 1

TOTAL (TO DATE): 1

BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
Suspected severe reaction to Cis-platinum in one patient at WRAMC

CONCLUSIONS:

The study is still open

PUBLICATIONS OR ABSTRACTS, FY-82:

NONE

DATE: OCT 82 WORK UNIT NO.: 6150 STATUS: INTERIM X FINAL
STARTING DATE: June 1982 DATE OF COMPLETION: 1985
KEY WORDS: Costs, cancer
TITLE OF PROJECT: Non Medical Costs of Childhood Cancer at WRAMC

PRINCIPAL INVESTIGATOR(S): Martha C. Lupo, CPT ANC

ASSOCIATE INVESTIGATOR(S):

FACILITY: WRAMC DEPT/SVC: Pediatric Hematology/Oncology

ACCUMULATIVE MEDICARE COST: ACCUMULATIVE CONTRACT COST: ACCUMULATIVE SUPPLY COST:

FY-83 MEDICARE: CONTRACT COST: SUPPLY COST: DATE OF COMMITTEE APPROVAL OF
N/A N/A N/A ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To identify the average monthly non medical cost incurred by parents of children with cancer, during the initial hospitalization period, and during the first month of OP care.

TECHNICAL APPROACH: Parents of cancer patients fill out questionnaire on expenses incurred during this time period.

PROGRESS DURING FY-82:

There have been no patients from WRAMC entered on this study from WRAMC in FY 82

NUMBER OF SUBJECTS STUDIED:

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
NONE

CONCLUSIONS:

The study is still open.

PUBLICATIONS OR ABSTRACTS, FY-82:
NONE

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| DATE: | Work Unit No.: 6151 | STATUS: INTERIM <input checked="" type="checkbox"/> FINAL |
| STARTING DATE: 15 July 1982 | DATE OF COMPLETION: September 1983 | |
| KEY WORDS: Memory, hydration | | |
| TITLE OF PROJECT: Effect of hydration status on short term memory | | |

PRINCIPAL INVESTIGATOR(S): Chandra M. Tiwary

ASSOCIATE INVESTIGATOR(S):

FACILITY: IRMHC DEPT/SVC: Pediatric

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| ACCUMULATIVE PFCASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
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| FY-83 PFCASE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT |
| | 3086 | | FEB 25 1983 |

STUDY OBJECTIVE: If short term memory is influenced by hydration status of the subject. If a correlation exists between the plasme vasopressin level and short term memory function.

TECHNICAL APPROACH:
No change

PROGRESS DURING FY-82: 8 subjects completed both part of the study two completed only one part of the study.

NUMBER OF SUBJECTS STUDIED:

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

CONCLUSIONS: Differences in various aspect of short term memory function are seen between the dehydrated and hydreated state. We do not know if the differences are statistically significant, results are encouraging and more subject should be studied.

PUBLICATIONS OR ABSTRACTS, FY-82: NIL

DATE: OCT 82 WORK UNIT No.: 6152 STATUS: INTERIM X Final

STARTING DATE: AUG 1982 DATE OF COMPLETION: 1985

KEY WORDS: Non-lymphoblastic lymphoma
TITLE OF PROJECT: FOG # 8106 High Dose Cyclophosphamide-High Dose Methotrexate
With Coordinated Triple Intrathecal Therapy for Stages III & IV Non Lymphoblastic
Lymphoma.

PRINCIPAL INVESTIGATOR(S): Frederick B. Ruymann, MD, COL, MC

ASSOCIATE INVESTIGATOR(S): Paul J. Thomas, MD, LTC, MC et al

FACILITY: WRAMC Dept/Svc: Pediatric Hematology/Oncology

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| ACCUMULATIVE MEDICASE COST: N/A | ACCUMULATIVE CONTRACT COST: N/A | ACCUMULATIVE SUPPLY COST: N/A |
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| FY-83 MEDICASE: N/A | CONTRACT COST: N/A | SUPPLY COST: N/A | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
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STUDY OBJECTIVE: To determine remission rates, remission lengths and survival rate for children, on a high-dose intensive chemotherapy. Study will document toxicity and complications of chemotherapy, and analyze for the influence of histologic ~~and complications of chemotherapy, and analyze for the influence of histologic~~ TECHNICAL APPROACH: subclassification (e.g. Burkitt vs non-Burkitt) and immunophenotype, on outcome.

Preventive Chemotherapy is given at the same time as conventional chemotherapy is
PROGRESS DURING FY-82: given, on this non-randomized study.

There have been no patients from WRAMC registered on this study in FY 82.

NUMBER OF SUBJECTS STUDIED:
FY-82: 0 TOTAL (TO DATE): 0 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
NONE

CONCLUSIONS:
The study is still open.

PUBLICATIONS OR ABSTRACTS, FY-82:
NONE

| | | |
|---|-----------------------------|--|
| DATE: 24/9/82 | WORK UNIT NO.: 7113 | STATUS: INTERIM X FINAL |
| STARTING DATE: Jan '82 | DATE OF COMPLETION: | |
| KEY WORDS: Interferon, ALS, Motor Neuron Disease | | |
| TITLE OF PROJECT: Interferon Therapy in ALS - A Pilot Study | | |
| PRINCIPAL INVESTIGATOR(S): Andres M. Salazar | | |
| ASSOCIATE INVESTIGATOR(S): | | |
| FACILITY: HRMC | DEPT/SVC: Neurology | |
| ACCUMULATIVE MEDICASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
| FY-83 MEDICASE: | CONTRACT COST: | SUPPLY COST: |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: 1) To determine the tolerance and safety of intrathecally administered interferon. 2) to determine its therapeutic efficacy in ALS.

TECHNICAL APPROACH: Weekly and then monthly intralumbar administration of nterferon to ALS patients.

PROGRESS DURING FY-82: No patient has yet been treated under this protocol due to unforeseen delays in delivery. Application for IND exemption has just been resubmitted to the FDA, and we expect to start the first patient in the next 30-60 days.

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 TOTAL (TO DATE): 0 BEFORE COMPLETION OF STUDY: 10

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
NONE

CONCLUSIONS: NONE

PUBLICATIONS OR ABSTRACTS, FY-82:

NONE

| | | |
|--|--------------------------------|--|
| DATE: 24/9/82 | Work Unit No.: 7114 | STATUS: INTERIM X FINAL |
| STARTING DATE: July, 1982 | DATE OF COMPLETION: July, 1984 | |
| KEY WORDS: Interferon, Poly-ICLC, Multiple Sclerosis | | |
| TITLE OF PROJECT: Poly-ICLC in the treatment of Multiple Sclerosis | | |
| PRINCIPAL INVESTIGATOR(S): Andres M. Salazar, COL, MC | | |
| ASSOCIATE INVESTIGATOR(S): Blaise Ferraracio, MD | | |
| FACILITY: WRAMC | DEPT/SVC: Neurology | |
| ACCUMULATIVE MEDICASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
| FY-83 MEDICASE: | CONTRACT COST: | SUPPLY COST: |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: To determine: 1) the safety of intravenously administered Poly ICLC in Chronic multiple sclerosis patients. 2) The therapeutic efficacy of Poly-ICLC in MS.

TECHNICAL APPROACH: Poly-ICLC is administered intravenously on a weekly basis for ten or more treatments to patients with chronic MS.

PROGRESS DURING FY-82: Five patients with chronic MS are currently under treatment.

NUMBER OF SUBJECTS STUDIED:

FY-82: 5 TOTAL (TO DATE): 5 BEFORE COMPLETION OF STUDY: 12

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): One patient died unexpectedly with massive pulmonary emboli; no relation to drug is suspected. (see disposition form submitted at time of occurrence.)

CONCLUSIONS:

No final conclusions to date, but Poly-ICLC appears to be safe in MS patients. Transient worsening of MS signs with fever is seen as expected in some patients. Two patients appeared to have improvement of their neurologic signs.

PUBLICATIONS OR ABSTRACTS, FY-82:

NONE

| | | |
|---|----------------------------------|--|
| DATE: 1/27/83 | WORK UNIT No.: 7116 | STATUS: INTERIM <input checked="" type="checkbox"/> FINAL |
| STARTING DATE: | | DATE OF COMPLETION: |
| KEY WORDS: | | |
| TITLE OF PROJECT: TREATMENT OF ACUTE INFLAMMATORY POLY NEUROPATHY WITH PLASMA EXCHANGE. | | |
| PRINCIPAL INVESTIGATOR(S): Preston C. Calvert, CPT, MC, USAR | | |
| ASSOCIATE INVESTIGATOR(S): Joan Kumar, MAJ, MC, USAR | | |
| FACILITY: WRMC | DEPT/SVC: Neurology/Pathology | |
| ACCUMULATIVE MEDICASE COST: 0 | ACCUMULATIVE CONTRACT COST: 0 | ACCUMULATIVE SUPPLY COST: 0 |
| FY-83 MEDICASE: | CONTRACT COST: | SUPPLY COST: |
| | 0 | 0 |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: Evaluation of plasmapheresis therapy of Guillain-Barre's syndrome.

TECHNICAL APPROACH: Multicenter randomized, controlled therapeutic trial.

PROGRESS DURING FY-82: Continued acquisition of patients toward study-wide goal.

NUMBER OF SUBJECTS STUDIED:

FY-82: 2 TOTAL (TO DATE): 4 BEFORE COMPLETION OF STUDY 10

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS:

Study in progress.

PUBLICATIONS OR ABSTRACTS, FY-82:

None

| | | |
|---|-------------------------------|--|
| DATE: 10/1/82 | WORK UNIT No.: 7117 | STATUS: INTERIM X FINAL |
| STARTING DATE: 1 Jul 82 | DATE OF COMPLETION: 1 Jul 83 | |
| KEY WORDS: Cholinergic Mechanism, Brain Stem Auditory Evoked Potential | | |
| TITLE OF PROJECT: Investigation of Cholinergic Transmission in Brain Stem's auditory system by observing changes of brain stem auditory evoked potentials in patients receiving high doses of Artane. | | |
| PRINCIPAL INVESTIGATOR(S): | Bahman Jabbari, M.D. LTC, MC | |
| | Carl H. Gunderson M.D. COL MC | |
| ASSOCIATE INVESTIGATOR(S): | Michelle Filling COL MC | |
| FACILITY: WRANC Evoke Lab | DEPT/SVC: Neurology | |
| ACCUMULATIVE PECCASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
| 0 | 0 | 0 |
| FY-83 PECCASE: | CONTRACT COST: | SUPPLY COST: |
| | | |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: To determine if a cholinergic neuro-transmitter transmits auditory signals in the brain stem.

TECHNICAL APPROACH: Patients on high doses of Artane are tested by Auditory Evoked Potentials before and during treatment. Changes of Latency and Morphology of waves are recorded.

PROGRESS DURING FY-82: One patient was treated before, while taking 20 mg. and while taking 40 mg of Artane daily. All Baep waves were slightly delayed at 40 mg daily dose but their interpeak latency did not change.

NUMBER OF SUBJECTS STUDIED:

FY-82: 1 TOTAL (TO DATE): 1 BEFORE COMPLETION OF STUDY: 4

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None.

CONCLUSIONS: On this single patient, absence of any interpeak latency change suggests that auditory signals in brain stem are not conveyed through a simple cholinergic neurotransmitter. Mild delay of all waves suggest a cholinergic mechanism at middle ear or cochlear level.

PUBLICATIONS OR ABSTRACTS, FY-82:

None.

| | | |
|--------------------------|-------------------------------|----------------------------|
| DATE: 1/28/83 | WORK UNIT No.: 7221 | STATUS: INTERIM XXXX FINAL |
| STARTING DATE: June 1980 | DATE OF COMPLETION: June 1983 | |

KEY WORDS:

TITLE OF PROJECT: The Effect of Hypnotic Intervention on the Electroencephalogram of Low, Medium and High Hypnotic Patients

PRINCIPAL INVESTIGATOR(S): Harold J. Wain, PhD

ASSOCIATE INVESTIGATOR(S): Glenn Harper, MD
Bahaman Jabbari, MD

FACILITY: WRAMC DEPT/SVC: Dept of Psychiatry
Neurology Svc

| | | |
|-----------------------------|-----------------------------|---------------------------|
| ACCUMULATIVE MEDICARE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
|-----------------------------|-----------------------------|---------------------------|

| | | | |
|-----------------|----------------|--------------|--|
| FY-83 MEDICARE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
|-----------------|----------------|--------------|--|

STUDY OBJECTIVE: To explore the effects of hypnotic intervention on the encephalographic tracings of low, medium and high hypnotic capacity patients before, during, and after the induction of a hypnotic trance.

TECHNICAL APPROACH: Each subject is to be evaluated for their hypnotic capacity. The subjects and then placed in low, medium and high hypnotic groupings. EEG recordings are then taken on one occasion before, during and after the induction of a hypnotic state.

PROGRESS DURING FY-82: Nine (9) subjects (3 more than in 1980) have been evaluated as of this date.

NUMBER OF SUBJECTS STUDIED:

| | | |
|----------|--------------------|--------------------------------|
| FY-82: 2 | TOTAL (TO DATE): 9 | BEFORE COMPLETION OF STUDY: 12 |
|----------|--------------------|--------------------------------|

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
None

CONCLUSIONS:

None at this time.

PUBLICATIONS OR ABSTRACTS, FY-82:
None.

DATE: 8 OCT 82 | WORK UNIT NO.: 7222 | STATUS: INTERIM X FINAL

STARTING DATE: 15 AUG 81 | DATE OF COMPLETION: 1 FEB 82

KEY WORDS: Schizophrenia, Rorschach

TITLE OF PROJECT: The Analyses of Thought Processes Using the Rorschach

PRINCIPAL INVESTIGATOR(S): Lawrence E. Klusman, Ph.D., CPT, MSC

ASSOCIATE INVESTIGATOR(S): Susan Colligan, LT, MSC, (USN)

FACILITY: WRAMC | DEPT/SVC: Psychology Service, Dept of Psychiatry

| ACCUMULATIVE MEDICASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
|-----------------------------|-----------------------------|---------------------------|
| 0 | 0 | 0 |

| FY-83 MEDICASE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT |
|-----------------|----------------|--------------|--|
| | | | FEB 25 1983 |

STUDY OBJECTIVE:

To determine the stage of impaired thought process in schizophrenics.

TECHNICAL APPROACH:

Time-restricted exposure of the Rorschach stimuli to schizophrenic subjects.

PROGRESS DURING FY-82:

All data collected and analyzed. Published as Ph.D. dissertation.

NUMBER OF SUBJECTS STUDIED:

FY-82: 36 | TOTAL (TO DATE): 36 | BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

NONE

CONCLUSIONS:

To be determined; final report to be submitted by 1 JAN 83.

PUBLICATIONS OR ABSTRACTS, FY-82:

Publication in journal form pending.

| | | |
|---|--|---|
| DATE: 10/82 | WORK UNIT NO.: 7223 | STATUS: <u>INTERIM</u> FINAL |
| STARTING DATE: August 1981 | DATE OF COMPLETION: Ongoing until 60 patients have been entered into study | |
| KEY WORDS: Extrapyramidal Syndromes | | |
| TITLE OF PROJECT: Incidence of Neuroleptic-Induced Extrapyramidal Syndromes in a Double-Blind Study Using Anticholinergic Prophylaxis | | |
| PRINCIPAL INVESTIGATOR(S): Antonio Blanco, MD, CPT, MC | | |
| ASSOCIATE INVESTIGATOR(S): Jon A. Shaw, MD, COL, MC Ralph Synakowski, LTC, ANC | | |
| FACILITY: WRAMC | DEPT/SVC: Psychiatry | |
| ACCUMULATIVE MEDICINE COST: NA | ACCUMULATIVE CONTRACT COST: NA | ACCUMULATIVE SUPPLY COST: |
| FY-83 MEDICINE COST: NA | CONTRACT COST: NA | SUPPLY COST: NA |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983 |

STUDY OBJECTIVE: To determine incidence of neuroleptic-induced extrapyramidal syndromes in patients treated with a high vs. a low potency neuroleptic agent and whether the prophylactic use of an anticholinergic agent significantly

TECHNICAL APPROACH: Sixty (60) patients will be evaluated at time of admission and during first 21 days of neuroleptic therapy. At the time of initiating the neuroleptic, the patient will be entered into a double-blind anticholinergic-placebo

PROGRESS DURING FY-82:

Due to change in principal and associate investigators, the study was re-started in July 1982.

NUMBER OF SUBJECTS STUDIED:

FY-82: 6 TOTAL (TO DATE): 6 BEFORE COMPLETION OF STUDY: 60

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
No serious/unexpected side effects.

CONCLUSIONS:

NA

PUBLICATIONS OR ABSTRACTS, FY-82:

None

Work Unit: 7223

Title: Incidence of Neuroleptic-Induced Extrapyramidal Syndromes in a Double-Blind Study Using Anticholinergic Prophylaxis.

STUDY OBJECTIVE: (Continued)
modifies the incidence.

TECHNICAL APPROACH: (Continued)
regimen on a twice a day dosage schedule in addition to the neuroleptic medication. Extrapyramidal reactions, if any, will be treated appropriately. After 21 days of treatment, the code will be broken. Evaluation of the patients for any movement disorders will be conducted twice a week during the study period using a standardized rating scale for extrapyramidal symptoms.

| | | | |
|--|-----------------------------|--|--|
| DATE: 8 OCT 82 | WORK UNIT No.: 7224 | STATUS: INTERIM | FISCAL X |
| STARTING DATE: | | DATE OF COMPLETION: May 30, 1982 | |
| KEY WORDS: Luria-Nebraska Neuropsychological Battery Slide Version | | | |
| TITLE OF PROJECT: | | | |
| A Comparison of Slide and Card Formats for the Luria-Nebraska Neuropsychological Battery | | | |
| PRINCIPAL INVESTIGATOR(S): Francis J. Fishburne, Ph.D., Chief, Psychology Service | | | |
| ASSOCIATE INVESTIGATOR(S): Mr. Kevin Parry | | | |
| FACILITY: IRMVC | | DEPT/SVC: Psychology Service, Dept of Psychiatry | |
| ACCUMULATIVE PECCASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: | |
| 0 | 0 | 0 | |
| FY-83 PECCASE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT |
| 0 | 0 | 0 | FEB 25 1983 |

STUDY OBJECTIVE:

To compare a slide format for presentation of the Luria-Nebraska neuropsychological TECHNICAL APPROACH: battery to the standard card format.
 The stimulus cards of the Luria-Nebraska were converted to 2 x 2 slides which are presented on a Kodak audio viewer.

PROGRESS DURING FY-82:

Ten subjects were presented the material in a counter-balanced design.
 NUMBER OF SUBJECTS STUDIED:
 FY-82: 10 TOTAL (TO DATE): 10 BEFORE COMPLETION OF STUDY: 10

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
 NONE

CONCLUSIONS:

There are no significant differences between a slide and card version of the Luria-Nebraska Neuropsychological Test Battery.

PUBLICATIONS OR ABSTRACTS, FY-82:

Paper is in preparation for submission to the Journal of Clinical Neuro-
 psychology.

DATE: 8 OCT 82 Work Unit No.: 7300 STATUS: INTERIM FINAL
STARTING DATE: October 1978 DATE OF COMPLETION: October 1983 (anticipated)
KEY WORDS: Neuropsychological Examinations, Normal Control
TITLE OF PROJECT:

LSD Followup Study - Establishment of Normal Controls for Neuropsychological Examination

PRINCIPAL INVESTIGATOR(s): Francis J. Fishburne, Ph.D., Chief, Psychology Service

ASSOCIATE INVESTIGATOR(s):

FACILITY: WRAHC DEPT/SVC: Psychology Service, Dept of Psychiatry

| ACCUMULATIVE WEDCASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
|--|-----------------------------|---------------------------|
| 0 | 0 | 0 |
| FY-83 WEDCASE: 0 | CONTRACT COST: 0 | SUPPLY COST: 0 |
| DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 | | |

STUDY OBJECTIVE:

SAME

TECHNICAL APPROACH:

UNCHANGED

PROGRESS DURING FY-82:

Approximately ten volunteer subjects have been recruited to complete the neuropsychological evaluation bringing the current total to 55 normal control
NUMBER OF SUBJECTS STUDIED: subjects evaluated.

FY-82: TOTAL (TO DATE): BEFORE COMPLETION OF STUDY: UNCHANGED

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

NONE

CONCLUSIONS:

N/A

PUBLICATIONS OR ABSTRACTS, FY-82:

| | | |
|---|--|---|
| DATE: 8 OCT 82 | Work Unit No.: 7301 | STATUS: INTERIM X FINAL |
| STARTING DATE: 3 JAN 1980 | DATE OF COMPLETION: OCT 1983 (anticipated) | |
| KEY WORDS: MMPI, Military Norms | | |
| TITLE OF PROJECT: | | |
| Baseline MMPI Profile for an Active Duty Military Population | | |
| PRINCIPAL INVESTIGATOR(s): Francis J. Fishburne, Ph.D., Chief, Psychology Service | | |
| ASSOCIATE INVESTIGATOR(s): Stephen C. Parkison, Ph.D. | | |
| FACILITY: WRMC | DEPT/SVC: Psychology Service, Dept of Psychiatry | |
| ACCUMULATIVE WECASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
| | | \$1,574.00 |
| FY-83 WECASE: NONE | CONTRACT COST: \$1,000 | SUPPLY COST: 0 |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: 23 1993 |

STUDY OBJECTIVE:

SAME

TECHNICAL APPROACH:

UNCHANGED

PROGRESS DURING FY-82:

At the present time approximately 2100 protocols have been collected from
 NUMBER OF SUBJECTS STUDIED: Army installations in the United States and Germany.

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: 5,000

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

NONE

CONCLUSIONS: Preliminary conclusions suggest that the Minnesota normative data typically used for interpreting the MMPI is inappropriate for the general military youthful population.

PUBLICATIONS OR ABSTRACTS, FY-82:

Symposium conducted on preliminary results at the American Psychological Association Convention, August 1982. Papers presented are attached.

| | | | | |
|---|------------------------------------|--|--|--|
| DATE: 8 Oct. 82 | | WORK UNIT No.: 8050 | STATUS: INTERIM X FINAL | |
| STARTING DATE: 1 October 1981 | | DATE OF COMPLETION: 30 September 1984 | | |
| KEY WORDS: Hyperthyroidism/hypothyroidism/cardiac function | | | | |
| TITLE OF PROJECT: Radionuclide assessment of cardiac functional reserve in patients with hyperthyroidism and hypothyroidism | | | | |
| PRINCIPAL INVESTIGATOR(S): Robert C. Smallridge, LTC MC | | | | |
| ASSOCIATE INVESTIGATOR(S): M. Goldman, K. Raines, D. Van Nostrand, K. Burman | | | | |
| FACILITY: WRAIC /WRAIR | | DEPT/SVC: Medicine/Clinical Physiology | | |
| ACCUMULATIVE MEDICASE COST: --- | ACCUMULATIVE CONTRACT COST: --- | | ACCUMULATIVE SUPPLY COST: --- | |
| FY-83 MEDICASE: --- | CONTRACT COST: --- | SUPPLY COST: --- | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 | |

STUDY OBJECTIVE: To determine whether patients with hyper- or hypothyroidism have impaired left ventricular (LV) functional reserve

TECHNICAL APPROACH: Multigated acquisition (MUGA) scans are performed before and after bicycle exercise. M-mode and 2-D echocardiograms are also done.

PROGRESS DURING FY-82: The hyperthyroid phase of the study is almost completed. Only three hypothyroid subjects have been studied.

NUMBER OF SUBJECTS STUDIED:

FY-82: 17 TOTAL (TO DATE): 17 BEFORE COMPLETION OF STUDY: 8-13

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS: Several patients have had abnormal ejection fractions after exercise. They will be re-examined after correction of their thyroid disorder to see if the abnormality is reversible.

PUBLICATIONS OR ABSTRACTS, FY-82:

None

| | | | | | |
|--|----------------|-----------------------------|--|---------------------------|--------|
| DATE: 8 Oct. 82 | | WORK UNIT No.: 8052 | STATUS: INTERIM X | | FISCAL |
| STARTING DATE: 1 July 1981 | | | DATE OF COMPLETION: 30 September 1983 | | |
| KEY WORDS: Angiotensin-converting enzyme/thyroid function | | | | | |
| TITLE OF PROJECT: Assessment of serum angiotensin-converting enzyme in euthyroid individuals and in patients with altered thyroid function | | | | | |
| PRINCIPAL INVESTIGATOR(S): Robert C. Smallridge, LTC MC | | | | | |
| ASSOCIATE INVESTIGATOR(S): P.S. Verma, CPT MSC; J. Rogers, GS-10 | | | | | |
| FACILITY: WRANC/WRAIR | | | DEPT/SVC: Medicine/Clinical Physiology | | |
| ACCUMULATIVE MEDICASE COST: | | ACCUMULATIVE CONTRACT COST: | | ACCUMULATIVE SUPPLY COST: | |
| --- | | --- | | \$1692.20 | |
| FY-83 MEDICASE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT | | |
| --- | --- | \$2,000.00 | FEB 25 1983 | | |

STUDY OBJECTIVE: To determine whether hyperthyroidism or hypothyroidism affects serum levels of angiotensin-converting enzyme (ACE)

TECHNICAL APPROACH: Serum ACE activity is measured using ¹⁴C-hip-his-leu as substrate and determining the amount of hippuric acid formed.

PROGRESS DURING FY-82: Additional subjects were studied, and sequential analyses were performed in those with abnormal thyroid studies initially.

NUMBER OF SUBJECTS STUDIED:

FY-82: 100 TOTAL (TO DATE): 250 BEFORE COMPLETION OF STUDY: 50-100

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS:

Serum ACE is elevated in hyperthyroidism and decreased in hypothyroidism. ACE activity returns to normal after therapy.

PUBLICATIONS OR ABSTRACTS, FY-82:

Data presented at the American Thyroid Association meeting, September, 1982.

DATE: 27 Jan '83 WORK UNIT No.: 9019 STATUS: INTERIM FISCAL X
 STARTING DATE: FY '79 DATE OF COMPLETION: FY '83

KEY WORDS: Hemoglobin S, Sickle cell anemia, pyridoxal phosphate
 TITLE OF PROJECT: Antisickling agents: alteration of hemoglobin oxygen affinity.

PRINCIPAL INVESTIGATOR(S): John A. Kark, LTC, MC
 ASSOCIATE INVESTIGATOR(S): Rudolfo Bongiovanni, CPT, MSC, Peter G. Tarassoff, CPT, MC
 FACILITY: WRMC, WRAIR DEPT/SVC: Hematology/Oncology, CIS, Hem, WRAIR

ACCUMULATIVE MEDICASE COST: ACCUMULATIVE CONTRACT COST: none ACCUMULATIVE SUPPLY COST: none

FY-83 MEDICASE: CONTRACT COST: SUPPLY COST: DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983

STUDY OBJECTIVE: 1. Compare and contrast antisickling activity of pyridoxal and pyridoxal phosphate.

TECHNICAL APPROACH: 1. Sickle cells were loaded with PLP or pyridoxal, using HPLC to measure hemoglobin modification. 2. Percent sickling was determined as a function of PO₂ and %oxy-Hb

PROGRESS DURING FY-82: Control experiments were conducted demonstrating no swelling of sickle RBCs in response to treatment. A paper was written submitted, and was accepted in December, 1982.

NUMBER OF SUBJECTS STUDIED:
 FY-82: 10 TOTAL (TO DATE): 20 BEFORE COMPLETION OF STUDY: 20

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
 None: patient participation involved only using venous blood which would otherwise have been discarded, being drawn for CCSSD study.

CONCLUSIONS:
 1. PLP has considerable antisickling activity. 2. Both pyridoxal and PLP modify intracellular hemoglobin and inhibit sickling, but PLP does this without increasing oxygen affinity, whereas pyridoxal does this only by increasing oxygen affinity of hemoglobin, thereby reducing oxygen transport function of the red cell.

PUBLICATIONS OR ABSTRACTS. FY-82: Kark, J.A., P. G. Tarassoff, and R. Bongiovanni. Pyridoxal phosphate as an antisickling agent in vitro. In press, Journal of Clinical Investigation (projected date, May, 1983).

DATE: 4 Oct 82 | Work Unit No.: 9020 | STATUS: INTERIM X Final
STARTING DATE: Jan 1979 | DATE OF COMPLETION: Jan '83
KEY WORDS: Antisickling agent, Vitamin B₆, Oxygen affinity, Red Blood Cell
TITLE OF PROJECT: The effects of B₆ aldehydes on red cell oxygen affinity

PRINCIPAL INVESTIGATOR(S): John A. Kark, LTC, MC
ASSOCIATE INVESTIGATOR(S): Peter G. Tarassoff, CPT, MC
FACILITY: WRANIC X | DEPT/SVC: Hematology
ACCUMULATIVE FEDCASE COST: 0 | ACCUMULATIVE CONTRACT COST: 0 | ACCUMULATIVE SUPPLY COST: 0
FY-83 FEDCASE: 0 | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: Establish the mechanism of effects of B₆ aldehydes on red cell oxygen affinity and on red cell sickling.

TECHNICAL APPROACH: Washed red cells were prepared from normal individuals and from those with sickle hemoglobinopathies, were modified by incubation with B₆, and the changes in oxygen affinity and sickling were noted.

PROGRESS DURING FY-82:

A paper was submitted to the J. Clin. Invest. and an additional control experiment was run in response to review, the revised manuscript

NUMBER OF SUBJECTS STUDIED: was re-submitted
FY-82: 10 | TOTAL (TO DATE): 20 | BEFORE COMPLETION OF STUDY: 20

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
none

CONCLUSIONS: Pyridoxal phosphate and pyridoxal have opposite effects on oxygen affinity of normal cells. Both inhibit sickling but by different mechanisms due to hemoglobin modification.

PUBLICATIONS OR ABSTRACTS, FY-82:

An article is now in review by J. Clin. Investigation.

| | | |
|--|--|--|
| DATE: | WORK UNIT No.: #9020-82 | STATUS: INTERIM <input checked="" type="checkbox"/> FINAL |
| STARTING DATE: November 15, 1982 | DATE OF COMPLETION: November 15, 1983 | |
| KEY WORDS: Sickle Cell Trait, Altitude Chamber | | |
| TITLE OF PROJECT: A pilot study of altitude chamber training for individuals with sickle cell trait (SCT) | | |
| PRINCIPAL INVESTIGATOR(S): John A. Kark, LTC, MC, Peter G. Tarassoff, CPT, MC, | | |
| ASSOCIATE INVESTIGATOR(S): Donald E. Butkus, COL, MC, Daniel B. Kimball, COL, MC, etc. | | |
| FACILITY: WRANC, AFIP, WRAIR | DEPT/SVC: Dept. Med, Aerospace Pathology, Hematology | |
| ACCUMULATIVE MEDICASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
| FY-83 MEDICASE: | CONTRACT COST: | SUPPLY COST: |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
| STUDY OBJECTIVE: To establish the risks of altitude hypoxia for SCT aviator candidates in NATO training. Pilot for future large field study. | | |
| TECHNICAL APPROACH: Physiologic evaluation of SCT and non-SCT subjects before, during, and after flights in the AFIP altitude chamber. Preliminary study added and consent forms modified in accord with AFIP review | | |
| PROGRESS DURING FY-82: Protocol cleared three Institutes and equipment purchased and set up. Procedures practiced in the laboratory. | | |
| NUMBER OF SUBJECTS STUDIED: | | |
| FY-82: 0 | TOTAL (TO DATE): 0 | BEFORE COMPLETION OF STUDY: 30 |
| SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): none | | |
| CONCLUSIONS: none | | |
| PUBLICATIONS OR ABSTRACTS, FY-82: none | | |

#9020-82

Principal Investigators:

John A. Kark, LTC, MC, Dept. Hematol. WRAIR
Peter G. Tarassoff, CPT, MC, Dept. Hematol/Oncol. WRAMC
Donald E. Butkus, COL, MC, Division Medicine, WRAIR
Daniel G. Wriqth, MAJ, MC, Depart. Hematol., WRAIR
David M. Posey, Aerospace Pathology Division, AFIP
Robert R. McMeekin, COL,MC, Division of Aerospace Pathology,
AFIP
Daniel B. Kimball, COL, MC, Dept. Medicine, WRAMC

Associate Investigators:

James P. Dixon, CPT, USAF, BCS, Aerospace Physiology Research
Branch
Douglas van Nostrand, Dept. Nuclear Medicine, WRAMC
Yancy Y. Phillips, MAJ,MC, Division of Pulmonary Medicine, WRAMC
James J. Jaeger, MAJ, MSC, Dept. Clinical Physiology, WRAIR
Andrew J. Young, CPT, MSC, Dept. Clinical Physiology, WRAMC
Claude J. Tellis, LTC, MC, Division of Pulmonary Medicine, WRAMC
Jack Moore, Jr., LTC, MC, Division of Nephrology, WRAMC
Daniel A. Nash, Jr., Division of Nephrology, WRAMC
Paul Whitmore, COL, MC, Department of Ophthalmology, WRAMC

DATE: 10/20/82 WORKS UNIT No.: 9021 STATUS: INTERIM X FINAL

STARTING DATE: 26 Feb 80 DATE OF COMPLETION: 1 Jul 83

KEY WORDS: Marrow transplantation; heterologous transplant

TITLE OF PROJECT: Human-Marrow-in-Mouse Chimera

PRINCIPAL INVESTIGATOR(S): COL William H. Crosby, MC

ASSOCIATE INVESTIGATOR(S): Mary Cutting, M.S.

FACILITY: WRMC /WRAIR DEPT/SVC: Hematology/Medicine

ACCUMULATIVE FDCASE COST: ACCUMULATIVE CONTRACT COST: ACCUMULATIVE SUPPLY COST:

FY-83 FDCASE: CONTRACT COST: SUPPLY COST: DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT 26 Jan 1982

STUDY OBJECTIVE: To transplant human (cadaver) marrow into a lethally irradiated mouse in order to repopulate him with human marrow and blood cells.

TECHNICAL APPROACH: Mice are irradiated (900r) with whole body radiation to ablate hematopoietic and immune systems after heterologous marrow core has been implanted subcutaneously ten days earlier. The radiation destroys the host and donor hematopoietic and immune systems, but not the stroma of the implanted core.

PROGRESS DURING FY-82: None. We have used rat marrow in mouse as a model because success has been reported by others. As yet, we cannot establish rat marrow in the lethally irradiated mouse.

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 TOTAL (TO DATE): 0 BEFORE COMPLETION OF STUDY: 10

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

CONCLUSIONS:

We have not yet begun to use cadaver marrow.

PUBLICATIONS OR ABSTRACTS, FY-82:

DATE: 4 Oct 82 | WORK UNIT NO.: #9021-82 | STATUS: INTERIM x FINAL
STARTING DATE: October, 1982 | DATE OF COMPLETION: OCTOBER '83
KEY WORDS: Red Cells, Sickle Cell Trait, anion
TITLE OF PROJECT: Anion Permeability of Sickle Cell Trait Red Cells

PRINCIPAL INVESTIGATOR(S): John A. Kark, LTC, MC

ASSOCIATE INVESTIGATOR(S):

FACILITY: WRMC

DEPT/SYC:

ACCUMULATIVE MEDICASE COST:
none

ACCUMULATIVE CONTRACT COST:
none

ACCUMULATIVE SUPPLY COST:
none

FY-83 MEDICASE: \$750 | CONTRACT COST: | SUPPLY COST:

DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To determine whether anion permeability of red cells is related to sickling or to increased membrane binding of polymorphic hemoglobins

TECHNICAL APPROACH: A prospective paired study of anion permeability of red cells of different hemoglobin phenotypes, using small samples of venous blood, and determining (35-Cl) efflux from red cells.

PROGRESS DURING FY-82: Equipment was purchased through WRAIR, and just arrived at the end of FY-82

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 | TOTAL (TO DATE): 0 | BEFORE COMPLETION OF STUDY: 70

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
none

CONCLUSIONS: None

PUBLICATIONS OR ABSTRACTS, FY-82:

Kark, JA, Hicks, CU. Enhanced anion permeability of membrane anion channels in sickle erythrocytes. Blood 58:60a, November, 1981.

DATE: 20 Oct 82 WORK UNIT No.: 9022 STATUS: INTERIM X FINAL

STARTING DATE: 9 Apr 80 DATE OF COMPLETION: 1 Jul 83

KEY WORDS: Iron Metabolism; Iron Absorption; Iron Deficiency

TITLE OF PROJECT:
Iron Tolerance Test (ITT)

PRINCIPAL INVESTIGATOR(S): COL William H. Crosby, MC

ASSOCIATE INVESTIGATOR(S): Mary Cutting, MS

FACILITY: WRAHC/WRAIR DEPT/SVC: Hematology/Medicine

ACCUMULATIVE FEDCASE COST: ACCUMULATIVE CONTRACT COST: ACCUMULATIVE SUPPLY COST:

FY-83 FEDCASE: CONTRACT COST: SUPPLY COST: DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To identify and interpret the variables in the "small dose ITT" that we have developed.

TECHNICAL APPROACH: To mildly iron deficient subjects we give a small dose (10-30 mg) of iron by mouth, then measure the plasma iron concentration at intervals for 8 hours. We modify the dynamics of the absorption curve by food, by changing the degree of iron deficiency, by varying the dose of iron.

PROGRESS DURING FY-82: The test gives predictable results. Tests of iron with foods have begun.

NUMBER OF SUBJECTS STUDIED:

FY-82: 132 TOTAL (TO DATE): 182 BEFORE COMPLETION OF STUDY: 300

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS: The test behaves predictably in replicate trials. Normally iron replete men have little or no change in plasma iron concentration. Iron deficient subjects (blood donors) show significant increases. Tests with food iron show a slower, shallower increase.

PUBLICATIONS OR ABSTRACTS, FY-82:

None

| | | |
|--|-------------------------------|--|
| DATE: 10/20/82 | WORK UNIT No.: 9023 | STATUS: INTERIM X FINAL |
| STARTING DATE: 5 Aug 81 | DATE OF COMPLETION: 1 Jul 83 | |
| KEY WORDS: Iron Absorption, Radioiron; Iron Deficiency | | |
| TITLE OF PROJECT: Measurement of Iron Absorption | | |
| PRINCIPAL INVESTIGATOR(S): COL William H. Crosby, MC | | |
| ASSOCIATE INVESTIGATOR(S): Mary Cutting, M.S. | | |
| FACILITY: WRANC/WRAIR | DEPT/SVC: Hematology/Medicine | |
| ACCUMULATIVE MEDICASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
| FY-83 MEDICASE: | CONTRACT COST: | SUPPLY COST: |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT 26 Jan 82 |

STUDY OBJECTIVE: To correlate the actual amount of iron absorbed with the dynamics of the changes of concentration of plasma iron following a small oral dose of iron.

TECHNICAL APPROACH: Normal subjects with mild iron deficiency (blood donors) are given small doses (1 μ Ci) of ^{59}Fe by mouth in carrier doses of various amounts (10-50mg of iron). The retention of radioactivity after 1 week, determined by whole-body counting, represents the percentage of iron absorbed.

PROGRESS DURING FY-82: We have performed a pilot study of absorption of large doses of iron: 60mg versus 120mg. 30% of the iron was absorbed from each dose: 18mg versus 36mg. The curve of ITT went twice as high with the larger dose.

NUMBER OF SUBJECTS STUDIED:

FY-82: 3 TOTAL (TO DATE): 6 BEFORE COMPLETION OF STUDY: 30

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

CONCLUSIONS: In a single pilot test there did seem to be a correlation between the highest of the curve and the total amount absorbed.

PUBLICATIONS OR ABSTRACTS, FY-82:
none

DATE: 1 Oct 82 | WORK UNIT NO.: 9025 | STATUS: INTERIM X FIRM

STARTING DATE: 1 Jan 81 | DATE OF COMPLETION: not determined

KEY WORDS: Myelopoiesis, Bone Marrow, Hematopoietic Stem Cells

TITLE OF PROJECT: Studies of the Proliferation of Myeloid Precursor Cells Isolated from Normal Human Bone Marrow

PRINCIPAL INVESTIGATOR(S): Dr. Daniel G. Wright

ASSOCIATE INVESTIGATOR(S): Dr. August Salvado

FACILITY: WRMC | DEPT/SVC: Hematology Medicine

| | | |
|-------------------------------------|-------------------------------------|-----------------------------------|
| ACCUMULATIVE MEDICASE COST: none | ACCUMULATIVE CONTRACT COST: none | ACCUMULATIVE SUPPLY COST: none |
|-------------------------------------|-------------------------------------|-----------------------------------|

| | | | |
|-------------------------|------------------------|----------------------|---|
| FY-83 MEDICASE: none | CONTRACT COST: none | SUPPLY COST: none | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
|-------------------------|------------------------|----------------------|---|

STUDY OBJECTIVE: To study naturally occurring mediators that regulate the production of myeloid cells in the bone marrow

TECHNICAL APPROACH: Collection of bone marrow aspirates from normal human volunteers; purification of myeloid precursor cells from marrow by density gradient and counter-flow elutriation techniques; in vitro culture of bone marrow cells.

PROGRESS DURING FY-82: Establishment of techniques to purify myeloid precursor cells (myeloblasts, promyelocytes, myelocytes) from normal human bone marrow aspirates.

2. Identification and characterization of cholinergic receptors on myeloid precursor cells.

NUMBER OF SUBJECTS STUDIED: 50 (approx.)

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

none

CONCLUSIONS:

on-going project

PUBLICATIONS OR ABSTRACTS, FY-82:

Wright, D.G., Meierovics, A.I., Schoomaker, E.B., Tang, L. and Lucas, D.: Muscarinic cholinergic receptors on human neutrophils during their development and function. Clin. Res. 30:382A, 1982

DATE: 9/18/82 WORK UNIT NO.: 9026 STATUS: INTERIM X FIRM

STARTING DATE: October 1981 DATE OF COMPLETION: July 1983

KEY WORDS: Intravenous Immunoglobulin

TITLE OF PROJECT: The Prophylactic Use of Intravenous Immune Globulin in Adult Neutropenic Patients with Hematologic Malignancy

PRINCIPAL INVESTIGATOR(S): Barbara M. Alving

ASSOCIATE INVESTIGATOR(S): Alan Cross, Gerald Sadoff, Howard Terebello, Phil Baldwin

FACILITY: WRAMC DEPT/SVC: Hematology/Oncology

ACCUMULATIVE FEBCASE COST: ACCUMULATIVE CONTRACT COST: ACCUMULATIVE SUPPLY COST:
~ 1500

FY-83 FEBCASE: CONTRACT COST: SUPPLY COST: DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983

STUDY OBJECTIVE: to determine if infusion of IV immune globulin into neutropenic patients will reduce incidence of infections

TECHNICAL APPROACH: A double-blind study is in Progress. Patients receive either immune globulin or albumin at start of treatment for leukemia. Dose at half-level will be repeated every two weeks as long as neutropenia persists.

PROGRESS DURING FY-82: Five patients have been entered into the protocol, four of whom are from WRAMC and one whom is from Letterman Army Hospital.

NUMBER OF SUBJECTS STUDIED:
FY-82: 5 TOTAL (TO DATE): 5 BEFORE COMPLETION OF STUDY: 60

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
No unexpected side effects have been noted.

CONCLUSIONS: The study is progressing extremely slowly even with the joint cooperation of the Hematology-Oncology Services at Brooke and at Letterman. We are therefore considering termination of the study. This will be discussed within the next month by the investigators. Although the Baltimore Cancer Research Center had initially promised to work with us, they were unable to fulfill the commitment because of funding problems.

PUBLICATIONS OR ABSTRACTS, FY-82:
None

DATE: Sep 30 82 | WORK UNIT No.: 9027 | STATUS: INTERIM X FINAL

STARTING DATE: 7/1/81 | DATE OF COMPLETION: 30 June 83

KEY WORDS: Antibiotic-associated colitis, clostridia difficile

TITLE OF PROJECT: Prevalence of antibiotic-associated colitis among patients on prolonged therapy

PRINCIPAL INVESTIGATOR(S): Alan S. Cross, M.D.

ASSOCIATE INVESTIGATOR(S): Arthur Dobek, Peter Gemski, Steven Opal, Charles Oster, Robert Redfield, Sara Rothman

FACILITY: WRANC

DEPT/SVC: Medicine

ACCUMULATIVE MEDICASE COST:
0

ACCUMULATIVE CONTRACT COST:
0

ACCUMULATIVE SUPPLY COST:
1500

FY-83 MEDICASE:
0

CONTRACT COST:
0

SUPPLY COST:
1588

DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: Not applicable

STUDY OBJECTIVE: To identify the relative frequency of antibiotic-associated colitis as a cause of antibiotic-associated diarrhea

TECHNICAL APPROACH: To obtain stool specimens from patients on antibiotic therapy, and to examine these stools for the presence of C. difficile and/or its toxin.

PROGRESS DURING FY-82: Progress during FY-82: We have now assayed a total of 46 stool specimens for the presence of C. difficile toxin. Of the 33 patients studied, 5(15%) were positive for C. difficile cytotoxin. C. difficile was isolated from 3

NUMBER OF SUBJECTS STUDIED: (see below)

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: 300

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): None

CONCLUSIONS: Need more patients

PUBLICATIONS OR ABSTRACTS, FY-82:

of the 5 toxin-positive specimens. Even with the shortened consent form, progress was significantly affected by the difficulty in obtaining informed consent for collection of stool specimens.

DATE: 9/20/82 WORK UNIT NO.: 9028 STATUS: INTERIM FUND: X

STARTING DATE: 1 July 1981 DATE OF COMPLETION: 1 December 1981

KEY WORDS: Coumadin HPLC

TITLE OF PROJECT: Measurement of Plasma Warfarin Levels With High Performance Liquid Chromatography

PRINCIPAL INVESTIGATOR(S): Barbara M. Alving

ASSOCIATE INVESTIGATOR(S): Robert Knight, Charles Barr, Pat Strickler, Ted Gegoux, Jeff Berenberg

FACILITY: HRMC DEPT/SVC: Hematology

ACCUMULATIVE MEDICASE COST: ACCUMULATIVE CONTRACT COST: ACCUMULATIVE SUPPLY COST:

FY-83 MEDICASE: CONTRACT COST: SUPPLY COST: DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1982

STUDY OBJECTIVE: To establish a procedure for accurate measurement of warfarin levels in plasma

TECHNICAL APPROACH: A plasma assay for warfarin levels that utilizes HPLC has been developed

PROGRESS DURING FY 82: 20 patients have had measurement of plasma levels of warfarin while taking this drug over a long time period.

NUMBER OF SUBJECTS STUDIED: Study is
FY-82: 20 TOTAL (TO DATE): 20 BEFORE COMPLETION OF STUDY: completed

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
None

CONCLUSIONS: A sensitive method for determination of plasma coumadin levels has been developed. Range for patients on adequate anticoagulation is 0.42 - 3.85µg/ml

PUBLICATIONS OR ABSTRACTS, FY-82:
Abstract: Alving, B.M., Strickler, M.A., Knight, R.D., Barr, C.F., Berenberg, J.F., and Gegoux, T.
Warfarin resistance: investigation of a rare phenomenon.
Clin. Res. 30, 309 A (1982).

DATE: 9/20/82 WORK UNIT NO.: 9029 STATUS: INTERIM X Final

STARTING DATE: November 1981 DATE OF COMPLETION: December 1982

KEY WORDS: Coumadin

TITLE OF PROJECT: Investigation of Hereditary Resistance to Coumadin

PRINCIPAL INVESTIGATOR(S): Barbara Alving, M.D.

ASSOCIATE INVESTIGATOR(S): Robert Knight

FACILITY: NRAMC

DEPT/SVC: Hematology/Oncology

ACCUMULATIVE PEDCASE COST:

ACCUMULATIVE CONTRACT COST:

ACCUMULATIVE SUPPLY COST:

FY-83 PEDCASE: CONTRACT COST: SUPPLY COST:

DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To determine if family members of our patient with coumadin resistance also are resistant to this drug.

TECHNICAL APPROACH: Normal volunteers were given coumadin (0.45 mg/kg) and prolongation of the prothrombin time was measured at 36 and 48 h.

PROGRESS DURING FY-82: 21 volunteers and four family members have been studied and the data analyzed.

NUMBER OF SUBJECTS STUDIED:

FY-82: 21 ^{normal} controls TOTAL (TO DATE): 25 BEFORE COMPLETION OF STUDY: 25
4 Family Members

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS: Two of 21 controls did not have a prolongation of the prothrombin time. Both are on diets rich in vitamin K. One family member also did not show a response to coumadin. We will study these three persons with a higher dose of coumadin (0.9 mg/kg). A resistant patient should show no response at this dose, while normals would have a prolonged prothrombin time.

PUBLICATIONS OR ABSTRACTS, FY-82:

Abstract: Alving, B.M., Strickler, M.P., Knight, R.D., Barr, C.F., Berenberg, J.F. and Gegoux, T. Warfarin resistance: investigation of a rare phenomenon. Clin. Res. 30, 309A (1982).

| | | |
|--|--------------------------------|---|
| DATE: 11 Oct 82 | WORK UNIT No.: 9030 | STATUS: INTERIM X FINAL |
| STARTING DATE: 1980 | DATE OF COMPLETION: Indefinite | |
| KEY WORDS: Ischaemic bowel, Surgery, Enzymes | | |
| TITLE OF PROJECT: Circulatory Serum Isoenzymes | | |
| PRINCIPAL INVESTIGATOR(S): Geoffrey Graeber, LTC | | |
| ASSOCIATE INVESTIGATOR(S): John W. Harmon | | |
| FACILITY: WRMC | DEPT/SVC: Surgery | |
| ACCUMULATIVE MEDICAL CASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
| FY-83 MEDICAL CASE: | CONTRACT COST: | SUPPLY COST: |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE:

To identify a serum marker for ischaemic bowel

TECHNICAL APPROACH:

To collect serum from patients with ischaemic bowel, as well as other conditions for controls, and measure levels of potential marker enzymes.

PROGRESS DURING FY-82:

Eight patients with ischaemic bowel have been studied. The results of these studies are being written up.

NUMBER OF SUBJECTS STUDIED: Indefinite

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
None

CONCLUSIONS: None

PUBLICATIONS OR ABSTRACTS, FY-82: None

DATE: 8 Oct 82 | Work Unit No.: 9031 | STATUS: INTERIM X FINAL
STARTING DATE: 1980 | DATE OF COMPLETION:
KEY WORDS: Stomach, Acid
TITLE OF PROJECT: Study of Control Mechanisms for Human Gastric Parietal Cells

PRINCIPAL INVESTIGATOR(S): John W. Harmon, LTC, MC

ASSOCIATE INVESTIGATOR(S): Samuel Batzri, PhD

FACILITY: WRAVC

DEPT/SVC: Surgery

ACCUMULATIVE FEDCASE COST:

ACCUMULATIVE CONTRACT COST:

ACCUMULATIVE SUPPLY COST:

FY-83 FEDCASE: CONTRACT COST: SUPPLY COST:

DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To study the control mechanisms of human parietal cells.

TECHNICAL APPROACH: To study gastric mucosal cells which have been dispersed using isolated cell technique

PROGRESS DURING FY-82: Further work has been done at USUHS gaining experience with the cell methodology

NUMBER OF SUBJECTS STUDIED: None

FY-82: TOTAL (TO DATE): BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): None

CONCLUSIONS:

None

PUBLICATIONS OR ABSTRACTS, FY-82: Attached are the results of 2 animal studies using this technique

| | | |
|---|--------------------------------|--|
| DATE: 11 Oct 82 | WORK UNIT No.: 9032 | STATUS: INTERIM <input checked="" type="checkbox"/> FINAL |
| STARTING DATE: 1980 | DATE OF COMPLETION: Indefinite | |
| KEY WORDS: Colon, Surgery, Ion transport | | |
| TITLE OF PROJECT: In Vitro Analysis of Human Colon Ion Transport | | |
| PRINCIPAL INVESTIGATOR(S): Harmon, John W. | | |
| ASSOCIATE INVESTIGATOR(S): RoyWong, Tai | | |
| FACILITY: WRAVC <input checked="" type="checkbox"/> | DEPT/SVC: Surgery | |
| ACCUMULATIVE MEDICASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
| FY-83 MEDICASE: _____ | CONTRACT COST: _____ | SUPPLY COST: _____ |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE:

To investigate transport mechanisms of the human colon

TECHNICAL APPROACH:

To study colonic mucosa from surgical specimens using Ussing Chamber technique

PROGRESS DURING FY-82:

No work was accomplished on this protocol in FY 82 because of the PCS of the key investigator R. Decker.

NUMBER OF SUBJECTS STUDIED: Indefinite

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS: None

PUBLICATIONS OR ABSTRACTS, FY-82:

None

DATE: 4 Oct 82 WORK UNIT No.: 9035 STATUS: INTERIM X FINAL

STARTING DATE: Jun 1977 DATE OF COMPLETION: --

KEY WORDS: Altitude, performance

TITLE OF PROJECT: Effects of altitude, mood, and dietary habits on performance of a choice-reaction time task

PRINCIPAL INVESTIGATOR(s): Dixon, J.P., CAPT, USAF, BSC

ASSOCIATE INVESTIGATOR(s): Ruehle, C. J., LT COL, USAF, MC

FACILITY: ~~None~~ AFIP DEPT/Svc: Aerospace Pathology

ACCUMULATIVE MEDICASE COST: ACCUMULATIVE CONTRACT COST: ACCUMULATIVE SUPPLY COST:

FY-83 MEDICASE: CONTRACT COST: SUPPLY COST: DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT Feb 27 1983

STUDY OBJECTIVE: To evaluate the subtle influence of mood, altitude, dietary habits and other stresses on performance and to relate these decrements to the job performance of military personnel.

TECHNICAL APPROACH:

(over)

PROGRESS DURING FY-82:

(over)

NUMBER OF SUBJECTS STUDIED:

FY-82: 9 TOTAL (TO DATE): 14 BEFORE COMPLETION OF STUDY: 6

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
None

CONCLUSIONS:

None

PUBLICATIONS OR ABSTRACTS, FY-82:

TECHNICAL APPROACH: By means of a choice-reaction time task, efficiency (number correct divided by average reaction time) will be used as the parameter to measure performance. Efficiency will then be related to the physiological parameters of oxygen saturation, respiration and heart rates at various altitudes. The test is undergoing refinement to include PAB tests as assigned by the Department of Military Medical Psychophysiology, WRAIR. This will include the more sensitive tests of logical reasoning and digit recall in which accuracy and reaction time are specifically ascertained. The mood scale is more extensively studied in this series.

PROGRESS: Due to learning effects, results in six subjects were rejected. The composite CRT performance of seven other subjects is not a sufficient data base from which to draw final conclusions. Further experimentation is needed, specifically to refine out the required 2-3 months of training needed to perform the task. Including the PAB tests from WRAIR will provide a computer test that is repeatable and requires possibly a week of training. Specifically, the logical reasoning test and the digit recall test will add 2-3 minutes of psychomotor testing each, and result in an efficiency grade that will reflect the subtle differences in performance at low altitude without extensive training.

DATE: 28 Jan 83 WORK UNIT NO.: 9036 STATUS: INTERIM * FINAL
STARTING DATE: June 28, 1977 DATE OF COMPLETION: Ongoing
KEY WORDS: myo-adenylate deaminase deficiency; lactate/ammonia exercise ratio
TITLE OF PROJECT: Urease and Deaminases in Chemistry and Medicine

PRINCIPAL INVESTIGATOR(S): William N. Fishbein, M.D., Ph.D.

ASSOCIATE INVESTIGATOR(S):

FACILITY: WRAMC

DEPT/SVC: Biochemistry Division

ACCUMULATIVE MEDICASE COST:

ACCUMULATIVE CONTRACT COST:

ACCUMULATIVE SUPPLY COST:

0

0

0

FY-83 MEDICASE: CONTRACT COST: SUPPLY COST:

DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: Development of a diagnostic clinical blood test for mADD

TECHNICAL APPROACH: Measurement of lactate and ammonia in antecubital vein blood drawn and after sponge-squeezing with partial venous obstruction.

PROGRESS DURING FY-82: Nine patients and 15 controls have now been tested without side-effects. No drugs or WRAMC funds have been used. The nine patients show no increase in NH₃ despite normal increase in lactate as reported

NUMBER OF SUBJECTS STUDIED:

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: 30

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): None

CONCLUSIONS: Test continues to look promising

PUBLICATIONS OR ABSTRACTS, FY-82:

DATE: 4 Oct 82 | WORK UNIT No.: 9038 | STATUS: INTERIM X FINAL

STARTING DATE: Aug 80 | DATE OF COMPLETION: --

KEY WORDS: Quinine, performance

TITLE OF PROJECT: Effects of low dose quinine on human performance of a choice reaction time task at ground level and at altitude

PRINCIPAL INVESTIGATOR(s): Dixon, J.P., CAPT, USAF, BSC

ASSOCIATE INVESTIGATOR(s): Wagner, G.N., CDR, MC, USN | Zaitchuk, J.T., COL, MC, USA
Chadwick, S.G., M.A.

FACILITY: ~~WONK~~ AFIP | DEPT/SVC: Aerospace Pathology

ACCUMULATIVE MEDCASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST:

FY-83 MEDCASE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To determine the singular effects of low dose quinine on reaction time, and the degree of synergism which may exist due to decreased oxygen saturation at altitude; to ascertain the ototoxic effects of quinine.

TECHNICAL APPROACH: To evaluate quinine's effect on a choice-reaction time task under normobaric and hypobaric conditions. To measure abnormalities in the electro-nystagmogram test series and audiogram due to repeated doses of quinine.

PROGRESS DURING FY-82:

No progress was made during this fiscal year.

NUMBER OF SUBJECTS STUDIED:

FY-82: 0 | TOTAL (TO DATE): 13 | BEFORE COMPLETION OF STUDY: 30

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

none

CONCLUSIONS:

none

PUBLICATIONS OR ABSTRACTS, FY-82:

DATE: 2/22/83 WORK UNIT No.: 9042 STATUS: INTERIM FISCAL XX

STARTING DATE: March 1981 DATE OF COMPLETION: Termination 1982

KEY WORDS: Vitamins Cancer

TITLE OF PROJECT: AN ASSESSMENT OF VITAMIN A, RIBOFLAVIN, VITAMIN G₆, AND VITAMIN E STATUS IN INDIVIDUALS WITH CANCERS OF EPITHELIAL TISSUE.

PRINCIPAL INVESTIGATOR(S): Thelma S. (Arnold) Hendricks, LTC ANC

ASSOCIATE INVESTIGATOR(S): Judy Driskell, PhD

FACILITY: WRAMC

DEPT/SVC: Food Service Directorate

ACCUMULATIVE MEDICASE COST:
NONE

ACCUMULATIVE CONTRACT COST:

ACCUMULATIVE SUPPLY COST:

FY-83 MEDICASE: CONTRACT COST: SUPPLY COST:
No WRAMC funds used.

DATE OF COMMITTEE APPROVAL OF
ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To evaluate the status of Vitamin A, riboflavin, Vitamin B₆ and Vitamin E status in individuals with a recent diagnosis of cancer involving epithelial tissues.

TECHNICAL APPROACH: Evaluation of: 1) Plasma retinal and alpha tocopheral - high pressure liquid chromatography; 2) Vitamin B₆ - plasma PO₄ and CO enzyme stimulation; 3) Riboflavin - erythrocyte

PROGRESS DURING FY-82: Vitamin B₆ was evaluated on (continued below) 15 patients at WRAMC using plasma PO₄ and co enzyme stimulation techniques.

NUMBER OF SUBJECTS STUDIED:

FY-82: 15

TOTAL (TO DATE):

BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

NONE

CONCLUSIONS: When compared with age matched controls, patients with cancer of epithelial tissues were found to have significantly lower pyridoxal PO₄ levels and higher co enzyme stimulation values indicative of Vitamin B₆ deficiency.

The study is terminated due to retirement of senior investigator.

PUBLICATIONS OR ABSTRACTS, FY-82:

NONE

Technical Approach (continued): glutathione reductase assay.

DATE: 1 Sept 82 WORK UNIT No.: 9043 STATUS: INTERIM FINAL XX

STARTING DATE: August 1980 DATE OF COMPLETION: September 1982

KEY WORDS: Quality Assurance, Operating Room Nursing, Process Criteria.

TITLE OF PROJECT: Development of a Methodology to Monitor Operating Room and Anesthesia Nursing Care.

PRINCIPAL INVESTIGATOR(S): MAJ Donna Sylvester/LTC Susan Shipley

ASSOCIATE INVESTIGATOR(S): N/A

FACILITY: WRAHC

DEPT/SVC: Nursing Research Service

ACCUMULATIVE MEDICARE COST:
\$5850.00

ACCUMULATIVE CONTRACT COST:

ACCUMULATIVE SUPPLY COST:
\$1776.01

FY-82 MEDICARE: CONTRACT COST: SUPPLY COST:
\$814.36

DATE OF COMMITTEE APPROVAL OF
ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To establish the statistical validity and reliability of a set of process criteria to monitor perioperative nursing practice.

TECHNICAL APPROACH: A set of process criteria were identified by a working committee and then ratified by a expert review panel. Each of six clinical facilities supplied a nursing observation team which was trained to monitor operating room (Cont)
PROGRESS DURING FY-82: Criteria field testing which began in August 1981 was concluded in January 1982 with a total of 794 worksheets completed by observers. Data has been analyzed using frequency distributions of criteria responses, item-total (Cont.)

NUMBER OF SUBJECTS STUDIED: Data collection is complete.

FY-82: TOTAL (TO DATE): BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
Work stopped on anesthesia criteria following the anesthesia nursing consultant's withdrawal of support for any further development or use of the tool in Army sites. (Cont.)

CONCLUSIONS: Sixty-four criteria were organized into a modified objective/subobjective structure. The Rush-Medicus scoring program was updated to generate quality indices for six objectives and 15 subobjectives. See attached summary for further details.

PUBLICATIONS OR ABSTRACTS, FY-82:

Continuation of Final Report for Work Unit 9043

Technical Approach: nursing practice, using the proposed criteria to review records, observe ongoing care, and interview staff and patients.

Progress During FY82: correlations, and coefficient alpha. Participating facilities received feedback on project results. Dissemination of project results included three presentations and four articles.

Serious/Unexpected Side Effects: See Intern Report for FY81.

DATE: 1 June 1982 WORK UNIT NO.: 9046 STATUS: INTERIM FINAL

STARTING DATE: 1 May 1981 DATE OF COMPLETION: 1 June 1982

KEY WORDS: Role of ANC Clinical Head Nurse in US Army Health Clinics

TITLE OF PROJECT: A Descriptive Study of the Role of the Clinical Head Nurse/Chief Nurse in US Army Health Clinics for ANC Officers.

PRINCIPAL INVESTIGATOR(S): Mary E. Buchanan, MPT, ANC

ASSOCIATE INVESTIGATOR(S):

FACILITY: WAMC DDC/ANC: Nursing Research Service/Department of Nursing

| ACCUMULATED MEDCASH COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
|---------------------------|-----------------------------|---------------------------|
| 0 | 0 | \$190.93 |

| FY-81: MEDCASH: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: |
|-----------------|----------------|--------------|---|
| 0 | 0 | \$190.93 | FEB 25 1982 |

STUDY OBJECTIVE: To describe the demographics of the study population. To describe the duties currently performed in the USAHC. To determine what the study population thinks the duties should be in the USAHC.

TECHNICAL APPROACH: A world-wide mail out questionnaire to the identified USAHC's with ANC clinical Head Nurse (Chief Nurses) (50) and Captains, Ambulatory Care Nursing Service (all MEDCASH/MEDCEN's) (50), with a follow-up mailing one month later to non-respondents.

PROGRESS DURING FY-81: See Completed report attached.

NUMBER OF SUBJECTS TO BE STUDIED BEFORE COMPLETION OF STUDY: 74

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT:

None

CONCLUSIONS: See completed report attached.

PUBLICATIONS OR ABSTRACTS, FY-81: Paper to be presented at Civilis J. Verhonic Research Course, 7 June 1982, Ft. Sam Houston, Texas

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|---|-----------------------------|-------------------------------|--|
| DATE: 20 Sep 82 | Work Unit No.: 9048 | STATUS: INTERIM | FINAL X |
| STARTING DATE: 1 Jul 81 | | DATE OF COMPLETION: 20 Sep 82 | |
| KEY WORDS: Patient falls | | | |
| TITLE OF PROJECT: Positive Use of Patient Fall Reports | | | |
| PRINCIPAL INVESTIGATOR(S): LTC Janet R. Southby, ANC, D.N.Sc. | | | |
| ASSOCIATE INVESTIGATOR(S): LTC R. Guida, MAJ B. Conrad, MAJ V. Johnson and MAJ J. Jolivet | | | |
| FACILITY: WRAMC Unit 52, 58, 79 DEPT/Svc: Nursing Research | | | |
| ACCUMULATIVE MEDICASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: | |
| 0 | 0 | 0 | |
| FY-83 MEDICASE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT |
| 0 | 0 | 0 | FEB 25 1983 |

STUDY OBJECTIVE:
 To decrease the number of patient falls which occur at WRAMC

TECHNICAL APPROACH:
 Same as stated in protocol

PROGRESS DURING FY-82:
 Data were analyzed and final report was prepared.

NUMBER OF SUBJECTS STUDIED:
 FY-82: 0 TOTAL (TO DATE): 408 BEFORE COMPLETION OF STUDY: 0

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
 Record review only

CONCLUSIONS:
 See attached abstract

PUBLICATIONS OR ABSTRACTS, FY-82:
 Two nursing inservice programs were conducted and a paper was presented at the Phyllis J. Verhonick Nursing Research Course, FSH, SAT, 7-11 June 1982. The abstract will be published in the proceedings of this course.

 Copy of final report is attached.

ABSTRACT

TITLE: Prevention of Patient Falls Through Use of an Assessment Tool

PURPOSE: To decrease the number of patient falls on three nursing units at Walter Reed Army Medical Center through use of an assessment tool. The objectives were:

1. To compare the number of patient falls that occurred during the study with the number of falls that occurred during the same period last year. The patient census and staffing levels for both periods will also be compared.
2. To compare the patients who fell with the patients who did not fall during the study with regard to age; activity, mental, and medication status; diagnosis; and length of hospital stay.
3. To describe specific characteristics held by the patient's who fell during the study as identified on the Analysis of Unusual Occurrence (WRAMC Form 322).
4. To revise the "Assessment Sheet -- Dynamics of Fall Accidents" to reflect more accurately the profile of the patient likely to fall during hospitalization so that intervention may be taken.

POPULATION DESCRIPTION: During the study period, July through September 1981, 701 patients were admitted to three nursing units and 408 were assessed in relation to the dynamics of fall incidents. Seventeen patients fell and were included in this sample. The medical records of 225 patients were reviewed to identify the study variables.

METHOD OF DATA COLLECTION: Nursing personnel used the "Assessment Sheet -- Dynamics of Fall Accidents" to compare how a specific patient at admission was similar to or different from the profile of patients prone to falls at Walter Reed. The nurse used this information, and additional factors identified in relation to patient falls, to evaluate the need for patient teaching regarding prevention of falls. The patient's orientation to the clinical unit included discussion of "Safety Tips to Prevent Patient Falls," familiarization with the hospital environment, and clarification of the patient's activity status.

Patients who fell during the study period were interviewed; a Report of Unusual Occurrence and an Analysis of Unusual Occurrence were initiated. In addition to these reports, Nursing Personnel Time Schedule and medical records of patients admitted to the nursing units were reviewed to obtain comparative data.

METHOD OF DATA ANALYSIS: Descriptive statistics and Chi Square test.

DISCUSSION OF FINDINGS AND CONCLUSIONS:

1. There was a slight decrease in both the number of patient falls and the average patient census during the study period. Also the ratio of patients to total staff improved slightly. It was noted that falls were more likely to occur when the patient to professional nurse ratio increased above the average.

2. The fall and no-fall groups were similar in composition with regard to age, sex, and diagnosis. The activity and mental status of the groups differed at admission. Almost 80% of the no-fall group was up ad lib whereas only slightly over half of the fall group was up ad lib on admission. A significantly greater proportion of the fall group was in the "up with assistance" or "bedrest" status and their mental status was confused, disoriented, or post ictal. Patients in the fall group received a greater number of medications than those in the no-fall group (an average of 5.3 versus 3.1). Patients in the fall group also experienced a significantly longer hospitalization than those in the no-fall group.

3. The day of hospitalization, time of day and day of week the fall occurred were not significant. There was a tendency for the mental and activity status to deteriorate from the time of admission to the time the fall occurred. Most falls occurred in the patient's room, at the bedside, while the patient was alone.

4. Five major characteristics were identified to indicate that a patient is prone to falling while hospitalized. These are: Sex - Male; Mental status - confused/disoriented/post ictal; Activity status - "up with assistance" or "bedrest"; Medication status; and Length of hospital stay - greater than two weeks.

RECOMMENDATIONS:

1. The authors believe that use of the Assessment Sheet as a separate component of the nursing assessment is unnecessary. However, the characteristics identified in the conclusion, to identify patients prone to falling needs to be incorporated as part of the continuing patient assessment.

2. The "Safety Tips to Prevent Patient Falls" should be incorporated as part of the Patient Safety Message given to each patient during orientation to the nursing unit.

3. When there is a decrease in the patient's mental status and/or a shift in activity status, consideration should be given to the use of siderails or restraints for the protection of the patient. While in a wheelchair, the patient should be under the direct observation of a health care provider.

4. Further study to compare and contrast the characteristics of the patients who fell in this study with the fall population of specific nursing units and of the hospital population during an extended period of time is recommended. In this way, verification of characteristics indicating a patient is prone to falling could be accomplished.

INVESTIGATORS:

LTC Janet R. Southby, Chief Nursing Research Service
LTC Robert Guida, C, Nursing Methods Division, Directorate of Resources
Management
MAJ Barbara Conrad, Assistant Area Coordinator, 5th Floor
MAJ Valerie Johnson, Clinical Coordinator, Ward 52
MAJ Joann Jolivet, Assistant Area Coordinator, 4th Floor

Date: 8 October 1982 Work Unit No: 9049 Status: Interim X Final

Starting Date: 1 August 1982 Date of Completion: 31 December 1983

Key Words: Patient Education, Coronary Artery Bypass Surgery

Title of Project:
Evaluation of a Preoperative and Postoperative Education Program for Coronary Artery Bypass Patients

Principal Investigator(s): Elizabeth A. Rimm, MAJ, ANC

Associate Investigator(s): LTC J.R. Southby, MAJ R. DeAngelis, CPT M. Rose

Facility: WRAMC Dept/Svc: Nursing Research Service

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| Accumulative MEDCASE Cost: 0 | Accumulative Contract cost: \$150.00 | Accumulative Supply Cost: 0 |
|---------------------------------|---|--------------------------------|

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| FY-83 MEDCASE: 0 | Contract Cost: 0 | Supply Cost: \$900.00 | Date of Committee Approval Of Annual Progress Report: FEB 25 1983 |
|---------------------|---------------------|--------------------------|--|

Study Objective: To evaluate an on-going teaching program for coronary artery bypass patients to determine whether it is providing the patient with the information he needs and wants to know, and if the use of a combination of patient education techniques and teaching tools has an effect on learning outcomes.

Technical Approach: As per protocol

Progress During FY-82: Knowledge questionnaires for phase I were pilot tested for reliability, revised and retested. Item analysis done on the final version of the questionnaire showed the mean index of difficulty to be 43% and the mean index of discrimination to be .40. Data collection began on phase I of the study in January 1982. Approximately half of the phase I sample group has been accumulated. See attachment for details.

Number of Subjects Studied:
FY-82 47 Total (To Date): 47 Before Completion of Study: 120

Serious/Unexpected Side Effects IN Subjects Participating in Project (If None So State):

NONE

Conclusions: See Attachment for data trends to date.

Publications or Abstracts, FY-82:

NONE

DATE: 2 Feb 83

WORK UNIT No.: 9050

STATUS: INTERIM XXX FINAL

STARTING DATE: 17 September 1981

DATE OF COMPLETION: December 1981

KEY WORDS: Stress of hospitalization; middle-aged & elderly patients

TITLE OF PROJECT: The Stress of Hospitalization in Middle-Aged and Elderly Patients

PRINCIPAL INVESTIGATOR(S): Lona K. Ambrose, MAJ,AMSC, University of MD, College Park, MD

ASSOCIATE INVESTIGATOR(S): Dana P. Schodt, MAJ, ANC

FACILITY: WRAMC

DEPT/SVC: Department of Nursing

ACCUMULATIVE MEDCASE
COST: N/A

ACCUMULATIVE CONTRACT
COST: N/A

ACCUMULATIVE SUPPLY
COST: N/A

FY-83: MEDCASE:
N/A

CONTRACT COST:
N/A

SUPPLY COST:
N/A

DATE OF COMMITTEE APPROVAL
OF ANNUAL PROGRESS RPT N/A
FEB 25 1983

STUDY OBJECTIVE: The purpose of the study is to determine the relationship between chronological age and self-perceived stress of hospitalization as measured by the Hospital Stress Rating Scale and the Profile of Mood State questionnaire.

TECHNICAL APPROACH: 60 Medical patients over the age of 45 given HSRS and POMS to determine events that have happened to them since being hospitalized and to determine general mood states for the week preceding the interview.

PROGRESS DURING FY-83: To this date the data collection is finished and is being analyzed. Expected date of completion is April 1983.

NUMBER OF SUBJECTS TO BE STUDIES BEFORE COMPLETION OF STUDY: 60

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT:

None

CONCLUSIONS: Pending (april 1983)

PUBLICATIONS OR ABSTRACTS, FY-83:

DATE: 4 Oct 82 Work Unit No.: 9051 STATUS: INTERIM FINAL

STARTING DATE: See below DATE OF COMPLETION: --

KEY WORDS: chloroquine, primaquine, performance

TITLE OF PROJECT: Chloroquine-primaquine effects on human performance of a choice-reaction time task at ground level and at altitude

PRINCIPAL INVESTIGATOR(S): Dixon, J.P., CAPT, USAF, BSC

ASSOCIATE INVESTIGATOR(S): Wagner, G.N., CDR, MC, USN

FACILITY: ~~KRANK~~ AFIP DEPT/SVC: Aerospace Pathology

ACCUMULATIVE PEDCASE COST: ACCUMULATIVE CONTRACT COST: ACCUMULATIVE SUPPLY COST:

FY-83 PEDCASE: CONTRACT COST: SUPPLY COST: DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT **FEB 25 1983**

STUDY OBJECTIVE: To evaluate the effects of therapeutic levels of chloroquine-primaquine on performance of a choice-reaction time task and compare their effects under normobaric and hypobaric conditions.

TECHNICAL APPROACH: To evaluate the singular effects of chloroquine-primaquine on reaction time, and the degree of synergism which may exist due to decreased oxygen saturation by testing subjects who are on this drug regimen at altitudes which will cause mild hypoxia.

PROGRESS DURING FY-82:
Research has yet to be initiated.

NUMBER OF SUBJECTS STUDIED:
FY-82: 0 TOTAL (TO DATE): 0 BEFORE COMPLETION OF STUDY: 21

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
none

CONCLUSIONS:
none

PUBLICATIONS OR ABSTRACTS, FY-82:

DATE: 20 Sep 82 Work Unit No. 9051B-82 STATUS: INTERIM FINAL X

STARTING DATE: September 1981 DATE OF COMPLETION: September 1982

KEY WORDS: Thumbsucking, security object

TITLE OF PROJECT:
The Current Status of Thumbsucking and Related Behaviors

PRINCIPAL INVESTIGATOR(S): LTC K.J. Ammon (Ret.), Asst. Professor, CUA

ASSOCIATE INVESTIGATOR(S): LTC J.R. Southby, ANC, D.N.Sc.

FACILITY: WRAHC Pediatrics DEPT/SVC: Nursing Research

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| ACCUMULATIVE MEDICASE COST: 0 | ACCUMULATIVE CONTRACT COST: 0 | ACCUMULATIVE SUPPLY COST: 0 |
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| FY-83 MEDICASE: 0 | CONTRACT COST: 0 | SUPPLY COST: 0 | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
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STUDY OBJECTIVE: To gain descriptive information concerning thumb-sucking, security seeking and feeding behaviors of children that would be useful in advising and counselling parents.

TECHNICAL APPROACH:
Same as stated in protocol

PROGRESS DURING FY-82: Questionnaires were distributed and returned; data were coded and analyzed; and final report was prepared.

NUMBER OF SUBJECTS STUDIED:
FY-82: 797 TOTAL (TO DATE): 797 BEFORE COMPLETION OF STUDY: 0

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
None

CONCLUSIONS:
See attached page.

PUBLICATIONS OR ABSTRACTS, FY-82:
Copy of final report is attached. Professional publication is planned.

Conclusions

1. Children who used the pacifier tended not to suck their thumb. Pacifier users who did thumbsuck stopped using the pacifier at a younger age than the nonthumbsuckers and more frequently discontinued pacifier use of their own accord. Perhaps the thumb was preferred in lieu of the pacifier.

2. Children who were thumbsuckers were more likely to have a security object; it seems that the thumb and blanket go together. Favored security objects were a blanket or cloth often having a smooth satin edge, stuffed toy, both blanket and toy, and a pillow. Children frequently selected security objects prior to age 1 year and let go after 3 1/2 years of age.

3. Children who were not thumbsuckers were, at present, more frequent in the high weight category. It may be that thumbsuckers pursue that habit for oral gratification when their nonthumbsucking

4. Children who were thumbsuckers began attending day care centers earlier than children who did not thumbsuck. Since children tend to suck their thumb when tired, sleepy, insecure, stressed or bored; a change from the familiar environment may produce any of these conditions. Also peers and school were cited as being associated with increased thumbsucking, so this occurrence could be expected.

5. Parents found doing nothing to discourage thumbsucking to be the most effective method of dealing with it. Apparently, the activity is comforting for the child and usually self-limiting in duration.

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| DATE: | WORK UNIT NO.: 9052A | STATUS: INTERIM | FISCAL X |
| STARTING DATE: | | DATE OF COMPLETION: | |
| KEY WORDS: | | | |
| TITLE OF PROJECT: CELLULAR DYNAMICS OF UTERINE EPITHELIUM. | | | |
| PRINCIPAL INVESTIGATOR(S): Drs. G.F. Bahr, P. Marcella and M. Thiel | | | |
| ASSOCIATE INVESTIGATOR(S): | | | |
| FACILITY: AFIP AFIP | | DEPT/SVC: Dept of Cellular Pathology | |
| ACCUMULATIVE MEDICAL CASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: | |
| FY-83 MEDICAL CASE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE:

TECHNICAL APPROACH:

PROGRESS DURING FY-82:

NUMBER OF SUBJECTS STUDIED:

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

CONCLUSIONS:

Study has been terminated because of unavailability of normal cervixes for it.

PUBLICATIONS OR ABSTRACTS, FY-82:

DATE: 30 Sept 82 WORK UNIT No.: 9052B STATUS: INTERIM X FINAL

STARTING DATE: 1 October, 81 DATE OF COMPLETION: 30 September, 84

KEY WORDS: Nasopharyngeal Carcinoma, Epstein-Barr Virus

TITLE OF PROJECT: Application of Epstein-Barr Virus Markers to Diagnosis and Prognosis of Nasopharyngeal Carcinoma in Occult Tumors of the Nasopharyngeal Area in the U.S.A.

PRINCIPAL INVESTIGATOR(S): Dennis K. Heffner, CAPT, MC, USN

ASSOCIATE INVESTIGATOR(S):

FACILITY: WRAVC / AFIP DEPT/SVC: Otolaryngic Pathology (AFIP)

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| ACCUMULATIVE MEDICASE COST: 0 | ACCUMULATIVE CONTRACT COST: 0 | ACCUMULATIVE SUPPLY COST: 0 |
|----------------------------------|----------------------------------|--------------------------------|

| | | | |
|----------------------|---------------------|-------------------|---|
| FY-83 MEDICASE: 0 | CONTRACT COST: 0 | SUPPLY COST: 0 | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
|----------------------|---------------------|-------------------|---|

STUDY OBJECTIVE: To cooperate with a group study of the usefulness of serum antibodies to EB virus antigens in confirming a suspected diagnosis of nasopharyngeal carcinoma (NPC) and in the follow-up of such patients.

TECHNICAL APPROACH: Identification of patients with NPC is made through the pathology consultation requests received by the Registry of Otolaryngic Pathology, and an initial request for serum is made. Further data are obtained in cooperation with the National Cancer Institute.

PROGRESS DURING FY-82: Twenty patients with NPC identified; 13 patients with neck metastases and suspected or possible NPC identified. Initial serum samples submitted to AFIP in nine instances (other initial and follow-up samples submitted through NCI

NUMBER OF SUBJECTS STUDIED:

FY-82: 33 TOTAL (TO DATE): 33 BEFORE COMPLETION OF STUDY: total identifi

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS: Pending

PUBLICATIONS OR ABSTRACTS. FY-82:

Levine, P.H., Pearson, G.R. et al. (incl. D. Heffner),
The reliability of IgA antibody to Epstein-Barr virus (EBV) capsid antigen
as a test for the diagnosis of nasopharyngeal carcinoma (NPC).
Cancer Detect. Prev., 4:307-312, 1981.

Project Number: U909

PROGRESS REPORT

1 October 1980 - 30 September 1981

Armed Forces Institute of Pathology
Washington, D.C. 20306

Title: Foveomacular Aging in the Rhesus Monkey

Work Unit No. 9052C

Investigator(s): Fine, B.S., M.D.
Broughton, W., M.D.; Eagle, R., M.D.; Font, R.L., M.D.;
Hidayat, A., M.D.; Perry, H.D., M.D.; Yanoff, M., M.D.;
Zimmerman, L.E., M.D.

Supported by a grant from National Institutes of Health (EY03060) - second year of support.

Our second paper on lipoidal degeneration of the retinal pigment epithelium involving the foveomacular region of aging rhesus monkeys was published.⁴ This work indicated that the degenerative vacuoles did indeed contain a lipoidal material in at least two morphologic forms both of which are easily extracted when using conventional fixation methods.

An additional 20 pairs of our series of aging rhesus monkey eyes were prepared for study.

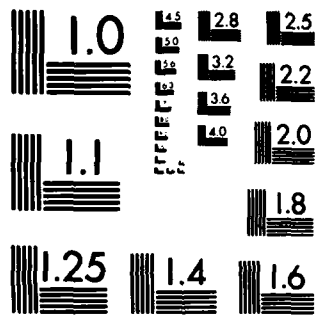
Ancillary work was carried out on cases of iris nevus syndrome,¹ keratoconus,² and on cases of glaucoma: a) unilateral glaucoma produced by an iris nevus,³ b) chronic open angle glaucoma,⁴ and c) congenital glaucoma.⁵

A manuscript is in preparation for work on the monkey foveomacula exposed to intense incoherent white light from a clinical instrument (i.e., indirect ophthalmoscope) in collaboration with Dr., L. Parver. Additional work in this area has also begun.

To date we have been unable to obtain material from very aged monkey eyes in our collaboration with Dr. T. Stafford in Chicago. However, we have been able to examine 3 eyes from humans who had documented (i.e., fluorescein angiography) evidence of pre-enucleation cystoid macular edema. A manuscript on this has been submitted for publication.

Additional studies on the vascular changes in the foveomacular region of an eye from a diabetic have been started and are being extended to an examination of changes that may occur in the nearby retina and optic nerve head.

Additional work was completed on a study of a new entity, "non-guttate corneal endothelial degeneration," in collaboration with Dr. R.L. Abbott in



MICROCOPY RESOLUTION TEST CHART
NATIONAL BUREAU OF STANDARDS-1963-A

Title: Foveomacular Aging in the Rhesus Monkey (cont'd.)

San Francisco. This report was presented to the American Academy of Ophthalmology in the fall of 1980 and a paper has been submitted to the journal, Ophthalmology.

Publications:

1. Eagle, R.C., Jr., Font, R.L., Yanoff, M., Fine, B.S.: The iris naevus (Cogan-Reese) syndrome: Light and electron microscopic observations. *Brit. J. Ophthalmol.* 64:446-452, 1980.

2. Perry, H.D., Buxton, J.N., Fine, B.S.: Round and oval cones in keratoconus. *Ophthalmology* 87:905-909, 1980.

3. Nik, N.A., Hidayat, A., Zimmerman, L.E., Fine, B.S.: Diffuse iris nevus manifested by unilateral open angle glaucoma. *Arch. Ophthalmol.* 99:125-127, 1981.

4. Fine, B.S., Yanoff, M., Stone, R.A.: A clinicopathologic study of primary open-angle glaucoma compared to normal eyes. *Am. J. Ophthalmol.* 91:88-105, 1981.

5. Broughton, W.L., Fine, B.S., Zimmerman, L.E.: Congenital glaucoma associated with a chromosomal defect. A histologic study. *Arch. Ophthalmol* 99:481-486, 1981.

6. Fine, B.S.: Lipoidal degeneration of the retinal pigment epithelium. *Am. J. Ophthalmol.* 91:469-473, 1981.

Title: The Degree of Burnout Experienced by Intensive Care Nurses

Purpose: While stress and stressors of intensive care nursing have been examined, it is not yet appropriate to presume a relationship between stress (cause) and burnout (effect). The question of whether burnout even exists among intensive care nurses requires systematic study before it can be answered. The purpose of this study was to assess, in intensive care nurses, the frequency and intensity of three aspects of the burnout syndrome as described by Maslach and Jackson (1981). The three aspects were: emotional exhaustion (EE), depersonalization (DP), and personal accomplishment (PA).

Sample description: The 90 subjects of this study were registered nurses currently practicing intensive care nursing. The CCU, NICU, SICU/RR, TICU, and MICU of a large Army medical center were used as the data collection sites. The majority of the subjects was military (66 percent), female (89 percent), and caucasian (74 percent). The mean age was 33±7.5 years. Of the 39 percent of subjects who were married, the mean number of years married was 3.6±6.8. The subjects' most common level of education was the baccalaureate degree (64 percent) and their most common level of position was that of staff nurse (78 percent). The mean number of months in nursing was 116.54±82.23 and the mean number of months in current job was 23.44±34.35.

Methods of Data Collection: This was a descriptive survey, with completely voluntary subject participation. The Maslach Burnout Inventory was used as the data collection tool. This is a self-reporting questionnaire with 22 items, each of which is answered twice, giving the frequency (F) and Intensity (I) responses, that is, EE:F, EE:I, DP:F, DP:I, PA:F, and PA:I. The syndrome of burnout would be demonstrated by increased EE:F, EE:I, and PA:I, DP:F, and DP:I scores and by decreased PA:F and PA:I scores. Reliability and validity of the tool is acceptable.

Methods of Data Analysis: Data from continuous variables were studied using correlational analysis. Data from discrete variables were studied using analysis of variance; a significance level of .05 was used. The means of the total group were compared, using the t Test, to the normative data of Maslach and Jackson.

Findings: The continuous variables of age, years married, and months in nursing showed low correlations indicating a definite but small relationship between these variables and some of the aspects of the burnout syndrome. Age was negatively correlated with EE:I and DP:I. Years married was negatively correlated with EE:F, EE:I and DP:I. Months in nursing was negatively correlated with EE:F, EE:I, DP:F, and DP:I.

The discrete variables indicated a significantly higher 1) EE:F and DP:I among military than civilian subjects; 2) EE:I among males than females; 3) EE:I, DP:F, DP:I and PA:I among caucasians than noncaucasians; 4) PA:F and PA:I among those with some college than those with BSN, Master's or other

levels of education; 5) EE:F and DP:F among those with baccalaureate degree than among those with other degrees or a diploma; 6) DP:I among clinical coordinators and senior clinical nurses than staff nurses, and 7) EE:F among subjects assigned to TICU than those on other units.

Considering the overall scores for the syndrome of burnout, the subjects demonstrated a level of burnout which was moderate when compared with the normative scores reported by Maslach and Jackson.

Conclusions and Recommendations: The rather scattered findings within the three aspects of burnout seem to indicate the need for extreme caution in presuming that burnout is the result of stress among intensive care nurses. Selected groups of intensive care nurses reported some of the aspects of burnout (feelings of increased emotional exhaustion, increased depersonalization, and decreased personal accomplishment), but none of the groups reported all of the aspects. Addressing the specific aspects reported by specific groups may assist nurses and nurse managers to better deal with the consequences of stress in intensive care nursing.

JOSEPH P. MALONEY, LTC, ANC
CLADUIA BARTZ, MAJ, ANC
Walter Reed Army Medical Center
Washington, DC

DATE: 6 Aug 82 | Block Unit No.: 9056-82 | STATUS: INTERIM | FINAL

STARTING DATE: APRIL 1982 | DATE OF COMPLETION: APRIL 1982

KEY WORDS: Health Beliefs, Breast Self-Examination

TITLE OF PROJECT: Nurse's Health Beliefs About Breast Cancer
And Breast Self-Examination

PRINCIPAL INVESTIGATOR(S): MAJ Dana Schodt, MAJ Donna Myzer

ASSOCIATE INVESTIGATOR(S):

FACILITY: WRAIC

DEPT/SVC: Department of Nursing

ACCUMULATIVE MEDICARE COST:

ACCUMULATIVE CONTRACT COST:

ACCUMULATIVE SUPPLY COST:

FY-83 MEDICARE:

CONTRACT COST:

SUPPLY COST:

DATE OF COMMITTEE APPROVAL OF
ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To determine if female registered nurses practice Breast Self-Examination and if they teach Breast Self-Examination to their female patients.

TECHNICAL APPROACH:

Survey questionnaire of 49 registered nurses at WRAIC and 50 registered nurses at a Baltimore City hospital

PROGRESS DURING FY-82:

Data Analysis Completed

NUMBER OF SUBJECTS STUDIED:

FY-82: 42

TOTAL (TO DATE): 42

BEFORE COMPLETION OF STUDY: NA

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

NONE

CONCLUSIONS:

See Attached Report

PUBLICATIONS OR ABSTRACTS, FY-82:

Methodology

A convenience sample of 50 female registered nurses from a local community hospital in Baltimore City, Maryland and 49 female registered nurses from a local military medical center in Washington, D.C. were asked to fill out a questionnaire devised by Margot Stillman in 1977 entitled "Women's Health Beliefs about Breast Cancer and Breast Self-Examination". The objective was to replicate her correlational study using one of the recommendations published in Nursing Research (March-April, 1977). "A study should be made of nurses in community health, industrial, high school, and hospital settings to determine the percentage who health teach about breast cancer and BSE, including the reasons for doing or not doing so".

Subjects

The subjects consisted of 99 female registered nurses. 50 questionnaires were distributed at the community hospital: 39 of the questionnaires were completed, 1 turned in blank, 2 were never received by the chosen nurses who were on leaves of absence, and 3 were not returned. At the military hospital, 49 questionnaires were distributed: 42 questionnaires were returned completed, 3 were returned after the data had already been tabulated, and 4 were not returned. 92% of the questionnaires were completed and analyzed.

Results

Section I (Knowledge). 44% of the sample selected the correct answer related to prevalence (less than 10% - letter a) while 56% overestimated the prevalence of breast cancer. 89% correctly believed that most breast lumps are not malignant (letter b). 80% of the sample in this study believed a woman's chances for developing breast cancer increases after age 30 or 40 (letters b and c), both of which were acceptable because the ages 35 and 40 are those most cited. In describing the woman more at risk for developing breast cancer, 89% of the sample knew about the relationship if relatives have breast cancer; 14% of the sample also believed that being married with no children or being single or post-menopausal were contributing factors, which they are. A Pearson's r of $-.21$ was obtained indicating no relationship between age of the subject and their knowledge as tested by the multiple choice questions in Section I.

Section II (Beliefs). 73% of the sample scored in the high range, with no subjects falling into the low range regarding perceived susceptibility. Sample scores ranged from 9 to 19 with a mean score of 18.7. Regarding perceived benefits, the majority of the sample (99%) scored in the high range, with no subjects falling into the low range. Sample scores ranged from 14 to 20 with a mean score of 18.7. An alpha coefficient of $.51$ was obtained for internal consistency. A t -test for independent samples yielded a $.8$, with $p > .05$ and $df 60$, indicating no significant difference in attitude (as measured by an individual's total score) and level of education. A second t -test for independent samples yielded $t=2.27$, p greater than $.05$, $df 60$, indicating no significant difference in the teaching of BSE with attitude.

Section III and IV (Practice of BSE). 99% of the sample answered that they do practice BSE at least monthly; 20% perform BSE 6-11 months out of the year; and 40% perform BSE less than 5 months out of the year.

A chi square was performed on frequency of performance and level of education which was not significant. A second chi square was performed on frequency of performance and teaching of BSE which was also not significant. A third chi square performed on age and frequency of performance was not significant. 85% of the sample are still having their menstrual periods with 67% performing BSE after their period. For those who no longer menstruate, they perform BSE whenever they think of it. 43% of the subjects had learned about BSE from a doctor while 47% had learned about BSE from a nurse. 55% of the subjects expressed confidence in the BSE technique. In relation to confidence in ability to discover something abnormal 30% were "not sure"; 70% replied yes; and 9% said no.

Section V (Demographics) The sample's mean age in years was 33 with a range of 42 (63 being high, 21 being low). The modal religion was Protestant (48%) with 43% Catholic, 3% Jewish, and 6% unspecified. 52% of the sample have a Bachelor of Science in Nursing, 26% are Diploma school graduates, 9% have an Associate Degree and 4% have their Master's Degree in Nursing. For purposes of the various test statistics performed using level of education, those with MSN's and BSN's were grouped together and those with Associate Degrees and Diplomas were grouped together. 53% of the subjects are married, 33% single, 12% separated or divorced, and 1% widowed. 46% of the sample have children. 79% of the subjects have no family history of cancer while 16% have had a lump removed from their breast. Only 1 person reported having had surgery for cancer. 95% care for cancer patients. A chi square for significance between level of education and the teaching of BSE was performed with no significance ($X^2=.58$, p greater than .05, df 1).

OTHER. 99% of the nurses do perform breast self-examination with 40% of the sample performing it on a monthly basis. 386 of the nurses in this sample do teach breast self-examination

to their patients. The 62% of the sample who do not teach BSE to their patients reported "lack of time" as the primary reason. Only 12% were not sure how to teach BSE and 6% reported embarrassment about the task.

Limitations. The tool itself needs to be redesigned and reevaluated. The review of the literature revealed multiple citations of Stillman's study yet the reliability of the tool had never been reported. The answers to the multiple choice questions in Section I pertaining to factual knowledge may need to be updated in regard to current social mores (i.e. being single versus married with no children as a predisposing factor for developing breast cancer). Furthermore, it was unclear how to score the multiple answers available for Item #4. Section III, Item 5 was ignored in this study due to its open-ended wording which was difficult to analyze from one individual to another although all of the responses given were appropriate. Section V, Item 6, needs to be reworded as the the age at which one delivered her first full-term fetus. Women who have their first child at or after the age of 35 are at an increased risk for developing breast cancer. Item 10 needs to be qualified as to the type of patient taught BSE, why, and how often an individual nurse does teach.

DATE: 1 Oct 82 WORK UNIT No.: 9053-82 STATUS: INTERIM FINAL X

STARTING DATE: 1 November 1981 DATE OF COMPLETION: 29 September 1982

KEY WORDS: Nursing, Job Satisfaction

TITLE OF PROJECT: A Survey of the Job Satisfaction of Nursing Personnel Assigned to the 5th Floor, Walter Reed Army Medical Center, during the period 1 November 1981 to 15 May 1982.

PRINCIPAL INVESTIGATOR(S): CPT Buchanan, LTC Kulm, MAJ Johnson, LTC Lobody, MAJ Greene, MAJ Synakowski, MAJ Pickering-Scott, MAJ Tushbant, MAJ Weigand, LTC Tollefson

ASSOCIATE INVESTIGATOR(S):

FACILITY: IRAMC DEPT/SAC: Nursing Research Service

ACCUMULATIVE MEDICARE COST: ACCUMULATIVE CONTRACT COST: ACCUMULATIVE SUPPLY COST:
0 0 0

FY-83 MEDICARE: CONTRACT COST: SUPPLY COST: DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983
0 0 0

STUDY OBJECTIVE: 1. To determine the level of job satisfaction felt by the nursing personnel assigned to the 5th floor, Walter Reed Army Medical Center, at the time of the surveys. (Cont)

TECHNICAL APPROACH: Survey - Resurvey

PROGRESS DURING FY-82: Completed

NUMBER OF SUBJECTS STUDIED:

FY-82: 250 TOTAL (TO DATE): 250 BEFORE COMPLETION OF STUDY: 0

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS: 1. First line supervisors can institute changes which can effect the satisfaction level on the nursing staff. 2. An improvement in other areas effecting satisfaction such as having designated, pleasant break areas, and giving the staff more responsibility in the arrangement of work assignments can have a positive effect on the perception of satisfaction with their pay or with their job.

PUBLICATIONS OR ABSTRACTS, FY-82: None

Study Objectives Con't - 2. To identify the job characteristics which contribute to the job satisfaction felt by the nursing personnel assigned to the 5th floor, Walter Reed Army Medical Center, at the time of the surveys. 3. To identify the job characteristics which contribute to the job dissatisfaction felt by the nursing personnel assigned to the 5th floor, Walter Reed Army Medical Center at the time of the surveys. 4. To identify the effects on job satisfaction of changes made on the unit between the administration of the two surveys.

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| DATE: 18 Oct 82 | Work No.: 9055 | STATUS: 1 | FIG. X |
| STARTING DATE: 1 March 1982 | | DATE OF COMPLETION: 1 July 1982 | |
| KEY WORDS: Burnout | | | |
| TITLE OF PROJECT: The Degree of Burnout Experienced by Intensive Care Nurses | | | |
| PRINCIPAL INVESTIGATOR(S): Joseph P. Maloney | | | |
| ASSOCIATE INVESTIGATOR(S): Claudia Bartz | | | |
| FACILITY: IRANC | | Dept/Svc: Department of Nursing | |
| ACCUMULATIVE MEDICARE COST: None | ACCUMULATIVE CONTRACT COST: None | ACCUMULATIVE SUPPLY COST: None | |
| FY-85 MEDICARE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983 |

STUDY OBJECTIVE: To Assess in Intensive Care Nurses the Frequency and Intensity of three Aspects of Burnout.

TECHNICAL APPROACH: Questionnaire

PROGRESS DURING FY-82: 90 Subjects completed the questionnaire

NUMBER OF SUBJECTS STUDIED:

FY-82: 90 TOTAL (TO DATE): 90 BEFORE COMPLETION OF STUDY: Completed

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
N/A

CONCLUSIONS:

See Abstract (Attached)

PUBLICATIONS OR ABSTRACTS, FY-82:

DATE: 10/18/82 | Work Unit No.: 9057-82.1 | STATUS: INTERIM FINAL

STARTING DATE: May 1982 | DATE OF COMPLETION: 27 Nov 82

KEY WORDS: Behaviors, Activities, Intraoperative

TITLE OF PROJECT: A Descriptive Study of the Behaviors, Activities and Cognitive Functions of the Registered Nurse During the intraoperative Phase of Surgery.

PRINCIPAL INVESTIGATOR(S): Major Jean M. Reeder

ASSOCIATE INVESTIGATOR(S): Major Donna Sylvester

FACILITY: WRMC | DEPT/SVC: Operating Room Nursing Service

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| ACCUMULATIVE FEDCASE COST: N/A | ACCUMULATIVE CONTRACT COST: N/A | ACCUMULATIVE SUPPLY COST: N/A |
|-----------------------------------|------------------------------------|----------------------------------|

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| FY-83 FEDCASE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
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STUDY OBJECTIVE: To Describe Nursing Activities and compare observed activities with the basic competencies of perioperative nursing from the Association of Operating Room Nurses.

TECHNICAL APPROACH: Qualitative Approach - direct observation, interviews and questionnaires

PROGRESS DURING FY-82: Proposal approved data collection, 1st 3 Chapters of thesis written and data analysis in progress.

NUMBER OF SUBJECTS STUDIED:

FY-82: 15 | TOTAL (TO DATE): 15 | BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS: Data analysis in progress; expect to be completed by 27 November 1982.

PUBLICATIONS OR ABSTRACTS, FY-82: Abstract submitted to AORN-Research Committee for consideration as a presentation at AORN Congress, April 1983. Status unknown.

DATE: 1/4/83 Work Unit No.: 9057-82 STATUS: INTERIM FISCAL YEAR XX

STARTING DATE: DATE OF COMPLETION: 17 Nov 83

KEY WORDS: Behaviors, Activities, Cognitive Functions, Intraoperative

TITLE OF PROJECT: A Descriptive Study of the Behaviors, Activities and Cognitive Functions of the Registered Nurse During the Intraoperative Phase of Surgery

PRINCIPAL INVESTIGATOR(S): Major Jean M. Reeder

ASSOCIATE INVESTIGATOR(S):

FACILITY: WRAVC DEPT/SVC: Operating Room Nursing Service

| ACCUMULATIVE MEDICASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
|-----------------------------|-----------------------------|---------------------------|
| 0 | 0 | 0 |

FY-83 MEDICASE: CONTRACT COST: SUPPLY COST: DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To describe nursing activities during the intraoperative phase of surgery.

TECHNICAL APPROACH: Qualitative

PROGRESS DURING FY-82: Study completed in November 1982

NUMBER OF SUBJECTS STUDIED:

FY-82: 15 TOTAL (TO DATE): 15 BEFORE COMPLETION OF STUDY: X

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): None

CONCLUSIONS: Approximately 70% of the Basic Competencies were observed during the intraoperative phase of surgery and 30% were not observed. Several areas were recommended for further nursing research.

PUBLICATIONS OR ABSTRACTS, FY-82:

DATE: 26 May 82 Hosp Unit No.: 9058-81 | STATUS: INTERIM FISCAL XX

STARTING DATE: October 81 | DATE OF COMPLETION: 16 Dec 1981

KEY WORDS:

TITLE OF PROJECT: An Identification of the Expressed Needs of Family Members of the Terminally Ill Patient in a Hospital Setting.

PRINCIPAL INVESTIGATOR(S): Mary E. O'Brien-Abt

ASSOCIATE INVESTIGATOR(S): N/A

FACILITY: WRAIC

DEPT/S/C: Nursing

ACCUMULATIVE MEDICARE COST:

ACCUMULATIVE CONTRACT COST:

ACCUMULATIVE SUPPLY COST:

N/A

N/A

N/A

FY-83 MEDICARE:

CONTRACT COST:

SUPPLY COST:

DATE OF COMMITTEE APPROVAL OF

N/A

N/A

N/A

ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: The purpose of this study was to identify the importance of needs of families of the terminally ill patient, if their needs were being met in nursing practice, and who were meeting these needs.

TECHNICAL APPROACH: An instrument consisting of three parts was utilized to collect the data. The parts were: participant information sheet, personal data sheet, and 45 statement information schedule. Twenty family members were interviewed.

PROGRESS DURING FY-82:

Completed as above

NUMBER OF SUBJECTS STUDIED:

FY-82:

TOTAL (TO DATE):

BEFORE COMPLETION OF STUDY: 20

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

N/A

CONCLUSIONS: The finding of this study indicated that the most important need was to have questions answered honestly. 66% of the needs were met > 50% of the time. The physicians and nurses met 31 or 86% of the needs.

PUBLICATIONS OR ABSTRACTS, FY-82: completed, a full report attached

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|--|-------------------------------------|-----------------------------------|---|
| DATE: 2/3/83 | WORK UNIT No.: 9080 | STATUS: INTERIM | FINAL XX |
| STARTING DATE: Sept 1978 | DATE OF COMPLETION: Oct 1983 | | |
| KEY WORDS: coronary heart disease, Type A behavior | | | |
| TITLE OF PROJECT: Coronary Artery Disease and Coronary-Prone Behavior. | | | |
| PRINCIPAL INVESTIGATOR(S): David Krantz, PhD, Assoc Prof, Med Psych USUHS | | | |
| ASSOCIATE INVESTIGATOR(S): James E. Davia, COL MC, C, Cardiology, WRAMC | | | |
| FACILITY: WRAMC & USUHS | | DEPT/SVC: Cardiology | |
| ACCUMULATIVE FEDCASE COST: None | ACCUMULATIVE CONTRACT COST: None | ACCUMULATIVE SUPPLY COST: None | |
| FY-83 FEDCASE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983 |
| STUDY OBJECTIVE: Same as report for previous years. | | | |

TECHNICAL APPROACH:

PROGRESS DURING FY-82:

Project completed.

NUMBER OF SUBJECTS STUDIED:

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS:

PROJECT COMPLETED.

PUBLICATIONS OR ABSTRACTS. FY-82:

- 1) Psychosomatic Medicine, 1982, 44, 273-284.
- 2) Journal of Human Stress, 1982, 8(3), 4-12.

Work Unit No.: 9082

Title of Project: Treatment and Rehabilitation of Knee Injuries at the United States Military Academy, West Point, NY 10996

Investigators:

Principal: LTC Walton W. Curl

Associate: LTC Keith L. Markey

Objectives: To develop predictive parameters and programs to lower the knee injury rate of cadets at the United States Military Academy. It is also the objective to analyze and develop better treatment modalities for those injuries which do occur.

Technical Approach: Cadets who are participating in the intramural and inter-collegiate football, wrestling, and lacrosse programs are being screened as part of the pre-season physical examination for multiple parameters which might effect knee injury rate. These parameters include: joint laxity, height, weight, body type, etc. This data and following the individuals through the sport season, determine what types of injuries they incur and it is hoped that a statistical correlation can be performed to relate these various parameters to knee injuries.

The treatment phase deals with the diagnosis and treatment of essentially isolated tears of the anterior cruciate ligament. Those who have a proven torn anterior cruciate ligament then undergo an acute repair and reconstruction of the torn anterior cruciate ligament utilizing the medial third of the patellar tendon. They are then casted with a long-leg cast with the bent knee at 60° for six weeks and then a cast-brace at 30-60° for six weeks. They are then started on a knee rehabilitation program. These patients are then followed at a 3 and 6 months, 1 year, 2 year, and 5 year, and 10 year intervals for long term sequelae.

Progress and Results: Preventive Phase: 198 intramural football players were examined and evaluated utilizing the Cybex II. The Cybex II was used to measure hamstring and quad strength at 5 rpm's and 30 rpm's on both the right and left knees. The average Cybex rating at 5 rpm's for the quadriceps was one knee was 95% the strength of the other knee. The range was from 74% to 100%, with the majority of knees being above 90% strength. Of the 198 individuals in this study, 22 injured their knees while play-intramural football. In both the injured group and the uninjured group, the Cybex rating was 6% difference in knees. This finding would therefore indicate that a pre-season Cybex rating of knees is not a good predictive parameter

for screening those individuals more prone to knee injuries while playing football. It was interesting to note that the average difference between the right and left knee was 6%. This is a useful parameter to know when rehabilitating a knee that one only need to rehabilitate the knee to approximately 90% strength in order for it to be considered in the normal range. The Cybex data will continue to be analyzed to see if there is any other more subtle correlations which can be made, however, it does not appear that it is a useful predictive parameter. A laxity study was also performed in a previous group which has been included in this protocol. The complete study is attached as an addendum.

Treatment phase: We currently have operated on 157 anterior cruciate ligament injuries using the medial one-third of the patella tendon to augment the repair of the anterior cruciate ligament. There have been no specific changes in the basic approach to the operation. The post operative immobilization was for three weeks at 60° and nine weeks in a hinged cast from 30° to 60°. The number of knees inputted into the study will be terminated as of the end of May 1982. The follow-up to these knee injuries will be on-going then over the next ten years to ascertain the efficacy of this operation over the long-term.

Conclusions: Again, the study continues to be on-going. The preventive phase has been concluded with the analysis of the Cybex data which has previously been discussed as being inconclusive. The laxity study which was done in conjunction with this study also proved to be of no value in providing a predictive parameter in this particular group of individuals. At present, we have been unable ascertain any type of predictive parameter in a routine screening test which has been able to identify those individuals who are prone to sustaining a serious knee injury during intramural football. We continue to have major problems in trying to have our data analyzed. We have recently obtained a computer terminal in the Orthopaedic Clinic where we are inputting our data into the computer at the present time into a data management system for analysis. Hopefully, by using this system, we will have an effective means to analyze data, using the computer and also will be able to use the computer for the long-term follow-up studies.

Funds Utilized, FY-82: The research secretary was funded for a part-time basis during FY-82. No other funds were utilized out of the clinical research investigation project.

Funding Requirements, FY-83:

Personnel: GS3 - This individual really should be hired on a full-time basis for FY 83 due to the increased amount of work to input data into the computer.

Equipment: Lenox Hill Braces for bracing anterior cruciate ligaments - Approx \$300.00 ea, estimated number required - 60.

Travel: \$1,000.00 for TDY for the purpose of presenting results as well as visiting other medical centers to discuss the role of the anterior cruciate ligament.

Supplies: None

Other: None

Publications & Abstracts FY-82: None as of yet.

DATE: 30 Sep 82 WORK UNIT No.: 9087 STATUS: INTERIM X FINAL

STARTING DATE: 30 March 1982 DATE OF COMPLETION: Unknown

KEY WORDS:

TITLE OF PROJECT: Intraocular Lens Implantation

PRINCIPAL INVESTIGATOR(S): ALLAN W. BERG, MD, LTC, MC

ASSOCIATE INVESTIGATOR(S): BENJAMIN LIBERATORE, MD, CPT, MC

FACILITY: WRAMC ^{Walton ACH} Fort Dix, NJ DEPT/SVC: Ophthalmology

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| ACCUMULATIVE MEDICASE COST: N/A | ACCUMULATIVE CONTRACT COST: N/A | ACCUMULATIVE SUPPLY COST: \$11,500 |
|------------------------------------|------------------------------------|---------------------------------------|

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|------------------------|-----------------------|-------------------------|---|
| FY-83 MEDICASE: N/A | CONTRACT COST: N/A | SUPPLY COST: Unknown | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983 |
|------------------------|-----------------------|-------------------------|---|

STUDY OBJECTIVE: To evaluate the correction of aphakia with intraocular lenses, to include primary and secondary implantation and adverse effects/complications.

TECHNICAL APPROACH: Standard cataract microsurgical techniques (extracapsular and intracapsular) followed by implantation of posterior or anterior chamber intra-ocular lenses.

PROGRESS DURING FY-82: Primary implantation, extracapsular with posterior chamber IOL: 14
Intracapsular with anterior chamber IOL: 2
Secondary implantation with anterior chamber IOL: 1

NUMBER OF SUBJECTS STUDIED:

FY-82: 17 TOTAL (TO DATE): BEFORE COMPLETION OF STUDY:

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS:

That, used appropriately, intraocular lenses are an acceptable means of correcting aphakia.

PUBLICATIONS OR ABSTRACTS, FY-82:

DATE: 14 Oct 81 | WORK UNIT No.: 9088 | STATUS: INTERIM X FINAL

STARTING DATE: 29 April 1980 | DATE OF COMPLETION: 30 July 1981

KEY WORDS: Obesity, Hypnosis- Cognitive Therapy, Group Therapy

TITLE OF PROJECT: A Comparison of the Use of Cognitive Therapy and Hypnosis in a Group Setting for Treating Obesity

PRINCIPAL INVESTIGATOR(S): Edmund G. Howe, M.D.

ASSOCIATE INVESTIGATOR(S):

FACILITY: HRAHC | DEPT/SVC: Psychiatry

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| ACCUMULATIVE MEDICASE COST: 0 | ACCUMULATIVE CONTRACT COST: 0 | ACCUMULATIVE SUPPLY COST: 0 |
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|----------------------|---------------------|-------------------|---|
| FY-83 MEDICASE: 0 | CONTRACT COST: 0 | SUPPLY COST: 0 | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
|----------------------|---------------------|-------------------|---|

STUDY OBJECTIVE: To determine whether the proposed treatment for obesity will be effective as a means of persons with obesity losing weight and maintaining weight loss. ~~To compare treatment and to generate hypotheses for further studies.~~

TECHNICAL APPROACH: Original study has been completed at this time. Analysis of data and writing up of results has yet to be done.

PROGRESS DURING FY-82: No further investigations were carried out. Modification described in 14 October 1981 interim report to take place over 10 weeks was not performed.

NUMBER OF SUBJECTS STUDIED: none

FY-82: _____ TOTAL (TO DATE): _____ BEFORE COMPLETION OF STUDY: _____

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): none

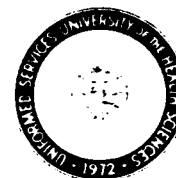
CONCLUSIONS: same

PUBLICATIONS OR ABSTRACTS, FY-82:

See abstract under FY 81 which is unchanged.



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SCHOOL OF MEDICINE
4301 JONES BRIDGE ROAD
BETHESDA, MARYLAND 20814



PEDIATRICS

15 October 1982

TEACHING HOSPITALS
WALTER REED ARMY MEDICAL CENTER
NATIONAL NAVAL MEDICAL CENTER
MALCOLM GROW AIR FORCE MEDICAL CENTER
WILFORD HALL AIR FORCE MEDICAL CENTER

SUBJECT: Annual Progress Report, FY-82, Clinical Investigational Program, Work Unit #9089, Etiology of Chronic Lymphadenopathy in Children and Adolescents.

THRU: COL Errol Alden, MC, USA - Professor and Chairman, Department of Pediatrics, USUHS *at*

COL George Hansen, MC, USA - Chief Pediatrics, Walter Reed Army Medical Center

TO: Timothy Boehm, M.D. - Chief, Clinical Investigation Service, Walter Reed Army Medical Center

1. Reference: Your DF dated 2 August 1982, suspense date of 8 October 1982 was not received until 8 October 1982.
2. It has been a policy for the past 12 years to calculate my data in reference to the above report at the end of the calendar year.
3. Because a large amount of statistical information will be extracted from over 200 patients I would be unable to give you a complete and detailed report until I have computed all of the patient data through 31 December 1982. This report would be submitted to your department NLT the 2nd week in January 1983. Also this annual report is sent to the Bureau of Biologics (FDA) for the annual report of IND# BB-IND-1267, PPD Skin Test study, and IND# BB-IND-1511 Cat Scratch Disease Antigen study, which constitutes a large part of the #9089 Clinical research study.
4. Please call me at 295-3136 if any questions arise.

A.M. Margileth

A.M. Margileth, M.D.
Professor and Vice Chairman
Department of Pediatrics, USUHS

DATE: 14 October '82 | WORK UNIT No.: 9089 | STATUS: INTERIM x FINAL

STARTING DATE: 1 January 1982 | DATE OF COMPLETION: 31 December 1982

KEY WORDS: Lymphadenopathy, skin test, PPD, Cat Scratch Antigen

TITLE OF PROJECT:

Infectious Etiology of Chronic Lymphadenopathy in Children & Adolescents

PRINCIPAL INVESTIGATOR(S): A.M. Margileth, M.D.

ASSOCIATE INVESTIGATOR(S): (1) Gerald Fischer, MD, USUHS (2) Richard Summers, MD, WRAMC
(3) Kenneth Hunter, ScD, USUHS (4) Monroe Vincent, USUHS

FACILITY: WRAMC

DEPT/SVC: Pediatrics

ACCUMULATIVE MEDCASE

COST: None

ACCUMULATIVE CONTRACT

COST: None

ACCUMULATIVE SUPPLY

COST: None

FY-83: MEDCASE: None CONTRACT COST: None SUPPLY COST: None | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE:

We propose to continue our studies to determine the etiology of chronic adenopathy in children and adolescents.

TECHNICAL APPROACH: Our approach will be to identify and purify the active component of CSD skin test material, and to determine the sensitivity and specificity as a diagnostic skin test antigen or as an agent for serologic testing of patients with adenopathy due to CSD. We would also determine the sensitivity and specificity of PPD atypical, PPD Battey and standard tuberculin PPD-T antigens in patients with (cont.)

Below

| PROGRESS DURING FY-82: Results 6 January 1982 thru 29 September 1982. | | | | |
|---|---------------------------|-----|------------------------------------|----|
| Skin tests | Cat Scratch Antigen Tests | 50 | Patients (Dual B&T Mantoux Tested) | |
| | PPD-T Tests | 258 | Cat Scratch Disease | 42 |
| | PPD-Battey Tests | 253 | Healthy persons, PPD-T Positive | 35 |
| | | 561 | Healthy persons, PPD-B Positive | 63 |
| | | | M. tuberculosis disease | 4 |
| | | | Nontuberculosis disease | 12 |

* NUMBER OF SUBJECTS TO BE STUDIED BEFORE COMPLETION OF STUDY: FY 82 206 Apprx. 156

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT:

None in past 21 years

CONCLUSIONS: Approximately 220 patients will be skin tested by 31 December 1982. See attached abstract paper (submitted for publication) of data from 1967 - 1980,

PUBLICATIONS OR ABSTRACTS, FY-82:

* Total (to date) 206 Before completion of study 160 patients each year

acute and chronic lymphadenopathy and in healthy individuals. Mycobacterial culture results still pending on several patients should be available by December 1982, thus allowing correlation of the PPD antigens with the specific mycobacterial isolate.

PUBLICATIONS AND PRESENTATIONS

1. Margileth, AM: Atypical Mycobacterial Infections in Children. PEDIATRICS Rudolph, A (Ed), 17th Edition, New York, Appleton-Century-Crofts, p-581, 1982.
2. Margileth, AM: Cat Scratch Disease. PEDIATRICS, Rudolph, A (Ed), 17th edition, New York Appleton-Century-Crofts, p-636, 1982.
3. Margileth, AM: Cat Scratch Disease, Cecil Textbook of Medicine, 16th ed., Wyngaarden, JB, and Smith, LH, Jr., Philadelphia, WR Saunders Co., 1982.
4. Margileth, AM: Infections with Nontuberculous (Atypical) Mycobacteria. Chapter 47 in Respiratory Tract Disorders in Children. WB Saunders Co., Philadelphia, PA. March 1983.
5. Margileth, AM: Nontuberculous (Atypical) Mycobacterial Infections: I Specificity of PPD Skin Tests in Children Compared to Mycobacterial Species. Accepted for publication. Abstract 14 Oct. 1982 enclosed.
6. Margileth, AM, Chandra, R, Altman, RP: Nontuberculous (Atypical) Mycobacterial Infections: II Clinical Features, Diagnostic Studies, Histopathology and Management in Children and Adolescents. In preparation.
7. Margileth, AM, London, W, Sever, J, and Curfman, B: Cat Scratch Disease, Failure of Material from humans to produce disease in Mammals. In preparation.
8. Cohen, GJ, Margileth, AM: Fungus Cultures in the Physicians Office: Comparison of DTM with Sabouraud's and Mycosei Media. Clinical Proc CHNMC, 1982.
9. Margileth, AM: Nontuberculous (atypical) Mycobacterial Infections. In Gellis, SS and Kagan, BM (Eds.). Current Pediatric Therapy, 11th edition, Philadelphia, PA, W.B. Saunders Co. 1983.
10. Margileth, AM: ABSTRACT, Atypical Mycobacterial Infections: Correlation of Atypical and Typical PPD Skin Tests with Mycobacterial Cultures. Pediatric Res. 1979;13:392.
11. Presented preliminary findings of this study to: Pediatric Faculties of University of Texas Medical School and Brooke Army Medical Center, San Antonio, Tx on 3 December, 1982.

REVISED 17 January 1983

A.M. Margileth, M.D.



UNIFORMED SERVICES UNIVERSITY
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PEDIATRICS

17 January 1983

TEACHING HOSPITALS
WALTER REED ARMY MEDICAL CENTER
NATIONAL NAVAL MEDICAL CENTER
MALCOLM GROW AIR FORCE MEDICAL CENTER
WILFORD HALL AIR FORCE MEDICAL CENTER

SUBJECT: Annual Progress Report, FY-82, Clinical Investigational Program, Work Unit #9089, Etiology of Chronic Lymphadenopathy in Children and Adolescents.

THRU: COL. Errol R. Alden, M.D., MC, USA - Professor and Chairman, Department of Pediatrics, USUHS

COL. George Hansen, M.D., MC, USA - Chief, Pediatrics, Walter Reed Army Medical Center

TO: Timothy Boehm, M.D. - Chief, Clinical Investigational Service
Walter Reed Army Medical Center

REFERENCE: Preliminary report, 15 October 1982, subject as above.

The results of our studies in 225 patients during 1982 are enclosed. During 1983 we plan to continue our clinical and experimental studies at USUHS, WRAMC, and NIH (see Dr. John Sever's ltr, Jan 1982). During 1982 little progress was made with the NIH cat scratch research. However, we were able to concentrate cat scratch antigen (CSAg) and show a linear increased reactivity to skin tests with the concentrated antigen in 6 patients (Appendix B). We will now attempt to identify the active component of CSAg.

We are also working with D.J. Wear, COL, MC, AUS, Chief, Geographic Pathology at AFIP, and T.L. Hadfield, Chief, Bacteriology of Microbiology at AFIP, on the possibility of isolating and identifying a microorganism in biopsy material of lymph nodes obtained from patients with cat scratch disease.

We have also prepared a new protocol to be resubmitted to the Grants Management Division at USUHS to obtain approval to perform a 3 year study of dual Mantoux (PPD-B & T) skin tests on freshman medical students attending airborne school each summer at Ft. Benning, GA. (see copy of letter from H.M. Meyer, Jr, Director, F.D.A., dated 11 June 1982)

No untoward nor unusual reactions have occurred in any patient tested to date. Two articles have been accepted for publication on the results of the PPD antigen studies.

Your suggestions and comments would be welcomed.

A. M. Margileth MD

A. M. Margileth, M.D.
Professor and Vice Chairman
Department of Pediatrics
USUHS

DATE: 17 Jan. '83 UNIT NO.: 9089 STATUS: RIM FINAL X

STARTING DATE: 1 Jan. '82 DATE OF COMPLETION: 31 Dec. '82

KEY WORDS: Lymphadenopathy, Skin Tests: PPD, Cat scratch Antigen

TITLE OF PROJECT:
Infectious Etiology of Chronic Lymphadenopathy in Children and Adolescents

PRINCIPAL INVESTIGATOR(S): A.M. MARGILETH, M.D.

ASSOCIATE INVESTIGATOR(S): (1) Gerald Fischer, M.D., USUHS (2) Richard Summers, M.D.
WRAMC
(3) Kenneth Hunter, ScD, USUHS (4) COL Wear, M.D., AFIP

FACILITY: Walter Reed Army Medical Center DEPT./SVC: Pediatrics

ACCUMULATIVE MEDCASE COST: None ACCUMULATIVE CONTRACT COST: None ACCUMULATIVE SUPPLY COST: None

FY-'83: MEDCASE: NONE CONTRACT COST: NONE SUPPLY COST: NONE DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983

STUDY OBJECTIVE: We propose to continue our studies to determine the etiology of chronic adenopathy in children and adolescents. We are now working with COL Wear, Geographic Pathology Section, AFIP on isolation and identification of an infectious agent for CSD.

TECHNICAL APPROACH: Our approach will be to identify and purify the active component of CSD skin test material, and to determine the sensitivity and specificity as a diagnostic skin test antigen or as an agent for serologic testing of patients with adenopathy due to CSD. We would also determine the sensitivity and specificity of PPD atypical, PPD Battey and a standard tuberculin PPD-T antigens in patients with acute and chronic lymphadenopathy and in healthy individuals. We plan to isolate the infectious agent of CSD using special culture media, and identify the agent by specific fluorescent antibody techniques now under development at the Geographic Pathology Section of AFIP.

PROGRESS DURING FY-'82: 1 Jan through 31 Dec '82

| | | |
|--------------------------|------------------------|---------------------------------------|
| <u>Skin Tests:</u> N=560 | <u>Patients:</u> N=222 | Cat scratch disease: 58 |
| Cat scratch antigen 74 | Dual B&T tests | PPD-T, healthy - 35 |
| PPD-T - 235 | | PPD-B, healthy - 70 |
| PPD-Battey - 251 | | M. Tuberculosis dis. - 4 |
| | | Non-Tuberculous dis. - 16 |
| | | Controls: other dis., healthy - 39 |

SEE APPENDIX A FOR DETAILS

*NUMBER OF SUBJECTS TO BE STUDIED BEFORE COMPLETION OF STUDY: FY-'82 200 (approx)

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT:

None in past 21 years

CONCLUSIONS: We anticipate identification of the etiologic agent of CSD in 1983. The 1981 and 1982 studies correlating PPD antigens with the mycobacterial isolates have shown similar results. Noted in the abstract attached, ref. #5.

PUBLICATIONS OR ABSTRACTS, FY-82:
See attached - Publications and Presentations.

ABSTRACT

Of 1288 patients tested with tuberculin PPD-T and nontuberculous mycobacterial (NTM) PPD antigens during a 13 year prospective study, 55%, 705, were PPD nonreactors. The remainder, 583 (45%), had findings to suggest tuberculous infection or were asymptomatic tuberculin (PPD and/or OT) test reactors. On the initial battery of PPD tests 553 patients had positive reactions; 513 (94%) could be classified as a human tuberculous reactor (HTR) or a nontuberculous reactor (NTR). Of the 553 patients 363 were asymptomatic and 190 had clinical disease. Fifty-nine patients had Mycobacterium tuberculosis (MTB) disease; 131 had NTM disease.

Mycobacterial isolates recovered in 71 (47%) of 150 patients cultured were compared to the initial and repeat PPD-T and NTM-PPD test results. There was 100% correlation between PPD-T and 22 MTB isolates, and 86% with the homologous NTM-PPD reaction and the species of 49 NTM isolates.

A PPD-T reaction of 5 to <15 mm suggested either an MTB or NTM infection while a PPD-T \geq 15 mm was strongly associated with MTB infection. Dual (PPD-T & PPD-Bathey) Mantoux testing in tuberculin positive children and adolescents can discriminate (88% of 26 MAIC culture positive subjects) between MTB or NTM infections and should be a valuable guide in their management.

14 October 1982

A.M. Margileth, M.D.

SKIN TEST PPD/CAT SCRATCH STUDY ANNUAL REPORT - 1982

| | <u>15 years</u> (1967-31DEC82) | <u>1980</u> | <u>1981</u> | <u>1982</u> |
|--|-----------------------------------|-------------|-------------|-------------|
| I. <u>Lymphadenitis or adenopathy</u> | | | | |
| Cat Scratch Disease | 706 | 46 | 59 | 58 |
| Mycobacterium (atypical) nontuberculous | 131 | 13 | 9 | 10 |
| Mycobacterium hominis | <u>22</u> | <u>0</u> | <u>2</u> | <u>1</u> |
| TOTAL | 859 | 61 | 70 | 69 |
| II. <u>Positive PPD skin test results</u> | | | | |
| <u>PPD-T (STU)</u> | | | | |
| Healthy reactors (chest x-ray normal) | 203 | 38 | 39 | 35 |
| Lymphadenitis | 22 | 0 | 2 | 1 |
| BCG itis | 2 | 1 | (2)* | 1 |
| Pulmonary disease | <u>39</u> | <u>0</u> | <u>0</u> | <u>1</u> |
| TOTAL | 266 | 39 | 41 | 38 |
| <u>Nontuberculous (Atypical) PPD (STU)</u> | | | | |
| Healthy Reactors (chest x-ray normal) | 345 | 42 | 43 | 70 |
| Lymphadenitis | 131 | 13 | 9 | 10 |
| Skin granuloma/splenitis | 7 | 1 | 0 | 2 |
| Pulmonary disease | <u>16</u> | <u>1</u> | <u>1</u> | <u>3</u> |
| TOTAL | 499 | 57 | 53 | 85 |
| GRAND TOTAL | 765 | 99 | 95 | 122 |
| III. <u>Negative PPD Tests</u> | | | | |
| Cat Scratch Disease | 598 | 33 | 50 | 32 |
| Adenitis or adenopathy: bacteria, viral, fungal | 59 | 0 | 1 | 1 |
| Other etiology diagnoses | 66 | 5 | 2 | 6 |
| Controls (no or minor disease) | <u>67</u> | <u>0</u> | <u>5</u> | <u>32</u> |
| TOTAL | 790 | 38 | 58 | 71 |

* BY P.H.

A. M. MARGILETH, M.D.
Rm. C-1066, (202)295-3136REVISED: 17 Jan. 1983

Mean (X) Skin Test reactions in mm and - = M

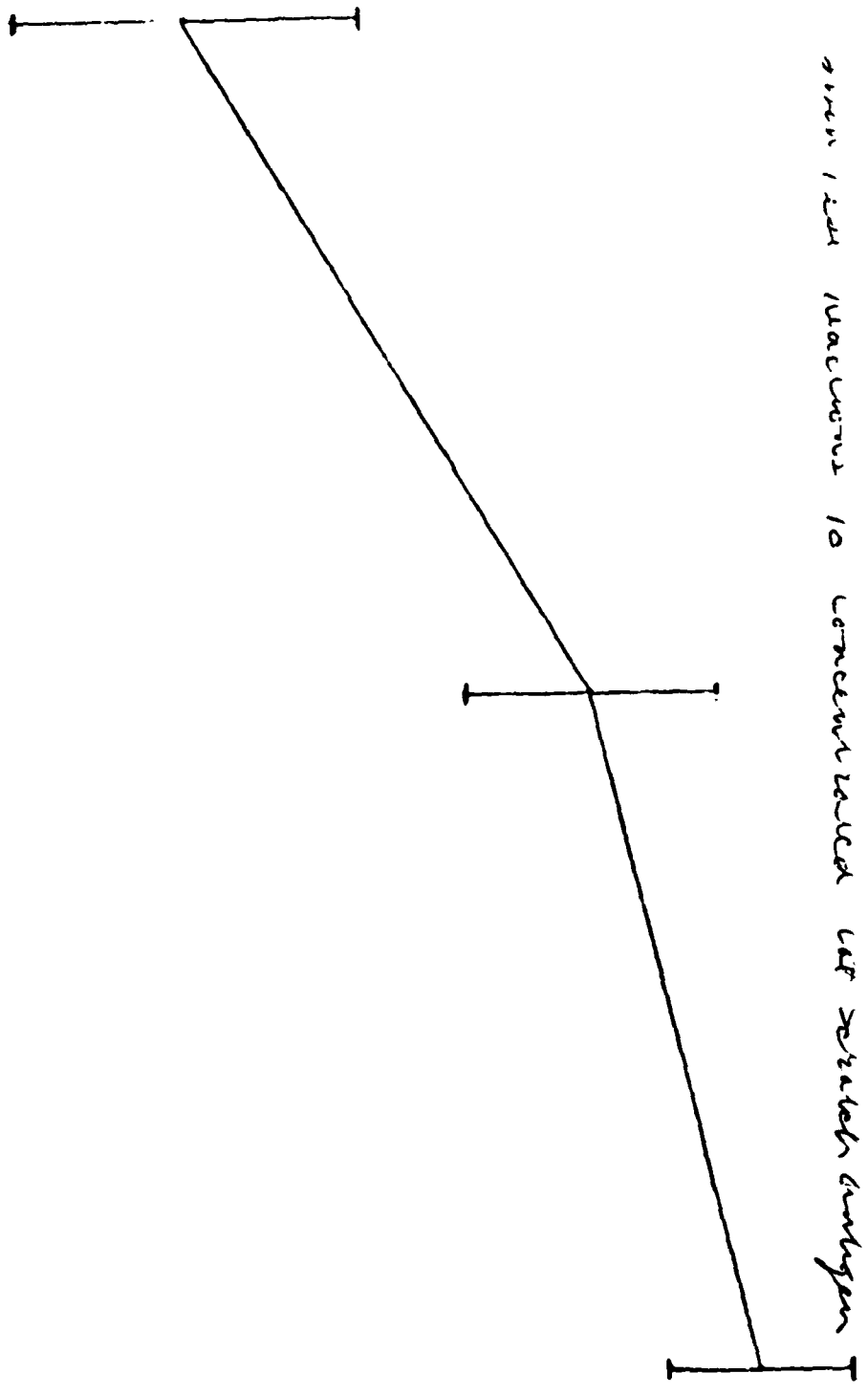
Cat scratch antigens Concentrations

X4

mean test reactions 10 concentrations cat scratch antigens

SEM I

Appendix B





PEDIATRICS

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15 January 1982



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SUBJECT: Annual Progress Report, FY-81, Clinical Investigational Program, Work Unit #9089, Etiology of Chronic Lymphadenopathy in Children and Adolescents.

THRU: COL. Errol R. Alden, M.D., MC, USA - Professor and Chairman, Department of Pediatrics, USUHS

COL. George Hansen, M.D., MC, USA - Chief, Pediatrics
Walter Reed Army Medical Center

TO: Timothy Boehm, M.D. - Chief, Clinical Investigational Service
Walter Reed Army Medical Center

REFERENCE: Preliminary report, 16 October 1981, subject as above.

The results of our studies in 153 patients during 1981 are enclosed. During 1982 we plan to continue our clinical and experimental studies at USUHS, WRAMC, and NIH (see Dr. John Sever's ltr, Jan 1982).

No untoward nor unusual reactions have occurred in any patient tested to date. Two articles have been prepared and submitted for publication of the results of PPD antigen studies. One has been accepted for publication.

Your suggestions and comments would be welcomed.

A. M. MARGILETH, M.D.
Professor and Vice Chairman
Department of Pediatrics

6 Incls

1. Detail Sheet (WRAMC CIS Form)
2. Abstract: NTM Infections
3. Publications/Presentations
4. Appendix A
5. Appendix B
6. John L. Sever, (ltr), M.D., Ph.D

CC:

1. Research Protocol
2. Assoc Investigators x 4
3. IND #s 1511 and 1267 office files
4. Gerald Fischer, M.D., Director, Pediatric Research

TELEPHONE: (202) 295-3136

DATE: 15 Jan 82 WORK UNIT No.: 9089 STATUS: INTERIM _____ FINAL x

STARTING DATE: 1 January 1981 DATE OF COMPLETION: 31 December 1981

KEY WORDS: Lymphadenopathy, skin test, PPD, Cat Scratch Antigen

TITLE OF PROJECT:
Infectious Etiology of Chronic lymphadenopathy in Children & Adolescents

PRINCIPAL INVESTIGATOR(S): A. M. Margileth, M.D.

ASSOCIATE INVESTIGATOR(S): (1) Gerald Fischer, M.D.-USUHS (2) Richard Summers, M.D. WRAMC
(3) Kenneth Hunter, ScD-USUHS (4) Monroe Vincent, USUHS

FACILITY: WRAMC DEPT/SVC: Pediatrics

| | | |
|------------------------------------|-------------------------------------|-----------------------------------|
| ACCUMULATIVE MEDCASE COST: None | ACCUMULATIVE CONTRACT COST: None | ACCUMULATIVE SUPPLY COST: None |
|------------------------------------|-------------------------------------|-----------------------------------|

FY-81: MEDCASE: _____ CONTRACT COST: _____ SUPPLY COST: _____ DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: To determine the etiology of chronic (≥ 3 wks) adenopathy in children and adolescents by skin tests with PPD-T and atypical (NTM) PPD antigens and cat scratch (CS) antigens.

TECHNICAL APPROACH: We will attempt to identify and purify the active component of CS antigen, and determine its sensitivity and specificity as a diagnostic skin test antigen. We will also determine the sensitivity and specificity of PPD-T and NTM antigens. Results are enclosed correlating these PPD skin test reactions with specific mycobacterial isolates.

PROGRESS DURING FY-81: Diagnoses made in 153 patients were:

| | |
|---------------------|----|
| Cat Scratch disease | 58 |
| PPD-T reactors | 42 |
| Healthy | 38 |
| lymphadenitis | 3 |
| BCG-itis | 2 |
| pulmonary disease | 1 |

* See bottom of pg, cont.

NUMBER OF SUBJECTS TO BE STUDIED BEFORE COMPLETION OF STUDY: 150-160 year

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT:
None in past 20 years in over 900 children, adolescents and adults.

CONCLUSIONS: Approximately 150-160 patients will be skin tested by 31 Dec 1981. See attached abstract paper to be submitted for publication of data from 1967-1980.

PUBLICATIONS OR ABSTRACTS, FY-81: Please see attached.

* PPD-(NTM) reactors , 53, healthy 43, lymphadenitis 9, pulmonary disease 1.
Negative Test: Cat scratch skin test 5, other diagnoses, PPD B&T tests 48, Appendix A.

| | | |
|---|------------------------------------|--|
| DATE: 8 Oct 82 | WORK UNIT No.: 9090 | STATUS: INTERIM <input checked="" type="checkbox"/> FINAL |
| STARTING DATE: 1 Sept 82 | DATE OF COMPLETION: 30 Sept 83 | |
| KEY WORDS: Immune Serum Globulin, Neonates | | |
| TITLE OF PROJECT: Modified Immune Serum Globulin in Neonates | | |
| PRINCIPAL INVESTIGATOR(S): Gerald W. Fischer | | |
| ASSOCIATE INVESTIGATOR(S): Leonard E. Weisman | | |
| FACILITY: WRAMC | DEPT/SVC: Newborn Medicine Service | |
| ACCUMULATIVE PEDCASE COST: 0 | ACCUMULATIVE CONTRACT COST: 0 | ACCUMULATIVE SUPPLY COST: 0 |
| FY-83 PEDCASE: _____ | CONTRACT COST: _____ | SUPPLY COST: _____ |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE:

Evaluate kinetics and safety of MISG in neonates

TECHNICAL APPROACH:

Infusion of MISG into neonates

PROGRESS DURING FY-82: Two patients have been enrolled at WRAMC. The patients tolerated the infusion well and no problems were noted. During the last year FAMC and MAMC have also contributed 12 patients to the project safely.

NUMBER OF SUBJECTS STUDIED:

FY-82: 2^{at FAMC} at WRAMC TOTAL (TO DATE): 2^{at FAMC} at WRAMC BEFORE COMPLETION OF STUDY: 30

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

No serious or unexpected side effects noted.

CONCLUSIONS:

The study will continue until completion sometime during the next fiscal year. Preliminary data is currently being tabulated and evaluated. Plans are being made for a multicenter efficacy trial once the pharmacokinetics trial are completed and results evaluated.

PUBLICATIONS OR ABSTRACTS, FY-82:

None

| | | |
|---|-----------------------------|--------------------------|
| DATE: 9/20/82 | WORK UNIT No.: 9092 | STATUS: INTERIM X FISCAL |
| STARTING DATE: 12/24/81 | DATE OF COMPLETION: 9/30/83 | |
| KEY WORDS: Heparin | | |
| TITLE OF PROJECT: Pharmacokinetic Modeling of Heparin Therapy | | |

| | | |
|--|-------------------------------------|---|
| PRINCIPAL INVESTIGATOR(S): Jeffrey L. Berenberg, MD, LTC, MC | | |
| ASSOCIATE INVESTIGATOR(S): Barbara Alving, MD, MAJ, MC, Carl Peck, MD, COL, MC | | |
| FACILITY: WRMC | DEPT/SVC: Medicine | |
| ACCUMULATIVE PECCASE COST: None | ACCUMULATIVE CONTRACT COST: None | ACCUMULATIVE SUPPLY COST: None |
| FY-83 PECCASE: | CONTRACT COST: | SUPPLY COST: |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983 |

STUDY OBJECTIVE: Development of acceptable and clinically useful mathematical model of heparin pharmacokinetics/pharmacodynamics

TECHNICAL APPROACH: Collection of coagulation tests in particular heparin levels. Computer fitting of heparin levels to metabolite inhibition and phagocytosis models on PROPHET computer. The study patients have venous thrombosis, pulmonary

PROGRESS DURING FY-82: After an initial period of difficulty in accrual, seven patients were entered into study since late June 1982. Coagulation tests are being performed at this time. No computer analysis has been done to date.

NUMBER OF SUBJECTS STUDIED:

FY-82: 7 TOTAL (TO DATE): 7 BEFORE COMPLETION OF STUDY: 20-30

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS: Too early to make a statement.

PUBLICATIONS OR ABSTRACTS, FY-82:

Technical Approach continued: embolus or arterial thrombosis. The latter category was approved in an addendum (29 June 1982).

DATE: 9 Oct 1982 WORK UNIT NO.: 9100 STATUS: INTERIM FINAL X

STARTING DATE: 30 September 1980 DATE OF COMPLETION: January 1982

KEY WORDS: Drug Interactions, Physician Education, Pharmacology

TITLE OF PROJECT:

Evaluation of Computer Assisted Drug-Drug Interaction Monitoring

PRINCIPAL INVESTIGATOR(S): Carl C. Peck, COL, MC

ASSOCIATE INVESTIGATOR(S): Brian Schuster, LTC, MC, Lawrence Fleckenstein, Pharm.D.,
James Wilson, Pharm.D.

FACILITY: WRAMC/USUHS DEPT/SVC: Clinical Pharmacology
Department of Clinical Investigation

ACCUMULATIVE MEDCASE
COST: 0

ACCUMULATIVE CONTRACT
COST: \$2500

ACCUMULATIVE SUPPLY
COST: 0

FY-82: MEDCASE: 0 CONTRACT COST: \$2500 SUPPLY COST: 0 DATE OF COMMITTEE APPROVAL OF
ANNUAL PROGRESS REPORT: FEB 25 1983

STUDY OBJECTIVE: Select high risk patients (receiving 10 drugs simultaneously) at WRAMC will be screened for potential drug interactions utilizing the MEDIPHOR computerized drug monitoring program developed at Stanford University. Information obtained will be provided primary physicians to assist them in their patient care and to educate them in the potential problems of multiple drug regimens.

TECHNICAL APPROACH: To evaluate the impact of a computer-based drug-drug interaction surveillance program on adverse drug interactions. We intend to evaluate the computer program MEDIPHOR for its clinical utility in detecting drug interactions and reducing the frequency of adverse drug reactions, and its impact on physicians prescribing of multiple drug regimens.

PROGRESS DURING FY-82: The study was completed and the results analyzed.

NUMBER OF SUBJECTS STUDIED:

FY-82: 14 TOTAL (TO DATE): 44 BEFORE COMPLETION OF STUDY: 44

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS: A total of 44 patients were studied. The study population had a mean age of 57.4 years, was 31.8% male, with 13 patients judged to have serious illness and 31 with moderate illness. The mean number of drugs at entry was 12.8 (range 10-17). A total of 77 potential drug-drug interactions (PDDI's) were detected by MEDIPHOR with a mean of 1.8 PDDI's/patient (range 0-5), and 42% of PDDI's were potentially life threatening or permanently damaging. Using strict criteria (JAMA 234:1236, 1975), only one probable and 4 possible adverse reactions were detected. We conclude that despite the high number of PDDI's detected in these potentially high risk patients, the detectable incidence of adverse reactions was low.

PUBLICATIONS OR ABSTRACTS, FY-82:

1. Schuster, et al., National Meeting, AFRC, February 1982.
2. Fleckenstein, et al., National Meeting, AFRC, February 1982.

DATE: 9 Oct 82 WORK UNIT NO.: 9101 STATUS: INTERIM x FINAL

STARTING DATE: April 1981 DATE OF COMPLETION:

KEY WORDS: WR 149024, Shock

TITLE OF PROJECT: PILOT STUDY OF WR 149024 IN SHOCK PATIENTS (IND NO 13518).

PRINCIPAL INVESTIGATOR(S): Craig J. Canfield, COL MC

ASSOCIATE INVESTIGATOR(S): Schuster, B.G.; Dimond, R.C.; and Tellis, C.

FACILITY: WRAMC /WRAIR DEPT/SVC: Exp Therapeutics, Pharmacology, Medicine

| | | |
|-----------------------------------|------------------------------------|----------------------------------|
| ACCUMULATIVE MEDCASE COST: -0- | ACCUMULATIVE CONTRACT COST: -0- | ACCUMULATIVE SUPPLY COST: -0- |
|-----------------------------------|------------------------------------|----------------------------------|

| | | | |
|------------------------|-----------------------|---------------------|---|
| FY-8 : MEDCASE: -0- | CONTRACT COST: -0- | SUPPLY COST: -0- | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
|------------------------|-----------------------|---------------------|---|

STUDY OBJECTIVE: 1) Determine whether WR 149024 produces improvement in CO measured of vital organs as evidenced by clinical signs; 2) Determine whether WR 149024 improves perfusion of vital organs as evidenced by clinical signs; 3) Determine whether WR 149024 can increase urine output in anuric or oliguric patients; 4) Determine the dose range at which hemodynamic improvement occurs; 5) Determine nature of any side effects; 6) Provisional opinions as to whether, on the basis of clinical signs, the drug WR 149024 may be effective in shock and deserving of further study.

TECHNICAL APPROACH: WR 149024 will be given in a rising dose regimen with continuous monitoring of various hemodynamic and clinical parameters of shock. Patients used in this study are those in whom all other modalities of therapy have been ineffective.

PROGRESS DURING FY-82: No patients have been entered on this study yet.

NUMBER OF SUBJECTS TO BE STUDIED BEFORE COMPLETION OF STUDY: 20

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT: None

CONCLUSIONS: NA

PUBLICATIONS OR ABSTRACTS, FY-82: None

Funding requested, FY-83: \$500.00 travel.

Work Unit Number: 9102

THE REACTOGENICITY OF C6/36 CELL CULTURE MEDIUM; A POTENTIAL VACCINE SUBSTRATE

PRINCIPAL INVESTIGATOR: ROBERT MCNAIR SCOTT M.D., COL, MC
DEPARTMENT OF VIRUS DISEASES
WRAIR

Type of Report: Final

Conclusion: Severe allergic reactions to the inoculation of C6/36 cell products were not expected to occur as a review of the available literature on mosquito sensitization identified no reports of anaphylactic or other reactions. However, as shown in the above report, humans are clearly sensitized to products contained in the supernatant of actively growing C6/36 cells and both immediate and delayed allergic reactions do occur. These reactions exemplify at least type I (immediate) and possibly type III (Arthus) and type IV (delayed or cell mediated) allergic responses. The PK tests showed that the immediate reactions were due to a heat labile transferable reaginic or homocytotropic antibody. As all of the subjects who were examined using the PK test had reaginic activity, this suggests that sensitization of humans to these antigens must be wide spread if not universal. Possible sources of sensitization are mosquito bites or the inhalation of antigens resulting from dead mosquitos. As the majority of the subjects have not lived in areas where Aedes albopictus may be found, and therefore had no opportunity to be exposed to Aedes albopictus antigens, the sensitization must be related to exposure to antigens perhaps resulting from other Aedes species or even antigens common to a wider range of insects. These questions require further investigation.

response was from one of the subjects who showed an immediate reaction. Heating the sera at 56° for 4 hours destroyed the transferable homocytotropic antibody in all cases; there were no reactions noted upon inoculation of the heated sera.

Subcutaneous Challenge: Subcutaneous inoculation of the C6/36 sham vaccine and the placebo was carried out in a double-blind fashion in one informed volunteer who had experienced an immediate reaction to the intradermal inoculation of the C6/36 vaccine. The volunteer was admitted to the medical intensive care unit for close observation. The inocula were administered in graduated doses at twenty minute intervals. The first dose of 0.05 ml resulted in slight itching at the site of the C6/36 sham vaccine injection. Injection of 0.1ml of the C6/36 sham vaccine led to the appearance of urticaria on the ipsilateral elbow followed by the development of urticaria on the cheeks, periorbital edema and itching of the hard palate. No other systemic reactions, such as bronchospasm, alterations in vital signs or hypotension, were noted. The reaction was terminated by the intravenous inoculation of 25mg of diphenhydramine hydrochloride (Benadryl).

Conclusion: Severe allergic reactions to the inoculation of C6/36 cell products were not expected to occur as a review of the available literature on mosquito sensitization identified no reports of anaphylactic or other reactions. However, as shown in the above report, humans are clearly sensitized to products contained in the supernatant of actively growing C6/36 cells and both immediate and delayed allergic reactions do occur. These reactions exemplify at least type I (immediate) and possibly type III (Arthus) and type IV (delayed or cell mediated) allergic responses. The PK tests showed that the immediate reactions were due to a heat labile transferable reaginic or homocytotropic antibody. As all of the subjects who were examined using the PK test had reaginic activity, this suggests that sensitization of humans to these antigens must be wide spread if not universal. Possible sources of sensitization are mosquito bites or the inhalation of antigens resulting from dead mosquitos. As the majority of the subjects have not lived in areas where Aedes albopictus may be found, and therefore had no opportunity to be exposed to Aedes albopictus antigens, the sensitization must be related to exposure to antigens perhaps resulting from other Aedes species or even antigens common to a wider range of insects. These questions require further investigation.

The delayed hypersensitivity, indicated by the development of induration and erythema within the first twenty-four hours, is unexplained. It occurs a little too early to be a classical type IV response. The timing of the development of the reaction suggests an Arthus reaction, particularly as the delayed reaction occurred only in subjects who received the subcutaneous injection of the C6/36 sham vaccine. The biopsy of one of the delayed reactions showed nonspecific round cell infiltration, compatible with either of these mechanisms. This study did not elucidate the etiology of these reactions and further investigation is indicated.

The heat labile transferable reaginic antibody is IgE. There was a remote possibility that IgG type 4 might be responsible, but, IgG antibodies are not heat labile. That there could be sufficient IgE antibody directed against components of the C6/36 cells in subjects to cause an anaphylactic response was unequivocally shown by the reaction occurring in the subject who underwent a subcutaneous challenge with the C6/36 sham vaccine.

Therefore, the use of the C6/36 cell line as a vaccine substrate is contraindicated, at least in its present form, because of the potential for widespread reactions in human subjects. Techniques for the identification and removal of the proteins responsible for the allergic reactions are presently being explored.

Acknowledgements: Drs. Artie L. Shelton and Richard J. Summers participated in this investigation.

Table 1

Reactions to Intradermal Skin Tests with C6/36 Sham Vaccine*

| Subject | Immediate | | | Delayed (12 hrs.) | |
|---------|-----------|-------|-------|-------------------|-------|
| | Wheal | Flare | Grade | Wheal | Flare |
| BLB | 4** | Neg | + | 4** | 6** |
| DDB*** | 11 | 35 | +++ | Neg | Neg |
| EAH**** | 5 | 9 | ++ | 10 | 11 |
| KDJ | Neg | Neg | 0 | 11 | 13 |
| MKG | Neg | Neg | 0 | Neg | 10 |
| MJB | 8 | 8 | ++ | 8 | 8 |
| MHS*** | 10 | 50 | +++ | Neg | Neg |
| NLG | Neg | Neg | 0 | Neg | Neg |
| RJS | Neg | Neg | 0 | Neg | Neg |
| RMS | Neg | Neg | 0 | 5 | 8 |
| WEB | 5 | 15 | ++ | Neg | 13 |
| WHB*** | 9 | 50 | +++ | Neg | Neg |

* 0.1 ml inoculated intradermally

** Millimeters

*** Positive immediate reaction, did not receive sham vaccine subcutaneously.

**** Delayed reaction biopsied.

Table 2

Reactions to the Prausnitz-Künster* Test

| Subject | Unheated | | | Heated | |
|---------|----------|-------|-------|--------|-------|
| | Wheal | Flare | Grade | Wheal | Flare |
| DDB | 8* | Neg | ++ | Neg | Neg |
| EAH | 11 | Neg | +++ | Neg | Neg |
| KDJ | 9 | Neg | +++ | Neg | Neg |
| MJB | 7 | Neg | ++ | Neg | Neg |
| MHS | 14 | 50 | ++++ | Neg | Neg |
| WEB | 8 | Neg | ++ | Neg | Neg |
| WHB | 9 | Neg | +++ | Neg | Neg |

* The Prausnitz-Künster test was performed using the back of RJS.

** Millimeters

| | | |
|---|----------------------------------|--------------------------------|
| DATE: 6 Oct 82 | WORK UNIT NO.: 9200 | STATUS: INTERIM X FINAL |
| STARTING DATE: 5 Dec 80 | DATE OF COMPLETION: 1 Oct 84 | |
| KEY WORDS: Head Injury, Epilepsy, Post Traumatic Sequelae | | |
| TITLE OF PROJECT: Vietnam Head Injury Study | | |
| PRINCIPAL INVESTIGATOR(S): LTC J. D. DILLON, MC | | |
| ASSOCIATE INVESTIGATOR(S): COL A. SALAZAR, MC | | |
| FACILITY: WRAMC | DEPT/SVC: Clinical Investigation | |
| ACCUMULATIVE MEDCASE COST: 0 | ACCUMULATIVE CONTRACT COST: 0 | ACCUMULATIVE SUPPLY COST: 0 |
| FY-83 MEDCASE: 0 | CONTRACT COST: 0 | SUPPLY COST: 0 |
| DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT | | |

STUDY OBJECTIVE:
To examine selected veterans who received head injuries in Vietnam

TECHNICAL APPROACH: Each subject receives a neurological exam, CT Scan, Speech Pathology exam, Motor exam, Auditory exam, and Electrophysiology battery. In addition, an American Red Cross case worker has interviewed each subject and family to complete a field study.

PROGRESS DURING FY-82:
428 protocols completed by ARC Field Study
35 Reinterview cases completed

NUMBER OF SUBJECTS STUDIED:
FY-82: 245 TOTAL (TO DATE): 278 BEFORE COMPLETION OF STUDY: 950

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
NONE

CONCLUSIONS:
NONE

PUBLICATIONS OR ABSTRACTS, FY-82:
 -Anatomical and Functional Sequelae of Head Injuries Incurred in Vietnam.
 -Hemispheric Representation of Simple Distal Motor Processes
 -Text Processing in Brain Lesioned Patients
 -AAN Scientific Program Abstract Form
 -The Brain Bases for Language Functioning: New Insights From Penetrating Head Injuries
 -Persistent Speech Dysprosody Following Penetrating Head Injuries
 -Staggered Spondaic Word Test
 -Dichotic Digit and CV Results for Individuals with Head Injuries

- Notes on Posttraumatic Epilepsy in Missile Wounds of the Brain
- An Analysis of Brain Abscess Following Penetrating Craniocerebral Injuries
- Prognostic Factors for the Occurrence of Post-Traumatic Epilepsy

631B

DATE: 4 Oct 82 WORK UNIT No.: 9201 STATUS: INTERIM X FINAL

STARTING DATE: 25 Aug 1981 DATE OF COMPLETION: 1 Oct 84

KEY WORDS: Head Injury, Heterotopic Ossification

TITLE OF PROJECT: Incidence, Location and Functional Significance of Clinically Significant Heterotopic Ossification in Head Injury Adults

PRINCIPAL INVESTIGATOR(S): MAJ Michael A. Smutok, AMSC; MAJ Jane Sweeney, AMSC

ASSOCIATE INVESTIGATOR(S): COL M. Levine, MC; COL V. Metcalf, AMSC

FACILITY: WRAMC DEPT/SVC: Clinical Investigation/VHIS

| | | |
|---------------------------------|----------------------------------|--------------------------------|
| ACCUMULATIVE MEDCASE COST: 0 | ACCUMULATIVE CONTRACT COST: 0 | ACCUMULATIVE SUPPLY COST: 0 |
|---------------------------------|----------------------------------|--------------------------------|

| | | | |
|---------------------|---------------------|-------------------|---|
| FY-83 MEDCASE: 0 | CONTRACT COST: 0 | SUPPLY COST: 0 | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
|---------------------|---------------------|-------------------|---|

STUDY OBJECTIVE: To ascertain the incidence location and significance of non-traumatic heterotopic ossification in subjects who received head injury in Vietnam.

TECHNICAL APPROACH: Shoulder, elbow, hip & knee joints of each subject are surveyed for loss of motion pain & presence of palpable mass about the joint. Joints with loss of motion or pain or palpable mass with no past history of trauma are X-rayed to rule out heterotopic ossification. Only subjects with neurologic dysfunction will be radiographed. Incidence, location and significance will be determined upon completion of VHIS

PROGRESS DURING FY-82: 245 Subjects surveyed
 34 Subjects met clinical criteria for x-ray in one or more joints
 30 Subjects were radiographed/ Heterotopic ossification identified in 3 subjects

NUMBER OF SUBJECTS STUDIED: (1 shoulder, 4 elbows, 2 hips)

| | | |
|------------|----------------------|---------------------------------|
| FY-82: 245 | TOTAL (TO DATE): 278 | BEFORE COMPLETION OF STUDY: 950 |
| | | Approx |

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT(IF NONE SO STATE):
NONE

CONCLUSIONS: Study not completed

PUBLICATIONS OR ABSTRACTS, FY-82:
NONE

| | | |
|--|--------------------------------|--|
| DATE: 24/9/82 | WORK UNIT NO.: 9202 | STATUS: INTERIM <input checked="" type="checkbox"/> FINAL |
| STARTING DATE: July, 1982 | DATE OF COMPLETION: July, 1985 | |
| KEY WORDS: Interferon, Poly ICLC, Guillain-Barre, Dysimmune polyneuropathy | | |
| TITLE OF PROJECT: Poly-ICLC in the treatment of Chronic Guillain-Barre Syndrome | | |
| PRINCIPAL INVESTIGATOR(S): Andres M. Salazar, MD | | |
| ASSOCIATE INVESTIGATOR(S): Albert Cuetter, MD | | |
| FACILITY: IRAMC | DEPT/SVC: NEUROLOGY | |
| ACCUMULATIVE MEDICASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST: |
| FY-83 MEDICASE: | CONTRACT COST: | SUPPLY COST: |
| | | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE:

To determine the therapeutic usefulness of Poly-ICLC in Chronic Guillain-Barre

TECHNICAL APPROACH:

I.V. administration of Poly-ICLC weekly for two or more months.

PROGRESS DURING FY-82: One patient has been treated to date with a slow but measurable improvement in leg strength.

NUMBER OF SUBJECTS STUDIED:

FY-82: 1 TOTAL (TO DATE): 1 BEFORE COMPLETION OF STUDY: 10

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
NONE

CONCLUSIONS: Poly-ICLC appears to be beneficial in the one patient currently under treatment, but no final conclusions can be reached.

PUBLICATIONS OR ABSTRACTS, FY-82:

NONE

| | | | |
|---|----------------------------------|------------------------------------|--|
| DATE: 15 NOV | WORK UNIT No.: 9251-82 | STATUS: INTERIM X FINAL | |
| STARTING DATE: 1 OCT 1982 | | DATE OF COMPLETION: | |
| KEY WORDS: Cholesterol, Apolipoprotein, HighPerformance liquid chromatography | | | |
| TITLE OF PROJECT: Quantitation of apolipoprotein and total cholesterol in human plasma lipoprotein by HPLC. | | | |
| PRINCIPAL INVESTIGATOR(S): CPT Patricia Young, PhD, MSC LTC Timothy M. Boehm, MC | | | |
| ASSOCIATE INVESTIGATOR(S): | | | |
| FACILITY: WRAVC | | DEPT/SVC: Clinical Investigation | |
| ACCUMULATIVE PEDCASE COST: 58,000 | ACCUMULATIVE CONTRACT COST: 0 | ACCUMULATIVE SUPPLY COST: 3,000 | |
| FY-83 PEDCASE: 45,000 | CONTRACT COST: NONE | SUPPLY COST: 5,000 | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |

STUDY OBJECTIVE: To quantitate component parts of human lipoproteins and to correlate these with various disease states.

TECHNICAL APPROACH: Classical lipoprotein preparation by ultracentrifugation followed by solvent extraction to prepare lipids and proteins for separation by HPLC.

PROGRESS DURING FY-82: We have developed a protein separation system on HPLC and have resolved apoLipoproteins from HDL. We have also developed a lipid quantitation protocol to determine cholesterol, cholesterylester and

NUMBER OF SUBJECTS STUDIED: triglyceride by HPLC.

FY-82: 1 TOTAL (TO DATE): 1 BEFORE COMPLETION OF STUDY: Not Known

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
No serious/unexpected side effects

CONCLUSIONS:

We conclude that it is possible to quantitate plasma lipids and proteins by HPLC techniques and shall apply these techniques to study lipid metabolism in various disease states.

PUBLICATIONS OR ABSTRACTS, FY-82:

NONE

DATE: _____ WORK UNIT No.: #9301 STATUS: INTERIM X FINAL

STARTING DATE: 26 July 1981 DATE OF COMPLETION: _____

KEY WORDS: Use of Computer Assisted Instruction (CAI) for foodservice employee training

TITLE OF PROJECT: Effectiveness of a Computer-assisted Instruction Program for Teaching Sanitation to Selected Hospital Foodservice Employees.

PRINCIPAL INVESTIGATOR(S): Wolf J. Rinke, Ph.D., R.D., MAJ

ASSOCIATE INVESTIGATOR(S): Kathleen P. Waddell, R.D., CPT

FACILITY: WRMC DEPT/SVC: Food Service Directorate

| | | |
|--|------------------------------------|-------------------------------------|
| ACCUMULATIVE MEDICASE COST: \$2550.00 (FY 81) | ACCUMULATIVE CONTRACT COST: --- | ACCUMULATIVE SUPPLY COST: 280.00 |
|--|------------------------------------|-------------------------------------|

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|------------------------|-----------------------|--------------------------|--|
| FY-83 MEDICASE: --- | CONTRACT COST: --- | SUPPLY COST: \$120.00 | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983 |
|------------------------|-----------------------|--------------------------|--|

STUDY OBJECTIVE: To determine efficacy of CAI, when used as training modality for foodservice employees.

TECHNICAL APPROACH: Sanitation lessons were sequenced and programmed on the Aids Teaching Machine. Program was tested by subject specialists for content validity. Volunteers were selected from the population to evaluate the effectiveness of the CAI program.

PROGRESS DURING FY-82: CAI program development was completed. Volunteers were selected. Study was administered. Finalization of the study is anticipated in early part of FY 83.

NUMBER OF SUBJECTS STUDIED:

FY-82: 90 TOTAL (TO DATE): 90 BEFORE COMPLETION OF STUDY: 90

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):

None

CONCLUSIONS:

PUBLICATIONS OR ABSTRACTS, FY-82:

Paper presentation and publication anticipated in early FY 83.

DATE: 15 Oct 82 | Work Unit No.: 9401 | STATUS: INTERIM X FINAL

STARTING DATE: 24 June 81 | DATE OF COMPLETION: In progress

KEY WORDS: Analgesic efficacy in third molar surgery

TITLE OF PROJECT: A double-blind, controlled study to evaluate the short-term analgesic efficacy of two different doses of Cl-583 (Meclomen^R) in comparison with Cl-757 (buffered aspirin) and placebo in patients with post-surgical dental pain.

PRINCIPAL INVESTIGATOR(S): KENNETH K. KEMPF, DDS
JOSEPH KONZELMAN, DDS

ASSOCIATE INVESTIGATOR(S):

FACILITY: WRAHC | DEPT/SVC: Oral Surgery Service,
Hospital Dental Clinic

ACCUMULATIVE MEDICASE COST: | ACCUMULATIVE CONTRACT COST: | ACCUMULATIVE SUPPLY COST:

FY-83 MEDICASE: | CONTRACT COST: | SUPPLY COST: | DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT FEB 25 1983

STUDY OBJECTIVE: Therapeutic, dose finding, placebo controlled, double-blind comparison with buffered aspirin.

TECHNICAL APPROACH: Subjects are randomly selected to participate in the study. Patients must require the removal of at least one third molar. 72 hrs follow-up via written forms and phone interviews is obtained.

PROGRESS DURING FY-82: 93 subjects have participated in the study.

NUMBER OF SUBJECTS STUDIED:

FY-82: | TOTAL (TO DATE): | BEFORE COMPLETION OF STUDY: 100

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE):
None

CONCLUSIONS: None at present

PUBLICATIONS OR ABSTRACTS, FY-82: None

DATE: Nov 82 WORK UNIT No.: 9500 STATUS: INTERIM x FINAL x

STARTING DATE: Feb 81 DATE OF COMPLETION: Oct 82

KEY WORDS: behavioral coping patterns based on stages of disease and family communication

TITLE OF PROJECT: Patterns of coping with the stages of cancer: The child-patient and his/her family

PRINCIPAL INVESTIGATOR(S): Major James L. Maury, ACSW

ASSOCIATE INVESTIGATOR(S): None

FACILITY: HRAVC DEPT/SVC: Social Work Service

ACCUMULATIVE MEDICASE COST: N/A ACCUMULATIVE CONTRACT COST: N/A ACCUMULATIVE SUPPLY COST: N/A

FY-83 MEDICASE: N/A CONTRACT COST: N/A SUPPLY COST: N/A DATE OF COMMITTEE APPROVAL OF ANNUAL PROGRESS REPORT: FEB 25 1983

STUDY OBJECTIVE: To identify the coping behaviors of the child-patient, the parents and the siblings and to study the association among stages of disease and patterns of family communication.

TECHNICAL APPROACH:

Through interviews with each parent and child.

PROGRESS DURING FY-82: 13 child-patients; 7 siblings; 22 parents

NUMBER OF SUBJECTS STUDIED:

FY-82: 42 TOTAL (TO DATE): 66 BEFORE COMPLETION OF STUDY: N/A

SERIOUS/UNEXPECTED SIDE EFFECTS IN SUBJECTS PARTICIPATING IN PROJECT (IF NONE SO STATE): N/A

CONCLUSIONS: see attached Abstract and summary chapter V.

PUBLICATIONS OR ABSTRACTS, FY-82:

Dissertation #117, The Catholic University of America

TABLE OF PUBLICATIONS AND PRESENTATIONS, FY-82

DEPARTMENT OF MEDICINE

Nephrology Service

Eil C, Fein HG, Smith TJ, et al: Nuclear binding of I²⁵I triiodothyronine in dispersed cultured skin fibroblasts from patients with resistance to thyroid hormone. J Clin Endocrinol Metab 55: 502-510, 1982.

Fitz JD, Sperling EM, Fein HG: Long-term treatment of obese diabetics with semi-starvation diet. Slide presentation at the 3rd Annual Meeting of the Society of Military Endocrinologists, San Francisco, CA, June 1982.

Moore J, Johnson JP, Bohan L, Austin H, Balow J, Antonovych T, and Wilson C: Therapy of anti-glomerular basement membrane antibody (A- GEM-Ab) Disease: A prospective study. Presented at the 14th Annual Meeting of the American Society of Nephrology, Chicago, Il, December 1982. (Abstract)

Moore J, et al: Radiocontrast dye induced nephrotoxicity: Relationship with uric acid excretion. Clin Rsch 30(2): 449A, 1982.

Weismann WP, and Webster HK: Abnormal deoxy adenosine metabolism in uremic erythrocytes. To be presented at 14th Annual Meeting of the American Society of Nephrology, Washington, DC, Nov 21-24, 1981.

Tang L, and Wiesmann WP: Calcium stimulated cGMP formation in human RBC treated with cholinergic agonists. To be presented at the Annual Meeting of the American Society of Hematology, San Antonio, Texas, Dec 5-8, 1981.

Henry AR, Moore J, Hasbargen JA, and Huggins M: Erythrocytosis in renal transplant recipients Clin Rsch 30(2), 450, 1982. (Abstract)

Cardiology Service

Zoltick JM, Patton J, Vogel J, Davia J, and Bedynek J: Cardiovascular screening evaluation to test for coronary artery disease in asymptomatic males over the age of forty. Amer Journ of Card, March 1982. (Abstract)

Publications and Presentations, FY-82 (continued)

Department of Medicine (continued):

Endocrinology-Metabolism Service

Abstracts:

Wray HL, Mehlman I, Butler V, Dawson E, and Bruton J. Effect of dietary phosphorous restriction on serum 1,25(OH)₂D in pseudohypoparathyroidism. Fifth Workshop on Vitamin D, February 1982.

Vigersky RA, Mazingo D, Eil C, Purohit V, and Bruton J. The anti-androgenic effects of testolactone (teslac) in vivo in rats and in vitro in human culture fibroblasts, rat mammary carcinoma cells, and rat prostate cytosol. Endocrinology 110:214, 1982.

Burman KD, Smallridge RC, Wannamacher RC, and Wartofsky L. Iodate restores the fasting induced decrement in TSH secretion. Clin Res 1982.

Glass AR, Smallridge RC, Vigersky RA, and Burman KD. High serum T3 in nephrotic syndrome: A reflection of increased T4 availability? Clin Res 1982.

Smallridge RC, Whorton NE, Burman KD, and Ferguson EW. Effect of physical conditioning and acute exercise on serum T4, rT3, TSH and PRL responses to TRH in man. Endocrine Society, June 1982.

Burman KD, Wartofsky L, and Smallridge RC. Iodate restores the fasting induced decrement in TSH secretion. 12th Annual Meeting European Thyroid Association, Brussels, Belgium, September 1982.

Wartofsky L, DeRuyter H, Smallridge RC, and Burman KD. Thyrotropin secretion in starved rats is enhanced by somatostatin antiserum. 12th Annual Meeting of the European Thyroid Association, Brussels, Belgium, September 1982.

Smallridge RC, Whorton NE, Ferguson EW, and Burman KD. Effect of physical conditioning and acute exercise on serum thyroxine (T4), thyrotropin (TSH), and prolactin (PRL) in man. Presentation to the Society of Air Force Physicians, Sacramento, CA, March 1982.

Fears WB, Yu J, Vigersky RA, Glass AR, and Ferguson EW. Mechanism of exercise-induced secondary amenorrhea. Presented at Air Force Regional ACP Meeting, 1982.

Glass AR, Smallridge RA, Vigersky RA, and Burman KD. High serum T3 in nephrotic syndrome: A reflection of increased T4 availability? Clin Research 30:490A, 1982.

Glass AR, Beach J, Anderson J, and Vigersky RA. Nephrotic syndrome: a model for hypothalamic-pituitary hypersensitivity to negative feedback effects of testosterone. Endocrinology 110 (Supp):407 9Abst 1311, 1982.

Department of Medicine (continued)

Endocrinology-Metabolism Service (continued)

Fears WB, Yu J, Ferguson E, Glass AR, and Vigersky RA. Mechanism of exercise-induced secondary amenorrhea. *Endocrinology* 110 (Supp):86 (Abst 26), 1982.

Glass AR, Anderson J, and Vigersky RA. Pubertal changes in underfed male rats: lack of correlation with body weight. Submitted to Society of Military Endocrinologists, 1982.

Glass AR, Anderson J, and Vigersky RA. Pubertal changes in underfed male rats: lack of correlation with body weight. Submitted to Triennial AIN/ASCN Meeting, 1982.

Vigersky RA, Rice M, Cole D, Shohet R, and Poplack D. Estrogen receptors in human peripheral lymphocytes. *Clin Res*, April 1982.

Smallridge RC, Glass AR, Wartofsky L, Ward KE, and Burman KD. Investigations into the etiology of elevated serum tri-iodothyronine (T3) levels in protein malnourished rats. 62nd Annual Meeting of the Endocrine Society, June 1980. *Metabolism* 31:538-542, 1982.

Glass AR and Vigersky RA. Testicular reserve of testosterone precursors in primary testicular failure. *Fertil Steril* 38:92-96, 1982.

Vigersky RA, Chapman RM, Berenberg J, and Glass AR. Testicular dysfunction in untreated Hodgkin's disease. *Am J Med* (in press).

Borst GC, Burman KD, Osburne RC, Georges LP, O'Brian JT. Effect of fasting in TRH responsiveness in hypothyroidism. Military Society of Endocrinology. San Francisco, June 1982 and American Thyroid Association Meeting, Quebec, Canada, Sep 82.

Wartofsky L, DeRuyter H, Smallridge RC, and Burman KD. Thyrotropin secretion in starved rats is enhanced by somatostatin antiserum. European Thyroid Association, Brussels, Belgium, Sep 82.

Burman KD, Djuh YY, Ferguson RW, Wartofsky L, and Latham KR. Beta receptors in peripheral mononuclear cells increase acutely during exercise. American Thyroid Association, Sep 82.

Zaloga GP, Chernow B, Burman KD, Rainey TG, and Lobe CR. Hemodynamic and catecholamine response to TRH in patients undergoing cardiac surgery. *Clin Res* 82.

O'Brian JT, Michenfelder J, and Burman KD. The effect of fasting and T3 upon urinary excretion of catecholamines. Submitted to Annual Air Force Physicians Meeting.

O'Brian JT, Michenfelder J, and Burman KD. The effect of cold climate upon T4, T4 and TSH response to TRH. Submitted to Annual Air Force Physicians Meeting.

Endocrinology-Catabolism Service (continued,

Abstracts (continued):

Baker J, Lukes YD, Smallridge RC, Burger M, and Burman KD. The development of a sensitive, rapid ELISA assay for TSH receptor binding antibodies. Submitted to American Federation of Clinical Research annual meeting.

Chernow B, Zaloga GP, Burman KD, Quinn T, Rainey TG, and Zajtchuk B. Cardiopulmonary bypass surgery rapidly alters thyroid function. Society of Critical Care Medicine Annual Meeting, Dec 82.

Chernow B, Zaloga GP, Burman KD, Chin R, Zajtchak P, Rainey TG, and Larfe CR. Diagnostic dosages of TRH raise blood pressure by a non-catecholamine mechanism. Society of Critical Care Medicine Annual Meeting, Dec 82.

Srinivasan U, Blatt J, Vigersky R, Wesley R, O'Neill D, Cole D, and Poplack D. Effect of sex-steroids on the survival of AkR mice. Am Assoc of Cancer Res, Apr 82.

Vigersky R, Barnes S, Beach J, Diehl L, and Berenberg J. Pituitary suppression fails to prevent testicular failure due to combination chemotherapy. Am Soc Andrology, Mar 83.

Newman FP, Levine MA, and Wray HL. Pseudohypoparathyroidism with apparent recessive inheritance in two sisters with normal erythrocyte G unit activity. Abstracts of Fourth Annual Scientific Meeting of Am Soc Bone Min Res, p. S43, 1982.

Publications and Presentations, FY-82 (continued):

Department of Medicine (continued)

Endocrinology-Metabolism Service (continued):

ARTICLES

Glass AR and Vigersky RA. Testicular reserve of testosterone precursors in primary testicular failure. *Fertil Steril* 38:92-96, 1982.

Smallridge RC, Glass AR, Wartofsky L, Latham KR, and Burman KD. Investigations in to the etiology of elevated serum T3 levels in protein-malnourished rats. *Metabolism* 31:538-542, 1981.

Glass AR, Steinberger A, Swerdloff R, and Vigersky RA. Pituitary-testicular function in protein-deficient rats. II. FSH hyperresponse to castration and supersensitivity of gonadotropin secretion to androgen negative feedback. *Endocrinology* 110:1542-1546, 1982.

deShazo R, Boehm TM, Kumar D, Galloway JA, and Dvorak HT. Dermal hypersensitivity reactions to insulin correlations of three patterns to their histopathology. *J Allergy and Clin Immunol* 229-240, 1982.

Thompson PT, Burman KD, and Wartofsky L. CSF iodothyronine levels. *J Clin Endocrinol Metab* 54:653-655, 1982.

Swartz M, Burman KD, and Salen G. Cerebrotendinous xanthomatosis: a potentially treatable lethal disease presenting with cataracts. *Amer J Medical Sciences* 283:147-152, 1982.

Burman KD, Smallridge RC, Wannamacher RC, and Wartofsky L. Iodate restores the fasting induced decrement in TSH secretion (submitted for publication).

Smallridge RC, Burman KD, and Wartofsky L. Etiology of elevated serum T3 levels in protein-malnourished rats. *Metabolism* 31:538-542, 1982.

Wartofsky L and Burman KD. Alterations in thyroid function in patients with systemic illness: The "euthyroid sick syndrome. *Endocrine Reviews* 3:164-217, 1982.

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