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SUBJECT: Study Report
A Prioritized Set of Physiological Measurements
for Future Spaceflight Experiments

This report identifies a set of desired experimental measurements to be obtained in future spaceflights in four areas of physiological investigation. The basis for identifying the measurements was the physiological systems analysis performed on Skylab data and related ground-based studies.

An approach for prioritizing the measurement list is identified and discussed with the use of examples.

Finally, a prioritized measurement list is presented for each of the following areas: Cardiopulmonary, Fluid-Renal- and Electrolyte, Hematology and Immunology, and Musculoskeletal. Also included is a list of interacting stresses and other factors present in spaceflight experiments whose effects may need to be quantified.

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Attachment
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PHYSIOLOGICAL MEASUREMENTS LIST

The list of measurements described in this report is intended to identify, in the view of the author, both the measurements which should be made in the upcoming Shuttle Human Spaceflight experiments and the relative importance of each measurement expressed as a category or priority.

The basis for selecting these measurements is the knowledge and experience gained in the integrated analysis and interpretation of Skylab data and related ground-based studies.

The assignment of priorities to physiological measurements on this list, even within a discipline subdivision, requires clear identification of the program objectives. These program objectives could include:

1. Further the basic understanding of the mechanisms involved in physiological adaptation to the spaceflight environment.
2. Development of specific countermeasures to reduce objectionable physiological effects of spaceflight (with frequent short term flights and extended duration missions).
3. To provide a basis of health care monitoring in space. This includes predictive capability for normal physiological changes for a relatively diverse population of exposed persons and interactions with additional environmental stresses, metabolic stresses, or disease states.

Although these program objectives have not been completely defined, as yet, it is apparent that both the second and third objectives listed are somewhat dependent on the first objective listed. Therefore the approach taken to prioritizing the measurements was to consider only the contribution to an enhanced understanding of spaceflight induced physiological changes. This approach will hopefully reflect the appraised value of the measurement to testing current hypotheses.

Organization

Physiological research during the Shuttle Program will be organized into investigative areas according to the major physiological systems

involved. The investigative areas and the major spaceflight effects considered are given in Table I. The same subsystem breakdown will be used in the development of this list.

The priority assigned to a particular measurement will, insofar as possible, be a function of its role in an integrated hypothesis which describes the total process of adaptation. The more central the effect, the more value assigned to it. As an example, the headward migration of blood from the legs into the thoracic cavity is an acute effect of zero-g exposure that has short term and long term consequences in the cardiovascular, fluid electrolyte control and hematological systems and suspected interactions with the pulmonary, musculoskeletal, and other physiological subsystems. Therefore, temporal characterization of the volume shifts, and associated pressures and flows will have considerable value as a primary stimulus for producing a wide range of the observed effects of spaceflight.

From these considerations, a set of categories can be defined to prioritize the suggested measurements in each investigative area. The categories are defined in Table II. As can be seen in the list, these categories do not necessarily dictate the overall priority of the measurement since the overriding considerations may be of a more subjective nature. The categories do, however, remain a descriptor of the perceived application of the measurement.

Modifying Factors

Once program objectives are defined in detail, the priorities for the suggested measurements could be modified accordingly. The development of countermeasures as a program objective would require identifying the most likely adaptive mechanisms involved, the degree of counteracting stimulus required, and the most effective means of providing the stimulus for the least resources (time, weight, power, dollar, subjective discomfort). For example, the rational development of exercise countermeasures would require differentiating the contributions of hypovolemia, decreased function of exercising, muscle fatigue, and additional spaceflight-induced biochemical changes on postflight exercise capacity. The ability to counteract the induced changes would be assessed, in this case by providing rapid rehydration or infusion of plasma, constituents, maintaining muscle function with

TABLE I

MAJOR EFFECTS OF SPACEFLIGHT OBSERVED TO DATE

Fluid, Electrolyte, and Hormonal

- Decrease in weight inflight
- Decrease in TBW (pre-post)
- Decrease in plasma volume (pre-post)
- Decrease in total body sodium (pre-post)
- Decrease in total body potassium (pre-post)
- No measured Henry-Gauer diuresis
- Increase in aldosterone excretion
- Decrease leg volume
- Increased upper body volume including puffy faces, nasal congestion
- Decreased plasma osmolality
- Increased cortisol excretion
- Decreased excretion of epinephrine and norepinephrine

Cardiovascular

- Decreased orthostatic tolerance (inflight, LBNP, postflight)
- Decreased exercise capacity (postflight)
- Decreased exercising cardiac output (postflight)
- Decreased effective circulating blood volume (postflight)
- Increased heart rate inflight

Musculoskeletal

- Decrease in bone mineral content (os calcis) related to mission duration
- Negative balance of calcium, phosphorus, and introgen inflight
- Muscular imbalance occasioned by functional disuse atrophy of anti-gravity muscles
- Decrease in lean body mass
- Negative energy balance first week inflight

Hematology and Immunology

- Decreased red cell mass not related to mission duration
- No evidence for increased destruction
- Apparent suppression of red cell production
- Decreased immunological function during and postflight
- Increased inflight hemaglobin concentration.

TABLE II

DEFINITION OF CATEGORIES

Category 1 - Critical to verify existing hypotheses involving more than one major effect of spaceflight (Table I).

Category 2 - Critical to a specific hypothesis involving a single major effect of spaceflight.

Category 3 - Confirmatory, amplifying or supporting, measurements related to one or more existing hypotheses.

Category 4 - Desirable to confirm or explain minor (not in Table I and not in mainstream of adaptive process) effects of spaceflight.

Category 5 - Desired to investigate suspected additional spaceflight effects.

specific inflight exercises, assuring adequate rest before the landing. The quantitative aspects of the therapy would be based on the amount of fluids lost in the first case and perhaps the amount of rest required in the last case. The therapeutic use of inflight exercise, however, would have at least the following parameters: 1) preflight level of subject conditioning to perform the exercise (aerobic capacity, perhaps), 2) muscle groups involved, 3) type of exercise indicated (viz, isokinetic, isotonic, isometric), 4) intensity and duration (may be a function of all the above factors). As can be readily seen, the number of potential experiments which could be performed to optimize countermeasures for maintaining exercise capacity is conceivably very large. As a program objective, this would require assignment of priorities to the measurements which will assess the functions and optimize the parameters discussed above.

An additional consideration in designing countermeasures and one which may be of particular concern in the development of physiological baselines for monitoring crew health (program objective #3) will be the sources of individual variation. The population of persons who will fly in the Shuttle program is much more diverse than the astronauts population of the previous programs in terms of age, sex, physical conditioning, and many other parameters affecting health status. These factors present an additional dimension in the requirements for experimental data collection. The priority for an experiment to quantitate these factors can be determined only by a clear program objective and possibly screening by using appropriate ground-based analogs.

Limitations

The greatest single limitation imposed upon this measurement list is the assumption that the only objective is one of advancing our basic understanding of the adaptive process. A great many other factors in the selection of experiments have been ignored. Some of the factors which affect the scientific desirability of investigations or which will play a role in the selection of experiments include:

1. Directness of measurement techniques
2. Experiment controls

FLUID, ELECTROLYTE, RENAL

Category	Measurement	Desired Timing, days after launch			
		0-1	1-5	>5	Recov.
(1)	Central Venous Pressure	X	X	X	X
(1)	Thoracic Blood Volume	X	X	X	X
(4)	Leg Volume, total	X		X	X
(1)	Vascular	X		X	X
(1)	Extravascular	X		X	X
(1)	Diuresis (well hydrated)	X			
(2)	Plasma ADH	X	X	X	X
(2)	H_2O Intake	X			X
(3)	Free Water Clearance	X	X	X	X
(3)	Renal Plasma Flow	X		X	X
(3)	GFR	X	X	X	X
(2)	Natriuretic Factor	X	X	X	X
(2)	Aldosterone Secretion	X	X	X	X
(4)	Evaporative Water Loss	X	X	X	X
(3,4)	K^+ - Nitrogen Relation	X	X	X	X
(3,4)	pH Plasma, Urinary	X	X	X	X
(4)	Na^+/Ca^{++} Urinary Factors	X		X	X
(3,4)	Intracellular Na^+, K^+, H^+	X	X	X	X
(4)	Cortisol Effects on K^+ Excretion	X	X	X	X
(4)	Total Body Water	X		X	X

3. Concomitant measurements with interpretive value
4. Probability of obtaining statistical significant results
5. Interference between experiments

The proposed list also ignores engineering and operational feasibility and resource requirements.

Much has been said and could be said about each element of the list presented, however, it should be pointed out that some desired measurements could be implied or inferred from other measurements, either with the addition of assumptions or a formal mathematical model of the physiological system. For example, in the acute phase of adaptation following launch, plasma volumes may be inferred from hematocrit data by assuming red cell volume does not change during this interval.

CARDIOPULMONARY

Category	Measurement	Desired Timing, days after launch			
		0-1 hr	1-5 days	>5 days	Post
(1)	Central Blood Pressure	X	X	X	
(1)	Total Blood Volume	X	X	X	X
(1)	Total Leg Volume	X	X	X	X
(1)	Leg Blood Volume	X	X	X	
(3)	Leg Blood Flow	X	X	X	X
(1)	Thoracic Blood Volume	X	X	X	
(1)	Renal Blood Flow	X	X	X	
(1)	Cardiac Output	X	X	X	X
	TPR	X	X	X	
	SV	X	X	X	
(2)	High Pressure Baroreceptor Activity	X			X
(3,4)	Venous Compliance	X	X	X	
(3)	Circadian Variability Plasma Vol.	X	X	X	
(5)	Blood Gas and pH	X	X	X	X
(2)	p^{50} Shifts on Oxyhemoglobin Sat.				X
(5)	Pre/Post Capillary Resistance in Various Tissue	X		X	
(3)	Plasma Proteins Conc.	X	X	X	X
(3)	Humoral Control Factors				
	Circulating catecholamines,	X		X	X
	renin/angio	X		X	X
(4)	Vital Capacity	X	X	X	X
(4)	Exercising RER	X	X	X	X
(1)	24-hour Metabolic Rate			X	
(3,4)	Basal Metabolic Rate			X	X
(5)	Direct Cardiac Function			X	X
(5)	Ventilation/Perfusion Ratio		X	X	X
(3,4)	MAX O_2 Uptake	X		X	X

MUSCULOSKELETAL

Category	Measurement	Desired Timing, days after launch			
		0-1	1-5 days	>5	Recov.
(1)	Skeletal Ca^{++} Losses				X
(1)	Distribution of Bone Mineral Loss				X
(3)	Ca^{++} plasma, urine	X	X	X	X
(3)	Urinary Hydroxyproline	X	X	X	X
(2)	Calcitonin	X	X	X	X
(2)	Vitamin D_3 (metabolites)	X	X	X	X
(2)	PTH plasma	X	X	X	X
(3)	PO_4 Excretion	X	X	X	X
(1)	Loss in Muscle Mass				X
(1)	Distribution of Muscle Mass Losses				X
(3,4)	Type of Muscle Fiber Lost				X
(3)	Energy Balance	X		X	X
(1)	24-hr. Energy Utilization	X	X	X	X
(3,5)	BMR, Thyroxine	X		X	X
(3)	Nitrogen-K^+ Excretion	X	X	X	X
(2)	Deformation Forces in Bone	X		X	X
(5)	GIT Transit Time	X		X	X
(4)	Absorption of Fat Soluble Vitamins	X		X	X

OTHER FACTORS OF INTEREST

Space Motion Sickness
Therapeutic Drug/Spaceflight Interaction
Acceleration (+gz)
Circadian Shifts (work/rest, sleep cycles)
Ionizing Radiation
Psychological Indices
Toxicity Monitoring
Thermal Anomalies

HEMATOLOGY & IMMUNOLOGY

Category	Measurement	Desired Timing, days after launch			
		0-1	1-5	>5	Recov.
(2)	Erythropoietin	X	X	X	X
(2)	Hematocrit	X		X	X
(2)	Hemoglobin vs. RCM	X		X	X
(1,3)	Renal Blood Flow	X		X	X
(4)	p50 Shift		X		X
(3)	RBC Life Span				X
(3)	Iron Uptake		X	X	X
(5)	Biliruben		X		X
(4)	Species Differences in Experimental Animal Models				
(1)	Mechanism of Immunosuppression				