STUDY REPORT:

SYSTEMS IDENTIFICATION AND APPLICATION SYSTEMS DEVELOPMENT FOR MONITORING THE PHYSIOLOGICAL AND HEALTH STATUS OF CREWMEN IN SPACE

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GENERAL ELECTRIC COMPANY

SPACE DIVISION - HOUSTON OPERATIONS

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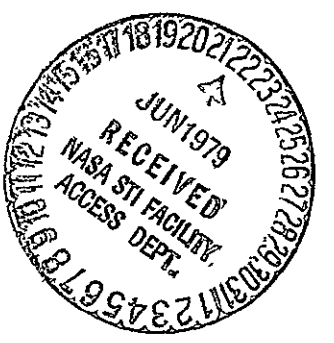

STUDY REPORT: SYSTEMS IDENTIFICATION AND APPLICATION SYSTEMS DEVELOPMENT FOR MONITORING CREW HEALTH STATUS DURING SPACEFLIGHT

TABLE OF CONTENTS

1.0 INTRODUCTION

The outset of man's exploration into space was accompanied by fundamental questions about his ability to survive, let alone perform well, in exceedingly demanding tasks. Medical monitoring was thus restricted to the measurement of vital signs in cardiac and respiratory systems. In later missions of the Gemini and Apollo era, with survival capacity established, task requirements were increased immensely and while the depth of pre- and postflight medical experiments was enhanced measurably, there was much less effort applied to an inflight biomedical program. Mercury, Gemini, and Apollo were primarily engineering programs not intended to produce biomedical data of general predictive value for use in the design of advanced space systems. Skylab represented the first mission program in which good quality baseline data were obtained as a starting point for comprehensive evaluation of all major physiological systems. While Skylab did much to permit extrapolation to major extensions in mission duration, it also raised many more questions. Thus, many of the same investigative areas which were identified prior to Skylab still remain as sources of concern and interest with regard to both a scientific and medical point of view; these include changes in cardiovascular control, fluid-electrolyte regulation, renal, endocrine, erythropoietic, vestibular, central nervous, musculoskeletal, and immunological systems. Still ahead is the task of determining the precise nature, the ultimate severity, and the fundamental etiology of many of these changes in man's functional capabilities during and following prolonged space flight.

Since long duration missions presuppose man's ability to perform indefinitely at a high level physically and mentally, it is apparent that systems and techniques to acquire and analyze biomedical data must meet pressing needs. At the very minimum this will involve: (a) establishing new standards for remote medical monitoring, diagnosis, and treatment;

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Since long duration missions presuppose man's ability to perform indefinitely at a high level physically and mentally, it is apparent that systems and techniques to acquire and analyze biomedical data must meet pressing needs. At the very minimum this will involve: (a) establishing new standards for remote medical monitoring, diagnosis, and treatment;

(b) evaluating crucial indices of health, fitness, and performance, (c) developing and testing novel instrumentation for measuring these parameters; and (d) designing and implementing sophisticated data acquisition and data analysis systems. This will mean a truly collaborative relationship between physical and life scientists to achieve efficient monitoring of man in the unique environment of space. All the elements of the long-duration mission should be viewed as portions of a totally integrated and mutually reinforcing system including temporal factors, engineering factors, operational factors, scientific factors, and human factors. Measures for the overall status of the crew at a given time during flight must be established and an accurate time profile of the adaptation of men to space conditions must be developed. An additional complicating factor is that information must be obtained not only from the whole-body but also from the whole-person. This means that intellectual, emotional, physical, and biochemical data must be integrated and directed toward the early detection of deteriorative trends and preserving good health. Because of the complexity of the system, which will be increased by its dynamic nature, the systems analysis approach should be advantageous in providing a common frame of reference for interdisciplinary planning and implementation.

The present research effort has been deeply involved in systems analysis application to biomedical and physiological systems. This has included the development of automated data base systems, data analysis systems, mathematical simulation models of major physiological systems and many techniques involved in identification of complex, large scale systems. It is the purpose of this report to relate some of the ideas and accomplishments developed during this contract to the task of developing automated biomedical systems for monitoring crew health status during space flight.

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2.0 DETERMINANTS OF CREW HEALTH STATUS

Problems Associated with Defining Crew Health

Throughout the manned space program the major objective in maintaining a healthy crew was to assure performance of inflight tasks, to maintain this integrity for reentry, and to minimize the effects of the flight during the recovery period. The criteria for crew health at any moment in time during the flight has been not only concerned with present performance and function, but also concerned with future performance and future physiological function. However, it appears that insufficient data and flight experience has precluded an accurate correlation of present function with future function. As a result it has been difficult to assign a "fitness" rating to a crew that would be meaningful with regard to their ability to withstand reentry and complete a successful recovery. As more experience is acquired and the normal physiological adaptation-to-weightless space flight is better understood, it will be possible to better assess the fitness of an individual crew member and predict future function based on present overall health status. This suggests an ongoing, intensive research effort to reveal more of the direct and indirect causes of impending abnormality as well as delineating the mechanisms that control the sequence of changes resulting in deterioration. These are the same research goals established for the terrestrial practice of predictive and preventive medicine[1], and as in that field, there is a promising role for automated computer data analysis and mathematical simulation models.

It has been recognized that the most important factor in predictive medicine is periodic examination (i.e., monitoring) in order to reveal changes and trends. Such trends could forecast oncoming illness, offer an opportunity to initiate early treatment and help evaluate the

effectiveness of the selected treatment. One of the most difficult problems associated with predictive medicine is determining which measurements shall be examined in order to predict any important disorder before it becomes an impairment to overall health. Diagnosing and treating an impending disorder has not been nearly as well studied as diagnosing and treating fully developed diseases. And yet that should be one of the challenges of space flight medicine. Until extensively equipped medical clinics are established in space, the costliness and the physical remoteness from earth of each mission dictates that maintenance of crew health be supported with the aid of the most sophisticated analytic tools possible. The potential spin-offs in developing these advanced biomedical systems as they apply to the nation's multi-phasic health care programs are obvious.

Inasmuch as an adequate definition of fitness for health is lacking (both in space and earth medicine), the problem of determining which onboard measurements are necessary during long-duration missions has not been adequately solved. The effects of prolonged weightlessness, possibly involving cellular and subcellular systems, might not give rise to familiar syndromes or illnesses and hence might be mis-diagnosed, at least with respect to etiology and the time course of the effects in terms of adaptation or progressive deterioration. This points up the need for "undirected" monitoring. On the other hand, previous experience with weightless flight suggests that in the absence of countermeasures, special attention should be given to monitoring specific physiological systems such as fluid-electrolyte balance, musculoskeletal deterioration, reduced blood volume, vestibular changes, etc. In addition, specific potential pathological problems have been identified as having a possibility of occurrence during spaceflight, including urinary calculus, chronic exposure to high levels of carbon dioxide, chronic

levels of heat exposure, radiation effects, respiratory and gastro-intestinal viral illnesses, and reaction to high mental and physical demands (e.g., fatigue). The problem of which parameters to monitor becomes more complicated of course, because all the normal physiological adaptive changes to weightlessness have not been recognized and investigated. One of the future challenges will be to separate as much as possible the adaptive changes from pathological changes and to determine whether pathology in space is modified or aggravated by weightlessness.

Implicit in the above discussion is the belief that techniques must be available to measure, at appropriate intervals, the crewmembers' physiological, psychological, and performance status inflight. It is still to be determined whether or not the employed clinical measurement techniques are sufficiently encompassing or sensitive to detect all occurring accommodative and acclimative processes as well as changes which reflect deterioration of body function. It is quite probable that many changes that occurred during previous space flights were not detected with the existing measurement techniques unless overt symptoms developed. Objective methods need to be developed which may be able to identify subtle physiological adaptive or insipient pathological conditions. Substantial research and development will be necessary to attain these goals. Among these efforts, the use of computer methodology, systems analysis techniques, and mathematical modeling seem warranted and necessary in order to synthesize the various bits of information obtained through empirical research.

In summary, three basic problems have been discussed: (a) an objective definition of crew health status is lacking; (b) as a result, the minimal number of parameters which must be monitored have yet to

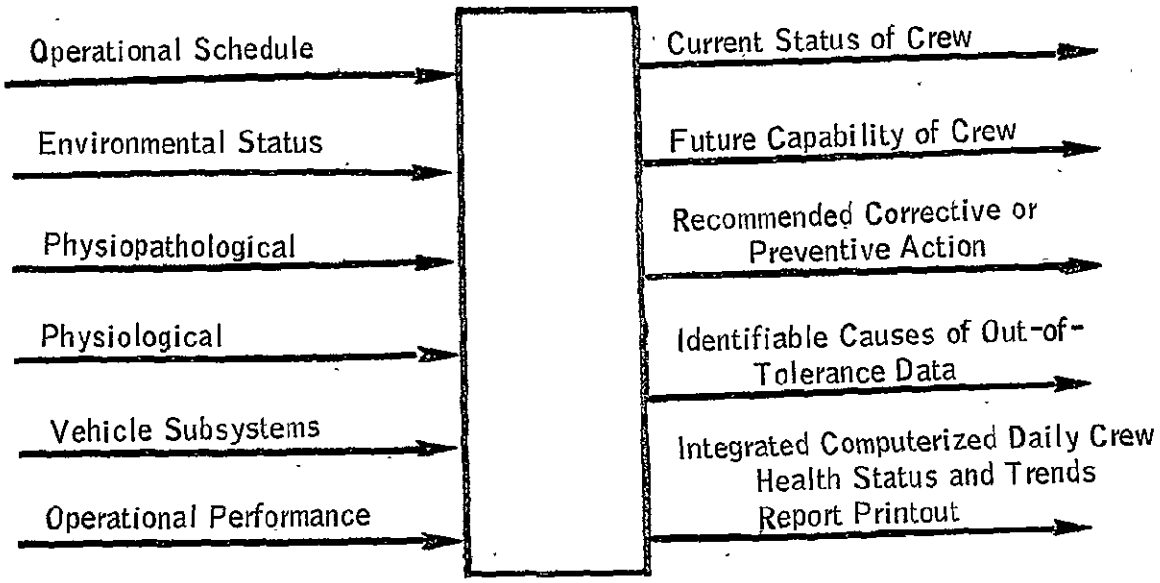
be defined; and (c) techniques, instruments, and analytical tools for measuring and processing these parameters must be developed and their sensitivity must be sufficient to quickly reveal the onset of adaptive or pathological processes. It is clear that solutions to these problems deserve intensive study and interdisciplinary collaboration. Previous studies have attempted to delineate important monitoring procedures and their results are summarized elsewhere in this report. However, these were not approached in a systematic manner and were based essentially on traditional, terrestrial medical practice which may not be adequate. As more is learned about the space environment and space medicine these studies should be reviewed and updated. It is apparent, however, that most investigators of these problems feel that inputs into a total monitoring system should consist of much more than physiological measurements. Thus, monitoring should include environmental factors, psychological factors, crew performance factors, results of special medical investigatory experiments, self-assessment reports, and physician-crew consultation. An automated physical examination that will include measurements of many of these factors and which can be performed easily and rapidly by each crewmember has been proposed for future flights[2]. One research tool that may become valuable in helping to define crucial measurement parameters and the conditions for obtaining these measurements is the simulation model developed especially for studying physiological function. The role of models in this regard will be discussed in a later section of this report.

In the remainder of this section an attempt will be made to identify important biomedical determinants of crew health status, including physiological, psychological, clinical, and environmental factors. Various study groups have previously identified hundreds of relevant

parameters that were thought to be essential to a complete inflight medical support system. This was the point of departure for this study. While such lists appear to be all-encompassing, little effort has been given to provide an objective rationale for suggesting these measurements, or for providing a basis for determining priority. It is not within the scope of this report to perform the type of cost-benefit analysis, task analysis, and sensitivity analysis that would be required to meet these objectives. However, it should be realized that such an approach would be necessary to truly consider all the scientific, technical, economic, and political factors involved in establishing a final configuration. An alternate but less rigorous approach would be to make recommendations for future flights based on identifying those determinants of crew health status which have been shown to be useful in past manned flights. This is the approach taken here.

Idealistic System for Crew Health Monitoring Compared with Current Capability

The flow of input and output information necessary to establish a crew health monitoring system is shown in Figure 1[3]. Inputs to the system would be the operational schedule, spacecraft environment, physiopathological, psychological, and operational crew performance measures and vehicle subsystem or hardware status data. The outputs would consist of current crew health status, predictions of future crew capability inflight and postflight, recommended corrective or preventive action, causes for deviation from expected values for physiological, psychological, and performance data (where it is identifiable) and integrated, computerized daily and weekly crew health status reports and trend printouts,



INPUT/OUTPUT INFORMATION FLOW OF IDEALIZED INFLIGHT HEALTH MONITORING SYSTEM

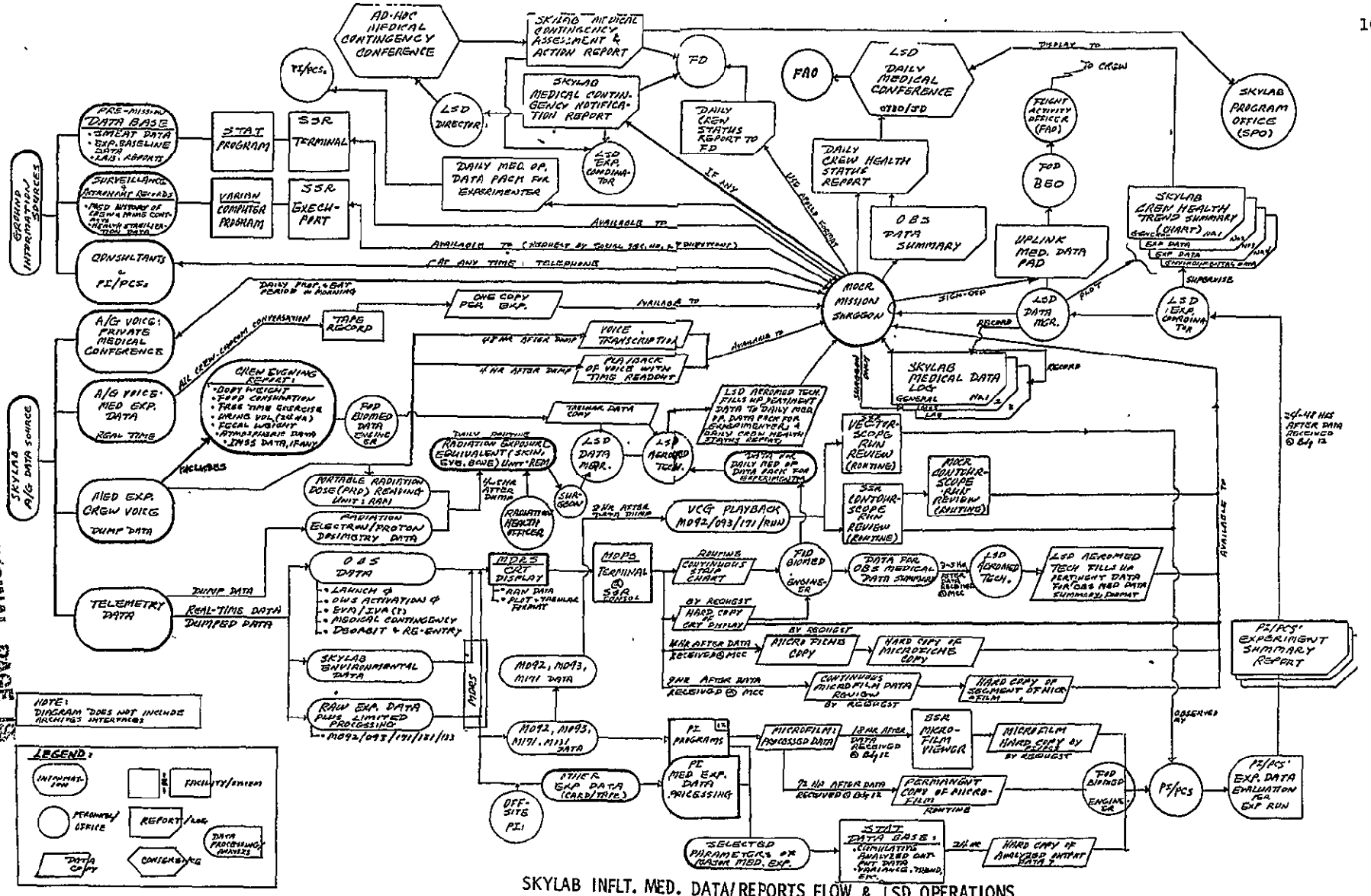
FIGURE 1

In Skylab, the capability to integrate crew health monitoring information and automatically prepare daily crew status reports did not exist. This function was performed manually in a rudimentary manner with the conventional parameters. They included, for example, the crew health trend charts, daily water intake and urine output, caloric intake, exercise, vitamin supplements, a daily crew health status sheet including medication, sleep, subjective clinical comments of crewmen, and preliminary results of major experiments represented by a few variables. It should be emphasized that the crew health trend charts and daily health status data in the Skylab missions lacked any predictive capability; major decisions depended solely on physician's clinical judgement and intuition. A large amount of manpower was consumed for the daily assembling and printing of an enormous volume of data. Such manual methods are quite costly and would be ineffective in oncoming Space Shuttle medical operations. The complexity of the Skylab medical operational data and reports flows are shown in Figure 2. This diagram is included merely to illustrate the point of departure upon which a new system must be developed.

The need for automatic integration of crew health data for the Shuttle medical operation is apparent when one sees its operational mode of multi-crewmen and passengers and rapid turnaround time (i.e., up to 40 flights per year by 1984) imposing a heavy overlap of pre, in-, and postflight crew monitoring. Recommendations regarding specific modes of operation of the monitoring system shown in Figure 1 will be discussed in Section 3.0.

Identification of Crew Health Monitoring Data

The contractor has been accumulating medical measurement variables and technological studies carried out by various space life science groups. A previous study by the contractor attempted to



SKYLAB INFLT. MED. DATA/REPORTS FLOW & LSD OPERATIONS

FIGURE 2

define a biomedical program for crew health monitoring on Shuttle missions[4]. A result of that study is shown in Table 1 in which a proposed crew health monitoring data checklist is summarized. A total of 202 measurements are listed and divided into three major investigative categories. The first column are those "minimum crew-safety assurance parameters" which are considered fundamental non-invasive measurements. The second and third columns represent typical parameters necessary to make diagnosis onboard the spacecraft in case of crew(s) becoming severely ill or incapacitated. It can be concluded that any manned spacecraft should always have a capability of onboard measurements as identified in these three columns regardless of mission objectives, spacecraft types, and/or onboard experiments.

Identification of Important Environmental and Clinical Factors

For purposes of this report, one can define the important environmental and clinical factors as all factors not being specifically monitored by the sensors associated with a particular experiment or analysis. For many purposes, it is sufficient to say a test environment is "normal," or "within limits." However, many parameter changes such as temperature and partial pressure of oxygen that can and do occur in space flight will effect physiological responses to stress tests and routine work. Some of these can be accounted for in simulation models if the data is made available. Other factors such as drug dosages and sensitivities and time at which tests are performed cannot at present be taken into account by models, but are important in interpreting physiological responses and deviations from simulation model predictions.

TABLE 1

MEDICAL MEASUREMENTS REQUIRED FOR CREW HEALTH MONITORING

MEASUREMENT CATEGORIES	MEDICAL/BEHAVIORAL MEASUREMENTS AND ENVIRONMENTAL MEASUREMENTS (MEASUREMENTS GROUPS)	REAL-TIME CREW SAFETY: MINIMUM CREW SAFETY ASSURANCE PARAMETERS	ONBOARD EMERGENCY DIAGNOSIS: PHYSICAL MEASUREMENTS FOR ONBOARD DIAGNOSIS	ONBOARD EMERGENCY DIAGNOSIS: LABORATORY MEASUREMENTS FOR ONBOARD DIAGNOSIS REQUIRING SPECIMEN SAMPLING
MUSCULOSKELETAL AND METABOLIC	Muscle Strength & Size			
	Body Mass Measurement (BMMD)		●	
	Specimen Mass Measurement (SMMD)			●
	Nitrogen Balance			
	Mineral Balance			
	Core Temperature (Ear Canal)			
	Average Skin Temperature	●	●	
	O_2 Consumption, CO_2 Production			●
	Caloric Intake			
	Body Fluid (including sweat)			
	Return of all Food Packages			
	Sweat Measurement & Sample Return			
	Bone Densitometry (Isotope Method)			
	Gastric Pressure and pH			
	Inflight Exercise (Ergometer output)			
	Net Weight of Feces			
	Return of Total Dry Stool			
	Fluid Intake Measurement (Water and Food)			●
	Fluid Output Measurement			●
NEURO/BEHAVIORIAL	Electroencephalogram (EEG)		●	
	Electromyogram (EMG)			
	Electrooculogram (EOG)			
	Galvanic Skin Response (GSR)			
	Ocular Counterrolling			
	Agravic Perception			
	Semicircular Canal Threshold			
	Angular Acceleration Threshold			
	Visual Task w/Head Rotation			
	Coriolis Sickness Susceptibility			
	Depth Perception			
	Brightness Threshold Discrimination			
	Visual Field Mapping			
	Absolute Brightness Threshold			
	Critical Fusion Frequency			
	Phorias			
	Visual Acuity			
	Dark Adaptation			
	Photo Stress			
	Color Perception			
	Absolute Auditory Threshold			
	Speech Intelligibility	●	●	
	Temporal Acuity			
	Pitch Discrimination			
	Time and Motion			
	Concentration			
	Pressure Threshold			
	Tracking			
	Multilimb Coordination			
	Steadiness			
	Reaction Time			
	Sensory Test Battery			
	Perceptual Evaluation			
	Memory - Short & Long Term			
CARDIOVASCULAR	Electrocardiogram (ECG)	●	●	
	Vectorcardiogram (VCG)		●	
	Venous Blood Pressure		●	
	Limb Plethysmogram		●	
	Phono/Vibrocardiogram		●	
	Impedance Cardiogram			
	Heart Rate	●	●	
	Arterial Blood Pressure	●	●	
	Pulse Wave Velocity (PWV)			
	Pulse Wave Contour			
	Ballistocardiogram (BCG)			
	Regional Blood Flow			
	Arterial Reactivity			
	Lower Body Negative Pressure (LBNP)			
	Elastic Leotards			
	Carotid Body Stimulation			
	Blood Rheology (RHE)			
	Cardiac Output		●	
RESPIRATORY	Respiratory Rate	●	●	
	Vital Capacity		●	
	Timed Vital Capacity		●	
	Inspiratory Capacity			
	Expiratory Reserve Volume			
	Tidal Volume			
	Minute Tidal Volume			
	Maximum Inspiratory Flow		●	
	Maximum Expiratory Flow		●	
	Maximum Breathing Capacity		●	
	Aveolar pO_2			
	Aveolar pCO_2			
	Respiratory Dead Space			
	Alveoral Ventilation			
	Residual Volume			
	Airway Resistance			
	Lung Compliance			
	Lung Diffusion Capacity			
	Cardio-Pulmonary Pathology(X-Ray)		●	
LABORATORY, BLOOD	Hemoglobin (Hb)			●
	Hematocrit (Hct)			●
	Blood pH			●
	Blood pO_2			●
	RBC Count			●
	WBC Count			●
	WBC Differential			●
	Platelets			●
	Reticulocyte Count			
	RBC Fragility			
	RBC Mass (Sod. Chromate 51)			
	Bleeding Time		●	
	Clotting Time			
	Prothrombin Consumption			●
	Immunoglobulins & Fibrinogen			
	Platelet Adhesiveness			
	Antibody Titration			●
	Fibrinolytic Activity			
	RBC Survival (Sod. Chromate 51)			
	RBC Morphology			
	Clot Retraction			
	Total Body Water			
	Plasma Sodium			●
	Plasma Potassium			●
	Plasma Chloride			●
	Plasma Calcium			
	Plasma Protein			●
	Plasma Glucose			●
	Plasma Phosphate			
	Plasma Volume			●
	SGOT			●
	SGPT			●
	Plasma Alkaline Phosphatase			
	Plasma Bilirubin			
	Serum ADH			
	Blood 17 - Hydroxycorticosteroids			
	Plasma Protein Electrophoresis			
	Serum Cholesterol			
	Blood Urea Nitrogen (BUN)			●
	Blood Uric Acid			
	Blood Bicarbonate			●
	Creatinine Phosphokinase (CPK)			
	Serum LDH & LDH Isoenzymes			
	Blood ACTH			
	Blood TBPA			
	Blood Histamin			
	Lymphocyte Kariotyping			
	WBC Mobilization			

● : Crew Health Monitoring Data

TABLE 1 - Continued

MEASUREMENT CATEGORIES	MEDICAL/BEHAVIORAL MEASUREMENTS AND ENVIRONMENTAL MEASUREMENTS / MEASUREMENTS GROUPS	REAL-TIME CREW SAFETY: MINIMUM CREW SAFETY ASSURANCE PARAMETERS	ONBOARD EMERGENCY DIAGNOSIS: PHYSICAL MEASUREMENTS FOR ONBOARD DIAGNOSIS	ONBOARD EMERGENCY DIAGNOSIS: LABORATORY MEASUREMENTS FOR ONBOARD DIAGNOSIS REQUIRING SPECIMEN SAMPLING
	Transferrins			
	Whole Blood Methemoglobin			
	RBC Enzyme Studies			
	Complement Titration			
	TSH			
	Blood, Growth Hormone			
	Thyroid Bound Globulin (T3)			
	Serum Parathyroid Hormone			
	Serum Calcitonin			
	Blood, pCO_2			●
	Insulin Assay			
LAB., BLOOD	Glucagon Assay			
	Blood Serotonin (5HIAA)			
	Blood Lipids			
	Angiotensin II			
	Membrane Assay & Cytogenetic Studies			
LABORATORY, URINE	Urine, Color			●
	Urine Specific Gravity			●
	Urine pH			●
	Urine Glucose			●
	Urine Protein			●
	Urine Bile			●
	Urine Blood			●
	Urine Microscopic Study			●
	Urine Calcium			●
	Urine Phosphate			●
	Urine Sodium			●
	Urine Potassium			●
	Urine Chloride			●
	Urine Acetone Bodies			●
	Urine Mucoproteins			
	Urine Pyrophosphates			
	Urine Hydroxyprolines			
	Urine Total Amino Acids			
	Urine Aldosterone			
	Urine ADH			
	Urine, 17-Hydroxycorticosteroids			
	Urine, 17 Ketosteroids			
	Urine, Vinyl Mandelic Acid (VMA)			
	Urine, Metanephrines			
	Urine, Catechols			
	Urine, Histamine			
	Urine, Serotonin (5HIAA)			
	Urine, Sulfate			
	Urine, Creatine and Creatinine			
ENVIRONMENTAL	Suit, Cooling Garment Fluid Temperatures	●	●	
	Suit, Pressure	●	●	
	Suit, Temperature & RH	●	●	
	Suit, pO_2	●	●	
	Suit, pCO_2	●	●	
	Electromagnetic Field			
	Acoustic Noise			
	Vibration			
	Acceleration/Gravitational Field			
	Ambient Temperature	●	●	
	Ambient RH			
	Ambient Pressure	●	●	
	Ambient pO_2	●	●	
	Ambient PCO_2	●	●	
	Ambient Radiation Dose	●	●	
	Light ($I_{\lambda x}$ vs λ)			
	Ambient Air Flow Rate			
LAB., BAC.	Bacteria and Fungi			●
	Virus			

The following list of parameters are based on particular experience with the Skylab missions and are currently being evaluated for their relevancy in interpreting integrated results from several biomedical experiments. Although they are in some respects repetitious of other lists in this report, they have been derived from different sources and are being used for special research purposes. They have been divided into six logical groups depending on the type of information they convey.

The following are useful parameters in describing the environment that could influence crew performance or health either immediately or from a long range point of view.

- o Ambient Pressure - Avg.
- o Ambient Temperature - Avg.
- o Partial Pressure of Oxygen
- o Partial Pressure of Carbon Dioxide
- o Humidity and/or Dewpoint
- o Radiation Exposure Dose to Crewmen

The following clinical factors are transient in nature, can be different for each crewman. These include:

- o Illness Events
  - Symptoms with time of onset and disappearance
  - Diagnosis/Etiology
  - Medications with time of administration
- o Circadian Rhythm Shift (wake time/bed time)
- o Amount of sleep
- o Length of work day
- o Major mission activity
- o Time of each meal
- o Timing of each medical experiment
- o Emotional upheaval

While the environmental data is quite limited in number of parameters, the clinical data can be broken up into logical groups based on the type of information. The following groups are based on experience with the other indicators of the crew physical conditions that should be monitored and are as follows:

- o Exercise duration
- o Exercise type
- o Liquid intake
- o Food quantity and type
- o Anthropometric measurements
  - Circumferences at various parts of the body
  - Height, preferably divided into lower and upper portions

The following items of information require special equipment to be onboard in order to obtain data which are of value in any long mission in monitoring crew physical condition.

- o Weight
- o Urine quantity
- o Urine specific gravity, etc.
- o Blood sampling equipment
- o Exercise quantity (ergometer)

The following items of each crewman's history should be immediately avilable in any data base, in addition to possibly many others that are of concern to a physician in evaluating an illness event.

- o Age
- o Preflight weight
- o Maximum heart rate
- o Maximum oxygen uptake
- o Drug sensitivity
- o ECG anomaly history

Realistic Assumptions of Shuttle Medical Operation

An effective development of an operational Shuttle crew health monitoring system must be based on realistic assumptions of the type of data available in actual Shuttle missions. Certain Shuttle flights will be devoted exclusively to life-science research and much biomedical data will be available from the inflight medical experiments. However, crew health monitoring is concerned with all manned flights regardless of their mission objectives.

Assuming four crewmen and a complement of four passengers fly every ten days by 1984, it is reasonable to assume that the mode of routine Shuttle crew health monitoring will be extremely limited and, therefore, should be highly efficient and effective. The basic assumptions for the definition of available data in a Shuttle crew health monitoring system include:

1. Measurements for specialized biomedical experiments will not be available.
2. Available crew time and medical measurements for the crew's routine health monitoring will be limited to a minimum except for the life sciences devoted missions.
3. Ground control crew surgeons will not be stationed at the Mission Control Center Medical Console on a round-the-clock basis, but will be on stand-by mode.
4. Air-to-ground private medical conferences will be furnished as needed.
5. Voice and television will be available for the telediagnosis as needed.
6. Radiation health data will be available.
7. An Inflight Medical Support System (IMSS) will be provided for the onboard medical tests and care and such data will be available to the ground crew surgeon.

8. Operational Bioinstrumentation System (OBS) data (including electrocardiogram, impendence, pneumogram, and metabolic rate) will be also used in Shuttle during the launch, EVA, and reentry phases in selected subjects.

9. Nutrition and caloric intake data will not be available inflight.

10. Data on the daily water intake (potable water only) and daily urine output will be available by automated sampling and computation system.

11. Body and Specimen Mass Measuring Systems data also will be available inflight.

12. Crew and passengers will conduct an instrumented exercise daily, which include measurements of workload, EKG/VCG, and spirometry. (This assumption is tentative at this time; other types of deconditioning countermeasures may be developed).

Minimum Available Crew Health Monitoring Data in Shuttle

Based on the foregoing discussion, it has been possible to estimate the minimum inflight crew health monitoring data that will be available in non-life science Shuttle missions. These are shown in Table 2. The variables are divided under major body systems and the desired frequency of measurement (during exercise; once/day; twice/day (b. i. d.) continuous; during OBS use; as occurred and as indicated) is indicated. Of the 68 parameters shown, 44 can be expressed as objective, quantitative indicators while the remainder are subjective measurements or observations. Only 17 measurements would be available on a daily basis. It may be concluded that while the list appears somewhat lengthy, it would be possible to detect physiological disorders only after overt symptoms have developed.

TABLE 2

Projected Minimum Available Inflight Crew Health Monitoring Data in Shuttle Missions*

SYSTEM	DATA	FREQUENCY
General	Body weight/mass	Once a day
	Oral temperature	b. i. d. **
	Water intake (potable water only)***	24 hrs.
	Injury	As occurred
	Fatigue complaint	As occurred
CARDIOVASCULAR	EKG/VCG and heart Rate	OBS & exercise
	Venous blood pressure	As indicated
	Circulation time	As indicated
	Arterial blood pressure	b. i. d.
	Heart sound (auscultation)	As indicated
	Cardiopulmonary symptoms complaint	As occurred
	Retinal examination	As indicated
	Skin, nail bed, and mucosal color	As indicated
	Venous distention	As occurred
RESPIRATORY	Impedance pneumogram (ZPN) & Respiratory rate	OBS, EVA
	O_2 consumption, CO_2 production	Exercise, EVA
	Breath holding time	As indicated
	Vital Capacity (with spirometry)	Exercise
	Maximum inspiratory/expiratory flow	Exercise
	Maximum breathing capacity	Exercise
METABOLISM	Exercise test (with EKG/VCG & spirometry)	Exercise
HEMATOLOGY	Complete blood cell count (CBC)	Weekly or as indicated
	Blood cell differential	Weekly or as indicated
	Hemoglobin (Hb)	Weekly or as indicated
	Hematocrit (Hct)	Weekly or as indicated
	Bleeding Time	Weekly or as indicated
	Clotting time	Weekly or as indicated

*Includes data obtained by using IMSS by trained crewmen

**b. i. d. = twice a day

***Water intake and urine output data will be available automatically only when module waste management system is added to current basic Shuttle configuration.

TABLE 2 (Cont'd)

SYSTEM	DATA	FREQUENCY
RENAL	Urine output***	24 hrs.
	Urinalysis (WBC, RBC, pH, sugar, protein, osmolarity, microscopic)	Weekly, or as indicated
	Voiding evaluation	As occurred
MUSCULOSKELETAL SYSTEM	Muscle, size, girth	Daily or weekly
	Joint motion range	Weekly, or as indicated
	Skin fold test	Weekly
	Anthropometry and circumference	Daily or weekly
DIGESTIVE SYSTEM	Bowel function evaluation & stool characteristics	Daily
	Eating habits, appetite, & time of meal	Daily
	Nausea & regurgitation evaluation, time of onset	As occurred
	Liver size	As indicated
NERVOUS SYSTEM	Electroencephalogram (EEG)	As indicated
	Speech intelligibility (A/G voice & dumped tape)	Continuous
	Sensation	As indicated
	State of Arousal	As indicated
	Reflex response & clonus evaluation	Weekly or as indicated
EYE, EAR, NOSE, THROAT (EENT)	Ophthalmoscopy	As indicated
	Visual field evaluation	As indicated
	Incidence of aerotitis media	As occurred
MICROBACTERIOLOGICAL	Fecal flora (sampling & preservation only)	Periodic
	Crew skin & mucosa microbial sampling & analysis	Periodic or as indicated
ENVIRONMENTAL	EVA, suit pressure	EVA, constant
	Suit, temperature & relative humidity	EVA, constant

TABLE 2 (Cont'd)

SYSTEM	DATA	FREQUENCY
ENVIRONMENTAL (Cont'd)	Suit pO_2, pCO_2	EVA, constant
	Metabolic rate & activity type	EVA, constant
	Radiation dose, rem, on skin, eye, bones (predicted)	Daily
	Acceleration, G±X during launch & reentry phases	OBS
	Ambient temperature	Continuous
	Ambient relative humidity	Continuous
	Ambient pressure	Continuous
	Ambient pO_2 & pCO_2	Continuous
	Ambient toxic gases and/or microbial particles	Periodic, or as indicated
WORK-REST CYCLE	Work-rest cycle with type of activity	Daily
	Awake-sleep time	Daily
	Sleep quantity, subjective	Daily
CLINICAL	Medication, dose, time of administration	As occurred
	Other signs and symptoms, time of onset, time of disappearance	As occurred
	Treatments other than medication & time	As occurred
	Private medical conference (Available to crew surgeon only)	As occurred

Detection of onset of disorders will require more intensive and sensitive measurements as indicated by the list of Table 1. The processing and integration of physiological and clinical measurements to obtain an overview of crew health status is a challenge to space medical research, especially when those measurements represent a minimal subset.

Examples of Crew Health Monitoring Data Display Formats

Implicit in any monitoring system is an effective method of displaying the measured information whether it be processed, analyzed, or integrated data. With respect to biomedical data that will be used to monitor crew health, consideration should be given to the appropriate grouping of data dependent upon its ultimate use. Thus, raw, filtered real-time data such as heart rate, ECG, and oxygen uptake may be required during extremely stressful periods such as launch, reentry, EVA's, or exercise stress tests. On the other hand, daily measurements or fluid intake, output, and body masses, may be delayed for display for longer periods of time. Blood and urine analysis, if they are required on a regular but infrequent schedule, can be processed and integrated with other data using statistical analysis or simulation models. In any case, attempts should be made to include all the available data by taking advantage of the most sophisticated techniques for data integration and data display, minimizing the delays associated with manual data manipulation. Time constraints have not permitted a thorough analysis of this problem and the examples shown here are for illustrative purposes only; much more development is needed in this area.

Figure 3 represents a plotting of real time data during the critical period between lift-off and orbital insertion showing heart rate for all three crew members superimposed on the G_x acceleration time

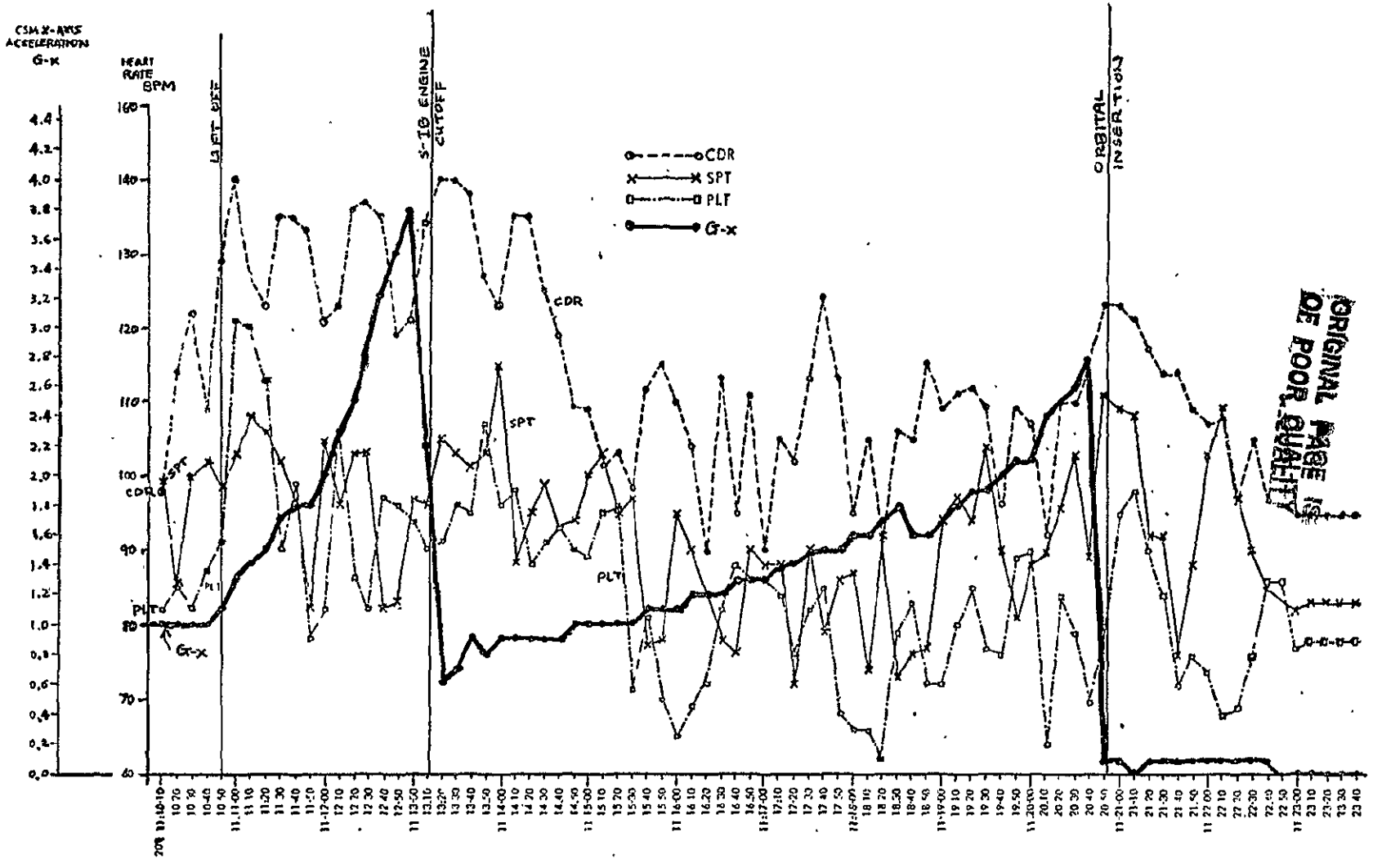


FIGURE 3 SL-3 CREW HEART RATES AND CSM X-AXIS ACCELERATION DURING LAUNCH

profile. The example shown was obtained from one of the Skylab missions. While there does not appear to be any correspondence between heart rate and G_x profile, there does appear to be large changes in heart rate of each crewman. Whether or not this is an appropriate response can be estimated by comparing these flight responses with previous flight responses or with pre-flight simulation data. This comparison could be accomplished in near real-time using automated techniques.

An example of a data display from a specialized biomedical research experiment is shown in Figure 4. Although these profiles were obtained from raw data during an actual Skylab LBNP experiment, they were constructed manually many hours following the test for the flight surgeon who wished to further investigate causes underlying early termination of the experiment. In this particular case it may have been possible to predict an oncoming presyncopal episode from the sudden changes in heart rate and blood pressure accompanying the higher levels of LBNP. From the study of the plots, it is apparent that if one sees real-time changes of physiological parameters in each test phase, it is possible to flag the rate and direction of these changes and their implications for crew safety as well as to detect abnormal responses before the subject or onboard observer can notice it. Hopefully, this can be accomplished without depending on the development of clinical presyncopal signs and symptoms of the subject. Rate, direction of change, and change of correlation coefficients in various phases of the preflight test can be compared as representing a crewman's own baseline response in such a way that warning and cutoff points can be defined.

Figure 5 is a display of a respiratory flow-volume contourograph obtained during a pulmonary function test. The outer contour (solid lines) represents a normal response while the inner contour

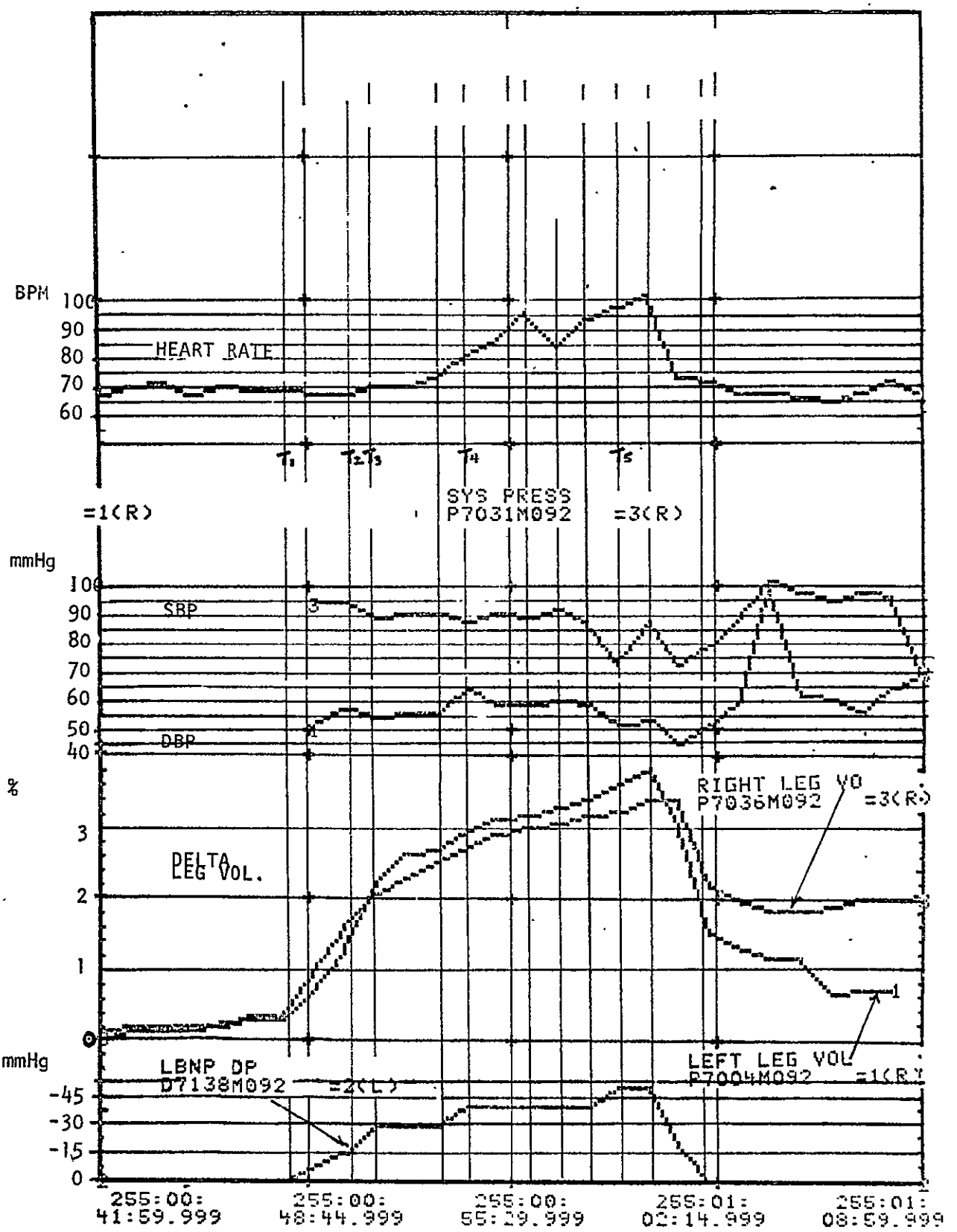


FIGURE 4 UTILIZATION OF MEDICAL EXPERIMENT RAW DATA FOR DAILY CREW HEALTH ASSESSMENT

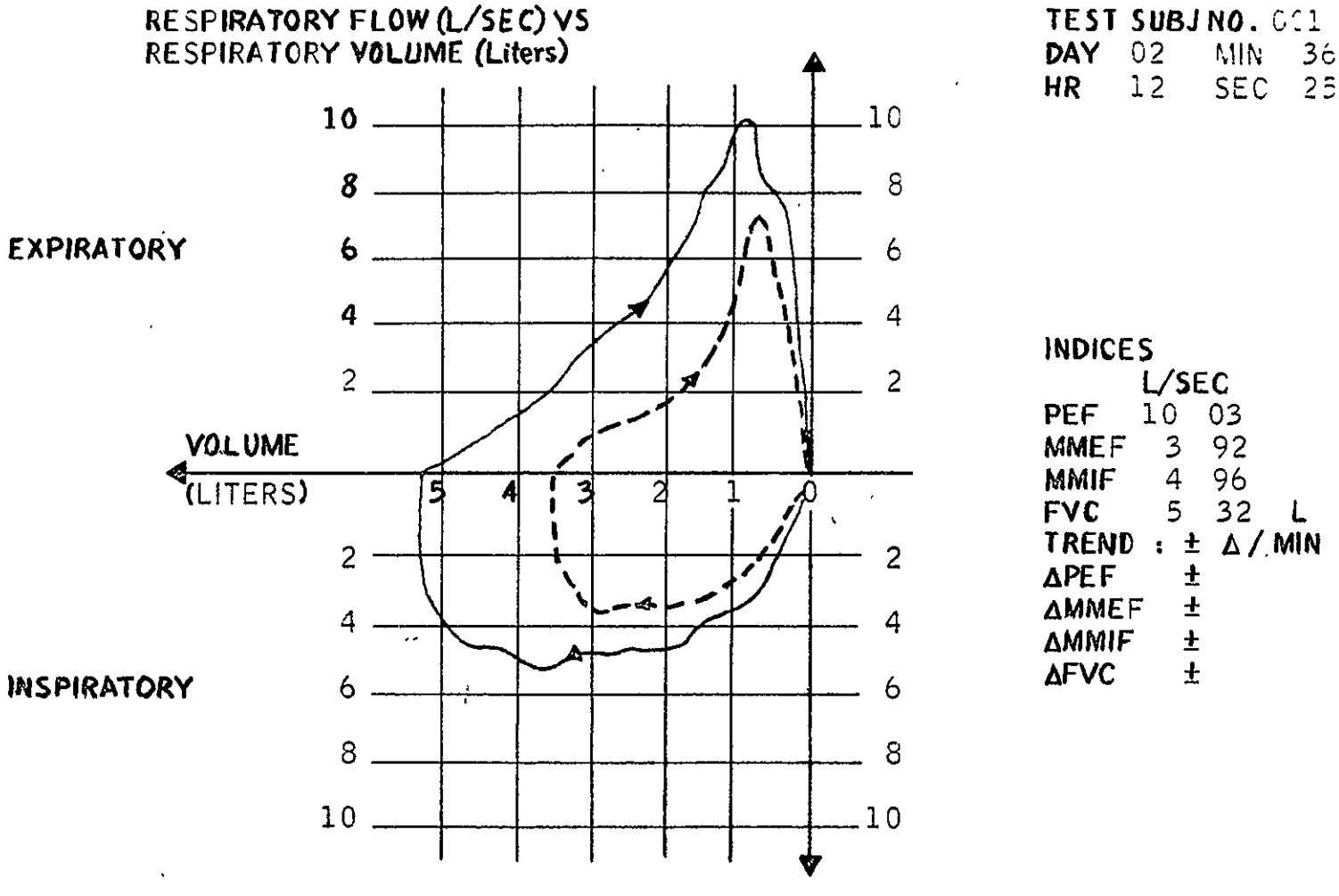


FIGURE 5 RESPIRATORY FLOW-VOLUME CONTOUROGRAPHY DISPLAY FORMAT

(dotted line) represents a possible emphysemic condition. The data analyzed in this fashion is highly sensitive to detecting airway resistance changes and is an example of the use of data display for supplementary diagnostic tests.

An example of a real-time crew health monitoring data display that attempts to compress a large amount of visual information is shown in Figure 6. This might represent a rather complete set of data obtained from an ongoing stress test or could also be an equally suitable display for results of urine and blood analysis. The large empty boxes would contain numeric display of the absolute magnitude of the particular parameter while the smaller boxes would be color codes to designate whether the measurement is nominal or off-nominal. A display of this type may be created using a subset of measured parameters selected by the flight surgeon for differential diagnosis. Further study is warranted to determine the utility of computing and displaying a matrix of correlation coefficients of selected inflight parameters in comparison with preflight control parameters.

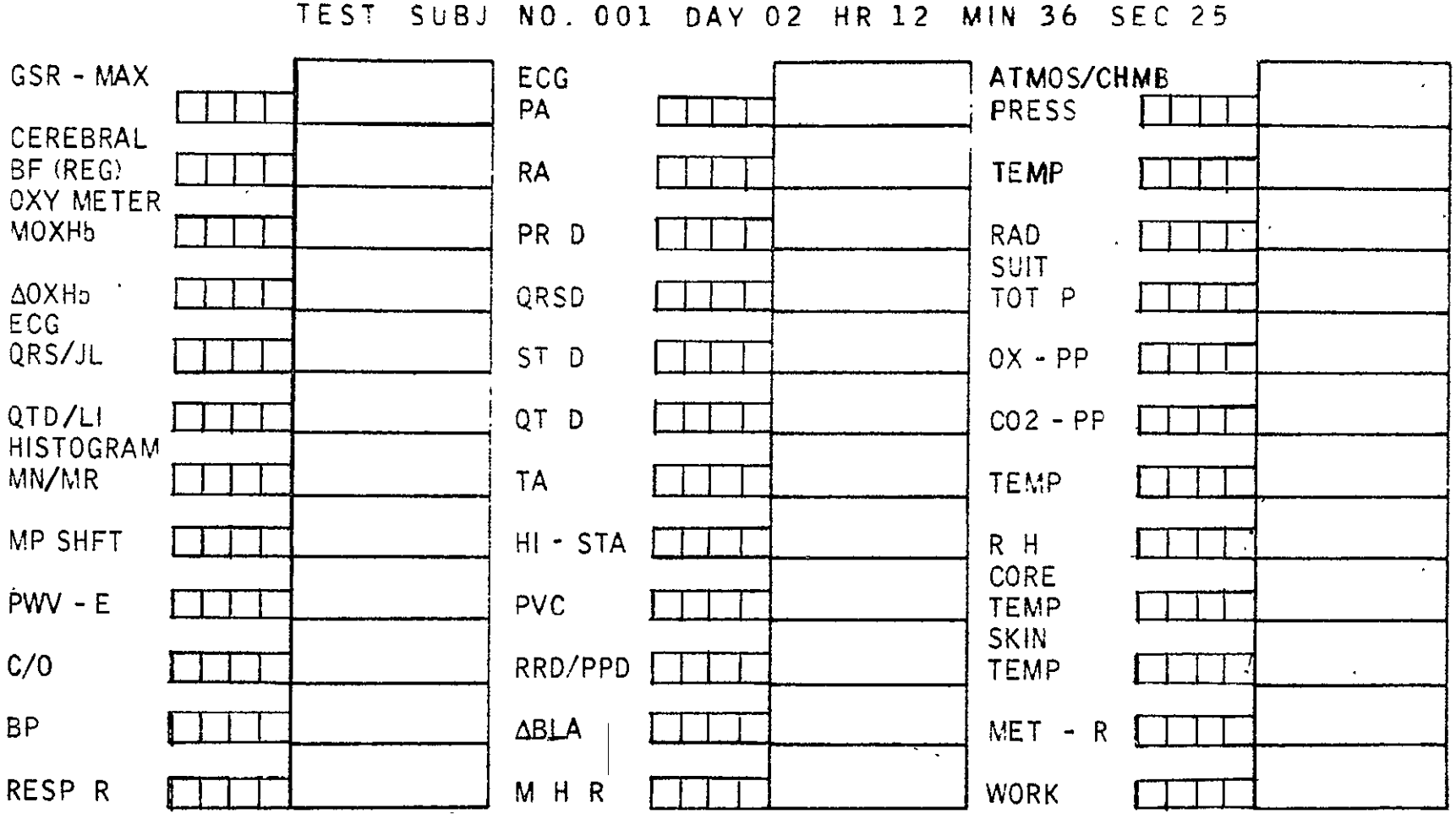


FIGURE 6 EXAMPLE OF REAL-TIME CREW SAFETY/HEALTH MONITORING DATA DISPLAY

3.0 ROLE OF SYSTEMS ANALYSIS AND MODELING IN MONITORING AND MAINTAINING CREW HEALTH

Identification of Subsystem Simulation Models

During the pre-Skylab manned space missions, many areas of significant physiological change as a result of weightlessness and other environmental factors were identified. Although all identifiable changes were reversible for flights lasting up to two weeks, it became apparent that much more intensive monitoring and experimentation would be required in order to better understand the physiological effects of weightlessness and recovery as well as to provide adquate countermeasures where necessary. During this time several scientific task groups directed their attention to identifying the specific areas of human and animal research that should be given priority during space flights lasting one to two months in an orbital research laboratory[2, 5, 6, 7]. Specific guidelines for each major investigative area including the anticipated experiments, measurements, instrumentation, etc., were established in an experimental program plan issued by the NASA Payloads Directorate[8]. Much of the Skylab medical experimentation and biomedical monitoring program was based on these guidelines. Table 3 is a summary of these major investigative categories, specific research areas and measurements required to fulfill the research task. While the Skylab medical experiments provided much insight into most of these areas, they still remain active areas of concern[9].

One of the prime objectives of this contractual effort is to develop mathematical simulation models for application in the life sciences effort of the space program. The choice of subsystem models and the manner of implementation was predicated to a large extent by the particular needs of the Life Sciences Directorate

as determined by the accumulative flight experience. Simulation models are most useful in those situations in which the objectives are clearly defined and in which there exists a data base to indicate directions for model refinement. The summary of research objectives as shown in Table 3, coupled with the results of the Skylab medical program, provide these minimal requirements. Thus, it is possible to identify specific areas in which simulation models may be useful in helping to understand and monitor physiological changes during space flight.

A literature review of currently existing simulation models has resulted in identification of many models related to the physiological systems singled out for intensive investigation in the Skylab era. These are shown in the last column of Table 3 (also see Appendix). In addition, the major parameters of each subsystem are identified by an asterisk if they are known to be utilized by these models. It should be mentioned that the literature review is by no means complete, but serves to indicate the diversity and relevancy of available models as well as pointing out areas of deficiency.

The model subsystems that would be investigated and evaluated in depth during the present contract were identified in the original statement of work. Trade studies were based largely on desired goals of the NASA Life Sciences Directorate and the technical monitor and on the availability and suitability of current models. This resulted in identifying several major subsystem models of the cardiovascular, respiratory, thermal regulatory, fluid balance, and renal/endocrine systems. These are indicated in Table 3 by a (+) designation and they are summarized more completely in Table 4. It is apparent that the models are capable of integrating a large quantity of information and predicting behavior of a great number of physiological variables, most of which have been previously identified as important elements in space flight biomedical

Table 3

MAJOR PHYSIOLOGICAL INVESTIGATIVE AREAS AND MATHEMATICAL SIMULATION MODELS AVAILABLE

MAJOR INVESTIGATIVE CATEGORY(1)	SPECIFIC RESEARCH AREA (1)	PRIMARY MEASUREMENTS REQUIRED (1),(2)	SIMULATION MODELS AVAILABLE (3)
NEUROPHYSIOLOGY	Vestibular Function - Head movement effects - Otolith and semicircular canal sensitivity - Sleep - Alertness - Biorhythms	Electroencephalogram * Occular counter-rolling * Eye tracking ** Body temperature Task performance	Vestibular System Vestibular-ocular System Eye Tracking Simulation Counter-rolling Simulation
CARDIOVASCULAR FUNCTION	Cardiovascular Deconditioning - Circulatory response to exercise - Blood volume effects on arterial pressure control - Peripheral venous compliance - Cardiac dynamics - Intraocular arterial blood pressure - Cardiac output Deconditioning Countermeasures - Lower body negative pressure device - Onboard centrifuge - Occlusive cuffs - Response to shock therapy	** Heart Rate ** Cardiac Output ** Arterial Blood Pressure ** Right Atrial Pressure ** Circulation Time ** Cardiac Filling Time ** Blood pO_2 ** Expiratory pO_2 and pCO_2 ** Body Temperature * BodyMass Electrocardiogram Phonocardiogram Ballistocardiogram * Plethysmogram (limb vol.) Urinary catecholamines ** Tidal volume * Respiratory Amplitude ** Hematocrit ** Blood Volume ** Plasma Volume ** Extracellular Fluid Volume ** Total Body Water ** Red Cell Mass	+Overall Circulatory Control +Systemic Flow, Pressure, and Volume Distribution +Cardiac Regulation +Capillary Exchange +Cardio-respiratory Integration Vectocardiogram Simulation +Exercise Simulation +Lower Body Negative Pressure +Tilt-Table Simulation +Hypo-/Hyper-volemic Simulation
RESPIRATION	Ventilatory Mechanics - Pulmonary mechanics - Respiratory control Pulmonary Efficiency - Blood gas exchange - Lung cleansing - Induced pulmonary infections - Blood flow distribution in lungs Atmospheric Condition Effects - Composition - Pressure - Contaminants - Oxygen toxicity - Carbon dioxide	** Respiration Rate * Airway Resistance Maximum Inspiratory and Expiratory Pressures Breath Holding Time * Lung Compliance * Respiratory Volumes ** Lung Gas Exchange ** Inspired pO_2 and pCO_2 ** Expired Air pO_2 and pCO_2 ** Blood pH, Bicarbonate, pO_2, pCO_2 ** O_2- Hb Saturation ** Body Temperature ** Ambient Temperature ** Ambient Pressure Trace Contaminant Conc. * White Cell Count	+Respiratory System Regulation +Cardio-respiratory Integration +Exercise Simulation +Hypoxia Simulation +Hypercapnia Simulation

(Continued on next page)

Table 3 (Continued)

MAJOR INVESTIGATIVE CATEGORY (1)	SPECIFIC RESEARCH AREA (1)	PRIMARY MEASUREMENTS REQUIRED (1),(2)	SIMULATION MODELS AVAILABLE (3)
GASTROINTESTINAL (GI)	GI Function and Motility - Motility and pH - Intestinal absorption General Renal Function - Stone formation - Renal infection	Peristaltic Contraction Rate and Intensity Stomach Volume Gastric pH Absorption Rates of Food * Body Mass Blood Urea Nitrogen ** Serum Electrolytes Serum Creatinine Urine Calcium and Phosphorus * Urine Osmolarity ** Urine Volume	+Thirst Regulation +Fluid-Electrolyte Regulation +Renal Circulatory Control Amino-Acid Regulation Intestinal Glucose Absorption Simulation
METABOLISM AND NUTRITION	General Metabolism - Metabolic rates - Carbohydrate, fat, and protein metabolism Fluid and Electrolyte Balance - Body fluid composition - Intake and output rates - Body fluid volumes Mineral Metabolism Muscle and Bone Metabolism Nutrition Cellular Metabolism	* Body Mass * Body Volume ** Body Temperature ** Inspiratory pO_2 and pCO_2 ** Expiratory pO_2 and pCO_2 * Nitrogen Intake * Urine Nitrogen Fecal Nitrogen * Serum Proteins ** Serum Electrolytes * Serum pH * Urine Osmolarity Urine creatine and creatinine * Serum, Urinary, and Fecal Calcium and Phosphorus * Fecal Mass * Blood and Urine Glucose * Blood Free-Fatty Acids ** Total Body Water ** Blood Volume ** Plasma Volume ** Red Blood Cell Mass ** Extracellular Fluid Volume	+Body Fluid Volume Control +Fluid-Electrolyte Regulation Glucose-Insulin Regulation Carbohydrate Metabolism Fatty Acid Metabolism Urinary Amino-Acid Regulation
MUSCULOSKELETAL	Skeletal Decalcification - Bone Density - Fracture healing - Calcium mobilization Work Capacity, Exercise, and Deconditioning - Muscle mass and strength	* Bone Density * Muscle Strength * Muscle Mass * Blood, Urine and Fecal Calcium and Phosphorus Serum Alkaline Phosphotase * Calcium Turnover Rate * Bone Formation Rate * Calcium Intake and Excretion Serum and Urine Creatine Serum and Urine Creatinine Blood Lactic Acid Electromyogram	Calcium Metabolism and Regulation Phosphate Metabolism Whole-body Biomechanical Models

(Continued on next page)

Table 3 (Continued)

MAJOR INVESTIGATIVE CATEGORY (1)	SPECIFIC RESEARCH AREA (1)	PRIMARY MEASUREMENTS REQUIRED (1),(2)	SIMULATION MODELS AVAILABLE (3)
ENDOCRINOLOGY	Stress Effects - Endocrine assays from: pituitary thyroid gonadal adrenal renal glands - Temperature regulation	** Expiratory pO_2 and pCO_2 ** Urine Volume and Osmolarity ** Fluid Electrolytes ** Ambient Temperature ** Skin and Core Temperature ** Humidity ** Blood Flow * Blood Iodine * Blood TSH * Sperm Count and Motility * Urinary 17-hydroxysteroids ** Urinary Aldosterone Urinary 17 ketosteroids Urinary Catecholamines Urinary Serotonin * Blood ACTH	+Fluid-Electrolyte Balance Thyroid Control System Adrenocortical Regulation Growth Hormone-Hypoglycemic Simulation +ADH Regulation +Aldosterone Regulation +Renin-angiotensin Regulation +Renal-electrolyte Regulation
HEMATOLOGY	Blood Cytogenetics - Chromosomal activity Blood Cell Dynamics - Erythrocyte dynamics - Leukocyte dynamics - Platelet dynamics Wound Healing Hemostatic Function - Blood coagulation	** Hematocrit ** Red Blood Cell Mass ** Red Blood Cell Survival Time Red Blood Cell Fragility * Reticulocyte Count * White Blood Cell Count ** Hemoglobin * Platelet Count Clotting Time	+Erythropoietic Regulation Bone Marrow Kinetics Ferrokinetic Models Granulocyte Kinetics
MICROBIOLOGY AND IMMUNOLOGY	Microbiology - Microbiological evaluation of environment - Microbiological evaluation of crewmembers Immunology - Immunological evaluation of crewmembers	Bacterial Identification and Enumeration Collection of Serum Immune Components	
PHARMACOLOGY	Drug Effects and Stability Pharmacological Manipulations of Sleep, Behavior, Biorhythms, etc. Dose Levels Drug Sensitivity Tests	Blood Concentrations of Drugs Dose response	Prediction of Drug Effects Prediction of dose regimens Drug Distribution Effects
RADIOBIOLOGY	Molecular and Cellular Changes Mammalian Systems Changes Combined Effects of Radiation and Other Stresses	Radiation in Spacecraft Radiation Crew Monitoring Rate of Mutation of Microorganisms	

Note (1) Ref."Experiment Program for Extended Earth Orbital Missions", Volume II, Office of Manned Space Flight, National Aeronautics and Space Administration, September 1969.

Note (2) * Appears as input parameter, system parameter, or predicted variable in at least one model listed in next column

Note (3) + Indicates capability of models developed for current contract

Selected bibliography of these models appears in Appendix

Table 4

CAPABILITY OF CURRENT MODELS TO UTILIZE AND PREDICT IMPORTANT PHYSIOLOGICAL PARAMETERS

SUBSYSTEM MODEL	VALIDATED SIMULATIONS	SYSTEM PARAMETERS (known or assumed)	OUTPUT VARIABLES (predicted)
CIRCULATORY DYNAMICS, FLUID-ELECTROLYTE BALANCE MODEL (5 Circulatory Compartments; 5 Body Fluid Compartments)	* Exercise * Salt loading Renal failure Proteinuria Intravenous infusions * Bedrest Congestive heart failure	* Fluid intake * Na^+ and K^+ intake * Evaporative water loss * Exercise work rate * Arterial oxygen saturation * Vascular compliances Ventricular strength factor Plasma protein production and destruction rates * Red cell production and destruction rates (Total number parameters = 100)	* Cardiac output * Heart rate * Stroke volume * Arterial pressure * Venous pressure * Peripheral resistance * Urine flow rate * Na^+ and K^+ excretion rates Renal and muscle blood flows * Blood volume * Extracellular fluid * Intracellular fluid * Total body water * Red blood cell mass * Hematocrit * Blood viscosity * ADH concentration * Aldosterone concentration * Renin and Angiotensin concentrations * Na^+ and K^+ plasma concentrations * Oxygen uptake (Total number variables - 350)
PULSATILE CARDIOVASCULAR MODEL (28 Compartments)	* Exercise * Tilt-table * LBNP Hemorrhage	* External workload Exercise efficiency * LBNP intensity * Tilt angle * Total blood volume * Compliances of veins, venules, arteries and arterioles Fixed flow resistances Stress relaxation sensitivity Length of vascular segments (Total number parameters = 100)	* Cardiac output * Heart rate * Stroke volume * Total peripheral resistance * Systolic blood pressure * Diastolic blood pressure * Heart period * Diastolic filling time Whole-body blood volume distribution Blood pressure (static and dynamic) profiles Pressure pulse profiles Whole-body blood flow distribution Resistances to flow (Total number variables = 350)
RESPIRATORY SYSTEM MODEL (4 Compartments)	* Hypoxia * Hypercapnia * Exercise	* Inspired O_2 * Inspired CO_2 Inspired N_2 * Barometric pressure * Metabolic rate * Total blood hemoglobin Blood and tissue-gas solubilities Blood-brain gas diffusivities * Tissue masses Blood transport delays (Total number parameters 30)	* Minute volume * Respiratory rate Dead space ventilation * Cardiac output * Heart rate * Arterial pO_2 and pCO_2 * Venous pO_2 and pCO_2 * Blood and brain pH Brain blood flow * Alveolar RQ * O_2-Hb Concentration (Total number variables 80)
THERMOREGULATORY SYSTEM MODEL (41 Compartments)	* Environmental heat stress * Environmental cold stress * Exercise * Effects of humidity, clothing, air velocity and pressure	* Total metabolic rate Tissue basal metabolic rates Useful work efficiency * Body surface area Body posture * Ambient temperature * Wall temperature * Ambient humidity * Ambient free air velocity * Ambient pressure * Gravity factor * Clothing factor * Emissivity of outerwear * Specific heat of atmosphere Tissue thermal conductivities Tissue heat capacities Convection and radiation coefficients Basal blood flows Sweat distribution factors Shivering distribution factors (Total number parameters = (330)	* Body temperature distribution * Sweating rate * Insensible water losses Sensible heat losses Heat storage Shivering rate Skin blood flow Muscle blood flows (Total number variables - 300)
ERYTHROPOIETIC CONTROL SYSTEM MODEL	* Hypoxia Anemia * Hypervolemia * Polycythemia	* Arterial pO_2 Blood flow * Plasma volume Tissue metabolism O_2-Hb capacity (Total number parameters = 10)	* Red cell mass * Hematocrit * Red cell production rate * Red cell destruction rate Tissue pO_2 * Venous pO_2 (Total number variables = 20)

NOTE: * Denotes stresses, parameters, and variables which have been identified by aerospace medical investigators for study and measurement aboard an orbital laboratory.

investigations. The list of system parameters in Table 4 is simplified to the extent that it does not include essential elements of the control system such as gains, set points, time delays, etc. Economic limitations precluded the evaluation of other very important subsystem models. These include the vestibular system, the calcium regulating system, certain hormonal systems, biomechanical locomotion models, and detailed biochemical/metabolic systems.

Identification of Important Parameters with the Aid of Simulation Models

The problem of defining parameters which represent crucial measurements in a health monitoring system has been traditionally approached by a combination of clinical and experimental experience as well as economic and technical considerations. Very often the final determination of measurements is decided by the availability and costliness of instruments. However, a more systematic approach to this problem of establishing measurement priorities can be borrowed from the use of specialized techniques associated with simulation models in certain research situations. Sensitivity analysis has been shown to be a systematic and quantitative method of identifying the most important parameters of a system; i.e., those that have the greatest influence on a given response variable. This method would provide a rational basis for deciding priority of measurements and cost allocations in both experimental and clinical situations. Error analysis, when combined with sensitivity analysis, can lead to an even more powerful ordering of priorities. This technique provides an estimate of the relative contribution of errors of the major system parameters to the final system response. This information can be used to define the limits of allowable instrument error and hence suggest acceptable measurement techniques.

Table 4 provides a list of what may be considered the most important parameters and output variables associated with a particular

system for the stresses of interest. It would be helpful to obtain measurements of all these factors, but this would, of course, be impractical. Using the techniques mentioned above, it would be possible to predict which parameters and variables should be measured during a particular stress to ascertain overall system response. Alternatively, if previous space flight experience indicates that weightlessness is more likely to affect certain parameters than others, it would be possible to predict the measurement accuracy of the variables which are most sensitive to these changes.

It should be emphasized that it is neither feasible nor desirable to investigate a single major physiological system without regard to concomitant efforts in other systems. An important part of the present contractual effort has been the design and implementation of a simulation model in which major physiological subsystems are integrated. The full power of the systems analysis approach has been shown to be effectively utilized only when the influence of all the major subsystems are fully accommodated in a dynamic sense. Thus, techniques such as sensitivity analysis, error analysis, and parameter estimation can more effectively be used to identify critical parameters and indices of system performance when they are applied to integrated models such as the whole-body algorithm.

Evaluating Crew Health Status with the Aid of Simulation Models

While the discussion in Section 2.0 pointed out many difficulties in arriving at an objective definition of crew health status, it would be a desirable goal of the space medicine program to assign some type of a quantitative "fitness rating" to every crew member throughout the pre-, in- and post-flight period. It is recognized, however, that fitness and health will invariably have a subjective component determined by the degree to which the systems which comprise total body function

are not understood. However, even subjective feelings can be quantitized in some manner. In addition, fitness is quite dependent on the desired performance. Thus, fitness for athletes is not the same as that for more sedentary people. Nevertheless, the techniques that determine fitness might be the same for both populations--only the standards would be different. Inasmuch as most simulation models require known quantities as input forcing functions or system parameters and describe quantitative behavior of predicted output variables, it would appear that a tangible, unambiguous definition of fitness would be an essential requirement for the efficient utilization of simulation models in predicting crew health status. Other models--stochastic and statistical models--are capable of dealing with probabilities, and in the final analysis health or fitness may more realistically be defined in this manner.

The practitioners of predictive medicine are placing increasing use on the ability of "stress tests" to identify abnormal or deteriorating body components that would otherwise remain undetected until more overt symptoms developed. Tests such as tilt-table intolerance, LBNP, exercise, glucose tolerance tests are examples of physiological stress tests. Investigators in the fields of human behavior and performance have also devised such methods. Some combination of stress tests would be an excellent starting point for evaluating fitness at any moment in time as well as predicting the probability of future performance. In terms of systems analysis, these tests have the following virtues: (a) they are amenable to modeling because they often involve identifiable subsystems and mechanisms as well as known and controlled forcing functions and output behavior, (b) the tests are usually highly reproducible, that is the noise level of the response is relatively low, a feature also of the simulation model, (c) they are capable of steady state as well as dynamic modes of

operation, a feature which takes full advantage of the dynamic capabilities of simulation models, and (d) a model that is capable of accurately simulating a particular stress is capable of being used as a research tool to help improve the design of the test, identify the sensitive parameters, specify the accuracy required for the measuring instruments, and utilize non-invasive measurements to predict values of difficult to measure invasive parameters. These abilities and model features exist at the present time as attested to by the accomplishments of the present research effort in simulating LBNP, tilt, exercise, hypoxia, hypercapnia, and thermal stresses. The ability to simulate other stresses using these and other models can be readily achieved.

There is a strong analogy between defining fitness in man and in determining a performance criterion in mathematical models. A previous report prepared under this contract has described the usefulness of sensitivity analysis in assigning relative importance to parameters in terms of their effects on a performance criterion[10]. A performance criterion is a measure of overall system performance and is usually defined as some combination of predicted variables (e. g., the performance criteria of a model designed to simulate the glucose tolerance test might be defined as the value of plasma glucose concentration at a certain instant in time). However, just as in the case of defining health it is not always easy to decide on a measure of system performance in a model of a real system. The choice of performance criterion cannot be decided by systems analysis alone but must be determined by understanding and weighing all the objectives of the program at hand. It should now be evident that a quantitative index of fitness based on physiological measurements may be translated directly into a performance criterion in a model of a physiological system in which these same measurements may be simulated. Once

this index can be established or even hypothesized, it would be feasible and desirable to utilize simulation models to help evaluate alternate hypotheses to forecast the relative value of measuring various crucial physiological parameters, to predict the accuracy required in measuring these parameters, and to design experiments which will establish the plausibility of the original hypothesis.

An example may help clarify this concept. Consider the tilt-table stress experiment. There is, at present, considerable uncertainty as to which variable provides the best measure of postural tolerance. Some investigators believe a rising heart rate to be the preferable index but others favor a declining systolic pressure or a combination of heart rate and blood pressure[11]. In addition to these easily measured variables, there are known to be various parameters that have a great effect on the tilt-table response, including vascular compliance, total blood volume and baroreceptor sensitivity. The pulsatile cardiovascular model developed under this contract has been shown to be capable of accurately simulating the tilt-table stress. It is possible therefore to hypothesize various indices of postural tolerance based not only on heart rate and blood pressure, but other variables such as stroke volume, carotid pressure, peripheral resistance, etc., which the model can simulate. It is also possible to quantitatively determine the sensitivity of each of these candidate indices to changes in compliance, blood volume, baroreceptor gain, or other identifiable critical parameters, by performing a sequence of simulations. This procedure --an example of sensitivity analysis--might very well suggest a much more sensitive index of postural tolerance than heretofore exists or might suggest that different indices be used under different conditions. Similar experiments could be performed in man to verify these results.

A model is usually formulated to simulate an average response to a particular stress.. However, it is possible to "customize" a model

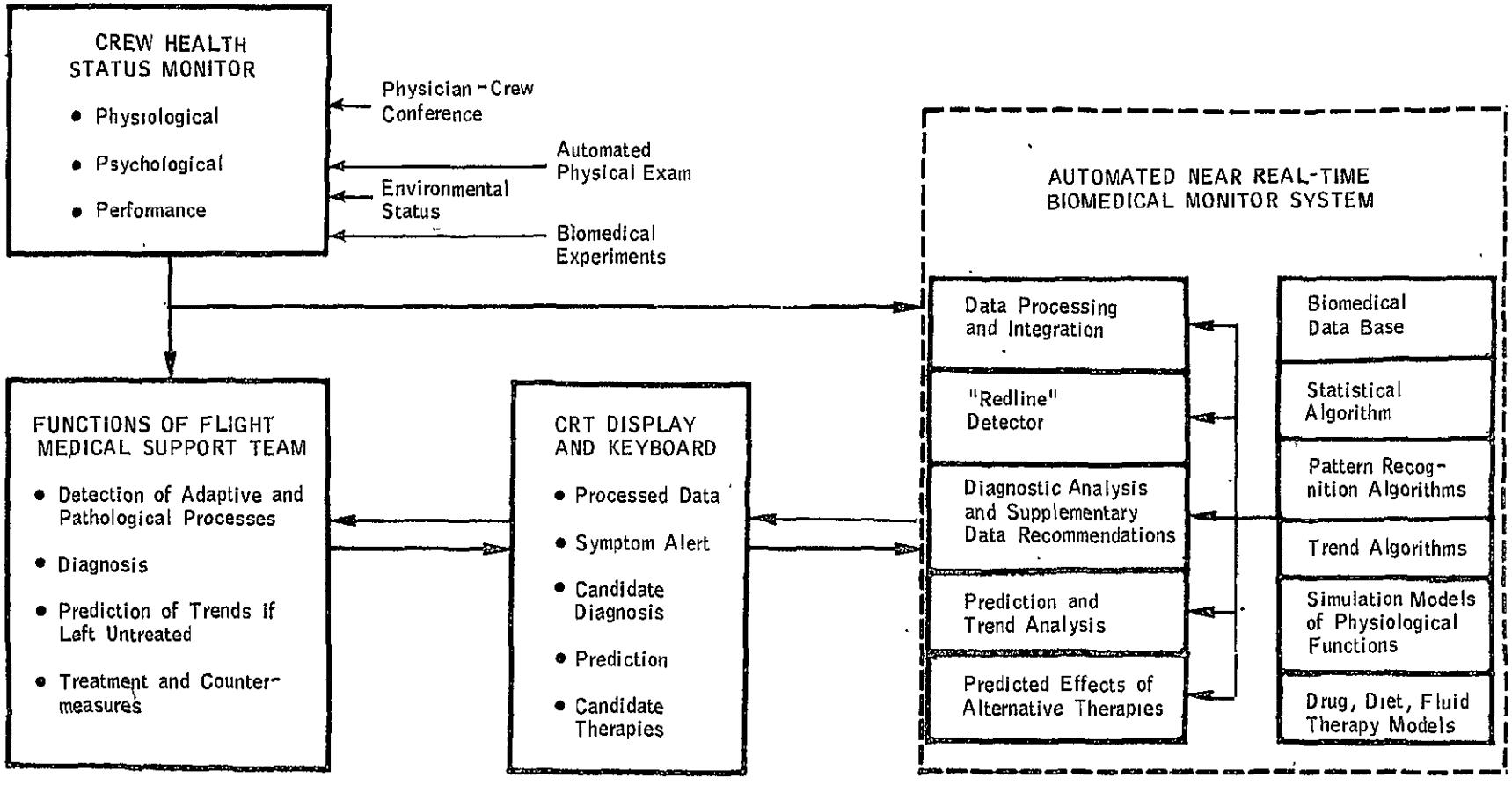
to an individual. This can be done by using measured values obtained from an individual for corresponding parameter values in the model or by using parameter estimation techniques to determine model parameters that are difficult to measure. Since models are themselves gross approximations of real systems, this procedure will not insure that the model is tailored precisely to a particular individual but, nevertheless, there are real advantages to using this technique. A model which is capable of reproducing a crewman's preflight response to a given stress test can detect changes in the inflight response pattern with greater fidelity than if the model was "tuned" for merely an average response. Another example of the usefulness of this technique is to allow the model to predict measurements which would ordinarily be performed with invasive methods. This is possible by using parameter estimation techniques which permits the model to correctly simulate those response variables which are easy to measure non-invasively. The ability of models to predict difficult to measure responses coupled with the ability to evaluate certain indices of fitness may suggest improved tests and criterion for selecting space flight crews. This is a relatively new area of physiological system model applications.

An Automated Biomedical System for Monitoring Crew Health Status

The biomedical monitoring programs of NASA have been designed to support two broad objectives. First, the development of a real-time system of data analysis and decision making to assure the greatest possible crew safety and mission success. Secondly, the acquisition of information about man's abilities, limitations, and characteristic reactions to weightless space flight which is necessary before future missions of longer durations can be planned and controlled. The medical experiments of the Skylab mission were primarily in the

second category but they also served to provide invaluable help to mission control in supplementing ground-based medical monitoring information. Pre- and post-flight measurements have also been required to detect and rectify any potential medical problems developing in the immediate pre-flight period, to identify and assess any residual changes in the physiological status of the crew as a result of space flight, and to establish baselines for interpreting inflight and reentry changes. It is expected that similar monitoring procedures will continue in future flights including pre- and post-flight measurements, inflight physical examinations, responses to experimental stress tests, astronaut self-assessments, and reporting of subjective and objective information. However, the task of acquiring, assembling and integrating this information as well as responding to any abnormal changes in crew health status will presumably take on much larger proportions in future flights as the mission duration and number of flights increase and as the likelihood of remedial action increases with a broader cross-section of space travelers.

Future requirements for medical monitoring will most likely include an increased emphasis on remote health care as well as development of on-board biomedical measuring equipment. While ultimate decisions will and should remain in the province of flight surgeons and their medical support teams, thoughtful consideration should be given to the advantageous role that could be provided by an automated biomedical analysis system[3]. A concept of such a system and the part it could play in monitoring and predicting crew health status is illustrated in Figure 7. Two ideas are expressed in this diagram. First, monitoring is not shown as an end in itself but rather the beginning of an entire health care process which includes the detection and diagnosis of patho-physiological conditions, prediction of the course of the abnormality if left untreated



CONCEPT FOR AUTOMATED BIOMEDICAL NEAR REAL-TIME MONITOR

FIGURE 7

and the application of necessary therapeutic countermeasures. Secondly, a candidate approach is suggested whereby sophisticated techniques can aid in each step of the health care process--from intergrating and analyzing raw data which indicates current crew health status--to using faster than real-time simulation models to predict the effectiveness of proposed therapeutic measures.

It is beyond the scope of this report to attempt to detail diagnostic and possible remedial treatment for the flight surgeon. Rather, the intent is to propose analytical and automated approaches to provide the medical support team with the information they can use in the shortest possible time. While most of the software systems shown in Figure 7 have not been developed sufficiently for immediate application to the space flight program, many are available in a form ready for serious development either as a result of work performed in the present contract, already in use in the NASA/JSC MEDICS system[12], or from the outside scientific community.

The biomedical data base would include individual crewmembers' medical history, pre-, post-, and in-flight data from previous flights as well as norms for many physiological parameters obtained from the general population. This data base would be updated using results from the post-flight analysis of every mission flown.

Data integration systems might consist of readily available reduction schemes for preprocessing raw unfiltered data and statistical algorithms for computing means, variances, auto-correlation coefficients and trend determinations. In addition, it is feasible to integrate data which has not been measured directly but instead has been derived from other data using mathematical models. For example, it should be possible to use present models to estimate evaporative water losses as a function of known metabolic rates and environmental

conditions or to predict blood volume on the basis of daily fluid-electrolyte input/output measurements.

It is also within the current state of computer arts to apply pattern recognition techniques to this processed data and to establish their relationship to accepted baselines. Deviations of some significant parameter (or combination of parameters) beyond these redline limits will signify onset of an abnormal condition. More research is necessary to establish these critical indices.

The diagnostic analysis function is one of the most significant parts of the automated biomedical system shown. Many techniques for deriving a diagnosis from combinations of symptoms or physiological measures have been investigated[13]. One of these--a Computer Assisted Differential Diagnosis program--has been initiated as a pilot program by GE. Since the final diagnosis in all cases must be made by the physician, the computer serves only as an initial screener of possible diagnoses. In this application, when an off-nominal physiological measure has been detected, the computer will interrogate simultaneously recorded environmental variables and crew control variables to establish whether the redline measurement is due to an external factor or is part of a general physiological or pathophysiological syndrome. When a set of possible responsible factors is identified and displayed, the pre-programmed algorithms will be capable of recommending specific supplementary tests to narrow down this candidate set. The use of simulation models in diagnostic analysis under certain conditions may also provide valuable information to the flight surgeon. A well understood pathological process can be modeled in the same manner as modeling normal physiological processes. The validated model could establish a "normal" response to candidate disease states under a particular environmental or metabolic stress

situation and the individual's response compared to it to establish a candidate diagnosis.

The purpose of the prediction and trend analysis function is to predict the future status of the flight crew on the basis of past and present analytic data assuming no remedial action is taken. This operation is perhaps the least developed of all those considered, but has the most potential reward since predictive data analysis can provide quantitative information on the urgency and type of remedial action. Prediction analysis will most likely lean heavily on the use of mathematical models (either deterministic, stochastic, or statistical models) based on accumulated and analyzed biomedical data. Models are presently available to predict certain physiological, psychological, and performance responses although models of the latter two categories are in need of much more development particularly since they are dealing with noisy systems which are not well understood.

Physiological models have been developed, validated, and utilized for a variety of purposes in the present study and their usefulness in space flight medical monitoring has already been discussed. Nevertheless, their major application to date has been devoted more to normal experimental physiological stresses and response predictions rather than to pathological situations. Simulation of physiological stress would certainly be useful (and feasible, as this study has shown) in research programs aimed at clarifying man's adaptation to weightlessness and to predict responses to metabolic and environmental stresses during space missions. Much more development is needed, however, in utilizing these same models of major physiological subsystems to the study of disease. Models are capable of predicting, better than human intuition, the response to multiple stresses; this includes combinations of normal adaptive stresses superimposed on pathological changes. For example, presently developed models are capable of predicting the effect that cardiovascular adaptations to

weightlessness might have on the susceptibility or the severity of such problems as heat disorders, hypoxia, and hypovolemic shock. Crucial to the successful predictive mode of model operation is the completeness of experimental and case-study data that is used to derive the initial model structure and parameter values and the ability of the model to accurately simulate the response of the real system to a given stress (or stresses) under controlled conditions.

The therapeutic function of an automated biomedical system would also lean heavily on simulation models as well as pattern recognition algorithms and Monte Carlo gaming techniques. This function consists of a search for remedial or corrective action alternatives with probabilities of success attached to each action. If suitable models were available, these candidate countermeasures could be evaluated on the model before administering to the individual. Some success has already been achieved in this area. Some notable examples include: predicting drug effects and proposing drug dosage regimens, predicting the corrective action of fluid therapy, and optimizing hemodialysis rates for patients with impaired renal function. Existing models can be applied directly to such relevant problems as the evaluation of diet and hormonal administration therapy to counteract calcium loss and musculoskeletal deterioration.

The use of models for either diagnosis or prediction of disease trends and therapeutic measures may become important in space because the classic symptoms from which diseases are normally diagnosed on earth may be significantly altered by the zero-g environment. A model which is capable of responding to a given disease state in a 1-g simulation and which has been verified as an accurate simulator of the space flight environment may be a powerful tool for translating these classic terrestrial responses into "classic" space

flight environment responses. Normal earthbound treatment procedures may be inadequate or inaccurate when applied to the spacebound patient. For example, distribution of drugs within the body may be different in weightlessness than on earth due to different fluid volumes and fluid distributions. In this situation, models would be able to help evaluate the effectiveness of drugs as well as the method of administration. Countermeasures for weightless deconditioning, such as exercise, LBNP, occlusive cuffs or garments, and centrifugation can also be evaluated with models and optimum treatment protocols can be suggested. This may be an area of fruitful study.

The biomedical system for monitoring and maintaining crew health described above should be viewed merely as a very broad concept. Details of the approach must be worked out in conjunction with mission planners, space flight medical support teams, biomedical investigators, and biomedical engineers. Except for certain obvious cases, no mention has been given as to which operations will be performed on-board or by the ground-crews. The scheme presented in Figure 7 does not do justice to the interactive man-machine mode of operation that is necessary and desirable at each step in the process. It is certainly not envisioned as an entirely automatic procedure but rather as an important aid to medical teams on the ground or to on-board physicians who will be far from their laboratories and reference materials. An important feature is its modular concept. No automated operation or function is dependent upon another, although interaction between functions can certainly exist if desired. Since much research and development is needed for some of these operations, those that are in more advanced stages of readiness such as data integration and analysis functions, can be included for earlier missions with others added at later dates. The planned Shuttle flights would provide an excellent testing ground for parts of this system to prove feasibility and provide confidence in its utility and operation.

4.0 SUMMARY

This report began with the recognition that central to the question of how crew health status should be monitored is the problem, still not fully resolved, of how crew health should be defined. It was suggested that automated, analytical techniques can be used quite advantageously to aid medical support teams provided an objective definition of crew health can be established. Recommendations were presented for characterizing crew health in terms of: (a) whole body function including physiological, psychological and performance factors, (b) a combination of critical performance indices which consist of multiple factors of measurable parameters, (c) specific responses to low noise level stress tests, and (d) probabilities of future performance based on present and periodic examination of past performance. The biggest scientific challenge of preventive space medicine was suggested to be the ability to detect the onset of patho-physiological disorders before the appearance of overt symptoms and debilitating function. Related to this is the technical challenge of developing flight ready instrumentation to monitor whole body and organ function and automated, analytical methods to process, integrate, and display these measurements.

A concept was proposed for a computerized real-time biomedical monitoring and health care system that would have the capability to: (a) automatically integrate space flight health monitoring data, (b) detect acute or chronic off-nominal conditions, (c) predict future health status assuming no remedial action is taken, and (d) search for alternative therapies with prediction of possible consequences and probabilities of success attached to each countermeasure. This capability would be provided by a computer software system consisting of an extensive biomedical data base and programs for data processing, pattern recognition, Monte Carlo searches, and statistical and trend

analysis. In addition, the utilization of mathematical simulation models of major physiological systems was suggested to have much potential in this biomedical monitoring process. Models were described to be most suitable as biomedical research tools for such uses as: (a) establishing indices most sensitive to particular changes in body function, (b) establishing acceptable tolerance limits for monitoring instruments, and (c) helping to distinguish between normal adaptive changes as a result of weightlessness and pathological conditions that might be modified by the space environment. Furthermore, a capability exists, still to be explored in depth, for operating simulation models in a near real-time predictive mode for such purposes as: (a) predicting difficult to measure parameters from non-invasive measurements, (b) predicting trends for pathological conditions, and (c) prediction of effects of alternative therapies for pathological states as well as countermeasures for normal adaptive states. The program of which this study is a part has demonstrated that techniques such as sensitivity analysis, error analysis, and parameter estimation can be used to identify critical parameters and indices of system performance when applied to integrated subsystem model simulations of environmental and metabolic stresses.

Consideration was given to a Shuttle medical monitoring system in the light of past and present crew health monitoring capabilities and resulted in the following conclusions: (a) much of the data processing previously performed manually could be computerized using existing software; this would provide the flight surgeon with integrated data as rapidly as possible, (b) more development should be devoted to compressed data displays using mass storage and color CRT devices so that off-nominal conditions may be quickly evaluated, and (c) the number of monitored parameters proposed for Shuttle missions may not be adequate to detect the onset of pathological conditions until

overt symptoms have developed. The next generation of Shuttle missions are visualized as unusual practical opportunities to: (a) provide information essential for decisions on what constitute significant physiological deviations, (b) identify potential problems in a reasonably large population exposed to the space environment, (c) develop the optimal techniques for acquiring the maximum amount of useful biological information from each crewman, (d) test monitoring devices to be carried on long-duration missions, and (e) develop and evaluate an automated real-time biomedical monitoring-data analysis system.

5.0 RECOMMENDATIONS

As a result of this study, the following specific recommendations are made:

(a) Utilize the research capabilities of simulation models and other analytical tools to develop sensitive indices of health especially in the area of stress testing. This would lead to more objective definitions of crew health, provide impetus to develop sophisticated instrumentation, and provide a sound basis for determining the critical parameters needed in a total biomedical monitoring system.

(b) Proceed with adapting existing data processing software to the problem of integrating and displaying biomedical data in near real-time model for the purpose of monitoring crew health and function. This includes the use of data base management systems, statistical analysis, pattern recognition algorithms and mathematical models.

(c) Develop a more complete real-time biomedical monitoring system to aid the flight medical support team which will include the functions of: detection of off-nominal conditions, diagnostic screening, prediction of physiological and pathological trends, and evaluation of proposed therapeutic countermeasures.

(d) Develop the use of mathematical simulation models for real-time predictive modes of operation. This would include predicting: important, difficult to measure parameters such as blood volume, cardiac output, baroreceptor sensitivity, etc.; effects of therapy measures such as drug dosages and fluid therapy; and the onset and development of pathological states.

(e) Extend the range of simulation capability to include: models of such systems as calcium regulation, vestibular function and biochemical/metabolic function; models of behavior and performance, and discrete and stochastic models.

(f) Continue biomedical research (especially with animals) in the weightless environment to distinguish between normal adaptive mechanisms and pathological conditions, and to determine if pathology is modified or aggravated by weightlessness.

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APPENDIX

APPENDIX

SELECTED BIBLIOGRAPHY OF SIMULATION MODELS

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