

JSC RESOURCE REQUIREMENTS

INFLUENCE OF SPACE FLIGHT ON THE BLOOD AND BLOOD-FORMING ORGANS

(BLOOD ALTERATIONS RTOP)

TASK NO.	TASK TITLE	RES AREA	FY76	TP	FY77	PRIORITY
1-02	Special Inflight Hematology (Kimzey/JSC)	2,4,5,6	50	10	50	
1-04	The Effects of Weightlessness on Tissue Proliferation (Crosby/Scripps)	6,7	50		50	
1-05	Regulation of Blood Volume (Johnson/Baylor)	1,2,3,5		20	30	
1-06	Influence of Space Flight on Red Cell Production: Structural and Functional Aspects (Larkin/Martinez VA)	2,6	20	20	20	
1-07	Functional Evaluation of Reticulocytes	6	(40)			
1-08	End-organ Sensitivity to Erythroid Stimulating Factor	5,6			40	
1-09	Plasma Inhibitory Factors of Erythroid Stimulation (Lang,Dunn,Chen/U of Tenn Knoxville)	5	40		20	
<i>NRW</i>	Computer Simulation of Erythropoieses	1-8		10	25	
<i>NEW</i>	* Hematology Experiment Definition (Kimzey/JSC)	1-8				
<i>NRW</i>	* Operational Support in Hematology (Kimzey/JSC)					

* IMS Support only

REGULATION OF BLOOD VOLUME DURING SPACE FLIGHT

DEFINITION OF BASIC QUESTION(S)

REGULATION OF RED CELL MASS (CIRCULATING ERYTHROCYTE VOLUME)

REGULATION OF PLASMA VOLUME

INTERRELATIONSHIP OF CONTROL MECHANISMS

SIGNIFICANCE TO HEALTH AND SAFETY OF CREW MEMBERS

PHYSIOLOGICAL LIMITS FOR FLIGHT

SIGNIFICANCE TO SHUTTLE-TYPE MISSIONS (7 to 30 DAYS)

IDENTIFICATION AND REQUIREMENTS FOR ANY COUNTER MEASURES

SCIENTIFIC SIGNIFICANCE

IDENTIFICATION AND CHARACTERIZATION OF BASIC MECHANISM(S)

SELECTION OF SUITABLE ANIMAL MODEL SYSTEM

DESIGN OF INFLIGHT EXPERIMENTS

DESIGN OF GROUND-BASED SIMULATIONS (MAN AND ANIMAL)

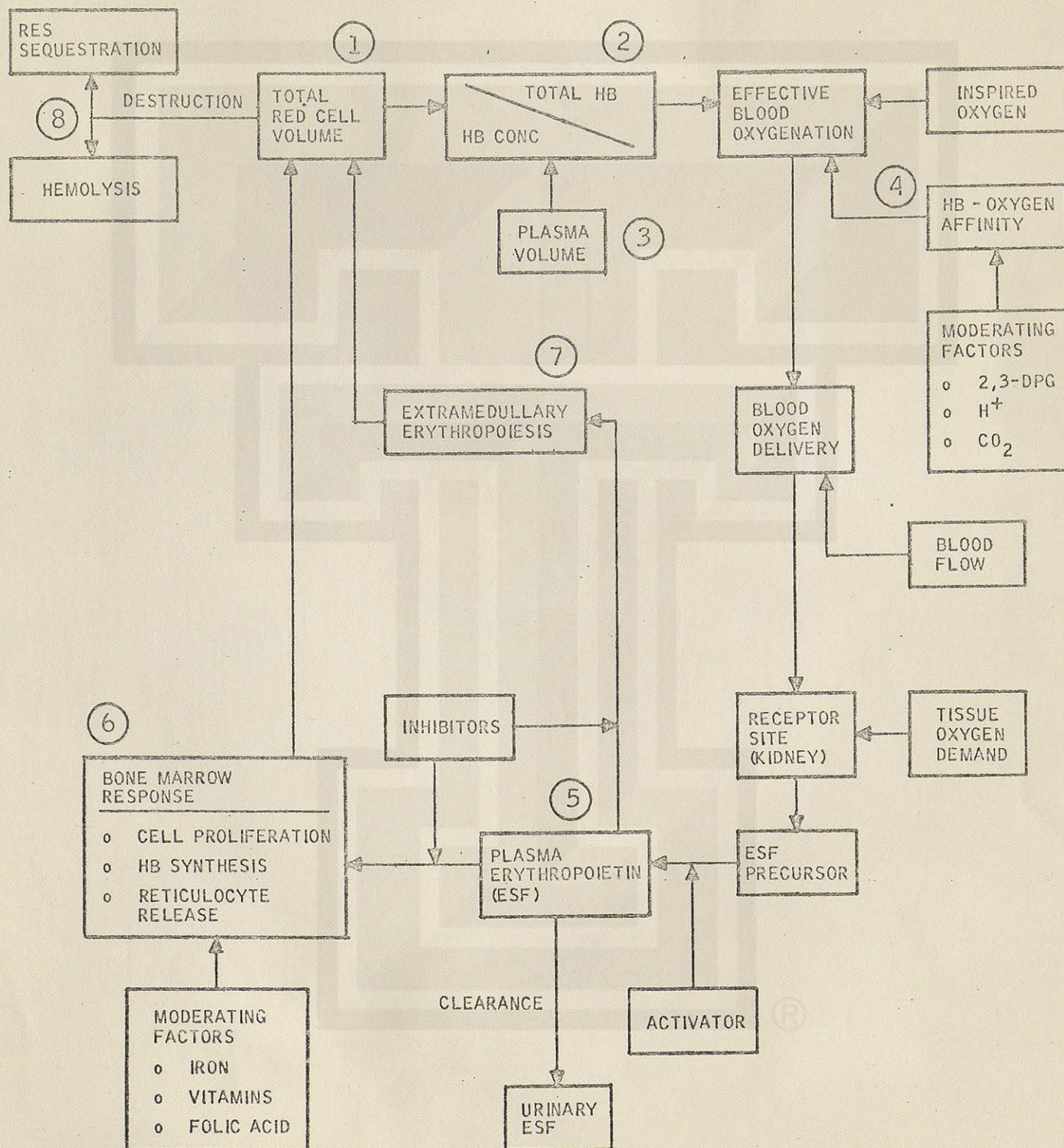
CONTRIBUTION TO BASIC UNDERSTANDING OF RED CELL REGULATION

CORRELATION WITH DATA FROM OTHER MEDICAL EXPERIMENTS

BIOCHEMISTRY, ENDOCRINOLOGY

EXERCISE PERFORMANCE, CARDIOVASCULAR RESPONSE

FLOW DIAGRAM FOR CONTROL OF ERYTHROPOIESIS



SYSTEMATIC STUDY OF THE CONTROL OF ERYTHROPOIESIS

<u>EXPERIMENT AREA</u>	<u>PRIORITY</u>
1. TOTAL RED CELL VOLUME	HIGH
2. HEMOGLOBIN	HIGH
A. TOTAL	
B. CONCENTRATION	
3. PLASMA VOLUME	HIGH
4. HEMOGLOBIN-OXYGEN AFFINITY	MODERATE
5. ERYTHROPOIETIN	HIGH
A. CONCENTRATION	
B. ACTIVATION	
C. INHIBITION	
6. BONE MARROW RESPONSE	MODERATE
A. CELL PROLIFERATION	
B. HB SYNTHESIS	
C. RETICULOCYTE RELEASE	
D. MODERATING FACTORS	
7. EXTRAMEDULLARY ERYTHROPOIESIS	LOW
8. RED CELL DESTRUCTION	LOW
A. RES SEQUESTRATION	
B. HEMOLYSIS	

HEMATOLOGY AND IMMUNOLOGY STUDIES
MISSION ASSIGNMENT CRITERIA

GROUND BASED STUDIES

BASELINE DATA

PROCEDURE DEFINITION AND/OR DEVELOPMENT

FLIGHT HARDWARE REQUIREMENT

DEFINITION OF EXPERIMENTAL SYSTEM

DEFINITION OF EXPERIMENTAL PROTOCOL

COMPUTER SIMULATIONS

SMS TEST

CREW TRAINING AND INFLIGHT PROCEDURE

EXPERIMENT TIMELINES

HARDWARE TESTING AND VERIFICATION

DATA SYSTEM TESTS

CARRY-ON EXPERIMENT

NON-IMPACT TYPE

PREFLIGHT AND POSTFLIGHT TESTING ONLY

7-DAY MISSION (DEDICATED TO LIFE SCIENCES)

30-DAY MISSION (DEDICATED TO LIFE SCIENCES)

EXTEND DURATION MISSION

HEMATOLOGY PROGRAM (OVERALL SCOPE)

ASTRONAUT PHYSICAL EXAMINATIONS AND CONTINUED SURVEILLANCE

ASTRONAUT DATA BASE (DEFINITION OF NORMAL VALUES)

DATA TREND ANALYSIS (PREDICTIVE SIGNIFICANCE)

APOLLO SOYUZ TEST PROJECT

OPERATIONAL SUPPORT (HEALTH ASSESSMENT)

FOLLOW-ON STUDIES BASED ON SKYLAB DATA (BLOOD VOLUME CHANGES)

GROUND-BASED SIMULATION STUDIES (BED REST, CHAMBER, 0-G FLIGHTS, ETC)

SHUTTLE PROGRAM

EXPERIMENT DEFINITION

INFLIGHT ANALYTICAL PROCEDURES

SUPPORT OF SIMULATIONS

SKYLAB DATA INTEGRATION AND ANALYSIS

CORRELATIONS

MATHEMATICAL SIMULATIONS

DEFINITION OF FUTURE EXPERIMENTS TO TEST HYPOTHESIS

RESEARCH PROGRAMS IN THE LIFE SCIENCES

SKYLAB FOLLOW-ON STUDIES IN HEMATOLOGY AND CELLULAR IMMUNOLOGY

EARLY DETECTION OF DISEASE PROGRAM

EDUCATIONAL PROGRAMS

AUTOMATED DATA ANALYSIS AND DATA MANAGEMENT

GENERAL SUPPORT FUNCTIONS UTILIZING CAL LAB CAPABILITIES

REGULATION OF BLOOD VOLUME DURING SPACE FLIGHT

CURRENT RESEARCH PROGRAM

EXTRAMURAL

STUDY OF TISSUE (BONE MARROW) PROLIFERATION (SCRIPPS CLINIC AND RESEARCH FOUNDATION)
W. H. CROSBY and M. TAVASSOLI

REGULATION OF BLOOD VOLUME (BAYLOR COLLEGE OF MEDICINE/METHODIST HOSPITAL)
P. C. JOHNSON, C. P. ALFREY and E. A. NATELSON

ULTRASTRUCTURE AND FUNCTION OF HEMATOPOIETIC TISSUE (MARTINEZ VA HOSP/UC DAVIS)
E. C. LARKIN

INTRAMURAL (INHOUSE AND COLLABORATIVE EFFORTS)

CORRELATION OF RED CELL SHAPE (SEM) WITH NATURAL AND EXPERIMENTAL HEMATOLOGIC DISORDERS

EVALUATION OF FUNCTIONAL STRESS TESTING OF RED CELL OSMOREGULATION PROCESSES

FLIGHT AND GROUND BASED EXPERIMENT DESIGN AND IMPLEMENTATION

SHUTTLE SIMULATION/SHUTTLE FLIGHTS

COSMOS

DATA INTEGRATION AND MATHEMATICAL SIMULATIONS OF ESF CONTROL

DEVELOPMENT OF TECHNIQUES FOR RETICULOCYTE EVALUATION (STRUCTURE/FUNCTION)

SUPPORT OF MISSION(ASTP) AND GROUND-BASED SIMULATION PROGRAMS IN HEMATOLOGY

EVALUATION AND IMPLEMENTATION OF SENSITIVE ESF ASSAY

SPECIAL INFLIGHT HEMATOLOGY

OBJECTIVES:

CONTINUE TO ADVANCE EXISTING METHODS FOR SINGLE CELL ANALYSIS FOR CHEMICAL AND STRUCTURAL INFORMATION. IMPROVE TECHNIQUES FOR INFLIGHT ACQUISITION AND ANALYSIS OF BLOOD SAMPLES. EXPAND DATA ANALYSIS CAPABILITY WITH EMPHASIS ON COMPUTERIZED PATTERN RECOGNITION AND DISTRIBUTION PROFILES OF CELLULAR CHEMICAL CONSTITUENTS. APPLY THIS INFORMATION FOR THE MEDICAL EVALUATION OF MAN RELATIVE TO HIS PHYSIOLOGICAL PERFORMANCE AT THE CELLULAR LEVEL DURING SPACE FLIGHT.

PROGRESS:

SEM CLASSIFICATION OF RBC'S ESTABLISHED AND APPLIED IN SKYLAB HEMATOLOGY EXPERIMENTS. SERIES OF STUDIES COMPLETED ON ION ETCHING/SEM EXAMINATION OF BLOOD CELLS AND RESULTS PUBLISHED. TECHNIQUE FOR FLUOROMETRIC ANALYSIS OF SPUTUM SAMPLES EVALUATED FOR EPA. CYTOPHOTOMETRY TECHNIQUES APPLIED TO SKYLAB EXPERIMENTS (M115 AND S015). INTERACTIVE DATA SYSTEM FOR SMP ANALYSIS INSTALLED. SUPPORT PROVIDED FOR EDPRO.

FUTURE PLANS:

AUTOMATED DATA SYSTEM FOR FLOW-THROUGH ANALYTICAL DEVICES BEING INSTALLED AND WILL BE APPLIED TO RAPID EVALUATION OF BLOOD CELL POPULATIONS. MICROANALYTICAL PROCEDURES WILL CONTINUE TO BE REFINED. FUNCTION AS A DEVELOPMENTAL OPERATION FOR NEW PROCEDURES WHICH ARE THEN UTILIZED IN SUPPORT OF OTHER JSC LIFE SCIENCES PROGRAMS IN HEMATOLOGY AND RELATED AREAS. THIS TASK ALSO SERVES AS A FOCAL POINT FOR THE COORDINATION OF MICROANALYTICAL TECHNIQUES FOR CELLULAR ANALYSIS AND AUTOMATED DATA PROCESSING.

EFFECTS OF WEIGHTLESSNESS ON TISSUE PROLIFERATION

OBJECTIVES:

DETERMINE THE CHRONOLOGY OF THE REPAIR PROCESSES IN SELECTED MAMMALIAN TISSUES WITH EMPHASIS BEING PLACED ON THE BONE MARROW AND ERYTHROPOIESIS. THE STUDY WILL ATTEMPT TO DETERMINE THE EFFECTS OF SUCH VARIABLES AS OXYGEN TENSION, AMBIENT PRESSURE AND THE PRESENCE OR ABSENCE OF NITROGEN ON THE PROLIFERATING TISSUES, USING A GROUND-BASED SIMULATOR.

THE SECOND PHASE OF THIS STUDY WILL BE CONCERNED WITH THE DESIGN OF INFLIGHT EXPERIMENTS TO DETERMINE THE EFFECTS OF WEIGHTLESSNESS ON THE ESTABLISHED KINETICS FOR SPECIFIC TISSUE PROLIFERATION. THESE EXPERIMENTS WILL BE DESIGNED TO HAVE MINIMUM IMPACT ON THE TIME OF THE FLIGHT CREW.

SIGNIFICANCE:

EXAMINATION OF TISSUE PROLIFERATION AT THE CELLULAR LEVEL HAS NOT BEEN EXTENSIVELY STUDIED IN RELATION TO ANY SPACE FLIGHT PROGRAM.

SOME OF THE CHANGES OBSERVED FOLLOWING SPACE FLIGHT COULD BE DUE TO A COMMON MECHANISM INVOLVED WITH NORMAL REGENERATIVE PROCESSES.

COORDINATION OF THIS EFFORT WITH OTHER RED CELL PRODUCTION STUDIES COULD YIELD ADDITIONAL DATA RELEVANT TO THE RED CELL MASS LOSS QUESTION.

INFLUENCE OF THE EXTERNAL PARAMETERS OF SPACE FLIGHT ON THE REGULATION
OF BLOOD VOLUME

OBJECTIVES:

INVESTIGATE THE EFFECTS OF EXTERNAL FACTORS SUCH AS BEDREST, ATMOSPHERE, EXERCISE AND SEVERE STRESS ON THE MECHANISMS CONTROLLING NORMAL BLOOD VOLUME IN MAN AND IN AN EXPERIMENTAL ANIMAL SYSTEM. THESE DATA WOULD BE APPLIED TO ELUCIDATE THE POSSIBLE CAUSES OF THE RED CELL MASS AND PLASMA VOLUME CHANGES OBSERVED DURING SKYLAB AND APOLLO MISSIONS.

TECHNICAL APPROACH:

TEST SUBJECTS WILL INCLUDE HUMAN AND ANIMAL (RATS)

TEST CONDITIONS WILL INCLUDE:

LONG TERM BEDREST (USPHS STUDIES?)
STRENUOUS EXERCISE
RESTRAINED CONDITIONS (ANIMALS ONLY)
VARIOUS ATMOSPHERIC CONDITIONS (ANIMALS)
LONG TERM STRESS (ANIMALS)

SPECIFIC MEASUREMENTS INCLUDE:

RED CELL MASS AND PLASMA VOLUME
ROUTINE HEMATOLOGICAL PARAMETERS
ERYTHROID STIMULATING FACTOR (ERYTHROPOIETIN) IN PLASMA AND URINE
SPECIAL HEMATOLOGY (FUNCTIONAL TESTS ON RED CELLS)
BONE MARROW STUDIES FROM ANIMAL EXPERIMENTS

INFLUENCE OF THE EXTERNAL PARAMETERS OF SPACE FLIGHT ON THE REGULATION
OF BLOOD VOLUME

OUTLINE OF STUDY:

1. APPLY EXPERIMENTAL TEST PROTOCOL TO
 - a. NORMAL ANIMALS (RATS)
 - b. RESTRAINED ANIMALS
 - c. NORMAL AND RESTRAINED UNDER DIFFERENT ATMOSPHERES
 - d. EXERCISED ANIMALS
2. DEVELOP DETAILED EXPERIMENTAL PROTOCOL FOR SHUTTLE-TYPE FLIGHT
3. ESTABLISH AND COMPARE ASSAY METHODS FOR ERYTHROPOIETIN
 - a. HYPOXIC MOUSE
 - b. TISSUE CULTURE METHOD (MOUSE FETAL LIVER CELLS)
 - c. IMMUNOLOGICAL ASSAY
4. APPLY PROTOCOL TO SUPPORT OF ASTP MISSION
5. APPLY PROTOCOL TO HUMAN SUBJECTS UNDER CONDITIONS OF
 - a. BEDREST
 - b. PROGRAMED EXERCISE LOADS

THE FUNCTIONAL AND ULTRASTRUCTURAL RELATIONSHIPS OF HEMATOPOIETIC TISSUE

SIGNIFICANT ALTERATIONS IN THE SURFACE TOPOGRAPHY OF CIRCULATING ERYTHROCYTES WERE OBSERVED DURING THE SKYLAB FLIGHTS. THESE RESULTS MAY HAVE A BEARING ON THE OBSERVED RED CELL MASS LOSS DURING THESE MISSIONS.

THE PURPOSE OF THIS STUDY IS TO EXAMINE AND CORRELATE THESE MORPHOLOGIC CHANGES IN THE RED CELL WITH BIOCHEMICAL AND BIOPHYSICAL CHANGES IN THE RED CELL AND ITS PRECURSORS UNDER A SERIES OF PATHOLOGIC AND EXPERIMENTAL CONDITIONS.

ALTERED IN VITRO INCUBATION CONDITIONS

PH OF MEDIA

IONIC STRENGTH OF MEDIA

ECHINOCYTOGENIC DRUGS (AND REAGENTS)

STOMATOCYTOGENIC DRUGS (AND REAGENTS)

PATHOLOGIC CONDITIONS

NUTRITIONAL ANEMIAS (IRON, FOLIC ACID, B12)

IN PATIENTS RECEIVING MEMBRANE-ACTIVE DRUGS

PATIENTS WITH HEMOGLOBINOPATHIES

IN VARIOUS HEMOLYTIC ANEMIAS

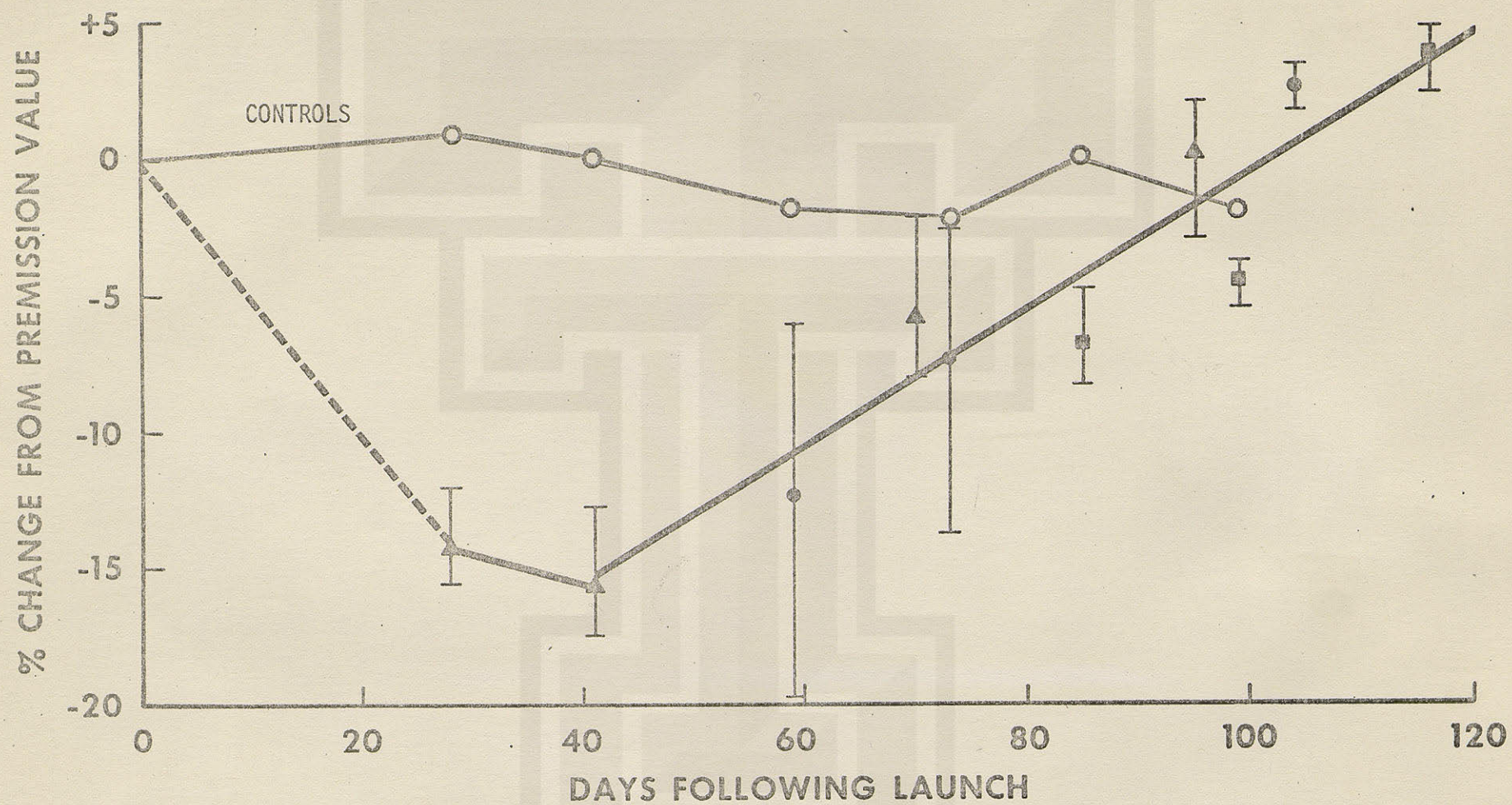
IN PATIENTS RECEIVING HIGH (40-100%) OXYGEN

ANIMAL EXPERIMENTS (RATS AND RHEUS MONKEY)

INITIAL STUDIES WILL CONCENTRATE ON RED CELL, BUT FUTURE INVESTIGATIONS WOULD INCLUDE RED CELL PRECURSORS AND LEUKOCYTES.

PRIMARY EMPHASIS WILL BE TO DEVELOP A FRAMEWORK WHEREIN THE RED CELL CHANGES SEEN IN SPACE FLIGHT CAN BE INTERPRETED, PARTICULARLY WITH RESPECT TO THE REDUCTION IN RED CELL MASS.

RED CELL MASS/SKYLAB



MISSION DURATION {
SL2 (▲)
SL3 (●)
SL4 (■)

NASA-5-74-4964

SKYLAB 3 AND 4

RELATIVE HEMOGLOBIN CONCENTRATION IN-FLIGHT

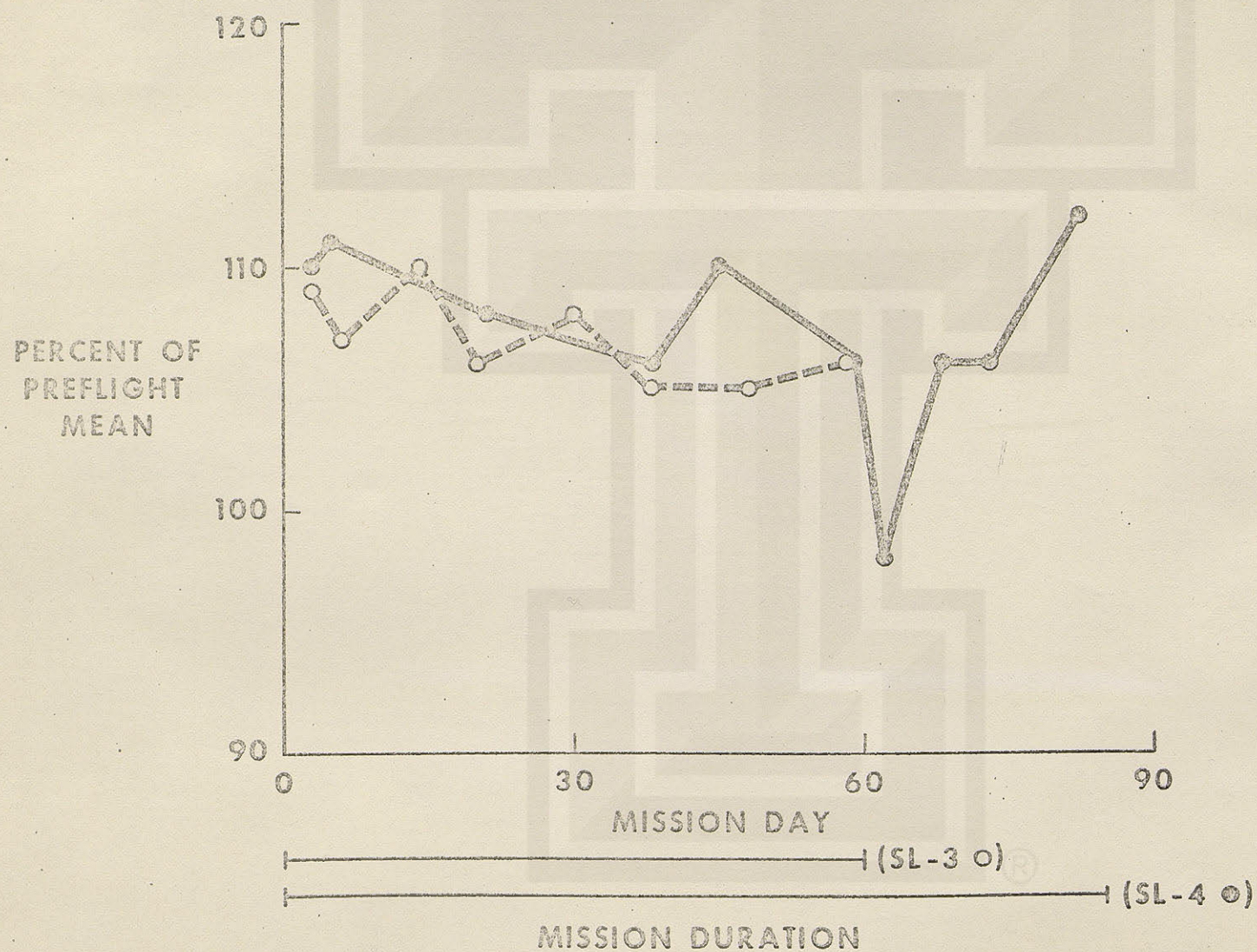
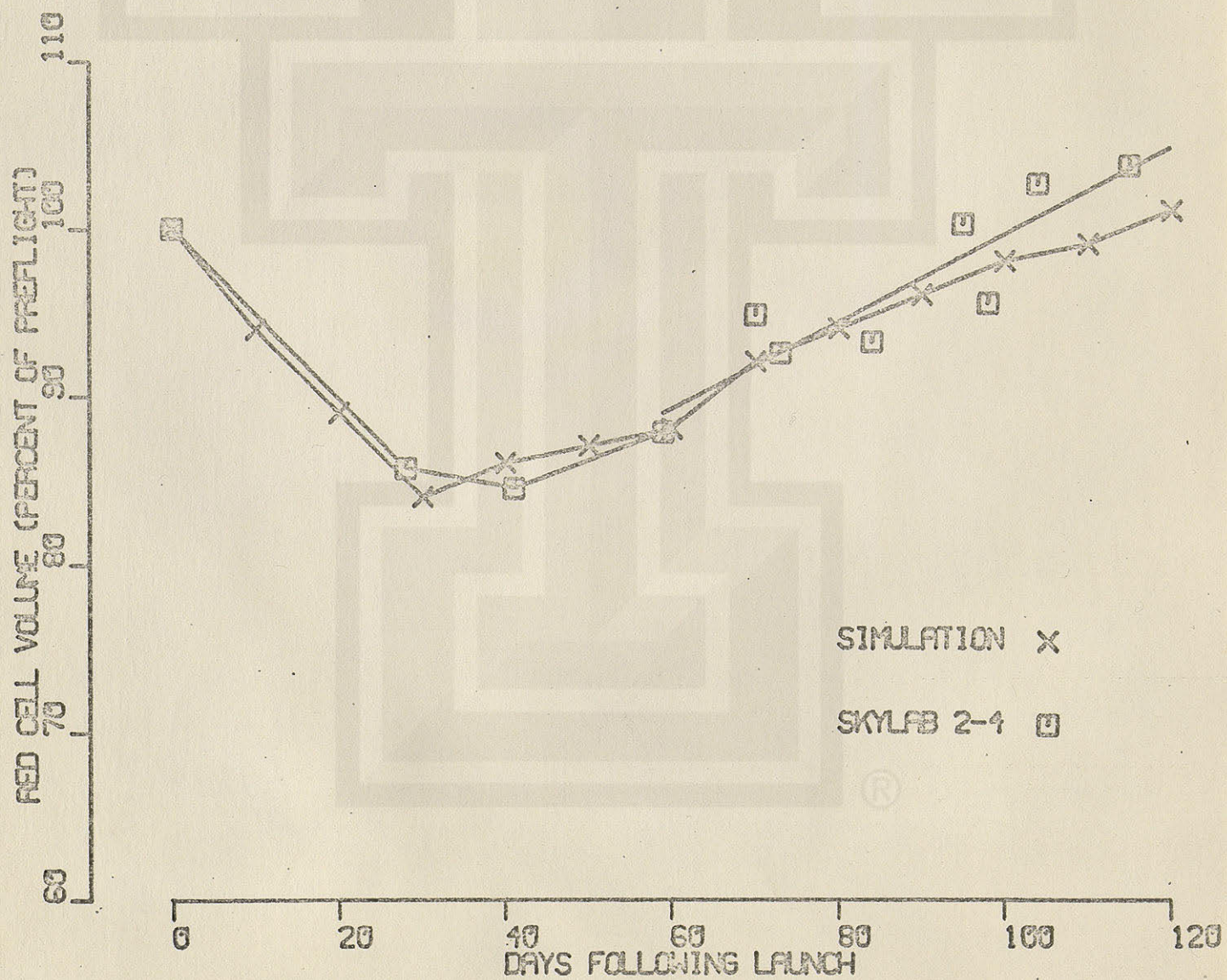


TABLE VI
COMPARISON OF SKYLAB HEMOGLOBIN CHANGES

CREWMAN	PREFLIGHT Mean \pm S.D.	R+0 (HB)	R+3 (HB)	PRE - R+0 % Change	PRE - R+3 % Change	R+0 - R+3 % Change
CDR-2	14.0 \pm .6	13.0	13.1	-7.1	-6.4	0.8
SPT-2	14.4 \pm .6	13.5	13.2	-6.3	-8.3	-2.2
PLT-2	14.3 \pm .4	13.6	13.2	-4.9	-7.7	-2.9
MEAN	14.2 \pm .2	13.4 \pm .3	13.2 \pm .1	-6.1	-7.5	-1.4
CDR-3	14.0 \pm .9	15.3	12.5	9.3	-10.7	-18.3
SPT-3	13.5 \pm .4	14.0	11.7	3.7	-13.3	-16.4
PLT-3	15.0 \pm .7	15.3	13.0	2.0	-13.3	-15.0
CDR-4	14.6 \pm .4	15.0	13.4	2.7	- 8.2	-10.7
SPT-4	13.3 \pm .5	14.0	11.6	5.3	-12.8	-17.1
PLT-4	14.6 \pm .4	14.9	12.7	2.1	-13.0	-14.8
MEAN	14.2 \pm 0.7	14.8 \pm .6	12.5 \pm .7	4.2 \pm 2.8	-11.9 \pm 2.1	-15.4 \pm 2.6

RCV CHANGES DURING SPACEFLIGHT

SKYLAB 3 SIMULATION



EARLY DETECTION OF DISEASE PROGRAM: EVALUATION OF THE CELLULAR IMMUNE RESPONSE

OBJECTIVES:

DETECT AND CHARACTERIZE CHANGES IN THE CELLULAR IMMUNE SYSTEM FOR THE EARLY DETECTION AND DIAGNOSIS OF RESPIRATORY INFECTIONS IN THEIR PRECLINICAL, ASYMPTOMATIC STAGES.

PROGRESS:

A DETAILED PROTOCOL USING THE MOST CURRENT PROCEDURES OF EVALUATION OF THE IMMUNE RESPONSE WAS DEVELOPED AND APPLIED OVER THE PAST TWO YEARS TO THREE GROUPS OF SUBJECTS: ASTRONAUTS, NON-INFECTED NON-ILL INDIVIDUALS, AND VOLUNTEERS GIVEN A VIRAL CHALLENGE. A DATA BASE OF 250 NORMAL INDIVIDUALS WAS ESTABLISHED AND ENTERED INTO THE JSC MEDICAL DATA COMPUTER SYSTEM (MEDICS).

FUTURE PLANS:

THE SURVEILLANCE STUDIES INITIATED PREVIOUSLY WILL CONTINUE TO BE APPLIED TO THE FOLLOWING GROUPS:

ASTRONAUT POPULATION (AS PART OF YEARLY PHYSICAL AND SPECIFIC INFECTIOUS AGENTS).

NORMAL POPULATION (SURVEILLANCE OF INDIVIDUALS IN SAME GENERAL AREA).

EXTENSION OF PROGRAM WILL INCLUDE DEVELOPMENT OF MORE SENSITIVE ASSAYS FOR DETECTION OF VIRAL ANTIGENS ATTACHING TO RECEPTOR SITES ON LYMPHOCYTE MEMBRANES. AS ASSAYS BECOME AVAILABLE THEY WILL BECOME A PART OF THE SURVEILLANCE STUDIES.

MARCH, 1976

AUTOMATED CYTOLOGY/COMPUTERIZED PATTERN RECOGNITION

OBJECTIVES:

UPDATE COMPUTER PROGRAMS FOR ACQUISITION OF SPECTRAL DATA FROM SCANNING MICROSCOPE PHOTOMETERS, X-RAY SCANNERS, AND PULSE HEIGHT ANALYZERS

ESTABLISH WORKING COMPUTER PROGRAMS FOR HIGH-SPEED REDUCTION AND EVALUATION OF DIGITAL SCAN DATA DERIVED FROM OPTICAL IMAGES OF BLOOD CELLS

IMPLEMENT EXISTING SOFTWARE FOR CLASSIFYING DISTRIBUTION-TYPE DATA FROM PULSE HEIGHT ANALYZER

DEFINE AND IMPLEMENT AUTOMATIC DECISION MAKING PROCEDURES FOR CLASSIFYING CELL TYPES AND/OR POPULATION PROFILES

PROGRESS:

THIS EFFORT WAS PLANNED FOR INITIATION IN FY74, BUT ACTIVITIES ASSOCIATED WITH SKYLAB PREVENTED SELECTION OF ADEQUATE CONTRACTOR TO ACCOMPLISH TASKS LISTED ABOVE. AN RFP IS IN PREPARATION WITH AN ANTICIPATED START DATE OF JANUARY 1975.

FUTURE PLANS:

UTILIZE THESE TECHNIQUES TO ESTABLISH REPRODUCIBLE CYTOPATHOLOGY STANDARDS FOR DETECTING CELLULAR FUNCTIONAL RESPONSES. APPLY IN EXISTING RESEARCH AND OPERATIONAL PROGRAMS FOR EVALUATING THE HEALTH STATUS OF POTENTIAL FLIGHT CREWS AND TO IMPROVE GENERAL DIAGNOSTIC CAPABILITY.

JSC HEMATOLOGY PROGRAM INTERRELATIONS

HEMATOLOGY STUDIES (RBC REGULATION)

BONE MARROW PROLIFERATION
(SCRIPPS)

REGULATION OF BLOOD
VOLUME (BCM)

HEMATOPOIETIC TISSUE
STRUC/FUNC (MARTINEZ VA)

COLLABORATIVE STUDIES
METHODIST HOSP
RICE UNIV
MED UNIV OF SC
UTMB, GAL
BCM

CELL. ANAL. LAB. INHOUSE RESEARCH

SPEC INFLT HEMATOLOGY
ROUT HEMATOLOGY
SPEC HEMATOLOGY
ELECTRON MICRO
CYTOPHOTOMETRY
DATA STORAGE SYST
INFLT ANALYSES

AUTOMATED CYTOLOGY
(UNIV OF ARIZONA)

SKYLAB DATA INTEGRATION
CORRELATIONS
ESF REGULATION

ASTRONAUT DATA BASE
DATA STORAGE
TREND ANALYSIS
LONG TERM EFFECTS

IMMUNOLOGY STUDIES (EDPRO/LYMPHOCYTE)

EDPRO: CELL IMMUNOL
(BCM/INHOUSE)

LYMPHOCYTE STRUC/FUNC
(BCM/INHOUSE)

LYMPH. RESPONSE
CHANGES, SKYLAB
(BCM/INHOUSE)

ASTP IMMUNOL EXPT.
MA031/MA032
(BCM/INHOUSE)

OTHER NASA PROGRAMS

ENDOCRINOLOGY

EXERCISE PHYSIOLOGY

BCM SKYLAB
SIMULATION

USPHS BED
REST STUDIES

JSC SHUTTLE
SIMULATIONS

USSR COSMOS
BIOSAT EXPT.

ASTRONAUT PHYSICAL EXAMS

(SIH)
(BM PROL.)
(BVOL REG)