NASA Technical Memorandum 58280

Results of the Life Sciences DSOs Conducted Aboard the Space Shuttle 1981 - 1986

May 1987

National Aeronautics and Space Administration

Lyndon B. Johnson Space Center
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CONTENTS

Section Four: Microbiology

Section Five: Space Motion Sickness

Section Six: Vision

Appendix A - Matrix Overview of the DSO Program

INTRODUCTION

Since 1983, the Space Biomedical Research Institute (SBRI) at the NASA Johnson Space Center has been conducting a program of investigations into man's physiological adaptation to spaceflight, with an emphasis on delineating detrimental effects and their operational impact. The primary vehicle for inflight research has been the Detailed Supplementary Objective (DSO), which provides a means of gathering crucial inflight data without interfering with primary mission objectives.

Data from the Apollo and Skylab programs pointed to a number of potential problems resulting from adaptation to microgravity. These included but were not limited to space motion sickness (SMS), cardiovascular deconditioning, and difficulty in delivering health care in the remote space environment. It became clear that an understanding of these problems and their operational impacts was essential to the success of the Space Program. While a number of Space Shuttle payloads dedicated to the Life Sciences were planned, a method for obtaining more immediate information was needed. The DSO provided a means of obtaining this information.

At the beginning of the Shuttle Program, the Space Transportation System (STS) Program Office established a procedure for testing and refining Orbiter and subsystem performance capabilities, and for evaluating new hardware and procedures. Procedures involving the Orbiter, its subsystems, and its support equipment were designated Development Test Objectives (DTOs). All other operationally relevant procedures were classified as DSOs. DSOs were by definition "supplementary." They were not to interfere with primary mission objectives but were to demand less on crew time, stowage volume, weight, and power requirements than did other payloads. The DSO seemed adaptable to inflight research into biomedical problems with operational impact.

During the Orbital Flight Test period (STS-1 through 4), postflight debriefings conducted by the Flight Surgeons provided biomedical information. STS-3 marked the first inflight use of a biomedical DSO protocol (fluid loading as a countermeasure to cardiovascular deconditioning - see p. 41). Beginning with STS-5 in 1982, biomedical DSOs involving hardware were manifested and flown on a regular basis. The creation of the SBRI in 1983 formalized the biomedical DSO program, providing direction for a systematic approach to the study of physiological adaptation to space flight. Since that time, biomedical DSOs have been used to study physiological adaptation as well as to test hardware and procedures that are operationally relevant to the Space Shuttle and Space Station programs.

The inclusion of biomedical DSOs on Shuttle missions has helped to fill the gap in biomedical data. Serious decrements in physiological function have been observed in Space Shuttle crewmembers. Some have been debilitated for several days early in the mission with the repeated nausea and vomiting of SMS, others have fainted postflight from the orthostatic intolerance induced by cardiovascular deconditioning, still others might have been unable to perform an emergency egress due to the combined physiological changes which occurred during their adaptation to microgravity. The DSO program has lent insight into understanding each of these problems as well as others. The study of altered distribution of drugs in the human space traveler has begun. Through the DSO program a partial countermeasure to cardiovascular deficiencies has been developed and applied in a successful, practical approach. Additionally, key hardware and procedures have been tested and verified as DSOs prior to use in support of more costly, complex life sciences investigations.

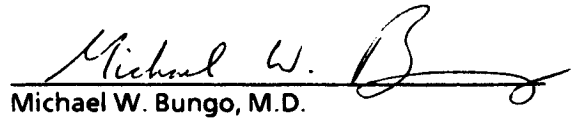
To varying degrees, biomedical DSOs have been a part of each Shuttle flight to date. Particular concentrations of these investigations occurred on Shuttle flights STS-8, STS 51-D, and STS 61-C. Over fifty biomedical DSOs have now been flown. This document presents the most significant scientific results of these investigations. It must be cautioned that in most cases the data are based on very small subject populations, and as a result hard, dogmatic

conclusions cannot be made. Further investigations must be performed to accomplish this goal, and the SBRI will continue in this direction.

As Shuttle flights resume, the future of the SBRI DSO program is not easily assessed; however, the work which has begun in these endeavors is too essential to the health and welfare of astronaut crews and the success of the U.S. space program to be given anything less than critical priority.

This report represents the combined efforts of many individuals. The investigators and their teams of support personnel have spent countless hours designing and developing hardware and procedures; collecting, reducing, and analyzing data; and reporting the results. The editors have tried to present the material in a manner that will concisely summarize their findings without compromising medical confidentiality for the individual subjects involved. It has been a monumental task, and would not have been possible without the help of many people. To all of them, the editors extend their thanks.

This document is a reprint of TM 58280.



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DSO PROGRAM DESCRIPTION

Life Sciences DSOs are managed by the SBRI Flight Projects (FP) office. When an investigator wishes to participate in the DSO program, he/she submits a proposal to the Director of the Institute. The proposal is peer-reviewed for scientific merit, and submitted to the Life Sciences Directorate through the Science Management Review Board (SMRB). The board verifies that it is appropriate to pursue the investigation as a DSO based on its operational relevance. The SMRB then directs the SBRI FP office to obtain the requested number of subjects on Shuttle missions.

The Flight Projects office provides assistance to the investigator in all aspects of preparation for flight, and is essentially a "start to finish" support system. Having received authorization from the SMRB, the FP office helps the investigator assess the hardware requirements for the DSO. The FP Engineering Support personnel work closely with the investigator, manufacturing, modifying, and readying the hardware as needed for flight certification.

All hardware that is to be flown in the Space Shuttle must undergo a strict certification process to assure that it will pose no hazard to the crew or to the vehicle. Since DSOs are not critical to Shuttle mission accomplishment, they are normally classified as "Class D" payloads. As such, they must be certified for safety and compatibility with the Orbiter and its environment by personnel of NASA Safety, Reliability and Quality Assurance organizations. FP Experiment and Engineering Support personnel ensure that all DSO hardware is tested and analyzed for compliance with all applicable requirements, including standards for: Electromagnetic Interference (EMI); Flammability/Odor/Offgassing (Toxicity); and Shock/Acceleration/Crash Safety/Vibration. The hardware is tested as necessary for functional interfaces with the Orbiter and cleaned in adherence to NASA standards for contamination control. FP Experiment Support personnel then prepare a Safety Analysis Report for the hardware, identifying potential hazards which could result from its use and describing measures taken to eliminate or minimize those hazards.

All investigations involving human subjects must be approved by the Human Research Policy and Procedures Committee (HRPPC). Concurrent to hardware certification, FP Experiment Support Personnel assist the investigator in preparing and submitting the required protocol to this committee to secure their evaluation and approval.

Having ascertained a feasible readiness date for the hardware and procedures, FP Experiment Support personnel examine the Shuttle mission schedule to identify flights of appropriate duration with adequate stowage space and crew time to accommodate the DSO. They then prepare a crew information package summarizing the objectives of the DSO, the scheduled pre-, post-, and inflight activities, and the investigator's plans for the data obtained, and send it to the crewmembers of the candidate missions for review. The FP office then arranges a science briefing for each candidate crew, during which the investigator can explain the DSO objectives and methods and answer any questions. These meetings have proven beneficial for all parties involved. By soliciting participation in person, the Investigator is better able to convey the importance of the DSO. The crewmen, in turn, are able to obtain better quality data when they are knowledgeable about the scientific objectives. They are often able to point out relevent factors peculiar to the spacecraft environment that the Investigator may not have considered in preparing the study, and to suggest appropriate changes in the protocol to maximize data return.

The DSO is then presented to the Mission Integration Control Board (MICB) for flight assignment. This board is composed of representatives from the Mission Operations and Payloads communities, and is chaired by Program Office personnel. They are tasked with fitting the various flight objectives together and planning a coherent, workable mission. These objectives are outlined in the Flight Requirements Document (FRD) issued for each flight.

Once the MICB approves a DSO for flight and includes it in the FRD for a given mission, the FP Experiment Support personnel work to see that all the requirements are met. They contact the crew schedulers to reserve time for training and data collection sessions; meet with Flight Activities Office personnel to ensure that the proper procedures are included in the Flight Data File checklists and that DSO activities are scheduled in the Crew Activity Plan, and support mission simulations and crew training to allow astronaut subjects to practice using the DSO hardware in a flight-like setting. The FP office also briefs Mission Control Center Flight Directors and Flight Control personnel so that DSO priorities and activities are understood should real-time rescheduling of crew activities be required during the mission.

Finally, critical hardware reviews and launch and landing activities are supported by FP office personnel as necessary. These services are provided for each DSO. After landing, FP office personnel follow the DSO hardware and data, and can be available for assistance with data reduction and analysis. They obtain the required Postflight reports from the investigators and forward them to the Shuttle Program Office so that DSO progress can be monitored.

Section One
Biochemistry and Pharmacology

A crewman collects a saliva sample as part of a DSO involving study of the action of drugs administered inflight. The noninvasive technique demonstrated here has been successfully employed in support of several DSOs in biochemistry and pharmacology.

COMBINED BLOOD INVESTIGATIONS

Investigators: C. S. Leach-Huntoon, Ph.D., H. Schneider, Ph.D., N. M. Cintron, Ph.D., and R. Landry

INTRODUCTION

A cephalad shift of fluid is thought to be one of the first responses of the human body to microgravity. Losses of body fluid and electrolytes, which have consistently been observed during space flight, may result from the body's attempt to compensate for a perceived increase in blood volume (Gauer and Henry, 1963; Leach, 1981).

It has been proposed that the redistribution of fluids initiates the following immediate responses: reflex peripheral vasodilation, suppression of the renin-angiotensin-aldosterone system, suppression of antidiuretic hormone (ADH), increased secretion of humoral natriuretic substances, and reduced thirst (Leach, 1981). To determine whether these predicted responses occur, it is necessary to measure key parameters that reflect the status of fluid and electrolyte metabolism at specific times after exposure to weightlessness. In addition to angiotensin, aldosterone and ADH, these parameters include cortisol, other hormones such as catecholamines, and the major electrolytes, sodium, potassium, chloride and calcium. Although many of these variables have been measured in blood samples obtained during other space flights, estimation of early changes has not been possible because of inflight scheduling priorities and constraints. Prior to Spacelab 1 and this investigation, the earliest blood draws had been done at 3-4 days inflight on Skylab. The most dramatic changes in the adaptive response to weightlessness are believed to occur in the first hours of a mission. Early sampling would allow determination of the sequence of changes, as well as whether changes are due to a metabolic disturbance or are adaptive. The primary objective of this investigation was to measure these select hormonal and electrolyte components of the blood as early in flight as possible.

Circulating levels of several hormones associated with the physiologic response to stress are increased during space flight (Leach and Rambaut, 1977). Among the key hormones associated with the control and maintenance of normal neuroendocrine processes and which are thought to be indicators of the body's adaptive response to space flight are adreno-corticotrophic hormone (ACTH), cortisol, ADH, and the catecholamines. Although measurements of many of these hormones have been made extensively in ground-based bedrest studies, the only inflight data currently available on the neuroendocrine changes during the initial phases of space flight are from four Spacelab crewmembers.

The primary objective of the neuroendocrine part of this study was to measure the changes in neuroendocrine function evoked early in flight. The lack of such information has precluded reliable evaluation of the initiation of the endocrine and metabolic effects observed in Shuttle crewmembers. Information about integrated neuroendocrine function has significance in formulating the total picture of the crewmen's health status and in delineating the effects of space flight on the individual.

PROCEDURES

The general design of this DSO consisted of blood sample collection at designated time intervals followed by analysis of the specified hormonal/biochemical variables using established analytical procedures. A total of six crewmembers on two missions participated in the study. Blood was collected during preflight and postflight phases of the missions in conjunction with scheduled physical examinations. For the first mission, three preflight samples were collected, and for the second, one sample was collected. Postflight samples were collected as soon as possible after landing (within 2 hours) and on the third day after landing. Samples for the first mission were also collected on the tenth day after landing.

Standard venipuncture techniques were used inflight, with the Inflight Blood Collection System (Fig. 1). Blood samples were drawn into

plain tubes or tubes containing EDTA or heparin as anticoagulants. They were centrifuged in Sarstedt separator tubes and stored frozen until return to the laboratory. Inflight samples were drawn twice during the first mission and three times on the second. The crewmembers on the first were on two different work/rest cycles, and during flight they collected blood samples during the postsleep activity period. This was 6:30 or 7:00 a.m. Houston time for two crewmembers and 5:00 or 6:00 p.m. for the other two. For two crewmembers, mission elapsed time for the first inflight draw (MD2) was 31 hours and for the other two it was 42 hours; mission elapsed times for the second draw (MD6) were 175 and 185 hours. On the second mission, blood was drawn inflight at the end of the work shift, for sample collection times of 35 (MD2), 82 (MD4), and 130 (MD6) hours mission elapsed time.

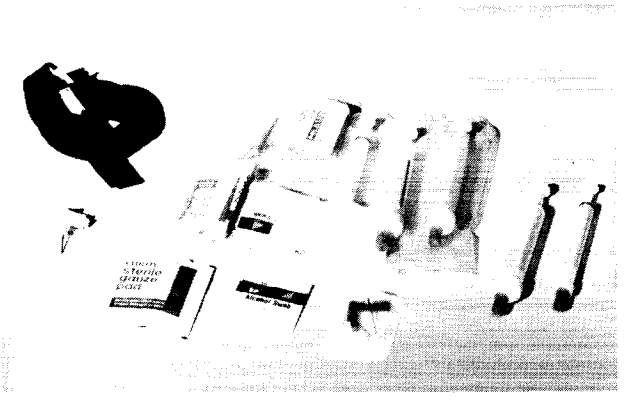

Figure 1. The inflight blood collection system.

Table 1

Two Shuttle Missions

Percent Change from Preflight

	Mission Day													
	MD2		MD4		MD6		MD7		L+0		L+3		L+10	
	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE	Mean	SE
Plasma hormones														
Angiotensin I	-50.0	12.5	70.1	18.1	131.4	18.7	43.5	9.3	201.0	77.7	73.9	26.1	-35.1	20.2
ADH	719*		157.9	77.1	172.3	70.0			9.6	9.6	.5†	4.3		
Aldosterone	-15.0	8.5	-34.5	9.8	-23.9	15.9	-4.3	11.4	37.3	22.4	24.1	11.4	18.9	14.6
ACTH	29.2	16.3	62.0	23.1	108.2	30.7	20.6	2.8	32.6	20.4	.3	6.6	32.8	4.3
Cortisol	41.2	16.9	-55.6	7.1	-43.7	10.1	27.4	15.4	65.4	25.4	21.2	17.5	52.5	3.2
Serum electrolytes														
Na	-1.0	1.0	-2.1	2.1	-.4	1.1	-1.1	.9	-.4	.8	.6	.4	1.6	.2
K	-4.1	6.1	-10.8	8.4	2.6	6.9	8.8	2.7	-4.9	3.4	-3.6	3.3	3.1	2.3
Cl	-1.9	.9	-3.8	1.9	.5	.5	-3.1	.7	-.3	1.4	.6	.3	2.2	.5
Ca	1.9	1.5	-3.2	1.1	-5.8	2.6	-1.0	1.2	-1.0	1.0	-5.2	1.3	-2.8	.7
Mg	-2.9	1.9	-6.9	2.7	-7.2	7.2	-2.3	1.3	-8.3	1.3	-1.3	2.9	-3.4	1.1
CO_2	-6.7	3.7					.05	3.2	-6.6	1.8	-5.3	4.0	-.1	1.9
Creatinine	2.3	2.3					-5.3	3.1	-2.8	2.8	12.6	2.5	9.8	4.1
n	5		2		2		4		6		6		4	

*n = 1
†n = 2

The following variables were measured by standard clinical laboratory methods: angiotensin I (Haber et al., 1969), aldosterone (Ito et al., 1972), ACTH (Vague and Oliver, 1972), cortisol (Foster and Dunn, 1974), sodium (Tietz, 1976), potassium (Tietz, 1976), chloride (Cotlove et al., 1958), calcium (Trudeau and Freier, 1967), magnesium (Trudeau and Freier, 1967), carbon dioxide (Tietz, 1976), creatinine (Owen et al., 1954), and ADH (LaRochelle et al., 1980).

RESULTS

The percent change from preflight to each inflight or postflight time point was calculated for each crewmember, using the preflight mean for the first mission and the single preflight value for the second mission. Means of these percent changes are presented in Table 1 and Figs. 2 and 3. Results for the two flights are combined. Statistical tests were not done because there were so few samples for some time points. Some results were highly consistent.

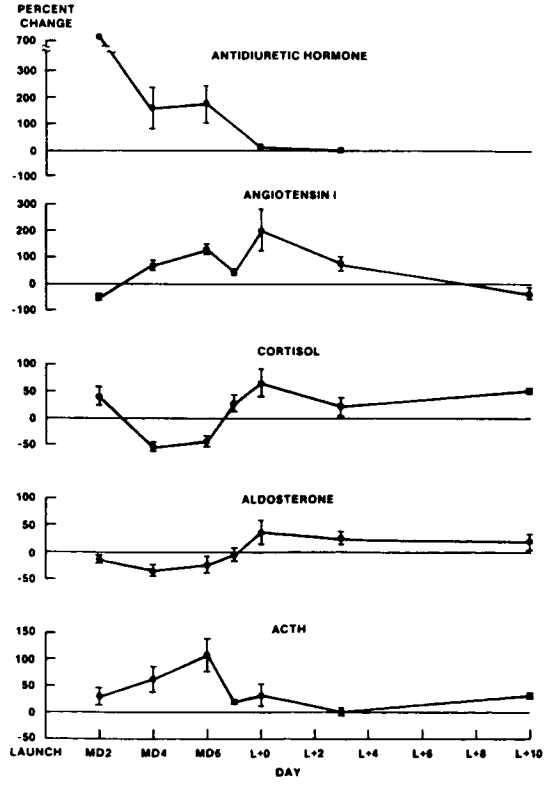

Figure 2. Mean percent change in plasma hormones measured inflight and postflight in crewmembers. Bars represent standard error.

Antidiuretic hormone, which unfortunately could not be measured in some of the samples because not enough sample was available, was increased over preflight levels every time it was measured in blood drawn inflight, but immediately after landing it had returned to preflight levels. Angiotensin I was slightly decreased on MD2 but was increased on MD4 and MD6. Cortisol had an opposite response for those days. Plasma aldosterone was decreased on all inflight days, and ACTH was increased on all inflight days. On landing day, angiotensin I, cortisol, aldosterone and ACTH were at least slightly increased. Levels of these four hormones were lower on day L + 3, but cortisol and ACTH levels had increased again by day L + 10.

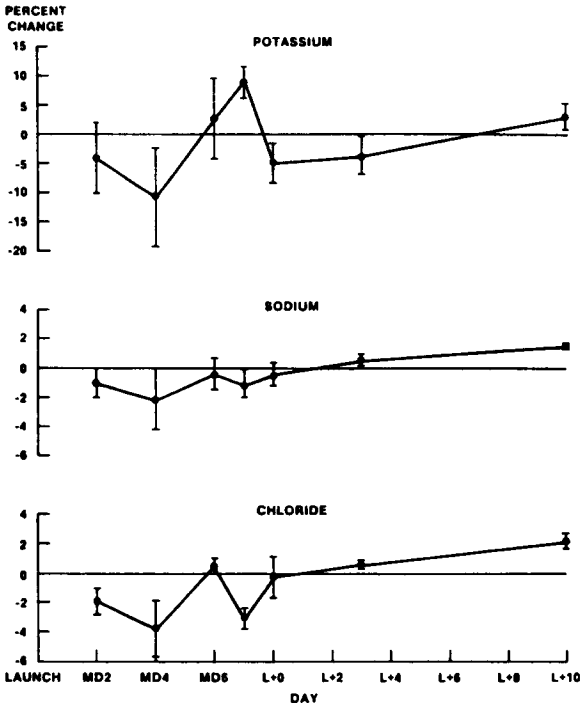

Figure 3. Mean percent change in serum electrolytes measured inflight and postflight in crewmembers. Bars represent standard error.

Serum sodium was decreased throughout the flights. There was variability among crewmembers, so that the decrease may not have been significant on any day. At landing, serum sodium was close to preflight levels. Although serum chloride had a pattern similar

to that of sodium, it appeared to decrease more on days MD2, MD4 and MD7. Serum potassium decreased through day MD4 but increased on MD6 and MD7 and decreased on L + 0. Levels of all three electrolytes measured were higher on day L + 10 than on any other postflight day.

DISCUSSION

Not all of the desired goals were achieved. Although blood was drawn early, 31 hours still may not have been early enough. The high levels of ADH were surprising because ADH had been thought to be suppressed during space flight, but an early transient suppression may have been missed. Apparently it is not effective in preserving blood volume. Secretion of ADH can be stimulated by the emetic reflex (Rowe et al., 1979), and this probably caused the increase in plasma ADH in at least one subject early in the flight. Another unexpected finding was that angiotensin I levels increased while aldosterone was suppressed inflight at the times measured. The increases in most hormones at landing were consistent with Apollo (Leach et al., 1975) and Skylab findings (Leach and Rambaut, 1977). Cortisol secretion appeared to have been stimulated by the high levels of ACTH, which decreased at the same time cortisol increased above preflight levels.

The blood levels of electrolytes in crewmembers of these two missions were consistent with previous results (Leach and Rambaut, 1977). Electrolyte concentrations generally decrease early in flight because of the loss of fluid. The suppression of aldosterone may have contributed to the mild hyponatremia observed during weightlessness, since aldosterone generally stimulates sodium retention. Serum potassium may be increased in space flight, probably because of a breakdown of muscle cells, and usually is excreted in urine samples. The reversal of serum potassium changes from the last mission day to landing was quite rapid, and serum potassium remained low for at least 3 days. Decreased serum potassium on landing day is characteristic of crewmembers who have ingested a physiological saline solution as a countermeasure against orthostatic intolerance, as the subjects in these studies did (Leach and Johnson, 1985).

With respect to hormones associated with the response to stress, the results of these studies were somewhat different from Skylab results. Plasma ACTH increased during flight in the Spacelab crewmembers whereas it decreased in Skylab; plasma cortisol decreased during part of the Spacelab flights, but in Skylab it remained elevated throughout the missions. The reasons for these differences are not immediately obvious, but it appears likely that either the Spacelab crewmembers were not as stressed as the occupants of Skylab or other factors were more important in determining the levels of the hormones measured.

CONCLUSIONS

These results indicate that some of the hypotheses put forward to explain physiologic changes during space flight need to be continually studied. They provide important evidence that some of the other factors recently found to participate in fluid and electrolyte regulation should be measured inflight. Some of these factors are prostaglandin E and the atrial natriuretic factor (Leach, 1981; Leach et al., 1985). The examination of renal clearance factors and of plasma or serum endocrine/electrolyte concentrations early (within hours of weightlessness) will greatly enhance the understanding of man's physical response to space flight.

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INFLIGHT ASSESSMENT OF RENAL STONE RISK FACTORS

Investigator: Nitza M. Cintron, Ph.D.

INTRODUCTION

Nephrolithiasis has been identified as a potential complication of space flight. Despite the limited available data, certain metabolic changes which ensue during space flight suggest an increased risk for the formation of renal stones.

Hypercalciuria, believed to be skeletal in origin, develops soon after space flight begins (1). The progressive rise in urinary calcium reaches a peak in 2 weeks and is sustained at that level thereafter. Urinary phosphate excretion is also increased during space flight, probably by the same mechanism. Both of these imbalances place an individual at an increased risk for stone formation by increasing urinary saturation of stone-forming calcium salts (calcium oxalate and calcium phosphate).

Two other factors which may contribute to stone formation during space flight are potassium deficiency and high urinary uric acid excretion (1,2). The exaggerated renal loss of potassium may reduce renal excretion of citrate, a well recognized inhibitor of the crystallization of calcium salts. To date, no measures of urinary citrate have been made during space flight. Urinary uric acid, on the other hand, may be high due to increased availability of purine substrate (via muscle degradation or high protein diet). The resulting hyperuricosuria may cause a predisposition to uric acid lithiasis or to calcium nephrolithiasis via monosodium urate-induced crystallization of calcium salts. The exaggerated renal loss of sodium may further promote the latter mechanisms. Additional factors which may aggravate the potential for stone formation in astronauts include high animal protein diets, high levels of exercise, and varying degrees of dehydration. Substantive clinical data exists suggesting that excessive consumption of animal protein (high in sulfate and purine) confers a significant risk for nephrolithiasis by increasing urinary calcium and uric acid and by lowering urinary citrate. Recently, preliminary data from Dr. C.Y.C. Pak (UTHSC, Dallas) indicate that strenuous exercise also accentuates this risk by reducing urine volume, causing acidosis, lowering citrate excretion, and increasing uric acid excretion.

The primary objective addressed by this investigation was to evaluate the potential of increased risk for the formation of renal stones as a consequence of space flight. This was to be accomplished by the analysis of 24-hour urine samples for urinary risk factors such as hypercalciuria, hyperuricosuria, hyperoxaluria, and hypocitraturia (3). Where possible, the urinary supersaturation with respect to stone-forming salts was to be estimated.

A secondary goal was to compare the stone-forming potential observed in normal subjects during bedrest to that observed during space flight. This would allow preliminary evaluation of the validity of bedrest as a model of weightlessness with respect to nephrolithiasis.

The limited amount of data obtained to date from a single crewmember (n = 1) precludes the appropriate assessment of the risks for renal stone formation associated with space flight. In this regard, the information presented here must be considered strictly as incomplete and preliminary.

PROCEDURES

STUDY DESIGN

The investigational design was comprised of three phases, the preflight control phase, inflight experimental phase, and postflight recovery phase. The overall protocol was identical for all phases and involved the collection of void-by-void 24-hour urine samples at designated times as summarized in Table 1. Both the pre- and postflight urine collection activities were scheduled in conjunction with

the routine crew physicals. Inflight, the procedure was repeated on a day early inflight and a day late inflight.

TABLE 1. STUDY PLAN AND SCHEDULE

Activity	Duration	Time
Preflight:		
1 Baseline Data Collection	24 hrs.	F-10 physical
Inflight:		
2 Data Collections	24 hrs. each	Early FD Late FD
Postflight:		
1 Data Collection	24 hrs.	L+2 physical

The one subject for this investigation was a male crewmember. Because of mission operations and schedule constraints, the two inflight collections were both obtained relatively early inflight (FD2 and FD4 vs FD2 and FD7) while the postflight collection was not obtained at all. In addition, two 24-hour urine specimens were collected during the preflight phase as opposed to the scheduled single collection.

The void-by-void 24-hour urine collection entailed discarding the first morning specimen on Day 1 and collecting all subsequent voids for 24 hours, including the first specimen on Day 2. Because no provisions for inflight refrigeration are available, all urine samples including pre- and postflight specimens were stored at ambient temperature in the presence of 1% boric acid until time of analysis. Inflight samples were collected using the Urine Collection Devices (UCD) flown on every flight as backup to the Shuttle Waste Collection System (WCS). After specimen collection, the UCD was sealed and placed in a ziplock bag. The time of collection was annotated, and the bag was subsequently discarded into the wet trash and recovered during post-landing activities.

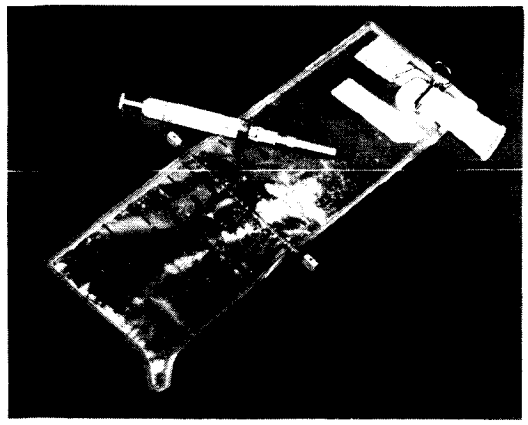

Figure 1. Urine collection device.

URINE BIOCHEMISTRY ANALYSIS

The specific laboratory assays and procedures, methods of analyses, and normal ranges for each parameter of relevance to renal stone potential measured in the 24-hour urine collections are detailed in Table 2.

TABLE 2. 24-HOUR URINE BIOCHEMISTRY

TEST	METHOD	REFERENCE	POPULATION NORMAL RANGE	ASTRONAUT NORMAL RANGE
Volume (ml)	Volumetric	(4)	800-1800 (M) 600-1600 (F)	760-2500 760-2500
Specific Gravity	Refractometry	(5)	1.003-1.030	1.010-1.024
Osmolality (mOsm)	Freezing Point Depression	(6)	500-800	327-900
Na (mEq/vol)	Ion Selective Electrode	(7)	27-287	23-275
K (mEq/vol)	Ion Selective Electrode	(7)	26-123	35-116
Cl (mEq/vol)	Amperometric Titration	(8)	110-250	85-268
Ca (mEq/vol)	Atomic Absorption	(9)	5.0-40.0	4.0-16.9
Mg (mEq/vol)	Atomic Absorption	(9)	5-13	5-13
IPO_4 (mg/vol)	Phosphomolybdate	(10)	300-1000	360-1200
Uric Acid (mg/vol)	Uricase	(11)	250-700	376-1182
Creatinine (mg/vol)	Alkaline Picrate	(12)	1000-2000	700-1900
Oxalate (mg/day)	Ion Chromatography	(13)	30-60	-
Citrate (mg/day)	Ion Chromatography	(14,15)	300-900	-
Sulfate (mg/day)	Ion Chromatography	(16)	0-30	-
pH	Bromothymol Blue	(4)	4.6-8.0	4.6-8.0

M = Male
F = Female

Ground-based control studies were performed to determine the effect of boric acid addition and storage of samples under the conditions anticipated during a mission. The results indicated that borate affects certain variables such as osmolality, creatinine, and pH. Although these parameters were measured, they were not considered for the overall evaluation of results. In addition, due to

scheduling and procedural modifications during urine sample collection and processing in the preflight activities, the baseline control measurements of oxalate and citrate were not obtained. Inflight values were compared to the established values for the general population.

mission phases, each set separated no more than 2 days. When compared to their preflight values, inflight data on a single void basis did not exhibit the development of trends with respect to changes in any parameter. As expected, there was significant variation from

TABLE 3. PREFLIGHT URINARY BIOCHEMISTRY* VOID-BY-VOID SAMPLE ANALYSIS

	Day of Sample	Time	TV ml	Specific Gravity	Osmo** mosm	Na mEq/TV	K mEq/TV	Cl mEq/TV	Ca mEq/TV	Mg mEq/TV	IP04 mg/TV	Uric Acid mg/TV	Creat** mg/TV
Preflight	L-34 Days	8:15 a.m.	41	1.030	1086	4	8	7	0.1	0.3	40	28	132
		11:10 a.m.	70	1.030	1195	9	13	13	0.2	0.6	95	40	197
		1:30 p.m.	51	1.031	1194	4	10	7	0.1	0.4	107	18	166
		6:30 p.m.	138	1.032	1215	25	24	22	0.3	1.4	284	94	364
		10:05 p.m.	57	1.030	1108	12	6	8	0.3	0.5	75	28	108
	L-33 Days	3:45 a.m.	222	1.027	1007	29	10	17	0.8	2.3	384	106	390
		7:00 a.m.	142	1.025	1001	18	11	22	0.5	1.4	142	49	224
	L-31 Days	8:56 a.m.	102	1.023	964	20	5	21	0.8	0.9	54	29	96
		10:24 a.m.	306	1.011	463	17	15	22	0.4	0.7	28	43	101
		12:41 p.m.	235	1.015	578	18	17	20	0.4	1.2	57	46	146
		2:46 p.m.	117	1.026	944	28	10	16	0.5	1.1	110	62	136
		4:37 p.m.	164	1.023	876	37	10	24	0.6	0.8	106	79	139
		6:14 p.m.	175	1.018	728	27	8	20	0.4	0.8	98	55	116
		8:32 p.m.	163	1.019	782	23	7	19	0.4	1.0	108	63	143
		9:23 p.m.	66	1.025	1050	16	2	13	0.6	0.7	52	39	78
		10:08 p.m.	12	1.026	1090	3	1	3	0.1	0.1	6	8	16
	L-30 Days	5:45 a.m.	95	1.026	1041	18	2	16	0.9	1.0	71	55	144

*Urine contains 1% boric acid
**Affected by boric acid addition and storage
L = Launch Date

TABLE 4. URINARY BIOCHEMISTRY* VOID-BY-VOID SAMPLE ANALYSIS

	MET†	Time	TV ml	Specific Gravity	Osmott mosm	Na mEq/TV	K mEq/TV	Cl mEq/TV	Ca mEq/TV	Mg mEq/TV	IP04 mg/TV	Uric Acid mg/TV	Creattt mg/TV
Inflight	**000	20:30	78	1.032	1202	12	7	13	0.1	0.9	11	1	239
	001	0 hr 44 min	326	1.016	476	22	13	27	0.8	2.5	177	129	346
		2 hr 22 min	256	1.011	435	20	8	24	0.6	1.3	54	79	174
		4 hr 22 min	276	1.010	385	22	9	25	0.4	0.9	76	51	127
		7 hr 01 min	303	1.010	380	25	5	25	0.8	1.6	133	60	145
		11 hr 01 min	305	1.015	604	46	10	45	1.4	2.6	206	108	287
		19 hr 11 min	200	1.022	844	29	11	30	0.8	2.1	306	36	364
	002	18 hr 11 min	67	1.025	1005	12	3	11	0.4	0.7	107	11	123
		22 hr 40 min	398	1.020	736	60	16	58	2.3	3.4	337	163	553
	003	0 hr 30 min	250	1.013	500	25	9	24	0.8	1.1	77	76	188
		9 hr 54 min	294	1.021	737	39	10	26	4.5	2.7	409	47	450
		13 hr 29 min	164	1.014	503	25	9	19	0.7	0.9	224	110	227
		17 hr 30 min	343	1.011	400	17	6	13	0.7	1.4	247	94	268

*Each urine collection bag contained 1 gram boric acid
**This void collection after arising at 20:30
†Mission Elapsed Time
††Affected by boric acid addition and storage

RESULTS

The values for urine chemistries determined from single voids collected from one crewmember during preflight and inflight phases of one mission are presented in Tables 3, 4, and 5. As mentioned earlier, two 24-hour collections were made during each of the

sample to sample in all parameters throughout the collection period. The latter is principally a consequence of the diurnal variation of individual parameters and the fluctuations in void volumes as a result of environmental influences.

The results of the urine analyses as standardized to a 24-hour specimen for both preflight and inflight data are summarized in

Table 6. Urine volume did not appear changed in this individual from the preflight control on

TABLE 5. INFLIGHT URINARY BIOCHEMISTRY*
VOID-BY-VOID SAMPLE ANALYSIS

	MET**	TIME	TV ml	CITRATE mg/TV	OXALATE mg/TV
Inflight	000	20:30	78	71.3	3.8
	001	0 hr 44 min	326	176.5	8.4
		2 hr 22 min	256	79.9	6.8
		4 hr 22 min	276	59.4	6.7
		7 hr 01 min	303	67.3	5.5
		11 hr 01 min	305	123.0	6.5
		19 hr 11 min	200	66.8	11.4
	002	18 hr 11 min	67	35.3	2.0
		22 hr 40 min	398	204.5	12.8
	003	0 hr 30 min	250	48.7	5.3
		9 hr 54 min	294	175.4	9.4
		13 hr 29 min	264	117.4	8.0
		17 hr 30 min	343	66.8	7.6

*Each urine collection bag contained 1 gram boric acid
**Mission Elapsed Time

either mission day. A trend to an increased excretion of calcium, phosphate, magnesium and uric acid was present. This is consistent with previous observations made in both space flight (1,2) and bedrest studies (Pak, personal communication). Urinary citrate and oxalate values early inflight were within the normal range of the general population. Observations made in bedrested subjects suggest that the development of hypocitraturia during space flight, if analogous to the ground-based model, would develop during the later adaptive phases of a mission when renal loss of potassium becomes significant. As seen in Table 6, potassium excretion did not appear elevated in the early flight days measured. This observation is tenuous at best in light of the limited data. Meaningful evaluation of all other urine parameters was equally limited due to the low number of data points available on a subject "n" of one in clinical parameters known to exhibit large variations from individual to individual.

Reliable assessment of the potential for urinary calculi during weightlessness will require the further analysis of urinary parameters and variables in a statistically valid population size over a wider range of mission days. The careful measurement of urinary parameters, including oxalate, citrate and saturation levels with respect to stone-forming salts, is warranted for inclusion in this evaluation (3). The importance of identifying pathogenic factors both of environmental and metabolic origin to future manned space flights of long duration are considered significant for proper safeguard implementation and timely institution of remedial measures when necessary.

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TABLE 6. URINARY BIOCHEMISTRY 24-HOUR COLLECTION

Mission Phase	TV ml/24 hr	Specific Gravity	Osmo mosm	Na mEq/24 hr	K mEq/24 hr	Cl mEq/24 hr	Ca mEq/24 hr	Mg mEq/24 hr	IP04 mg/24 hr	Uric Acid mg/24 hr	Creat mg/24 hr	Oxalate mg/24 hr	Citrate mg/24 hr
Preflight													
F-30	721	1.029	1090	101	82	96	2.3	6.9	1127	363	1581	-	-
F-33	1435	1.021	696	205	77	174	5.1	8.3	690	479	1116	-	-
Inflight													
MD2	1666	1.014	505	164	56	177	4.8	11.0	952	463	1443	45.3	572.9
MD4	1549	1.016	585	166	50	140	9.0	9.5	1294	490	1686	43.1	612.8

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INFLIGHT PHARMACOKINETICS OF ACETAMINOPHEN IN SALIVA

Investigators: Nitza M. Cintron, Ph.D., Lakshmi Putcha, Ph.D., and James M. Vanderploeg, M.D., M.P.H.

INTRODUCTION

The observation that a wide range of physiological and biochemical changes occur during space flight suggests that these changes may alter the pharmacodynamics of drugs administered to crewmembers during flight. Conventional methods of therapeutic and pharmacokinetic evaluation of drugs using concentration profiles in the blood are invasive and require special technical expertise. These methods, therefore, are not suitable for space flight applications. In the recent past, salivary concentrations of certain drugs were reported to be useful for clinical drug monitoring and pharmacokinetic evaluations (1). Since saliva sampling is simple and noninvasive, this method may be successfully employed for pharmacokinetic assessment of drugs administered to crewmembers during space flight.

The usefulness of salivary concentrations for predicting blood levels depends upon the detectability of drug concentrations in saliva and the consistency of saliva/plasma ratios over a wide range of plasma concentrations (2). Earlier reports on salivary levels of acetaminophen, a commonly used pain relief medication, indicate that there is a positive correlation between plasma and saliva concentrations, and that the saliva concentrations are higher than those in plasma (3). Preliminary studies conducted in the investigators' laboratory to verify the feasibility of using salivary drug levels for predicting blood concentrations of acetaminophen following oral administration have indicated that therapeutic concentrations of the drug can be successfully detected in saliva. The saliva/plasma ratio of the drug was consistent and remained close to 1 over a wide range of plasma concentrations during the pre- and post-absorptive phases of drug dynamics. These data suggested that acetaminophen might be a suitable candidate for reliable pharmacokinetic evaluation and therapeutic drug monitoring using salivary drug concentration profiles. The widespread use of acetaminophen as a common pain medication and its relatively insignificant side effects encouraged the use of this drug for a preliminary investigation to assess the usefulness of salivary drug monitoring for space medical operations in the future.

The present investigation constitutes the beginning of a comprehensive pharmacokinetic characterization of drugs administered to crewmembers during space flight in general, and of acetaminophen as a representative drug in particular, by using salivary concentrations.

The limited inflight data obtained to date precludes the appropriate assessment of pharmacokinetic alterations associated with space flight. In this regard, the information presented here must be considered strictly as incomplete and preliminary.

Figure 1. A crewman poses with the vial (floating, foreground) and kit used for saliva collection.

PROCEDURES

The investigational design was comprised of two phases, a preflight control phase and an inflight experimental phase (Fig. 1). The overall protocol for both phases was identical and involved oral administration of the drug and collection of saliva samples at regular time intervals for 8 hours after dosing. The details of this experiment are as follows.

The participating crewmember was requested to collect preflight control samples any time between L-30 and L-15 days. Before initiating the study, the crewmember fasted from at least one hour before the sleep period until one hour post-dosing. No drinks were allowed for one hour before and after dosing.

The crewmember ingested two 325-mg tablets of acetaminophen with 100 ml of water followed by a thorough rinsing of the mouth with an additional 100 ml of water. Saliva samples were collected at 0.25, 0.5, 1, 2, 3, 4, 5, 6, and 8 hours post-dosing. Samples were collected using a cotton ball placed at the back of the mouth between the jaws for 5 minutes or until the cotton ball was saturated with saliva, whichever was earlier. Constant rolling of the cotton ball in the mouth facilitated saturation. Stimulation of saliva secretion was achieved by chewing on a teflon square for 30-60 seconds prior to sampling. Saliva samples were collected and stored in designated sample collection tubes until they were analyzed.

The concentration of acetaminophen in each saliva sample was determined later using an established HPLC analysis method (4).

RESULTS

The saliva concentration-time profiles of acetaminophen following oral administration during preflight and inflight conditions in five crewmembers from three separate missions are depicted in Figures 2 to 4. It appears from these profiles that concentration-time profiles of acetaminophen change significantly during space flight when compared to their control counterparts.

Table 1. Absorption Parameters of Acetaminophen

SUBJECT NO.	PEAK CONCENTRATION (mg/ml)		TIME TO REACH PEAK (h)	
	Control	Inflight	Control	Inflight
1*	9.6	6.4	0.5	1.1 (MD4)
2	8.9	6.1	0.5	1.0 (MD4)
3	9.8	14.1	0.5	1.0 (MD3)
4	12.6	14.8	0.5	$\leq$0.25 (MD2)
5	13.0	15.6	0.5	$\leq$0.25 (MD2)

*MD3 data (Fig. 2A) from this subject were inadequate to estimate these parameters.

Preliminary evaluation of the data collected from all five crewmembers suggests that significant changes in the absorption phase of drug disposition occurred, as shown in Table 1, while the elimination of the drug appeared to be unaffected. The peak concentration of the drug decreased in two subjects during space flight and increased in the other three subjects, when compared to the respective control values. The time to reach peak concentration increased in three subjects and decreased in the other two during space flight. While intersubject variability in peak concentration and time to reach the peak concentration was minimal during the ground-based control phase, large variations in these two parameters were noticed between the subjects during flight.

DISCUSSION

Preliminary evaluation of the inflight results indicated that the degree and magnitude of the pharmacokinetic changes observed in crewmembers during flight appear to be dependent on a number of inflight variables that could not be controlled or documented in this study. Some of these contributing parameters that are unique to space flight are discussed below.

SUSCEPTIBILITY TO SPACE MOTION SICKNESS (SMS)

The limited pharmacokinetic data collected in flight (during three missions) suggest that there may be a correlation between the pathophysiological condition of the crewmember and the disposition changes of acetaminophen during flight. In one crewmember who experienced severe SMS symptoms, the peak concentration of acetaminophen and the overall disposition of the drug appeared to be erratic, with an unexpectedly high peak concentration and faster than normal elimination. While experimental artifacts such as contamination of the first two saliva samples by a residual dose in the mouth due to inadequate rinsing after ingestion of the drug cannot be ruled out, symptoms of SMS, such as regurgitation and dehydration, may also have contributed to the abnormal disposition of the drug in this crewmember. Information regarding the incidence of SMS in other crewmembers was not available; therefore, a correlation between the physiological responses to space flight and the disposition kinetics of the drug could not be investigated.

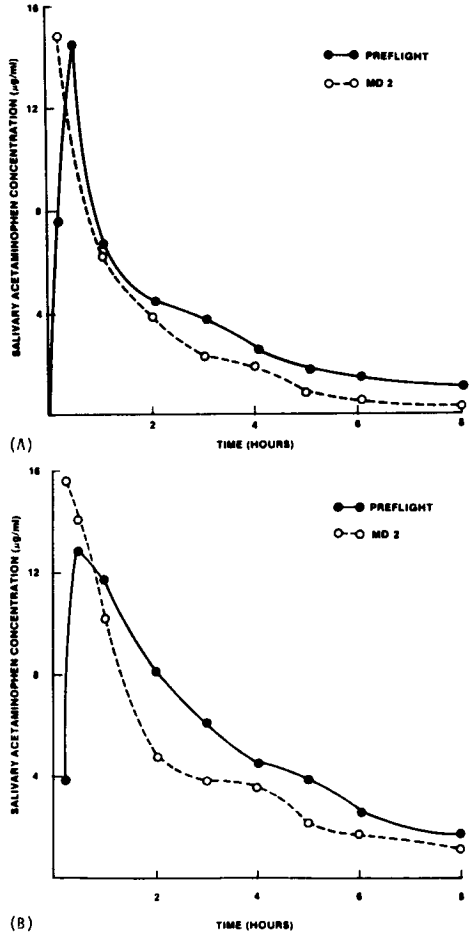

Figure 2. Salivary concentration-time profiles of acetaminophen following oral administration of 650 mg to crewmembers on mission day 2.

MISSION DAY

Among the studies completed so far during the three missions, two crewmembers implemented the study protocol on MD2, one

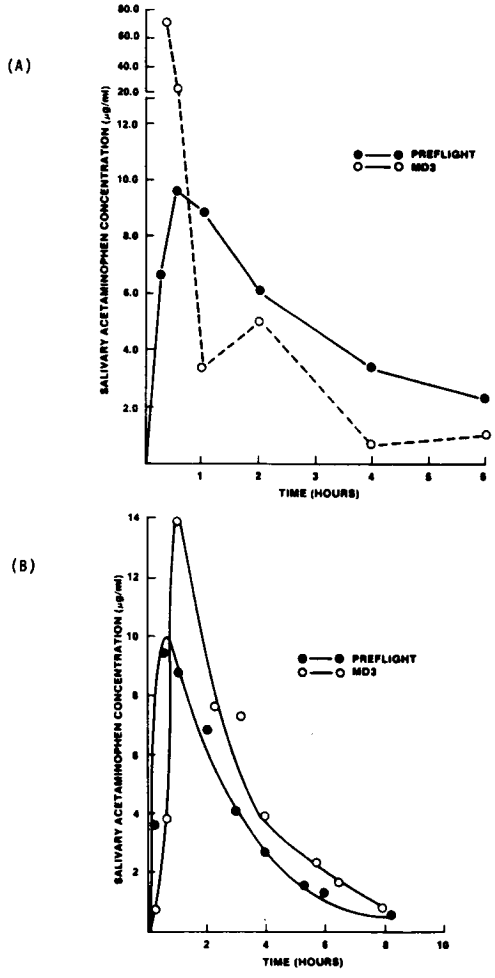

Figure 3. Salivary concentration-time profiles of acetaminophen following oral administration of 650 mg dose to crewmembers on mission day 3.

on MD3, one on MD4, and the other twice during one mission on MD3 and 4. On MD2, both crewmembers had a higher peak drug concentration and a faster time to reach peak concentration than during the preflight phase (Fig. 2). On MD3, the crewmember who had SMS manifestation showed an erratic disposition profile of acetaminophen while the other crewmember had a slower absorption but a higher peak concentration (Fig. 3).

On MD4, when the physiological adaptation to weightlessness may have reached an equilibrium, both crewmembers had a significant decrease in the absorption of acetaminophen as indicated by smaller peak concentrations reached later than during preflight (Fig. 4). These preliminary evaluations

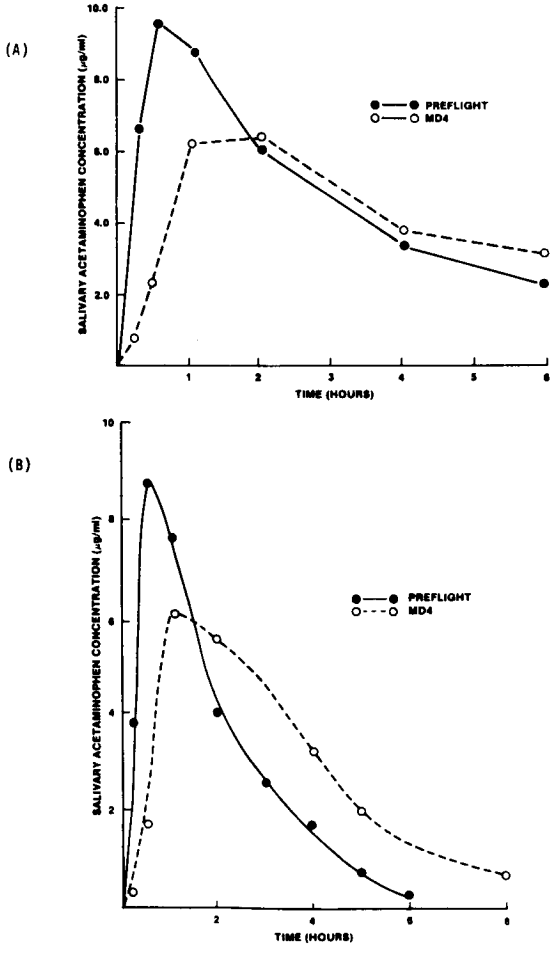

Figure 4. Salivary concentration-time profiles of acetaminophen following oral administration of 650 mg dose to crewmembers on mission day 4.

of the inflight data indicate that conducting the study on the same mission day may reduce the large differences in the experimental results.

INTERSUBJECT VARIABILITY

While no significant differences in pharmacokinetic parameters have been noticed between crewmembers during preflight control studies, large differences in the values of the same parameters between the same crewmembers have been observed during missions. These results suggest that the inter-individual differences in the physiological response to space flight may cause intersubject variability of drug disposition during space flight. In addition, any flight-specific activities such as exercise and ingestion of SMS medications like scopolamine may also contribute to the intersubject variability.

CONCLUSIONS

These limited results of an inflight drug pharmacokinetics investigation that is still in progress indicate that following oral administration of acetaminophen to crewmembers, the rate and extent of absorption of the drug are altered significantly. Earlier reports on acetaminophen absorption from tablets in ground-based studies indicate that delayed esophageal tablet transit caused by either inadequate water wash or supine position after dosing alters the absorption profile of acetaminophen in three ways (5). First, absorption rate is reduced in the first 60 minutes; second, peak plasma concentration is significantly reduced; and third, the time of peak plasma concentration is delayed. These results are similar to the ones observed on MD4. This suggests that changes in the absorption of acetaminophen during the flight may have been affected by the insufficient water intake reported during the mission. More importantly, dehydration and weightlessness, two conditions that prevail during missions, may directly induce changes in absorption similar to those described above. Such absorption changes decrease the effectiveness of acetaminophen as an analgesic (5). Similar changes in disposition have also been noticed with scopolamine, an anti-motion

sickness drug, in crewmembers during missions. These results are being reported separately. Changes in absorption of drugs could render them ineffective or lead to unfavorable therapeutic consequences when the drugs are administered by conventional dosing practices to crewmembers during space flight.

The limited inflight data accumulated thus far are inadequate for characterization of the degree and magnitude of the space flight-induced pharmacokinetic changes because of a number of interfering variables influencing the disposition profiles and kinetic parameter estimates of drugs. While information on some of these variables (such as mission day) is available, information about such factors as the incidence of space motion sickness, ingestion of other medications during the flight, and the overall physical and physiological responses of each participating crewmember to microgravity are unavailable. A thorough and comprehensive evaluation of inflight pharmacokinetics of drugs can only be accomplished under controlled experimental conditions, where some of the factors contributing to the variability in data can be monitored if not controlled. When a comprehensive characterization of observed changes in drug disposition and of the contributing physical, physiological, and biochemical factors is achieved in the future, this knowledge can be applied to predict the therapeutic consequences of operationally critical drugs administered to crewmembers during space flight. This information will assist in the design and development of safe and effective dosage regimens for optimum therapeutic efficiency and avoidance of undesirable side effects from drugs administered to crewmembers during Space Shuttle flights and other manned space missions of the future.

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INFLIGHT SALIVARY PHARMACOKINETICS OF SCOPOLAMINE AND DEXTROAMPHETAMINE

Investigators: Nitza M. Cintron, Ph.D., Lakshmi Putcha, Ph.D., Yu-Ming Chen, Ph.D., and James M. Vanderploeg, M.D., M.P.H.

INTRODUCTION

The need for elucidating the pharmacokinetic changes occurring during space flight has been widely recognized, but the technical and operational constraints of collecting multiple blood samples for such studies limit their implementation during space flight. The usefulness of salivary concentration profiles as an alternate, noninvasive method for clinical monitoring of certain drugs has been established (1). The feasibility of such an application for salivary drug monitoring depends upon the distribution of detectable levels of the drug into saliva and establishment of a consistent saliva/plasma (S/P) ratio over the entire disposition profile of the drug (2). To determine the applicability of noninvasive salivary drug monitoring for pharmacokinetic evaluation of therapeutic agents during space flight, three drugs that are frequently used by crewmembers have been selected for inflight study - acetaminophen, a relatively innocuous, common pain relief medication whose disposition characteristics have been well established, and a scopolamine/dextroamphetamine combination, an operational medication used for the treatment of space motion sickness during missions.

Ground-based, in-house investigations to establish the S/P ratios of scopolamine have been conducted in normal subjects. Following IV and oral administration, scopolamine readily distributes into saliva with consistent S/P ratios over the entire disposition profile. In this preliminary investigation, the pharmacokinetics of scopolamine/dextroamphetamine following oral administration to crewmembers before and during space flight are being evaluated using salivary concentrations to estimate the disposition parameter changes of anti-motion sickness agents during missions.

The limited inflight data obtained to date preclude the appropriate assessment of pharmacokinetic alterations associated with space flight. In this regard, the information presented here must be considered strictly as incomplete and preliminary.

PROCEDURES

Participating crewmembers received an oral dose of 0.4 mg scopolamine and 5 mg dextroamphetamine in combination as a

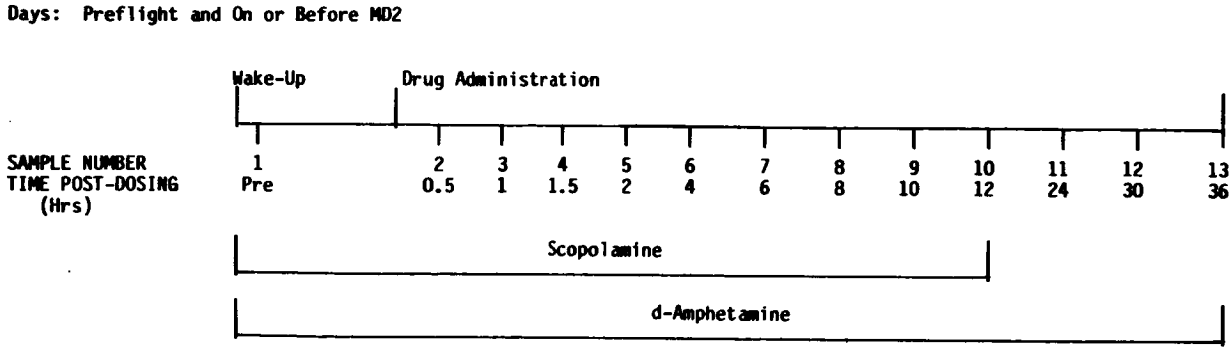

Figure 1. Saliva sample collection schedule.

capsule (SMS medication), twice on separate occasions during ground-based studies and once during space flight. Saliva samples were collected at designated time periods for 36

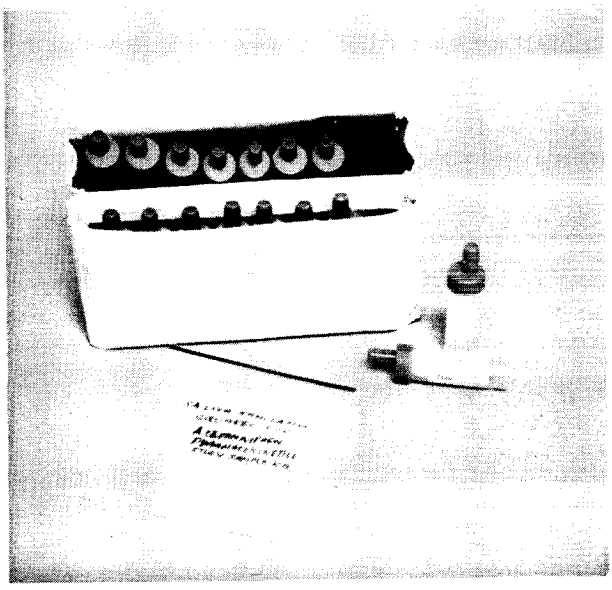

Figure 2. Salivary sample collection kit.

hours as shown in Figure 1, using the cottonball saliva collection kit designed and developed at the JSC (Figure 2). The saliva samples collected during the first 12 hours post-dosing were divided into two aliquots. Scopolamine concentrations were determined using the RPLC-receptor binding assay (3) in one set of the 12-hour sample aliquots. The remainder of the samples for the entire 36 hour duration of the study were frozen for later analysis to determine dextroamphetamine concentrations.

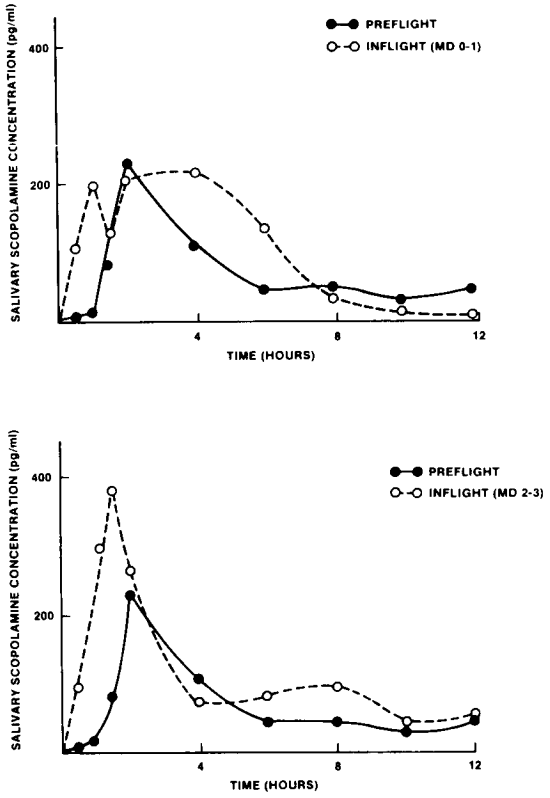

Figure 3. Salivary concentration-time profiles of scopolamine following oral administration of 0.4 mg scopolamine and 5 mg dextro-amphetamine to a crewmember.

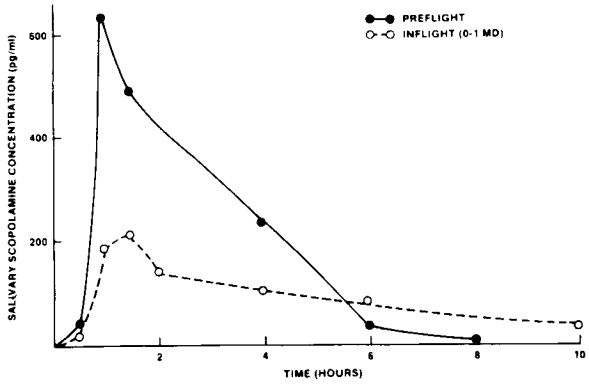

Figure 4. Salivary concentration-time profiles of scopolamine following oral administration of 0.4 mg scopolamine and 5 mg dextro-amphetamine to a crewmember.

RESULTS

Preliminary results from three crewmembers who participated in the study on two separate missions have been compiled and are presented in Figures 3-5. Preliminary evaluation of the salivary concentration-time profiles indicated that large deviations in the concentration-time profiles of scopolamine in crewmembers occur during space flight when compared to their ground-based control profiles. In one crewmember, a significant decrease in the peak concentration and an increase in the time to reach peak concentration were observed, while opposite results were obtained for another crewmember.

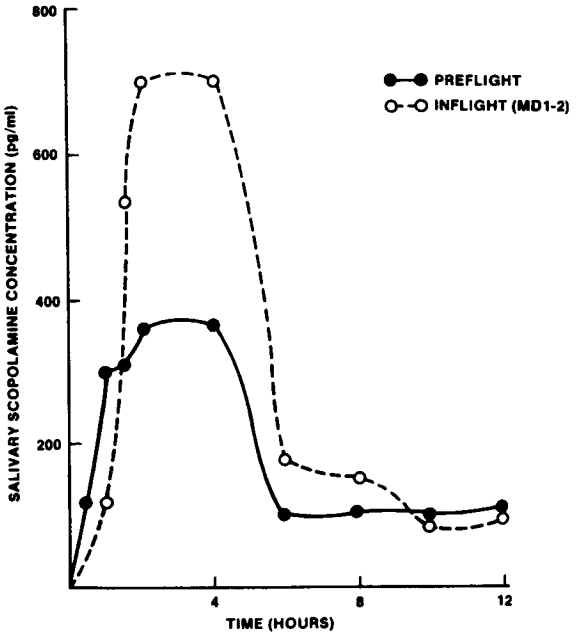

Figure 5. Salivary concentration-time profiles of scopolamine following oral administration of 0.4 mg scopolamine and 5 mg dextroamphetamine to a crewmember.

The third crewmember repeated the study twice during the mission, and the changes in both instances were relatively small when compared to the results from the other crewmembers. These preliminary results are summarized in Table 1. These data indicate that there was a large intersubject variability during flight, while preflight differences were minimal.

Table 1. Absorption Parameters of Scopolamine in Crewmembers

Subject No.	Peak Saliva Concentration (pg/ml)		Time to Reach Peak Concentration (h)	
	CONTROL	INFLIGHT	CONTROL	INFLIGHT
1	227	216 (MDO-1)	2.0	4.0 (MDO-1)
		383 (MD2-3)		1.5 (MD2-3)
2	633	212	1.0	1.5 (MDO-1)
3	356	690	3.0	3.0 (MD1-2)

DISCUSSION

The limited number of results collected so far indicate that the absorption of scopolamine, when administered to crewmembers as a combination SMS medication, may be influenced by the physical and physiological changes caused by weightlessness during space flight. However, the degree, nature, and magnitude of the pharmacokinetic changes could not be evaluated due to the limited number of results obtained thus far. Furthermore, large intersubject variability caused by a number of experimental differences such as mission day and concomitant ingestion of other drugs, in addition to inadequate sample size, make interpretation of the results difficult. Some of the flight-specific factors that may contribute to the variability are discussed below.

INTERSUBJECT VARIABILITY

Scopolamine, being an amine, has a poor absorption profile in humans when administered orally (4). In a preliminary investigation conducted in our laboratories to evaluate the pharmacokinetics of scopolamine in normal subjects, bioavailability of the drug was less than 25 percent of the administered oral dose. Peak saliva concentrations ranged between 600 and 800 pg/ml and were attained in less than 0.5 h after oral administration. The SMS medication used in the present study is a combination of scopolamine and dextro-

amphetamine, both of which are poorly absorbed from the gastrointestinal tract (4). The less than normal peak concentrations (227 and 356 pg/ml) noticed in two crewmembers during ground based control studies may be the result of an absorption interaction between the two drugs which should be evaluated in ground-based studies before definite conclusions can be drawn from inflight results. The crewmember whose salivary concentrations were in the normal range during the ground control study had a significant decrease in the peak saliva concentration during mission and an increase in the time to reach peak concentration. The results obtained from the other two crewmembers were highly variable.

MISSION DAY

As noticed in a similar study with acetaminophen, mission day may also influence the inflight results. This may be due to the fact that the physiological adaptation to space flight conditions is a dynamic process, and the degree and magnitude of these changes may influence the dynamics of drug disposition differently depending upon when the study was performed. The preliminary results obtained so far are from different mission days which makes interpretation of the data difficult.

SAMPLE SIZE

Since scopolamine causes dryness of the mouth in addition to the possible dehydration caused by SAS, adequate samples were not recovered for a large number of sampling times, especially during the absorption and distribution phases of the drug dynamics. This sample inadequacy might have resulted in less than efficient estimation of saliva concentrations in a large number of samples collected during the early phases of the study. Therefore, these results were insufficient for a comprehensive evaluation.

Preliminary evaluation of these limited results indicate that while significant changes in the disposition of scopolamine may occur during space flight, the degree and magnitude of these changes have to be evaluated in more crewmembers before reliable conclusions can be drawn.

CONCLUSIONS

The limited number of results obtained with three crewmembers from two separate missions suggests that scopolamine saliva concentration-time profiles were significantly different during space flight when compared to their preflight counterparts. Absorption of the drug during the flights appeared to be altered as indicated by peak concentration levels and time to reach the peak concentration. Large intersubject variability, inadequate sample volumes, and insufficient data make it very difficult to reliably assess the pharmacokinetic behavior of scopolamine in crewmembers during space flight. These intersubject variabilities may be due to a combination of contributing factors, such as different physical and physiological responses of the crewmembers to space flight, simultaneous ingestion of other medications, and the physiological condition of the participating crewmember on the day the study was conducted. In addition, the pharmacokinetic interaction of scopolamine and dextroamphetamine when administered concomitantly may influence the disposition of scopolamine inflight as well as the preflight study results. All of these factors need to be evaluated in both ground-based and inflight studies. These results, therefore, warrant a comprehensive evaluation of the pharmacokinetic behavior of SMS medications with a minimum number of variables that contribute to the disparity of inflight data. The results of such a comprehensive evaluation of SMS medications and other therapeutic agents for the treatment of pathophysiological disorders induced by space flight are important for determining the therapeutic efficiency and for predicting the incidence of undesirable side effects of drugs administered to crewmembers during missions. Furthermore, the results from the pharmacokinetic and bioavailability studies during space flight will provide information for the successful design and development of effective therapeutic regimens for both short and long duration missions.

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SALIVARY CORTISOL LEVELS DURING THE ACUTE PHASES OF SPACE FLIGHT

Investigator: Nitza M. Cintron, Ph.D.

INTRODUCTION

The complexity of the physiological response to weightlessness has stimulated research into identifying biochemical and endocrine parameters which might provide insight into the underlying mechanisms operative in the overall adaptation process. Available data from earlier inflight and ground-based studies substantiate the value of performing correlative studies to evaluate and assess the neuro-endocrinologic mechanisms associated with the various conditions of space flight-induced stress (1-3). As expected, these investigations clearly indicated the central involvement of autonomic neurotransmission in the etiology of stress-related imbalances (e.g. immunosuppression, motion sickness) and pointed to the potential of correlating early changes to hormonal alterations.

Cortisol, under the direct influence of adrenocorticotrophic hormone (ACTH), is one of the key hormones associated with the control and maintenance of normal neuroendocrine processes and with the response and onset of stress-related conditions. Plasma concentrations of cortisol have been found to increase during space flight (1). However, no data are currently available on its changes immediately after the achievement of weightlessness. It is during these first hours of a mission that the most dramatic changes are thought to occur as part of the adaptive response to weightlessness.

The lipophilic and neutral chemical nature of steroids have been shown to effect their rapid equilibration into saliva from plasma by passive diffusion (4). As a result, steroid concentrations in saliva represent those of the free fraction in the circulation and are independent of variations in salivary flow rate. For cortisol, salivary levels have been demonstrated to correlate with the free steroid fraction in both plasma (5) and serum (6). Recent improvements in steroid immunoassay and salivary extraction techniques have made feasible the routine assessment of adrenal activity by monitoring cortisol levels in saliva (7,8). For inflight application, collection of saliva represents a stress-free, non-invasive means of obtaining information about adrenal activity during the early inflight period; many samples can be collected with a minimum of disturbance of crewmembers' activities.

The primary objectives of this investigation were to determine the feasibility under operational Shuttle conditions of collecting saliva samples for cortisol analysis and, more importantly, to examine the key facets of endocrine function (i.e. adrenal activity) during the acute and adaptive phases of space flight as derived from the resultant cortisol measurements. Information about adrenal activity and about integrated neuroendocrine function have significance in formulating the total picture of the crewmen's health status and in predicting, in conjunction with all other available metabolic data, the possible duration of man's stay in weightlessness.

PROCEDURES

The general design of the overall investigation involved the serial collection of saliva samples throughout a specified 24-hour period during pre- and inflight phases of a mission (Figure 1). Saliva collection activities consisted of collecting 4 samples throughout each 24-hour period at approximately the same times (± 1 hour) during the sleep/activity cycle. To avoid an interruption of the sleep period, the first sample was collected soon after wake-up; the second sample at wakeup plus 5 hours (± 1 hour); the third sample at wake-up plus 10 hours (± 1 hour); and the fourth sample, shortly before the sleep period. These operations were performed once preflight at approximately one month prior to launch and twice inflight, once early and once late in the mission. All inflight

data were compared to preflight baseline data. A total of 6 subjects were required for appropriate assessment and evaluation of results.

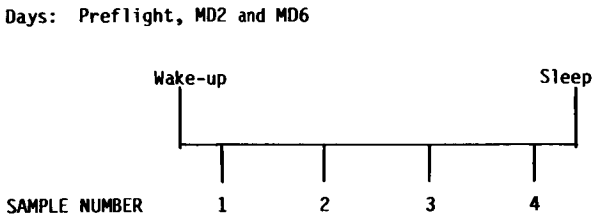

Figure 1. Inflight salivary cortisol sample collection schedule.

To date, two crewmembers have participated in this investigation. As scheduled, four samples were collected from each participating crewmember at approximately 6-hour intervals during a 24-hour period about a month before launch. During flight the crewmembers collected samples on mission days 1, 3 and 6.

Saliva samples were obtained using the Salivary Collection Assembly which consisted of a beta cloth pouch with foam inserts to retain Sarstedt syringe tubes, each containing a dental cotton roll (Figure 2). The syringe barrels had a screw cap on one end and a sliding plug on the other end into which the syringe plunger screwed, so that the barrels functioned as tubes for collection of samples as well as syringes for retrieval of the samples. Squares of Teflon film which could be chewed to stimulate salivation were also stowed in the pouch. Samples were collected by placing a roll of dental cotton between the lower teeth and cheek toward the back of the mouth. The cotton roll remained in place until it was saturated or for 20 min, whichever occurred first. The saliva samples were then stored in the designated tubes for subsequent analysis.

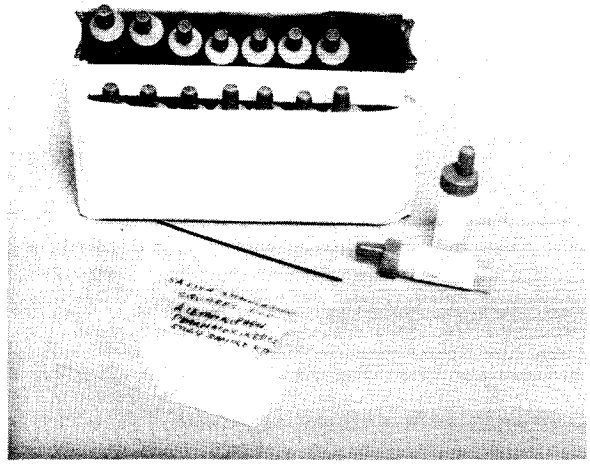

Figure 2. The saliva collection assembly with the Sarstedt syringe tubes containing dental cotton rolls and with the Teflon film squares used for stimulating salivation. The kit configuration shown is that used for saliva collection in conjunction with the Salivary Acetaminophen Pharmacokinetics investigation.

Samples were frozen at -70° C as soon as possible after landing. They were thawed and a plunger was inserted into each syringe. The contents of the cotton roll were squeezed into a 50-ml tube which was centrifuged with the syringe in a Beckman J-6B centrifuge. The roll was squeezed again so that as much sample as possible was transferred to the 50-ml tube. Samples were analyzed for cortisol by the radioimmunoassay described by Foster and Dunn (9).

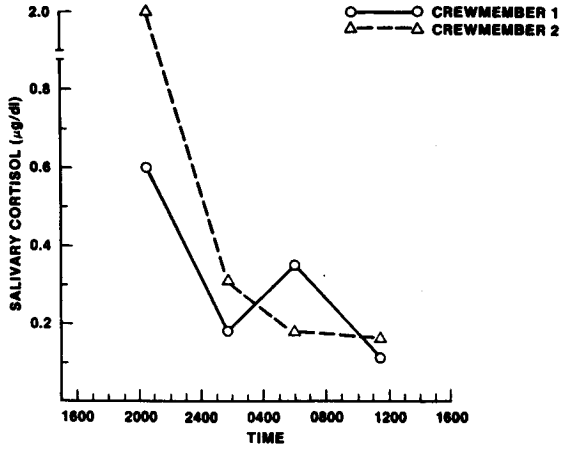

Figure 3. Preflight diurnal variation of salivary cortisol for Crewmembers 1 and 2. Samples were collected throughout a 24-hour period 30 days before flight and cortisol was determined by radioimmunoassay.

RESULTS

For both crewmembers the sample taken late at night (2030 hours) contained the highest concentration of cortisol (Figure 3). The concentration had dropped by at least two-thirds by the next sampling time (0140 hours).

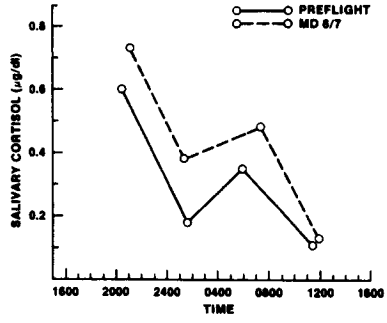

Figure 4. Comparison of preflight and inflight diurnal variation of salivary cortisol in Crewmember 1. The inflight samples were collected on mission day 6/7.

Only one complete set of inflight samples in which cortisol could be measured was obtained. It was collected on Mission Day 6/7. The graph of cortisol levels in these samples was almost parallel to the graph of cortisol in the same crewman's preflight samples (Figure 4); each of the samples taken on MD6/7 contained more cortisol than its preflight counterpart. For this crewmember (Crewmember 1) cortisol levels on day MD1 were higher than they were on MD3 (Table), but for the other crewmember the opposite was true (Table). Since the samples taken early in the flight were not taken at the same times of day as the preflight or MD6/7 samples (Table), cortisol levels in the samples from MD1 and MD3 could not be strictly compared to those from the other days.

Some of the samples collected by Crewmember 2 did not contain enough saliva for detection of cortisol.

CONCLUSION

Salivary cortisol is now considered by some investigators to give a more accurate picture of adrenal cortisol function than serum cortisol (7). Results show that saliva can be collected in zero gravity in quantities sufficient to measure cortisol. The noninvasive methods used in this experiment are highly advantageous for collecting samples frequently and with minimum disruption of the crewmembers' other work. The only problems encountered were insufficient saturation of the cotton rolls (possibly due to dryness of the mouth, a common side effect of antimotion sickness drugs), and inadequate labeling of some tubes. There may also be some difficulty with collection of samples at the same time on every day of the experiment, because of other demands on the crewmembers' time. It should

Table. Diurnal variation of salivary cortisol before and during space flight in two Shuttle crewmembers

Mission Day	Time	Cortisol µg/dl Crewmember 1	Crewmember 2
Preflight	2030	.60	2.04
	0140	.18	.31
	0600	.35	.18
	1130	.11	.16
MD1	2245	.55	.31
	0330	.28	.22
MD3	2215	.37	.53
	0345	.34	.42
	0850	.29	NS*
	2200	.16	NC+
MD6	2110	.73	NS
	0125	.38	NS
	0725	.48	NS
	1200	.13	NS

*NS = sample size not sufficiently large
+NC = not collected

be possible to solve these problems with further training and crew orientation.

The peak in plasma cortisol concentration generally occurs about 0700 hours (10), but for the two crewmembers in our study the peak occurred much earlier, not later than 2030 hours. This might be due to the strenuous preflight training schedule. There are not enough inflight data to draw any conclusions about the early effects of flight on cortisol levels in the body or on their diurnal variation, but in at least one crewmember the diurnal rhythm was the same after about a week of flight as it was preflight.

In conclusion, collection of saliva samples for measurement of cortisol during space flight appears to provide a feasible approach for studying change in adrenal function during adaptation of the body to weightlessness. Specific information regarding the status of adrenal activity in the initial phases of space flight will require additional data for the appropriate assessment of changes. In this regard, the current limited data must be considered strictly as preliminary.

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Section Two

Cardiovascular Effects and Fluid Shifts

A crewman prepares containers of drinking water and salt tablets to be consumed by his crewmates prior to reentry. DSO 402 demonstrated that fluid loading is an effective countermeasure to orthostatic intolerance upon return to gravity. Fluid loading is now a standard procedure on all Shuttle flights. The device on the crewmember's right hip is recording his blood pressure and heart rate as part of another DSO.

BLOOD PRESSURE AND HEART RATE DURING ORBIT AND ENTRY

Investigators: William E. Thornton, M.D., and Thomas P. Moore, M.D.

INTRODUCTION

Postflight orthostatic hypotension has been noted since the Mercury flights and can be expected after exposures to weightlessness. The problem is thought to arise from fluid shift and subsequent fluid loss, from decreased peak physical loads, and probably from neurological adaptation. There had been sufficient concern over hypotension during STS entry to provide the crew with anti-g suits (AGS). A commercial blood pressure-heart rate recorder was used in SMS studies on several missions, and by one crewmember during entry with anti-g suit activation and deactivation.

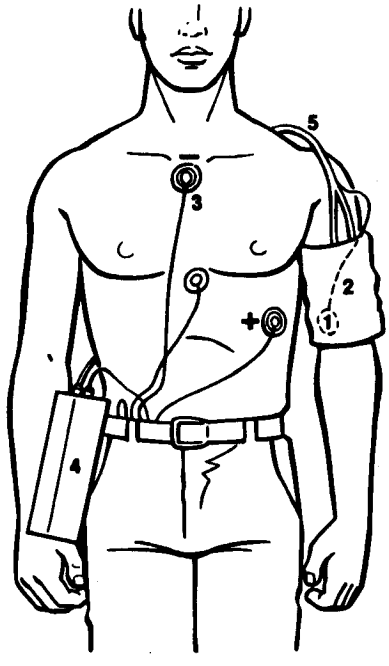

Figure BP-1. Installation of commercial BP-HR recorder showing conventional cuff (2), with microphone (1), over brachial artery and EKG electrodes (3), used to generate timing and rate signals. K-sound signals and cuff pressure are transmitted by cable and tubes (5), to recorder (4).

After several near-syncopal episodes on Shuttle missions following seat egress, presumed to be orthostatic hypotension, it was agreed to make a series of blood pressure and heart rate studies during entry and egress.

PATIENT: 0 DATE: 05-05-85

LINE#	TIME	SYS-TOLIC	DIA-STOLIC	HEART RATE	PULSE PRESSURE	MEAN PRESSURE	PR PRODUCT
1	1:21PM	113	85	95	28	94	10735
2	1:24	115	90	70	25	98	8050
3	1:31	109	83	70	26	91	7630
4	1:39	113	84	68	29	93	7684
5	1:46	116	85	70	31	95	8120
6	1:53	110	82	95	28	91	10450
7	2:01	*					
8	2:01	112	85	64	27	94	7168
9	2:09	118	86	74	32	96	8732
10	2:16	109	82	64	27	91	6976
11	2:24	106	84	63	22	91	6678
12	2:31	97	82	63	15	87	6111
13	2:39	105	80	62	25	88	6510
14	2:46	110	84	63	26	92	6930
15	2:54	112	92	64	20	98	7168
16	3:01	107	80	71	27	89	7597
17	3:09	98	80	64	18	86	6272
18	3:16	110	88	67	22	95	7370
19	3:23	119	85	64	34	96	7616
20	3:31	116	80	60	36	92	6960
21	3:38	115	80	61	35	91	7015
22	3:46	125	80	62	45	94	7626
23	3:53	117	84	71	33	95	8307
24	4:01	131	88	68	43	102	8908
25	4:08	117	83	71	34	94	8307
26	4:16	114	82	62	32	92	7068
27	4:23	112	80	63	32	90	7056
28	4:31	118	92	88	26	100	10384
29	4:38	121	85	74	36	97	8954
30	4:46	121	89	64	32	99	7744
31	4:53	114	84	69	30	94	7866
32	5:01	104	76	66	28	85	6864
33	5:08	115	83	65	32	93	7475
34	5:16	101	78	67	23	85	6767
35	5:23	119	86	70	33	97	8330
36	5:30	116	78	90	38	90	10440
37	5:38	113	79	72	34	90	8136
38	5:45	117	82	70	35	93	8190
39	5:53	114	79	70	35	90	7980
40	6:00	112	78	71	34	89	7952
41	6:08	98	85	80	13	89	7840
42	6:15	115	78	77	37	90	8855
43	6:23	114	85	77	29	94	8778
44	6:30	123	100	87	23	107	10701
45	6:38	101	81	90	20	87	9090

Figure BP-2. Record of digital data, generated by recorder and stored in memory (time, HR, SBP, and DBP). Other data shown are calculated from this by the replay unit. The missing line has been manually deleted for artifacts.

PROCEDURES

The BP-HR recorder was an extensively tested and used, commercially available, ambulatory unit modified only to the extent of decreasing minimum automatic sample time to 3.5 minute intervals. It used a conventional cuff

and K-sounds (Rivi-Rocci technique), was completely automatic, and was capable of recording and storing up to 200 lines of data (time, BP, and HR) internally. Equipment placement is shown in Figure BP-1. Postflight, these data were transferred to a standard digital format (Figure BP-2) and plotted by a companion data reduction unit. Accuracy of the unit has been examined and reported by a number of investigators who have used it in both clinical and aerospace applications. Each unit was repeatedly checked for accuracy by simultaneous comparison of its results with manual determinations made with a calibrated sphygmomanometer. Mean errors were typically less than 4 mmHg systolic and 3 mmHg diastolic.

RESULTS

Blood pressure and heart rate were obtained with this device pre- and postflight on Launch -59 days and Return +2 days and inflight on Mission Day 7 and through entry and egress on one subject. The records were edited and artifactual values removed. Results were then plotted and are shown in Figures BP-3, BP-4, BP-5 and BP-6.

CONCLUSIONS

The first record, Figure BP-3, was made during a one-g simulation. BP was approximately 120/80 and resting HR approximately 55 beats per minute (bpm). The inflight record, Figure BP-4, is equally unremarkable with lower systolic and diastolic BP and a low HR in spite of personal "acrobatics" performed during a portion of the record. Essentially the same values are seen during entry preparation with increase in BP and HR during seat ingress and then an increase in BP with onset of g-loads and an increase in and an upward trend of HR, Figure BP-5.

Thirty-two ounces of fluid with 8 gm of NaCl was ingested prior to entry and the AGS was worn and inflated to 1 psi. Blood pressure peaked during touchdown and egress and systolic pressure remained slightly elevated during the remainder of the record. It was during this period that the subject had symptoms which might have been characterized as orthostatic hypotension had the individual's BP and HR not been known. The most striking record was obtained on R + 2, Figure BP-6, when the HR is above 70 bpm and systolic BP is slightly elevated except during the period of 1415 to 1520 when systolic BP and pulse pressure (systolic BP minus diastolic BP) were decreasing and HR increasing. While there was no diary for this period, such a BP-HR signature is consistent with orthostatic stress, possibly caused by standing. All symptoms were denied during this period.

In summary, there was little change in HR and BP during an inflight record. During entry and seat egress, BP was normal for the situation with minimal HR changes in spite of being symptomatic on seat egress. Two days later there was a persistently elevated (for this individual) HR and one period consistent with orthostatic stress but without reported symptoms.

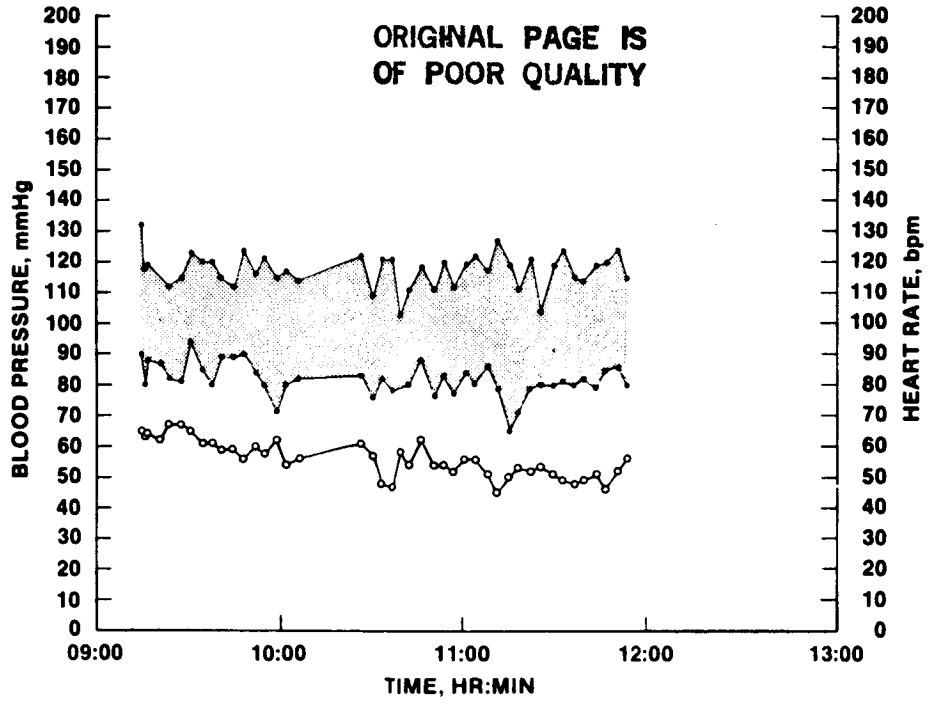

Figure BP-3. Blood pressure (shaded area) and heart rate (open circles) during simulation of entry preparation. The only remarkable feature is the low heart rate.

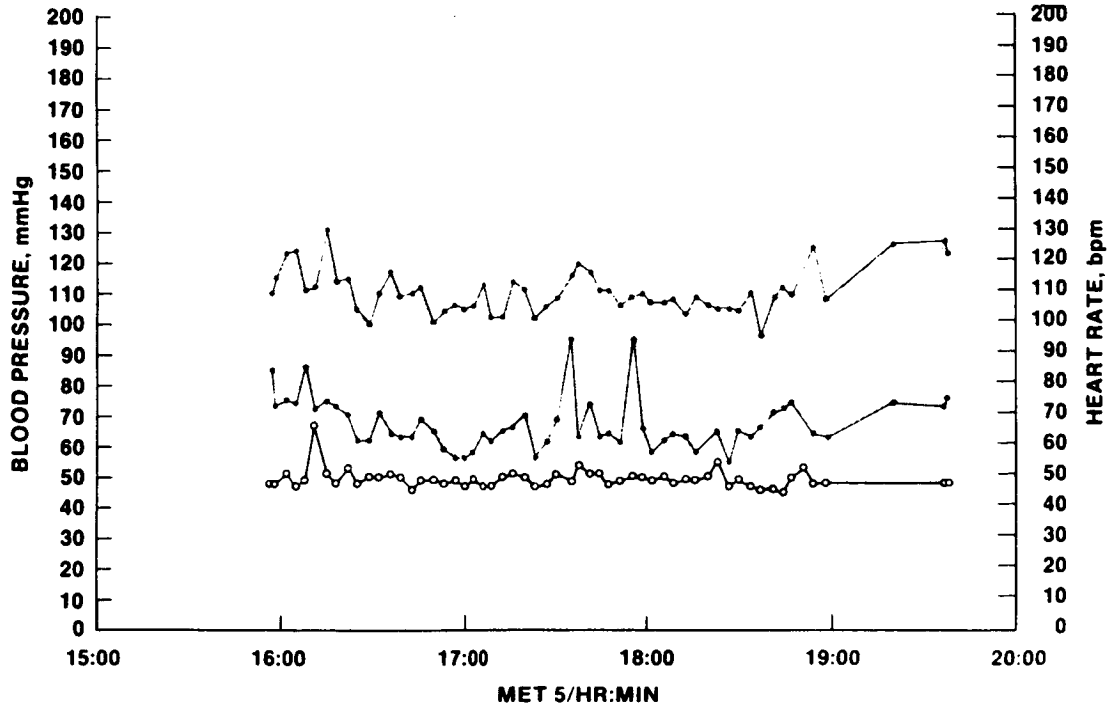

Figure BP-4. Blood pressure and heart rate during day prior to entry. Heart rate was equivalent to supine resting rate prior to entry.

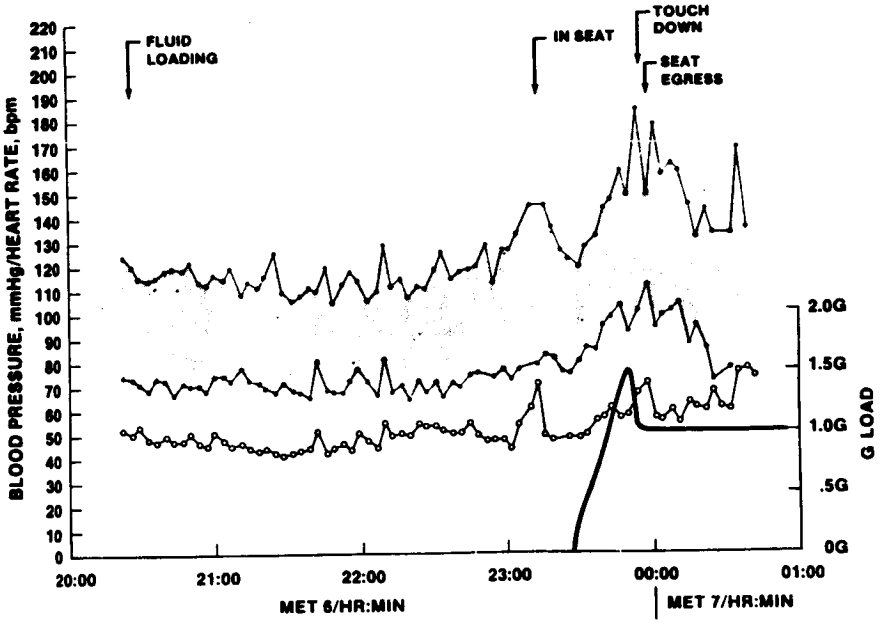

Figure BP-5. Blood pressure and heart rate prior to and during entry. Transient elevation at 2300 caused by activity associated with strapping into seat. Second increase is typical response to entry loads. Heart rate is relatively low for reexposure to one-g.

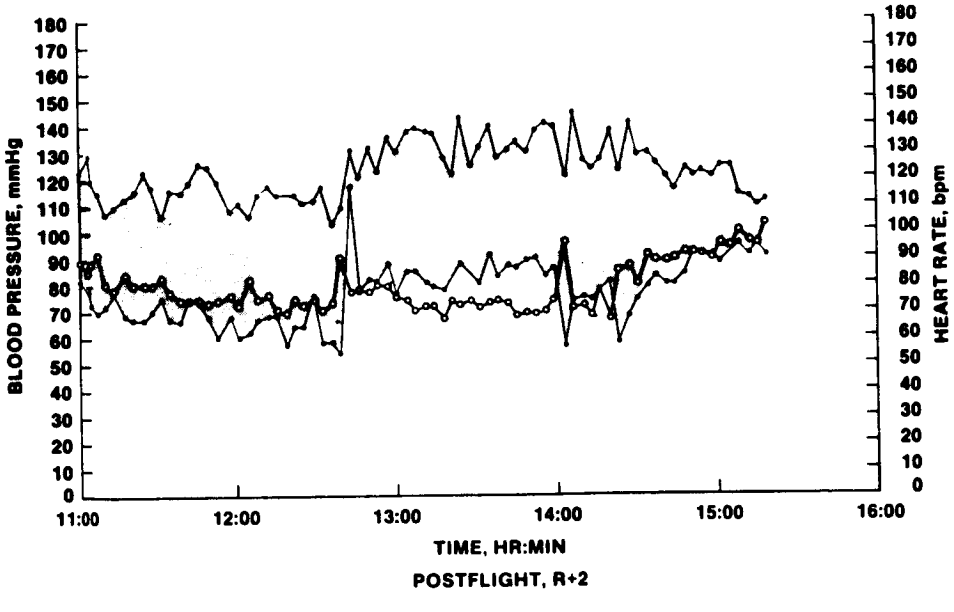

Figure BP-6. Blood pressure and heart rate on second day after entry. Note high average heart rate. Activity diary was not available but was presumably sitting 1100 to 1245 and then erect. Falling SBP and pulse pressure with increasing heart rate near end of record is typical of orthostatic stress.

CARDIOVASCULAR DECONDITIONING DURING SPACE FLIGHT AND THE USE OF SALINE AS A COUNTERMEASURE TO ORTHOSTATIC INTOLERANCE

Investigators: Michael W. Bungo, M.D., John B. Charles, Ph.D., and Philip C. Johnson, Jr., M.D.

INTRODUCTION

Early in the manned space flight program it was noted that the cardiovascular system undergoes several adaptive changes when subjected to the microgravity environment. Experimentation during NASA's Skylab missions demonstrated that fluid was shifted from the lower extremities to the more central and cephalad portions of the circulation. The results of this redistribution and of other alterations in the controlling mechanisms of the circulation which were not well defined were termed "cardiovascular deconditioning." The term deconditioning was felt to be appropriate because those individuals who were tested during or immediately after space flight demonstrated less orthostatic tolerance when provoked with lower body negative pressure (LBNP), higher submaximal oxygen consumptions at equivalent workloads, and higher resting heart rates when compared to their responses preflight (12). Numerous ground-based studies were performed using water immersion, bedrest, and headdown bed rest in an attempt to duplicate the cardiovascular adaptations observed in microgravity (3,14). Fluid volume shifts had been quantified, and the time course of events had been characterized (1). Several methods of reversing the deleterious effects of deconditioning were also suggested, such as the use of anti-G suits (including elastic leotards), liquid cooling garments, lower body negative pressure, electrical stimulation of the muscles, and various pharmacologic agents, mineralocorticoids being the most prominent among them (2).

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With the advent of the Space Shuttle, it was known that astronauts would receive the effects of reentry deceleration in the +Gz axis (head-to-toe), compared to earlier space flights in which these forces were directed +Gx (chest-to-back). The combination of this more stressful acceleration loading with the deconditioned state of the human cardiovascular system following space flights increased efforts directed at developing suitable countermeasures. Most were rejected for actual use in the Space Shuttle due to either complex hardware requirements or objections by flight crews. Even the anti-G suit, considered by many as the only acceptable alternative at the inception of the Shuttle program, was not regarded favorably. Therefore, the development of other, more suitable countermeasures to post-space flight orthostatic intolerance took on greater importance.

Earlier bedrest studies had revealed the usefulness of oral rehydration using normal saline, in the more palatable form of bouillon, in providing a degree of protection against the loss of LBNP (10,11) and acceleration (4) tolerance by expanding the circulating plasma volume. In one study, six male volunteers underwent 15 d of bed rest to "decondition" their cardiovascular systems in a physiological simulation of weightlessness (11). On each of the last 3 d of bed rest, each subject was stressed by LBNP at -50 mm Hg in one of three randomly-assigned conditions: employing no candidate countermeasures; having ingested 1 L of bouillon alone as a countermeasure; or following ingestion of the bouillon during 3 h of LBNP at -30 mm Hg, as a combined countermeasure. The results showed that the combination of oral rehydration and prolonged LBNP provided a more sustained increase in plasma volume and reduction in stressed heart

rate response. However, oral rehydration alone provided a larger increase in plasma volume and essentially the same reduction in stressed heart rate response, but for a period of only a few hours. Considering the constraints of Space Shuttle operations, especially the inconvenience of providing for the appropriate LBNP treatment of the entire crew during the last 24 h of space flight, the relatively short-lived protection of oral rehydration alone was deemed the superior treatment. Accordingly, the simple technique of oral rehydration shortly before reentry into the earth's atmosphere was evaluated during several Space Shuttle flights.

PROCEDURES

On the day prior to Shuttle landing, all 26 crewmembers were to consume at least 3 quarts (2.7 L) of fluids as part of their usual meal and snack routine. This was intended to offset any dehydration due to low intake during the period of adaptation to weightlessness, or to high insensible loss; it was not expected that this consumption would alter the physiological adaptation to microgravity.

Preliminary testing revealed that Shuttle crewmembers found isotonic saline unpalatable even in bouillon form. Therefore, the crews were provided with salt (sodium chloride) tablets (1 g each) and advised to take one tablet with each four ounces (114 ml) of water consumed, to a total of 8 tablets and 912 ml of water. This concentration approximated isotonic saline. On the day of landing, starting 2 hours before entry into the earth's atmosphere, the participating crewmember was to begin oral intake of fluid and salt at a rate dictated by personal comfort. It was stressed that regardless of the total fluid volume consumed, the tablet-to-volume ratio be kept constant as prescribed. During the interval between 1 and 2 hours after landing, each crewmember's heart rate and blood pressure responses to a Passive Stand Test (9) were recorded, for comparison with their preflight values. During the Stand Test, the electrocardiogram was recorded continuously, and blood pressures were measured each minute for 5 minutes while the crewmember was in the supine position, and for 5 additional minutes immediately thereafter while the crewmember was standing The individual stood with his/her feet six inches (15 cm) apart and nine inches (23 cm) from a wall, and leaned slightly backwards against the wall for support. Passive standing had previously been validated as a test of orthostatic intolerance (9).

Heart rate was determined from the electrocardiographic record as the number of QRS complexes occurring during each 1-minute interval. Mean blood pressure was calculated as one-third the sum of the systolic blood pressure plus two times the diastolic blood pressure. The average heart rate, systolic blood pressure, and diastolic blood pressure during the equilibrated portion of each 5-minute segment of this stand test were used in all calculations. In addition, the minute-by-minute group mean values for heart rate and mean blood pressure were plotted to illustrate the differences in the dynamic adjustments of cardiovascular function before and after space flight, and with and without the countermeasure. The results were similar to the averaged data.

A means of estimating the degree of cardiovascular deconditioning was formulated which standardizes each individual by his/her preflight testing response. This Cardiovascular Index of Deconditioning (CID) is defined as: CID = ΔHR - ΔSBP + ΔDBP, where ΔHR = heart rate (bpm) standing postflight minus heart rate standing preflight; ΔSBP = systolic blood pressure (mm Hg) standing postflight minus systolic blood pressure standing preflight; and ΔDBP = diastolic blood pressure (mm Hg) standing postflight minus diastolic blood pressure standing preflight.

The CID is a unitless index that reflects the numerical increase in heart rate and decreases in systolic and pulse pressures resulting from cardiovascular deconditioning, as documented in both space flight and bedrest experience (13). Therefore, as the numeric value of CID increases, the response of the cardiovascular system is greater, and the level of deconditioning (i.e., orthostatic susceptibility) more profound.

The experiment results were analyzed statistically using a two-factor mixed design analysis of variance (one factor between groups, and one within). The mean steady-state value of each variable during each 5-minute phase of the Stand Test, both preflight and postflight, was analyzed as a separate treatment.

RESULTS

All crewmembers from the first eight Space Shuttle flights were considered as the subjects of this investigation, for a total of 26 data sets from 24 individuals (two individuals flew twice). Of these subjects, 17 utilized the countermeasure and 9 did not. The space flights lasted from 54 hours to 192 hours, and flight length did not appear to correlate with the deconditioning parameters examined in this study.* Crewmembers participated in the study on a voluntary basis. Those that did not take the countermeasure did not use other countermeasures for the Stand Test and were considered the control population. The astronauts using the countermeasure consumed fluid and salt according to personal preference. Some drank water while others preferred various on-board beverages, especially fruit juices. Salt tablets were taken as prescribed or less than directed but not in excess. The operational environment in which the space-borne portion of this investigation took place made it impossible to control these individual variations. As a result, the amount of fluid consumed ranged from 0.5 L of hypotonic solution to 1 L of isotonic solution. Occasionally, crewmembers who had used the countermeasure prior to reentry consumed additional fluids postflight before the Stand Test was performed. Because of this pattern of compliance, any attempt at volume loading with salt and fluids prior to reentry was considered a use of the countermeasure.

* Subsequent to this analysis, additional data were collected which suggested an effect of flight duration on crewmembers using the countermeasure, but not on those who did not. This will be treated in more detail in a future publication.

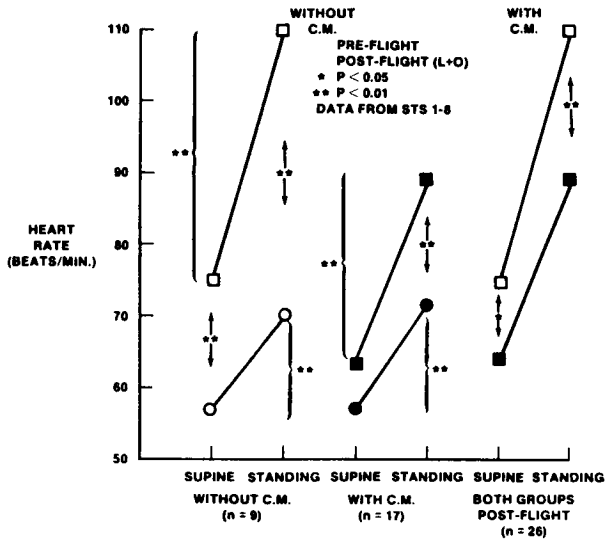

Figure 1. Responses of heart rate to orthostasis pre- and post-spaceflight, with or without countermeasure (C.M.).

The postflight Stand Test usually took place during the interval between 1 and 2 hours after landing. The heart rate responses to the orthostatic stress are summarized in Fig. 1. Both groups had mean supine heart rates of 57 bpm preflight, which upon standing increased to 70 bpm in the control group and 71 bpm in the countermeasure group. These changes in heart rate were statistically significant ($p < 0.01$), and the responses of the groups were essentially identical. Postflight, the control group's mean supine heart rate of 75 bpm was significantly elevated over the preflight supine value ($p < 0.01$). Their mean postflight standing heart rate rose to 110 bpm, a significant increase over both their postflight supine ($p < 0.01$) and preflight standing ($p < 0.01$) values.

In the group utilizing the countermeasure, the postflight mean supine heart rate of 64 bpm was only slightly elevated and increased ($p < 0.01$) to 89 bpm with standing. The postflight heart rates were significantly lower in the group using the countermeasure than in the control group, in

both the supine ($p<0.05$) and standing ($p<0.01$) positions.

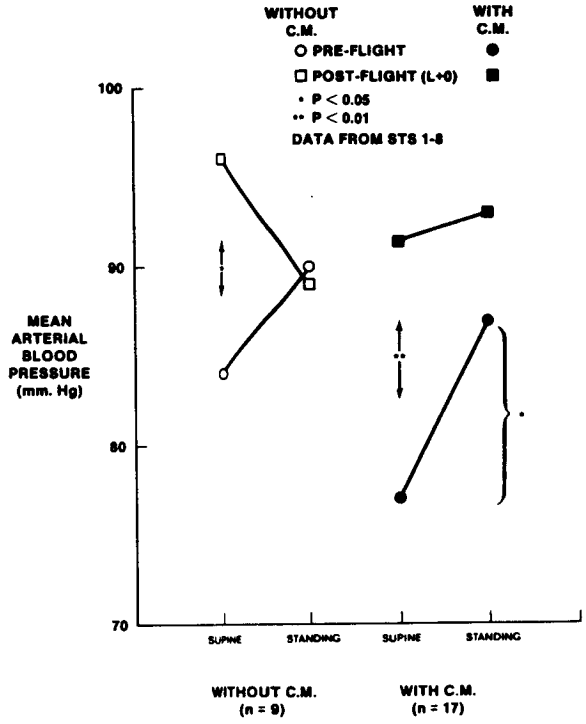

Figure 2. Responses of mean blood pressure to orthostasis pre- and post-spaceflight, with or without countermeasure.

Mean blood pressure responses to the orthostatic stand test are summarized in Fig. 2. The preflight response to assuming the upright posture was a 6 to 10 mm Hg rise in mean blood pressure. Postflight, the control group's mean blood pressure dropped 7 mm Hg when the astronaut assumed the standing position. In the group which utilized the countermeasure, the mean blood pressure rose 2 mm Hg when changing from supine to upright posture. In both the control and experimental groups, the supine mean blood pressure was significantly higher ($p<0.05$) postflight than preflight.

The individual responses to orthostasis before and after space flight are presented in Table I. The Cardiovascular Index of Deconditioning (CID) was calculated for each crewmember and listed in Table II. For those who did not use the countermeasure, the average CID was 49.4 ± 9.6 S.D. For those crewmembers utilizing the countermeasure, the average CID was 21.4 ± 15.9 S.D., a significantly ($p<0.003$) lower value than for the abstainers. Of the two crewmembers who had more than one Shuttle flight, one individual did not use the countermeasure either time; his CID values were 45 and 63. The other crewmember did not use the countermeasure on his first flight (CID = 46), but did use a partial countermeasure on his second flight (CID = 24).

Of the 26 crewmembers on the first eight Shuttle flights, 1 suffered an episode of outright postflight orthostatic syncope, and 2 had episodes of presyncope. None of these three individuals had utilized either the fluid loading or any other countermeasures for the Stand Test.

DISCUSSION

The use of orally consumed salt tablets and water has been shown in these studies to have a beneficial effect on orthostatic tolerance as measured by heart rate and blood pressure responses to a post-space flight stand test. The cardiovascular adaptation to microgravity, termed "deconditioning," therefore apparently has fluid redistribution and subsequent elimination as a significant component. Nevertheless, employing the countermeasure did not completely reverse the effects of space flight. This might be due to inadequate utilization of the volume loading protocol. However, given the complexity of the cardiovascular system's control mechanisms, and their potential susceptibility to alteration by space flight factors, it is probably also a result of other such alterations which are not so readily reversed. Future basic research will aid in discriminating these factors.

Although not providing the fine increments of orthostatic stress that a tilt table or lower body negative pressure device might generate, the stand test produced reproducible provocation that was clinically simple to use and easy to evaluate.

Since the countermeasure was utilized to various degrees of adherence to the protocol, the larger spread of CID values in the experimental group is not surprising, yet the statistical difference from the control group is maintained.

The instance of the crewman who used the countermeasure only after his second and

longer space flight demonstrates its effectiveness. The lower value of the CID after his second flight clearly implies that his orthostatic tolerance with the countermeasure was improved over that without the countermeasure.

The Cardiovascular Index of Deconditioning is a simplistic reflection of a complex, as yet unsolved, clinical research problem. However, this index can be helpful to those responsible for making operational judgements with minimal facilities for data acquisition. Certainly it can serve as an indication of the obvious clinical effects of deconditioning.

Oral rehydration using salt and fluids has also been evaluated for use during Soviet space flights (8), and is employed in the Salyut space station program (5-7, 15-17). During the final 1-3 weeks of their long-duration space flights, the Salyut crewmen have spent time in their "Chibis" LBNP garments (5-7, 15-17) to reaccustom the vasculature of the lower limbs to blood pooling. Some crewmembers also drank "15 sips" of water about 20 min prior to the later LBNP sessions (16), although they apparently did not take salt, as was done in the Americal bed rest study (11). On the last day of flight, the cosmonauts consumed 30 g of salt (in tablet form) and drank 300-400 ml of water at each meal (6,7,16,17), in preparation for the return to earth, sometimes before or during LBNP exposure (6,7). However, the salt and water countermeasure is apparently not used by the visiting crews of the week-long Soyuz resupply missions, who stay in space for periods comparable to American Shuttle crews (Jean-Loup Chretien, French spationaut on Soyuz T-6/Salyut-7: personal communication).

The ability of an astronaut to perform his duties during the +Gz forces of reentry is of considerable concern to the NASA organization. This is the first time a countermeasure to the physiologic changes occurring during space flight has been applied acutely in a successful manner. In this instance, success is judged by the

Table 1

INDIVIDUAL STAND TEST RESULTS

Subject number	Time in flight (hours)	Counter-measure yes/no	Preflight						Postflight						
			Supine			Standing			Supine			Standing			
			HR	SBP	DBP	HR	SBP	DBP	HR	SBP	DBP	HR	SBP	DBP	CID
1	54	N	61	127	88	73	145	92	61	120	80	99	110	80	49
2	54	N	59	129	76	65	137	86	66	140	110	85	135	110	46
3	54	N	78	118	76	102	118	76	103	117	75	126	90	62	38
4	54	N	54	110	70	71	105	68	80	118	82	111	118	86	45
5	192	N	52	118	80	70	105	80	77	140	84	120	120	98	53
6	192	N	53	100	70	65	100	72	77	118	82	137	104	70	66
7	169	Y	57	110	68	65	98	66	69	108	78	93	100	68	28
8	169	Y	53	130	80	60	118	78	69	128	84	97	126	82	33
9	122	Y	58	103	65	68	112	77	67	120	88	89	110	90	36
10	122	Y	68	100	60	86	107	73	65	119	75	92	110	80	10
11	122	Y	49	100	67	67	117	79	51	106	60	71	116	79	5
12	122	Y	57	102	68	66	110	74	60	114	56	82	122	72	2
13	120	Y	69	109	68	90	120	80	69	119	80	79	109	86	6
14	120	Y	65	108	63	82	120	80	59	137	88	90	129	96	15
15	120	Y	48	110	69	62	118	78	77	106	62	120	114	69	53
16	120	Y	49	95	50	60	110	68	50	112	57	74	113	77	20
17	146	Y	59	96	60	71	120	82	72	149	101	87	136	106	24
18	146	Y	53	100	60	72	119	76	72	132	96	94	125	103	43
19	146	Y	51	96	60	66	110	70	57	122	79	77	116	80	15
20	146	Y	55	80	60	78	90	65	64	124	92	91	96	63	5
21	146	Y	71	100	60	83	120	72	61	126	80	83	114	79	13
22	145	N	52	100	60	64	112	72	79	110	70	120	105	72	63
23	145	Y	52	90	60	66	113	72	47	110	72	82	112	83	28
24	145	Y	53	100	58	73	110	75	75	100	73	107	116	89	42
25	145	N	54	98	60	59	110	72	68	109	78	105	112	72	44
26	145	N	52	100	60	64	118	78	61	122	83	89	84	60	41

Legend: SBP = systolic blood pressure
DBP = diastolic blood pressure
HR = heart rate
CID = Cardiovascular Index of Deconditioning (see text)

Table 2

SPACE SHUTTLE

CARDIOVASCULAR INDEX OF DECONDITIONING - INFLUENCE OF SALINE COUNTERMEASURE

With Countermeasure	Without Countermeasure
28	49
33	46
33	38
10	45
5	53
2	66
6	63
15	44
53	41
20	49.4 ±SD9.6
24	
43	
15	
5	
1	
28	
42	
21.4 ±SD15.9	

Legend: Difference between two CID values is significant to the $p<0.003$ level

CID = ΔHR - ΔSP + ΔDBP (see text)

acceptance and regular utilization of a technique by the crewmembers, and the objective demonstration of statistically significant beneficial physiological effects. Indeed, this success has resulted in the official adoption of oral fluid and salt loading as an operational countermeasure for all Space Shuttle crewmembers.

In addition, a clinically useful index, the CID, has been developed to assist the flight surgeon in his assessment of the degree of deconditioning.

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CHANGES IN TOTAL BODY WATER DURING SPACE FLIGHT

Investigators: Carolyn S. Leach, Ph.D., L. Daniel Inners, Ph.D., and John B. Charles, Ph.D.

INTRODUCTION

The objective of this experiment was to measure the changes in total body water (TBW) occurring in humans as a consequence of exposure to microgravity.

It was hypothesized that total body water decreases by about 1.0-2.0 liters within the first three days of weightlessness and is maintained at that level for the duration of a 7-10 day flight.

Fluid shifts occurring during the first few hours of weightlessness have been identified as the probable cause of early adaptive responses of the human cardiovascular and renal/ endocrine systems (3). Fluid shifts have also been implicated as possible contributory factors in altered vestibular function. Despite this role in triggering the response of major pathways of adaptation, the timing and extent of the exchanges of water and electrolytes between compartments is unknown.

TBW measurements are particularly important to the goal of tracking fluid shifts. Not only are the overall changes in total water content of interest, but also changes in intracellular fluid volume cannot be calculated without reliable estimates of TBW.

Although exposure to weightlessness has long been known to affect the distribution of body fluids, previous measurements of total body water have been confined to preflight and postflight periods. Leach and Rambaut (4) measured TBW pre- and postflight on Skylab Missions 2, 3, and 4 on a total of nine subjects, using tritiated water as the tracer. Comparison of pre- and postflight measurements indicated a mean decrease of 1.7 % in postflight TBW relative to preflight. On the other hand, the ratio of TBW to body mass was observed to increase slightly in this comparison.

With the development of noninvasive techniques employing stable isotopes (5), it was possible to make direct, precise measurements of TBW at almost any conceivable time during a mission while making very minor demands on crew and spacecraft resources. Moreover, these newer methods are capable of a resolution of events separated by only three to six hours.

PROCEDURE

SUBJECTS

The subjects for this experiment were three male crewmembers. Height, age, percent body fat, and preflight body mass are summarized in Table 1.

Table 1. Height, body mass, percent body fat, and age for the three subjects who participated in this experiment. All data except body mass were recorded as part of the previous annual physical exam for the crewman. Body mass was taken from F-33 preflight data.

Subject	Height (cm)	Body Mass (kg)	% Body Fat	Age
A	178.5	80.6	14.7	39
B	170.0	68.5	14.2	35
C	177.7	71.9	14.4	43

Table 2. Body mass of subjects.

Subject	F-33	F-30	F-24	F-7	L+0	L+3
A	80.6		81.2	83.9	80.6	79.7
B	68.5		69.6	70.3	67.1	68.9
C	71.9	72.2		73.5	70.8	71.0

The proposed schedule of the experiment is summarized in Figure 1. The design included no special control group or control experiment. Instead, all inflight and postflight data were compared to preflight baseline data. Because of a delay in the launch of the mission and the unavailability of some crewmembers during the immediate pre- and postflight periods, the first preflight measurements were at F-34 to F-30, while some measurements were missed entirely. The actual schedule of measurements was as indicated in Table 3.

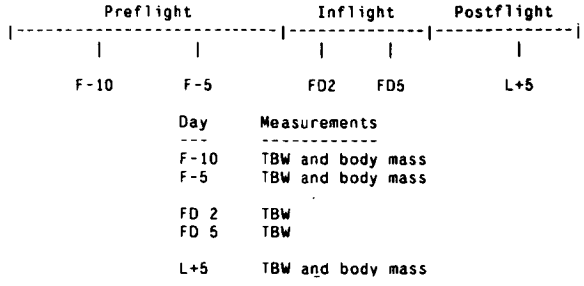

Figure 1. Nominal schedule of experimental sessions for measurement of total body water.

TBW was measured by the isotope dilution technique utilizing oxygen-18-labeled water ($H_2{}^{18}O$) as the tracer. Briefly, this method requires the ingestion of a known mass of ^{18}O water followed by sampling of representative body fluids such as urine or saliva over a period of several hours following the administration of the tracer. The protocol for a typical measurement is shown in Figure 2. The measurements were initiated immediately after a sleep cycle with the crewman in a fasted state. After the collection of background samples the dose was consumed followed by at least 50 ml of fruit juice or galley water. The subject was allowed to consume a light breakfast 30 min after dose administration and was requested to abstain from caffeine-containing beverages for the duration of the experiment. All food consumed during the experiment was recorded on a log sheet.

Table 3. TBW Measurements. Total body water in kg for three crewmembers, A, B, and C, on the mission days indicated. This is the unbalanced data matrix used for the general mixed model analysis of variance.

Hour		F-34	F-31 F-30	F-3	FD 2	FD 4 FD 5	L+6
	A	47.33	47.87	49.65	44.87	46.82	50.05
3 hr	B	40.02	40.19	41.41	43.46	39.20	41.32
	C	44.41	47.53		43.74	46.58	
	A	47.14		49.94	44.38		
5 hr	B	40.83	42.01	42.79	41.80		43.42
	C	47.18	47.43		44.17	45.71	

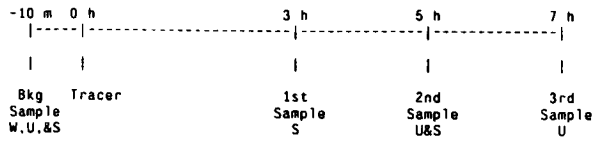

Figure 2. Schematic representation of a typical inflight experimental session (U = urine sample, S = saliva sample, W = galley water sample).

A sample of galley water was collected on FD 2. The experimental design called for galley water sampling on all days on which TBW was measured, since it had been observed on several previous occasions, including STS 51-D, that water sampled from the galley was enriched in ^{18}O content. Urine samples collected during inflight testing of the Urine Monitoring System on Spacelab 3 also exhibited ^{18}O enrichment.

Dental cotton rolls were used for saliva collection. All cotton used in the experiment was from one batch, and rolls were packaged individually in vapor-tight, 10-ml glass lyophilization vials (Wheaton) in a single operation lasting about 30 min. Once closed, the sample vials were opened only for sample collection and sample removal. The sample collection vials were packaged in a Nomex kit (Figure 3) for inflight use.

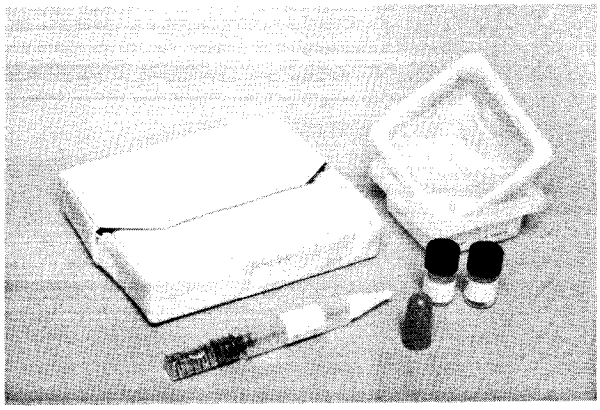

Figure 3. The Nomex dose syringe kit, an assembled dose syringe, the syringe cap, two saliva sample vials, and two beverage containers used to collect Shuttle galley water samples. A similar, separate kit was used for stowing the sample vials.

^{18}O water (95-98 %) was purchased from Mound Laboratories, Miamisburg, OH. The dose was approximately 6 g. The labeled water was filtered directly into a sealed, sterile syringe vial through a nonsterile 13-mm Millipore Type HA filter (0.45 micrometer pore) using a disposable filter holder. The syringe used was a two-piece disposable type manufactured by IMS (El Monte, CA), consisting of a glass vial containing the dose and a separate plastic injector with a lavage tip (Figure 3). This syringe was weighed three times: empty, filled with the labeled water, and after use to determine the dose delivered and the amount remaining in the syringe (usually about 0.3 ml). Syringes were stowed in a separate kit similar to that used for the sample vials. To ingest the dose, a crewman removed the protective caps, assembled the syringe, and delivered the contents directly into his mouth. Used dose syringes were left assembled with the tips capped and stowed in an empty food locker.

A test subject collected saliva by placing a dental cotton roll under his tongue for several minutes and then replacing the saturated cotton in the vial. It was determined in supporting studies that samples could be stored for over a week at ambient temperature without affecting isotope content, provided they were protected from evaporation. Sample vials were replaced in the original kit and stowed in a different locker from the used dose syringes. This precaution was taken to minimize the possibility of accidental contamination of the sample vial contents. The samples were frozen at -70° C after being returned to the laboratory.

The usefulness of the TBW measurement is greatly enhanced if body mass can be measured as well, since this enables the calculation of the TBW to total body mass ratio. Body mass measurements were obtained on days F-33, F-30, F-24, F-7, L + 0, and L + 3 (Table 2). Since these measurements were obtained at three different locations and presumably under three different protocols, their interpretation is difficult.

OXYGEN-18 ANALYSIS

Analyses of the samples were carried out in ground-based facilities of the Stable Isotope Laboratory at Baylor College of Medicine. Frozen samples were thawed and approximately 0.3-0.5 g aliquots were transferred to preweighed 20-ml Vacutainer serum tubes using disposable plastic tuberculin syringes. The tubes were reweighed to determine the mass of the sample. The tubes were then filled with 5% carbon dioxide, 95% nitrogen and equilibrated for 48-72 hours at 25° C. The cryogenically purified carbon dioxide was analyzed using a Model 3-60 Gas Isotope Ratio Mass Spectrometer (Nuclide Corp., University Park, PA). Details of the analytic procedure and calculation are found in Schoeller et al. (5,6).

RESULTS

The results of the experiment are summarized in Table 3. The eight gaps in this table represent five missing samples, one sample collected late, and two values which were spuriously high, perhaps owing to inadvertent dilution of the sample during collection. The values in the table are not corrected for fluid intake during the period of the experiment.

The data were analyzed according to the general mixed model analysis of variance, utilizing BMDP module BMDP3V (BMDP

Statistical Software, Los Angeles, CA). Subject was treated as a random variable, while mission day and sample time were regarded as fixed variables. Various null hypotheses were tested to identify the source of the variance. These are listed in Table 4. In addition, the multiple comparisons test (1,2) was applied to test for significantly different means of TBW for the different phases of the mission. This test is summarized in Table 5.

No attempt has been made at this time to make a similar analysis using the ratio of TBW to body mass.

In agreement with previous observations, the galley water was found to be enriched in ^{18}O, i.e., the enrichment was approximately 40 parts per thousand. The actual ratio of ^{18}O to ^{16}O in galley water was 0.00216, which may be compared with the ratio observed in normal surface water, 0.00208. The source of this enrichment has not been identified, although it is possibly due to boil-off during ground storage of the liquid oxygen used in the fuel cells.

Table 4. Results of analysis of variance using the general mixed model.

Source of variation	Type of factor	Chi-squared	df	p-value
Subject	random	10.729	1	0.001
Hour	fixed	2.538	1	0.111
Day	fixed	10.931	5	0.053
Hour * Day	fixed	7.060	5	0.216
Hour * Subject	random	0.0	1	0.998
Day * Subject	random	9.514	1	0.002
Hour * Day * Subject	random	0.0	1	0.998

The analysis summarized in Table 4 was based on the assumption that the day of measurement, i.e., the phase of the mission, was a fixed treatment effect. Under the hypothesis that this treatment had no effect, the resulting ratio of variances would be observed with a probability of 0.053, indicating that day of observation was a significant factor in explaining the observed variance. According to the usual convention of rejecting a null hypothesis for p-values smaller than 0.05, the decision to reject was borderline at this level of probability.

Table 5. Multiple comparisons test for arithmetic means of test days.

Comparison	F	Critical F p=0.05	Critical F p=0.10
Preflight vs. Inflight	5.145	6.61	4.06
Preflight vs. Postflight	0.254		
Inflight vs. Postflight	2.073		
FD 2 vs. FD 4,5	1.852		

From Table 5 it is apparent that the preflight values of TBW are significantly different from the inflight values at the 0.10 level. The fact that the inflight vs. postflight means are not significantly different can possibly be traced to the limited number of measurements conducted postflight.

It is clear from the foregoing discussion that additional measurements under similar conditions are highly desirable. Future measurements would ideally be made on the same schedule as was actually obtained on this flight, even though this schedule departed from the planned protocol.

CONCLUSIONS

It was concluded that TBW probably decreases by about 3% during exposure to microgravity. On the other hand, the differences between FD 2 and FD 4,5 were not significant, suggesting that the decrease had occurred by the second day inflight. These tentative conclusions were based on a limited number of observations on a small number of subjects, and must therefore be accepted with a degree of reservation until further measurements can be made under closely similar conditions.

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HEIGHT CHANGES IN MICROGRAVITY

Investigators: William E. Thornton, M.D., and Thomas P. Moore, M.D.

INTRODUCTION

Variations in height with position, from supine to upright and vice versa, and slow decreases in height from time of arising through the course of the day have been noted for some time. Difficulties were experienced by some crewmen in donning their unyielding space suits inflight and on the moon.

Changes in height during weightlessness were first documented on Skylab Mission 4, and again demonstrated on the Apollo Soyuz Test Project. Supine and upright height variations on Earth and the time course of these changes with and without varying loads have been investigated by Thornton and others. A series of inflight studies was also performed on the Shuttle missions. These studies and experiences resulted in adding an inch to the spacesuit torso length.

Results from the studies are consistent; the intervertebral discs expand or compress with changing load in a biphasic fashion. There is an immediate change in height with load followed by a slower change with a time constant of hours.

While the magnitude of such changes is fairly well established for weightlessness, their time course was unknown; this was studied as follows.

PROCEDURES

The barefooted subject was positioned standing fully erect, back against a wall and exerting downward pressure with his hands to ensure maintaining solid contact with the floor, Figure 1. A square jig was placed against the wall with its top just touching the subject's vertex, and an index mark was made on the wall. Pre- and postflight measurements were made in a similar fashion and the changes were measured to 1/16 of an inch.

RESULTS / CONCLUSIONS

The height data for one subject are tabulated in Table 1 and plotted in Figure 2. The model proposed by the investigator, and independently by Kazarian, predicts an exponential increase in height under flight conditions. When plotted in semilogarithmic fashion, all but one of the points follow such a curve with a time constant (1/e point) of 10 hours.

Table 1. Height of Subject Crewmember

Height, in.								
Preflight	Inflight*							Postflight
	02:40	04:20	08:00	23:30	29:30	50:32	73:30	R+1.5 h
71.5	72.00	72.50	72.50	72.75	73.00	73.00	73.00	71.5
	.5	1.0	1.25	1.5	1.6	1.5	1.5	0
%	(.70)	(1.40)	(1.75)	(2.10)	(2.10)	(2.10)	(2.10)	

*MET - Mission Elapsed Time

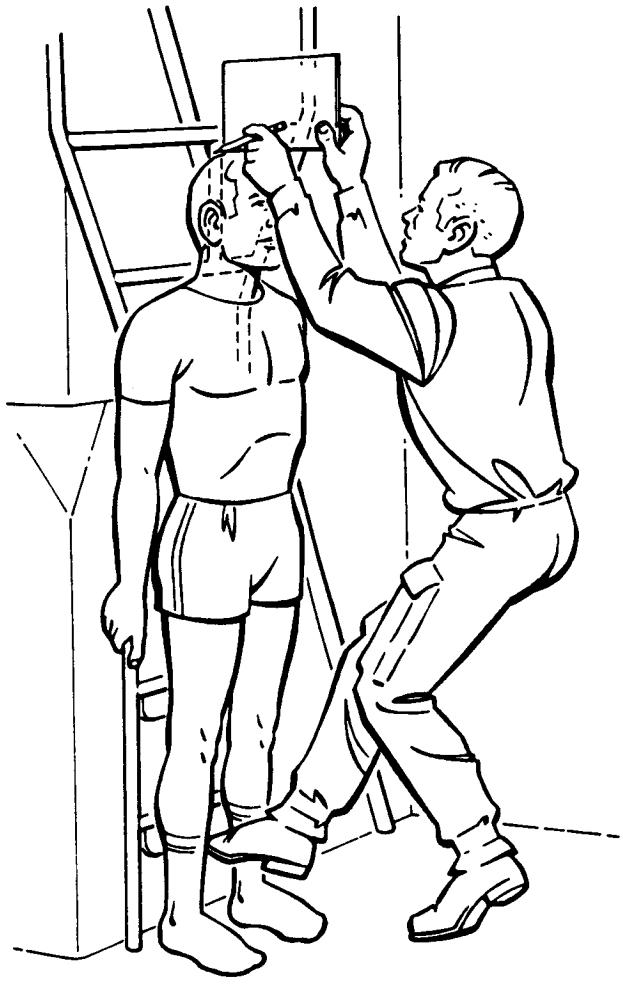

Figure 1. Sketch of inflight height determination. Level of mark above floor was measured and recorded.

COMMENTS

This was the first opportunity to follow the time course of these changes in weightlessness and the results were consistent with the theory of the phenomenon. The absolute value of observed change was 1.5 inches.

It would seem reasonable to extend this measurement to a population large enough to be statistically significant. Should it ever become necessary to accurately allow for such changes, as in equipment design, prediction procedure might be developed by studying the correlation of inflight to one-g changes in the same subject from a suitable population; if a consistent relationship were found, the flight value could be predicted from one-g changes.

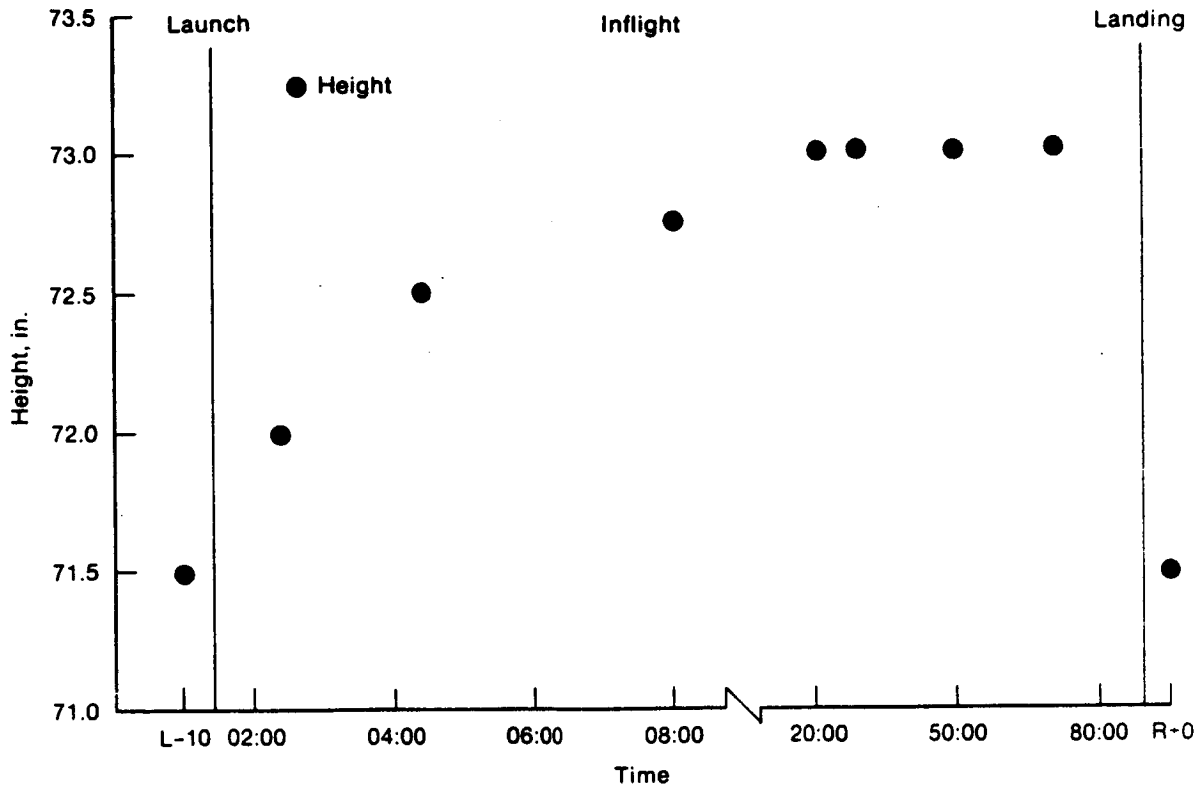

Figure 2. Pre-, in-, and postflight height changes for one subject. Note that time was truncated between 08:00 and 20:00.

INFLIGHT AND POSTFLIGHT FLUID SHIFTS MEASURED BY LEG VOLUME CHANGES

Investigators: Thomas P. Moore, M.D., and William E. Thornton, M.D.

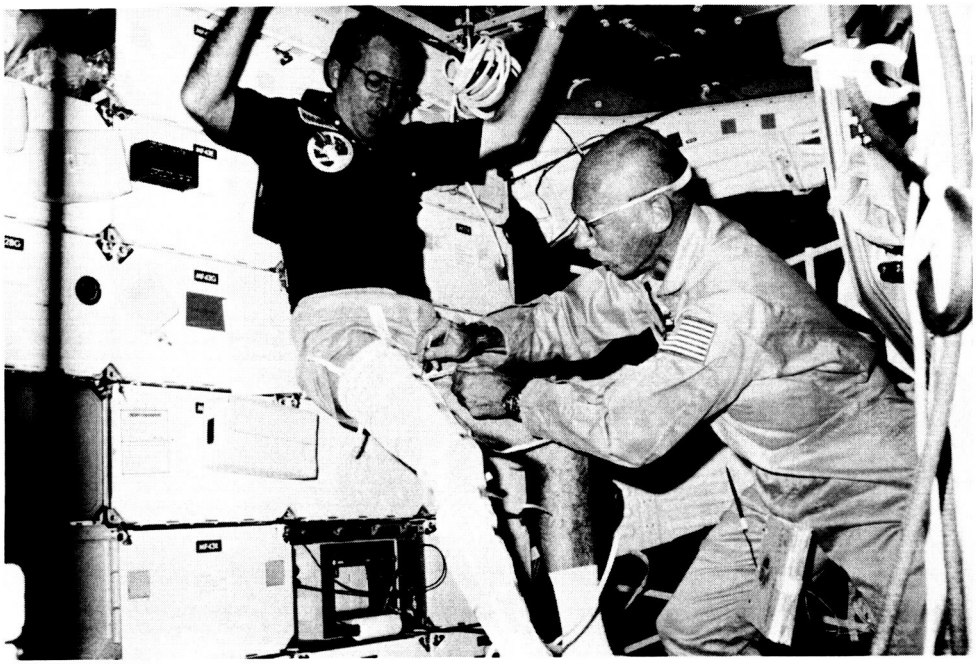

Figure 1. Shuttle crewmembers taking plethysmograph measurements.

INTRODUCTION

Signs and symptoms secondary to fluid shifts in weightlessness were among the first physiologic effects noted in the manned spaceflight program. These effects included puffy faces, nasal congestion, inflight and postflight weight loss, orthostatic hypotension, cardiovascular changes and the "bird legs of space"(1). The headward shift of body fluids, both intravascular and extravascular, results from the absence of the 1-G hydrostatic gradient.

Measurement of changes in leg volume were made pre- and postflight on Apollo 16 and 17 and subsequently on Skylab 2, 3, and 4 by Hoffler et. al (3). The volume measurement was accomplished by using a modification of a measurement system for fitting support stockings. Single-point calf girth measurements were also done inflight on Skylab 2, 3, and 4. The postflight leg volume measurements made on these missions were late in the recovery period after the return of fluid was largely over. The inflight calf measurement was subsequently shown not to be characteristic of the entire leg volume, and hence neither the time course nor magnitude of the changes were appreciated.

On Skylab 4, inflight changes in leg volume were documented using a tape measure system. The results showed volume losses of several liters from the legs (5). This data provided the initial groundwork for formulation of a basis of understanding of postflight weight loss, orthostatic hypotension and other observed space flight phenomena.

A repeat of the leg volume study was performed on the Apollo-Soyuz Test Project (ASTP) which confirmed the volume changes but raised questions on the time course of the fluid shifts (2). While these studies answered a

fundamental question regarding the approximate magnitude of fluid shifts, many significant details remained unknown, including the time course during launch and recovery, the volume distribution as a function of time, and the volume and distribution during orthostatic stress.

On the third Skylab mission, SL-4, the first inflight volume measurement was made on Mission Day 3 (MD-3). From this data it was concluded that the major volume change had occurred prior to the MD-3 measurement. On the ASTP one crewmember was able to obtain a measurement at a Mission Elapsed Time (MET) of 06:00 hours. This value reflected only a portion of the shift observed to occur during the subsequent inflight measurements which started at 32:00 hours MET. From the ASTP data the investigators hypothesized and concluded that the major shift of fluid volume from the legs did not occur in the first few hours of orbital exposure; rather, the time course of the fluid shift was likely to assume an exponential form with maximal rate of decrement within the first 24 hours and a distant plateau evident by 3 to 5 days.

PROCEDURES

The methodology used for these studies was tedious and time consuming. There was no opportunity for repeat studies until the Space Shuttle became operational. Other methods of volume determination, such as water displacement, are impractical in the weightless environment of space or are logistically difficult and time and equipment intensive. A simpler, much more rapid scheme for obtaining volumes was therefore devised and resulted in the stocking plethysmograph used during the Shuttle program (Fig. 2). This scheme was routinely used on several Shuttle flights (Fig. 1). Inflight data from early Shuttle missions was obtained at 11:00 and 13:00 hours MET (4). The conclusion from these data was that by the time of these measurements the fluid shift from the legs was essentially complete since later inflight measurements showed no further significant leg volume loss. Therefore, this experiment was designed to obtain data during the critical early on-orbit time frame as well as throughout the mission, in order to define and delineate the time course and hopefully to further understand the dynamics of the fluid shifts.

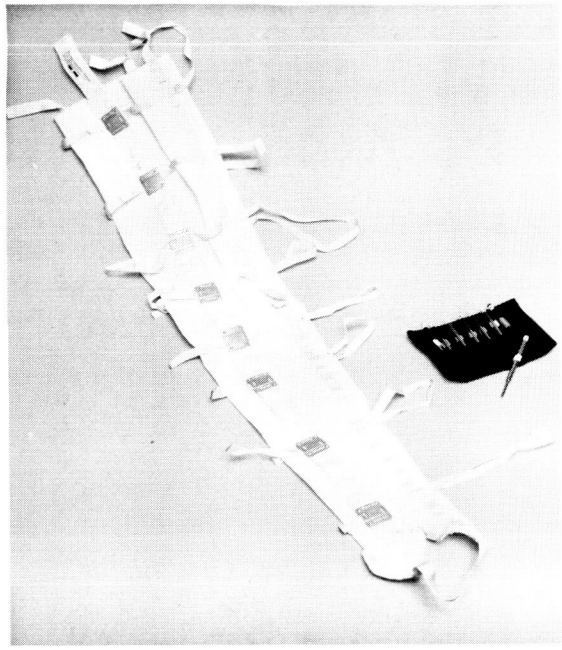

Figure 2. The stocking plethysmograph.

The measurement of body segment volumes presents problems since they are irregular and compressible. The stocking plethysmograph employed the use of direct girth-length measurements. From a series of circumferential measurements, volume was calculated under the assumption that a truncated cone represents a reasonable approximation of a leg volume segment. Using the formula for the frustum of a cone, $V = \pi L/3(R_1^2 + R_1 R_2 + R_2^2)$, the volumes of individual leg segments were calculated. Leg girths were measured to the nearest 5mm and the volume derived for each volume segment with total volume determined by the summation of these volume segments (Fig. 3). This assumption represents the first source of error in this method since the human leg is not shaped as a perfect cone. However, with the number and location of the volume segments used, this error was minimized. Another potential source of error existed in reproducing vertical location of the measuring tapes over successive measurements. Nonelastic longitudinal tapes were used to ensure consistent vertical location of the circumferential measuring tapes.

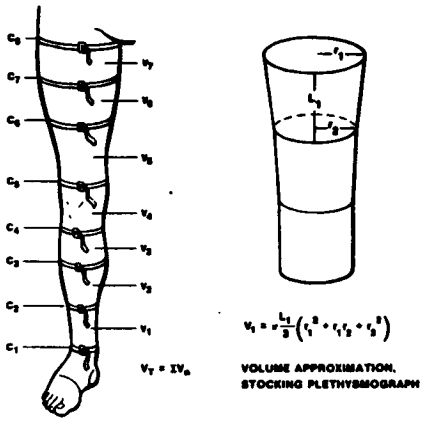

Figure 3. Volume approximation, stocking plethysmograph.

Physiological and anatomical factors produce a series of potential errors. Changes in relaxation or contraction of muscles and the anatomical position of leg segments will produce volume changes. Changes in body position as one moves from the supine to the standing position cause minor shifts in tissue volume and subsequent volume changes. Similar changes in tissue shapes and volumes are induced when going from 1-G to the weightlessness environment.

These potential sources of errors were realized and, insofar as possible, were examined or controlled. It was decided to anatomically divide the leg into 7 volume segments, 3 above the knee, 3 below the knee and 1 including the knee. Therefore, the stocking plethysmograph utilized 8 circumferential measuring tapes. Specific anatomical landmarks and locations were used for the determination of position of the 8 circumferential tapes. Eight different colored pens were used to mark the circumferential tapes and record the mission elapsed time (MET) directly onto the stocking. Each circumferential tape was then measured upon return from flight.

A large effort was put into the design, selection of materials, and design testing of the stocking plethysmograph. Due to limited development time for the first flight of the stocking, a plastic marking window was used. It was found that it did not produce uniform friction on the measuring tapes, introducing significant errors in measurements. A uniform and consistent metal marking window was then designed and used on subsequent missions.

A series of repeatability and validity tests was run, comparing the stockings to a tape measure. For repeatability, multiple tests of 5 on and off repetitive measurements were made. The standard deviation of the circumference measurement of the stocking was .25 cm versus .36 cm for the tape measure. The average difference between the stocking measurement and the tape measure was +.27 cm for the stocking method. In looking at the vertical variation of the location of the 8 circumferential tapes, a standard deviation for repeated measurements of .50 cm was found.

When comparing the stocking method versus the water displacement method, a mean difference of + 380 mls was found for the stocking method. This was believed to be well within acceptable limits taking into account the compressive effects of hydrostatic pressure associated with the water displacement method.

RESULTS

The leg volume changes from the Shuttle Program with comparison to Skylab and ASTP are illustrated in Table 1. Volume determinations were made on subjects on 5 different Space Shuttle flights. Two of the subjects made measurements on 2 separate Shuttle missions as indicated. Over 140 inflight measurements were made. The inflight volumes, illustrated in the table, reflect the mean of all measurements made during the missions except for early-on-orbit measurements (Mission Day 1) made on 3 subjects on two separate missions. These measurements were not included because they reflect volume determinations made during the time periods of active shifting of fluids from the legs (launch position). The data for these three subjects are presented in Tables 2 to 4 and Figures 4 to 6.

Table 1. SUMMARY OF LEG VOLUME CHANGES FOR THE SPACE SHUTTLE PROGRAM, SKYLAB, AND ASTP

	PREFLIGHT TOTAL VOLUME (ml)	INFLIGHT VOLUME CHANGE (ml)	INFLIGHT PERCENTAGE CHANGE	LANDING VOLUME CHANGE	LANDING PERCENTAGE CHANGE	POSTFLIGHT VOLUME CHANGE	POSTFLIGHT PERCENTAGE CHANGE
SHUTTLE CREWMAN A (1)	8,549	952	11.1	-	-	229	2.7
SHUTTLE CREWMAN B	7,735	962	12.4	439	5.7	-	-
SHUTTLE CREWMAN C	9,003	1,069	11.9	380	4.2	305	3.4
SHUTTLE CREWMAN D	8,227	860	10.5	370	4.5	291	3.5
SHUTTLE CREWMAN E	9,028	1,116	12.4	517	5.7	394	4.4
SHUTTLE CREWMAN F (2)	10,612	1,790	16.9	951	8.0	714	7.0
SHUTTLE CREWMAN G	8,656	1,096	12.7	326	3.8	337	3.9
SHUTTLE CREWMAN H (1)	8,422	685	8.3	200	2.4	88	1.0
SHUTTLE CREWMAN J (2)	10,540	1,164	11.4	+89	+.8	43	.4
SHUTTLE CREWMAN K	8,011	855	10.7	597	7.5	402	5.0
SHUTTLE CREWMAN L	7,560	740	9.8	119	1.6	30	.4
MEAN	8,758	1,026	11.6	381	4.3	283	3.2
SKYLAB	7,679	931	12.2	574	6.6	312	3.2
ASTP	7,957	803	10.0	477	6.0	387	4.9

(1) (2) - INDICATES THE SAME CREWMEMBER ON DIFFERENT MISSIONS

The volume change and percentage change are all compared with the preflight volume determinations. The landing measurements were made within 1.5 hours of touchdown. The postflight measurements were made during the first week postlanding through recovery plus 6 days (R + 6). It should be noted that the 1-G leg volume measurements for Skylab and ASTP were made with the crewmembers in the supine position, whereas the measurements in the Shuttle program were made with the crewmembers standing. When going from standing to supine, there is a shift of approximately 300ml of blood out of the legs.

This should be recognized and taken into account when comparing the data from these different space flights. There was an average inflight shifting of 1026ml, or 11.6% per leg. This compares with the Skylab findings of 931ml and 12.2% and ASTP of 803ml and 10%. Landing volume determinations showed a mean decrease of 381ml or 4.3%. Postflight measurements taken at various times from recovery plus 1 day through 1 week post recovery show a residual volume decrement as compared to preflight of 283ml or 3.2%.

Table 2. SEGMENTAL LEG VOLUME CHANGES FOR SHUTTLE CREWMAN G

	PREFLIGHT (n = 23)		INFLIGHT MD 1 (n = 1)	INFLIGHT MD 2-7 (n = 8)	POSTFLIGHT (n = 3)
ABOVE KNEE	5656 ml	(Volume)	5025 ml	4867 ml	5440 ml
		(Vol Change)	- 631	- 789	- 216
	65.3% OF TOTAL	(% Change)	11.1%	14.0%	3.8%
BELOW KNEE	3000 ml	(Volume)	2825 ml	2693 ml	2879 ml
		(Vol Change)	- 175	- 317	- 121
	34.7%	(% Change)	5.8%	10.6%	4.0%
TOTALS	8656 ml		7850 ml	7560 ml	8319 ml
		(Total Volume Change)	- 806	- 1096	- 337
		(Total % Change)	9.3%	12.7%	3.9%

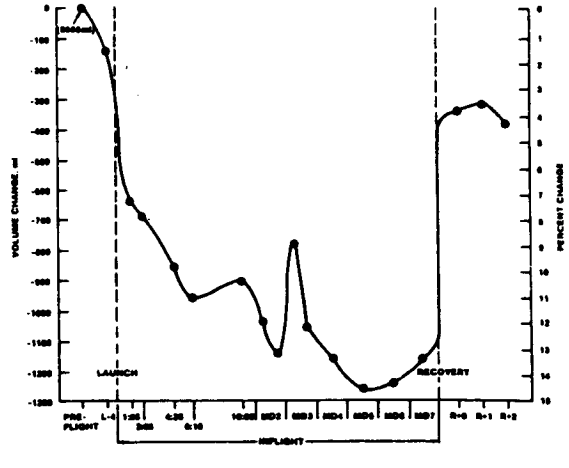

Figure 4. Leg volume changes for Shuttle crewman G.

Table 3. SEGMENTAL LEG VOLUME CHANGES FOR SHUTTLE CREWMAN K

	PREFLIGHT (n = 9)		INFLIGHT MD 1 (n = 5)	INFLIGHT MD 2-7 (n = 4)	POSTFLIGHT (n = 6)
ABOVE KNEE	5656 ml	(Volume)	4402 ml	4300 ml	4575 ml
		(Vol. Change)	- 442	- 544	- 268
	60.5% OF TOTAL	(% Change)	9.1%	11.2%	5.6%
BELOW KNEE	3000 ml	(Volume)	2957 ml	2856 ml	3034 ml
		(Vol Change)	- 210	- 311	- 133
	39.5%	(% Change)	6.6%	9.8%	4.2%
TOTALS	8011 ml		7359 ml	7156 ml	7609 ml
		(Total Volume Change)	- 652	- 855	- 402
		(Total % Change)	8.9%	10.7%	5.0%

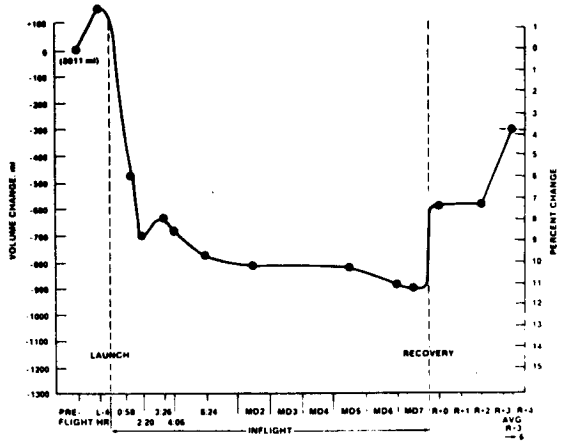

Figure 5. Leg volume changes for Shuttle crewman K.

Tables 2 to 4 and Figures 4 to 6 show the leg volume changes in the 3 crewmembers who wore the stocking plethysmograph during launch and were able to make a series of measurements during Mission Day 1 (MD1). Figures 4 to 6 illustrate the time course of the volume changes throughout the missions as compared with the mean of preflight measurements. The measurements represented are: one taken 4 hours prior to launch, five inflight volumes during MD1 (represented by mission elapsed times [MET] on the graph), those taken on MD2 through MD7, one taken at recovery, and those made postflight through the sixth day after landing.

The leg volumes in Tables 2, 3 and 4 are broken down into above- and below-knee values and percentages along with the relative changes inflight and postflight in these two regions of the leg. The mean MD1 volume change ranged from a decrease of 573ml (7.6%) in Subject L to 806ml (9.3%) in Subject G. MD2-7 volume decreases were also greatest in Subject G of 1096ml or 12.7%, with the lowest being 740ml or 9.8%. All of the crewmembers exhibited significantly greater absolute volume changes as well as relative percentage changes occurring above the knee as opposed to below the knee.

Table 4. SEGMENTAL LEG VOLUME CHANGES FOR SHUTTLE CREWMAN L

	PREFLIGHT (n = 8)		INFLIGHT MD 1 (n = 5)	INFLIGHT MD 2-7 (n = 3)	POSTFLIGHT (n = 7)
ABOVE KNEE	4819 ml	(Volume)	4397 ml	4296 ml	4822 ml
		(Vol. Change)	- 442	- 532	+ 3
	63.7% OF TOTAL	(% Change)	8.8%	10.9%	0%
BELOW KNEE	2741 ml	(Volume)	2590 ml	2524 ml	2708 ml
		(Vol Change)	- 151	- 217	- 33
	36.3%	(% Change)	5.5%	7.9%	1.2%
TOTALS	7560 ml		6987 ml	6820 ml	7530 ml
		(Total Volume Change)	- 573	- 740	- 30
		(Total % Change)	7.6%	9.8%	.4%

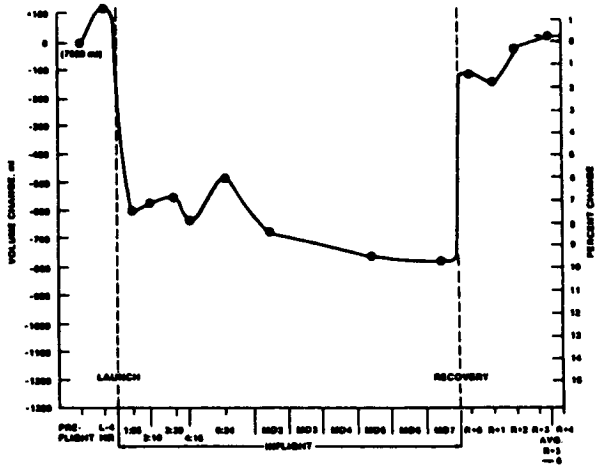

Figure 6. Leg volume changes for Shuttle crewman L.

The postflight residual volume decrement ranged from 30ml (.4%) to 402ml (5.0%).

The mean data of the 3 crewmembers (G, K, L) are presented in Table 5. Again, breakdowns of the total volumes above- and below-knee are illustrated for the preflight, inflight and postflight leg volumes. For these two regions, the volume, volume change from preflight, percentage of the total volume change that comes from that region, and the absolute percentage change along with the total change are shown. There was an average MD-1 volume change of 677ml or 8.4% and a MD2 through MD7 change of 897ml or 11.1%. An average 619ml or 69% of this volume change came from above the knee or the thigh with only 287ml or 31% arising from below the knee. There was a postflight volume decrease of 257ml or 3.2% as recorded during the first week postflight.

Table 5. MEAN SEGMENTAL LEG VOLUME CHANGES ON TWO SHUTTLE FLIGHTS (CREWMEN G, K, AND L)

	PREFLIGHT		INFLIGHT MD 1	INFLIGHT MD 2-7	POSTFLIGHT
ABOVE KNEE	5107 ml	(Volume)	4608 ml	4488 ml	4946 ml
		(Vol. Change)	- 499 ml	- 619 ml	- 161 ml
		(% of Total Change)	74%	69%	63%
	63.2% OF TOTAL	(% Change)	9.8%	12.1%	3.2%
BELOW KNEE	2969 ml	(Volume)	2791 ml	2691 ml	2873 ml
		(Vol Change)	- 178 ml	- 278 ml	- 96 ml
		(% of Total Change)	26%	31%	37%
	36.8%	(% Change)	6.0%	9.4%	3.2%
TOTALS	8076 ml		7399 ml	7179 ml	7819 ml
		(Total Volume Change)	- 677 ml	- 897 ml	- 257 ml
		(Total % Change)	8.4%	11.1%	3.2%

DISCUSSION

The inflight volume changes found in the 11 subjects from the Shuttle program demonstrated a mean volume change of 1026ml or 11.6% with a range from 1790ml or 16.9% to 685ml or 8.3%. The majority of the subjects had a 10% to 12% volume change. This compares with the 12.2% from Skylab and 10.0% from ASTP. The source of this leg volume change is a relatively rapid shift of blood followed by interstitial fluid and probably intercellular fluid, with some tissue loss secondary to muscle atrophy. It should be noted that one crewmember (Subject F, J) had a significantly larger volume change on his first flight (1790ml, 16.9%) than the mean, and also the volume change of his second flight was considerably smaller than the first (1164ml, 11.4%). There is no good explanation for these findings. No procedural or experimental error was identified, and the same stocking plethysmograph was used on both flights. The crewmember did experience Space Motion Sickness symptoms on both missions. He related that he believed his level of hydration was the same for both flights; however, there was noted a greater weight loss on his first flight (11 lbs. versus 7 lbs. for the second flight). The three crewmembers from whom data were obtained shortly after launch and throughout MD1 provided valuable information concerning the dynamics of the fluid shift. The actual fluid shift is complicated by the prelaunch position of lying on one's back in the spacecraft with the legs elevated for up to 2 hours prior to liftoff. The crewmembers universally commented that they believed this position is a stimulus to shifting of fluid prior to launch because of noted bladder distension and the common need to urinate while still on the launch pad. Another environmental stimulus to the fluid shift is the increase in G forces encountered during the launch profile. As stated, the crewmember is positioned on his back at T-zero; then, as the Space Shuttle rotates to an inverted position shortly after clearing the launch tower, the crewmember is also rotated to an inverted position. While in this position throughout the launch and entry profile, +G forces are exerted and reach a maximum of 3.4 G's during the approximate 8 minutes prior to main engine cut-off, orbit insertion and weightlessness. Taking into account these factors, the total volume curves show a logarithmic decrement for approximately the first 6 to 10 hours on orbit, after which there appears to be a plateauing with slight downward slope, with some variability in the daily measurements. The variability may be related to circadian rhythm variations. This is not consistent with the ASTP data, where a subject showed only a 260 ml change from his launch minus 1 day volume at an MET of 0600 hours, reflecting only a 30% shift of his mean total inflight volume reduction of 900 ml. The repeated measurents of these three crewmembers at the various time intervals on the two missions gives one more assurance of accuracy. Of great interest is the source of shift.

The reduction in leg volume is not evenly distributed, with the mid-thigh losing more than 12% of its volume versus 9.4% from the lower leg. When the much larger volume of the thigh is considered, the importance of the upper leg can be appreciated; e.g., more than twice the volume was removed from the thigh versus lower leg (619 versus 278ml- see Table 5). Possibly of more interest than this removal is the replacement of fluid upon return to earth and the gravity environment. Landing and postflight data from Table 1 shows the inflight reduction in leg volume was not totally restored following landing and postflight. However, it does appear that the majority of volume return was complete within 1.5 hours after landing. On the Shuttle crewmembers there was a reduction of 381ml or 4.3% 1.5 hours after landing and 283ml or 3.2% postflight. Skylab and ASTP had higher landing volume reductions and similar postflight reductions. This phenomena was previously observed and the assumptions are that (A) fluid redistribution under 1-G is more rapid than loss in weightlessness (such an assumption is consistent with the difference in driving forces), and (B) the remaining volume deficit is lost tissue due to atrophic changes from deconditioning. As noted, there is considerable variation between subjects which could reflect variations in weight loss. No consistent and reliable prelaunch and landing crewmember weights are recorded. However, in personal conversations, the crewmembers usually note a 3 to 7 pound weight loss during the missions.

Because of medical confidentiality, it is not indicated on Table 1 which crewmembers experienced symptoms of Space Motion Sickness (SMS). However, it may be reported that 7 of the 11 subjects did experience SMS. There was no difference in the leg volume change in those with SMS (11.6% change) when compared to those without SMS (11.7% change).

CONCLUSIONS

This was a study of the inflight and postflight leg volume changes associated with spaceflight. The results of this study show that there typically is an inflight volume change of 2 liters in the lower extremities, 1 liter from each leg. The vast majority of this change appears to be a shift in body fluids, both intravascular and extravascular. The fluid shift occurs rapidly on Mission Day 1 (MD-1), being essentially complete by 6 to 10 hours. The regional origin of shift and leg volume change shows that a far greater absolute volume and percentage of the total change comes from the thigh as compared to the lower leg. Postflight, the return of fluid to the lower extremities occurs rapidly with the majority of volume return complete within 1.5 hours postlanding. There is a residual postflight volume decrement that is probably due to tissue loss secondary to atrophic deconditioning and weight loss.

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INFLIGHT HOLTER MONITORING

Investigators: Michael W. Bungo, M.D., and John B. Charles, Ph.D.

INTRODUCTION

The incidence of cardiac rhythm abnormalities during Space Shuttle Extravehicular Activities (EVAs) is about 40% in individuals who do not exhibit such abnormalities during equivalent preflight stresses. It was hypothesized that some aspect of the space flight EVA environment was the instigating factor. Potential candidates included: a physiological response to microgravity (including fluid volume loss due to diuresis and/or vomiting; uncorrected electrolyte imbalance due to diuresis and/or vomiting) which is detected only during EVA due to the lack of ECG information during other flight phases; a response to the EVA workload; a response to the EVA environment of pure oxygen at 4.3 p.s.i.; a response to other environmental factors, such as low humidity. Strenuous activities during previous U.S. manned space flights did not produce equivalent frequencies of arrhythmias, for reasons that are unknown. Therefore, efforts to document the current phenomenon are considered of operational importance.

PROCEDURES

Baseline responses to treadmill stress testing were recorded during the physical exams. In addition, the subject wore a Holter recorder for 24 hours at some time during the preflight period.

Training included maintenance and use of a Holter recorder, familiarization with the STS onboard treadmill and its accessories, and familiarization with the Operational Bioinstrumentation System ECG harness assembly.

As planned preflight, the proposed test procedures were to be as follows: During the last 24 hours inflight, the subject was to instrument himself with ECG electrodes, attach and activate the Holter recorder, and go about his normal activities. During this period, he was to don the Operational Bioinstrumentation System (OBS) harness, mount the treadmill, don the bungee restraint cords, and "stand" quietly on the treadmill for 5 minutes. He was then to exercise at 70-85% of his maximum heart rate for a period of about 30 minutes. Following the exercise period, he was to remove the OBS harness, stow the treadmill, replace any ECG electrodes loosened by sweat, and resume his normal daily activities.

The subject was to continue wearing the Holter recorder through deorbit preparations, landing, seat egress, and arrival at the medical facility for post-flight testing.

FLIGHT EVENTS

The subject attempted to perform the experimental protocol exactly according to the Medical Check List; however, because of real-time changes in the flight timeline and minor equipment malfunctions, the events are summarized as follows.

The Holter Monitor was placed as appropriate on the morning of the treadmill run. The treadmill test was begun according to established procedure. At the end of a twenty minute treadmill run, it was noted that the Treadmill Data Recorder was not functioning, and the recorder was recycled and began functioning correctly. Thirteen additional minutes of exercise were performed. Treadmill speed was approximately 2.5 m.p.h. during the duration of the run. After 9-10 minutes of exercise (a heart rate of 130-135 b.p.m.) it was noted that the pulse meter was not tracking well and the subject voluntarily increased his work load to 150-155 b.p.m. for the remainder of the thirteen minute exercise period. At the end of that flight day it was noted that the Holter Monitor had jammed and most of the data had been lost. A backup Monitor was donned and worn for the remainder of the

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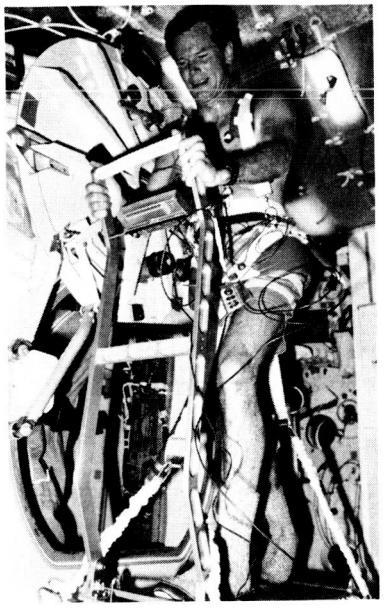

Figure 1. Subject performs an inflight treadmill stress test.

flight (shut off for a period of time because of a delay in landing) which included the entry profile. In all, 22 hrs. of recording were obtained on the inflight Holter Monitor and an additional exercise period as above recorded on the Treadmill Data Recorder. Two 24 hr. preflight Holter records were made as baseline data. All hardware discrepancies were investigated and corrected.

RESULTS

Preflight monitoring revealed a rare Ventricular Premature Beat (VPB) and rare Atrial Premature Beat. The inflight recording revealed four isolated VPBs during the recording period, and none during exercise nor entry.

CONCLUSIONS

There was no increase in ectopic activity in this crewmember during space flight and/or exercise in contrast to increased dysrhythmias seen during previous Shuttle EVA activities. This may be due to the natural variability between subjects or may relate more specifically to the particular environmental conditions unique to EVA. Further investigations are suggested.

NONINVASIVE ESTIMATION OF CENTRAL VENOUS PRESSURE USING A COMPACT DOPPLER ULTRASOUND SYSTEM

Investigators: John B. Charles, Ph.D., and Michael W. Bungo, M.D.

INTRODUCTION

The headward fluid shift encountered during space flight involves the redistribution of body fluids from the legs and abdomen into the thorax and head. This fluid shift is believed to initiate the cardiovascular read aptation syndrome (CRAS) of responses to space flight by stimulating arterial and cardiopulmonary sensors. The physiological responses to this stimulation may include reduction in plasma volume and resetting of cardiovascular reflexes controlling vascular volume and tone. These adaptive changes are appropriate for space flight, but inappropriate for life on earth after the space flight. The ability to counter those changes which are deleterious requires a complete understanding of the changes involved in CRAS, starting with a thorough documentation of the fluid shift and its effects. One means of tracking the fluid shift is by observing its effects on the central venous pressure (CVP), which is the filling pressure of the heart. A technique for the rapid, convenient and noninvasive estimation of CVP in space flight crewmembers would provide important insights into the reflex control of the cardiovascular system both in space flight and on earth.

METHODS

The method of Durr et al. (1) was used. Briefly, a small uni-directional vascular doppler flow detector was used to monitor the jugular venous blood flow while end-expiratory intrathoracic pressure was increased by partially occluded expiration. The intrathoracic pressure (mouth pressure, as indicated by a digital display on an electronic manometer) which transiently interrupted jugular blood flow was taken as an estimate of central venous pressure.

One crewmember was the subject for this experiment (Fig. 1). Preflight control measurements were made in the supine position at 34, 33, 31, and 10 days before launch. Inflight measurements were made at regular intervals during the first, second, third, fourth, and sixth days.

Figure 1. Subject performing an inflight CVP estimation.

RESULTS

The averaged values from each flight day are shown in Figure 2 [with the Spacelab 1 values from Kirsch et al. (2) for comparison]. The averaged values for each inflight data collection session are shown in Figure 3 (NB: the pressure axis is not corrected to cm. H_2O). Preflight supine values averaged about 4.2 cm. H_2O. Inflight values were always lower than the

preflight average, and decreased over the first three flight days to their minimum, where they remained for the duration of the flight. Measurements during the first two flight days indicate an increase in CVP over the awake period; measurements from flight days 3-5 suggest a small increase followed by a pronounced decrease in CVP over the awake period.

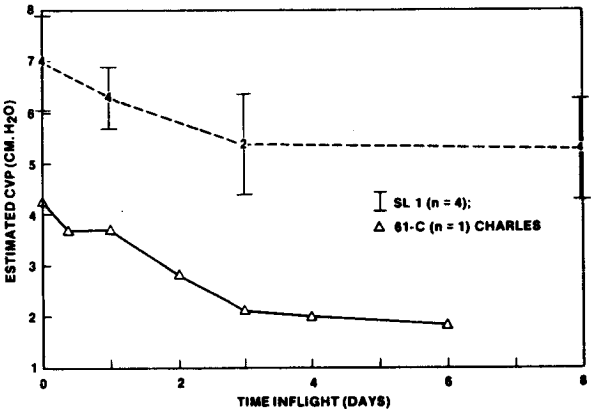

Figure 2. Estimated CVP during space flight.

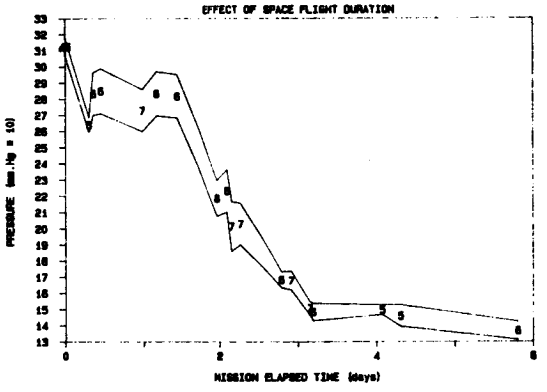

Figure 3. Jugular venous stop flow pressure.

DISCUSSION

The noninvasive estimates of CVP reported here for one subject parallel the average of the invasive measurements from 4 subjects during the Spacelab 1 flight, suggesting that the method has application for monitoring the time course of changes in CVP during space flight. The noninvasive data are of a smaller absolute magnitude than the invasive data, suggesting that the noninvasive technique is actually measuring a parameter directly related to CVP rather than CVP itself. However, the data of one of the Spacelab subjects are similar in magnitude, indicating that individual variability may explain the difference. Such an "offset" has not been detected in measurements on earth (1), but may exist during space flight. This hypothesis may be tested in a future space flight by comparing estimated CVP using the noninvasive method with CVP measured simultaneously using a right atrial catheter.

The applicability of this technique to repeated measurements will allow the testing of hypotheses regarding the acute and chronic redistribution of body fluids during space flight. For example, this flight data set suggests diurnal variations in CVP. A hypothesis (3) based on Skylab data is that inflight tolerance of lower body negative pressure (LBNP, which causes blood volume redistributions similar to standing upright) is higher in the morning than in the afternoon because the frequent use of the legs during the day for station keeping and propulsion causes a headward distribution of blood, prompting an acute decrease in leg interstitial fluid. LBNP stress during the afternoon sequesters some of the circulating volume in the "dehydrated" interstitium, decreasing the blood volume available for cerebral perfusion and reducing orthostatic tolerance. This hypothesis may be tested quickly and easily by the noninvasive estimation of CVP periodically throughout the waking hours. Similarly, the acute redistribution of fluid by exercise can be tracked by CVP measurements before and after treadmill exercise.

Another application is the determination of the influence of space motion sickness (SMS) on fluid volume adjustment. From the limited evidence to date, SMS may be associated with high levels of circulating antidiuretic hormone. Thus, afflicted individuals will retain fluid until they have adapted to space flight, while the unafflicted should begin diuresis soon after reaching orbit. These differences may be discernible in the time course of changes in CVP. Confirmation of this hypothesis could lead to new treatments for some of the effects of SMS.

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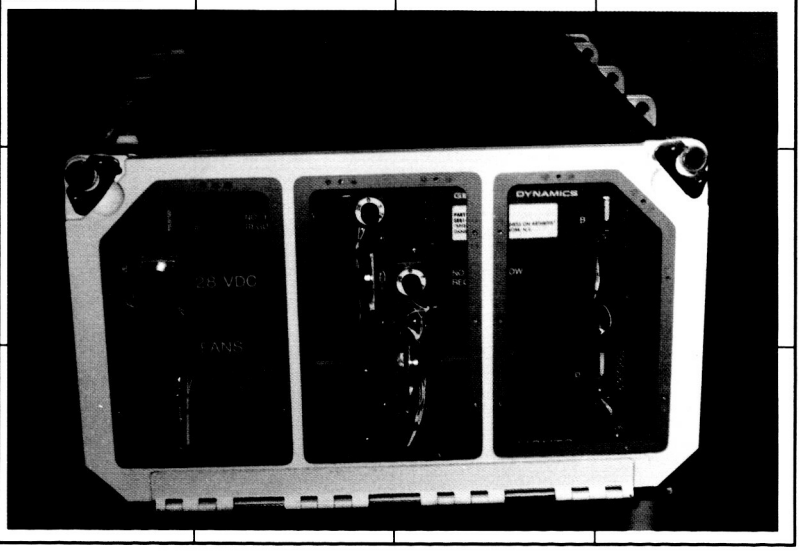
Section Three

Equipment Testing and Experiment Verification



One important function of the DSO program is evaluation of hardware prior to its use for a complex experiment. These photographs show the Animal Enclosure Module, a self-contained habitat for small laboratory animals that was tested as a DSO. The AEM fits into a standard Shuttle middeck locker (right).

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ANIMAL ENCLOSURE MODULE INFLIGHT TEST

Investigators: Malcom C. Smith, Jr., D.V.M., Philip C. Johnson, M.D., and Adrian LeBlanc, Ph.D.

INTRODUCTION

"Verification of the Mid-deck Animal Enclosure Module (AEM)" was flown as a DSO to test the efficacy of the AEM in supporting healthy animals without compromising crew safety and comfort. This study represents the first attempt to fly animals in the crew compartment of a United States space vehicle, and ground testing was accordingly rigorous.

Ground testing and logistical support procedures for the DSO are described in two reports: JSC #18858, dated March 21, 1983, "Test and Implementation Plan for Verification of the Mid-deck Animal Enclosure Module for STS DSO-0421" and JSC #19204, dated July 15, 1983, "Logistical and Operational Support Requirements for DSO-0421".

DESCRIPTION

FLIGHT HARDWARE

The AEM was originally built to support a Shuttle Student Involvement Project (SSIP) experiment entitled, "Effects of Weightlessness on Arthritis." Modifications to the AEM for flight qualification and to improve its operation included:

1. Microbial filter material on the exhaust side of the cage was glued to the metal housing to overcome leaks which occurred as a result of stitching.
2. Improved the seal of the filter housing to the cage to prevent channeling and leakage around the housing.
3. Installed a microbial filter on the inlet side of the cage to prevent back flow of unfiltered air into the cabin.
4. Provided an air-tight seal of the Lexan covers of the filter areas and the animal habitation area.

The AEM was installed in a mid-deck locker in the Shuttle Orbiter. Operation of the AEM required a 28 v DC power supply to operate air intake/exhaust fans and interior lights. Otherwise, it was a self-contained system designed to maintain 6 adult rats (250-300 g each) for seven days.

Exhaust air filtration in the AEM was accomplished by a 4-layer filter system. Layers consisted of Fiberglass (H_3PO_4 treated), Activated Carbon (H_3PO_4 treated), Fiberglass (H_3PO_4 treated), and a microbial filter (0.3-.5 μ) held between two 6 mm wire grids. Make-up air was pulled into the AEM from the Orbiter mid-deck environment by four axial flow fans. Food for the full 7-day mission was provided by a solid bar of nutrients (Teklad autoclaveable rat diet). Water was provided from raw potatoes. The AEM was tested at JSC with 6 live rats, a combination of 2 live and 4 dead rats, and 6 dead rats. In each instance there were no objectionable odors detected by a panel of "smellers" in the exhaust gases after periods of 6 to 10 days of operation.

Testing to assure that the crewmembers would not be exposed to obnoxious or noxious odors and pathogenic microorganisms was accomplished. Inflight crew involvement in the experiment was limited to activating lights to maintain nominal circadian rhythms, a 10-minute video tape on days 2 and 5, and daily observation of animal behavior. At no time did the crew handle the animals outside of the AEM.

TEST ANIMALS

Six Specific Pathogen Free (SPF) male albino rats (Lewis Wistar strain), age 56 days and weighing approximately 275 g at launch were to be used for flight. A group of 6 controls and 6 flight back-ups were required. However, the animal supplier could not guarantee that the rats would be free of one of the microorganisms on the restricted list, *Klebsiella pneumoniae*. Therefore, it was determined that germfree

(cesarian derived and isolator reared) rats would be required in order to meet all of the microbiological requirements. These germ-free rats were stabilized with a "cocktail" of *Lactobacillus* spp 4 days prior to shipment from the vendor's facility to the Life Science Support Facility (LSSF) at Kennedy Space Center (KSC). Only 15 of the germ-free rats were available, and these were subsequently divided into one group of 6 flight animals, one group of 6 back-up flight animals, and one group of 3 controls.

FACILITIES AND PROCEDURES

Housing facilities preflight were provided by the KSC LSSF in Hanger L. Procedures for handling and maintaining germ-free animals at this facility are as specified by the Association for Laboratory Animal Science. Procedures and equipment at the KSC LSSF were consistently within specification and animal comfort and exposure to microbial contamination was not compromised.

Animals were received in the LSSF on 18 August 1983 (F-12 days). Physical exams and microbiological analyses were accomplished upon receipt, at F-5 days, and at F-18 hours.

RESULTS

Average pre- and postflight body weight changes in the flight animals and in the various controls, Table I, are not remarkable if taken as a whole. Flight animals lost an average of 11 g (3.7%) in side A of the cage or gained an average of 3 g (1.3%) in side B. Controls gained an average of 5, 29, and 2 g (1.7%, 11%, 0.6%). The flight rats failed to gain weight at their expected rates and some even lost weight while the ground based controls either gained weight as expected or gained slightly less than expected.

Flight rats were at a disadvantage in that their food supply was glued to the sides of the cage and was slightly more difficult to access than the food in the cages of the controls. Flight animals consumed an average of 175 g of food whereas controls consumed 223 g. Control group KSC-1 did not gain at the expected rate, probably due to the fact that this group was anesthetized for a blood sample on 8-30-83. Control group ARC-5 did not gain at their expected rate due to the fact that this group was disturbed by transfer from KSC to ARC, and they had no food supply for about 24 hours.

Gnotobiotic rats were used in this test for reasons previously mentioned. These animals were isolator reared and had not been handled since birth. Birth dates varied from 6-10-83 to 7-5-83 which resulted in a group of animals varying in age of from 46 to 81 days at the time of launch. Selection of the flight animals resulted in a "small" group of 3 weighing an average of 228 g each and a "large" group of 3 weighing an average of 293 g each.

Postflight examination of the flight animals revealed that they were in good physical condition. They were alert and were actively grooming themselves and each other. Their supply of water in the raw potatoes was exhausted on Side A and nearly exhausted on Side B. Their hair coat was slightly discolored and stained which was probably due to their inadvertent rubbing against the food bars in microgravity. Postflight examination of the cage and inflight video tapes indicated that the air flow through the cage was not great enough to quickly pull urine, feces, and debris out of the cage area and onto the exhaust filter grid. Therefore, coprophagy was not prevented.

Microbiological analyses of the flight animals, food supply, water supply (raw potatoes), and AEM were accomplished by microbiology laboratories at KSC and JSC. Complete results of these tests are contained in separate reports but there was good general agreement between the laboratories.

Preflight microbial testing of the animals yielded *Lactobacillus* spp as expected, but no organism on the exclusion list was found. Testing of the raw potatoes revealed a variety of organisms in spite of using ionizing radiation and a chlorine scrub to provide a sterile potato. The potato-borne organisms were not on the exclusion list.

Postflight microbial testing of the animals yielded two organisms in the animals which had not been recovered preflight. These were *Streptococcus vividans* and *Staphylococcus aureus*, and it is presumed that these organisms were introduced by the raw potatoes and/or by the lack of complete sterility of the AEM. These organisms were not recovered from the exhaust ports of the AEM, and this supports the contention that the AEM is an effective

microbial isolator and does not result in contamination of the external environment.

CONCLUSIONS

The AEM successfully maintained 6 healthy rats for the duration of the mission (6 days). Improvements in the water supply (to provide a margin of safety of at least 20%) and an increase in the rate of air flow through the AEM are highly desirable. The AEM can be used for a variety of flight experiments using small laboratory animals without impairing crew time, crew safety, and crew comfort.

Table I - Animal Enclosure Module (AEM)

Average Body Weight Change

Flight	Preflight(g) (8-29-83) n=3	Postflight(g) (9-5-83) n=3	(g)	(%)	Food Consumed(g)	Potatoes Consumed(g)
Side A	293	282	-11	3.7	186	1170
Side B	228	231	+3	1.3	165	1162
Controls						
KSC-1	278	283	+5	1.7	216	1054
*KSC-4	264	293	+29	11.0	252	1059
ARC-5	292	294	+2	0.6	202	1155

* KSC-4 were true controls. KSC-1 gave a blood sample on launch day and ARC-5 were transported to NASA-ARC on launch day.

Table II - CBC Data

	Control Animals Pre Flight		Flight Animals 2 Hours Post Flight		Flight Animals 10 Days Post Flight	
	Mean	SE	Mean	SE	Mean	SE
WBC	9.8	0.7	15.2	2.4	10.5	0.4
RBC	8.7	0.2	9.8*	0.2	9.1	0.1
Hgb	17.6	0.2	19.6*	0.4	16.7	0.2
Hct	45.6	1.0	54.6*	1.5	48.3	0.4
MCV	52.2	0.3	55.9*	0.5	52.8	0.5
MCH	20.1	0.1	20.0	0.2	18.3*	0.2
MCHC	38.5*	0.4	35.8	0.3	34.6	0.4
Plt	539	59	752	42	600	
Retics	1.2	0.4	1.3	0.2		

* Significantly different from the two other means at the .01 level as determined by Analysis of Variance and Multiple Range Test

PROTOCOL/HARDWARE VERIFICATION OF THE SPACELAB-3 AUTOGENIC FEEDBACK TEST EXPERIMENT #3AFT23

Investigator: Patricia S. Cowings, Ph.D.

INTRODUCTION

A "pilot study" of the Spacelab-3 experiment, "A Preventive Treatment for Zero-Gravity Sickness" (#3AFT23), was flown as a DSO to examine the efficacy of inflight procedures planned for the subsequent formal experiment. There were three opportunities to speak to the one subject post-flight: a private, 2-hour debrief between the crewman and two of the investigators; a 2-hour public debrief, which was held by Johnson Space Center SBRI personnel; and a telephone conversation. A number of unforeseen problems arose inflight and were corrected for the subsequent flight after discussion of possible solutions with the crewman. The information obtained from this mission that was relevant to proposed changes in inflight procedures for the SL-3 mission is outlined below.

PROCEDURES / RESULTS

PREFLIGHT DONNING OF AFT HARDWARE AND EQUIPMENT CHECKOUT

The preflight donning procedures book developed for SL-3 was used. No modifications were recommended. Preflight donning of the Autogenic Feedback Test (AFT) hardware and STS garments took approximately 30 minutes for the one crewman. Participants in this study should perform this task while the flight crew receives their weather briefing. A maximum of 45 minutes to one hour may be needed for 4 crewmen as only two Ground Support Equipment units are available for "check-out."

URINE COLLECTION DEVICE (UCD) MODIFICATION TO THE AFT GARMENT

It was recommended that all crewmembers participating in this study allow a UCD modification for the AFT garments used during launch. The material of the flap may "bunch-up" in the crewman's back causing discomfort while seated in the launch chair. Further, the snaps on this flap prevent the garment from "riding-up" while the crewman sits in launch configuration. Lastly, this modification would save time post-insertion in that the crewman will not have to snap the flap into place while in zero-g (again, to prevent the garment from riding up).

AUTOGENIC FEEDBACK SYSTEM (AFS) ACTIVATION PRELAUNCH

The feedback display was carried to the Orbiter by close-out crew and handed to the crewman after seat ingress. The close-out crew turned the powerswitch of the AFS on before exiting the orbiter. It is recommended that at this time, the crewman follow the AFS activation cue card (mounted before each seat). However, after the unit is in "check-out mode" (refer to flight data file book, NOM-2, AFS activation) only one additional button push is required to start the tape recorder. It was strongly recommended that this final button push not occur until the L-10 minute hold. Because each tape operates for 7 hours, if all crewmen activated the recorder at the same time (i.e., L-10 minutes), it would then be possible to accurately time-line the cassette change on the first mission day (refer to Flight

Data File Book [FDFB], NOM-5). After this final button press, the crewmen should remove the display from their wrists and place them in FDFB pouches mounted on the sides of each launch chair: this location was chosen for its convenience and because the high vibration environment of launch might make the display fall off the wrist mount.

POST-INSERTION PROCEDURES

FEEDBACK DISPLAY

It was recommended that upon orbital insertion all crewmembers participating in this study remove the feedback display from the FDFB pouch on their launch chairs. Treatment subjects should re-attach the display to their cable harnesses at this time. Controls may place the display in a pocket. It became apparent that crewmembers should keep this display with them at all times while on shift. The display must be available for Treatment Subjects (i.e., feedback) and is used by all crewmen to input "events" to the recorder, (i.e., indicating the onset of symptom episodes if and when they occur). This display may also be kept in the AFS pouch pocket used for holding the belt.

MIDDECK PROCEDURES

Most of the following post-insertion procedures were practiced during a class held in the 1-g trainer. Input from the crew was welcomed, especially from those crewmen who had flown before. After consultation among the investigators, it was determined to be imperative to obtain continuous in-flight physiological monitoring. The first mission day was particularly important in this regard. Therefore, the requirement for reconnecting the AFS to the crewmember's cable harness within one hour post-insertion was maintained. The crewman indicated that tugging the under-seat pouches (containing the AFS) may produce unnecessary head movements. He recommended that these may be avoided by unbolting the launch chairs from the deck, leaving them in the air (or velcroing them to the wall), and then removing the pouches. This procedure could also save time in reconfiguration activities performed post insertion. Further, if this procedure were done one chair at a time with crewmembers assisting one another, it could reduce the time required.

AFT FLIGHT DECK PROCEDURES

This procedure must be considerably modified to accommodate MS-1, located on the flight deck. Because this crewman is responsible for payload activation and must perform many of his tasks in the confined area of the flight deck, it may not be possible for him to attach his AFS unit for up to 5 hours post insertion. This would result in a significant loss of critical data to this experiment. Nominally, MS-1 remains in his launch seat until the completion of OMS-2 (approximately 42 minutes). Instead, it was recommended that he brace himself in the hatch to the right of his seat such that his head is level with the underseat pouches, remove the AFS from the pouch, and connect it to his cable harness during this time. Because of his location, this activity should not disturb other critical flight tasks underway. Further, the recommended changes to the AFS pouch/belt assembly (see below, E.1.) should facilitate his attachment of the AFS and enable his unimpeded performance of mission-related activities in the flight deck.

INFLIGHT OPERATION OF TIME-LINED AND SYMPTOM-CONTINGENT PROCEDURES

MODIFICATION TO AFS POUCH/BELT ASSEMBLY

There was no Spacelab flown on this mission and the subject crewmember was required to make numerous translations from the middeck to the flight deck. Because the hatch connecting the two decks was significantly narrower than the "tunnel" leading to Spacelab, the AFS unit tended to "hang-up" on obstructions. This necessitated his making twisting and turning motions - again unnecessary head movements. After discussion of this

matter with the crewman post-flight, it was agreed that this problem could be avoided by making the AFS pouch detachable from the belt while remaining connected to the cable harness. In this way, the AFS could be held above the crewman's head (or between his legs) during translation. If working in confined spaces, the unit could be attached to the bulkhead with velcro, while the crewman remained tethered. The crewman recommended that the shoulder strap be used in-flight because it stabilized the AFS unit. The size of the AFS unit did not impede his movement or performance of mission related activities while he was in a relatively open volume of space (middeck and flight deck), as he was able to slide the unit (on the belt) to his back, side, or front, if needed. It was also recommended that a square of velcro be placed on the AFS unit itself to facilitate battery change-out procedures (refer to FDFB, NOM-6).

EVALUATION OF THE "RING" TRANSDUCER

The crewman did not have any difficulty using his fingers and hands to perform mission-related activities. The ring transducer did not get in his way. It was recommended that SL-3 crewmen keep a roll of elastoplast tape in the Spacelab should it be necessary to re-attach the ring transducer for any reason. This type of tape did hold the transducer firmly in place.

USE OF WRITTEN PROCEDURES - FLIGHT DATA FILE BOOK AND CUE CARDS

Explicit detail is required in the FDFB and on cue cards. No matter how well trained, an individual may "forget" a critical step in one or more of the flight procedures. Examples of this are discussed below under Section G., Paragraph 1. "Use of Foot Restraints;" and Section H., "De-Orbit Prep."

USE OF DIAGNOSTIC LOG BOOK OR VOICE CASSETTE RECORDER

It was essential to the science of this investigation that crewmembers provide a subjective report of their malaise levels during time-lined and symptom-contingent episodes inflight. The crewman used a voice microcassette recorder to perform these tasks. He did use the diagnostic book as a "cue card" so that his reports used the standardized terminology of the diagnostic scale. It is recommended that the use of a written log or taped report be made a crew option. It was observed that one crewman (during an early SL-3 simulation), attached his voice recorder with velcro to his flight suit (left side of chest) so that it would be convenient for verbal reports.

PRE-SLEEP DOFFING PROCEDURES

Removal and stowage of the AFS hardware and garment proceeded within timeline allowances (less than 10 minutes). This crewman further reduced the necessary time by leaving his cable harness attached while removing the garment.

POST-SLEEP DONNING PROCEDURES

USE OF FOOT RESTRAINTS

Post-sleep donning required 45 minutes. This was largely due to: a. difficulty with the Basal Skin Resistance (BSR) cable snap lead (see below, paragraph 2, "Modification of BSR electrode snap leads"); and b. failure to use foot restraints during donning. Although this crewman (and two from SL-3) participated in a class on the KC-135 zero-g flights which documented the fact that use of foot restraints shortened donning time from 45 to 15 minutes, this procedure was not performed inflight. It was strongly recommended that foot restraints be placed permanently in the vicinity of the stowage lockers for SL-3, and that instructions to use these restraints be written into the flight

data file book. Further, use of restraints reduces unnecessary head movements which might be made while "floating as you dress".

MODIFICATION OF BSR ELECTRODE SNAP LEADS

The snaps on the disposable BSR electrodes worn on the crewman's wrist tended to tear off the electrodes and remain mated to the cable harness. This tended to slow down donning procedures as the crewman had to find an implement (i.e., screw driver) to remove the snaps. For SL-3, these BSR snap leads were replaced on the harness so that this would not occur.

PRE-STRINGING THE CABLE HARNESS

The crewman discovered that donning time could be reduced by attaching the cable harness to the AFT garment before putting it on. Appropriate changes to the FDFB were made.

PROPOSED MODIFICATION TO AFS GARMENT

On the second mission day, the crewman noted that the garment felt uncomfortably tight, particularly in the abdominal region. He emphasized in his debriefing that he did not know if this was unique to himself or if others were likely to also feel discomfort caused by the garment. A possible solution to prevent the recurrence of the problem on SL-3 was to modify the AFT garment by inserting a second zipper on the right side (alternatively, the existing zipper could be modified to open from the bottom, rather than the top). This would loosen the fabric around the abdominal region and result in the loss of the abdominal respiration signal and relative respiratory tidal volume. However, the chest respiration gauge will remain intact and respiration rate will still be available as feedback to the treatment group crewmember. The experimenters would still be able to assess the effects of respiration rate on cardiovascular measures.

DE-ORBIT PREP PROCEDURES

It was strongly recommended that a de-orbit prep check-list be written and followed carefully. The crewman took great care in his preparations for re-entry. This essentially amounted to performing post-insertion procedures in reverse (i.e., mounting the AFS under the middeck seat, and performing AFS activation). However, it was discovered that although the AFS worked as is should, no re-entry tape was made. It is believed that the crewman inadvertently failed to make the final button press (which starts the tape running) before he removed his wrist display.

In summary, the results of this mission were extremely valuable to the SL-3 experiment.

Section Four
Microbiology

Two DSOs were successful in demonstrating the attachment of cells to microcarrier beads in zero gravity, as is evident in this scanning electron photomicrograph. These findings have exciting implications for bioprocessing in space.

CELL ATTACHMENT IN MICROGRAVITY

Investigators: Dennis R. Morrison, Ph.D., and Marian L. Lewis, Ph.D.

INTRODUCTION

Before cells can be cultured in space for electrophoretic separation or as mini-factories for producing selected natural cell products such as urokinase, studies must be done to assess growth characteristics of cells in the microgravity environment. Human kidney cells survive and proliferate in culture only when attached to growth surfaces such as flasks or microcarrier beads. On STS-7, a very simple study was conducted with the objective to determine if cells could attach to microcarrier beads in microgravity. The experiment was conducted at ambient cabin temperature rather than at optimal conditions in a 37° C incubator since an incubator was not available for STS-7. The study was designed to simply demonstrate feasibility of seeding cultures in microgravity. A subsequent experiment in an incubator was performed as a DSO on STS-8 to investigate attachment and proliferation at 37° C.

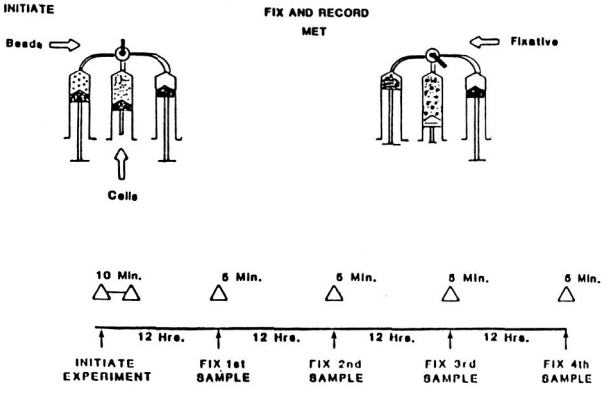


Figure 1. Cell attachment procedure.

PROCEDURES

Human kidney cells were maintained in four different syringe packs during launch. Early in the first day of orbit, beads were transferred into the syringes containing the cells. At 12 hour intervals, thereafter, fixative was added to a syringe according to the schematic procedure shown in Figure 1.

Figure 2a shows one of four cell bead packs. The pack consisted of an aluminum tray with a three-way valve attached to the tray and to three 5 ml syringes. One syringe contained the bead suspension, one contained cells, and

TABLE 1. MATERIALS

CELLS:	HUMAN EMBRYONIC KIDNEY (HEK)-(M.A. BIOPRODUCTS, USA)
GROWTH MEDIUM:	1:1:1 - MEM ALPHA, DULBECCO'S MEM, AND M-199 (GIBCO, USA) PLUS 10% FETAL CALF SERUM (BIOLABS, USA) AND OTHER CELL GROWTH SUPPLEMENTS
MICROCARRIER BEADS:	CYTODEX 3 - COLLAGEN COATED - (PHARMACIA, SWEDEN)
TRYPSIN-EDTA:	(GIBCO) 0.05% EACH IN Ca^{++} Mg^{++} FREE PBS
GLUTARALDEHYDE:	(TOUSIMAS, USA) DILUTED TO 2.5% IN DULBECCO'S PBS

GENERAL METHODS

PRE-LAUNCH	IN-FLIGHT (MICROGRAVITY)	POST-FLIGHT
1. TRYPSINIZE PRIMARY CULTURES 2. SUSPEND CELLS IN MEDIUM 3. SUSPEND BEADS IN MEDIUM 4. LOAD FIXATIVE SYRINGES	1. INJECT BEADS INTO CELL SUSPENSION 2. MIX BY SHAKING GENTLY 3. *FIX AT SELECTED TIMES* BY INJECTING GLUTARALDEHYDE	1 EVALUATE ATTACHMENT CELL/BEAD COUNTS (MICROSCOPE)

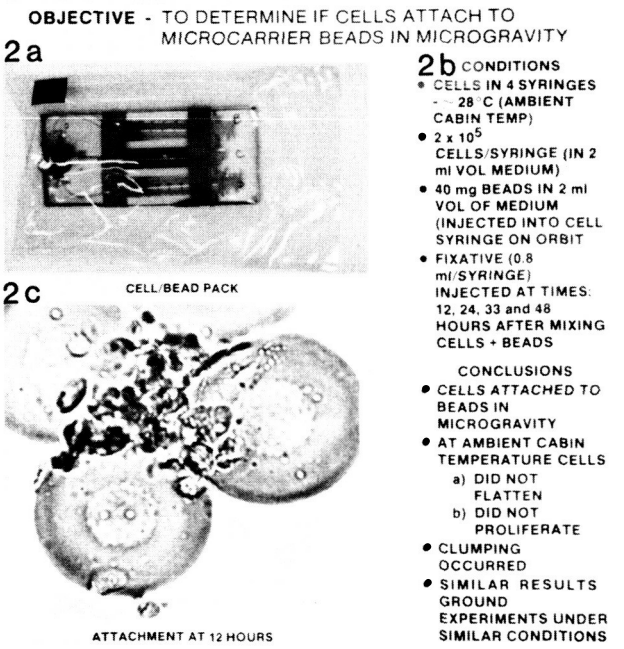


Figure 2. STS-7 cell/bead packs.

the third had glutaraldehyde as a fixative. The whole tray assembly was sealed in a plastic bag.

Materials and methods are described in Table 1 for each pack. The experimental conditions are listed in Figure 2b.

RESULTS

Figure 2c shows attachment of single cells and a large clump of cells for a sample fixed 12 hours after mixing of cells and beads on orbit. At ambient temperature the attached cells did not flatten or grow on bead surfaces. To evaluate the number of beads with cells attached, beads were arbitrarily divided into three categories; 1) beads with no cells, 2) beads with 1-10 cells and, 3) beads with clumps of cells attached. Each of the bead packs was divided into two aliquots for counting. Table 2 shows results of bead counts.

TABLE 2. CELL ATTACHMENT TO BEADS UNDER MICROGRAVITY CONDITIONS

CELL BEAD PACK # AND ALIQUOT	FIXED AT TIME (Hrs)	BEADS WITH 0 CELLS		BEADS WITH 1-10 CELLS		BEADS WITH CELL AGGREGATES		TOTAL NUMBER OF BEADS COUNTED
		NO.	MEAN % OF TOTAL COUNT ± SD	NO.	MEAN % OF TOTAL COUNT ± SD	NO.	MEAN % OF TOTAL COUNT ± SD	
1 A	12	55	84 ± 6	14	16 ± 6	ND	ND	69
B		117		16		ND		133
2 A	24	102	70 ± 14	47	20 ± 11	21	20 ± 11	170
B		91		14		9		114
3 A	33	114	60 ± 0	42	25 ± 4	34	25 ± 4	190
B		109		40		30		179
4 A	48	151	64 ± 4	42	18 ± 0	36	18 ± 0	229
B		114		34		40		188

By 12 hours after mixing cells and beads on orbit, 84% of beads counted had no cells and 16% of beads already had 1-10 cells. As time increased up to 33 hours, the number of beads with no cells decreased as the number with 1-10 cells and clumps of cells increased. No mixing was performed after the initial procedure at time zero. This confirmed that cells attach to growth surfaces while free floating in suspension under microgravity conditions. By 48 hours under less than optimal conditions of temperature, no statistical increase in cells attached to beads was apparent. Ground based experiments showed similar results.

CONCLUSIONS

Clearly, epithelial human kidney cells can attach to microcarrier beads under microgravity conditions even though the opportunities are based on initial mixing and thereafter to random collisions due to Brownian motion of the cells during the experiment period.

In ground based simulations, cells which were incubated at 37° C attached to beads, flattened on the bead surfaces, and began to grow. This indicated that the cells used in this experiment were viable and grew normally under optimal conditions. The aggregation of cells to cells was not an artifact of the glutaraldehyde fixative. In ground based experiments fixed at 24 and 72 hours after mixing cells and beads hardly any clumping was observed. This finding suggests that clumping may be due to a microgravity effect or to cell-cell interaction in the syringes during launch and orbit insertion prior to mixing cells with beads on orbit. It was apparent that the cells attach to each other if beads were not available. It was also obvious that considerable attachment occurred in the first 24 hours of this experiment. Under normal incubator temperatures cell metabolism would be greater, therefore, cell attachment may be even more pronounced.

This DSO was successful in that it met the objective of the experiment. Cells were shown to attach to growth surfaces in microgravity. Recommendations for the next flight DSO experiment included: (1) optimizing cell survival conditions by mixing cells and beads in culture chambers in a 37° C cell culture incubator, (2) designing the experiment to quantitate the relative attachment which occurs in the first 24 hours after mixing cells and beads on orbit, (3) counting larger numbers of cells and beads for statistical analyses post flight, and (4) evaluating the way in which cells are attached to beads by scanning electron microscopy.

INCUBATOR CELL ATTACHMENT TEST (ICAT)

Investigators: Dennis R. Morrison, Ph.D., Marian L. Lewis, Ph.D., A. Tschopp, Ph.D., and A. Cogoli, Ph.D.

INTRODUCTION

The microgravity environment of space provides unique advantages for the production and purification of pharmaceutical type natural cell products. Because of the potential of space bioprocessing, there is a new requirement to assess the behavior of cells in microgravity. Eventually, cells will be cultured in space in bioreactors and the desirable cell products will be harvested, purified and returned to Earth. Many of the target products, such as urokinase, are produced by cells which survive and grow only when attached to a substratum.

The attachment of cells to growth surfaces on Earth is normally affected by the settling of cells onto surfaces of flasks or other culture vessels. The experiments reported herein were designed simply to answer the fundamental questions: Do cells a) attach to and b) proliferate on growth surfaces as well in microgravity as on Earth.

Feasibility of cell-to-bead attachment at ambient temperature was shown on STS-7. The STS-8 Incubator Cell Attachment Test (ICAT) represented a cooperative effort between NASA and European Space Agency scientists. The test was initially designed to check out the Carry-on Incubator, developed and manufactured at the E. T. H. - Zentrum Zurich, Switzerland, before it was used for a lymphocyte experiment on Spacelab-1 and to assess cell attachment efficiencies at normal culture temperatures. On STS-8, kidney cells and microcarrier beads were incubated at 37° C in the carry-on incubator. The attachment of the kidney cells to beads is the subject of this report.

PROCEDURES

INCUBATOR

The apparatus, described in detail elsewhere (Cogoli and Tschopp, 1982), consisted of a carry-on box capable of maintaining a temperature of 37° C either with batteries or with on-board power, and which could be fixed to a front panel installed in the Space Shuttle's flight deck (Figure 1) or in a rack of the Spacelab module. The incubator contained four cell culture chambers sealed with a mobile piston, four syringes loaded with the microcarrier beads and four syringes with glutaraldehyde as fixative (Figure 2).

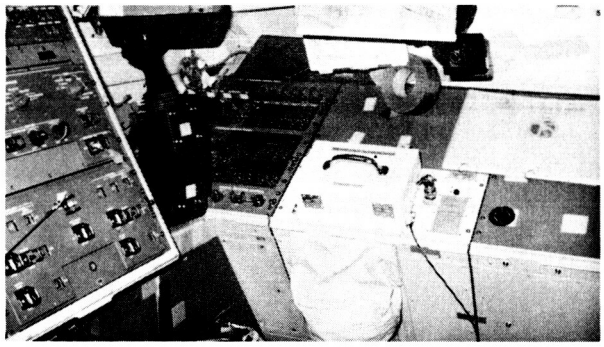


Figure 1. Incubator in place - Orbiter flight deck.

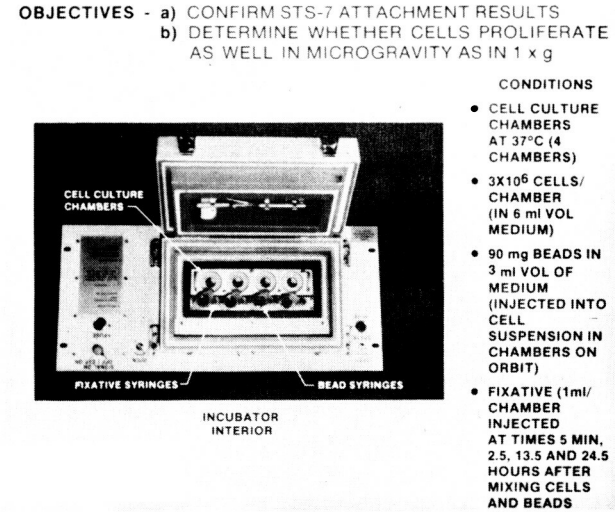


Figure 2. STS-8 ICAT.

CELLS AND MEDIUM

Frozen suspensions of human embryonic kidney cells were purchased from M. A. Bioproducts, Walkersville, MD. The cells were grown in medium consisting of one part each of Medium 199, MEM alpha, and Dulbecco's Modified Eagle Medium (Gibco Laboratories, Grand Island, NY) supplemented with 1.2 g/L of bactopeptone (Difco Laboratories, Detroit, MI), 0.02 g/L of folic acid, 0.72 g/L of i-inositol, 0.1 g/L of nicotinic acid, 16.2 g/L of NaHCO (Sigma Chemical Co., St. Louis, MO), 10% fetal bovine serum (Biolabs, Northbrook, IL), 20 mM HEPES (Research Organics Inc., Cleveland, OH) and 100 units/ml of penicillin and 100 mg/ml of streptomycin sulfate (Gibco Laboratories).

BUFFER AND ENZYME SOLUTIONS

Calcium and magnesium-free phosphate-buffered saline (CMF-PBS) consisted of 2.65 mM KCL (Pfaltz and Bauer Inc., Stamford, CN), 1.46 mM KH_2HPO_4 (Mallinckrodt Chemical Works, St. Louis, MO), 136.9 mM NaCl and 8.0 mM Na_2HPO_4 (J. T. Baker Chemical Co., Phillipsburg, NJ). Trypsin (Gibco Laboratories) and EDTA (Sigma Chemical Co.) were combined at 0.05% each in CMF-PBS.

GLUTARALDEHYDE FIXATIVE

A 50% aqueous ultra-pure TEM grade solution of glutaraldehyde (Tousimas Research Corporation, Rockville, MA) was further diluted with Dulbecco's PBS' to a concentration of 2.5%. One ml was loaded into each syringe.

MICROCARRIERS

Cytodex 3 microcarriers (Pharmacia Fine Chemicals, Uppsala, Sweden) were prepared for use according to the manufacturer's instructions by swelling and hydrating in CMF-PBS. The microcarriers were sterilized in 70% ethanol overnight. Prior to use, beads were washed three times in CMF-PBS and once in culture medium. The microcarriers were suspended in culture medium at a concentration of 30 mg/ml and loaded into the syringes.

GROUND PROCEDURES

Preflight operations were performed in the Life Sciences Payloads Facility at NASA Kennedy Space Center. Cells at passage level one were used for the experiment. The cells, previously grown in primary culture and stored frozen, were thawed, suspended in culture medium and planted in 75 cm^2 growth surface flasks (Corning 25110) five days prior to the scheduled time of stowage on the Shuttle. At launch time T-14 hrs, cells were approximately 90% confluent and were removed from flask surfaces with trypsin-EDTA. The cells were suspended in culture medium at a concentration of 464,000 cells/ml, and 6 ml of the cell suspension were then pipetted into each of the four cell culture chambers. Ground-based control cells were prepared in the same manner as for flight. The ground control experiment was run at NASA Johnson Space Center, Houston, TX.

FLIGHT PROCEDURES

The incubator with cultures and syringes was installed on board 14 hrs before launch and kept at ambient temperature. Four hrs after launch the incubator was switched on and 3.5 hrs later the experiment was started by injection of the beads into the cell chambers. Samples 1-4 were fixed by injection of glutaraldehyde 5 min, 3 hrs, 13.5 hrs and 24.5 hrs after addition of the beads espectively. Finally the incubator was switched off and the samples remained stored within the incubator until the end of the mission 6 days later. They were returned to the investigators 6 hrs after landing of the Shuttle and transported to the Bioprocessing Laboratory at the Johnson Space Center in Houston.

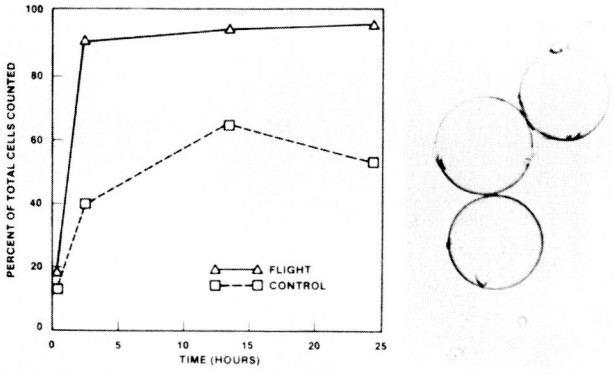
RESULTS

After return of the incubator to the laboratory, the cell/bead suspensions were removed from the growth chamber. An aliquot was taken from each suspension for scanning electron microscopy and the remaining suspension was evaluated for cell to bead attachment, cell-cell aggregation and individual

floating cell counts. For cell and bead counts, four slides were prepared for each sample fixed at each of the four times after mixing cells and beads on orbit or in the ground control. Figure 3 shows the ratio and percent of single (not clumped) cells counted which were attached to beads at each time. Significantly more single cells attached at each fixation time in the flight experiment than in the ground control. Statistical analyses of the cell counts were done by the non-parametric procedure of Cochran.

FIXATIVE ADDED

CHAMBER NO.	AT TIME AFTER MIX. CELLS AND BEADS (HOURS)	FLIGHT	% OF TOTAL	GROUND	% OF TOTAL
1	0.083	56/300	18.7	40/300	13.3
2	2.5	215/236	91.9	41/100	40.0
3	13.5	147/154	95.0	65/100	65.0
4	24.5	76/79	96.0	53/100	53.0



- FLIGHT - SIGNIFICANTLY MORE SINGLE CELLS ATTACHED AT EACH SAMPLE TIME (STATISTICAL ANALYSIS BY NON PARAMETRIC PROCEDURE OF COCHRAN)
- THIS DATA SUPPORTED BY BEAD EVALUATIONS

Figure 3. Attached single cell counts.

The number of cells per clump in aggregates which were not attached to beads is shown in Figure 4. In the ground control, by 2.5 hours only eight unattached clumps of cells were counted in the four prepared slides. In the flight samples, there were approximately three times more unattached clumps and there appeared to be more cells per clump. In 1-G the clumped cells tended to settle rapidly and had an opportunity to adhere to beads; whereas, in microgravity clumps free-floated until coming into contact with a bead. It appeared that cell-to-cell clumping occurred more frequently in flight than on the ground at the 2.5 hour time.

		0.083 HOURS	2.5 HOURS	13.5 HOURS	24.5 HOURS
GROUND CONTROL	NO. OF CLUMPS	261.00	8.00	1	ND
	MEAN CELLS/CL	4.11	2.88*	6	ND
	STANDARD DEV.	3.15	1.36	0	ND
FLIGHT	NO. OF CLUMPS	141.00	25.00	19.00	8.00
	MEAN CELLS/CL	3.48	8.44*	4.26	3.25
	STANDARD DEV.	2.45	6.23	3.48	1.49

*AT 2.5 HOURS - FLIGHT, MORE CELLS/CLUMP THAN CONTROL. INTERESTING IF DUE TO STICKY FLIGHT CELLS ATTACHING TO ONE ANOTHER IF NO BEADS AVAILABLE IN VICINITY.

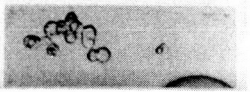


Figure 4. Number of cells/clump (unattached).

There was no significant difference in the number of cells attached to beads per clump of aggregates in flight versus control. However, statistically the average number of attached cells per clump in both the flight and ground control increased with time, indicating normal growth once the cells were attached (Figure 5).

- NUMBER OF CELLS/CLUMP ATTACHED - NO SIGNIFICANT DIFFERENCE FLIGHT VS. CONTROL
- AVERAGE LOG OF NUMBER OF CELLS/CLUMP ATTACHED INCREASED WITH TIME - INDICATES SOME CELL GROWTH FLIGHT AND CONTROL

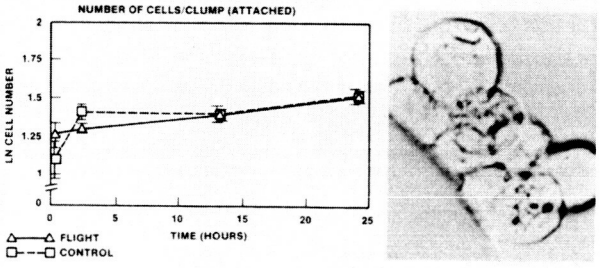
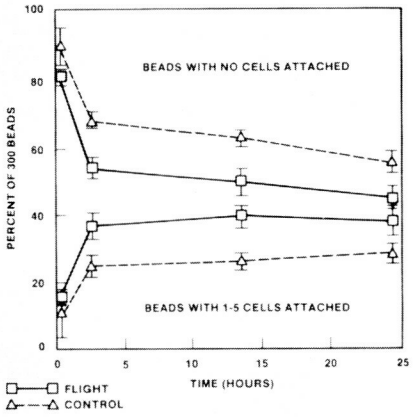


Figure 5. Estimation of cell clumping in microgravity.

As another approach to evaluating cell attachment to beads in flight compared to the ground control, 300 beads from each fixation time were scanned on each of four slide preparations. Beads were categorized as having no cells, 1-5 cells, 6-10 cells, or greater than 10 cells per bead for each of the four slides. Multivariate analysis of variance was applied to statistically determine the mean and standard deviation in the bead count categories. Figure 6 shows evaluations of beads with no cells and 1-5 cells per bead. The flight experiment had significantly more beads with 1-5 cells than the ground control. The number of beads with no

cells decreased with time as those with 1-5 cells increased. For categories of 6-10 and greater than 10 cells per bead there were very few beads; thus, there were large standard deviations for counts of the four replicate slides (Figure 7). The trend of the mean counts indicates an increase in the number of cells per bead with time. There was no significant difference between flight and control in the greater than 5 cells per bead categories. To determine if there were morphological differences in the way cells attached between flight and ground samples, scanning electron micrographs were examined. Figure 8 reveals no discernible differences between flight and ground samples. In both cases, the cells attached, flattened and increased in number as shown by the almost confluent state of some beads.

A TOTAL OF 300 BEADS WERE SCANNED PER SLIDE AND CLASSIFIED AS HAVING 0, 1-5, 6-10 OR > 10 CELLS/BEAD. (MEAN AND STANDARD DEVIATION OF FOUR SLIDES) (STATISTICS - MULTIVARIATE ANALYSIS OF VARIANCE.



- **FLIGHT - SIGNIFICANTLY MORE BEADS WITH 1-5 CELLS/BEAD THAN GROUND CONTROL - CONSTANT AT ALL SAMPLING TIMES**
- **BEADS WITH NO CELLS DECREASED AS NUMBER OF BEADS WITH 1-5 CELLS/BEAD INCREASED**

Figure 6. Evaluation of beads, ≤ 5 cells attached.

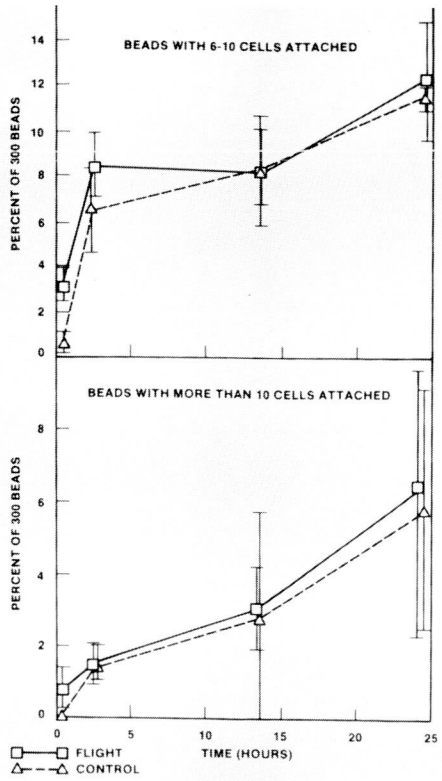


Figure 7. Evaluation of beads, ≥ 6 cells attached.

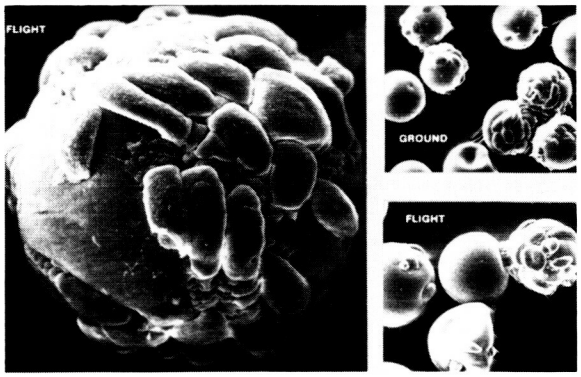


Figure 8. Scanning electron micrographs of cell/bead attachment fixed 24.5 hours after mixing cells and beads.

DISCUSSION / ANALYSIS

One concern was that cell attachment would be less in microgravity since the only opportunity for contacts between cells and beads would be based on random collisions while floating free in the culture chambers. These results show very clearly that considerable

attachment occurs quite quickly when cells and beads are mixed together in microgravity. At 37° C the number of attached cells was higher in the flight samples than in the ground control. This was possibly due to greater surface area availability at low-g, since all surface area of the beads would be available to cells, while on Earth only the top hemisphere of settled beads is available. Most of the cell adhesion occurred within the first 3 hr, and cell growth and replication appeared normal after cells had attached to microcarriers. Unspecific adhesion of cells by covalent attachment through an activation of the Cytodex carriers by glutaraldehyde can be excluded. If the attachment were nonspecific there would not be a difference between counts at the different times. In the flight experiment, there also appeared to be more cells per unattached aggregate than in the ground control. This could be due to cell to cell collisions rather than cell to bead collisions, resulting in cell clumping.

There were no problems with the incubator and no malfunctions occurred in this DSO.

CONCLUSIONS

Results of this DSO show clearly that anchorage-dependent human kidney cells attach to beads as well, or better, in microgravity than on Earth. Fifty percent more single cells had attached by 2.5 hours than in the ground control. There were no apparent differences in cell spreading and proliferation on the beads and no discernable differences in the manner of attachment observable by scanning electron microscopy.

These findings are extremely significant to the future of bioprocessing in space. They show that cells may be seeded on beads and initiated in microgravity for culture in a bioreactor or that cells may be grown in microgravity for electrophoretic separations. The selected subpopulations of high product-secreting cells may be seeded on beads for production of target pharmaceuticals. Cells separated by continuous flow electrophoresis may now be collected in receptacles containing microcarrier beads, thereby allowing attachment and better survival while the samples are waiting for return to Earth-based laboratories for culture and analyses.

Recommendations for further study include flying other DSOs to investigate effects of long term culture of cells on beads in microgravity, secretion of target products, effects of microgravity habitation on the cytoskeleton, and secretion of attachment proteins.

PUBLICATIONS BASED ON THIS DSO

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2. Tschopp, A., Cogoli, A., Lewis, M.L., and Morrison, D.R. (1984). Bioprocessing in Space: Human cells attach to beads in microgravity. Jour. Biotechnology (1984) 287-293.

3. Lewis, M.L., Cogoli, A., Morrison, D.R., and Tschopp, A. Anchorage dependent cells attach to microcarrier beads in microgravity. Abstract #263 - presented at the 8 International Biophysics Congress, Bristol, UK., 1984.

MICROBIAL SCREENING

Investigator: Duane L. Pierson, Ph.D.

INTRODUCTION

Microbial contamination during spaceflight presents a variety of health hazards to the crew and deterioration of essential materials. The level of airborne microbial contaminants has been established as an important factor in the dissemination of infectious diseases. The Shuttle/Spacelab serves as a small closed environmental system with a limited ability for the removal of airborne microbes. Microbially laden droplets and particulates generated by coughs, sneezes, and crew activities are removed from the air in minutes at one g; however, these droplets can remain suspended for hours in microgravity.

The JSC Microbiology Laboratory implemented a Microbial Contamination Control Plan at the onset of the STS missions. One facet of the plan was the quantitation and identification of airborne microbial contaminants. The cabin air was evaluated preflight and postflight to assess the efficacy of the environmental control system in removing such contaminants. The presence of an open hatch and the activities of various ground support personnel during sample collection jeopardizes the scientific validity of such studies. Inflight monitoring was the only scientifically sound method for assessing the levels and types of airborne microbial contaminants during a mission. The impact of the length of mission, number of crewmembers, and the inclusion of animals and other biological specimens upon the microbial load of the Orbiter's air can be assessed only by the evaluation of inflight air samples.

PROCEDURES

Evaluation of the airborne microorganisms was achieved by the use of the Reuter Centrifugal Air Sampler (RCS). Two-minute air samples were taken with the RCS using trypticase soy agar strips or rose bengal agar strips. Samples were taken during the preflight, inflight, and postflight phases of the missions. The sample sites were located on both the mid-deck and the flight deck. The microorganisms collected on all air strips were quantitated and identified.

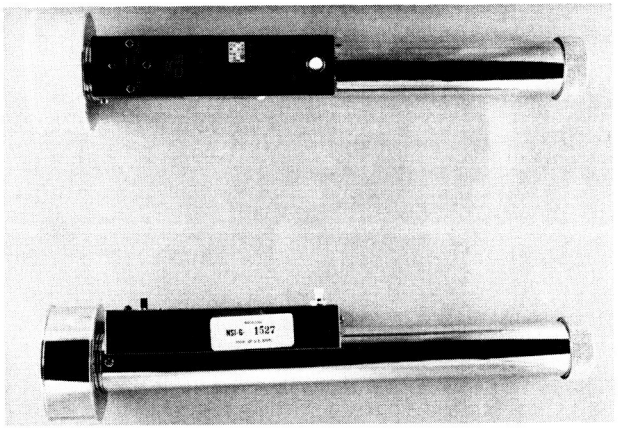


Figure 1. The Reuter Centrifugal Air Sampler.

The RCS is a completely portable instrument which can be hand-held and requires relatively little maintenance. The body consists of a metal tube 336.5 cm in length and 3.8 cm in diameter with an open end drum on one end, a power pack attached to the side, and a screw cap for access to the batteries on the end opposite the drum (Figure 1). The power pack is 3.5 cm X 13.9 cm X 1.3 cm and has an indicator light, main power ("ON-OFF") switch, time settings, and a start button. The indicator light detects weak or nonfunctioning batteries when the "ON-OFF" switch is in the "ON" position. The time setting selectors determine the length of time the sampler will run and the volume of air that will be sampled. The open end drum assembly is 7 cm in diameter and 3.2 cm deep and houses a removable ten blade impeller (Figure 2). The impeller blade assembly is removed for cleaning and/or sterilization as required by gently pulling on the knob attached to the center of the blade assembly; the drum can then be unscrewed from the instrument.

The inside of the drum is grooved to hold the agar strip in place.

Figure 2. RCS impeller.

The RCS employs the principle of air centrifugation, whereby the air is drawn in by the action of the impeller blades. The microbial particles present in the air are impacted onto the surface of the agar in the strip. The air flow is shown in Figure 3. The operating speed of the RCS is 4092 rpm and it draws 40 liters of air per minute. The flow rate remains constant by means of an electronic control which counts impulses reflecting from the rotating blades.

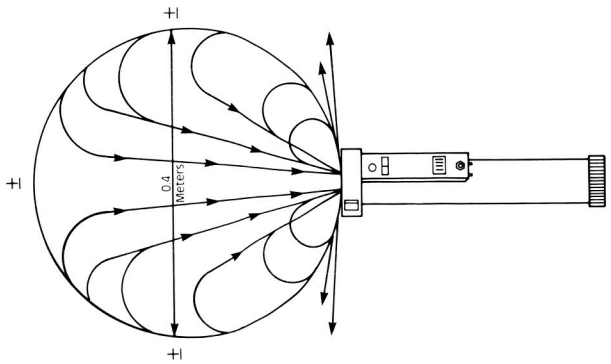


Figure 3. Air flow schematic.

Media Strips: Two types of agar strips were used. One contained nutrient agar for growth of bacteria. The other contained rose bengal agar for growth of fungi. Except for the agar, the strips were identical.

The agar strip used in the centri fugal air sampler was specially designed to give a surface area of 34 cm^2 (2 rows of 17 wells measuring 1 cm^2). This design allowed the strip to bend without cracking the agar as it was inserted into the open end drum, and also aided in the counting of the colonies. The agar strip was 21.2 cm X 2.5 cm X 0.3 cm and was packaged in a clear rigid plastic wrapper 23.5 cm X 3.2 cm X 0.9 cm with a seal on the cover (Figure 4). The agar strip was positioned in its wrapper so that the agar surface was facing away from the top of the wrapper. The agar strip may be stored at 4° C for at least three months or at room temperature for one month.

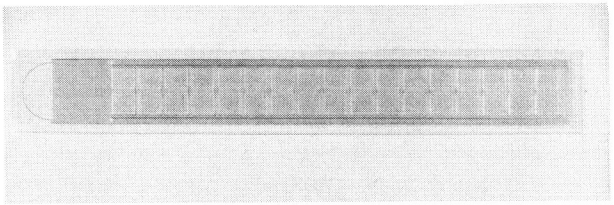


Figure 4. Agar strip.

Sample Procedures: The cabin air was monitored on both the middeck and flight deck. Samples were taken at the following times:

Preflight 24 hours before flight
Inflight #1 2nd day of mission
#2 mid-mission day
#3 next to last day
Postflight 6 hours after landing

The agar strips used inflight were stowed in the equipment area until postlanding destowage. The strips were packaged in wet ice and returned to the JSC Microbiology Laboratory where they were analyzed both quantitatively and qualitatively.

RESULTS

The results obtained from the microbial monitoring of the Orbiter air environment from STS missions 1-9 and mission 11 are given in Figures 5-8. Pre- and postflight sample analysis are shown for all the missions. Inflight sample analyses are shown for STS missions 6, 7, and 11. Inflight samples were also taken during another STS mission; however, the samples were compromised due to destowage and

transportation conditions. The agar strips were not destowed at the designated time and were subsequently exposed to temperatures incompatible with microbial recovery.

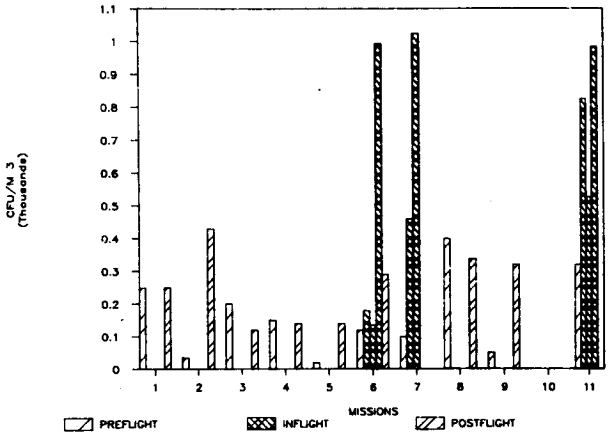


Figure 5. Airborne bacteria, mid deck.

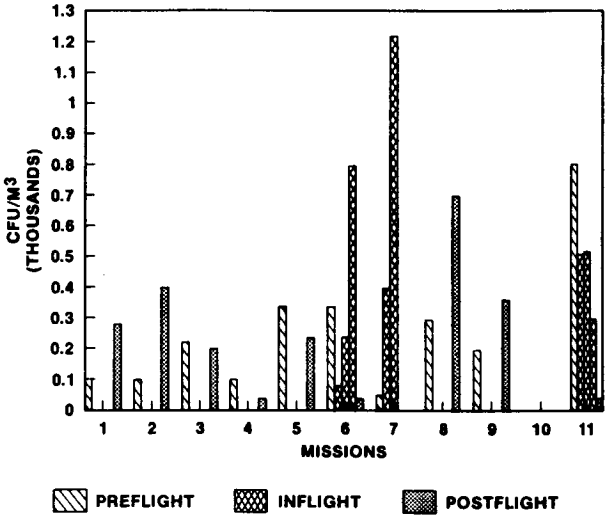


Figure 6. Airborne bacteria, flight deck.

Postflight microbial levels were generally 20-80% higher than preflight levels. However, the inflight measurements were more useful in evaluating the microbial levels of crew exposure during the mission. Four slight dropsin the microbial load were experienced during the first part of the mission, but this was followed by a rapid increase as the mission proceeded. The last inflight levels increased as much as 200-400 percent over the first inflight levels.

A qualitative analysis of each strip was also performed. This consisted of isolating and identifying each type of microorganism on the strip. A number of potential pathogens were isolated and are shown in Figure 9.

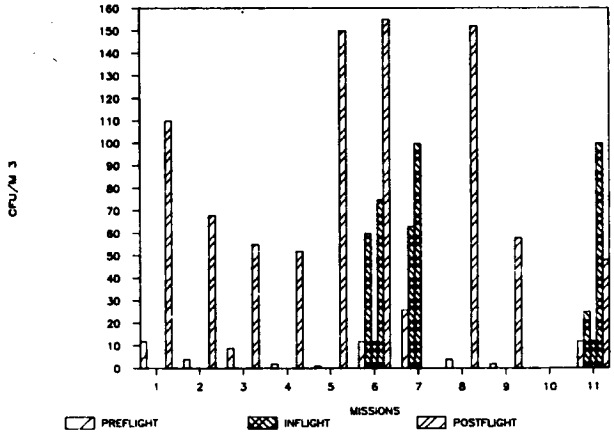


Figure 7. Airborne fungi, mid deck.

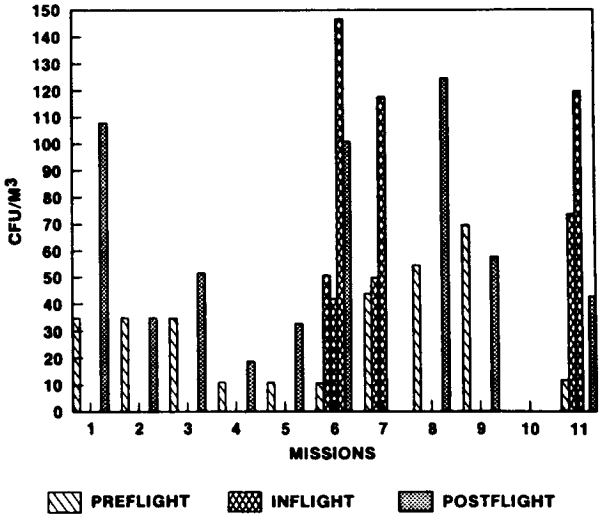


Figure 8. Airborne fungi, flight deck.

DISCUSSION

Inflight monitoring of the air proved to be a useful means of quantitating microbial changes that occurred during missions. A slight drop in the level of microorganisms in the air

was common during the early stages of the missions. This would indicate that the filtration system was adequate to clean the air at that time. However, as the mission progressed, the filtration system was no longer able to clear the air; the levels of contamination increased as the mission proceeded. This may have been due to the clogging of the filters with debris. It is logical to assume that longer missions and larger crews would increase the levels of contamination even more.

FUNGI

Alternaria alternata
Aspergillus amstelodami
Aspergillus flavus var columnaris
Aspergillus niger
Aspergillus sydowi
Aspergillus versicolor
Curvularia senegalensis
Drechslera hawaiiensis
Geotrichum candidum
Rhodotorula rubra
Trichosporon pullulans

BACTERIA

Acinetobacter calcoaceticus
Acinetobacter calcoaceticus (Iwoffi)

Figure 9. Microorganisms identified.

A number of potentially pathogenic fungi were isolated. The fungi have become increasingly important with the advent of the reusable spacecraft. Although the fungi are relatively slow growers, they are also very resistant to adverse conditions and remain viable for long periods of time. They remain dormant under adverse conditions but resume growth when conditions become more favorable. They pose a threat to the health of the crewmembers as 1) agents of infection, 2) allergens, and 3) producers of toxic metabolites. In addition, they are able to synthesize a vast array of enzymes enabling them to deteriorate practically every organic compound known.

CONCLUSIONS

The importance of the microbial monitoring of the air environment of the Shuttle missions, and eventually the Space Station, cannot be over emphasized. This monitoring serves 1) to evaluate cleaning procedures used between flights, 2) to evaluate microbial build-up in the orbiter during flight, and 3) to obtain data on contamination due to introduction of plants, animals and microorganisms.

A continual build-up of airborne contaminants was demonstrated by sequential sampling during several missions. While postflight monitoring of the air has always shown an increase in the microbial level, it does not truly reflect the levels of airborne microorganisms during the flight.

It is highly recommended that inflight monitoring of the airborne microbial contaminants be continued until a clear trend emerges. It is essential to evaluate the ability of the Orbiter's environmental control system to maintain acceptable levels of airborne microbes prior to the establishment of the Space Station.

MICROBIOLOGY REPORT IN SUPPORT OF THE SPACELAB 3 MISSION

Investigators: D. Pierson, Ph.D., and K. Gaiser

INTRODUCTION

The Spacelab 3 mission was unique for several reasons. The flight represented the first use of the Spacelab as an animal facility for biomedical investigation. The mission also served as the Flight Verification Test of the Research Animal Holding Facility (RAHF). The DSO, "Microbial Monitoring of the Spacelab 3 Mission," was developed and implemented to evaluate the impact of the animals in the Spacelab environment and to determine the ability of the RAHF to contain microorganisms.

Microbiological testing conducted on previous Space Shuttle flights has shown that some microbial buildup occurs in the closed crew environment during the course of the mission (1-2). The inclusion of animals in the crew environment represents a potential source of microbial contamination that may result in cross-contamination between the animals and crewmembers.

The first flight utilizing the RAHF required a more extensive microbial sampling protocol to monitor the microbial flora of the spacecraft and the crewmembers and to assess the containment capabilities of the RAHF. The microbiology effort for this mission was comprehensive and involved the Ames Research Center, Kennedy Space Center and the Johnson Space Center. This report describes the JSC effort. Included are the sample sites, methods, and the laboratory results obtained from the microbiological investigations conducted during the flight of Spacelab 3.

MATERIALS AND METHODS

SAMPLING PROTOCOL

Table 1 summarizes the sample sites, times, and types collected during the pre-, in-, and postflight phases of the Spacelab 3 mission. All samples described in this study were analyzed in the Microbiology Laboratory at JSC.

SAMPLE COLLECTION

CREWMEMBER

Samples from the crewmembers' ears, nose, throat, and hands were collected by the Culturette System during all sampling periods. With the exception of the throat cultures, all other samples were obtained after moistening the Culturette swab with 0.8 mM sterile phosphate buffer. After sampling, the Culturettes were stored at ambient temperature until processing.

Sputum and fecal specimens were collected in appropriate sterile containers and stored at 5° C until processing.

A 10 ml blood sample was collected from each crewmember for the determination of antibody titers to specific viral agents such as Hepatitis A and B, Epstein-Barr, and *Herpesvirus saimiri*, etc. A throat swab was collected from each crewmember for isolation of any viral agents that may have been present. The throat swab was placed in Veal Infusion Broth for stabilization and maintained at 5° C until processing.

SURFACE SAMPLES

Preflight and postflight surface samples from the Orbiter, Spacelab, and RAHF were collected using two sterile calcium alginate swabs moistened with 0.8 mM sterile phosphate buffer for each site. One swab was placed in trypticase soy broth for bacterial analysis; the other swab was placed in yeast malt broth for fungal analysis. All swabs were stabilized at 5° C until processing

Inflight surface samples of the RAHF and crewmembers' gloves were collected using the Culturette system. One Culturette per site was used. The Culturette was moistened with 0.8 mM sterile phosphate buffer before sampling. The samples were stored at ambient temperature until processing.

AIR SAMPLES

Air samples were collected in the Orbiter, Spacelab, Life Sciences Support Facilities (LSSF), and the JSC and KSC Crew Quarters using a Reuter Centrifugal Air Sampler. Two strips were taken at each site. One strip contained trypticase soy agar for bacterial analysis and the other contained rose bengal agar for fungal analysis. Additionally, particulate samples were taken inflight using the same air sampler with a modified Biotest sampling strip. All samples were maintained at ambient temperature until processing. Particulates were enumerated by light microscopy and further analyzed by scanning electron microscopy.

ANIMAL FECAL SAMPLES

Fecal samples were collected at the LSSF from the rats and squirrel monkeys. Samples were stabilized at 5° C and delivered to JSC for processing.

SAMPLE PROCESSING AND ANALYSIS

Specific details of sample processing and analysis techniques for all types of samples collected are outlined in Spacelab 3 Microbial Contamination Control Plan In Support of DSO 0437.

RESULTS

CREWMEMBERS

PREFLIGHT

As part of the routine F-10 preflight physical exam, samples were collected from the ears, nose, and throat of each crewmember. In addition to the routine samples, fecal and serum samples were collected from each crewmember. The fecal samples were analyzed for the presence of ova and parasites and pathogenic bacteria and fungi. The serum sample was assayed for antibody titers to specific viral agents. A sputum sample was received from one crewmember. Additional throat cultures were taken at F-0 on all crewmembers.

There were no microorganisms of medical concern recovered preflight from any of the crewmembers' specimens (Tables 2-5). The predominant microbial genus recovered immediately preflight from the throat cultures in six of the seven crewmembers was *Streptococcus*.

Air samples were taken preflight at F-30 (KSC) and F-10 (JSC) to assess the microbial load in the Crew Quarters prior to crew occupancy of these facilities. Overall, the microbial levels obtained at KSC (Table 6) and JSC (Table 7) were consistent with those observed from preflight sampling for previous missions. Three types of potentially pathogenic fungi were isolated from the Crew Quarters (Tables 6 and 8). These organisms are common fungal atmospheric contaminants, and no action was taken.

INFLIGHT

Throat and hand cultures were collected from selected crewmembers on MD1, MD2, MD4, and MD6. Table 9 shows the microorganisms recovered from the inflight throat samples. With the exception of the *Bacillus* sp. and *Saccharomyces cerevisiae*, all other microorganisms were isolated from the crewmembers preflight throat samples. Neither of these microbial species are considered to be fecal contaminants or of probable animal origin.

Table 10 illustrates the microorganisms isolated from the hand swab samples. In some cases, samples were collected after the hands had been cleaned with alcohol wipes. This sampling method may explain the apparent lack of growth in some of the cultures. The only microorganism of interest was *Streptococcus faecalis* which was isolated on MD2 from the hands of crewmember 7. This microorganism was recovered from preflight rat and squirrel monkey fecal samples collected at F-30. This species is also a common isolate of human feces. A waste tray changeout occurred immediately preceding the hand sampling procedure and may have been the source of the microbe. This microorganism was not isolated at any later time from any crewmembers' hands.

POSTFLIGHT

Ear, nose, throat, and sputum cultures were collected at L + O and again at L + 3 with the exception of the sputum samples. Microflora recovered from these samples was similar to preflight findings. Postflight samples do not indicate any cross-contamination between the animals and the crewmembers. *Pseudomonas aeruginosa, Pseudomonas fluorescens* (Table 2) and *Penicillium sp.* (Table 3) were isolated at L + 3 and are not considered to be of flight origin.

SPACECRAFT

PREFLIGHT

Orbiter

Surface swabs were collected at F-30 after alcohol cleaning and again at F-0 just prior to crew entry. Analysis of these samples did not demonstrate any unusual microbial levels (Table 11). However, a small number of samples collected from the Waste Management System (WMS) at F-0 showed very high levels of non-pathogens. This was attributed to improper temperature control of the samples prior to processing at JSC. The microorganisms of significance are listed in Table 12.

Bacterial and fungal air samples were collected at F-30 and F-0 for baseline data (Figs. 1, 2). The microbial levels were approximately

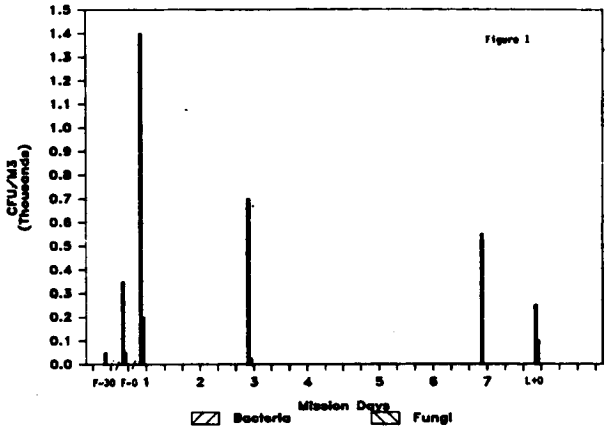


Figure 1. Bacterial and fungal counts, mid deck.

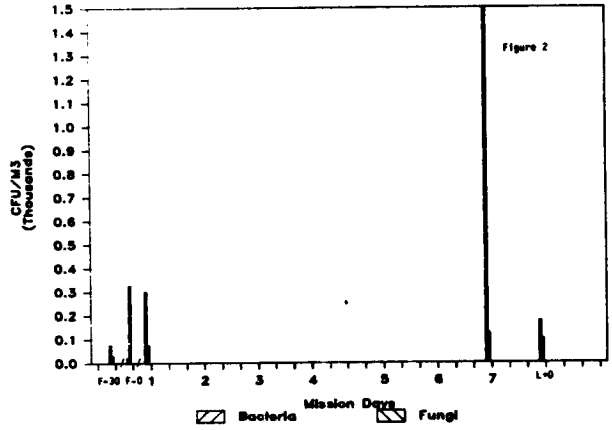


Figure 2. Bacterial and fungal counts, flight deck.

the same as seen in preflight sampling periods from previous missions. The particulate strips were not collected preflight.

Spacelab

Surface swabs were collected from six locations in the Spacelab module at F-30 after the wipedown and during the landing simulation exercises. The module was closed out upon completion of the exercises. No bacteria were isolated from any of the sites. Only 10 fungal colonies were recovered from the workbench handrail and were not of medical or epidemiological interest (Table 13).

A duplicate set of surface swabs was collected from twenty-two locations on the interior and exterior surfaces of the primate and rodent RAHFs. These samples were collected to

evaluate the cleaning procedures and to establish the baseline microbial levels for the RAHFs. Analysis of these samples showed low to moderate levels of microbial contamination (Table 14). Only two species of potentially pathogenic fungi were isolated from the primate RAHF (Table 15). Both are common environmental fungal species and represented no significant problem.

Bacterial, fungal, and particulate air strips were collected at F-30 during the landing simulation exercises prior to the final closeout (Fig. 3). Microbial levels were comparable to data obtained from Orbiter samples taken during previous missions. The particulate strips were not stored properly and, consequently, could not be processed.

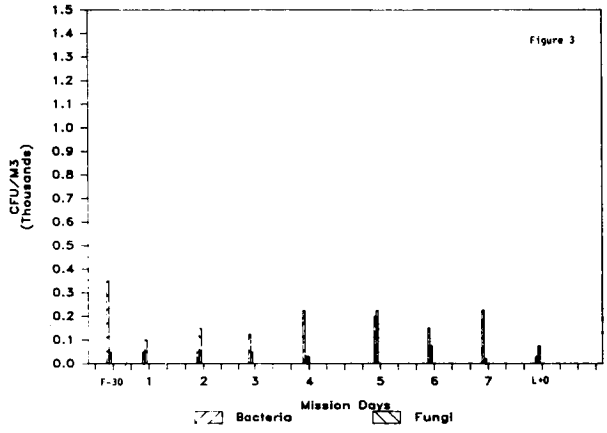


Figure 3. Bacterial and fungal counts, Spacelab.

INFLIGHT

Orbiter

No surface samples were collected from the Orbiter inflight. Bacterial, fungal, and particulate air sampling strips were collected on MD1, MD3, and MD7 on both the Mid Deck and the Flight Deck. Figures 1 through 3 illustrate the quantitation of the microorganisms and particulates recovered at each sampling period. Bacterial levels were markedly elevated on the Mid Deck on MD1 and decreased steadily throughout the mission (Fig. 1). Conversely, bacteria on the Flight Deck increased tenfold during the course of the flight (Fig. 2). No significant changes were observed in fungal levels during the flight. The majority of potential pathogens were fungi of the *Aspergillus* genus. *Staphylococcus aureus* was the only pathogenic bacterial species isolated (Table 17). No microorganisms of probable animal origin were isolated from the Orbiter inflight samples. Particulates on the Mid Deck decreased during the flight (only 2 samples) in much the same manner as the bacterial levels (Fig. 4). However, Flight Deck particulate values were high throughout the mission (Fig. 5). The elevated values for bacteria and particulates on the Flight Deck may be a result of the directional airflow from the Spacelab to the Flight Deck.

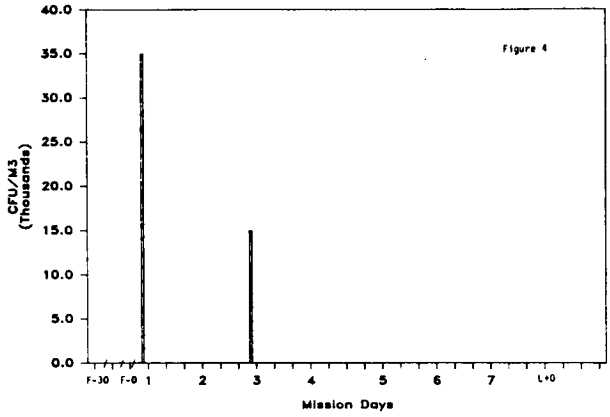


Figure 4. Particle counts, mid deck.

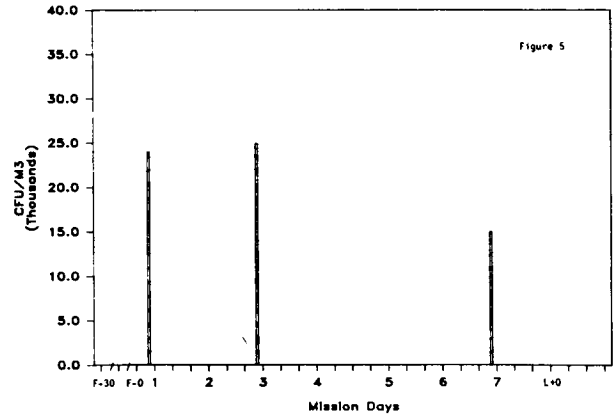


Figure 5. Particle counts, flight deck.

Spacelab

No samples from the Spacelab surfaces were collected inflight. Air samples were collected daily in conjunction with the waste tray changeout procedure. Bacterial, fungal, and particulate levels remained nearly constant

throughout the flight. An increase in particulate counts was noted during and following the waste tray changeout on MD4 (Fig. 6). *Aspergillus* sp. was the only potentially pathogenic microorganism isolated during the inflight sampling period (Table 16).

Five swab samples from the rodent RAHF and two swab samples from the primate RAHF were taken immediately following waste tray changeout on MD2, MD4, and MD6. All sample sites were external surfaces of the RAHFs. Additional samples were taken from crewmembers' gloves. Table 17 lists the microorganisms isolated from these sites. No fecal coliforms, indicative of fecal contamination, were isolated.

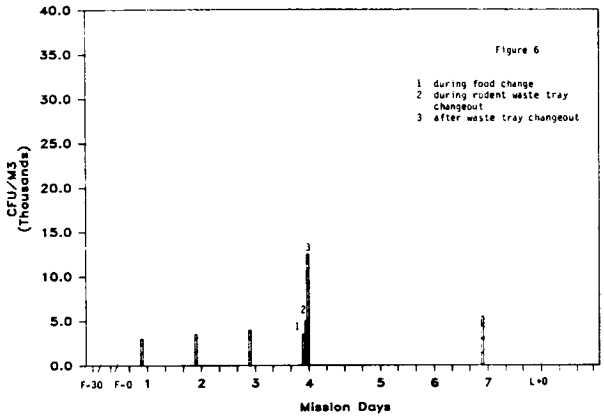


Figure 6. Particle counts, Spacelab.

POSTFLIGHT

Orbiter

Bacterial and fungal swab samples were collected at L + 0 at twenty-one sample sites. An approximate ten-fold increase from the preflight counts was seen in the number of bacteria in 11 of the 22 sites (Table 11). The number of fungal organisms did not increase significantly during the mission. Only two microbial species of interest, *Escherichia coli* and *Klebsiella pneumoniae*, were detected. *E. coli*, a fecal contaminant, was recovered from the air inlet ring and the slide valve which are two interior components of the Orbiter Waste Management System. This microbial species has been routinely recovered from these sites on previous flights. *K. pneumoniae* was isolated from the air return of the Aft Flight Deck. The origin of this contaminant is uncertain; *K. pneumoniae* was isolated immediately preflight from flight squirrel monkey #384-80 (sampling and analysis conducted by KSC). Bacterial and fungal air samples were collected at L + O. Postflight data correlates with the bacterial and fungal levels observed preflight (Figs. 1, 2). The particulate strips were not collected postflight.

Spacelab

Surface swabs were collected at L + O from the same six locations that were sampled preflight. Increases in bacterial growth were observed on five of the six locations (Table 13). No fungal growth was detected. *Staphylococcus aureus* was the only potential pathogen isolated.

Bacterial, fungal, and particulate air strips were collected at L + 0 immediately following the opening and ventilation of the Spacelab module. Bacterial and fungal levels were similar to preflight values (Fig. 3). The postflight particulate strip could not be enumerated due to the presence of numerous fine particles, presumably dust, which contaminated the Spacelab module during the ventilation procedure.

Postflight sampling of the RAHFs followed the preflight sampling protocol. Swab samples were collected from the twenty-two sites taken preflight. These samples were taken immediately after animal cage removal. A slight overall increase in bacterial growth was observed in samples from L + O (Table 14). The only organisms of significance were the fecal markers, *E. coli* and *S. faecalis*, and *Staphylococcus aureus*. All three species were isolated only from interior RAHF surface samples (Table 15). No appreciable change was observed in the number of fungal organisms.

ANIMAL MONITORING

At F-30 fecal samples were taken from selected rats and squirrel monkeys. Air samples were collected from the KSC LSSF during the same sampling period.

Table 18 lists all the microorganisms recovered from rat fecal samples. No microorganisms on the exclusion lists (Table 20 and 21) as defined by the JSC Human Research

Policy & Procedures Committee were isolated. Table 19 lists all the microorganisms recovered from the squirrel monkey fecal samples. Only one species on the exclusion list, *K. pneumoniae*, was isolated from monkey #3495. This animal was not selected for flight. However, immediately preflight *K. pneumoniae* was cultured from flight squirrel monkey #384-80 (sampling and analysis conducted by KSC-designated laboratories).

The air sample data collected from LSSF is shown in Table 22. The microbial levels were low and consistent with previous sampling data. Only common fungal environmental contaminants were isolated.

DISCUSSION

A total of 175 preflight, 81 inflight, and 98 postflight samples (354 total) were collected for quantitation and identification of the microbial flora present in the crew environment during the Spacelab 3 mission. The sampling protocol included samples from the air, various environmental surfaces, animals, and crewmembers.

Crewmember reports clearly documented the RAHF containment problems experienced during the flight. Comprehensive microbiological testing of the crewmembers and their environment during the SL-3 mission revealed no unusual microbial accumulations during the course of the mission. Levels of airborne microorganisms in the Spacelab were low compared to values obtained from the Orbiter during previous missions.

Fecal microorganisms, such as *E. coli* and *S. faecalis* were used as marker microorganisms for indication of fecal contamination. *E. coli* was detected only in the Orbiter Waste Management System and was probably of crew origin. *E. coli* and *S. faecalis* were also isolated from the interior surfaces of the RAHF postflight. In only two instances were microbial species of possible animal origin isolated external to the RAHF. *S. faecalis*, a fecal marker organism, was isolated on mission day 2 from a crewmember's hand immediately following waste tray changeout. *K. pneumoniae* was isolated postflight from an air return screen on the Orbiter Flight Deck. Unequivocal determination of origin, crewmember or experimental animal, was not possible.

The anomalies experienced during the SL-3 mission clearly demonstrated the value for redundancy in issues pertaining to the health of the crew. The use of Specific Pathogen Free animals (SPF) assured the safety of the crew when the RAHFs' containment system malfunctioned. It is strongly recommended that strict adherence to the SPF list be followed for all flights utilizing any biological specimens.

REFERENCES

1. NASA Technical Memorandum 58240 STS-1 Medical Report, December 1981.

2. NASA Technical Memorandum 58252 Shuttle OFT Medical Report - Summary of Medical Results from STS-1, STS-2, STS-3 and STS-4, July 1983.

Table 1. Microbial Samples Collected

Sample Sites	Sampling Times[a]		
	Preflight	Inflight	Postflight
Crew			
Ear	F-10		L+0, L+3
Nose	F-10		L+0, L+3
Throat	F-10, F-0	MD1, MD2, MD4, MD6	L+0, L+3
Feces	F-10		
Sputum	F-7		L+0
Hands		MD1, MD2, MD4, MD6	
Plasma	F-10		L+60
Spacecraft			
Surface	F-30, F-2		L+0
Air	F-30, F-2	MD1, MD7	L+0
Spacelab			
Surface	F-30		L+0
Air	F-30	MD2, MD3, MD4, MD5, MD6	L+0
RAHF			
Surface	F-30	MD2, MD6	L+0
Crew Quarters			
KSC	F-30		
JSC	F-10		
LSSF			
Air	F-30		
Animals			
Feces	F-30		

[a]F refers to days prior to flight, e.g., F-10 is 10 days preflight
L refers to days after landing, e.g., L+3 is 3 days post landing
MD refers to mission day

Table 2. Medically Important Microorganisms Isolated From Crewmember's Throat

	Preflight													Postflight												
	F-10							F-0						L+0							L+3						
CREWMEMBER	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
BACTERIA																											NS	
Acinetobacter calcoaticus bio anitratus	X																											
Branhamella catarrhalis													X															
Citrobacter sp.																										X		
Corynebacterium sp.		X		X	X			X		X				PO			PO	PO		PO	PO			PO	PO			PO
Enterobacter aerogenes																												X
Enterobacter cloacae																						X						
Haemophilus aphrophilus											X																	
Haemophilus sp. not influenzae								X					X	X						X				X	X			
Haemophilus parahaemolyticus		X					X																					
Haemophilus parainfluenzae	X	X	X	X	X	X	X		X			X			X	X						X	X			X		
Haemophilus parainfluenzae Biotype I																	X	X	X	X								
Haemophilus parainfluenzae Biotype II												X									X							
Haemophilus parainfluenzae Biotype III																												X
Kluyvera sp.												X																
Micrococcus sp.			X	X	X	X		X	X			X			X	X				X								
Neisseria sp.	X	X	X	X	X	X	X		X			X			X	X			X	X	X	X	X			X		X
Neisseria lactamicus																									X			
Pseudomonas aeroginosa																							X					
Pseudomonas fluorescens																						X						
Serratia rubidaea												X																
Staphylococcus aureus		X	X			X		X		X				X		X					X	X	X					
Staphylococcus epidermidis						X	X										X	X						X				X
Alpha-hemolytic Streptococcus	X	PO	PO	PO	PO	X	PO	PO	X	X	X	PO	PO	X	PO	X			PO		X					PO		
Gamma-hemolytic Streptococcus	PO	X	X	X	X	PO	X	X	PO			X			X				X					X	X	X		
Streptococcus equinus																							X					
Streptococcus morbillorium																	X											
Streptococcus mitis																						PO	PO					
Streptococcus pneumoniae										PO																		
Streptococcus salivarius											PO		X	X		PO												
Streptococcus sanguis																						X						
FUNGI																												
Aspergillus flavus group																			X									
Candida albicans			X						X	X							X									X		
Candida pseudotropicalis							X																					
Candida tropicalis													X															
Rhodotorula rubra		X																										

PO = Predominant organism
NS = No sample taken

Table 3. Medically Important Microorganisms Isolated From Crewmembers' Nose

CREWMEMBER	Preflight							Postflight															
	F-10							L+0							L+3								
	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7		
BACTERIA																				NS			
Citrobacter sp.											PO								X				
Corynebacterium sp.	PO	X	X	PO	PO		X	PO	X			PO					X	X	PO				
Enterobacter aerogenes	X						X									X					X		
Enterobacter cloacae															X								
Micrococcus sp.				X																			
Proteus mirabilis		X														X							
Staphylococcus aureus	X	PO	X			PO		X	PO	PO	X		PO		PO	PO	PO						
Staphylococcus epidermidis	X	X	PO	X	X	X	PO	X	X	X	X	X	X	PO	X	X	X	PO	X		PO		
FUNGI																							
Candida albicans															X								
Penicillium sp. 1												X							X				
Penicillium sp. 2												X											
Scopulariopsis brevicaulis						X																	

PO = Predominant organism
NS = No sample taken

Table 4. Medically Important Microorganisms Isolated From Crewmembers' Ears

CREWMEMBER	Preflight							Postflight															
	F-10							L+0							L+3								
	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7		
BACTERIA																				NS			
Bacillus sp.		X						X															
Corynebacterium sp.				PO	PO	X						X			PO	PO	X	X	PO				
Enterobacter aerogenes	X																						
Enterobacter cloacae															X								
Lactobacillus sp.									X														
Micrococcus sp.	PO	X	PO		X	X	X	X	X		X												
Staphylococcus sp.																							
Staphylococcus aureus													PO	PO									
Staphylococcus epidermidis		PO	X	X	X	PO	PO	PO	PO	PO	PO	PO	X	X	X	X	PO	PO	X		PO		
FUNGI																							
Aspergillus sp.		X							X														
Candida parapsilosis		X																					
Fusarium sp.					X																		
Penicillium sp.																X		X					

PO = Predominant organism
NS = No sample taken

Table 5. Microbiological Analysis of Sputum from Crewmembers

CREWMEMBER	MICROORGANISMS	
	PREFLIGHT	POSTFLIGHT
1	NS	Alpha-hemolytic Streptococcus (PO) Neisseria sp. Gamma-hemolytic Streptococcus Corynebacterium sp. Micrococcus sp. Haemophilus sp. not influenza Candida albicans
2	NS	Alpha-hemolytic Streptococcus (PO) Neisseria sp. Gamma-hemolytic Streptococcus Staphylococcus aureus Staphylococcus epidermidis
5	Alpha-hemolytic Streptococcus (PO) Gamma-hemolytic Streptococcus Neisseria sp. Corynebacterium sp. Haemophilus sp. not influenzae	Alpha-hemolytic Streptococcus (PO) Neisseria sp. Gamma-hemolytic Streptococcus Micrococcus sp.
6	NS	Corynebacterium sp. (PO) Micrococcus sp. Haemophilus sp. not influenza Candida albicans
7	NS	Corynebacterium sp. (PO) Haemophilus parainfluenzae,- Biotype II Staphylococcus epidermidis

NS = No samples taken

Table 6. Quantitation of Airborne Microorganisms in the Kennedy Space Center (KSC) Crew Quarters at F-30

AREA	CFU/m^3 OF AIR[a]		POTENTIAL PATHOGEN
	BACTERIA	FUNGI	
BEDROOM 1B	38	438	
BEDROOM 2B	50	238	
BEDROOM 3B	50	363	
BATHROOM B	100	175	
BEDROOM 1C	138	100	
BEDROOM 2C	38	113	Drechslera hawaiiensis
BEDROOM 3C	75	163	
BATHROOM A	88	88	
GYM	50	75	
DINING ROOM	12	88	
LIVING ROOM	38	50	
KITCHEN	12	188	
CONFERENCE ROOM	12	150	
LIVING ROOM A	0	50	

[a]Colony forming units per cubic meter of air

Table 7. Quantitation of Air Borne Microorganisms Isolated from the Johnson Space Center (JSC) Crew Quarters at F-10

TRAILER #	LOCATION	CFU/m^3 of Air	
		BACTERIA	FUNGI
1	Bedroom #1	1000	3500
	Bathroom	2050	3750
	Kitchen	500	1500
	Living Room	300	1200
	Bedroom #2	50	400
	Hall	550	900
	Bedroom #3	100	200
	Bedroom #4	150	750
2	Bedroom #1	500	1350
	Bathroom #1	600	1600
	Kitchen	150	800
	Living Room	500	1250
	Bedroom #2	150	200
	Hall	200	500
	Bathroom #2	150	300
	Bedroom #3	50	250
Outside Trailer	Bathroom	450	600
	Area between Trailer 1&2	50	300
3	Food Storage Room	300	200
	Bathroom	200	1250
	Hall	300	500
	Living Room	650	1400
	Dining Room	800	600
	Kitchen	150	950
4	Bedroom #1	550	1850
	Bathroom #1	800	2150
	Kitchen	300	1300
	Living Room	700	1750
	Bedroom #2	500	400
	Hall	0	550
	Bathroom #2	150	950
	Bedroom #3	900	450

Table 8. Potential Pathogens Isolated from Johnson Space Center (JSC) Crew Quarters at F-10

Potential Pathogen	Location
Aspergillus sp.	Trailer 1, Bedroom #2 Trailer 2, Bedroom #2 Trailer 2, Hall Trailer 3, Bathroom Trailer 4, Kitchen Trailer 4, Bathroom #2
Aspergillus flavus	Trailer 1, Living Room Trailer 1, Hall
Drechslera hawaiiensis	Trailer 1, Bedroom #1 Trailer 1, Bathroom #1 Trailer 1, Bedroom #2 Trailer 2, Bedroom #1 Trailer 2, Bathroom #1 Bathroom between Trailers 1 & 2 Trailer 4, Bedroom 1

Table 9. Medically Important Microorganisms Isolated From Crewmembers' Throat (Inflight)

	Inflight																									
	MD1							MD2							MD4							MD6						
CREWMEMBER	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7	1	2	3	4	5	6	7
BACTERIA	NS	NS	NS	NS			NS	NS	NS	NS		NS	NS		NS	NS												
Bacillus sp.											PO																	
Corynebacterium sp.					X	PO								X				PO	PO									
Haemophilus sp. not influenzae																						X	X	X		X	X	
Micrococcus sp.					X																			X				
Neisseria sp.																						X	X	X	X	X		X
Staphylococcus aureus																							X		X			
Staphylococcus epidermidis					PO						X			PO			PO	X	X	PO		X	X	X	X	X	X	X
Alpha hemolytic Streptococcus											X											PO	PO	PO	X	PO	X	PO
Gamma hemolytic Streptococcus						X												X				X	X	X	PO		PO	
Streptococcus salivarius																				PO								
FUNGI																												
Aspergillus flavus group																												X
Candida albicans					X									X			X		X		X			X	X	X		X
Saccharomyces cerevisiae						X														X							X	

PO = Predominant organism
NS = No sample taken

Table 10. Medically Important Microorganisms Isolated from Crewmembers' Hands (Inflight)

Crewmember	MD1	MD2	MD4	MD6
3	NS	No growth	Aspergillus flavus group	Staphylococcus epidermidis
4	NS	No growth	Aspergillus flavus group	Staphylococcus epidermidis
5	No growth	NS	No growth	Aspergillus flavus group Cryptococcus albidus var albidus
6	NS	Aspergillus flavus group	Aspergillus flavus group	Penicillium sp.
7	NS	Streptococcus faecalis	No growth	No growth

NS = No samples taken

C-2

Table 11. Quantitation of Microorganisms Isolated from Orbiter Surface

SAMPLE SITE	SAMPLE PERIOD[a]					
	Bacterial			Fungal		
	F-30	F-0	L+0	F-30	F-0	L+0
Urine collection device	$1.5X10^1$	$2.4X10^{3b}$	$3.8X10^2$	0	0	0
Air Inlet Ring	$1.5X10^1$	$1.0X10^{4b}$	$1.0X10^3$	0	$1.0X10^1$	0
Slide valve	$5.2X10^2$	$2.4X10^{4b}$	$1.3X10^3$	0	0	$1.0X10^1$
WCS handle	$7.5X10^0$	$4.9X10^{2b}$	$2.3X10^2$	0	$2.1X10^1$	$1.0X10^1$
WMS Trash Bag (MF43H)	NS	$2.0X10^{4b}$	$4.1X10^2$	NS	$1.0X10^1$	0
Air supply vent, Mid Deck	$4.5X10^1$	$1.7X10^{4b}$	$7.7X10^2$	$5.0X10^0$	$6.3X10^1$	$9.4X10^1$
Wall above hatch	$2.3X10^1$	$4.5X10^1$	$7.5X10^1$	0	0	0
Water dispenser needle	0	$9.0X10^0$	$3.8X10^1$	0	0	$6.3X10^1$
Personal hygiene nozzle	$3.0X10^1$	$9.0X10^0$	NS	$1.5X10^1$	0	NS
Food locker (MF14E)	NS	0	$5.3X10^2$	NS	0	0
Food trays (MF23H)	NS	$9.0X10^0$	$1.2X10^2$	NS	0	$1.0X10^1$
Food warmer (MF23H)	0	$9.0X10^0$	$3.0X10^1$	0	0	$1.0X10^1$
Sleep restraint (2)	NS	$9.0X10^0$	$1.1X10^2$	NS	0	$1.2X10^2$
Air supply vent, sleep station	$1.1X10^2$	$9.0X10^0$	$9.6X10^1$	$3.5X10^1$	$1.0X10^1$	$3.2X10^1$
Wet trash	$2.3X10^2$	$7.5X10^1$	$8.3X10^1$	0	$1.0X10^1$	0
CO_2 Absorber (B) latch handle	NS	0	NS	NS	0	NS
Window 8 gasket	$1.7X10^2$	$3.8X10^1$	$4.9X10^2$	$5.0X10^0$	0	0
Air supply vent, flight deck	$1.5X10^1$	$9.0X10^0$	$3.8X10^2$	$2.0X10^1$	$1.0X10^1$	$1.0X10^1$
Control stick, Commander	$2.3X10^1$	$9.0X10^0$	$7.5X10^0$	0	0	0
Control stick, Pilot	$9.8X10^1$	$9.0X10^0$	$2.9X10^2$	0	0	0
Data file case	$7.5X10^1$	$9.0X10^0$	$1.4X10^2$	$5.0X10^0$	0	0
Air return, Aft flight deck	NS	$9.0X10^0$	$1.2X10^3$	NS	$3.0X10^2$	$2.1X10^2$

[a]Quantitation given in colony forming units per cm^2
[b]Sample not refrigerated after collection
NS=No Sample taken

Table 12. Potential Pathogens Isolated from Orbiter Surface - STS 51-B

SAMPLE PERIOD	POTENTIAL PATHOGENS	ORBITER LOCATION
F-30	*ASPERGILLUS* SP.	AIR SUPPLY VENT - SLEEP STATION
		AIR SUPPLY VENT - FLIGHT DECK
	ASPERGILLUS FLAVUS	AIR SUPPLY VENT - SLEEP STATION
	CURVULARIA LUNATA	DATA FILE CASE
	PENICILLIUM SP.	AIR SUPPLY VENT - SLEEP STATION
F-0	*ACINETOBACTER CALCOAETICUS*	WMS TRASH BAG (MF43H)
	ALTERNARIA SP.	WCS HANDLE
	ASPERGILLUS SP.	AIR SUPPLY VENT - MID DECK
		AIR SUPPLY VENT - FLIGHT DECK
		AIR RETURN - AFT FLIGHT DECK
	ASPERGILLUS FLAVUS	WET TRASH
	ASPERGILLUS NIGER GROUP	WCS HANDLE
	GRAM NEGATIVE ROD CDC GROUP VE-2	AIR SUPPLY VENT - MID DECK
	STAPHYLOCOCCUS AUREUS	WMS TRASH BAG (MF43H)
		AIR SUPLY VENT - MID DECK
		SLEEP RESTRAINTS
L+0	*ACREMONIUM* SP.	WCS HANDLE
		AIR SUPPLY VENT - SLEEP STATION
	ASPERGILLUS SP.	AIR RETURN - AFT FLIGHT DECK (2 SPECIES)
		AIR SUPPLY VENT - MID DECK
	ASPERGILLUS NIGER GROUP	WATER DISPENSER NEEDLE
		SLEEP RESTRAINT (2)
	ENTEROBACTER AEROGENES	WINDOW 8 GASKET
		AIR RETURN - AFT FLIGHT DECK
	ESCHERICHIA COLI	AIR INLET RING - WMS
		SLIDE VALVE - WMS
	KLEBSIELLA PNEUMONIAE PENICILLIUM SP.	AIR RETURN - AFT FLIGHT DECK SLIDE VALUE
		AIR RETURN - AFT FLIGHT DECK
	STAPHYLOCOCCUS AUREUS	FOOD TRAYS (MF23H)

Table 13. Quantitation of Microorganisms Isolated from the Spacelab Surface

Sample Site	Sample Period[a]			
	Bacterial		Fungal	
	F-30	L+0	F-30	L+0
Air Vent	0	$9.0x10^{0}$[b]	0	0
Workbench Handrail	0	$5.3x10^{1}$	$1.0x10^{1}$[c]	0
Utility Box Latch	0	$4.0x10^{1}$	0	0
CO_2 Absorber Latch	0	$3.0x10^{1}$	0	0
Workbench Surface - Center	0	0	0	0
Trash Container (2 loops)	0	$1.4x10^{2}$	0	0

[a]Quantitation in colony forming units/cm^2
[b]Potential pathogen Staphylococcus aureus, isolated
[c]Potential pathogen Penicillium sp., isolated

Table 14. Quantitation of Microorganisms Isolated from the RAHF Surface

Sample Site	Sample Period[a]					
	Bacterial			Fungal		
	F-30A	F-30B	L+0	F-30A	F-30B	L+0
Primate RAHF						
Quick disconnect, lixit, slot 1	$1.0x10^{2}$	0	0	0	0	0
Inner door, inner surface slot 1	0	$7.5x10^{1}$	$1.9x10^{2}$	0	0	0
Quick disconnect, lixit, slot 2	0	0	0	$2.0x10^{1}$	0	0
Inner door, inner surface, slot 3	$1.0x10^{2}$	0	$8.3x10^{1}$	0	0	0
Case air inlet plenum, slot 2	0	0	$2.4x10^{3}$	0	0	0
Case air outlet plenum, slot 2	0	$7.5x10^{1}$	$9.8x10^{1}$	0	0	0
Outer door, outer surface, slot 2	$1.0x10^{2}$	0	$9.0x10^{0}$	0	0	0
Outer door, outer surface, slot 4	0	$7.5x10^{1}$	0	0	0	0
Bleed air outlet port	0	0	$4.5x10^{2}$	$5.0x10^{0}$	0	$1.4x10^{2}$
Bleed air inlet port	$3.0x10^{1}$	0	$1.3x10^{5}$	0	0	0
Rodent RAHF						
Lixit, front, slot 4	$1.0x10^{2}$	0	$1.9x10^{2}$	0	0	0
Lixit, rear, slot 6	$2.1x10^{3}$	0	$2.5x10^{3}$	0	0	0
Inner door, inner surface, slot 6	0	0	0	0	0	0
Lixit, front, slot 8	0	0	$2.8x10^{3}$	0	0	0
Lixit, rear, slot 10	$2.3x10^{1}$	0	$9.0x10^{0}$	0	$5.0x10^{0}$	0
Case air inlet plenum, slot 10	0	0	$9.0x10^{0}$	0	$2.5x10^{1}$	0
Case air outlet plenum, slot 10	$1.4x10^{1}$	0	$9.0x10^{0}$	0	$5.0x10^{0}$	0
Inner door, inner surface, slot 10	0	$7.5x10^{1}$	$9.0x10^{0}$	0	0	0
Outer door, outer surface, slot 1	0	0	$9.0x10^{0}$	0	0	0
Outer door, outer surface, slot 3	$1.0x10^{2}$	0	0	0	0	0
Bleed air outlet port	$1.0x10^{2}$	0	0	0	0	0
Bleed air inlet port	$1.0x10^{2}$	$7.5x10^{1}$	$1.0x10^{3}$	$5.0x10^{0}$	0	0

[a]Quantitation given in colony forming units/cm^2

Table 15. Potential Pathogens Isolated from the Primate and Rodent Research Animal Holding Facilities (RAHF) During Pre- and Postflight

Sample Period	Potential Pathogens	RAHF Location
F-30	Aspergillus sp. Penicillium sp.	Bleed air outlet port - primate Quick disconnect, lixit, slot 2 - primate
L+0	Escherichia coli	Lixit, rear, slot 6 - rodent
		Lixit, front, slot 8 - rodent
	Penicillium sp.	Bleed air outlet port - primate
	Pseudomonas acidovorans	Inner door, inner surface, slot 3 - primate
	Staphylococcus aureus	Case air inlet plenum, slot 2 - primate
		Lixit, rear, slot 10 - rodent
		Bleed air inlet port - rodent
	Streptococcus faecalis	Inner door, inner surface, slot 1 - primate
		Lixit, rear, slot 6 - rodent
		Case air inlet plenum, slot 10 - rodent
		Case air outlet plenum, slot 10 - rodent
		Inner door, inner surface, slot 10 - rodent

Table 16. Potential Pathogens Isolated from Spacecraft Air

Sample Period	Potential Pathogens	Orbiter Location
F-30	None Isolated	
F-0	Aspergillus sp. (2) Aspergillus glaucus	Flight Deck
MD1	Aspergillus sp. Aspergillus flavus group	Mid Deck
MD2	Aspergillus flavus group	Spacelab
MD3	Aspergillus sp. Aspergillus flavus group	Spacelab
MD4	Aspergillus sp.	Spacelab
MD5	Aspergillus sp. Aspergillus flavus group	Spacelab
MD7	Aspergillus sp. Staphylococcus aureus	Spacelab Flight Deck
L+0	Aspergillus sp. (2)	Flight Deck

( ) number of species isolated

Table 17. Inflight Surface Samples

Rodent RAHF			
	MD2	MD4	MD6
Cage 1 3 5	No growth No growth No growth	No growth No growth Aspergillus flavus group	Aspergillus flavus group No growth Staphylococcus epidermidis
Outlet Port	No growth	No growth	Staphylococcus epidermidis, Gram-negative rod CDC VE-2
Slot 6/8	No growth	Aspergillus flavus group	Staphylococcus epidermidis Aspergillus flavus group

Primate RAHF			
	MD2	MD4	MD6
Cage 1 4	NS NS	NS NS	NS NS
Outlet Port	Aspergillus flavus group Dematiaceous fungus	Staphylococcus aureus	Staphylococcus epidermidis
Slot 1/2	Bacillus sp. Dematiaceous fungus	No growth	Bacillus sp.

Gloves			
	MD2	MD4	MD6
	Staphylococcus epidermidis, Micrococcus sp. Aspergillus flavus group	Staphylococcus epidermidis	Staphylococcus epidermidis
*MD5 - Gloves Aspergillus flavus group			

NS = No samples taken

Table 18. Microbiology and Parasitology Analysis of Rat Feces (F-30)

Rat ID Number	1	2	4	6	7	14	17	32	34	40	42	61	63	64	95	111	112
Bacteria																	
Citrobacter amalonaticus		X									X						
Enterobacter cloacae														X			
Escherichia coli	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Proteus mirabilis																X	
Streptococcus avium										X		X					
Streptococcus faecalis	X			X	X	X		X	X		X						
Fungi																	
Moniliaceous fungi (no conidia)													X				
Penicillium sp.	X							X	X	X		X		X			
Ova & Parasites																	
None Observed	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

Table 19. Microbiology and Parasitology Analysis of Squirrel Monkey Feces (F-30)

Monkey ID Number	3165*	3483	3495	384-80*
Bacteria				
Escherichia coli		X	X	
Klebsiella pneumoniae			X	
Proteus mirabilis	X	X	X	X
Staphylococcus aureus	X			
Streptococcus faecalis			X	
Ova and Parasites				
None Observed	X	X	X	X

*Flight animals

Table 20. SPF Criteria for Rats

MICROORGANISM	CULTURE SITE/MATERIAL OR IDENTIFICATION TEST
BACTERIA:	
Streptobacillus Moniliformis	Oral
Spirillum Minor	Oral
Streptococcus Pneumoniae	Oral, Nasal
Streptococcus, Beta Hemolytic	Oral, Nasal
Pseudomonas Aeruginosa	Oral, Fecal
Salmonella sp.	Fecal
Leptospira sp.	Urine
Klebsiella Pneumoniae	Fecal, Oral, Nasal
Klebsiella Oxytoca	Fecal, Oral, Nasal
Campylobacter sp.	Fecal
VIRUSES:	
Lymphocytic Choriomeningitis Virus	Blood
Sendai Virus	Blood
FUNGI	
All Dermatophytes	Skin
ECTO PARASITES	Skin, Hair
ENDO PARASITES	Feces, Caecal Contents

Table 21. SPF Criteria for Squirrel Monkeys

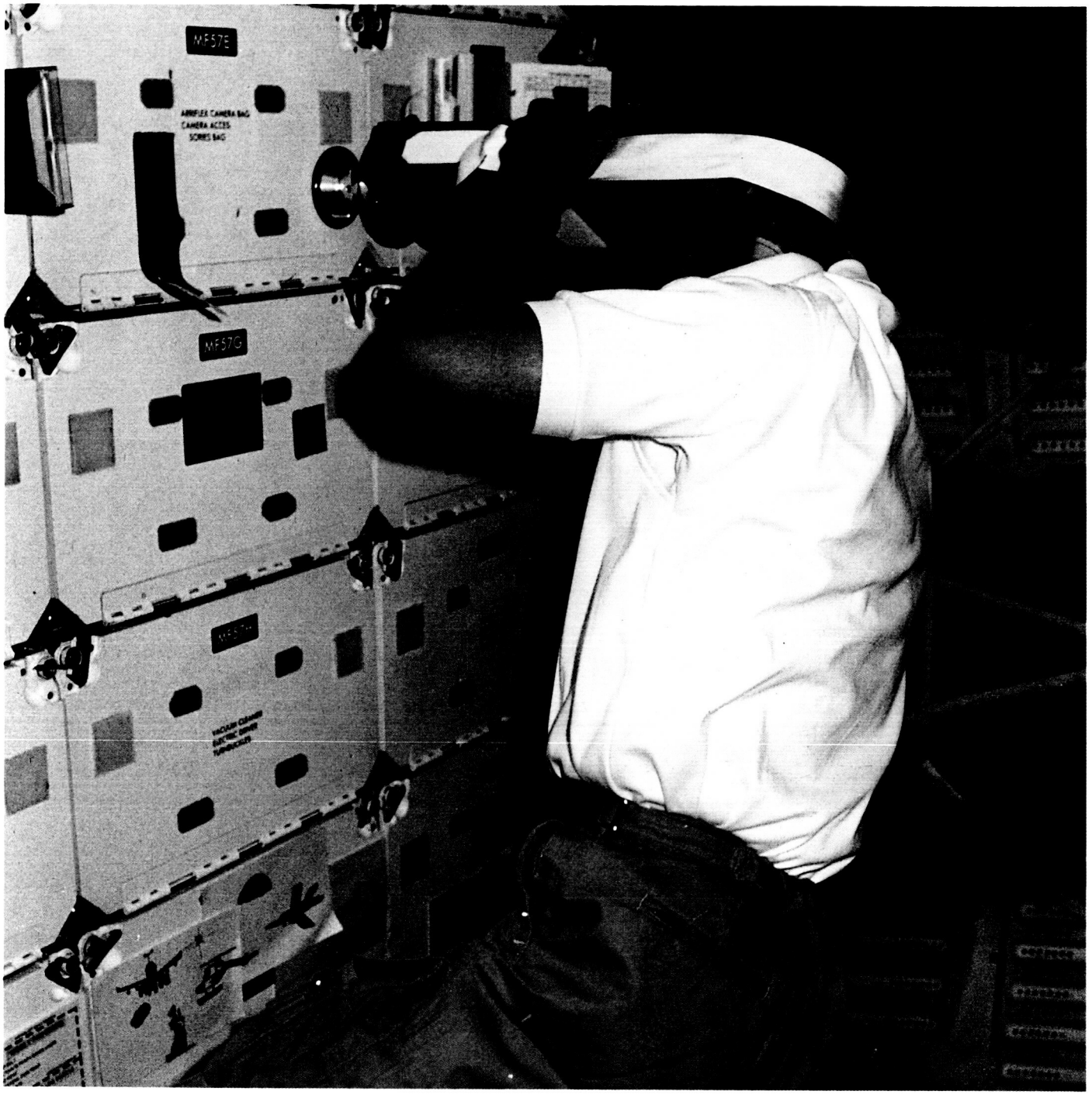
MICROORGANISM	CULTURE SITE/MATERIAL OR IDENTIFICATION TEST
BACTERIA:	
Shigella sp.	Fecal
Salmonella sp.	Fecal
Streptococcus pneumoniae	Oral, Fecal
Klebsiella pneumoniae	Oral, Fecal
Mycobacterium tuberculosis	Skin Test, X-Ray
Pasteurella multocida	Nasal, Fecal
Campylobacter sp.	Fecal
Leptospira sp.	Urine
Streptococcus, Beta Hemolytic (Group A)	Oral, Nasal
VIRUSES:	
Lymphocytic choriomeningitis virus	Blood (Serology)
Herpesvirus tamarinus	Blood (Serology)
Herpesvirus saimiri	
ENDOPARASITES:	
Trichomonas	Oral
Acanthocephlans	Feces
Strongyloides	Feces
Entamoeba histolytica	Feces
Hemoprotozoa	Blood
FUNGI:	
All Dematophytes	Skin

Table 22. Quantitation of Airborne Microorganisms
Life Sciences Support Facility (LSSF) at F-30

Sample Site	CFU/m^3 of Air		
	Bacteria	Fungi	Potential Pathogens
Hall	0	$1.5X10^2$	*Aspergillus* sp. (3)
X-Ray	0	$1.1X10^2$	*Aspergillus* sp. (2)
Cental Supply	0	$8.8X10^1$	*Aspergillus flavus* *Aspergillus* sp. (3)
AHR 2	0	$7.5X10^1$	*Aspergillus* sp. (2)
AHR 5	0	$1.9X10^2$	*Aspergillus* sp.
AHR 6	0	$2.7X10^2$	*Aspergillus* sp. (4)
AHR 7	$1.5X10^2$	0	

( ) number of different species isolated.

Section Five
Space Motion Sickness



An understanding of vestibular and somatosensory roles in adaptation to microgravity may hold the key to prevention and treatment of Space Motion Sickness. This crewmember is using a device designed to measure ocular counterrolling in microgravity conditions. The neck brace is to "decouple" somatosensory receptors in the neck.

A CURRENT STATUS OF SMS EXPERIENCE IN SHUTTLE CREWMEMBERS

Investigators: James M. Vanderploeg, M.D., Donald F. Stewart, M.D., and Jeffrey R. Davis, M.D.

INTRODUCTION

Space motion sickness (SMS) is a problem that has been associated with space travel for over twenty years and is the most clinically significant medical phenomenon during the first four days of spaceflight. Upon entry into micro-gravity, the body begins to adapt to this novel environment. The sensory-motor system, among others, must learn to function appropriately for the new conditions. Adaptation of the vestibular system and, more generally, the sensory-motor system is of particular importance in the development and resolution of symptoms of SMS.

Throughout the United States space program information concerning SMS has been collected by the NASA flight surgeons examining and debriefing the crewmembers postflight. Information collected during the Space Shuttle program makes up the substance of this paper.

INCIDENCE

During the United States manned spaceflight programs SMS has been reported by crewmembers during Apollo, Skylab, and Shuttle flights. The reason astronauts did not experience and report SMS symptoms during the Mercury and Gemini flights is felt to be largely due to the marked limitation of motion of the crewmembers in these small space capsules. As mobility increased in the larger Apollo, Skylab, and Shuttle spacecraft, susceptible crewmembers experienced one or more of the motion sickness symptoms listed in Table 1.

The incidence of SMS symptoms across the United States manned spaceflight programs, through the first 19 Shuttle flights, is given in Table 2. The percent incidence shown in Table 2 is total incidence for each program and includes cases of SMS ranging from mild through severe. As is shown, the incidence of SMS during the Shuttle flights has been 53 percent.

TABLE 1. SMS SYMPTOMS

HEADACHE	CENTRAL NERVOUS SYSTEM
MALAISE	
LETHARGY/APATHY	
DROWSINESS	
DISEQUILIBRIUM	
ANOREXIA	GASTRO-INTESTINAL SYSTEM
STOMACH AWARENESS	
NAUSEA	
VOMITING	

TABLE 2. SMS INCIDENCE

- MOST CLINICALLY SIGNIFICANT MEDICAL PHENOMENON DURING THE FIRST SEVERAL DAYS OF SPACEFLIGHT

UNITED STATES	INCIDENCE
MERCURY	0%
GEMINI	0%
APOLLO	35%
SKYLAB	60%
APOLLO-SOYUZ	0%
SHUTTLE	53%

This high incidence is of increased significance in the Shuttle program for two reasons. First, because Shuttle flights generally are only 5 to 7 days in duration, SMS symptoms are present during one-third to one-half of the flight and are a nuisance to crewmembers both in terms of personal comfort and in decreased work efficiency. Second, since the Shuttle is flown back to Earth like an airplane and requires crewmember control, an emergency requiring an early landing could result in a sick astronaut having to pilot the spacecraft.

CLINICAL CHARACTERISTICS

In order to apply a uniform assessment of SMS symptoms and severity across all Shuttle flights, a classification of symptom severity was developed by Homick and coworkers (1). Four categories of SMS severity were identified based on type, duration and severity of individual symptoms. Using information provided by the crewmembers during their medical debriefings after each mission, the interviewing flight surgeon assigned each crewmember into one of the four categories: none, mild, moderate, or severe space motion sickness. The description of each of these categories of SMS can be found in Table 3.

TABLE 3. SMS CATEGORIZATION

NONE (0):	NO SIGNS OR SYMPTOMS REPORTED WITH EXCEPTION OF MILD TRANSIENT HEADACHE OR MILD DECREASED APPETITE
MILD (1):	ONE TO SEVERAL SYMPTOMS OF A MILD NATURE; MAY BE TRANSIENT AND ONLY BROUGHT ON AS THE RESULT OF HEAD MOVEMENTS; NO OPERATIONAL IMPACT; MAY INCLUDE SINGLE EPISODE OF RETCHING OR VOMITING; ALL SYMPTOMS RESOLVED IN 36-48 HOURS
MODERATE (2):	SEVERAL SYMPTOMS OF A RELATIVELY PERSISTENT NATURE WHICH MAY WAX AND WANE; LOSS OF APPETITE; GENERAL MALAISE, LETHARGY AND EPIGASTRIC DISCOMFORT MAY BE MOST DOMINANT SYMPTOMS; INCLUDES NO MORE THAN TWO EPISODES OF VOMITING; MINIMAL OPERATIONAL IMPACT. ALL SYMPTOMS RESOLVED IN 72 HOURS
SEVERE (3):	SEVERAL SYMPTOMS OF A RELATIVELY PERSISTENT NATURE THAT MAY WAX AND WANE; IN ADDITION TO LOSS OF APPETITE AND STOMACH DISCOMFORT MALAISE AND/OR LETHARGY ARE PRONOUNCED; STRONG DESIRE NOT TO MOVE HEAD; INCLUDES MORE THAN TWO EPISODES OF VOMITING; SIGNIFICANT PERFORMANCE DECREMENT MAY BE APPARENT; SYMPTOMS MAY PERSIST BEYOND 72 HOURS

The first 19 Shuttle flights covered the period from April 1981 through August 1985. Seventy-one different individuals flew on these missions. With several individuals flying more than once, these people represent a total of 93 crewperson-flights. Symptoms of SMS were experienced by 49 of these 93 crewpersons for a total incidence of 53 percent. Twenty-four of the cases were mild, constituting 49 percent of the cases or 26 percent of the total; 18 were moderate in severity, making up 37 percent of the cases or 19 percent of the total; and 7 were judged to be severe cases, representing 14 percent of the cases or 8 percent of the total crewpersons flown. These data are summarized in Table 4.

TABLE 4. SMS EXPERIENCE ON FIRST 19 SHUTTLE FLIGHTS

STS-1 APRIL 1981	THROUGH	STS-51-F AUGUST 1985	
	NUMBER	PERCENT OF CASES	PERCENT OF TOTAL
TOTAL CREWPERSONS	93		
TOTAL CASES OF SMS	49		53%
MILD	24	49%	26%
MODERATE	18	37%	19%
SEVERE	7	14%	8%

Each of the 49 cases of SMS was evaluated according to the specific symptoms experienced by each crewmember. The results are summarized in Table 5. The most commonly experienced symptoms, taking all cases, were loss of appetite (82 percent), vomiting (82 percent), stomach awareness (57 percent), malaise (57 percent), headache (53 percent), and lethargy (51 percent). Of interest is the fact that the incidence of nausea was only 45 percent compared to an 82 percent incidence of vomiting. Many of the crewmembers who vomited reported that they frequently had little, if any, nausea precedent to vomiting and if nausea was present it often began only a few seconds to minutes before frank vomiting occurred. Anorexia and vomiting were found in all of the individuals with moderate or severe SMS while only 63 percent of the crewmembers classified as mild cases had these symptoms. It is also interesting to note that, whereas 63 percent of the mild cases described anorexia and vomiting, only 38 percent experienced malaise. This apparent discrepancy is explained by the fact that a number of astronauts indicated that they felt quite well before and after vomiting and denied any sensation of malaise. They found that the vomiting was very sudden in onset without precedent nausea or malaise.

TABLE 5. INCIDENCE OF SYMPTOMS

	MILD (n = 24)	MODERATE (n = 18)	SEVERE (n = 7)	TOTAL (n = 49)
HEADACHE	12 (50%)	9 (50%)	5 (71%)	26 (53%)
MALAISE	9 (38%)	13 (72%)	6 (86%)	28 (57%)
LETHARGY	9 (38%)	11 (61%)	5 (71%)	25 (51%)
DROWSINESS	2 (8%)	6 (33%)	4 (57%)	12 (24%)
DISEQUILIBRIUM	3 (12%)	7 (39%)	1 (14%)	11 (22%)
ANOREXIA	15 (63%)	18 (100%)	7 (100%)	40 (82%)
STOMACH AWARENESS	12 (50%)	11 (61%)	5 (71%)	28 (57%)
NAUSEA	8 (33%)	9 (50%)	5 (71%)	22 (45%)
VOMITING	15 (63%)	18 (100%)	7 (100%)	40 (82%)

In addition to the specific symptoms, the time course of the symptoms was also of interest. The time of onset of symptoms, the time of peak intensity, and the time period in which the symptoms of SMS completely abated were obtained during the medical debriefing. Symptoms during the first 36 hours were grouped in 6-hour time blocks; symptoms occurring thereafter were grouped in 12-hour time blocks. The majority of susceptible crewmembers developed the onset of their symptoms during the first 6 hours of flight. The onset of symptoms has been seen from as early as 15 minutes after launch to as late as the end of the second day of a mission. The symptoms tend to reach peak intensity either near the middle of the first flight day or the middle of the second day. In the majority of cases the symptoms resolved by the end of the third day of the flight. Figure 1 shows the time course of onset, peak, and resolution of symptoms plotted against the mission elapsed time. The dip in the time of peak intensity at 18 to 24 hours most likely represents the abatement of symptoms during the first sleep period when the movements of crewmembers are minimized. When the time course of symptoms was plotted for each severity category, as is shown in Figures 2, 3, and 4, essentially the same patterns were seen as in the plot for the combined grouping, with the exception of the onset of symptoms. All the individuals who experienced symptoms of moderate or severe intensity had the onset of their symptoms within the first 6 hours of flight.

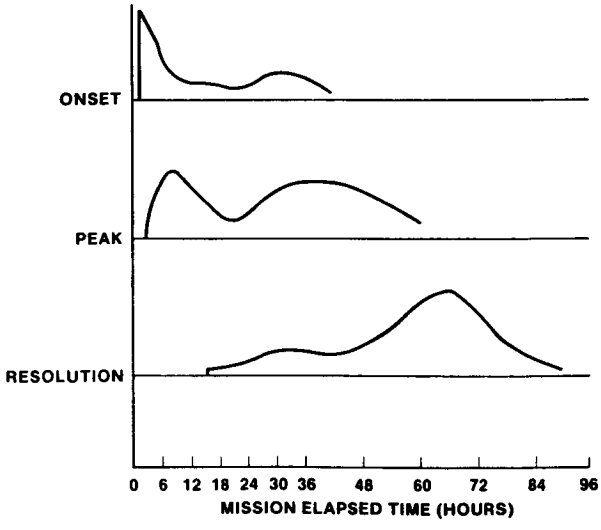


Figure 1. SMS symptom time course: all cases.

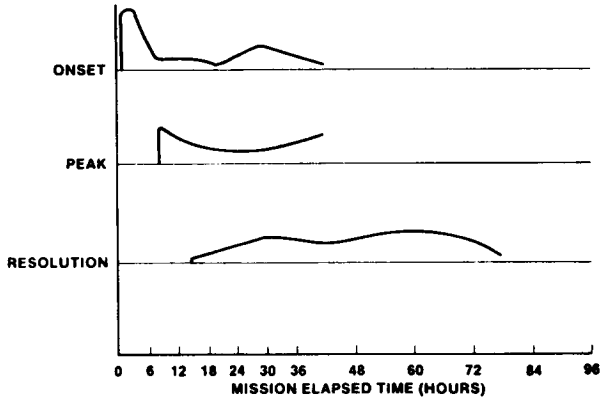


Figure 2. SMS symptom time course: mild cases.

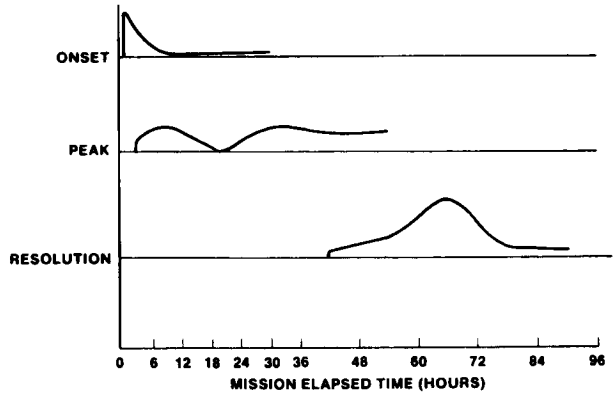


Figure 3. SMS symptom time course: moderate cases.

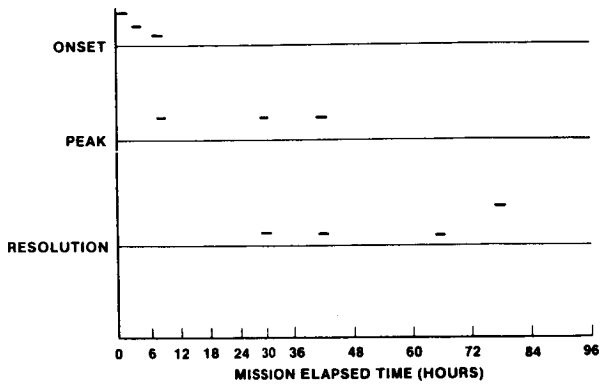


Figure 4. SMS symptom time course: severe cases.

PREDICTION

Prediction of susceptibility to SMS has long been an elusive goal. A variety of ground based tests and test-batteries have been evaluated in an effort to develop the capability to predict which crewmembers will be susceptible to Space Motion Sickness. None of these tests has thus far proven to be sufficiently accurate to be useful in the operational setting. In this study the intent was to evaluate the effect of repeat spaceflight on the incidence and severity of SMS. In particular it was hoped to determine whether the occurrence of SMS on one flight would predict its development and its severity on subsequent flights.

TABLE 6. SHUTTLE CREWMEMBERS' SMS EXPERIENCE ON FIRST FLIGHT*

	NUMBER	PERCENT OF CASES	PERCENT OF TOTAL
TOTAL CREWMEMBERS	71		
TOTAL CASES OF SMS	42		59%
MILD	18	43%	25%
MODERATE	17	40%	24%
SEVERE	7	17%	10%

*SIX SHUTTLE CREWMEMBERS ACTUALLY HAD THEIR FIRST FLIGHTS ON VEHICLES OTHER THAN THE SHUTTLE. THEIR MOTION SICKNESS EXPERIENCE WAS IDENTICAL TO THEIR FIRST SHUTTLE FLIGHT: FOUR HAVING NO SMS AND TWO HAVING MODERATE SYMPTOMS.

On the first 19 Shuttle flights 71 different individuals served as crewmembers. Forty-two of these 71 people experienced SMS symptoms on their first flight, for an incidence of 59 percent. The severity distribution of these cases is shown in Table 6.

Among the crewmembers of the first 19 Shuttle missions were 22 astronauts who flew in space more than once. Eleven of these were affected by SMS on their first flight. However, on their second flight only 9 of these 11 experienced the sickness. This represents a reduction from 50 percent to 41 percent. None of the 11 who were not sick on their first flight developed symptoms on any subsequent flight. In addition to a reduction of the total number affected by SMS on their second flights there was also a reduction in the severity of symptoms of some of those who were still sick on their second flight. These data are summarized in Table 7.

TABLE 7. SMS EXPERIENCE OF REPEAT SPACE FLIGHT

SMS INCIDENCE
FIRST FLIGHT: 11 CASES = 50%
SECOND FLIGHT: 9 CASES = 41%

PATTERN: SEVERITY	1ST FLIGHT	2ND FLIGHT
NONE	11	13
MILD	3	6
MODERATE	7	3
SEVERE	1	0

Table 8 shows the change in severity level from first flight to second flight. It should be noted that 2 of the 3 individuals who experienced moderate symptoms on both their first and second flights had their first spaceflight experience 10 years prior to their Shuttle flights. Overall, 5 individuals experienced the same type and severity of symptoms on their second flight while 6 had a decrease in severity. These data suggest that previous spaceflight motion sickness experience is a good predictor for subsequent flights. First flight presence of SMS correctly predicted the occurrence of SMS on a second flight in 91 percent of the cases. This compares quite favorably with the 64 percent correct prediction reported by Homick and coworkers (Ref. 1) utilizing ground based motion sickness tests.

These data also suggest that there may be a carryover of adaptation from one flight to the

next. Of the 9 astronauts who flew twice on the Shuttle and were sick on the first flight, 6 had a decrease in symptoms on their second flight.

TABLE 8. SMS SEVERITY CHANGE FROM FIRST TO SECOND FLIGHT

1ST FLIGHT	2ND FLIGHT	NUMBER
NONE	NONE	11
MILD	MILD	2
MODERATE	MODERATE	3
MILD	NONE	1
MODERATE	NONE	1
MODERATE	MILD	3
SEVERE	MILD	1
	TOTAL	22

COUNTERMEASURES

A search for effective and operationally useful countermeasures for Space Motion Sickness continues to be conducted by scientists both within NASA and in the academic research community. Three general areas of countermeasures--Drugs, Preflight Adaptation Training, and Autogenic Feedback Training--are under investigation at the present time.

DRUGS

Various drugs have been tried in a preventive or therapeutic regimen for SMS but none has been entirely satisfactory. Of key importance in selecting a pharmacologic approach to deal with SMS is the need to avoid drugs with side effects which are more debilitating than the sickness itself. Many of the traditional anti-motion sickness medications have a sedative effect as well as an antiemetic effect and consequently may be more detrimental to the astronaut than the symptoms themselves. Table 9 lists the various anti-motion sickness drugs that have been tried during the Shuttle program. Scopolamine with Dexedrine, Scopolamine alone, Transderm Scop, and Metoclopramide have been used in both a preventive mode and a therapeutic regimen. The remaining medications have been used for treatment of symptoms only. None of the drugs has been tested in adequately controlled studies. Consequently, conclusions about the efficacy of any of the drugs are based only on anecdotal accounts. Two lines of investigation are currently underway at the Johnson Space Center. One investigation is studying the pharmacokinetics of Scopolamine and Dexedrine inflight while the other investigation will study, in a controlled double-blind manner, the effect of Scopolamine and Dexedrine in preventing SMS.

TABLE 9. SHUTTLE CREWMEMBER ANTI-MOTION-SICKNESS DRUG USAGE SUMMARY

	NUMBER OF CREWMEMBERS		
DRUG NAME	TOTAL	WITH SMS	WITHOUT SMS
SCOPOLAMINE (.4 mg) + DEXEDRINE (5 mg) - ORAL	31	20	11
SCOPOLAMINE (.4 mg) - ORAL	1	1	0
PHENERGAN (25 mg) - SUPPOSITORY	3	3	0
PHENERGAN (25 mg) + EPHEDRINE (25 mg) - ORAL	1	1	0
METOCLOPRAMIDE (10 mg) - ORAL	22	19	3
COMPAZINE (10 mg) - SUPPOSITORY	3	3	0
TRANSDERM SCOP - CUTANEOUS	1	0	1
DIAZEPAM (5 mg) - ORAL	1	1	0

PREFLIGHT ADAPTATION TRAINING

The concept of developing training procedures by which adaptation of the sensory-motor system can be accomplished prior to spaceflight has arisen from experimental results supporting the otolith tilt-translation reinterpretation hypothesis (2 and 3). In this countermeasure concept for SMS, a training devise is used in which the subject is exposed to conflicting visual-vestibular inputs which produce the same eye movement responses that are seen in the immediate postflight period. By repeated exposure to this simulated situation on the ground prior to spaceflight it is hoped that the crewmember can adapt in such a manner that he will be much less susceptible to SMS. Preliminary studies, as reported by Parker and co-workers (3), indicate that it is possible to induce such an adaptation. Figure 5 shows conceptually how the relationships between otolith responses associated with the subject's movements and the visual scene presented to him are systematically altered. For example, in the trainer, leftward head roll results in

translation of the visual scene toward the left without rotation. It remains to be seen whether this will be an effective countermeasure for SMS.

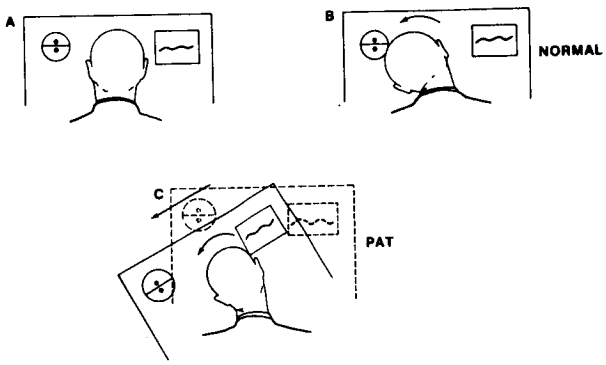


Figure 5. Concept for preflight adaptation training (PAT).

AUTOGENIC FEEDBACK TRAINING

A third area of investigation in the development of SMS countermeasures is the study of autogenic feedback training. In this technique the crewmember is taught to control certain autonomic nervous system functions, such as heart rate, skin temperature, and muscle tension, with the goal that this training will carry over into the control of motion sickness symptoms (4 and 5). This technique has been tried on two Shuttle flights under the direction of Dr. Cowings of the NASA Ames Research Center. Thus far too few subjects have been evaluated to draw a conclusion about the efficacy of this countermeasure.

SUMMARY

The incidence of space motion sickness during flights of the Space Shuttle continues to run between 50 and 60 percent. Although there has not been a serious deleterious effect on Shuttle mission objectives to date, the symptoms are unpleasant and reduce crew efficiency. The impact of SMS is potentially greater in flights which, planned or otherwise, are completed in less than four days. Approximately half of the cases of SMS are mild in nature and resolve fairly quickly. The remainder of the cases are in the moderate to severe categories and include multiple episodes of vomiting, suppression of appetite, and contribute to dehydration of the crewmembers. Most of the crewmembers who become sick do so within the first 6 hours after launch, reach the peak of their symptoms in the middle of the first or second day of flight, and feel back to normal by the end of the third day of the mission.

Previous spaceflight experience with SMS is an accurate predictor of subsequent susceptibility to the sickness. There does, however, appear to be a partial retention of adaptation from one flight to the next, particularly if the time interval between space flights is less than two years.

A search for effective and operationally useful countermeasures continues. In order for a countermeasure to be useful it not only must be effective in preventing or minimizing symptoms but must also be free of side effects which could reduce crew performance. There is active ongoing research in three general areas: anti-motion sickness drugs, preflight adaptation training, and autogenic feedback training. In all likelihood the ultimate solution to the problem will involve a combination of countermeasures tailored to each individual's specific needs.

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EFFECTS OF PROLONGED WEIGHTLESSNESS ON SELF-MOTION PERCEPTION AND EYE MOVEMENTS EVOKED BY ROLL AND PITCH

Investigators: M. F. Reschke, Ph.D., and D. E. Parker, Ph.D.

INTRODUCTION

Responses to three types of motion were examined before and after 5-7 days of orbital flight. Self-motion perception and eye movements were recorded during roll and pitch stimulation. Postural orientation was assessed using video tape recordings of voluntary body movements.

The research described in this paper was derived from the otolith tilt-translation reinterpretation model (1,4,5). This model suggests that on Earth the otoliths respond to both linear motion and head tilt (pitch or roll) with respect to gravity. In space, however, the otoliths no longer respond to head tilt with respect to gravity. Following adaptation to weightlessness, otolith signals apparently are interpreted by the brain as always indicating linear motion.

Three research hypotheses were examined: (i) roll or pitch stimulation would result in translational self-motion perception during reentry and immediately postflight; (ii) within the first 1-2 hr after landing, roll would elicit increased (relative to preflight) horizontal eye movements and pitch would elicit reduced vertical eye movements; (iii) overshoots in torso bending would be observed when a standing astronaut attempted to tilt (roll and pitch) 20 deg off-vertical immediately postflight.

Those parts of the first and second hypotheses concerning effects of roll were derived from data obtained from three astronauts and were reported previously (1). It was anticipated that the previous observations would be replicated.

Hypothesized response changes associated with pitch stimulation were based on the otolith reinterpretation model. If otolith signal reinterpretation persists immediately after landing, anterior-posterior displacement of the otoliths should be correlated with translation along the astronaut's X body axis and with ocular accommodation and convergence changes (but not vertical eye movements). After adaptation to weightlessness and while still on orbit, vertical eye movements during pitch head motion should be driven entirely by the semicircular canals. Immediately after landing, otolith signals associated with pitch head motion should stabilize the eye and oppose the vertical eye movement signal generated by semicircular canal stimulation; therefore, the gain of the vertical eye movement evoked by pitch should be reduced.

The third hypothesis was derived from anecdotal observations and the otolith reinterpretation model. Vestibular, proprioceptive, and visual signals normally provide feedback as a person attempts to bend from the waist to a particular tilt angle. If visual signals are eliminated and if the otolith output is not interpreted as tilt immediately postflight, the magnitude of the feedback signal during voluntary tilting should be reduced. Consequently, the astronauts should bend too far as they attempt to perform roll or pitch movements.

PROCEDURES

SUBJECTS

Eight astronauts who participated in four different shuttle missions contributed to the results reported here. Data from Astronauts 1-3 have been reported previously (1). Due to last-minute change of the landing site, postflight eye movement data from Astronauts 7 and 8 are incomplete.

APPARATUS AND PROCEDURES

The apparatus used to passively move Astronauts 1-6 during self-motion perception and eye movement recording was the Miami University Parallel Swing (1). The astronaut was restrained in the prone position with his head dorsal-flexed about 45 deg. A cloth shroud enclosed the head-end of the cylinder and eliminated motion cues from air currents and light.

For roll stimulation, the aluminum cylinder was oscillated at 0.26 Hz around the subject's Z body axis (X head axis). Roll amplitude was ±5 deg from the head-upright position for self-motion perception and ±15 deg for eye movement recording.

Preflight observations from Astronauts 7 and 8 were obtained using a newly-constructed pitch-and-roll device (PARD-Fig. 1). The astronauts were restrained by belts located at the feet, legs, hips, waist, shoulders and arms. The head was restrained by ear pads and a bite board. A light-tight shroud covered the entire body. Self-motion perception was recorded following stimulation at 0.2 Hz and ±5 deg from the head-up position. Eye movements were recorded during stimulation at 0.1, 0.2 and 0.4 Hz at ±15 deg for the higher frequencies and ±30 deg at 0.1 Hz.

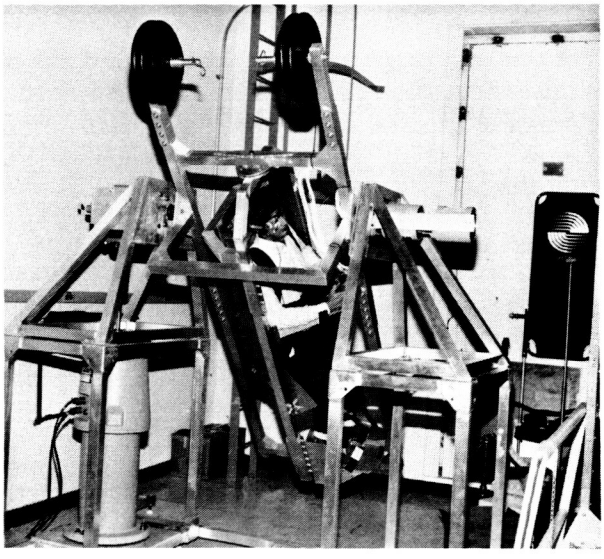

Figure 1. Pitch and roll device.

SELF-MOTION REPORTING

Responses to three motion stimuli produced by the parallel swing were obtained from Astronauts 1-6. The motions consisted of pure linear motion at 100 cm/sec/sec, pure roll at ±5 deg, and phase-locked combined roll and linear motion. Three cycles of each type of motion stimulus were presented. The data collected consisted of drawings and verbal reports (recorded on a VCR) of perceived self-motion path.

Self-motion and visual-surround-motion perception reports during pitch, roll and yaw voluntary head motion (±15 deg, 0.25 Hz) were voice recorded during reentry and while the orbiter was stationary on the runway from Astronauts 7 and 8. Less formal observations were performed by Astronauts 5 and 6. The voice tapes were reviewed with the subjects during a video-taped debriefing two days after landing.

EYE MOVEMENT RECORDING

Eye movements were recorded using an infra-red sensitive video camera and with Electrooculogram (EOG) electrodes. For the video recordings, the camera was focused on the subject's left eye with the aid of extender rings. The light source was an array of infrared-emitting diodes mounted on the camera lens. The camera output was recorded on 3/4 inch tape. For EOG recording, signals from "vertical" and "horizontal" electrode pairs were preamplified and recorded using an LSI-11/23 computer system.

VOLUNTARY TILT

The astronauts were placed adjacent to a wall on which a 20 deg off-vertical line was located. They were required to tilt from the waist until their torso was aligned with the line. Video tape records were obtained while the subjects rolled to their left or pitched forward first with their eyes open and then closed (Astronauts 4-6) or only with their eyes closed (Astronauts 7 and 8).

RESULTS

PERCEIVED SELF-MOTION

PARALLEL SWING OBSERVATIONS

Drawings indicating perceived self-motion path during roll from Astronauts 1-6 are illustrated in Fig. 2. Preflight, all reported that cylinder roll produced primarily roll self-motion perception. Immediately postflight, they reported increased horizontal displacement during the roll stimulation.

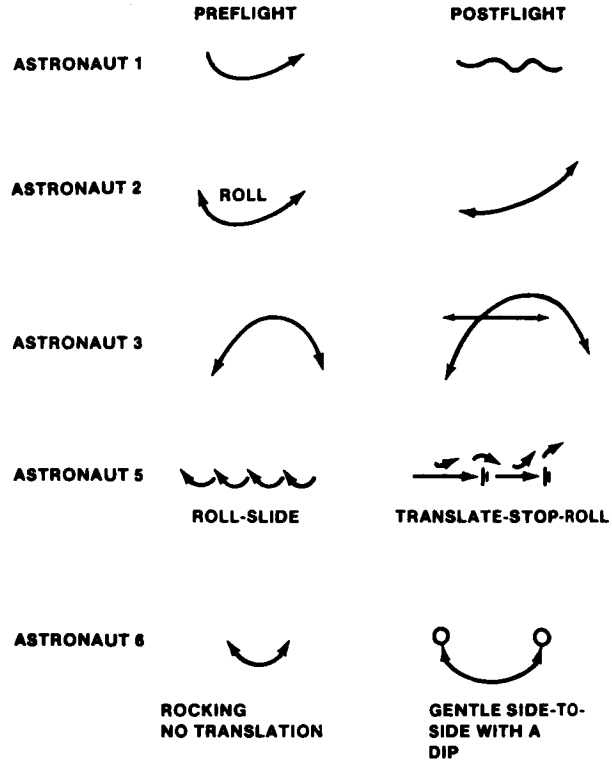

Figure 2. Drawings of self-motion perception during roll from Astronauts 1-6. The postflight reports were obtained within 2.5 hours after landing.

REENTRY OBSERVATIONS

Astronaut 6 reported self-motion perception associated with pitch, roll and yaw head motion during reentry Forward pitch motion initially resulted in the perception of backward translation. This perception was reported as unexpected. Subsequently during reentry, pitch and roll elicited translational self-motion perception in the same direction as the head movement.

Astronaut 7 reported strong sensations of self- and surround-motion associated with pitch and yaw during reentry and after the orbiter had stopped on the runway. No unexpected sensations were associated with roll head movement. As previously reported by Astronaut 6, the translation component of the self-motion was perceived to be in the direction of the tilt. Astronaut 8 reported that head motions during reentry and subsequently on the ground made him dizzy and elicited motion sickness symptoms.

EYE MOVEMENTS

Data suitable for Fourier analysis were recorded from Astronauts 4-6 postflight and from Astronauts 7 and 8 preflight. Following digital filtering and cosine tapering, the digitized eye movement and roll stimulus records were analyzed employing Fourier transforms. Stimulus power, ocular response power, transfer function gain, phase and coherence at the stimulus frequency were determined.

Figure 3 illustrates horizontal eye movements recorded during roll stimulation from Astronaut 6 two hours (Fig. 3-A) and three days (Fig. 3-B) after landing. On the day of landing (R + 0), the horizontal eye position trace led the roll position signal by 33 deg; three days after landing (R + 3) the eye position trace led the roll signal by 165 deg.

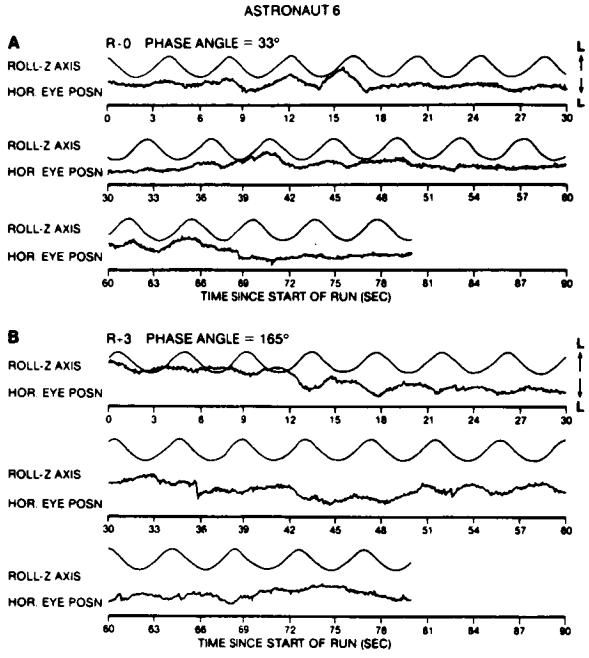

Figure 3. Eye movement records from Astronaut 6 during roll stimulation at 0.25 Hz 2 hr (R + 0) and 3 days (R + 3) after landing. Note that the phase relationship between horizontal eye movements and head roll changed.

Eye movement phase angle and coherence data from Astronauts 4-6 are plotted in Fig. 4. The EOG records from Astronaut 6 indicate a 132 deg phase shift during roll stimulation immediately postflight relative to later postflight observations. Leftward roll was associated with leftward horizontal eye movement for Astronauts 4 and 5 across all recordings and for Astronaut 6 three days after landing.

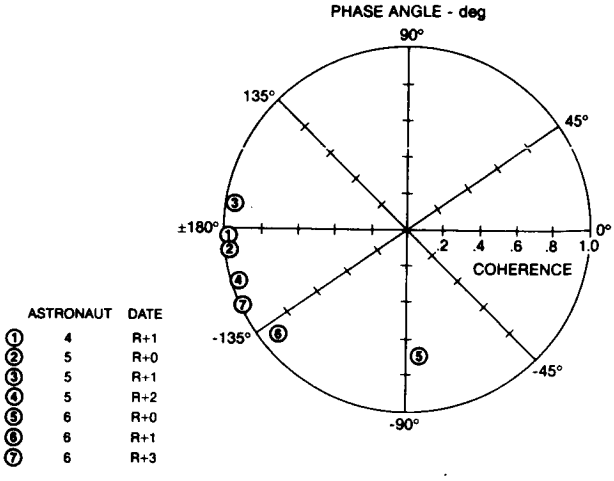

Figure 4. Phase relationships and coherence between horizontal eye position and roll position signals from Astronauts 4-6 postflight.

Eye movement responses elicited by stimulation with the PARD apparatus are illustrated in Fig. 5. Unfortunately, the shuttle made a contingency landing at Edwards AFB, whereas the PARD was located at Kennedy Space Center; consequently, no postflight eye movement data were collected from Astronauts 7 and 8.

VOLUNTARY TILT

Pitch and roll voluntary body tilt immediately postflight was not different from preflight. Astronaut 5 indicated that he relied more than usual on waist joint receptor cues when performing voluntary tilt with his eyes closed. He stated also that he probably could not have performed the task within minutes after landing. Astronaut 6 deviated leftward when attempting to pitch forward and reported "digging in" his toes.

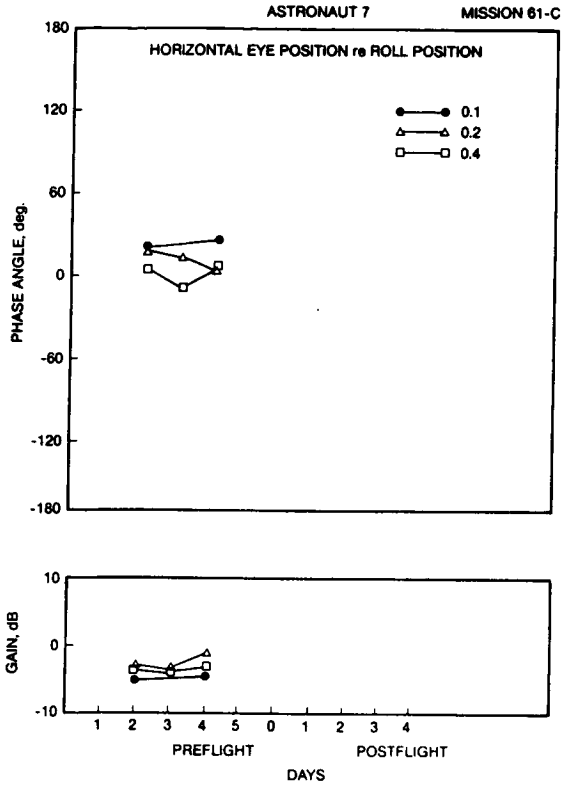

Figure 5. Phase and gain of horizontal eye movements during roll stimulation in a newly constructed pitch and roll device. No postflight data were collected due to the landing of the shuttle in California rather than Florida.

CONCLUSIONS

PERCEIVED SELF MOTION

The data reported here confirm previous reports of increased translational self-motion perception during roll stimulation immediately after extended orbital flight. The reports from Astronaut 6 and 8 regarding perception during reentry strongly confirm the basic observations.

Three astronauts performed slow pitch and roll head motions during reentry or while stationary on the runway immediately after a mission. All three reported unusual self- or surround-motion perception while performing the head movements. Astronaut 6 reported self-motion initally in the direction opposite to the head tilt and subsequently in the same direction as the tilt. Astronaut 8 reported that his perception of translational self-motion was always in the direction of the head tilt.

Following the otolith tilt-translation reinterpretation model, we hypothesized that weightlessness-adapted astronauts would report translational self motion in the direction opposite to head pitch or roll immediately postflight. Figure 6 summarizes a possible resolution of the discrepancy between this prediction and the astronauts' reports.

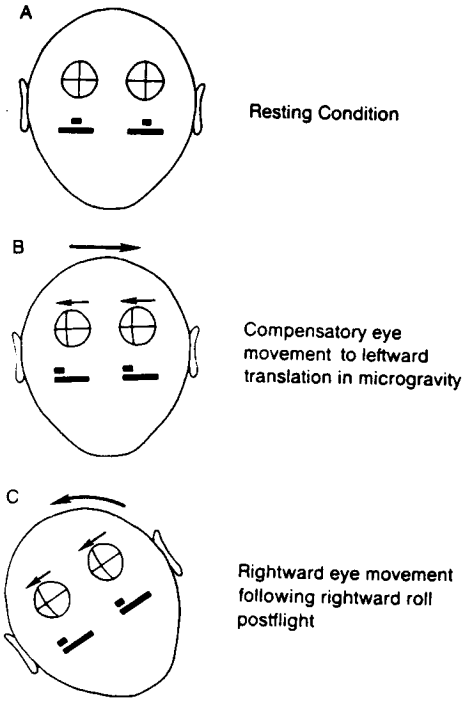

Figure 6. Otoconia displacement and associated compensatory horizontal eye movements developed during adaptation to microgravity.

An astronaut's eyes and the otoconia located above the utricular maculae are illustrated in Fig. 6-A. In microgravity, leftward translation would be associated with rightward displacement of the otoconia and a rightward compensatory horizontal eye movement, as illustrated in Fig. 6-B. When the astronaut returns to a gravity environment, rightward head roll would produce rightward displacement of the otoconia. If he relies only on the signals from the otolith organs, the astronaut should perceive leftward translational self motion because rightward otoconia displacement has been associated with leftward translation during adaptation to microgravity. Alternatively, suppose the astronaut's eyes are

open while he rolls his head. The rightward compensatory horizontal eye movement developed during adaptation to weightlessness should persist (Fig. 6-C). This compensatory eye movement would cause the image of the stationary visual surround to slip across the retina in a leftward direction. This leftward retinal slip could be interpreted by the astronaut as rightward self motion in the same manner as the well-known linear and circular vection reactions. Conversely, the retinal image slip might be interpeted by the astronaut as inappropriate surround motion. (As one astronaut said, "I tilted my head and the middeck lockers that had been in front of me slid off to one side.")

Given this analysis, it is not surprising that the reports of motion during head pitch or roll postflight are contradictory. Unless trained to make careful observations, an astronaut may be able to report only that his "gyros were tumbled." Careful observations from appropriately trained astronauts will be required to resolve these issues.

Astronaut 8 was exposed to the basic sensory rearrangement produced by a prototype preflight adaptation trainer (2,3). He reported that the trainer produced sensations similar to those that he had experienced during pitching head movements while seated in the shuttle on the runway immediately after landing except that the phase relation between visual surround motion and head tilt was incorrect by 180 deg.

EYE MOVEMENTS

The altered head movement/eye movement phase relationship recorded from Astronaut 6 was not found for Astronaut 5. This may be due to the fact that the observations were performed with Astronaut 5 about 45 minutes after those with Astronaut 6. Consequently, he may have been more completely readapted to the normal-gravity environment. Alternatively, this may reflect individual differences in adaptation or readaptation processes.

Astronaut 5 reported erratic self motion/head motion relationships during reentry and that locomotion during this period was guided solely by visual cues. He reported strong "pitching over" sensations associated with any off-vertical head position during the first minutes after landing. Although he did not report translation, the direction of the relationship between head motion and self-motion perception is similar to that reported by Astronaut 6.

The failure of this investigation to obtain predicted increases in horizontal eye movement amplitude from Astronauts 5 and 6 may have been due to motion apparatus and data analysis limitations. The newly developed PARD apparatus and associated data analysis procedures will allow this prediction to be assessed.

The failure of this investigation to obtain predicted overshoots during voluntary body tilt was also surprising, particularly in view of the report from Astronaut 4. In the future, voluntary body tilt will be examined with the astronauts' ankles "decoupled" (by standing on a foam rubber pad) or with vision stabilized.

The basic findings from this investigation, particularly the self-motion reports during reentry, are consistent with the otolith tilt-translation reinterpretation model and the concept for preflight prophylactic adaptation training (1).

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GASTRO-INTESTINAL MOTILITY IN SPACE MOTION SICKNESS

Investigators: William E. Thornton, M.D., Tom Moore, M.D., and Sam Pool, M.D.

INTRODUCTION

Motion sickness (MS) signs and symptoms have traditionally been divided into those of 'head' and 'stomach', with nausea and vomiting being cardinal signs. With adequate stimulus, vomiting is the final stage of motion sickness (14). With continued stimulus repeated vomiting may occur, to the point of prostration in some cases (15).

The neurological control mechanism for emesis has been studied and discussed in detail (2,4,19) and a simplified rendition of the currently accepted scheme of this mechanism is shown in Figure 1. There are connections from the vestibular system to the vestibular nuclei and from the nuclei to the emesis center, which produces vomiting by way of the respiratory and abdominal musculature plus some gastroduodenal activity.

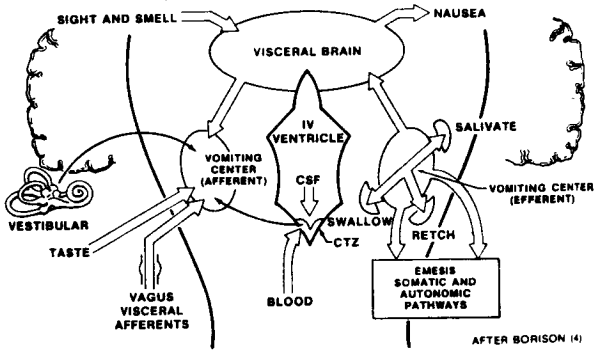

Figure 1. Currently accepted schema of emesis center and its major inputs. The center itself coordinates and directs the action of vomiting by stimulation of the respiratory and somatic abdominal musculature with some G.I. activity. After Borison.

Many investigators report the nausea of motion sickness to be accompanied by a reduction of gastrointestinal activity (16). Others have found that vestibular and other stimulation produces strong duodenal antiperistalsis (1,10). Crampton reported that vomiting in MS-susceptible cats can be prevented by plugging the aqueduct between the third and fourth ventricles, implying a possible cerebral spinal fluid (CSF) carrier role with a humoral pathway (6). Several investigators have shown decreased GI motility accompanied by increased endorphin levels with caloric stimulation (17,18). Borison found that the Chemoreceptor Trigger Zone (CTZ, area postrema) is not necessary for vomiting from motion sickness in cats (3).

The current theory is that as stimulus duration/intensity increases, hypersalivation, swallowing, nausea, and finally retching/vomiting will occur. If the stimulus level is maintained vomiting will be repeated. At lower stimulus levels only salivation or nausea may be sustained. Less frequently, nausea and vomiting may occur suddenly with or without any or all of the prodromal symptoms.

Early in the Shuttle program there were reports of sudden, brief bouts of vomiting without prodrome (including nausea). Considerable periods of time, usually hours, could elapse before the event was repeated unless food or water was ingested, in which case vomiting typically followed in less than an hour. Vomitus was usually clear, but occasionally bile stained. Any food present was undigested. There were one or two reports of vomiting coincident with seeing the Earth "inverted" but such cases were a small minority; it usually occurred in ordinary circumstance and often with lights out. Nausea was sometimes present, but was more often absent.

Vomiting of this nature was so different from that of ordinary motion sickness that a crewman who had experienced both summed up his opinion by stating, "I don't know what it is but it isn't sea sickness!" This difference was one of the major reasons for an inflight investigation begun by the Astronaut Office and Flight Medicine. As part of this

investigation, an on-board physician noted that bowel sounds were absent in those with Space Motion Sickness (SMS) for the duration of the syndrome but present after recovery and in those unaffected. It was concluded that the GI problem was a temporary ileus. Electronic recording of bowel sounds and direct and electronic ascultation performed on one flight confirmed the earlier findings. Metoclopramide (MCP) was taken in an attempt to reestablish bowel activity and seemed to be effective in two subjects.

An improved sound recording system was devised and 18 inflight records of sounds have been made, including 6 during SMS and 3 while taking MCP. An electro-gastro-graphic study was done on 1 subject, a single trial of intravenous MCP and Naloxone was done, and frozen plasma from 2 subjects with SMS was obtained for analysis of possible transmitter substances. The following results are from an ongoing study.

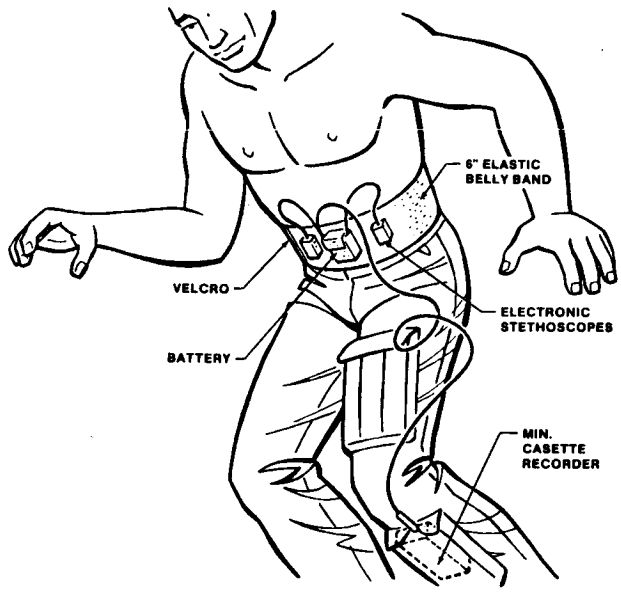

Figure 2. Inflight recording of bowel sounds. The recorder is small enough to be carried in a pocket.

PROCEDURES

Electronic stethoscopes (with a battery life of 14 days) were incorporated into an elastic, velcro-secured belt (Figure 2). They were located over the right and left upper quadrants of the abdomen. Output was recorded by a professional quality, miniature dual channel tape recorder typically carried in a flight suit pocket. Frequency response of the microphones was 30 to 500 Hz (3 db. points) in contact with skin. They were embedded in foam to improve the sealing of the microphone cavity to the body. Validated frequency response of the recorder was 40 to 15,000 Hz (3db), with 1 percent distortion and wow and flutter of less than 0.14 percent with a speed accuracy of 0.3 percent. Cassette tapes with 45 minutes recording time per side were used. No attempts were made to control conditions or activities during the recording period, including ingestion of food, since this would have inevitably conflicted with inflight operations and would have further reduced recording opportunities. Where possible, the conditions were documented.

Data were reduced by the investigator by monitoring both channels of the recorded sounds with wide response earphones. Sounds were graphically recorded by a high-frequency (DC-15 kHz) electrostatic recorder after band pass filtering from 400 Hz - 3 kHz (24 db/oct. roll-off). The nominal graphic recording speed was 1 cm./sec. so that only sound envelopes were distinguishable. An event marker, manually controlled by a push button, was actuated for every sound ranging from single brief "tinkles" through prolonged "rushes." Figure 3 is an example of a scored record. If several distinct sounds were present in an event they were scored. No allowance was made for differences in amplitude, and events were frequently too rapid for manual counting. The result was that a quiet bowel was overscored and an active one underscored. Obviously, this was semiquantitative at best. The events were counted for each one minute epoch, summed, and plotted for 5 minute epochs.

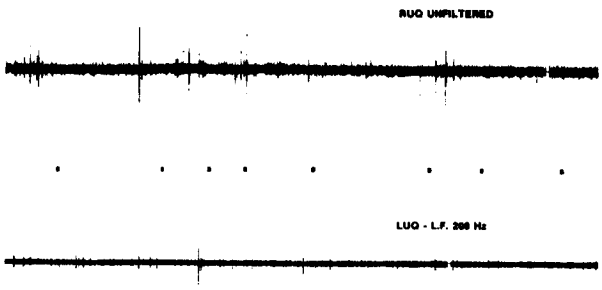

Figure 3. Section of a scored bowel sound recording made inflight on one mission. Identified sounds are indicated by the marker signals between channels.

The planning matrix in Figure 4 was done to allow the comparisons shown. Twenty recordings were also made before, during, and after acutely induced MS on the rotating chair using this system on ordinary subjects. A series of recordings over extended periods during normal activities was also made.

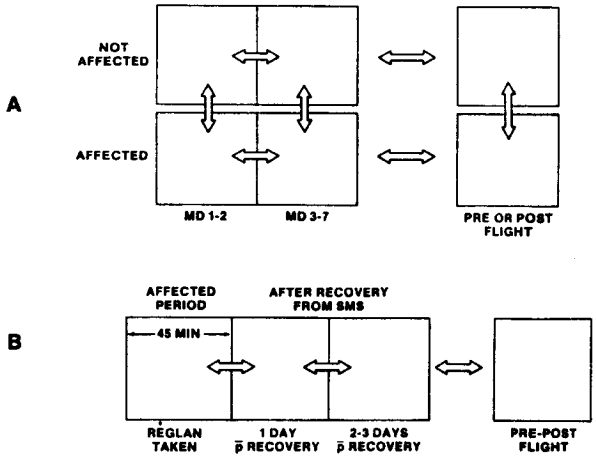

Figure 4. Planned matrix for comparison of sound activity of two hypothesized populations, affected versus unaffected, plus another with medication, in 3 possible circumstances. 'A' allows comparison of affected versus unaffected under various conditions while 'B' examines the effect of MCP on individuals affected.

RESULTS

Nineteen individuals have made at least 1 recording inflight. Of these, 6 affected subjects, one of whom flew 3 times, have made recordings that met the horizontal or temporal requirements of the study; i.e., 1g baseline and recording during and after SMS. None of these had simultaneous inflight controls. One subject, unaffected by SMS, made an adequate total number of recordings. Two of the recordings included the use of MCP. Other recordings were randomly scattered in time.

The collected data does not allow for significant comparisons as planned (Figure 4) other than between the level of activity preflight and inflight during SMS in those affected, and between those affected and unaffected during the same periods.

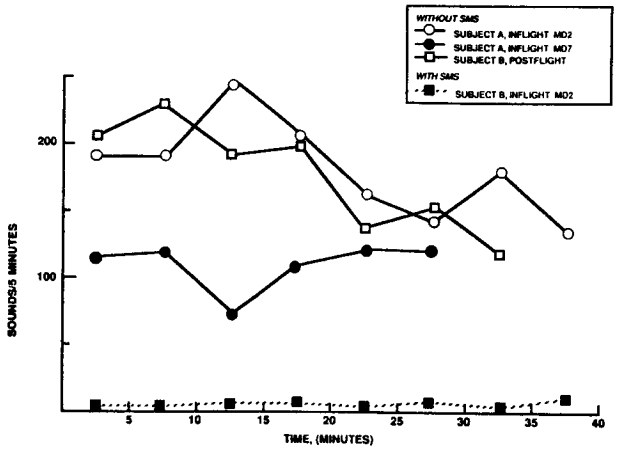

Figure 5. Plot of means of sounds counted per five minutes versus time during the period of SMS inflight and after recovery. Subject A was unaffected while B had a typical course of SMS. Inflight MD2 on subject A was made during the susceptible period while inflight MD7 was made after this period.

Typical plots of sound activity versus time for individuals with and without SMS are shown in Figure 5. Of particular interest was one recording made over the period of recovery. In Figure 6, the 5-minute means of counts are shown over this period. The means of such activity for all subjects versus the period in which they were gathered are plotted in Figure 7. Normalized activity, i.e., counts during the period of SMS divided by 1g baseline counts, are also plotted here.

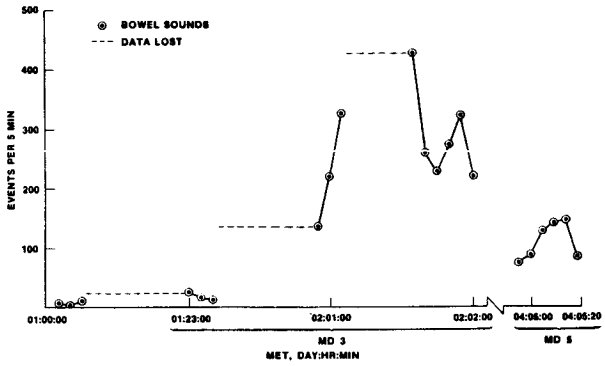

Figure 6. Record of sound activity from a subject during recovery from SMS. The rapid resolution and period of hyperactivity is consistent with indirect observations of this process. MET is mission elapsed time and MD is mission day; i.e., recordings on MD3 were made on the morning of the third day.

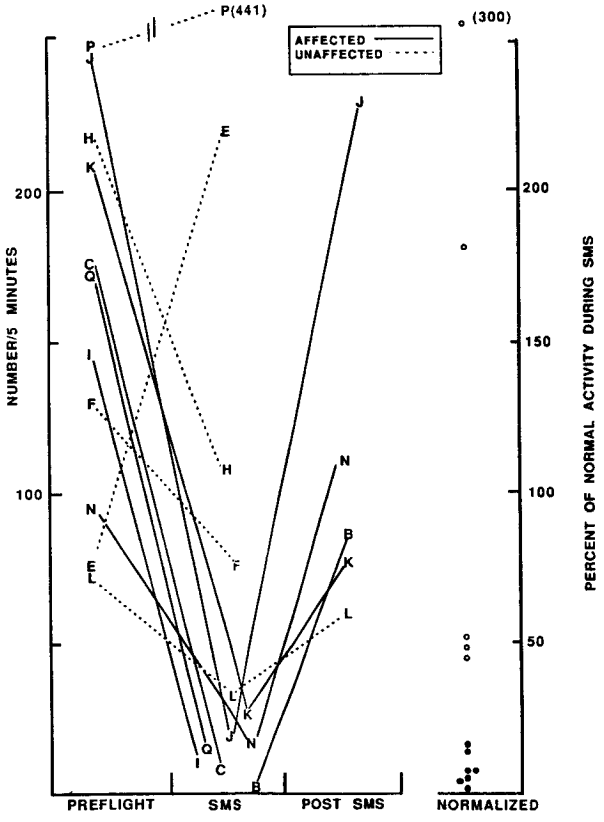

Figure 7. Means of counts from recordings made of all subjects, preflight and during periods of SMS and recovery. Affected individuals have solid lines, while those unaffected are dotted. Percentage of activity during SMS versus preflight are plotted on the right side with those affected in solid circles and those unaffected in open circles.

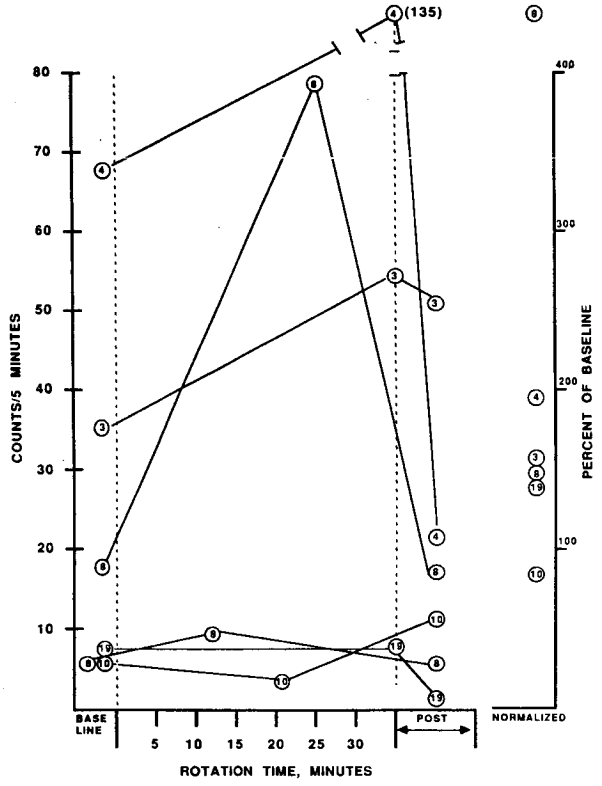

Figure 8. Mean of sound activity in 6 normal subjects during and after off-vertical rotation. Level of sickness reached by Graybiel criteria is shown in the numbered circles which also show time at which the rotation was stopped. On the right side, the mean activity during the period of symptoms is plotted as a percentage of pre-stimulus activity levels.

In addition to these data, a number of flights have had physicians aboard who listened to the bowel sounds of those with and without SMS. They have confirmed a great reduction or virtual absence of sounds in those with SMS as compared to activity after recovery or in those without SMS. Such reductions have been observed in all but one case of recorded or observed subjects to date. One subject appeared to develop marked hyperactivity during SMS, but medication was present. In contrast, most who were unaffected have had normal or hyperactivity during this period. The change was so striking that a number of nonmedical astronauts have monitored their gut activity with stethoscopes. The sound activity of normal subjects with acutely induced MS is shown in Figure 8. In every case monitored during off-vertical rotation, the activity was increased or unchanged.

Only 3 monitored studies of metoclopramide were done; one on a normal subject and two on subjects with SMS. There were no striking changes produced by this drug in the bowel activity of either of the latter cases. Intravenous metoclopramide and naloxone were each tried in one case without significant difference.

On one subject, a naso-gastric catheter with transducer was passed from oral cavity to duodenum, and pressure recordings were obtained, but this was after recovery from SMS. It probably would not have been possible during SMS.

There have been numerous ground-based electrogastrogram (EGG) studies, but only one flight study has been performed, and that was after SMS had resolved.

CONCLUSIONS

Reasonably accurate measurement of GI motility is difficult under laboratory conditions on Earth. Radiographic methods or nuclear-tagged meals are not currently possible inflight. Radiotelemetry pills leave much to be desired even on Earth. The multi-port perfused catheter is technically feasible, but operationally unacceptable. This was obvious during passage of the naso-gastric catheter on orbit, which was more difficult than in 1g and would have been unlikely with SMS present. It is more difficult to relate motility to the electrogastrogram (11) than to bowel sounds, and the recording technique is more complex for the EGG.

There is an indirect relationship of sounds to mechanical activity and especially to coordinated activity (5,7,8,9,12,13,20). Conversely, life and death decisions are still routinely based on this technique. In short, it was the best that could be done under the circumstances. The methodology is robust and reliable albeit inefficient and time-consuming, requiring approximately two times the actual recording time for assessment.

In addition to the limitations inherent in estimation of motility by auscultation there is also the wide variation that may occur with uncontrolled sampling; for example, the large changes in normal activity level from mealtime to mealtime, and under other conditions.

In spite of this and with the limited results, it seems safe to say that a significant ileus is present in the majority of subjects during SMS, and appears to last for the duration of symptoms. Such a state of the bowel is also consistent with other signs such as the vomiting of virtually all ingested food and in most cases any significant amounts of water. The vomiting of true SMS is therefore probably secondary to distension of the stomach which then stimulates the emesis center by vagal afferents. There are many and varied ramifications and possible complications of this simple scheme, both in practice and theory.

Some of the facts that must be accounted for include: vomiting may occur within minutes of orbital insertion, long before significant accumulation of liquids could occur. It seems likely, in this case, that simple motion sickness secondary to launch stresses may be present, although in every such case to date signs and symptoms of SMS have followed. In rare cases there has been bile staining of vomitus which would indicate a relaxed pylorus or retrograde duodenal peristalsis. In the latter case, bowel sounds should be present at some point, possibly prior to emesis. Much more complex is the question of why the majority of subjects was not nauseated. The two final questions are how is this related to 1g motion sickness and what is the mechanism?

In both cases there is neither the experimental, nor theoretical knowledge to answer. If the currently accepted scheme of vestibular (system) conflict → emesis center → nausea/vomiting is correct, then it seems at odds with the findings here. The question of GI activity during 1g motion sickness has not been satisfactorily answered, for while some investigators find reduced or absent activity, others have reported increased sounds and duodenal anti-peristalsis with caloric stimulation. This limited study of sounds in acutely induced motion sickness supports increased gut activity which may well be retrograde.

As to the mechanisms of this ileus, there is no certainty. At first glance it would seem to be simple vagal inhibition; but in view of animal and human studies which show large changes in endorphin levels and upper GI motility with caloric stimulation, and the blocking of effects of endorphins on motility in animals, it may not be this simple. A further note of caution may

have been raised by recent studies of Koch and Stern (personal communication) in which vagotomized patients had gastric responses to motion sickness stimulation by circumvection.

The failure of MCP and Naloxone(a) was disappointing, for if some agent could be found to restore motility a major portion of the SMS problem might be resolved. It appears that we may have to await more knowledge of the GI system itself, as well as a better understanding of brain-gut pathways to attack the ileus logically.

A better means of motility measurement is needed, and while the bowel sound methodology could obviously be improved, there is little else of promise at this time.

Conversely, the absence or reduction in bowel sounds is the first consistent sign, the first reliable marker, of SMS. It promises to be an objective means of detecting and following SMS and also offers a research path to increased knowledge of SMS, possibly back to its origin.

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(a) An n of 1 cannot be unequivocably called a failure, but it produced absolutely no effects in a good trial case.

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OCULAR COUNTERROLLING

Investigators: M. E. Reschke, Ph.D., D. E. Parker, Ph.D., and N. Skinner

The Otolith Tilt-Translation Reinterpretation (OTTR) hypothesis says in part that adaptation to space flight is a function of sensory rearrangement and that signals from the otolith organs during orbital flight are reinterpreted as linear displacements.

An important question relating to this concept concerns the maintenance or substitution by other sensory systems of information to the central nervous system which will replace missing or altered vestibular inputs. Specifically, this study asks the question: "Can neck receptors substitute for otolith receptor input to maintain ocular torsion during space flight?"

The measurement of ocular torsion is difficult under the best of circumstances. When coupled with the additional constraints imposed by orbital flight, very careful consideration had to be given to the mechanism and procedures that were to be used. The device and procedures had to be simple enough that the experiment could be performed by one crewperson at a time, while meeting size, weight, and safety requirements.

To meet these criteria a method of measuring ocular torsion first used about 140 years ago was selected. In this method an after-image of a target is formed on the retina. Any eye torsion occurring while the after-image is visible produces a tilting of the after-image relative to an objective reference target.

Figure 1 shows the apparatus developed to obtain ocular torsion with the after-image method. This device is a goggle arrangement housing an electronic flash to place the after-image on the retina, and a digital read out to indicate angular position of the target. A small voice-activated tape recorder was attached to the goggle so that the subjects could verbally report the position of the target as well as their head position. A neck brace was used to eliminate proprioceptive cues from the neck as a control measurement during the flight.

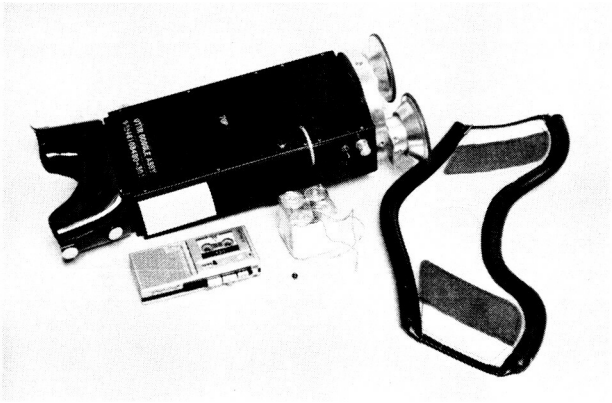

Figure 1. Ocular counterrolling measurement goggles, voice recorder, neck brace, and battery pack.

During use, the head was held in place with a set of flexible rubber eye goggles that were fixed to the main body of the device. A wide velcro strap was used to secure the head to the goggles. The device was fixed to a smooth wall for ground-based testing or to the forward bulkhead lockers during flight with a set of large suction cups. The interface between the main body of the goggle assembly and the suction cups was fitted with a tilt mechanism. This allowed the goggles to be tilted in 15 degree increments from the horizontal position up to plus or minus 60 degrees. Each position had a positive engagement detent to hold the goggles at the desired angle. Each of the nine possible tilt positions was marked with a letter rather than the actual degree of rotation to limit knowledge of head position. During ground baseline testing a level was used to insure that the goggles in the zero tilt position were perpendicular to the gravity vector.

Upon looking into the goggles, the subject saw a digital display indicating the amount of target rotation. The digital display provided a 2000 count output for displacements between plus and minus 20 degrees. This allowed a resolution of 1.2 minutes of rotation

per count. There was a small amount of hysteresis in the controls used to move the reference target and in the potentiometer used for measurement of the angular torsion. This resulted in an absolute accuracy of 10 minutes of rotation.

During the execution of this experiment the subject verbally reported the digital read out. During data reduction the values reported were converted to actual degrees of rotation.

The target used to place an after-image on the subject's right retina consisted of an aluminum disk into which an inverted "T" reticle had been machined. Behind the target disk were an electronic photo flash tube and ready light positioned so that they were visible to the subject through the inverted "T."

The target was rotated by a gear and belt driven mechanism operated by means of a thumbwheel.

Also incorporated in the apparatus was a low intensity light strobe that flashed at 2 hertz. This stroboscopic illumination refreshed the retinal after-image.

During pre- and postflight data collection, the subject set the target to the gravitational vertical with the thumbwheel. The vertical position corresponded to a value of 1000 on the digital display. Then, while following a checklist, the subject tilted his head and the goggles to a predetermined and randomized angle. Once the subject achieved the tilt angle, that position was maintained for approximately 30 seconds. Following the 30 second period the electronic flash was enabled and triggered to place an after-image on the retina.

With the after-image in place, the subject returned the goggles to the upright position. The subject shut his eyes and displaced the target slightly with a thumbwheel in either the clock wise or counterclockwise direction. Once the target was displaced from the vertical, the subject opened his eyes, set the target reticle with the thumbwheel so that it matched the angular position of the after-image, and read a displacement value from the LED's. The subject repeated this procedure in the upright position twice more for that angle, always displacing the target in the opposite direction between each measurement. This entire procedure was then repeated for each of the remaining 8 angles of head tilt.

The inflight procedures differed only slightly from those used on the ground. In one condition the subject's feet were restrained in foot restraints. This condition required the subject to flex his neck to obtain the tilt angles just as he did on the ground. The control condition required the subject to wear a neck brace and to float freely such that his whole body was tilted to match the angle of the goggle tilt.

Measurements were obtained during one Shuttle flight. It was hoped to have measurements made as early inflight as two or three hours. Unfortunately, the goggle unit failed during its early use. However, the crew was able to repair it and obtain data beginning on the third day of the flight.

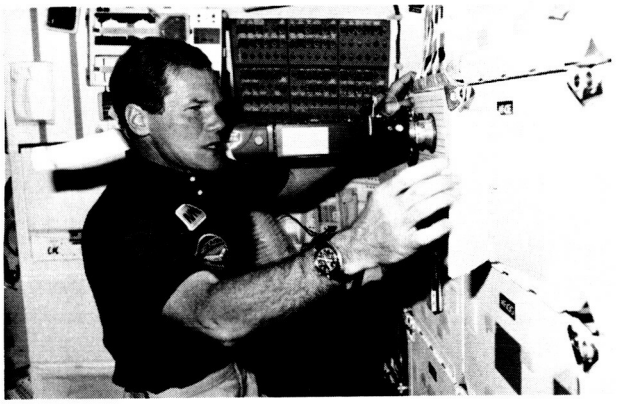

Figure 2. The ocular counterrolling measurement goggles in use during flight.

Figure 3 shows the preflight average response obtained from the two crewmen that were tested. The amount of eye torsion is indicated on the y-axis, and the head tilt position is located on the x-axis.

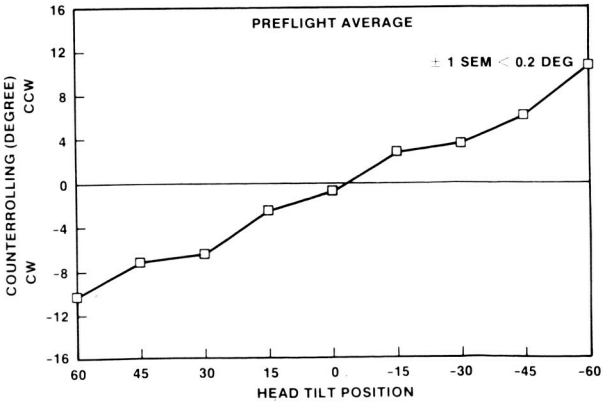

Figure 3. Preflight average data.

Four preflight measurements were obtained from one crewman and 6 from the second crewman. Each point on the plot represents 30 trials at that angle of head tilt. The variance for each data point, expressed as plus or minus one standard error of the mean, was less than 0.2 degrees.

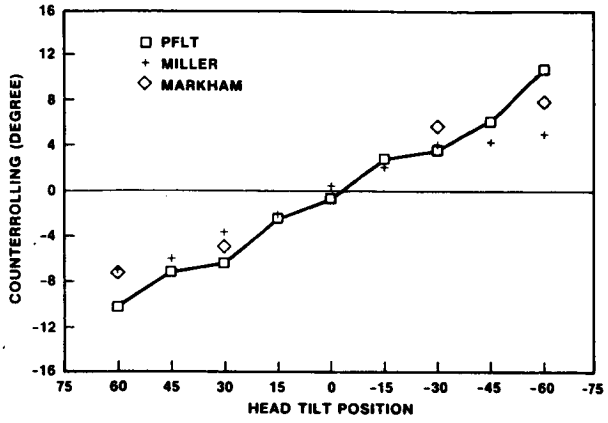

Figure 4. Preflight average vs. published data.

Because the method of measuring ocular counterrolling that was chosen is subjective in nature, it was interesting to compare these data with those from others who had used a more objective approach.

Figure 4 illustrates the preflight average data compared with data that have been published both by Miller (1) during his time at Pensacola and by Dr. Charles Markham (2). Note that for the range between plus or minus 15 degrees the data are comparable. It is at the extremes that this study shows a greater degree of eye torsion than the more objective camera data. However, the lack of correspondence between these data and those of others has no impact on the primary objective of this experiment.

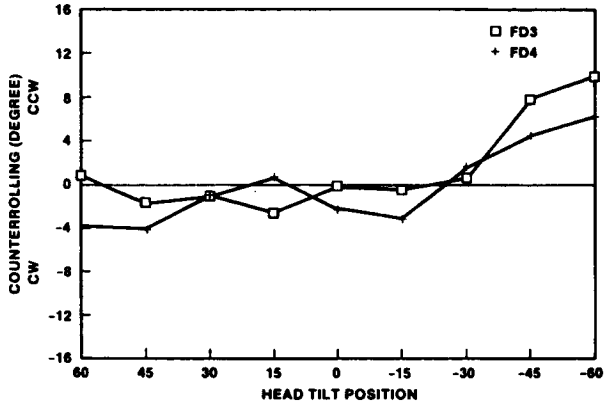

Figure 5. Data for flight days 3 and 4.

Figure 5 shows the data obtained during the flight. Measurements were only obtained from one crewman on the third day of the flight. However, both crewmen were measured on flight day 4. Note that there is some counterrolling present particularly to a rightward head tilt and that there appears to be more torsional eye movement to a head tilt early in the flight.

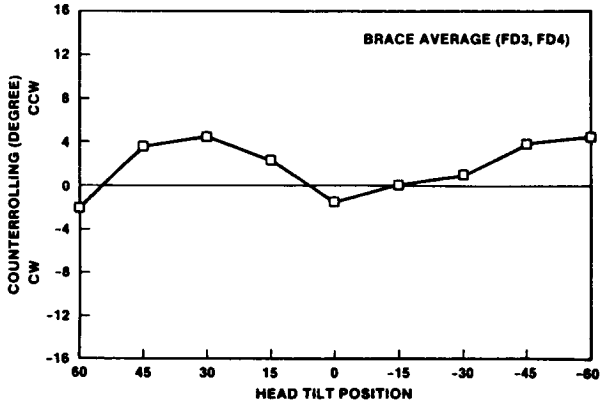

Figure 6. Neck brace average data.

Figure 6 shows the data obtained when the neck brace was worn. Note that the data appear random and do not exhibit a particular trend.

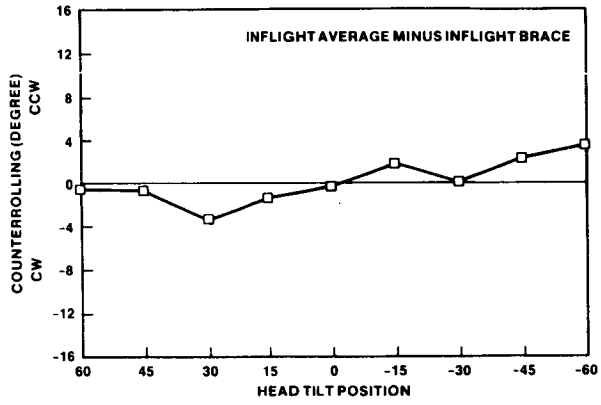

Figure 7. Inflight average minus inflight brace data.

Because of the variability of the data obtained with the neck brace, the absolute difference between the inflight experimental trials and the inflight control data was taken. That difference is depicted in Figure 7. Note that very little eye torsion is evident. The amount that is present represents the variability of this measurement inflight.

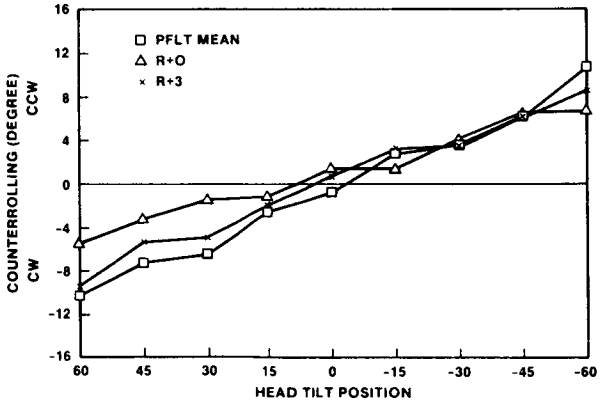

Figure 8. Postflight data.

Figure 8 shows the torsional eye data obtained after the flight. The eye movements measured immediately after the flight show some slight reduction from those obtained preflight. By the third day postflight the amount of counterrolling was essentially equivalent to that seen prior to the flight. This trend was particularly noticeable to a leftward head tilt. It is interesting to note that the compensatory eye movements to a left-ward tilt inflight showed the greatest reduction.

CONCLUSIONS

Based on the data obtained from a single flight with only two subjects it appears that the eyes show a compensatory torsional movement to head tilt. This compensatory torsional eye movement appears to be elicited by the neck receptors.

These findings support a concept of sensory substitution, in this case the substitution of neck receptors for missing otolith information.

If these findings are replicated on future flights, the otolith tilt-translation reinterpretation hypothesis may be modified to incorporate these results. As one might expect, adaptation to space flight is a complex process that is just beginning to be understood.

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OTOLITH TILT-TRANSLATION REINTERPRETATION FOLLOWING PROLONGED WEIGHTLESSNESS: IMPLICATIONS FOR PREFLIGHT TRAINING*

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INTRODUCTION

Three major points were considered in this investigation. First, this research addressed the problem of space motion sickness. Secondly, this research suggested concepts that provide a basis for understanding space motion sickness. Thirdly, on the basis of these concepts, a proposal for preflight prophylactic adaptation training was presented.

This investigation assessed changes in responses associated with otolith receptor activity following prolonged space flight. The results led to the development of an otolith tilt-translation reinterpretation hypothesis which, in conjunction with the sensory conflict hypothesis, provides a conceptual framework for comprehending space motion sickness.

Possible effects of weightlessness on spatial orientation system (13) responses have been considered by several investigators during the past two decades (10). Some have focused on the consequences of altered stimulation of the otolith receptors while others have suggested changes in the "gains" assigned by the brain to orientation information from visual, vestibular, and somatic receptors (9, 10, 13).

The vestibular otolith receptors respond to linear motion and gravity. If motion cues from visual and skin receptors were reduced or eliminated, responses to roll and linear translation attributable primarily to the otolith receptors could be examined. The Miami University parallel swing and its associated restraint system allowed this.

This investigation examined two types of responses associated with roll and linear translation stimulation: perceived self-motion path and eye movements. These responses were examined before and after orbital flight. Because the otoliths are gravity receptors, it was hypothesized that adaptation to the loss of stimulation due to gravity during flight would alter responses to which the otoliths contribute.

Both perceptual and motor responses associated with the vestibular receptors adapt to rearrangements of either vestibular or visual stimulation. This adaptation phenomenon accounts for the observation that motion sickness symptoms resolve during the initial 48-72 h of orbital flight. Rearrangements that have been investigated previously include ocean travel, slow rotation, image reversing glasses and weightlessness (3,7,17,23). Return to a "normal" stimulus environment following prolonged exposure to rearranged stimulation is associated with a period of readaptation. Responses seen during readaptation suggest that mechanisms of response change during the initial adaptation to the rearrangement.

After preliminary observations (15), the otolith tilt-translation reinterpretation hypothesis was proposed: on Earth, information from the otolith receptors is interpreted by the brain as linear motion or head tilt with respect to gravity. Because stimulation from gravity is absent during orbital flight, interpretation of otolith responses as tilt is meaningless. Therefore, the brain adapts to weightlessness by reinterpreting all otolith receptor output as linear motion (Fig. 1). Immediately following return to earth and before the brain readapts to the normal gravity environment, this reinterpretation of otolith responses persists.

Following the otolith tilt-translation reinterpretation hypothesis, it was predicted that roll stimulation would elicit roll self-motion perception preflight but that this stimulation would be associated primarily with linear

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translation self-motion perception immediately postflight.

It was also predicted that roll stimulation would elicit increased horizontal eye movements and decreased ocular counterrolling immediately postflight relative to preflight and later postflight observations. Vestibular-ocular reflexes serve to stabilize the direction of gaze during head motion. If the weightlessness-adapted brain interprets otolith signals as indicating translation, the appropriate compensatory eye movement during head roll would be horizontal eye deviation.

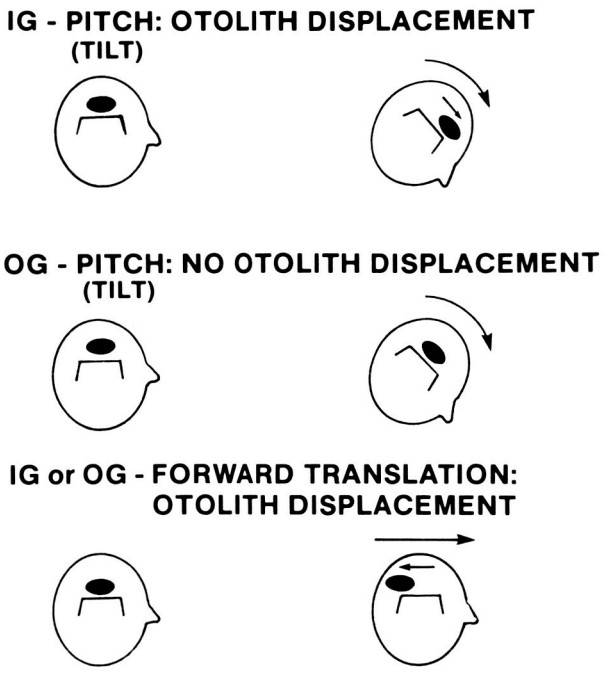

Figure 1. Diagram of vestibular otolith displacement.

PROCEDURES

PERCEIVED SELF-MOTION PATH

SUBJECTS

Three astronauts from two missions served as the subjects in this experiment.

APPARATUS

The motion apparatus employed was the Miami University Parallel swing (Fig. 2). The swing was a four-pole pendulum that produced "linear" (translation) oscillation at 0.26 Hz. For translation, the swing was moved manually by the experimenter. The swing restraint system included an aluminum cylinder which was connected to a motor drive and could be rolled at amplitudes up to ±20° and frequencies between 0.1 and 0.5 Hz. Objective measures of translation and roll motion were provided by appropriate transducers.

The subject was encased in a styrofoam body mold inside of the aluminum cylinder. Head restraint was provided by ear pads and a bite board. The subject was placed in the restraint in the prone position, and his head was dorsal-flexed about 50°. A cloth shroud, which eliminated motion cues from light and air currents, enclosed the head-end of the cylinder.

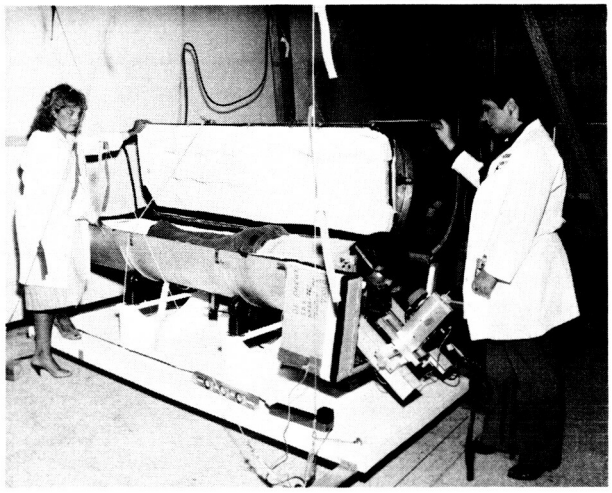

Figure 2. Parallel swing.

PROCEDURE

Responses to three types of motion stimuli were obtained. These were linear translation at 100 cm/s^2 peak; roll at ±5°; and phase-locked, combined roll and linear translation. Translation was in the direction of the subject's Y axis. Roll motion was around the subject's Z body axis (X head axis). For both types of motion, the oscillation frequency was 0.26 Hz.

Three cycles of each type of motion stimulus were presented. The subject's

responses consisted of drawings and verbal reports of his perceived self-motion path.

EYE MOVEMENT RECORDING

SUBJECTS

Two astronauts from one mission participated in this study.

APPARATUS

The apparatus was the same as that used in the self-motion path perception study with the addition of eye movement recording capability. Eye movements were recorded using an experimental RCA infrared video camera. The peak sensitivity of the camera was 890 nanometers. The camera was focused on the subject's left eye with the aid of extender rings. The light source was an array of twelve 100-mw infrared-emitting diodes mounted on the camera lens. The camera output was recorded with a video cassette recorder.

PROCEDURE

Eye movements were recorded during roll ± 15°) and Y axis linear translation oscillation (200 cm/s^2 peak). The oscillation frequency was 0.26 Hz. The goal was to record during five consecutive cycles of movement. The subject's "arousal level" was not controlled.

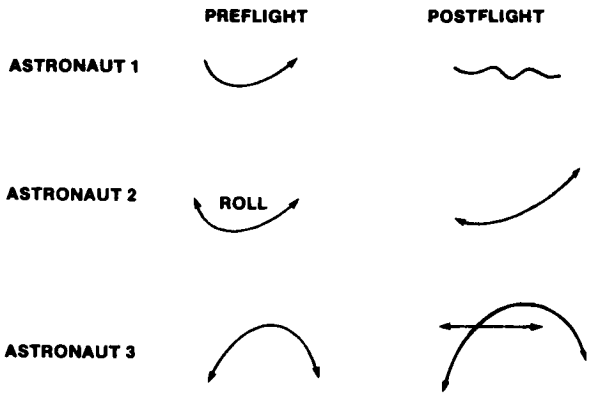

Figure 3. Astronauts' drawings of self-motion perception following roll stimulation.

RESULTS

PERCEIVED SELF-MOTION PATH

Drawings indicating perception of self-motion path during roll are shown in Figure 3. Preflight, the three astronauts reported that cylinder roll produced nearly pure roll self-motion perception, which they illustrated by drawing a "U" shape with arrows at the ends, and that linear translation oscillation produced nearly pure horizontal linear self motion. Immediately postflight, roll stimulation was perceived as translation self motion with a small angular motion component. The verbal reports and drawings were congruent.

EYE MOVEMENTS

Analyzable data during roll oscillation were obtained from both subjects on days 2 and 3 after landing. Fewer usable data were obtained during linear translation.

Because of the poor quality of the video tape records, quantitative analysis focused on transient horizontal eye movements. Horizontal nystagmus during roll stimulation was greater immediately postflight than 2 or 3 days after landing or preflight. The data suggest depression of horizontal eye movements during roll on day 2 after landing and some rebound on day 3. Data obtained during translation stimulation suggest enhancement of the horizontal eye movement response on the second and third day after landing.

Qualitatively, the recording during roll from Astronaut 2 immediately postflight appears different from the other recordings. This record shows the "classic" phase reversing horizontal nystagmus seen ordinarily during oscillation around the Z head axis.

Eye movements were difficult to assess immediately postflight because of the movement of the astronaut's head in the restraint relative to the camera, poor image quality, and the inability of the subjects to maintain straight-ahead gaze.

The video tape records showed a clear ocular counterrolling for Astronaut 3 during roll stimulation. The counterrolling was observable 150 minutes after landing as well as preflight

and on the second and third days after landing. Because of the poor image quality, no attempt was made to analyze counterrolling quantitatively.

CONCLUSIONS

OTOLITH REINTERPRETATION

The results of this experiment support the hypothesis that the brain adapts to prolonged weightlessness by reinterpreting all otolith signals as indicating linear translation. This tilt-translation reinterpretation is reasonable in view of the normal functions of the otolith receptors and analysis of how these functions must change in weightlessness. In weightlessness, no changes in otolith signals are associated with head tilts; only linear translations elicit responses from these receptors. Therefore, it is reasonable to expect that the adaptive brain would learn to interpret all otolith signals as indicating linear translation and that both eye movement reflexes and self-motion perception would be altered accordingly.

Melvill-Jones (9) may have been the first to note that adaptive changes during orbital flight could leave the brain temporarily unresponsive to otolith stimulation by the steady "G" vector. Young, Oman, and their colleagues (10) suggested "otolith reinterpretation" as one of several possible consequences of prolonged weightlessness.

Roll stimulation immediately postflight elicited complex self-motion reports. The self-motion perception included both linear and angular motion components. Also, both horizontal eye deviation and ocular counterrolling were elicited by roll stimulation within the 150-min period after landing. These results are interpreted as follows: Upon return to the normal-gravity environment, the brain persisted in interpreting otolith signals as linear motion. Therefore, the otolith signals produced by roll (tilt) elicited horizontal eye deviation and were perceived as linear motion. Because oscillatory roll also stimulates the semicircular canals, the self-motion path was perceived as a combination of roll and translation, and ocular counterrolling was present.

Results from five other life sciences space experiments are congruent with those reported here. Immediately postflight, astronauts exhibited decreased postural stability with their eyes closed (24), slightly decreased ocular counterrolling during tilt (22), improved ability to null lateral linear motion in the "closed loop otolith nulling task" (24), and unchanged linear oscillation detection thresholds (16, 22). One subject noted that the "rooftop illusion," ordinarily experienced during translation on the U.S. Lab Sled, was absent during the immediate postflight period.

These additional postflight observations are consistent with the otolith tilt-translation reinterpretation hypothesis for the following reasons. Decreased postural stability and ocular counterrolling should be associated with failure to interpret otolith responses following roll stimulation as head tilt. If all otolith signals are interpreted as linear motion, performance of the closed-loop nulling task, which requires precise linear motion detection, should be improved. Because motion detection would be independent of the particular class of motion perceived (translation or tilt), self-motion detection thresholds during linear oscillation should be unchanged. Finally, if all otolith output is interpreted as linear translation, the rooftop illusion (10,13) should be lost.

These observations led Young et al. (24) to propose a tilt-translation reinterpretation hypothesis that is nearly identical to the one developed independently by this study (15,16).

A sixth observation suggests an additional type of otolith reinterpretation. Reschke, Anderson, and Homick (18) examined vestibulospinal reflex and perceptual responses elicited by "drops" before, during, and after the Spacelab 1 mission. Pre- and postflight, the subject was dropped over a short distance using a quick-release helicopter cargo hook. The subject suspended himself above the floor by grasping a T-shaped handle. At random time intervals after suspension, the release was activated and the subject fell to the floor. Because gravity was absent inflight, the drops were produced by pulling the subject to the Spacelab floor using calibrated bungee cords. Modulation of the Hoffman reflex (H-reflex) and perception of self motion were recorded.

During the early period of space flight, sudden drops were perceived as "falls," but by the sixth day of flight the drops were perceived

as linear translations but not as falls. The subjects reported that drops early in the flight felt much as they did preflight. The H-reflex changes associated with these drops also were similar to those recorded preflight. Later in the flight, the drops were perceived as sudden, fast, and hard. The subjects were not aware of where their legs and feet were and exhibited difficulties in maintaining "balance" following "landing." Late in flight, the H-reflex was not potentiated by the drops. Postflight, the drops were perceived just as they were by the sixth day inflight. That is, the subjects were unaware of where their feet were, and the drops were perceived as unexpected and hard (19).

These observations support an otolith reinterpretation hypothesis. Under normal-gravity conditions, a sudden drop is perceived as a "fall" and elicits an otolith-spinal reflex if the body's Z axis is parallel to the gravity vector. Ordinarily, falls are produced by gravity acting on the body mass and the fall is in the direction of the gravity vector. The reflex response prepares the body for the impact deceleration of landing following the fall.

During space flight, a fall, defined as linear translation parallel to gravity, is meaningless because gravity is absent. The "drops" produced on orbit were linear translations but were not falls. Consequently, the adaptive brain learned to interpret all otolith signals as linear translations but not as falls; reflex and perceptual responses ordinarily elicited by falls were lost.

Certainly the data from the space experiments conducted to date are not ideal, and firm conclusions based on observations from only seven subjects are problematic. Nevertheless, converging lines of evidence appear to support an otolith reinterpretation hypothesis.

SPACE MOTION SICKNESS

Motion sickness during the early period of orbital flight and, to a lesser extent, disorientation during re-entry are among the problems associated with space flight. A substantial body of evidence suggests that these problems may be related to alteration of vestibular responses following prolonged weightlessness (4,5).

Sensory conflict appears to be the basic mechanism underlying space motion sickness (5). During the initial period of exposure to weightlessness, signals from the otolith receptors would conflict with those from the semicircular canals and the eyes. Following roll or pitch head motions, movements of the visual scene and signals from the semicircular canals would indicate that the expected head motion had occurred; however, an appropriate signal from the otolith receptors would be lacking. Many astronauts have reported that pitch head motions during the initial period of orbital flight evoke motion sickness symptoms (12,21). These reports support the sensory conflict approach to space motion sickness as well as an otolith tilt-translation reinterpretation hypothesis.

Alteration of otolith receptor response during prolonged weightlessness also could be related to disorientation following return to a normal-gravity environment. In fact, some crewmembers noted horizontal oscillopsia (visual field motion) during head roll motions while in the re-entry phase of flight.

PREFLIGHT PROPHYLACTIC ADAPTATION TRAINING

Based on the otolith tilt-translation reinterpretation hypothesis and the sensory conflict approach to space motion sickness, it is proposed to develop prophylactic adaptation training (PAT) procedures and apparatus for use by astronauts prior to flight. The proposed training is based on the concept that the brain can be forced to "recalibrate" relationships between otolith and visual signals in a manner that would be appropriate to weightlessness. After training, eye movement reflexes, postural muscle reflexes, and self motion experiences in relationship to visual scene movements would be appropriate to the weightlessness-adapted state. It is hypothesized that the training would afford astronauts significant relief from space motion sickness symptoms during the early phase of orbital flight.

BACKGROUND

As noted previously, people adapt to sensory rearrangements such as those produced when they are placed in slowly-rotating rooms (17) or wear optical devices that reverse or invert the visual scene (7,20). Exposure to these sensory rearrangements frequently elicits motion sickness symptoms.

Weightlessness is a form of sensory rearrangement (6,8,13). Because gravity is absent, the vestibular and skin receptor signals elicited by postural orientation and body motion are different from those experienced on earth. Consequently, the relationships between orientation and motion signals from the visual receptors are rearranged with respect to those from the vestibular and skin receptors.

Following adaptation to visual-vestibular sensory rearrangement, vestibular-ocular reflex and self-motion perception response changes indicate neural recalibration of the relationships between visual and vestibular motion signals (1,2,11). These response changes can be used to assess the current state of adaptation and to determine the adequacy of a prophylactic adaptation training protocol.

PROPHYLACTIC ADAPTATION TRAINER

It is proposed to alter, systematically, the relationships between otolith response changes associated with the subject's movements and the visual scene presented to him (14). Relationships between visual scene and subject motion are illustrated in Figure 4. Normally, when the subject's head is rolled toward his left shoulder, the visual scene rotates around the corneal-retinal axis in the direction opposite to the head tilt.

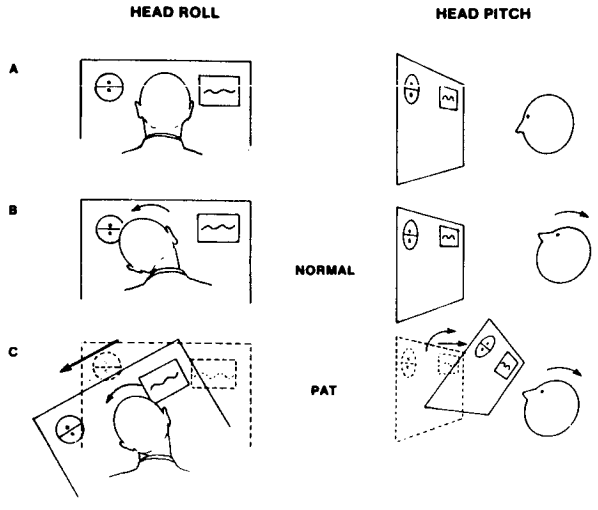

Figure 4. Relationships between head movements and visual scene during PAT.

In the trainer, a leftward head roll would result in a translation of the visual scene toward the left without rotation; i.e., the vertical axis of the scene would remain aligned with the vertical retinal meridian. Normally, when the subject's head is pitched backward, the visual scene moves downward in the visual field. In the trainer, pitch backward would be associated with apparent flow of the visual scene toward the subject, but the horizontal axis of the scene would remain aligned with the horizontal retinal meridian. The relationships between the visual scene and head movements in the trainer would mimic those that are experienced in weightlessness, as revealed by the results of inflight observations.

Several possible concepts for constructing a prophylactic adaptation trainer are currently being pursued.

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PREDICTION OF SUSCEPTIBILITY TO SPACE MOTION SICKNESS*

Investigators: J. L. Homick, Ph.D., M. F. Reschke, Ph.D., and J. M. Vanderploeg, M.D.

INTRODUCTION

Space motion sickness (SMS) is experienced by about 50% of crewmembers during the first several days of exposure to the microgravity space flight environment (1,2,3). Predominant symptoms of the syndrome are headache, depressed appetite, general malaise, lethargy, gastrointestinal discomfort, nausea, and vomiting. As in other forms of motion sickness, the syndrome may reduce self-motivation and result in decreased ability to perform demanding tasks. The syndrome is self-limiting. Complete recovery from major symptomatology, in other words adaptation to the space flight environment, occurs within two to four days. After complete adaptation occurs, crewmembers appear to be immune to the development of further symptomatology.

The overall incidence to date of SMS in the U.S. and Soviet manned space programs is summarized in Figure 1. Available data indicates that the frequency of occurrence of this syndrome has been approximately equal in both countries. An important feature of these data is that with the advent of larger spacecraft in the U.S. program (i.e., Apollo, Skylab and Shuttle) that permit greater mobility of crewmembers, the incidence of SMS has increased.

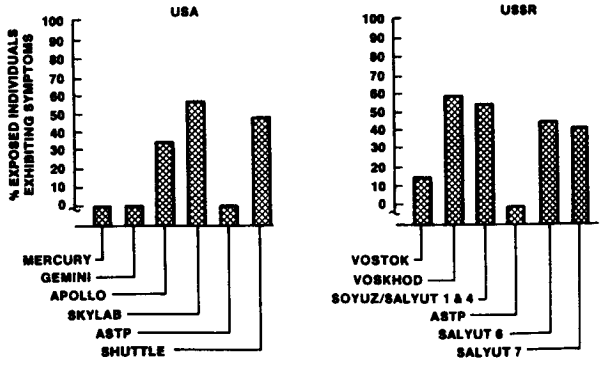

Figure 1. SMS experience.

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In an effort to resolve the SMS or at least minimize the operational impact of the syndrome, NASA has significantly expanded its research efforts in this area. As part of this expanded effort, a systematic program of operationally oriented motion sickness data collection was implemented on most individuals assigned to Shuttle flights from April 1981 to April 1985. The primary objective of this program was to collect preflight, inflight and postflight data on the crewmembers in an effort to begin validating ground based tests which may be predictive of susceptibility to the syndrome. The development of reliable predictors is operationally important because they would permit the a priori identification of individual crewmembers for whom special preventative measures should be taken. A secondary objective of the program was to acquire data which could be used to validate countermeasures for the syndrome.

PROCEDURES

Preflight data collection involved several different procedures. Approximately three to six months prior to flight, each crewmember completed a questionnaire designed to elicit information regarding past experiences with various types of motion environments and responses to those environments.

Also during the three to six months before flight each crewmember was tested at least one time for susceptibility to experimentally induced motion sickness. Three different laboratory test procedures were used to provide a ground-based data point against which inflight susceptibility could be compared.

For the first nine Shuttle missions, which involved 29 different crewmembers, a standard Coriolis Sickness Susceptibility Index test (CSSI),

originally developed by Miller and Graybiel (4) was used. This procedure, which stimulates primarily the semi-circular canals, requires the performance of head movements while rotating at a constant velocity in a servo-controlled chair. Prior to the start of the test the crewmember was instructed on how to report his or her symptoms of motion sickness to an observer who was skilled in the recognition of signs and symptoms of motion sickness. The signs and symptoms were recorded and scored according to the diagnostic categorization shown in Table 1 (4). The test was terminated when the blindfolded crewmember reached the Malaise III level of motion sickness or performed 150 head movements, whichever occurred first. The higher the score, the longer the subject continued the test, indicating a greater resistance to motion sickness. A majority of the crewmembers on the first nine Shuttle missions were tested at least one additional time with the CSSI procedure in order to evaluate the efficacy of an anti-motion sickness medication. The medication most frequently evaluated was oral scopolamine (.4 mg) plus dexedrine (5 mg).

TABLE 1. DIAGNOSTIC CATEGORIZATION OF ACUTE MOTION SICKNESS LEVELS

	PATHOGNOMONIC	MAJOR	MINOR	MINIMAL	AQS *
CATEGORY	16 POINTS	8 POINTS	4 POINTS	2 POINTS	1 POINT
NAUSEA SYNDROME	NAUSEA III,+ RETCHING OR VOMITING	NAUSEA II	NAUSEA I	EPIGASTRIC DISCOMFORT	EPIGASTRIC AWARENESS
SKIN		PALLOR III	PALLOR II	PALLOR I	FLUSHING/ SUBJECTIVE WARMTH ± II
COLD SWEATING		III	II	I	
INCREASED SALIVATION		III	II	I	
DROWSINESS		III	II	I	
PAIN					HEADACHE (PERSISTENT) ± II
CENTRAL NERVOUS SYSTEM					DIZZINESS (PERSISTENT) - EYES CLOSED ± II EYES OPEN - III
LEVELS OF SEVERITY IDENTIFIED BY TOTAL POINTS SCORED					
FRANK SICKNESS (FS) - 16 POINTS	SEVERE MALAISE (M III) 9 - 15 POINTS	MODERATE MALAISE A (M IIA) 5 - 7 POINTS	MODERATE MALAISE B (M IIB) 3 - 4 POINTS	SLIGHT MALAISE (M I) 1 - 2 POINTS	

* AQS - ADDITIONAL QUALIFYING SYMPTOMS
III - SEVERE OR MARKED, II - MODERATE, I - SLIGHT

The second motion sickness susceptibility procedure used was a modified version of an off-vertical rotation or OVR test originally developed by Graybiel and Miller (5). The OVR produces a rotating linear acceleration and is essentially an otolith stimulus. During this procedure crewmembers were blindfolded and restrained in the rotating chair with lap, shoulder and leg straps. The head was also restrained. While in the vertical position the chair was accelerated to a velocity of 20 rpm and rotated for 5 minutes. Following stabilization of 0° tilt the angle of tilt of the chair was increased in 5° increments at 5 minute intervals until the crewmember reached the Malaise III level of symptoms or the chair had been maintained at 30° tilt for 5 minutes. The OVR test was performed on 29 individual astronauts most of whom flew subsequent to the ninth Shuttle flight.

The third procedure used was a modified version of an eyes open sudden-stop test developed by Graybiel and Lackner (6). This test assessed susceptibility to a vestibulo-visual interaction stimulus. Visual stimulation was provided by a stationary optokinetic field which surrounded the chair in which the crewmember was restrained. The chair was accelerated to a velocity of 50 rpm and held at that velocity for 30 seconds. The chair was then decelerated at 150°/sec to a complete stop and maintained at zero velocity for 30 seconds, after which the sequence was repeated for a total of 20 clockwise and 20 counterclockwise stops or until the Malaise III level of symptoms was reached, whichever occurred first. Data were collected on only six crewmembers with this procedure.

Inflight data collection was limited to the use of a microcassette tape recorder and a motion sickness symptom checklist. The checklist was similar in content to the diagnostic scale shown in Table 1 and allowed comparisons between the pattern of symptoms that occurred during the preflight pro vocative tests and those that occurred inflight. The checklist also required crewmembers to report on preventative measures used such as anti-motion sickness drugs and voluntary restriction of head and body movements. Each crewmember was required to use the recorder and checklist each mission day to report any symptoms or sensations that had been experienced during that day.

Questions pertaining to SMS, vestibular sensations, and performance were also asked of each crewmember on the day of landing and during postflight medical debriefings.

Both the inflight and postflight crew debriefing data were used to categorize crewmembers as susceptible or non-susceptible to SMS. Those who were defined as being susceptible were further classified into mild, moderate and severe subgroups for subsequent data analysis. Operational definitions for SMS categorization are given in Table 2.

TABLE 2. SMS CATEGORIZATION

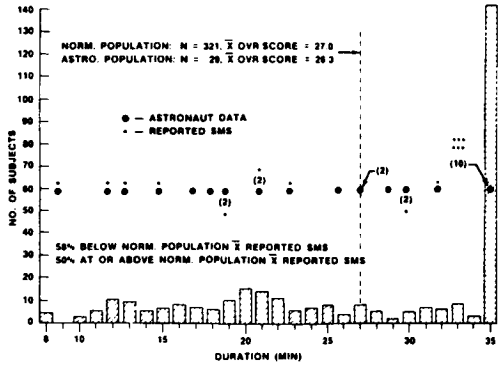
NONE (0):	NO SIGNS OR SYMPTOMS REPORTED WITH EXCEPTION OF MILD TRANSIENT HEADACHE OR MILD DECREASED APPETITE
MILD (1):	ONE TO SEVERAL SYMPTOMS OF A MILD NATURE; MAY BE TRANSIENT AND ONLY BROUGHT ON AS THE RESULT OF HEAD MOVEMENTS; NO OPERATIONAL IMPACT; MAY INCLUDE SINGLE EPISODE OF RETCHING OR VOMITING; ALL SYMPTOMS RESOLVED IN 36-48 HOURS
MODERATE (2):	SEVERAL SYMPTOMS OF A RELATIVELY PERSISTENT NATURE WHICH MAY WAX AND WANE; LOSS OF APPETITE; GENERAL MALAISE, LETHARGY AND EPIGASTRIC DISCOMFORT MAY BE MOST DOMINANT SYMPTOMS; INCLUDES NO MORE THAN TWO EPISODES OF VOMITING; MINIMAL OPERATIONAL IMPACT, ALL SYMPTOMS RESOLVED IN 72 HOURS
SEVERE (3):	SEVERAL SYMPTOMS OF A RELATIVELY PERSISTENT NATURE THAT MAY WAX AND WANE; IN ADDITION TO LOSS OF APPETITE AND STOMACH DISCOMFORT MALAISE AND/OR LETHARGY ARE PRONOUNCED; STRONG DESIRE NOT TO MOVE HEAD; INCLUDES MORE THAN TWO EPISODES OF VOMITING; SIGNIFICANT PERFORMANCE DECREMENT MAY BE APPARENT; SYMPTOMS MAY PERSIST BEYOND 72 HOURS

RESULTS

Results include preflight and inflight symptomatology data, antimotion sickness drug data and preflight versus inflight motion sickness susceptibility data.

As indicated in Table 3 there is a striking difference in the pattern of symptomatology generated inflight versus during the ground-based tests. Subjective warmth, sweating, and pallor, which were dominant ground-based test symptoms, were almost nonexistent inflight. In contrast, vomiting, anorexia, headache, malaise and lethargy were dominant inflight symptoms. The vomiting episodes often occurred abruptly with little or no prodromal nausea, although a sensation of stomach fullness or discomfort was often present prior to vomiting. In most cases, vomiting resulted in relief from the uncomfortable stomach sensations, although for some crewmembers the discomfort would gradually return.

TABLE 3. INCIDENCE OF PREFLIGHT VS. INFLIGHT SYMPTOMATOLOGY



The specific nature and time course of inflight symptomatology tends to be highly variable. Some crewmembers reported that symptoms appeared within the first one to two hours of the mission. Others did not become aware of symptoms until the second day of flight. In general, however, symptoms began during the first day of flight, plateaued between 24-48 hours and gradually diminished between approximately 48-96 hours. During this time the symptoms usually waxed and waned in severity. Unquestionably, head and body movements exacerbated the symptomatology. Accelerometric data obtained by Oman during the Spacelab 1 mission (STS-9), and subsequently confirmed by verbal reports from a number of crewmembers, indicate that in microgravity head movements in the pitch and roll planes are the most provocative (7,8).

Anti-motion sickness and/or anti-emetic medication was used by 40 of the 65 crewmembers included in this study. As indicated in Table 4 the oral scopolamine plus dexedrine combination was the most frequently used with 25 crewmembers taking one or more doses during the first few days of flight. Oral metoclopramide was used by 18 crewmembers in an effort to restore gastric motility and alleviate nausea and vomiting. Of the 31 crewmembers who experienced symptoms, 29 used medication during the course of their symptomatology.

TABLE 4. SHUTTLE ANTI-MOTION-SICKNESS DRUG USE SUMMARY

DRUG NAME	NUMBER OF CREWMEMBERS
SCOPOLAMINE (.4 MG) + DEXEDRINE (5 MG) - ORAL	25
SCOPOLAMINE (.4 MG) - ORAL	1
PHENERGAN (25 MG) - SUPPOSITORY	3
PHENERGAN (25 MG) + EPHEDRINE (25 MG) - ORAL	1
METACHLOPRAMIDE (10 MG) - ORAL	18
COMPAZINE (10 MG) - SUPPOSITORY	1
TRANSDERM SCOP	1

Results related to a comparison of preflight motion sickness data with SMS are by no means unequivocal.

The motion experience questionnaire indicated that all of the crewmembers had a minimal history of susceptibility to terrestrial forms of motion sickness. The questionnaire revealed that a few had experienced some motion sickness during past exposures to aerobatic flight, parabolic flight, and heavy sea conditions. The questionnaire results, however,

did not correlate with the actual incidence of SMS reported.

Table 5 provides an overall summary of group mean differences between the SMS susceptible and non-SMS susceptible subgroups for each of the preflight motion sickness susceptibility tests used. The subgroups of astronauts who experienced SMS were slightly more susceptible to the preflight motion sickness tests than were the non-SMS susceptible astronauts. However, the test score ranges for all subgroups are large and the difference between the means of the subgroups for each test are not statistically significant. In a further attempt to establish a relationship between the ground-based tests and SMS, correlation coefficients between the ground-based test scores and the scores assigned for the inflight level of severity of SMS symptoms were computed. The correlation coefficients were non-significant for all three ground-based tests.

TABLE 5. PREFLIGHT MOTION SICKNESS TEST RESULTS VS. SMS

SYMPTOM	*INFLIGHT NUMBER	*INFLIGHT PERCENT	PREFLIGHT
VOMITING	26	40	0
ANOREXIA	23	35	0
HEADACHE	20	31	0
MALAISE	18	28	0
STOMACH AWARENESS	17	26	18
LETHARGY	15	23	0
NAUSEA	13	20	55
DROWSINESS	6	9	3
DISEQUILIBRIUM/DIZZINESS	6	9	3
SALIVATION	0	0	18
PALLOR	?	?	85
SWEATING	0	0	75
SUBJECTIVE BODY WARMTH	0	0	48

*BASED ON 65 INDIVIDUALS, 31 OF WHOM REPORTED SMS

As an alternative approach to determining whether or not the preflight susceptibility tests might have some predictive value for SMS, the astronaut data for each test was compared to a frequency distribution of non-astronaut normative data. The normative data were collected over the past several years by the Johnson Space Center Neurophysiology Laboratory. Figure 2 summarizes the CSSI test data. The hatched bars are the normative data and the closed circles are the astronaut data. The "star" symbol indicates astronauts who reported SMS. The astronaut mean CSSI score is 28.7 while the normative population mean CSSI score is 14.0. Of potentially greater significance is the finding that 67% of the astronauts whose CSSI score was below the population mean experienced SMS, while only 40% whose scores were above the population mean experienced SMS.

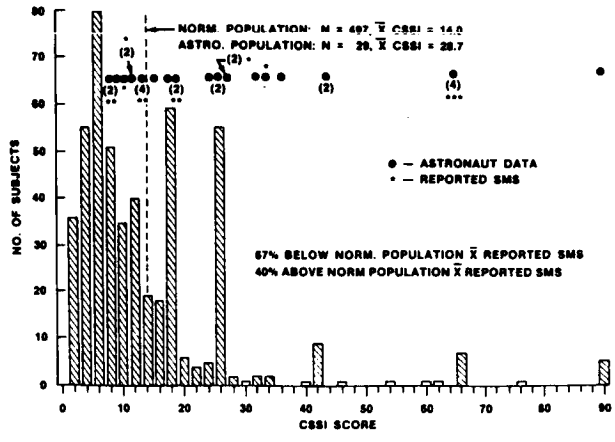


Figure 2. CSSI test.

Data from the OVR test are shown in a similar fashion in Figure 3. Here there is virtually no difference between the astronaut and normative population data. The mean OVR test scores are almost identical and there were as many crewmembers above the normative population mean who reported SMS as there were below the mean.

	CSSI		OVR		SST (EO)	
IN FLIGHT	*SMS	NO SMS	SMS	NO SMS	SMS	NO SMS
N	14	15	15	14	3	3
%	48	52	52	48	50	50
PREFLIGHT						
X̄ =	27.4	30.9	25.7	27.1	10.0	19.7
RANGE	8.4-64.5	11.2-90.0	17.0-35.0	9.0-35.0	2.0-26.0	6.0-40.0
**F =	.192		.201		.545	
P =	.69		.66		.51	

* SMS REPORTED
** ONE WAY ANOVA

Figure 3. OVR test.

Figure 4 summarizes the sudden-stop test data. The number of astronaut data points are too few to permit drawing any meaningful conclusions. However, it is of interest to note that two astronauts who were very susceptible to the preflight sudden stop test experienced SMS.

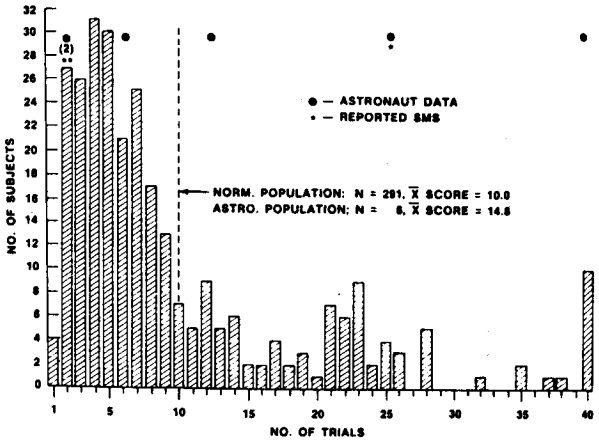


Figure 4. Sudden-stop test.

All of the data summarized thus far in this report have compared SMS susceptibility to a single preflight test. Table 6 compares a weighted ground-based test score with SMS susceptibility for each of 11 crewmembers on whom data were collected on two or more of the preflight tests. The weighted score is the algebraic sum of the differences between the astronaut's test scores and the normative population means for each test. It would be predicted that a positive weighted score (i.e., greater than average resistance to experimentally induced motion sickness) should relate to a lack of SMS and a negative weighted score should be related to the presence of SMS. A correct match was obtained in 64% of the cases.

TABLE 6. WEIGHTED GROUND-BASED TEST SCORES VS. SMS

WEIGHTED SCORE = Σ(CREW Δ'S FROM NORM POPULATION $\bar{X}$)

HYPOTHESIS:

- **POSITIVE WEIGHTED SCORE SHOULD BE RELATED TO LACK OF SMS**
- **NEGATIVE WEIGHTED SCORE SHOULD BE RELATED TO PRESENCE OF SMS**

CREW MEMBER				WEIGHTED SCORE	SMS
1	(SST = -8)	+ (OVR = +3)	=	-5	1
2	(SST = -8)	+ (OVR = -7)	=	-15	1
3	(SST = +16)	+ (OVR = +5)	=	+21	1
4	(SST = +3)	+ (OVR = -1)	+ (CSSI = +19) =	+21	1
5	(SST = -4)	+ (OVR = +7)	=	+3	0
6	(SST = +30)	+ (OVR = +8)	+ (CSSI = +77) =	+115	0
7	(OVR = +8)	+ (CSSI = +51)	=	+59	0
8	(OVR = -10)	+ (CSSI = -2)	=	-12	0
9	(OVR = +3)	+ (CSSI = -1)	=	+3	0
10	(OVR = -4)	+ (CSSI = -1.5)	=	-4.5	1
11	(OVR = +8)	+ (CSSI = -3)	=	+6	2

HITS	MISSES
7 OUT OF 11 64%	4 OUT OF 11 36%

CONCLUSIONS

On the basis of data collected during this study it can be generally concluded that the prediction of SMS susceptibility on an individual crewmember basis remains a difficult and challenging task. Certainly the use of a single ground-based parameter or test procedure is inadequate. The use of a composite index or weighted score which takes into account several response parameters appears to have greater predictive potential. A larger sample size of composite scores based on the collection of preflight CSSI, OVR and sudden-stop data on Shuttle crewmembers would be desirable. The data needed to derive these composite scores do not exist, nor do plans currently exist to collect these data.

Despite inability to identify preflight, ground-based predictors of SMS susceptibility, there does appear to be one reasonably accurate predictor and that is space flight itself. Out of 16 individuals who have flown two or more space missions only 3 changed their response pattern from one flight to the next. Out of the remaining 13, 7 individuals were symptom free on all of their flights, while the other 6 experienced symptoms on each of their flights. Obviously, the routine use of space flight as the method of identifying SMS susceptible individuals is impractical. Thus the need to identify and validate ground-based methods remains an important issue.

It is important to emphasize that efforts in this area have not been abandoned. The collection of inflight and postflight symptom reporting data is continuing as a standard operating procedure. Improved methods for characterizing the exact nature and time course of SMS are being evaluated. Also, various pre-, in- and postflight measurements of vestibular function are being conducted, the data from which may be useful in our attempts to develop predictors of SMS susceptibility.

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SPACE MOTION SICKNESS: CHARACTERIZATION AND ETIOLOGY

Investigators: William E. Thornton, M.D., Tom Moore, M.D., and Sam Pool, M.D.

INTRODUCTION

Whenever man is placed in environments of motion to which he is unaccustomed, either real or simulated, a sizeable percentage of the population will develop the characteristic syndrome of motion sickness (23). This is a nuisance, or worse to many individuals. It is a significant problem to modern military forces, and much of the study of motion sickness has been sponsored by the military in World War I and II (24). Dr. Graybiel's work in the U.S. Navy is an archetype of such research (6,7,8,9). With the development of a numerical scoring system of signs and symptoms (12) and means with which to rapidly induce motion sickness, research became almost stylized. It was possible to develop such a scoring system only because susceptible individuals develop characteristic signs and symptoms on continued exposure to an environment which produces major sensory conflict.

If such exposure is continued, vomiting and retching may be prolonged, sometimes with prostration (25). After varying amounts of exposure, the majority of subjects develop resistance to the specific stimuli (26). Medication, habituation, and training may be effective in prevention or treatment to varying degrees (27). In addition to the above symptoms, Graybiel proposed a 'sopite' syndrome (10). This may be intertwined with motion sickness and may occur under prolonged mild stimuli, or as a variant of motion sickness under strong stimuli. Features of this syndrome, as proposed, include yawning, drowsiness, disinclination for physical or mental work, and lack of participation in group activities.

Prior to space flight it was predicted that a conflict between the gravity-sensitive statolith organs and unaffected canals would occur in weightlessness and produce a variety of symptoms (20). Early in the Soviet space program, cosmonauts complained of disorientation, illusions, malaise, nausea and vomiting (4). Similar complaints were expressed later by American astronauts in the Apollo Program (15). Based upon these reported symptoms, it was reasonable to consider this motion sickness and treat it accordingly. By the end of Skylab, however, there was reason to doubt that the sickness in space was absolutely identical to that on Earth. There was little correlation between susceptibility on Earth and in space; the medications effective on Earth had questionable efficacy in space, and after a few days of exposure to weightlessness individuals became remarkably resistant to coriolis stimulation, a unique non-specific adaptation (11). After the third Space Shuttle flight, it was obvious that the Shuttle Program also would have to contend with the problem (13,14). There were repeated attempts to document signs and symptoms by means of questionnaires and debriefings, but the first scheduled inflight study (Spacelab 1) was still 18 months away.

An objective inflight investigation of the problem with major emphasis on operational concerns was necessary. This was especially so with accumulating verbal information describing differences between sickness inflight and on Earth. An operationally oriented program by the JSC Astronaut Office and Flight Medicine was mounted on Shuttle flights 4 through 8, and astronaut physicians were added to two of the crews. A large number of investigations were developed and flown as Detailed Supplementary Objectives (DSOs). Some studies of this series have been continued to the present under the aegis of JSC's Space Biomedical Research Institute (SBRI). These investigations used clinical procedures where possible and had the major goals of:

1. Clinical characterization
2. Investigation of etiology
3. Investigation of possible treatment

A listing of studies is given in Table 1. These investigations included personal observations and anecdotal accounts from Astronaut flight experience.

TABLE 1

LISTING OF INFLIGHT SMS STUDIES

Study	Number of Subjects (With SMS)
Head and Eye Motion (EOG) During Launch & Reentry (a)	5 (4)
Head and Eye Motion (EOG) On Orbit(a)	11 (5)
Kinesthetic Repeatability(b)	14 (7)
Eye-hand Tracking Task(b)	12 (7)
Audiometry, pure tone(a)	6 (3)
Physical Examination(a)	7 (4)
With Ophthalmoscope	7 (4)
Intraocular pressure(a)	1
Evoked Potentials: audio, short and mid-latency(a)	7 (4)
visual	1 (1)
Fluid Balance(a)	1 (1)
Ambulatory monitoring	
Heart Rate and Blood Pressure(a)	2 (2)
EKG(a)	2 (2)
Heart Rate and Blood Pressure on Reentry(b)	8
Bowel Sound Recording(b)	12 (7)
Leg Plethysmography(b)	10 (5)
Tissue Tonometry(a)	5 (2)
Serum for Causative Agents(b)	3 (3)

(a) Study begun in Astronaut Office and Flight Medicine Inflight Investigation.

(b) Study begun in Astronaut Office and Flight Medicine Inflight Investigation and continued under Space Biomedical Research Institute (SBRI).

CLINICAL CHARACTERIZATION

SYMPTOMS

MOTION SENSITIVITY

These studies observed an amazingly wide and variable range of symptoms in space motion sickness (SMS). Typically, the first indication was hypersensitivity to angular head motion, either alone, or combined with body motion. In many subjects this sensitivity was predominant in the pitch plane, in others it was in yaw; but in most cases it was also present in all other angular axes. This hypersensitivity became noticeable from zero to 1 to 2 hours after exposure. It typically increased to a plateau in several hours and remained at that level until resolution, when it rapidly diminished. It could only be described as a thoroughly unpleasant sensation not to be repeated if possible. One simply wanted a quiet immobile spot during this period of altered sensitivity.

It did not produce visual disturbance or illusion, nor did it obviously produce stomach symptoms as, for example, does out-of-plane head motion in a spinning chair. If anything, it was increased with eyes closed. The sensation strength appeared to be related to the magnitude of the velocity or possibly to the rate of acceleration of movement.

Translation, even reciprocating translation, did not produce these symptoms.

ILLUSIONS, VISUAL DISTURBANCE, ORIENTATION

Illusion of both position and motion was reported as a major symptom in the Russian Program (18) and in some of the Apollo experiences (3). Many Shuttle Astronauts have been questioned after flight and there has been no admission of either visual disturbance or illusion on launch or orbit, except from one pilot. He was not motion sick and claimed an illusion of being in a static pitched-down position for several hours after orbital insertion. Great care was taken during questioning to insure that illusions and vertigo were explained and understood.

Much has been made of the 'egocentric' ability or referencing surroundings to one's own axis; for example, the ability to place the Earth above one's head rather than being inverted above the earth. Some crewmembers who were able to do this easily reported that it did not prevent SMS. Sensitivity to scenes out of alignment with one's own reference, such as inverted Earth or inverted crewmen, appears to have been disturbing to a few, but not to the majority. A common illusion may occur in experienced aircraft pilots observing the Earth while strapped in the Commander or Pilot seats with the Shuttle nose down: one feels as if it is pitching further. This may be avoided by releasing the seat belt. Dr. Lackner has reported similar experience in zero-g aircraft (19).

GASTROINTESTINAL

These signs and symptoms appeared from minutes to several hours after weightlessness and often consisted of a very brief bout of unproductive retching, but usually of sudden vomiting without nausea or other prodrome. There have been several reported episodes of vomiting, often repeated, within a few minutes of orbital insertion. One such case was observed and although sweating and pallor were absent, it is suspected that the vomiting was evoked by the launch-insertion environment (i.e., ordinary motion sickness). However, these subjects all had continuing symptoms of SMS.

Typically, vomiting due to SMS was strenuous, brief, and appeared to empty the stomach of whatever contents were present, undigested. The contents were rarely bile-stained. Subjective relief was commonly claimed afterward. In the absence of eating or drinking, these events, which produced clear vomitus, were sometimes repeated one or more times, usually with hours of spacing between events. Vomiting was not prolonged; there were no dry heaves nor frequent bouts. Typically all significant amounts of ingested food or drink were lost, usually within thirty minutes to an hour or more. The majority of subjects denied nausea, but in some this was a major symptom or a presenting symptom. This nausea sometimes waxed or waned but was not necessarily related to other activity (although some motions were avoided by SMS-affected individuals). Loss of appetite was almost universal. A variety of non-specific epigastric symptoms have been reported, the most common being a "knot in the stomach." Lower bowel functions, as judged by flatus and defecation, seemed normal.

SWEATING AND PALLOR

There was virtually no incidence of sweating, and flushing was more common than pallor. The absence of sweating cannot be attributed to the "cool, dry environment of Spacelab" (37), since it was the same environment as most test labs on Earth.

OTHER SYMPTOMS

Malaise, lack of initiative, and irritability were nearly universal during this time. Headache was common, usually mild, non-specific and with various locations in different individuals. Malaise typically increased in the first few hours and then plateaued. Somnolence was very common and may have caused brief periods of sleep given the opportunity. This was frequently a symptom which developed early and persisted until resolution. It may have been complicated by lack of usual sleep.

EFFECTS OF ACTIVITIES

Demanding activities such as the Commander's duties, the responsibility for satellite launch, or Remote Manipulator System (RMS) operations appeared to reduce the perceived discomfort, if not the actual level of SMS. Excessive movement early on orbit may have precipitated or increased the symptoms. In any event, cessation of activity, even sleeping, sometimes decreased the discomfort, but did not cure the problem.

INCIDENCE

Two interrelated questions are the incidence of SMS and the horizontal overlap of symptoms in those affected versus those unaffected. The presence of symptoms from

other causes must also be considered. Incidence depends upon the criteria used and the accuracy of reporting of symptoms; estimates vary widely among investigators, from 30% to as high as 70%. While there were variations in severity with some mildly affected, there was a distinct clustering of well versus sick subjects. In some cases without frank SMS some features of the sopite syndrome were present. There was also ample stimulus available for ordinary motion sickness; e.g., vertical launch and visually inverted flight with up to 3.5G "eyeballs-in" terminating in weightlessness, plus a host of other new sensations. Consequently, diagnosis of SMS must be made with some care.

OBJECTIVE STUDIES

ELECTROOCULOGRAPHY (EOG)

Because of the unique relation between eye motion and the greater vestibular system (1,16,21), electrooculography was intensively studied (29).

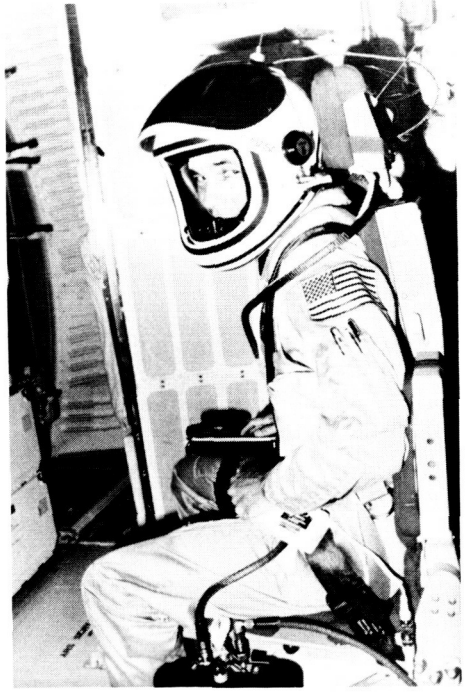

Figure 1. Crewman instrumented for EOG and recording of head position prior to launch. Data was recorded and transmitted continuously during launch and entry.

Horizontal and vertical EOG were recorded during launch on one flight and during entry on two flights, with 3 subjects. Horizontal EOG and head motion were monitored during 3 ascents and entries with a total of 4 subjects.

Conventional calibration, electrode configurations and equipment standards were employed (2,34). Standardized voluntary head oscillations with eyes open and fixed on a target, and with vision occluded by blind goggles were made before, during, and after ascent and entry. Continuous recordings were made during launch and entry (Figure 1). No abnormalities were seen, not even brief nystagmus.

On-orbit a more or less conventional EOG exam was performed (Table 2), without Hallpike maneuver or caloric stimulation, and with voluntary head oscillation substituted for an oscillating chair (Figure 2).

TABLE 2

ON ORBIT EOG PROTOCOL AND NUMBER OF PARTICIPATING SUBJECTS

Procedure	Number of Subjects (With SMS)
Gaze, Eyes open and closed, Horzontal and Vertical Deviation	17 (6)
Saccadic Tracking, Calibration	17 (6)
Head Oscillation with:	
Eyes open, fixed target	17 (6)
Eyes closed, fixed target	17 (6)
Eyes closed, shielded, Fixed Target	9 (4)
Eyes open, head synchronized target	15 (6)
Pursuit tracking, head fixed	4
Optokinetically induced nystagmus	4 (2)
Head turns	17 (6)
Head and Body Rotation - sinusoidal Eyes open, closed and shielded with fixed target	2 (2)

Again conventional standards were adhered to although the equipment had to be designed to fit the situation. Forty-one records were made on orbit, 7 during SMS, with 57 preflight and 19 postflight controls. This series can be summarized as clinically normal (29). Two isolated records contained distortion during the head oscillation which seemed most likely to be artifactual.

Figure 2. Crewman during EOG study with sinusoidal rotation on STS-8. A two axis gyroscope is mounted on the head.

AUTONOMIC NERVOUS SYSTEM RESPONSES

Another major effort was documentation of autonomic changes during SMS, including facial color, pupillary size, temperature, heart rate and blood pressure. These have proven extraordinarily difficult to obtain for non-technical reasons and there is not an adequate statistical sample to date; however, attempts continue. Objective studies of pupillary size were made by macro-photography under controlled and measured light conditions. Pallor/flushing studies were also done by photography with color control to be analyzed by chromatic micro-densitometry. Depending upon the individual, observation showed pallor or flushing with apparently normal pupillary size. Ambulatory monitoring of the heart rate and blood pressure of one subject showed them to become remarkably low as the symptoms plateaued the first day (33). Ambulatory monitoring of a subject during recovery from SMS showed a significant increase in basal heart rate during this period.

BOWEL SOUNDS MONITORING

As part of these studies, an onboard physician observed that bowel sounds were absent during the course of SMS. This finding has been subsequently confirmed by auscultation in nearly every case observed, and objectively studied (31). At least one case of hyperactive sounds during SMS with nausea and vomiting has been seen. It was possible that this hyperactivity was anti-peristaltic duodenal activity which has been seen with nausea.

Objective studies consisted of recording sounds from the right and left upper quadrants of the abdomen preflight and during and after SMS in parallel with unaffected controls. The records were semiquantitatively scored by counting the rate of audible events by standard criteria. Weightlessness did not greatly alter the rate or quality of bowel sounds in those unaffected, although some individuals may have been hyperactive the first day. Conversely, SMS greatly depressed or virtually eliminated sounds during the course of the syndrome. This phenomenon bears a constant relation to the presence of SMS. There is some evidence of rebound activity for the first hours after recovery followed by normal activity.

PERFORMANCE DURING SMS

This was the most difficult evaluation to make. Even under normal circumstances, tests of performance are, at best, tenuously related to actuality. While it is obvious that a person is hors de combat during vomiting, this is brief. Conversely, trained astronauts have in every case performed assigned tasks, though there have been two precautionary delays of scheduled EVAs. While there was a lack of initiative during SMS, tasks trained for and scheduled were done and done well. Many of these required concentration as well as good neuromuscular and eye-hand coordination. There have been cases of Payload Specialists, who have not had extensive training and

mission simulations, being unable to complete all assigned tasks.

In an effort to study effects of SMS on performance, two areas have been examined: neuro-muscular performance and mental processing. The first consisted of returning hand or arm to a fixed linear position after voluntary displacement and manual tracking of a visual target on a linear scale which moved in a series of regular and aperiodic functions. A second study used the relatively common Sternberg test. This consisted of the timed indication of presence or absence of a single digit in a previously displayed number. Neither of these tests have shown any decrement in performance in the few cases examined to date.

TEMPORAL PROFILE OF SYMPTOMS

As noted, with an exception which will be treated later, onset of symptoms occurred within minutes to 1 to 2 hours of exposure to weightlessness (Figure 3). This progressed in intensity over a period of hours to a plateau which for a given condition remained stable. There were typically both head and gut symptoms although one or the other sometimes predominated. In some subjects, the gut symptoms may have been the only ones recognized, but in almost every case the gut remained quiet. Vomiting was often more frequent at the beginning. In some cases, after one or two episodes, it did not recur in the absence of intake.

The resolution of symptoms was typically sudden and dramatic, and most frequently occurred between 30 to 48 hours, but has been seen after only 12 hours, and possibly as long as 72 hours. During and after resolution there was a marked change in attitude, loss of malaise, return of stomach activity and usually appetite, and marked decrease in motion sensitivity. This typically occurred in a matter of hours or less. There was occasionally some residual motion sensitivity which decreased to normal over the next 2 to 3 days. With determined effort this sensitivity could be aggravated (37), but was not a problem with reasonable movement. Anorexia sometimes remained also, but hunger was more common. at this time or in the days immediately following, resistance to all forms of motion sickness developed. This included the out-of-plane head motions in the rotating chair as was first demonstrated in Skylab (11).

DELAYED ONSET

There was a sub-group of 4 crewmen who had significantly delayed onset of symptoms, one for 48+ hours. This crewman was very active and symptom-free for the first 2 days, yet developed a moderate case which persisted for 24+ hours. Common in these four were

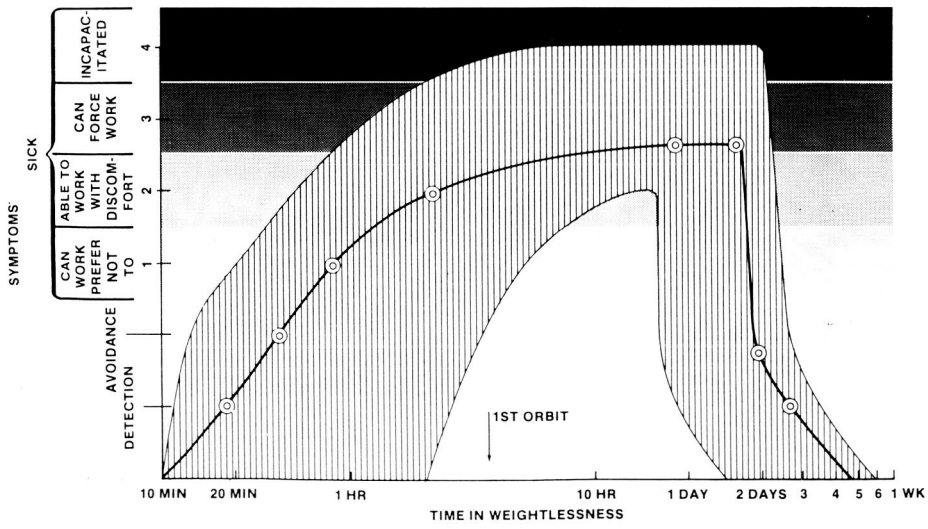

Figure 3. Time course of symptoms of SMS. The range of symptoms that have been recorded on Shuttle crewmembers is shown in the shaded area Note that the time scale is logarithmic.

medication with ScopDex and onset of symptoms after discontinuation of the medication. This was the most convincing evidence seen to date of the efficacy of a drug to combat SMS, but it represented only a small number of subjects having taken this medication. It is probably significant that symptoms were not prevented, only delayed.

REENTRY AND POSTFLIGHT

In the American program, there have been few instances of recurring symptoms after landing, although this is reported to be common in the Russian Program (18). During reentry and for hours thereafter head turns have provoked a sense of disequilibrium in some subjects, including those not affected by SMS, but not with the sense of unpleasantness experienced by those with SMS inflight (Figure 4). One subject without SMS reported developing motion sickness symptoms on reentry while making head motions as part of an investigation. A few subjects have noted an illusion of translation during head turns hours after return to 1g. This phenomenon could not be elicited in flight from any subject including one who experienced it briefly on return. Inflight detection of motion, both angular and linear, was correct and had a nominal threshold as judged by manual movement of blindfolded crewmen without tactile stimulation.

Several changes in sensation were transiently present postflight. One of these postflight changes is an apparently delayed resistance to all forms of motion sickness or even disequilibrium. This has not been adequately studied. There have been anecdotal reports of such increased postflight resistance to unpleasant motion sensations and motion sickness, especially in aircraft, even from those who did not experience space motion sickness. One crewman repetitively tried every maneuver possible in the T-38 for 19 days after his first flight, and could elicit nothing. Two crewmen also rode the coriolis chair with head motions postflight, without any effect, although on the day of landing one had been hypersensitive to it. This lack of sensitivity appeared to last for

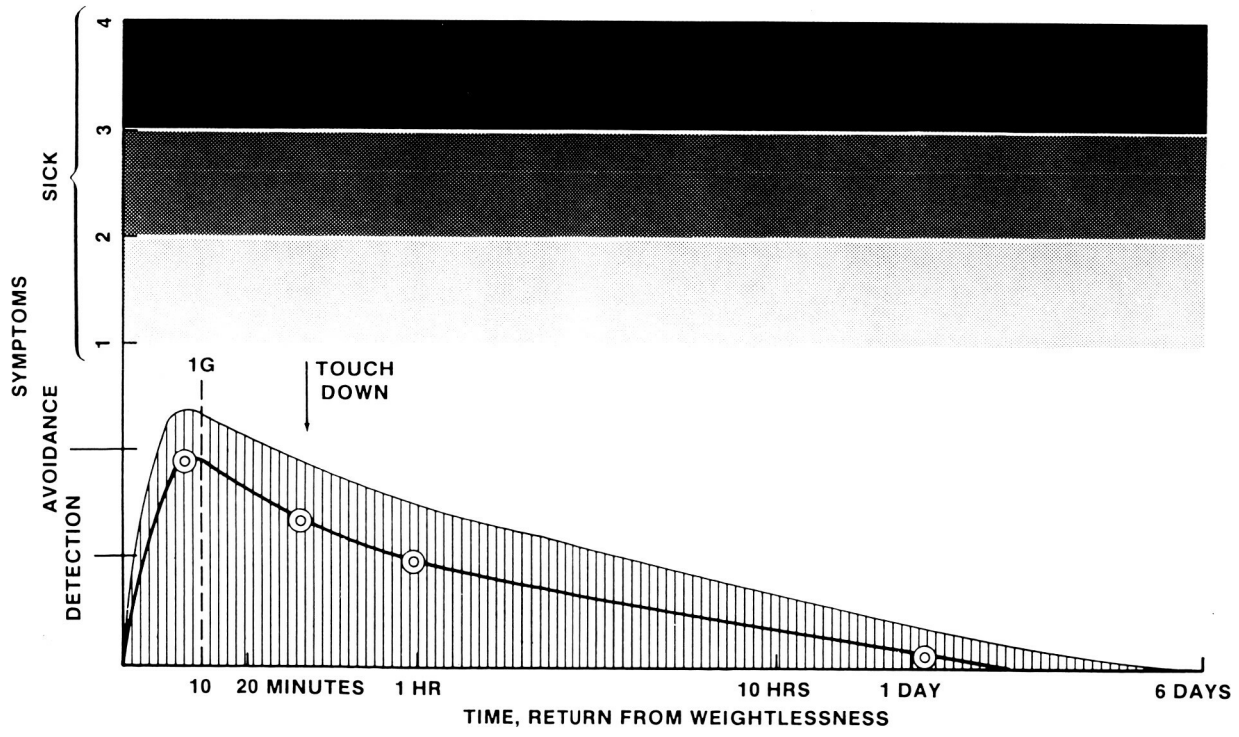

Figure 4. Time course of symptoms during neurological readaptation upon return to Earth.

weeks, but is one of many questions which need quantitative answers.

ACQUIRED RESISTANCE

The question of acquired resistance to SMS has not been adequately documented. At one time it was considered part of flight readiness to have gone through informal but vigorous acclimatization by repetitive, violent maneuvers in the T-38 and in some cases prolonged sessions in the spinning chair. Some of the subjects most resistant to motion sickness during such maneuvers suffered most from SMS.

Conversely, there is increasing evidence, largely undocumented, that prior spaceflight produces resistance to SMS. This is supported by several gastrointestinal motility studies done on individuals who have flown more than once. Previous flight appears to have no effect after a period of 10 years or more. For those who have flown within 2 to 3 years there was wide individual variation with some showing relatively small effects, even with flights as recent as 7 months, while one crewman was symptom-free on his second flight after a delay of 2 + years. In some there was no reduction in symptoms, but a reduction in duration, while in others there was a significant reduction in severity of symptoms.

It seems very significant that in no case in the American program has there been a failure to adapt to weightlessness, nor has there been redevelopment of symptoms once resolved.

ETIOLOGY OF SPACE MOTION SICKNESS

There is insufficient space to review theories of etiology of motion sickness on Earth except to say that the sensory conflict theory currently best fits our existing knowledge. We can find a number of situations involving major sensory modalities: vision, somatosensory and vestibular, which in continued conflict will produce the classic symptom complex of motion sickness. The mechanism whereby the conflicting temporal profiles of neurological impulses are translated into the symptoms remains unknown.

Significant differences between SMS symptoms and those of classic motion sickness have been seen. There are other factors to consider in SMS, such as the large and rapid cephalad fluid shifts on exposure to weightlessness (22,30,32). Taking into account the symptoms of malaise, lethargy, headache, sudden vomiting and reports of illusions, one could not reasonably exclude the possibility of malfunctioning end organs, nor even of increased intracranial pressure. At the time the inflight investigation was started a number of possible causes had to be considered and investigated (Table 3). They were based on clinical experience and a word of explanation may be in order for each.

Table 3

POSSIBLE ETIOLOGIES OF SMS

DISCORDED FUNCTION	ANOMALOUS SIGNALS
Vestibular Hydrops	Visual
Increased intracranial pressure	Vestibular
Cervical Vertigo	Semicircular Canals
	Statolith Organs
	Somatosensory
	Visceral

POSSIBLE CAUSES

DISCORDED FUNCTION

Vestibular hydrops or in this case pseudo Meniere's disease could result from a sudden shift of labyrinthine fluid pressure or composition (36). In the same way, changes in intracranial pressure or composition were also possible. It was known that in the absence of hydrostatic pressure several liters of fluid are shifted from legs alone and that part of the fluid was retained as edema in facial tissue and in mucous membranes (30). Under these circumstances intracranial changes could not be overlooked.

Cervical vertigo is a variously described but apparently real syndrome usually resulting from trauma to the neck's somatic sensors. This

may produce vertigo, nausea and other motion sickness symptoms (5). It is known that significant expansion of the intervertebral discs occurs in weightlessness, usually beyond that seen in bed rest on Earth (28,30). There is also a change in the carrying angle of the head in weightlessness (30). These two factors could conceivably produce distortion in cervical sensors and their signals.

ANOMALOUS SIGNALS

Weightlessness can, indeed must, produce anomalous signals in some of our normal Earth-based sensory systems. There was little reason to think that it would directly affect the visual system. In many ways the visual image should remain the standard of comparison. Conversely, many correct scenes in space are inconsistent with previous experience and might well produce symptoms. For example, rapid angular maneuvers or positions incongruent with local orientation which are not possible on Earth will not have been previously experienced.

There is an inherent conflict between canal and statolith organs in weightlessness, for the dynamic angular responses of each overlap and weightlessness will grossly distort the statolith organ's signal. While the static component of this signal is correct, it will conflict with previous experience and with visual and possibly other sensory signals.

Many of the somatosensory signals a crewman encounters when weightless have never been experienced before. Relatively little is known of visceral signals beyond the fact that they occasionally reach consciousness during motion, particularly vertical accelerations, and that they are capable of producing a variety of upsets.

INFLIGHT INVESTIGATIONS

An investigational program was designed to study as many potential etiologies as possible with minimum resources. For example, EOG may provide information on several of the above categories. Because of its nature, determination of etiology was not possible with techniques currently available; rather, it was feasible to reasonably exclude most of the possibilites and focus on the most probable cause. There is not space to give the usual details of procedures or detailed results, so only summaries are offered, treating each of the potential causes listed previously.

DISCORDED CNS FUNCTION

Vestibular Hydrops

Illusions and visual field disturbances were denied; clinical neurological exam was normal; EOG exam was normal (13); there was no difference in audio threshold sensitivity or audio-evoked potentials between those affected and unaffected (13); and no significant difference was seen in volume of fluid shifted from legs in those with and without SMS.

Increased CNS Pressure

Illusions and other neurological disturbances were denied; clinical neurological exam was normal; there were no changes in fundus; EOG was normal (13); one intraocular pressure was normal; audio evoked potentials including midlatency studies were normal (13); eye-hand tracking was normal; one visual evoked potential was normal; and no difference was seen in fluid volume shifted from legs in those with and without SMS (22).

Cervical Vertigo

Illusions and other neurological disturbances were denied; clinical neurological exam was normal; EOG was normal; there was no difference in height increases in those with and without SMS; and cervical loading was without affect in one subject. In summary, there was not positive evidence for altered sensory or CNS function.

ANOMALOUS SIGNALS

When potential roles of various sensory inputs are examined there is less hard evidence, and subjective symptoms are open to many interpretations. Looking at sensory modalities for effects of weightlessness:

Visual

Visual disturbances were denied, and visual acuity and extraocular motion were normal, as were reflexes to light and accommodation. The visual tracking function for saccadic, pursuit and nystagmoid motion was normal, as was optokinetic nystagmus; i.e., the purely visual inputs were normal. The absence in this study of oscillopsia, or pathological nystagmus, and the ability to normally track a head-synchronized target during SMS argue against other sensory modalities disturbing visual function; i.e., the visual information should be valid.

Vestibular Function

Canal function appeared to be normal, for while there were changes in VOR gain as could be determined from eyes occluded head oscillation, the differences appeared random in time and between subjects. The strongest evidences for the role of vestibular inputs were the overwhelming conscious sensations that occurred during motions. In many, the pitch plane was most sensitive while in others it was yaw, but in any event it was a potent sensation. Stopping all motion sometimes caused some improvement in feeling, but it did not cure SMS, and there is evidence from gastrointestinal studies to support this. Stopping motion probably only removed the unpleasant sensations from motion and had little objective effect on the underlying process. An example of this is one subject who simply clung to a supporting structure with eyes closed for two nights and a day without improvement.

Somatosensory Inputs

The only direct studies of this system were the kinesthetic position sense and eye-hand tracking. These did not look at senses which would most likely be involved in gravity produced signals, hence it could be argued they are irrelevant. The number of studies during SMS are small and not statistically significant to date, but no significant changes have been seen in performance during or after SMS. One subject was loaded to the equivalent of his own weight by the treadmill harness and stood quietly for a prolonged period without improvement in symptoms.

Visceral Inputs

No means were available to study this. Other than the gastric symptoms noted, visceral sensation did not reach consciousness.

In summary, this study showed no evidence for the role of altered or disturbed sensory or neurological systems and considerable evidence against such. At the same time there is strong theoretical argument for a sensory conflict between the canal and statolith organ signals. This argument is consistent with the phenomena observed. Visual signals are not altered and should be consistent with canal signals, both of which conflict with dynamic statolith signals. Visual scenes may produce conflicts with stored information from previous experience or possibly with static information from statoliths or somatosensory signals. The role of somatosensory or visceral inputs is unknown.

Neuroanatomy also seems to be consistent with a major role for vestibular conflict since there are known pathways, through nuclei, connecting the end organs to the one area which is consistently affected by SMS, the upper gastrointestinal tract (28,32). It may be significant that the vestibular nuclei, the nuclei which control the digestive tract, the chemoreceptor trigger zone, and the emesis center are in very close proximity around and under the 4th ventricle.

CONCLUSION

COMMENT

The current problem is ignorance of basic mechanisms. The pathways and the nature of the signals that cause the ileus of the upper gastrointestinal tract and the head symptoms are unknown. There are two basic possibilities: neurological transmission and/or humoral transmission. This remains an open question. While it is felt that the neurological pathway is more likely, nevertheless serum has been collected in a search for strange agents. One subject received an injection of naloxone, an opioid blocker, during SMS without effect.

The question of whether or not cerebral spinal fluid might be a pathway has been raised

by one set of experiments. This certainly deserves consideration.

An important aspect of these investigations was the demonstration that useful, objective data can be gathered quickly and with minimum resources during operational missions.

SUMMARY

Space Motion Sickness is a probable variant of 1g motion sickness with major differences in many aspects. It has not been incapacitating to trained individuals, who have still performed demanding tasks with it. It has been universally self limiting in the American experience, usually clearing within 36 hours. It has not recurred on continued exposure, and appears to be moderated by repeated experience. It appears to have produced an upper gastrointestinal ileus in almost all of those affected and vomiting has been secondary to this ileus, not a primary event. Restriction of food and drink has helped to minimize vomiting.

At this time it appears that an intra-vestibular conflict is the primary cause with unknown contributions from other modalities. Current knowledge of the neuronal mechanisms in volved is inadequate for understanding the process. Some breakthrough, some drug, or some method of stimulating the conflict on Earth might be found, but until then SMS must be studied in the only place it occurs - space.

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Section Six
Vision

This crewman is performing a DSO to test for changes in near-vision acuity. An understanding of visual function changes due to microgravity is important for on-orbit operations.

ORIGINAL PAGE IS
OF POOR QUALITY

EFFECTS OF SHORT-TERM SPACE FLIGHT ON SEVERAL VISUAL FUNCTIONS

Investigators: H. Lee Task, Ph.D., and Col. Louis V. Genco

INTRODUCTION

Since the early days of the Gemini space program there has been an interest in the possible effects of the space environment on visual capability. During the Gemini program S.Q. Duntley headed an effort to determine the effects of space on visual acuity at two different contrast levels. His approach was to develop a portable, compact vision tester to fly aboard the Gemini capsule and compare these results with the astronauts' ability to see similar target patterns constructed on the ground. These methods provided limited visual acuity data on a total of 4 astronauts.

Duntley originally planned to measure a number of visual functions, but due to various limitations only the visual acuity under two contrast conditions was measured. Very little quantitative work on vision in space has been done since that time.

In order to explore the area of vision in space, a series of visual function testers (VFT) was developed to measure several visual functions. The first of these (VFT-1) measured visual acuity, stereopsis, torsional phoria, lateral and vertical phoria, critical fusion frequency and eye dominance. VFT-2 was designed to measure contrast thresholds for several types of optical patterns.

These first two VFTs were flown on several shuttle flights. A total of 16 astronauts have been tested on VFT-1 and 5 have been tested on VFT-2.

PROCEDURES / RESULTS

VFT-2: MEASUREMENT OF CONTRAST SENSITIVITY

VFT-2 was designed to measure visual contrast threshold for several test patterns. The amount of contrast required to see a pattern or to extract specific information concerning the pattern (e.g. orientation) increases as the size of the pattern (or information detail) becomes smaller. A standard method of presenting this data is to take the reciprocal of the contrast (designated contrast sensitivity) and graph it against the reciprocal of size (spatial frequency).

The observer was instructed to increase the contrast of the pattern until the specified detail was detected. At this point, readings of the luminance values of the target pattern and background were taken with internal light sensors. This insured accurate calibration of the instrument.

Four types of test patterns were employed. Six upper squares each contained a square-wave pattern of a single spatial frequency (light & dark bars per degree of visual angle). The six spatial frequencies tested were: 4, 8, 12, 16, 22 and 30 cycles per degree. The lower left square contained an array of tri-bar targets with 8 spatial frequencies represented (the 8 rows) and 8 tri-bars at each spatial frequency in random orientations (vertical or horizontal). The lower center square was a continuous resolution fan test pattern ranging from 10 to 70 cycles per degree and the lower right square contained Blackwell disks of six different sizes (six rows).

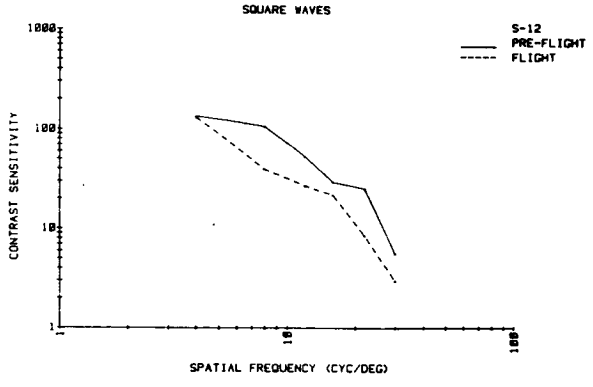

Figure 1

SQUARE-WAVE CONTRAST SENSITIVITY RESULTS

Figures 1, 2, and 3 show the square-wave contrast sensitivity for the three astronauts who participated in the use of the VFT-2. Subjects S-12 and S-15 tended to show a decrease in square-wave contrast sensitivity during flight compared to pre-flight tests while S-13 showed a minor improvement in contrast sensitivity during flight compared to pre-flight. As a group, there was no statistically significant change in contrast sensitivity during spaceflight compared to the pre-flight baseline. Further investigation is required to determine if the individual changes are significant and repeatable.

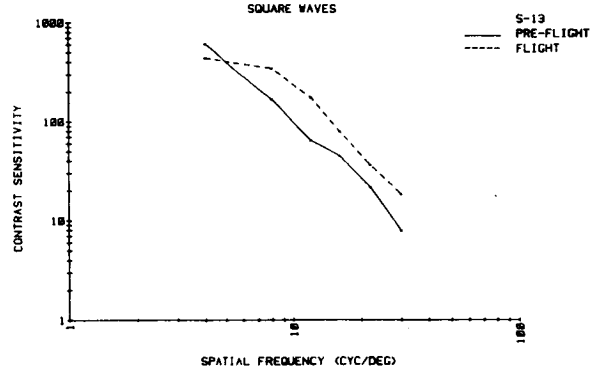

Figure 2

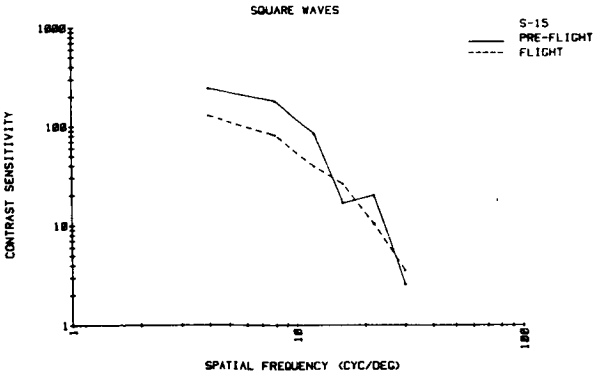

Figure 3

BLACKWELL DISK CONTRAST SENSITIVITY RESULTS

The Blackwell disk contrast sensitivity graphs (Figures 4, 5, and 6) for the same three subjects show results that are very similar to the square-wave contrast sensitivity. Again S-12 had a lower contrast sensitivity during flight than pre-flight. S-15 showed essentially no difference between the two conditions. The overall group results indicate that there is no significant group effect due to space flight. Again, further research is required to determine if the individual changes are repeatable.

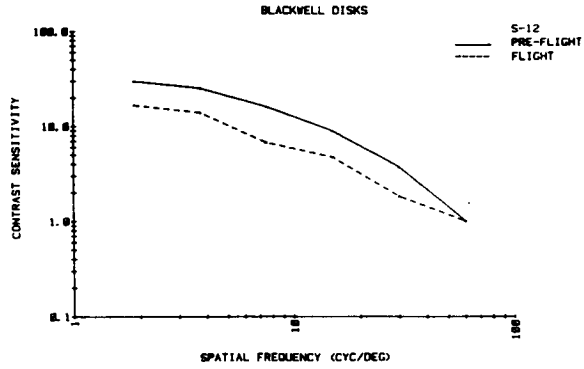

Figure 4

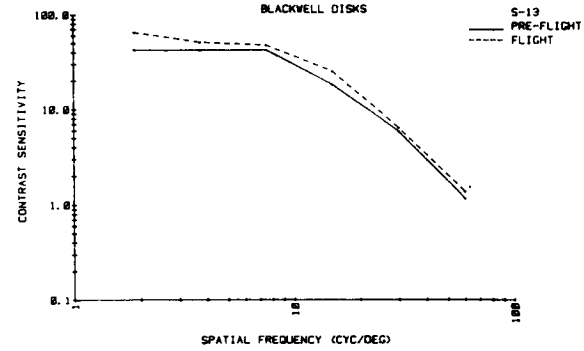

Figure 5

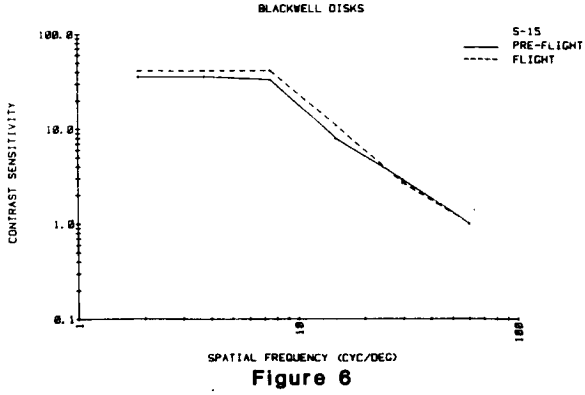

Figure 6

TRI-BAR CONTRAST SENSITIVITY RESULTS

The tri-bar results are highly similar to the Blackwell disk and square wave contrast sensitivity results as can be seen from the graphs

(Figures 7, 8, and 9). One significant finding from this study so far is that the results from the different test pattern types are so close that future study in this area need only use one of the pattern types to investigate changes in contrast sensitivity. Since the Blackwell disks or tri-bars require much less space than the square-wave patterns and yield the same results, it is most probable that future efforts will concentrate on one of these two pattern types.

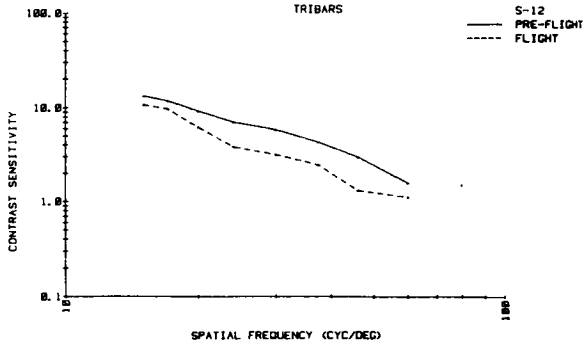

Figure 7

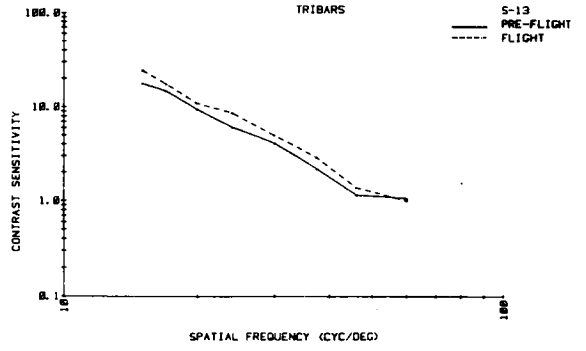

Figure 8

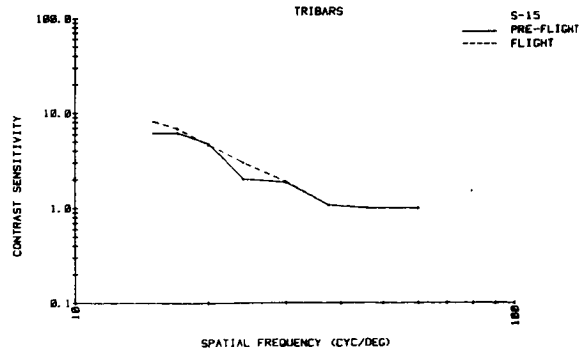

Figure 9

VFT-2 COMPARISON WITH OTHER CONTRAST SENSITIVITY MEASUREMENT METHODS

Figures 10 and 11 show a comparison between contrast sensitivity measured using the square-wave test patterns of VFT-2 and two other methods using sine-wave test patterns. The Optronix y/n tracking method uses a TV display to produce a sine-wave test pattern to which subjects respond. The other method uses a photographically printed array of sine-wave patterns of different contrasts and spatial frequencies. The graphs below show a good correspondence between the VFT-2 measurement and the photographic charts method. The specific TV method used resulted in somewhat higher measures of contrast sensitivity as evidenced by the graphs below. These graphs are part of a validation study that was conducted to compare the VFT-2 methods of measuring contrast sensitivity with other methods.

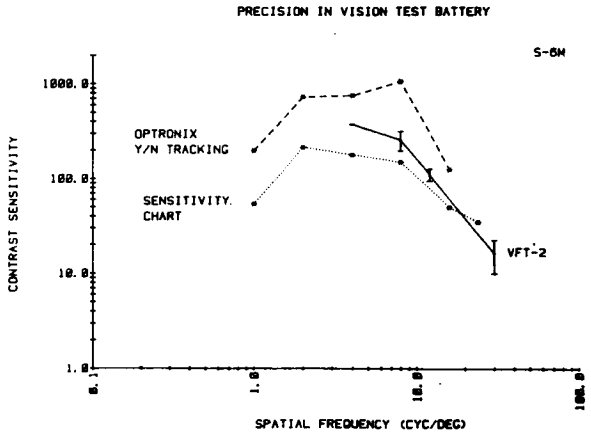

Figure 10

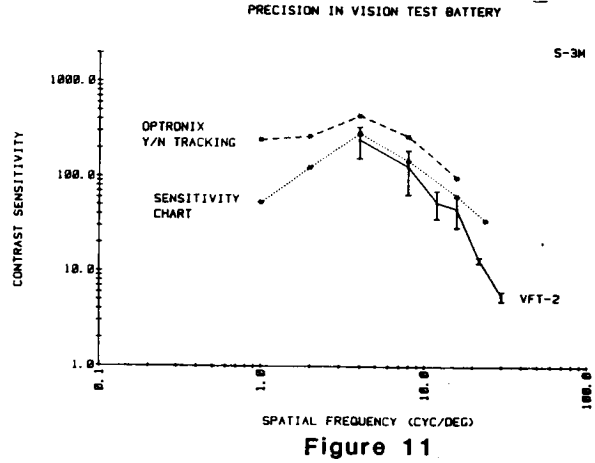

Figure 11

PHORIA OR EYE MUSCLE BALANCE RESULTS

Figures 12, 13, and 14 summarize the results of eye muscle balance effects due to space flight for all 15 astronauts tested. There was no significant group effect for cyclophoria, vertical phoria or horizontal phoria. Additionally, there did not appear to be any evidence of individual changes in eye muscle balance due to weightlessness.

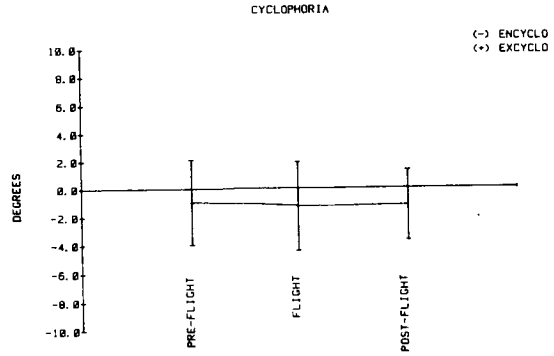

Figure 12

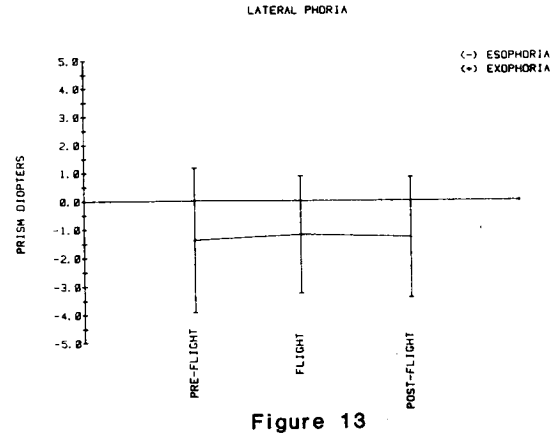

Figure 13

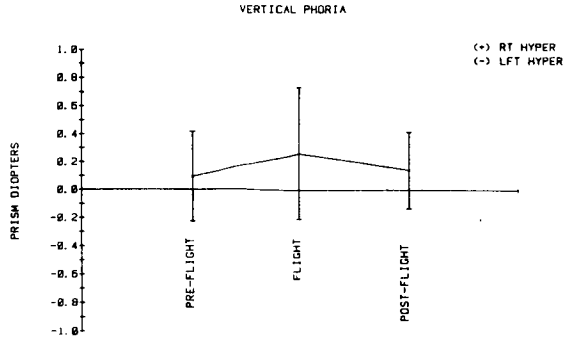

Figure 14

EYE DOMINANCE

The change in eye dominance as measured by the VFT-1 was not statistically significant. The changes evident on the graphs (Figures 15, 16 and 17) may have been a result of repeated exposure to the method of testing (essentially learning). As noted on the graphs, data for this test was only available for six astronauts: S-1 to S-6.

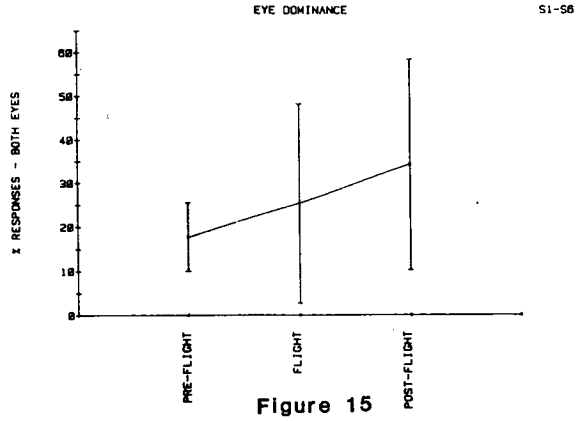

Figure 15

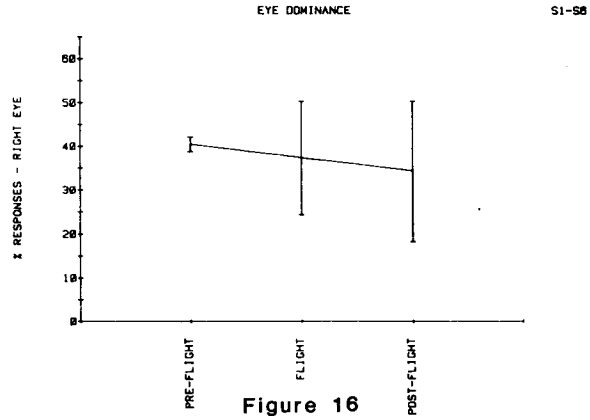

Figure 16

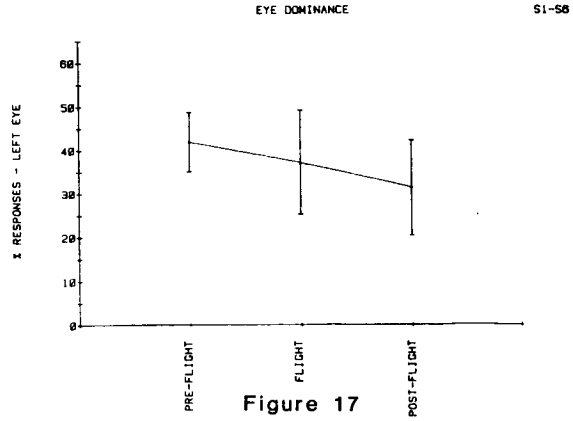

Figure 17

CRITICAL FLICKER FREQUENCY

The critical flicker frequency was measured both foveally (center of the retina) and peripherally (about 15 degrees off center) for all astronauts. As is obvious from the graphs (Figures 18 and 19), there were no significant changes in either of these parameters due to weightlessness.

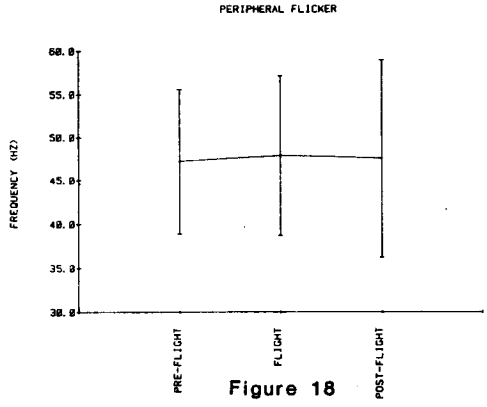

Figure 18

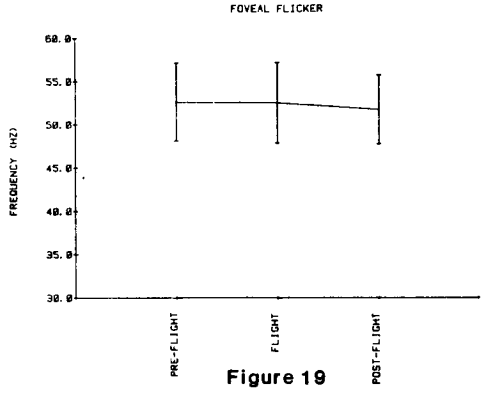

Figure 19

STEREOPSIS AND ACUITY

These two visual functions are interesting for different reasons. Initial reactions of some of the early astronauts indicated that they felt they could see better in space during space to ground observations. This would mean an improvement in their far visual acuity. From Figure 20 it is apparent that visual acuity was slightly (not statistically significant) worse during flight than pre or post flight.

Stereopsis showed the largest group change of all the parameters tested. Although the change was not statistically significant, the change was particularly interesting because it shows an apparent improvement in stereo acuity due to space flight. There is no explanation nor any hypothesis of a mechanism for why this might occur.

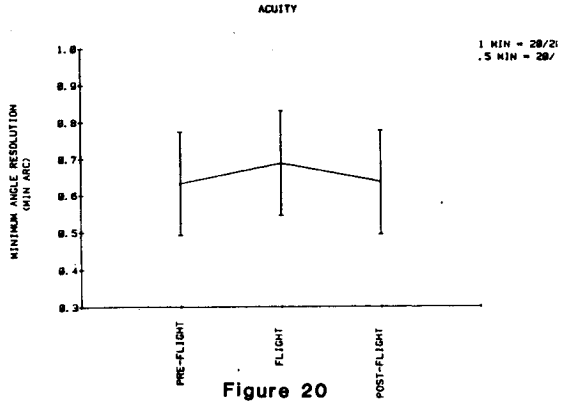

Figure 20

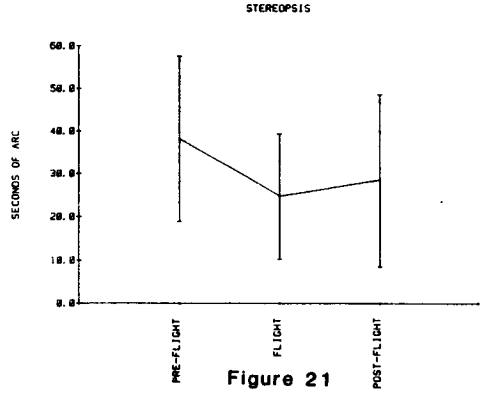

Figure 21

INDIVIDUAL EFFECTS

None of the parameters tested showed a significant change due to space flight. However, some of the individual data were interesting in that there appear to be some effects on some individuals. Figures 22, 23, and 24 are the most striking examples of possible individual effects. Two individuals seemed to show a significant improvement in stereopsis during space flight and one showed an apparent decrease in visual acuity during space flight. There is no way to satisfactorily test the statistical significance of these effects since these data are post facto selected from the data collected. However, the possibility exists that weightlessness affects the visual system of different individuals differently, as does space adaptation syndrome. The best way to

determine if the graphs are significant is to retest these subjects on future flights if the opportunity arises.

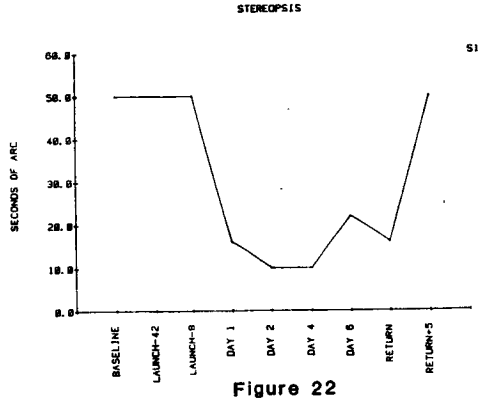

Figure 22

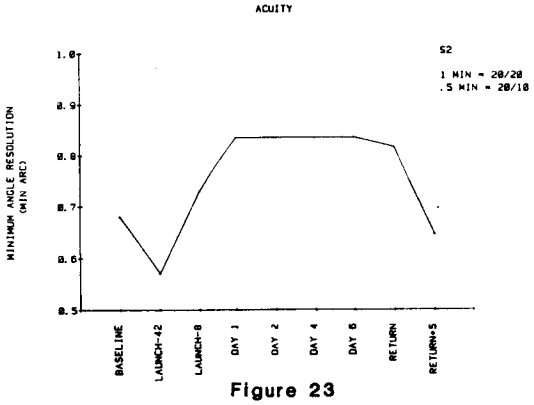

Figure 23

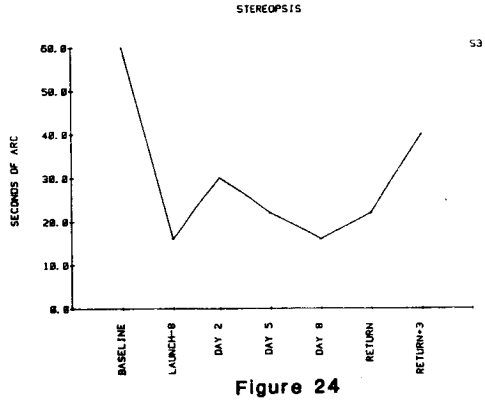

Figure 24

CONCLUSIONS

The VFT-1 and VFT-2 tested for changes in visual acuity, stereopsis, vertical and lateral phoria, cyclophoria, critical flicker frequency, eye dominance and contrast sensitivity. None of these visual parameters showed a statistically significant group change due to weightlessness. A total of 15 astronauts participated in VFT-1 experiments and 3 in the VFT-2 study.

Although there were no group changes in these parameters, some individuals appeared to show significant differences in acuity and stereopsis during space flight. Without further study it is impossible to determine if these effects are real or simply a happenstance of the data.

Two of the parameters studied seemed to show some (not statistically significant) group effect. These were a minor decrease in visual acuity and a relatively large increase in stereo acuity.

It should be remembered that all of these data were collected on short duration shuttle flights. It is quite possible that significant visual effects may become evident during extended space habitation stays as would occur on a space station. This remains as an area of study for the future.

VISION IN SPACE: NEAR VISION ACUITY AND CONTRAST SENSITIVITY

Investigators: Arthur P. Ginsburg, Ph.D., and James Vanderploeg, M.D.

INTRODUCTION

Both American and Soviet astronauts have reported conflicting experiences with visual capability in space (1). While some astronauts report considerable increases in visual capability, some report marked decreases in capability, and still others report no change. Since weightlessness causes disruption of the vestibular-ocular system and a redistribution of fluid throughout the body which could cause cerebral edema and changes in eyeball shape, changes in visual capability would not be unexpected. Studies using two different testing methods, near visual acuity and contrast sensitivity, were undertaken to determine the effects of weightlessness on vision. Near visual acuity was selected to determine changes in accommodation and other possible changes affecting vision. Contrast sensitivity testing was selected as a more precise measure of general vision loss as well as an aid in determining the possible physiological location and nature of vision changes. Evidence shows that significant losses in contrast sensitivity can occur with little or no effect on visual acuity (2-6).

PROCEDURES

Twenty-three crew members were tested for near vision acuity. Sixteen crew members were evaluated for contrast sensitivity. Using the near point of accommodation, near vision acuity was measured in diopters from a Krimsky rule. Contrast sensitivity was measured using five specially designed contrast sensitivity charts. The contrast levels and orientations of the test patches for each chart were randomized to control for guessing and memorization. Six spatial frequencies of 1, 2, 4, 8, 12, and 24 cycles per degree were tested at a distance of 18 inches. Luminance differences between ground and space testing were controlled Measurements were taken at thirty days preflight, ten days preflight, during flight, at landing, and seven days postflight.

TABLE 1. NEAR VISION ACUITY

Crew-member	Change in Diopters (Space - Ground)	
1	0.20	
2	1.20*	
3	-0.45	
4	0.05	
5	0.00	
6	-0.20	
7	0.07	
8	-0.22	
9	0.04	Range -2.2
10	-0.25	to 1.45
11	-0.83	Mean -0.068
12	-0.80	Std Dev 0.74
13	0.15	
14	-2.20*	
15	-0.10	
16	0.20	
17	-0.45	
18	-0.47	
19	1.45*	
20	0.20	
21	1.10*	
22	-0.40	
23	0.15	

*Clinically Significant (>1 Diopter Change)

RESULTS

Near vision acuity data were analyzed for differences in the near point of accommodation among the preflight, inflight, postflight, and average of pre- and postflight measurements (Table 1). Paired t-tests and analysis of variance with repeated measurements showed that no significant differences in diopter measurements existed among the three phases of flight. Contrast sensitivity data were analyzed for

differences between the average preflight contrast sensitivity data and those obtained inflight, at landing, and postflight (Figure 1). Statistically significant individual differences in contrast sensitivity changes in space were found. Crewmembers exhibited different magnitudes of change at different spatial frequencies.

CONCLUSIONS

No clinically significant changes in near vision acuity in the micro-gravity environment of space were found during space shuttle flights. However, changes in contrast sensitivity were seen under these conditions. Alterations in contrast sensitivity occurring in the low and middle but not the high spatial frequencies cannot be readily attributed to changes in accommodation, but reflect more central effects. In general, the changes in contrast sensitivity are less than a factor of two and would not be expected to cause major visual performance increases or decreases. The possible physiological reasons for the changes in contrast sensitivity during space flight will require further research.

Figures 1 - 6. Changes in contrast sensitivity of crewmembers from initial (baseline) measurements. The data of these six crewmembers are typical of the largest changes found. Note that there are significant increases and decreases in sensitivity over different spatial frequencies for these crewmembers. Further research will be required to fully understand these changes. Since these changes are generally a factor of two or less, no major visual gains or losses are indicated for crewmembers in space.

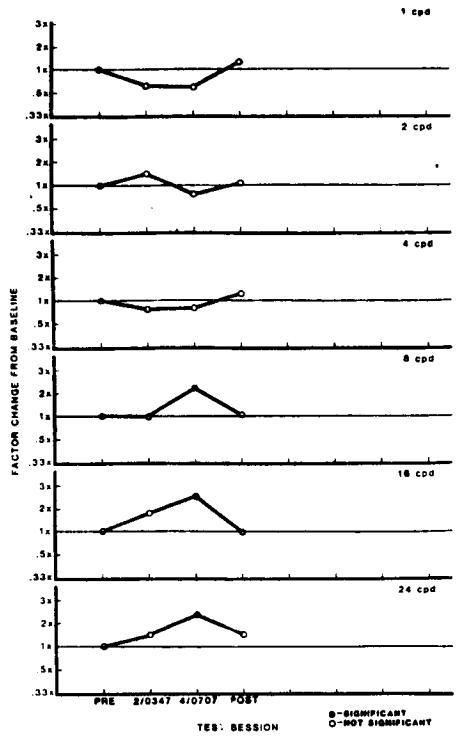

Figure 1. Crewman A.

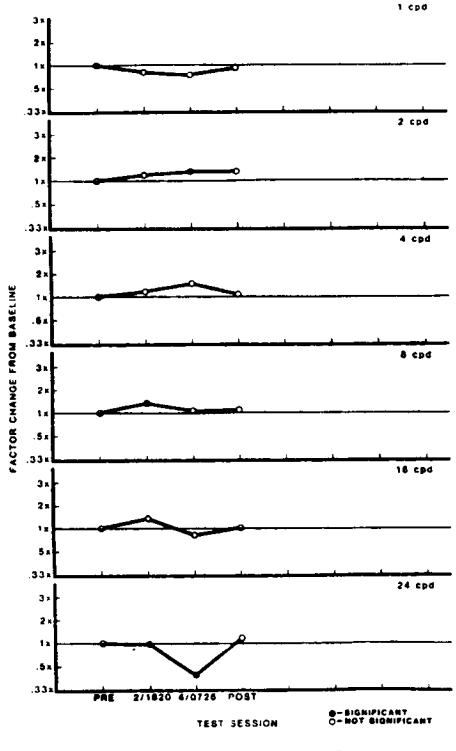

Figure 2. Crewman B.

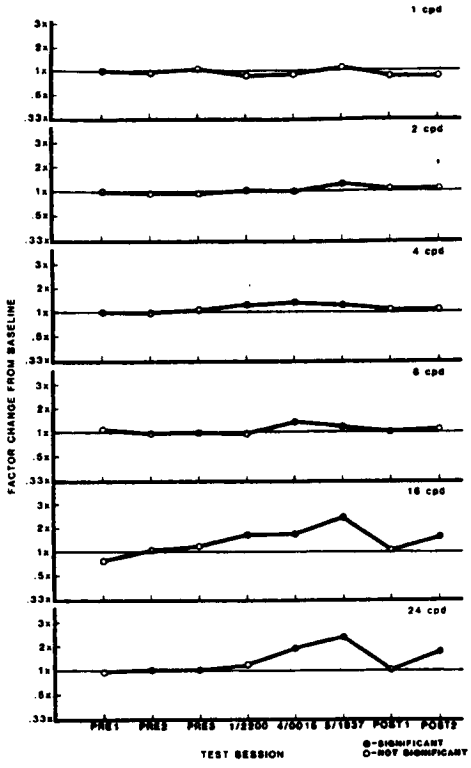

Figure 3. Crewman C.

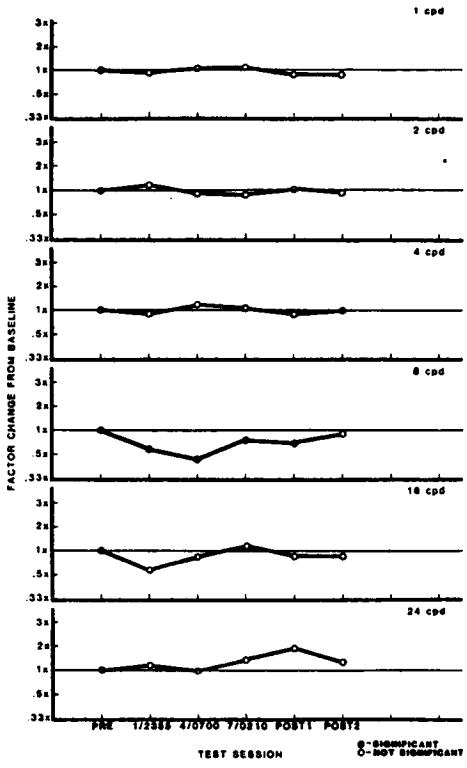

Figure 5. Crewman E.

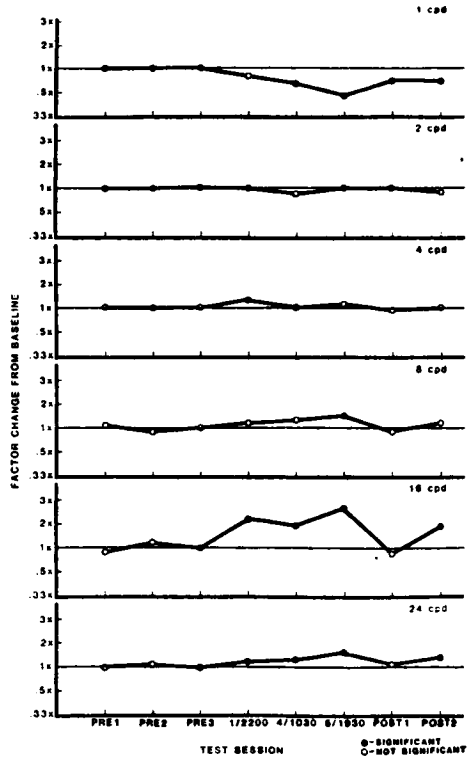

Figure 4. Crewman D.

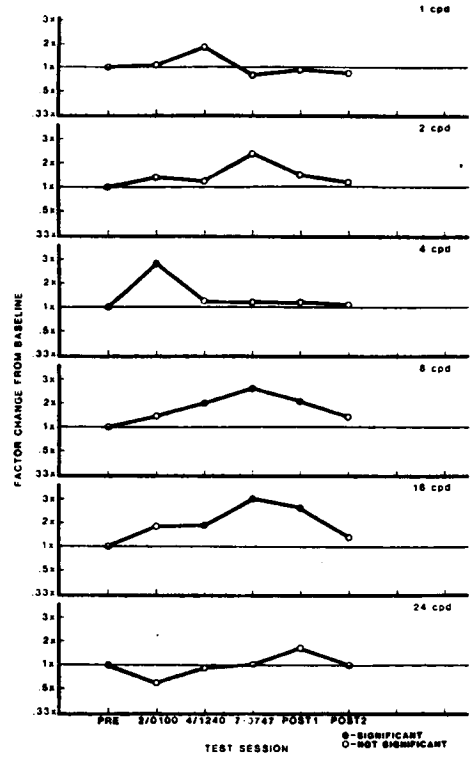

Figure 6. Crewman F.

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6. Committee on Vision, National Research Council: Emergent Techniques for the Assessment of Visual Performance, Washington, D.C., National Academy Press, 1985.

7. Ginsburg, A.P.; A New Contrast Sensitivity Vision Test Chart, Am. J. Opt. Physiol. Opt., 61(6), 1984, 403-407.

Appendix A: Matrix Overview of the DSO Program

MATRIX 1: MEDICAL DSOs LISTED BY NUMBER AND TITLE Prepared 02-20-87 by SBRI Flight Projects/MAB

DSO	TITLE	INVESTIGATOR(S)	FLIGHT HISTORY	COMPLETION STATUS	SUMMARY OF RESULTS
401	Validation of Predictive Tests and Countermeasures for Space Motion Sickness	Dr. J. L. Homick	Performed on 16 missions: STS-1 through 9, 41B, 41C, 41D, 41G, 51A, 51C, & 51D	This study is complete. All 58 requested subjects were obtained.	Predicting susceptibility to SMS by using ground based test results is difficult, but shows some promise. Reporting of SMS symptoms is now SOP on all Shuttle flights. See page 153 of this report.
402	Cardiovascular Deconditioning Countermeasure Assessment	Dr. M. W. Bungo and Dr. P. C. Johnson	12 Flights: STS-1 thru 9, 41B, 41C, 41D	This study is complete. All 46 requested subjects were obtained.	Prelanding "fluid loading" is an effective countermeasure for orthostatic intolerance. Fluid loading prior to reentry has been made SOP on all Shuttle flights. See page 41 of this report.
403	Head and Eye Motion During Ascent and Entry	Dr. W. E. Thornton	STS-5 through 8 (4 Flights)	Complete; all 5 requested subjects were obtained.	No abnormalities have been seen with or without SMS. See pages 162 and 167 of this report.
404	On-Orbit Head and Eye Tracking Tasks	Dr. W. E. Thornton	STS-5 through 8 (4 Flights)	Complete; 16 subjects were obtained.	No evidence of disordered and organs or of increased CNS pressure. See pages 162 & 167 of this report.
405	Acceleration Detection Sensitivity	Dr. W. E. Thornton	STS-5, 7, and 8 (3 Flights)	Complete: 2 subjects were obtained.	Hardware performance was inadequate; undesired angular oscillations made detection of linear motion questionable.
406	Kinesthetic Ability	Dr. W. E. Thornton	STS-5, 7, and 8 (3 Flights)	Complete; 3 or 4 subjects obtained.	No conclusions were reported.
407	Photographic Documentation of Body Fluid Shift	Dr. W. E. Thornton	STS-6, 7, and 8	Complete; 7 subjects obtained.	Photographs are adequate, but analysis is incomplete.
408	Near Vision Acuity and Contrast Sensitivity	Drs. A. Ginsberg & J. M. Vanderploeg	Nine flights: STS-5, 6, 7, 8, 41B, 41C, 41D, 41G and 51C	Complete; 32 of 36 requested subjects were obtained.	Some changes in contrast sensitivity were observed; changes in acuity were insignificant. See page 179 of this report.
409	Microbial Screening	Dr. D. L. Pierson	Four flights: STS-6, 7, 8, and 41B	Complete; data was collected on 4 flights as requested.	A continual buildup of airborne contaminants was demonstrated. See page 93 of this report.

MEDICAL DSOs LISTED BY NUMBER AND TITLE (Continued)

DSO	TITLE	INVESTIGATOR(S)	FLIGHT HISTORY	COMPLETION STATUS	SUMMARY OF RESULTS
410	Audiometry	Dr. W. E. Thornton	STS-6, 7, and 8	Complete; 13 subjects were obtained.	Results are questionable. Audio evoked potentials are preferred to this method.
411	Simple Mass Measurement	Dr. W. E. Thornton	STS-8	Complete; 1 subject was obtained.	Concept is valid, but balance time constant was too long for accurate measurements.
412	Treadmill Operation	Dr. W. E. Thornton	STS-7 and 8	Complete; 2 subjects obtained.	Data points were incompatible with analysis procedure.
413	Cell Attachment in Microgravity	Dr. D. R. Morrison	STS-7	Complete	Cells can attach to a growth surface in microgravity. (This study continued with an incubator as DSO 432.) See page 85 of this report.
414	Ophthalmoscopy	Dr. E. L. Shulman	STS-7 and 8	Complete; 4 subjects were obtained.	No indication of increased intracranial pressure. See page 167 of this report.
415	Tissue Pressure Tonometry	Dr. W. E. Thornton	STS-7 and 8	Complete; 5 subjects obtained.	Data were nominally obtained. See page 160 of this report.
416	Ambulatory Monitoring	Dr. W. E. Thornton	STS-7 and 8	Complete; 2 subjects obtained.	Bowel sounds may be reliable as a "marker" for SMS. See page 163 of this report.
417	Inflight Countermeasures for SAS	Dr. W. E. Thornton	STS-7 and 8	Complete; 1 subject obtained.	Physical countermeasures seemed to have little effect, yet one pharmacological agent initially showed great promise. See page 134.
418	Eye-Hand Coordination	Dr. W. E. Thornton	STS-8	Complete; 5 requested subjects obtained.	No obvious changes were noted. See page 164 of this report.
419	Evaluation of Food Flavor Perception in Zero Gravity	R. L. Sauer	---	Disapproved	---
420	Evaluation of Taste Acuity in Zero-g	R. L. Sauer	---	Disapproved	---

MEDICAL DSOs LISTED BY NUMBER AND TITLE (Continued)

DSO	TITLE	INVESTIGATOR(S)	FLIGHT HISTORY	COMPLETION STATUS	SUMMARY OF RESULTS
421	Animal Enclosure Module Inflight Test	Dr. M. C. Smith	STS-8	Complete; data was collected on 1 flight as requested.	Six rats were successfully kept healthy without impairing the safety of the crew. See page 75 of this report.
422	Anatomical Observation	Dr. W. E. Thornton	STS-8	Complete; all 5 requested subjects were obtained.	Many changes were noted using auscultation and palpation; percussion was not possible.
423	Study of Inflight Fluid Changes	Drs. W. E. Thornton and C. S. Leach	STS-8	Complete; 1 subject was obtained as requested.	Fluid shift of up to 4 liters occurs within hours of exposure to zero gravity.
424	Evoked Potentials	Dr. W. E. Thornton	STS-8	Complete; 4 subjects obtained as requested.	No evidence of abnormalities was found. See pages 160 & 167 herein.
425	Intraocular Pressure	Dr. S. L. Pool	STS-8	Complete; 1 subject obtained as requested.	No apparent difference from preflight. See pages 160 & 167 herein.
426	Denitrogenation Procedures Validation	J. M. Waligora and D. J. Horrigan	---	Withdrawn	---
427	Soft Contact Lens Application Test	Drs. W. E. Thornton and L. R. Young	STS-8	Complete; 1 subject obtained as requested.	Lens would not adhere using the prescribed procedure.
428	Unassigned	---	---	---	---
429	Unassigned	---	---	---	---
430	Unassigned	---	---	---	---
431	Unassigned	---	---	---	---
432	Engineering Test of Carry-on Incubator and Cell Attachment in Microgravity	Drs. D. R. Morrison and A. Cogoli	STS-8	Complete; data was collected on 1 flight as requested.	Cell attachment inflight was greater than in ground control samples and much improved over DSO 413 results; there are exciting implications for bioprocessing in space. See page 87 of this report.

MEDICAL DSOs LISTED BY NUMBER AND TITLE (Continued)

DSO	TITLE	INVESTIGATOR(S)	FLIGHT HISTORY	COMPLETION STATUS	SUMMARY OF RESULTS
433	Preflight and Postflight Parallel Swing Tests	Drs. D. E. Parker and M. Reschke	STS-8, 41B, and 51D	Complete; 5 of 6 requested subjects obtained (including those obtained as part of DSO 449).	Findings support the Otolith Tilt-Translation Reinterpretation Hypothesis. Was renamed DSO 449 prior to STS-51D. See page 145 of this report.
434	Unassigned	---	---	---	---
435	Unassigned	---	---	---	---
436	Inflight Monitoring as a Reflection of Cardiovascular Deconditioning	Dr. M. W. Bungo	---	Withdrawn	---
437	Microbial Monitoring	Dr. D. L. Pierson	STS 51-B	Active; data has been collected on 1 flight and is to be collected on all flights with animals.	Adherence to the Specific Pathogen Free criteria for animals protected the crew when the RAHF failed. See page 97 in this report.
438	Unassigned	---	---	---	---
439	Documentation of the Action of Metoclopramide	Dr. W. E. Thornton	STS-41D, 41G, 51C, 51D*, 51B	Complete; 9 of 12 requested subjects were obtained.	SMS causes cessation of bowel activity. MCP is an ineffective treatment. See page 138 in this report.
440	Crew Visual Performance	Lt. Col. L. V. Genco and Dr. H. L. Task	STS-41D, 41G, and 51C	Complete; 10 of 11 requested subjects were obtained.	Acuity is marginally poorer; stereopsis shows marked improvement. All values tend toward norms on return. See page 173 herein.
441	Blood Pressure Monitoring During Reentry	Drs. W. E. Thornton and T. P. Moore	STS-8, 41D, 41G, 51C, 51D*, 51B, and 51F	On hold; 9 of 9 requested subjects were obtained.	No evidence of orthostatic hypotension during the flight phase; there are questions about the seat egress phase. See page 37 herein.

*As part of DSO 456.

MEDICAL DSOs LISTED BY NUMBER AND TITLE (Continued)

DSO	TITLE	INVESTIGATOR(S)	FLIGHT HISTORY	COMPLETION STATUS	SUMMARY OF RESULTS
442	Autogenic Feedback Training (AFT)	Dr. P. S. Cowings	STS-51C	Complete; 1 subject was obtained as requested.	Provided valuable suggestions for improvement of hardware and procedures for the AFT experiment on Spacelab 3. See page 79 herein.
443	Seqmental Fluid Shift	Drs. J. S. Logan, R. J. Luciani, L. D. Montgomery, and G. R. Coulter	---	On hold	---
444	Unassigned	---	---	---	---
445	Thoracic Impedance Measurements	Drs. T. P. Moore and W. E. Thornton	STS-8 (not as 445)	On hold; 1 subject was obtained.	No conclusions were reported.
446	Leg Plethysmography	Drs. T. P. Moore and W. E. Thornton	STS-51B, 51D*, and 51J (as DSO 446); 61B and 61C (as DSO 461)	Complete; 9 of 8 requested subjects were obtained (including those obtained as part of DSO 461).	There is typically a 1 liter volume change in each leg, largely due to shifts in body fluids. The shift occurs in the first 6-10 hours after launch. Postflight return is rapid, but a decrement persists. See page 59 herein.
447	Causative Agents During SMS	Dr. W. E. Thornton	---	---	Was incorporated into DSO 453 and flown under that designation.
448	Echographic Evaluation of Cardiovascular Deconditioning	Dr. M. W. Bungo	---	N/A	Resubmitted as a Form 100 Experiment (American Flight Echo).
449	Preflight and Postflight Parallel Swing Tests	Drs. D. E. Parker and M. Reschke	STS-8, 41B, and 51D	Complete; 5 of 6 requested subjects obtained (including those obtained as part of DSO 433).	Findings support the Otolith Tilt-Translation Reinterpretation Hypothesis and provide the basis for proposing a Preflight Adaptation Trainer (PAT). See page 145 in this report.
450	Salivary Cortisol During Acute Phases of Spaceflight	Dr. N. Cintron	STS-41G and 51L	Active; 1 of 6 requested subjects has been obtained.	Saliva collection is a viable tool for measurement of inflight cortisol levels. See page 31 in this report.

*As part of DSO 456.

DSO	TITLE	INVESTIGATOR(S)	FLIGHT HISTORY	COMPLETION STATUS	SUMMARY OF RESULTS
451	Eye-Hand Coordination During SMS	Drs. W. E. Thornton and T. P. Moore	STS-51D*, 51B, 51J, and 61C	On hold; 5 of 10 requested subjects have been obtained.	No changes are apparent due to zero-G alone; data during SMS are under analysis. See page 164 in this report.
452	Leg Volume Changes	Drs. T. P. Moore and W. E. Thornton	---	On hold	---
453	Combined Blood Investigations	Drs. W. E. Thornton, C. Leach-Huntoon, H. Schneider, N. Cintrol, and Mr. R. Landry	STS-51B and 51F	Complete; 6 of 8 requested subjects have been obtained.	Some hypotheses about physiologic changes during spaceflight need additional study; new evidence indicates additional factors should be studied. See page 7 herein.
454	Clinical Characterization of SMS	Drs. W. E. Thornton and J. Vanderploeg	See DSO 455	See DSO 455	Redesignated DSO 455 before flight. See DSO 455 results.
455	Clinical Characterization of SMS	Drs. W. E. Thornton and J. Vanderploeg	STS-51D*, 51G, 51I, 51J, 61B, 61C, and 51L	Active; 7 of 12 requested subjects have been obtained.	Lack of bowel sounds may be a reliable indicator of SMS. Other data are being analyzed (pupillary size, skin color, etc.). See page 159 of this report.
456	Medical Tests and Measurements for the STS-51D Payload Specialist	Drs. Vanderploeg, Pool, Cintron, Charles, Inners, Reschke, Parker, Thornton, and Moore	STS-51D	Complete; 1 subject was obtained as requested.	This was a combination of many studies, including all or parts of DSOs 439, 441, 446, 449, 451, 455, 458, and 460. See results of individual studies.
457	Salivary Pharmacokinetics of Scop-Dex	Drs. N. Cintron and L. Putcha	STS-61B and 61C	Active; 3 of 6 requested subjects have been obtained.	There are apparent changes in the distribution of Scopolamine; a Dextroamphetamine assay is underway. See page 25 herein.
458	Salivary Acetaminophen Pharmacokinetics	Drs. N. Cintron and L. Putcha	STS-51D*, 51I, 61B, and 61C	Active; 5 of 6 requested subjects have been obtained.	A significant change has been noted in the disposition of acetaminophen taken inflight, in both drug concentration and time course. See page 19 of this report.

*As part of DSO 456.

MEDICAL DSOs LISTED BY NUMBER AND TITLE (Continued)

DSO	TITLE	INVESTIGATOR(S)	FLIGHT HISTORY	COMPLETION STATUS	SUMMARY OF RESULTS
459	Otolith Tilt-Translation Reinterpretation	Drs. M. Reschke and D. E. Parker	STS-61C and 51L	Active; 2 of 8 requested subjects have been obtained.	Pitch motion immediately after reentry was perceived as translation. Ocular counterrolling was observed inflight, but of a lower magnitude than preflight. These data will be of great help in designing a Preflight Adaptation Trainer (PAT). Due to late change in landing site, the most critical data (early postflight measurements) were not obtained. Subjective accounts of sensory perceptions were elicited in interviews. See pages 125 and 141 of this report.
460	Changes in Total Body Water During Spaceflight	Drs. C. S. Leach, L. D. Inners, and J. B. Charles	STS-51D* and 61C	Active; 3 of 5 requested subjects have been obtained.	Total body water decreases about 3% by day 2 of exposure to zero-G, then remains stable. See page 49 of this report.
461	Leg Plethysmography	Drs. T. P. Moore and W. E. Thornton	STS-51B, 51D*, and 51J (as DSO 446); 61B and 61C (as DSO 461)	Complete; 9 of 8 requested subjects were obtained (including those obtained as part of DSO 446).	There is typically a 1 liter volume change in each leg, largely due to shifts in body fluids. The shift occurs in the first 6-10 hours after launch. Postflight return is rapid, but a decrement persists. See page 59 herein.
462	Noninvasive Estimation of Central Venous Pressure	Drs. J. B. Charles and M. W. Bungo	STS-61C	Active; 1 subject has been obtained.	The technique is viable and produced good results. CVP decreased over the first three flight days, then remained at a constant value. See page 69 in this report.
463	Inflight Treadmill Stress Test	Drs. M. W. Bungo and J. B. Charles	STS-61C	Complete; 1 subject was obtained as requested.	No increase in ectopic activity was seen in this crewmember in contrast to the increase in dysrythmias seen during EVAs on previous STS Flights. See page 67 in this report.

*As part of DSO 456.

DSO	TITLE	INVESTIGATOR(S)	FLIGHT HISTORY	COMPLETION STATUS	SUMMARY OF RESULTS
464	Inflight Assessment of Renal Stone Risk Factor	Dr. N. Cintron	STS-61C	Active; 1 subject has been obtained.	Urine volume did not appear changed from preflight. A trend to increased excretion of calcium, phosphate, magnesium, and uric acid was present. See page 13 in this report.
465	Preflight and Postflight Echocardiography	Drs. J. B. Charles and M. W. Bungo	STS-61C	0 of 12 requested subjects was obtained. Will be supplanted by DSO 466.	Due to a last-minute change of landing site, no postflight data were collected. DSO 466 will replace 465 when flights resume.
466	Variations in Supine and Standing Heart Rate, Blood Pressure, and Cardiac Size as a Function of Space Flight Duration and Time Postflight	Drs. J. B. Charles and M. W. Bungo	Awaiting flight assignment	66 subjects from flights of varying durations have been requested.	TBD

MATRIX 2

MEDICAL DSOs - FLIGHT ASSIGNMENTS & SUBJECT COUNTS

Prepared by SBRI Flight Projects/MAB 2/27/87

DSO	SHORT TITLE	SUBJECTS APPROVED vs OBTAINED FOR EACH SHUTTLE FLIGHT																									TOT REQ vs OBT
		STS 1	STS 2	STS 3	STS 4	STS 5	STS 6	STS 7	STS 8	STS 9	STS 41B	STS 41C	STS 41D	STS 41G	STS 51A	STS 51C	STS 51D	STS 51B	STS 51G	STS 51F	STS 51I	STS 51J	STS 61A	STS 61B	STS 61C	STS 51L	
401	Predictive Tests	2 2	2 2	2 2	2 2	4 4	4 4	4 4	4 4	5 5	5 5	5 5	6 6	4 4	3 3	2 2	4 4	STANDARD OPERATING PROCEDURE ----------									58 58 C
402	Fluid Loading	2 2	2 2	2 2	2 2	4 4	4 4	5 5	5 5	4 4	5 5	5 5	6 6	STANDARD OPERATING PROCEDURE ----------													46 46 C
403	Head & Eye Motion					1 1	1 1	1 1	2 2																		5 5 c
404	Head & Eye Tracking					? 2	4 4	? 5	5 5																		? 16 c
405	Acceleration Detection					? 0		? 0	0 2																		? 2 C
406	Kinesthetic Ability					? 0		? 1	? ?																		? 3-4C
407	Body Fluid Shifts						? 0	? 2	? 5																		? 7 C
408	Near Vision Acuity					4 4	4 4	5 5	5 5		2 0	5 5	2 2	4 2		5 5												36 32 C
409	Microbial Screening						1 1	1 1	1 1		1 1																4 4 C
410	Audiometry						4 4	? 4	5 5																		? 13 C
411	Mass Measurement								? 1																		? 1 C
412	Treadmill Operation							? 2	? ?																		? 2 C
413	Cell Attachment							1 1																			1 1 C
414	Ophthalmoscopy							2 2	? 2																		? 4 C

DSO	SHORT TITLE	SUBJECTS APPROVED vs OBTAINED FOR EACH SHUTTLE FLIGHT																									TOT REQ vs OBT
		STS 1	STS 2	STS 3	STS 4	STS 5	STS 6	STS 7	STS 8	STS 9	STS 41B	STS 41C	STS 41D	STS 41G	STS 51A	STS 51C	STS 51D	STS 51B	STS 51G	STS 51F	STS 51I	STS 51J	STS 61A	STS 61B	STS 61C	STS 51L	
415	Tissue Tonometry							? 1	? ?																		? 5 C
416	Ambulatory Monitoring							1 1	1 1																		2 2 C
417	SMS Countermeasures							? 0	1 1																		1 1 C
418	Eye-Hand Coordination								5 5																		5 5 C
419	Flavor Perception	DISAPPROVED ----------																									N/A
420	Taste Acuity in 0-G	DISAPPROVED ----------																									N/A
421	Animal Enclosure Module								1 1																		1 1 C
422	Anatomical Observation								5 5																		5 5 C
423	Inflight Fluid Changes								1 1																		1 1 C
424	Evoked Potentials								4 4																		4 4 C
425	Intraocular Pressure								1 1																		1 1 C
426	Denitrogenation	WITHDRAWN ----------																									N/A
427	Soft Contact Lens Test								1 1																		1 1 C
428	Unassigned																										N/A
429	Unassigned																										N/A
430	Unassigned																										N/A
431	Unassigned																										N/A

DSO	SHORT TITLE	SUBJECTS APPROVED vs OBTAINED FOR EACH SHUTTLE FLIGHT																									TOT REQ vs OBT
		STS 1	STS 2	STS 3	STS 4	STS 5	STS 6	STS 7	STS 8	STS 9	STS 41B	STS 41C	STS 41D	STS 41G	STS 51A	STS 51C	STS 51D	STS 51B	STS 51G	STS 51F	STS 51I	STS 51J	STS 61A	STS 61B	STS 61C	STS 51L	
432	Cell Attachment								1 1																		1 1 C
433/ 449	Parallel Swing Tests								1 1		2 2						3 2										6 5 C
434	Unassigned																										N/A
435	Unassigned																										N/A
436	Cardio Deconditioning	WITHDRAWN ----------																									N/A
437	Microbial Monitoring																	1 1									1 1 A
439	Action of Reglan												3 1	4 4		2 2	1 1	2 1									12 9 C
440	Visual Performance												2 2	4 3		5 5											11 10 C
441	BP Monitoring								1 1				1 1	2 0		1 1	2 2	2 2		2 2							9 9 H
442	Autogenic Feedback															1 1											1 1 C
443	Segmental Fluid Shift	ON HOLD ----------																									1 0 H
444	Unassigned																										N/A
445	Thoracic Impedance	ON HOLD ----------																									8 0 H
446/ 461	Leg Plethysmography																1 1	3 3				2 2		2 2	1 1		8 9 H
447	SMS Causative Agents	INCORPORATED INTO DSO 453 ----------																									N/A
448	Echocardiography	RESUBMITTED AS A FORM 100 EXPERIMENT ----------																									N/A
449	Parallel Swing Tests	SEE DSO 433 ----------																									6 5 C

DSO	SHORT TITLE	SUBJECTS APPROVED vs OBTAINED FOR EACH SHUTTLE FLIGHT																								TOT REQ vs OBT
		STS 1	STS 2	STS 3	STS 4	STS 5	STS 6	STS 7	STS 8	STS 9	STS 41B	STS 41C	STS 41D	STS 41G	STS 51A	STS 51C	STS 51D	STS 51B	STS 51G	STS 51F	STS 51I	STS 51J	STS 61A	STS 61B	STS 61C	STS 51L	
450	Salivary Cortisol													2 1											2 0	6 1 A
451	Eye-Hand Coordination																1 1	5 1				2 2			1 1		10 5 H
452	Leg Volume Changes	ON HOLD ----------																									5 0 H
453	Blood Investigations																	4 2		4 4							8 6 C
454/ 455	Characterization of SMS																3 0		2 2		2 0			0 1	4 4	2 0	12 7 A
456	Tests & Measurements																1 1										1 1 C
457	Salivary Scop-Dex																							2 1	2 2		6 3 A
458	Salivary Acetaminophen																1 1				1 0			2 2	2 2		6 5 A
459	Otolith Tilt-Trans																								2 2	2 0	8 2 A
460	Total Body Water																1 0								3 3		5 3 A
461	Leg Plethysmography	SEE DSO 446 ----------																									8 9 H
462	Estimation of CVP																								1 1		1 1 H
463	Holter Monitoring																								1 1		1 1 H
464	Renal Stone Risk																								1 1		1 1 H
465/ 466	Pre & Postflight Echo																								1 0		66 0 A

NOTES:
1. Top numbers in the "Subjects Approved vs Obtained" columns represent the number of subjects approved by the Mission Integration Control Board (MICB) for each flight listed.
2. Bottom numbers in the "Subjects Approved vs Obtained" columns represent the number of subjects obtained on each of the flights listed.
3. Numbers in the "Total Requested vs Obtained" column represent the total number of subjects requested by the investigator(s) (top number) versus the number obtained to date (bottom number). The MICB attempts to schedule a DSO on an appropriate series of flights until the desired number of subjects is obtained.
4. Letters in the "Total Requested vs Obtained" column indicate the status of the DSO:
   C = Complete
   A = Active
   H = On hold. Data is to be reviewed before the DSO is scheduled for reflight.
5. A question mark in a column indicates that the number is unknown or was not specified.
6. The protocols used in DSOs 401 and 402 have been adopted as Standard Operating Procedure to be used by Shuttle flight crews.
7. DSO 437 is to be flown on all flights on which animals will be exposed to cabin air.

MATRIX 3

DSO Investigators Prepared 2/19/87 by SBRI Flight Projects/MAB

INVESTIGATOR	ORG CODE	DSO NUMBER	SHORT TITLE OF DSO
Dr. M. W. Bungo	SD5	402	Cardiovascular Deconditioning Countermeasures
		462	Estimation of Central Venous Pressure
		463	Inflight Treadmill Stress Test
		465	Pre- and Postflight Echocardiography
Dr. J. B. Charles	SD5	460*	Total Body Water
		462	Estimation of Central Venous Pressure
		463	Inflight Treadmill Stress Test
		465	Pre- and Postflight Echocardiography
Dr. N. Cintron	SD4	450	Salivary Cortisol During Spaceflight
		453	Combined Blood Investigations
		457	Salivary Pharmacokinetics of Scop-Dex
		458*	Salivary Acetaminophen Pharmacokinetics
		464	Inflight Assessment of Renal Stone Risk Factor
Dr. P. S. Cowings	ARC	442	Autogenic Feedback Training (AFT)
Lt. Col. L. V. Genco	USAF	440	Crew Visual Performance Testing
Dr. A. Ginsberg	USAF	408	Near Vision Acuity (Contrast Sensitivity)
Dr. J. L. Homick	SD	401	Predictive Tests and Countermeasures for SMS
Dr. L. D. Inners	SD4	460*	Total Body Water
Dr. P. C. Johnson	SD	402	Cardiovascular Deconditioning Countermeasures
Dr. C. S. Leach	AC	423	Study of Inflight Fluid Changes
		453	Combined Blood Investigations
		460*	Total Body Water
Dr. T. P. Moore	SD5	441*	Blood Pressure Monitoring During Re-entry
		446/461*	Leg Plethysmography
		451*	Eye-Hand Coordination During SMS
		456	Medical Tests and Measurements (51D P/S)
Dr. D. R. Morrison	SD3	413	Cell Attachment in Microgravity
		432	Carry-on Incubator/Cell Attachment in Micro-G
Dr. D. E. Parker	SD5	433/449*	Pre- and Postflight Parallel Swing
		459	Otolith Tilt-Translation Reinterpretation
Dr. D. L. Pierson	SD4	409	Microbial Screening
		437	Microbial Monitoring
Dr. S. L. Pool	SD	425	Intraocular Pressure

INVESTIGATOR	ORG CODE	DSO NUMBER	SHORT TITLE OF DSO
Dr. L. Putcha	SD4	457	Salivary Pharmacokinetics of Scop-Dex
		458*	Salivary Acetaminophen Pharmacokinetics
Dr. M. Reschke	SD5	433/449*	Pre- and Postflight Parallel Swing
		459	Otolith Tilt-Translation Reinterpretation
Dr. H. Schneider	SD4	453	Combined Blood Investigations
Dr. E. L. Shulman	CB	414	Ophthalmoscopy
Dr. M. C. Smith		421	Animal Enclosure Module Inflight Test
Dr. W.E. Thornton	CB	403	Head and Eye Motion During Re-entry
		404	On-Orbit Head and Eye Tracking Tasks
		405	Acceleration Detection Sensitivity
		406	Kinesthetic Ability
		407	Photographic Documentation of Body Fluid Shift
		410	Audiometry
		411	Simple Mass Measurement
		412	Treadmill Operation
		415	Tissue Pressure Tonometry
		416	Ambulatory Monitoring
		417	Inflight Countermeasures for SAS
		418	Eye-Hand Coordination
		422	Anatomical Observation
		423	Study of Inflight Fluid Changes
		424	Evoked Potentials
		427	Soft Contact Lens Application
		439*	Documentation of the Action of Metoclopramide
		441*	Blood Pressure Monitoring During Re-entry
		446/461*	Leg Plethysmography
		451*	Eye-Hand Coordination During SMS
		453	Combined Blood Investigations
		454/455	Clinical Characterization of SMS
		456	Medical Tests and Measurements (51D P/S)
Dr. J.M. Vanderploeg	SB	408	Near Vision Acuity (Contrast Sensitivity)
		454/455	Clinical Characterization of SMS
		456	Medical Tests and Measurements (51D P/S)

* Included as part of DSO 456.
AC, CB, SB, SD, SD3, SD4, and SD5 are NASA JSC mail codes.
ARC - NASA Ames Research Center.
USAF - United States Air Force.

MATRIX 4

MEDICAL DSOs LISTED BY DISCIPLINE Prepared by SBRI Flight Projects/MAB 2/19/87

DISCIPLINE	DSO	SHORT TITLE	INVESTIGATOR(S)
Biochemistry and Pharmacology	447*	Causative Agents During SMS	
	450	Salivary Cortisol During Spaceflight	Dr. N. Cintron
	453	Combined Blood Investigations	Drs. C. S. Leach et al.
	456	Medical Tests and Measurements (51D P/S)	Drs. W. E. Thornton et al.
	457	Salivary Pharmacokinetics of Scop-Dex	Drs. N. Cintron and L. Putcha
	458	Salivary Acetaminophen Pharmacokinetics	Drs. N. Cintron and L. Putcha
	464	Inflight Assessment of Renal Stone Risk Factor	Drs. N. Cintron
Cardiovascular Effects and Fluid Shifts	402	Cardiovascular Deconditioning Countermeasures	Drs. M. W. Bungo and P. C. Johnson
	407	Photographic Documentation of Body Fluid Shift	Dr. W. E. Thornton
	412	Treadmill Operation	Treadmill Operation
	415	Tissue Pressure Tonometry	Dr. W. E. Thornton
	423	Study of Inflight Fluid Changes	Drs. W. E. Thornton and C. S. Leach
	436#	Monitoring of Cardiovascular Deconditioning	Dr. M. W. Bungo
	441	Blood Pressure Monitoring During Re-entry	Drs. W. E. Thornton and T. P. Moore
	443#	Segmental Fluid Shift	Dr. J. S. Logan, et al.
	445	Thoracic Impedence Measurements	Drs. T. P. Moore and W. E. Thornton
	446	Leg Plethysmography	Drs. T. P. Moore and W. E. Thornton
	448@	Echocardiographic Evaluation of Deconditioning	Drs. M. W. Bungo and J. B. Charles
	452#	Leg Volume Changes	Drs. T. P. Moore and W. E. Thornton
	456	Medical Tests and Measurements (51D P/S)	Drs. W. E. Thornton, et al.
	460	Changes in Total Body Water During Spaceflight	Drs. C. S. Leach, D. L. Inners, et al.
	461	Leg Plethysmography	Drs. T. P. Moore and W. E. Thornton
	462	Estimation of Central Venous Pressure	Drs. M. W. Bungo and J. B. Charles
	463	Inflight Treadmill Stress Test	Drs. M. W. Bungo and J. B. Charles
	465	Pre and Postflight Echocardiography	Drs. M. W. Bungo and J. B. Charles
	466	Variations in Supine & Standing ... Heart Size ...	Drs. M. W. Bungo and J. B. Charles
Equipment Testing and Experiment Verification	411	Simple Mass Measurement	Dr. W. E. Thornton
	421	Animal Enclosure Module Inflight Test	Dr. M. C. Smith
	426#	Denitrogenation Procedures Evaluation	Dr. J. M. Waligora and D. J. Horrigan
	442	Autogenic Feedback Training (AFT)	Dr. P. S. Cowings
Microbiology	409	Microbial Screening	Dr. D. L. Pierson
	413	Cell Attachment in Microgravity	Dr. D. R. Morrison
	432	Carry-on Incubator/Cell Attachment in Micro-G	Drs. D. R. Morrison and A. Cogoli
	437	Microbial Monitoring	Dr. D. L. Pierson

MEDICAL DSOs LISTED BY DISCIPLINE (Continued)

DISCIPLINE	DSO	SHORT TITLE	INVESTIGATOR(S)
Space Motion Sickness and Space Adaptation Studies	401	Predictive Tests and Countermeasures for SMS	Dr. J. L. Homick
	403	Head and Eye Motion During Re-entry	Dr. W. E. Thornton
	404	On-Orbit Head and Eye Tracking Tasks	Dr. W. E. Thornton
	405	Acceleration Detection Sensitivity	Dr. W. E. Thornton
	406	Kinesthetic Ability	Dr. W. E. Thornton
	410	Audiometry	Dr. W. E. Thornton
	414	Ophthalmoscopy	Dr. E. L. Shulman
	416	Ambulatory Monitoring	Dr. W. E. Thornton
	417	Inflight Countermeasures for SAS	Dr. W. E. Thornton
	418	Eye-Hand Coordination	Dr. W. E. Thornton
	419!	Food Flavor Perception in Zero Gravity	R. L. Sauer
	420!	Taste Acuity In Zero Gravity	R. L. Sauer
	422	Anatomical Observation	Dr. W. E. Thornton
	424	Evoked Potentials	Dr. W. E. Thornton
	425	Intraocular Pressure	Dr. S. L. Pool
	427	Soft Contact Lens Application Test	Drs. W. E. Thornton and L. R. Young
	433	Pre- and Postflight Parallel Swing Tests	Drs. D. E. Parker and M. L. Reschke
	439	Documentation of the Action of Metoclopramide	Dr. W. E. Thornton
	447*	Causative Agents During SMS	Dr. W. E. Thornton
	449	Pre- and Postflight Parallel Swing Tests	Drs. D. E. Parker and M. L. Reschke
	451	Eye-Hand Coordination During SMS	Drs. W. E. Thornton and T. P. Moore
	454/455	Clinical Characterization of SMS	Drs. W. E. Thornton and J. Vanderploeg
	456	Medical Tests and Measurements (51D P/S)	Drs. W. E. Thornton et al
	459	Otolith Tilt-Translation Reinterpretation	Drs. M. L. Reschke and D. E. Parker
Vision	408	Near Vision Acuity & Contrast Sensitivity	Drs. A. Ginsberg and J. M. Vanderploeg
	440	Crew Visual Performance Testing	Lt. Col. L. V. Genco and Dr. H. L. Task

LEGEND:

* Was incorporated into DSO 453 and flown under that designation

\# Withdrawn

@ Resubmitted as a Form 100 Experiment; flown as American Flight Echocardiograph (AFE)

! Disapproved

MATRIX 5

CURRENTLY ACTIVE MEDICAL DSO Prepared 02-20-87 by SBRI Flight Projects/MAB Page 1 of 1

DSO	TITLE	PRINCIPAL INVESTIGATOR(S)	STATUS
437	Microbial Monitoring	Dr. D. L. Pierson	To be flown when animals are on board
450	Salivary Cortisol During Acute Phases of Spaceflight	Dr. N. Cintron	5 additional subjects are needed to reach the approved total.
455	Clinical Characterization of SMS	Drs. W. E. Thornton and J. Vanderploeg	Need additional subjects with SMS (minimum of 6 more)
457	Salivary Pharmacokinetics of Scop-Dex	Drs. N. Cintron and L. Putcha.	3 additional subjects are needed to reach the approved total.
458	Salivary Acetaminophen Pharmacokinetics	Drs. N. Cintron and L. Putcha	1 additional subject is needed to reach the approved total.
459	Otolith Tilt-Translation Reinterpretation	Drs. M. Reschke and D. E. Parker	6 additional subjects are needed to reach the approved total.
460	Changes in Total Body Water During Spaceflight	Drs. C. Leach-Huntoon, L. D. Inners, and J. B. Charles	2 additional subjects are needed to reach the approved total.
462	Noninvasive Estimation of Central Venous Pressure	Drs. M. W. Bungo and J. B. Charles	Initially approved only for STS-61C; additional subjects have been requested.
464	Inflight Assessment of Renal Stone Risk Factor	Dr. N. Cintron	Initially approved only for STS-61C; additional subjects have been requested.
465/466	Pre and Postflight Echocardiography	Drs. M. W. Bungo and J. B. Charles	DSO 465 was approved for STS-61C and later supplanted by DSO 466. 66 subjects on missions of various durations are needed.

MATRIX 6

STS FLIGHT HISTORY

Prepared by SBRI Flight Projects/MAB 2/26/87

FLIGHT NUMBER	VEHICLE	LAUNCH DATE	DURATION (DAYS)	LANDING SITE	CREWMEMBERS	PAYLOADS	MED DSOs	COMMENTS
STS-1	Columbia	4-12-81	2.25	EAFB	John W. Young Robert L. Crippen	DFI	401 402	First Orbital Flight Test (OFT) of the Space Shuttle System.
STS-2	Columbia	11-12-81	2.25	EAFB	Joe H. Engle Richard H. Truly	DFI OSTA-1 ACIP	401 402	Second OFT; first test of Remote Manipulator System (RMS); mission cut to 2 days by fuel cell failure.
STS-3	Columbia	3-22-82	8.00	EAFB	Jack Lousma C. Gordon Fullerton	DFI OSS-1 ACIP GAS EEVT MLR PDP	401 402	Third OFT; student experiments; test of hardware for electrophoresis operations (EEVT); landing site changed to Northrop Strip (White Sands, NM) due to water on lakebed at Edwards AFB; landing delayed one day due to weather at the alternate landing site.
STS-4	Columbia	6-27-82	7.04	EAFB	Thomas K. Mattingly Henry Hartsfield	DFI MLR CFES GAS IECM NOSL ACIP	401 402	Fourth OFT; included a DOD payload; first flight of Continuous Flow Electrophoresis System (CFES).
STS-5	Columbia	11-11-82	5.08	EAFB	Vance D. Brand Robert Overmyer William Lenoir Joseph Allen	TELESAT-E SBS-C	401-406 408 (7 DSOs)	First operational flight; first deployment of satellites.
STS-6	Challenger	4-04-83	5.00	EAFB	Paul J. Weitz Karol J. Bobko Donald H. Peterson F. Story Musgrave	TDRS-A CFES MLR NOSL GAS	401-406 407-410 (8 DSOs)	First flight of Challenger; first Shuttle EVA (Peterson, Musgrave); TDRS failed to reach geosynchronous orbit due to IUS guidance failure.

STS FLIGHT HISTORY (Continued)

FLIGHT NUMBER	VEHICLE	LAUNCH DATE	DURATION (DAYS)	LANDING SITE	CREWMEMBERS	PAYLOADS	MED DSOs	COMMENTS
STS-7	Challenger	6-18-83	6.08	EAFB	Robert L. Crippen Frederick H. Hauck Sally K. Ride John M. Fabian Norman E. Thagard	TELESAT PALAPA B-1 SPAS-01 OSTA-2 CFES	401-410 412-417 (16 DSOs)	Physician crewman (Thagard) to study SMS; use of RMS to deploy and retrieve the Shuttle Pallet Satellite (SPAS-1); scheduled landing at KSC waved-off due to bad weather (changed to EAFB).
STS-8	Challenger	8-30-83	6.04	EAFB	Richard H. Truly Daniel C. Brandenstein Guion S. Bluford Dale A. Gardner William E. Thornton	INSAT 1-B PFTA	401-412 414-418 421-425 427 432-433 441 (26 DSOs)	First Shuttle night launch & landing; physician crewman (Thornton) made use of DSOs to continue inflight study of SMS.
STS-9	Columbia	11-28-83	10.32	EAFB	John W. Young Brewster H. Shaw Robert A. Parker Owen K. Garriott Byron Lichtenberg Ulf Merbold	Spacelab 1	401-402 409	Two-shift, 24 hr/day operations; astronomy, physics, materials sciences, and biomedical research (neurovestibular, cardiovascular, hematological, immunological, & psychological adaptation to space flight); first non-US crewmember (Merbold-Germany).
STS 41-B	Challenger	2-03-84	7.97	KSC	Vance D. Brand Robert L. Gibson Bruce McCandless II Robert L. Stewart Ronald E. McNair	SPAS-01A PALAPA B-2 WESTAR-VI	401-402 408 433	First test of MMU, first KSC landing; both satellites failed to reach geosynchronous orbit due to PAM failures.
STS 41-C	Challenger	4-06-84	6.99	EAFB	Robert L. Crippen Francis R. Scobee Terry J. Hart James D. van Hoften George D. Nelson	LDEF-1	401-402 408	Rendezvous, repair, and redeploy of Solar Max satellite; student experiment (bees); highest STS altitude to date (269 nautical miles).
STS 41-D	Discovery	8-30-84	6.04	EAFB	Henry W. Hartsfield Michael L. Coats Richard M. Mullane Stephen A. Hawley Judith A. Resnik Charles D. Walker	OAST-1 SBS-D TELSTAR 3C SYNCOM IV-1 CFES	401-402 408 439-441 (6 DSOs)	Evaluation of the deployable solar array (OAST-1); first "frisbee" type satellite deployment (SYNCOM); first commercial payload specialist (Charles Walker).

STS FLIGHT HISTORY (Continued)

FLIGHT NUMBER	VEHICLE	LAUNCH DATE	DURATION (DAYS)	LANDING SITE	CREWMEMBERS	PAYLOADS	MED DSOs	COMMENTS
STS 41-G	Challenger	10-05-84	8.23	KSC	Robert L. Crippen Jon A. McBride David D. Leestma Sally K. Ride Kathryn D. Sullivan Paul D. Scully-Power Marc Garneau	OSTA-3 LFC/ORS ERBS IMAX GAS (8)	401 408 439-441 450 (6 DSOs)	First American woman to perform an EVA (Sullivan); first seven person crew; first American orbital fuel transfer; first Canadian crewman (Garneau).
STS 51-A	Discovery	11-08-84	7.99	KSC	Frederick H. Hauck David M. Walker Dale A. Gardner Joseph P. Allen Anna L. Fisher	MSL-1 SYNCOM IV-2 TELESAT	401	2 EVAs for retrieval of PALAPA-B-2 and WESTAR VI satellites from STS-11
STS 51-C	Discovery	1-24-85	3.06	KSC	Thomas K. Mattingly Loren J. Shriver Ellison S. Onizuka James F. Buchli Gary E. Payton	DOD	401 408 (6 DSOs)	First dedicated DOD mission; test of hardware for SL-3 Autogenic Feedback Experiment (DSO 442).
STS 51-D	Discovery	4-12-85	7.00	KSC	Karol J. Bobko Donald E. Williams M. Rhea Seddon Jeffrey A. Hoffman S. David Griggs Charles D. Walker E. J. "Jake" Garn	SYNCOM IV-3 TELESAT-I CFES	401 456	SYNCOM failed to activate after deployment; unscheduled EVA to attach "fly swatters" to RMS for attempt to trip the activation switch; American Flight Echocardiograph (AFE) provided first American heart images inflight; U.S. Senator as payload specialist.
STS 51-B	Challenger	4-29-85	6.96	EAFB	Robert F. Overmyer Frederick D. Gregory Don L. Lind Normal E. Thagard William E. Thornton Lodewijk van den Berg Taylor G. Wang	Spacelab 3 NUSAT GLOMR	437 451 439 453 441 462 (6 DSOs)	Crystal growth and materials science experiments; Auroral photography; test of Research Animal Holding Facility (failure caused contamination); test of Autogenic Feedback Training for effectiveness in combatting SMS.

STS FLIGHT HISTORY (Continued)

FLIGHT NUMBER	VEHICLE	LAUNCH DATE	DURATION (DAYS)	LANDING SITE	CREWMEMBERS	PAYLOADS	MED DSOs	COMMENTS
STS 51-G	Discovery	6-17-85	7.07	EAFB	Daniel C. Brandenstein John O. Creighton Shannon W. Lucid John M. Fabian Steven R. Nagel Patrick Baudry Sultan S. A. Al-Saud	ARABSAT-A TELSTAR-3D SPARTAN 101/MPESS MORELOS-A	455	The French Echocardiograph Experiment (FEE) and French Posture Experiment (FPE) provided data on physiological adaptation to Space Flight.
STS 51-F	Challenger	7-29-85	7.95	EAFB	C. Gordon Fullerton Roy D. Bridges F. Story Musgrave Anthony W. England Karl G. Henize Loren W. Acton John-David Bartoe	Spacelab-2	441 453	Around-the-clock astronomy studies, including extensive solar observation; blood collection for bitamin D metabolites; plant growth.
STS 51-I	Discovery	8-27-85	7.10	EAFB	Joe H. Engle Richard O. Covey James Van Hoften John M. Lounge William F. Fisher	SYNCOM IV-4 ASC-1 AUSSAT-1 MSL-2 CFES	455 458	Rendezvous with failed SYNCOM from mission 51-D; EVA for capture and repair; redeploy.
STS 51-J	Atlantis	10-03-85	4.07	EAFB	Karol J. Bobko Ronald J. Grabe Robert C. Stewart David C. Hilmers William A. Pailes	DOD	451 461	Second dedicated DOD mission; first flight of Atlantis.
STS 61-A	Challenger	10-30-85	7.00	EAFB	Henry W. Hartsfield Steven R. Nagel Bonnie J. Dunbar Guion S. Bluford James F. Buckli Reinhard Furrer Wubbo Ockels Ernst Messerschmid	Spacelab D-1 GLOMR	---	First 8 person crew; first foreign dedicated Spacelab (West Germany); life sciences experiments (neurovestibular, cardiovascular, immunological) and materials sciences.

STS FLIGHT HISTORY (Continued)

FLIGHT NUMBER	VEHICLE	LAUNCH DATE	DURATION (DAYS)	LANDING SITE	CREWMEMBERS	PAYLOADS	MED DSOs	COMMENTS
STS 61-B	Atlantis	11-26-85	6.87	EAFB	Brewster H. Shaw Bryan D. O'Connor Mary L. Cleave Sherwood C. Spring Jerry L. Ross Charles D. Walker Rodolfo Neri	MORELOS-B SATCOM Ku-2 AUSSAT-1 EASE/ACCESS CFES IMAX	455 457 458 461	2 EVAs for assembly of EASE and ACCESS truss structures to evaluate Space Station construction techniques.
SIS 61-C	Columbia	1-12-86	5.09	EAFB	Robert L. Gibson Charles F. Bolden Franklin Chang-Diaz George D. Nelson Steven A. Hawley Bill Nelson Robert J. Cenker	SATCOM Ku-1 MSL-2 GAS Bridge	451 455 457-465 (11 DSOs)	U.S. Congressman payload specialist performed 10 biomedical DSOs; landing at KSC delayed two days and waved-off due to weather.
STS 51-L	Challenger	1-28-86	---	---	Francis R. Scobee Michael J. Smith Judith A. Resnik Ellison S. Onizuka Ronald E. McNair Gregory Jarvis Sharon C. McAuliffe	TDRS-B SPARTAN- Halley	450 455 459	Explosion claims crew and orbiter at 73 seconds into the flight.

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15. Supplementary Notes

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16. Abstract

Results are presented for a number of life sciences investigations sponsored by the Space Biomedical Research Institute at the NASA Lyndon B. Johnson Space Center and conducted as Detailed Supplementary Objectives (DSOs) on Space Shuttle flights between 1981 and 1986. An introduction and a description of the DSO program are followed by summary reports on the investigations. Reports are grouped into the following disciplines: Biochemistry and Pharmacology, Cardiovascular Effects and Fluid Shifts, Equipment Testing and Experiment Verification, Microbiology, Space Motion Sickness, and Vision. In the appendix, the status of every medical/life science DSO is presented in graphical form, which enables the flight history, the number of subjects tested, and the experiment results to be reviewed at a glance.

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