Clinical Characterization and Etiology of Space Motion Sickness

WILLIAM E. THORNTON, M.D., THOMAS P. MOORE, M.D., SAM L. POOL, M.D., and JAMES VANDERPLOEG, M.D.

Astronaut Office, NASA/Johnson Space Center, Houston, Texas; Methodist Hospital of Indiana, Inc., Department of Medical Research, Indianapolis, Indiana; and Medical Sciences Division, NASA/Johnson Space Center, Houston, Texas

THORNTON WE, MOORE TP, POOL SL, VANDERPLOEG J. *Clinical characterization and etiology of space motion sickness.* Aviat. Space Environ. Med. 1987; 58(9, Suppl.):A1–8.

An inflight, clinically-oriented investigation of SMS was begun on STS-4 and revealed the following: compared to motion sickness on Earth, autonomic signs are significantly different in space motion sickness (SMS) vs. motion sickness (MS) in that sweating is not present, pallor or flushing may be present, and vomiting is episodic, sudden, and brief. Nausea may be present but is more often absent. Onset ranges from minutes to hours, plateaus, and rapidly resolves in 8–72 h with 36 h as average. Postflight reactions have been mild unless deliberately provoked in the early period of re-exposure to gravity. Postflight there is a period of resistance to all forms of motion sickness. There is some evidence for individual reduction in sensitivity on repeated flights. Etiology could not be proven objectively; however, the sensitivity to angular motion, often pronounced in pitch, and theoretical considerations make an intravestibular conflict the most likely cause. Electro-oculogram (EOG), audio-evoked potentials, measurement of fluid shifts, and other studies are inconsistent with a transient vestibular hydrops or increased intracranial pressure as a cause.

WHENEVER MAN is placed in environments of motion to which he is unaccustomed, either real or simulated, a sizable 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 (23). Dr. Graybiel's work in the U.S. Navy is an archetype of such research (6–9). Development of a numerical scoring system of signs and symptoms (12) and means with which to rapidly induce motion sickness allowed research to become almost stylized. Such a scoring system is possible 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 (23). In addition to the above symptoms, Graybiel proposed a 'sopite' syndrome (10). This may be intertwined with motion sickness, occur under prolonged mild stimuli, or as a variant of motion sickness under strong stimuli. Features of this syndrome include yawning, drowsiness, disinclination for physical or mental work, and lack of participation in group activities.

After varying amounts of exposure, the majority of subjects develop resistance to the specific stimuli to motion sickness. Medication, habituation, and training may be effective in prevention or treatment to varying degrees (23).

Prior to spaceflight 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 (19). 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 reports, it was not unreasonable to consider these symptoms as motion sickness and treat them accordingly. By the end of the Skylab Program, 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 exposure to weightlessness, individuals became remarkably resistant to Coriolis stimulation, a unique non-specific adaptation (11). After the third flight, it was obvious that the Shuttle Program also would have to contend with this problem (13,14). Repeated at-

Address reprint requests to: William E. Thornton, M.D., who is currently a NASA Scientist-Astronaut, Dept. CB, NASA/Johnson Space Center, Houston, TX 77058.

tempts to document signs and symptoms during early Shuttle missions by means of questionnaires and debriefings left much to be desired.

Operational Inflight Investigation: Prior to STS-4, individuals in the JSC Astronaut Office and in Flight Medicine felt that objective inflight investigation of the problem with major emphasis on operational concerns was necessary, especially since accumulating anecdotal information described further 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, with astronaut physicians on the last two. Some studies of this series have been continued to the present under the control of JSC's Space Biomedical Research Institute (SBRI). This investigation used accepted, objective clinical procedures where possible and had the major goals of: (1) clinical characterization, (2) investigation of etiology, and (3) investigation of possible treatment.

A listing of studies is given in Table I. Regular and repeated, pre-, in- and postflight examinations of 10 crewmembers, 4 of whom had SMS, were made by two physicians who had been flown for the study of SMS on two flights. Close observation of seven additional subjects, four with SMS, were also made on ground and inflight by the same physicians on a second flight. Specific postflight debriefings were conducted by the author on a total of 32 subjects, 16 of whom had SMS, and who had participated in some phase of this study. In addition, informal discussions were held on the subject by the author with every person flying on Shuttle except some crewmembers of SL-1 and D-1 missions.

Symptoms

Motion Sensitivity: There is an amazingly wide and variable range of symptoms in SMS. Typically, the first indication is hypersensitivity to angular head motion, either head alone, or from combined head and body motion. In many subjects this sensitivity is predominantly in the pitch plane, in others it is in yaw, but in every case it is also present in all other angular axes. This hypersensitivity may become noticeable from zero to 1 to 2 h after exposure. It can be described as a thoroughly unpleasant sensation involving the head, not to be repeated if possible. It does not produce visual disturbance or illusion, nor does it obviously produce stomach symptoms as, for example, does out-of-plane head motion in a spinning chair. If anything, it is increased with eyes closed. The sensation strength appears to increase with increased velocity or possibly acceleration of movement. Voluntary translation, even reciprocating translation, does not produce these symptoms. This hypersensitivity typically increases to a plateau in several hours and remains at that level until resolution when it rapidly diminishes. One simply wants a quiet immobile spot during this period of altered sensitivity.

TABLE I. LISTING OF INFLIGHT SMS STUDIES.

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

* Astronaut Office and Flight Medicine Inflight Investigation
** Study continued under SBRI

Illusions, Visual Disturbance, Orientation: Illusion of both position and motion was reported as a major symptom in the Russian Program (17) and in some of the Apollo experiences (3). With the exception of SL-1 and D-1 crews, the principal author has questioned all Shuttle astronauts postflight and has been unable to elicit any experience of either visual disturbance or illusion on launch or orbit except in one pilot who 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 to insure that illusions and vertigo were explained and understood.

Some workers have suggested that an "egocentric" orientation, a strong reference to one's own axis, the ability to place the Earth above one's head rather than being inverted above the Earth, would alleviate symptoms. It was possible to do this easily, but it did not prevent SMS. Another well-known inflight phenomena is the 'automatic' alignment of external surroundings with one's own reference; e.g., one may elect to work feet to "ceiling" and after a brief period, usually seconds, the ceiling becomes "down" and the floor "up" with no sense of discomfort to the individual. If one then returns to the floor, the scene will initially appear inverted, but after a brief time, "snap" into normal alignment. This holds true for any position and all crewmen questioned. It does not appear to play a role in 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 the majority. Another common illusion unrelated to SMS 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 (18).

Gastrointestinal Symptoms: These signs and symptoms may also appear from minutes[a] to several hours after weightlessness and often consist of a very brief bout of unproductive retching but usually of sudden vomiting without nausea or other prodrome. The vomiting is strenuous, brief, and appears to empty the stomach of whatever contents are present, undigested; rarely, the contents are bile-stained.

[a] There have been several reported episodes of vomiting, often repeated, within a few minutes of orbital insertion. The first author observed one such case and although sweating and pallor were absent, he suspected it was evoked by the launch-insertion environment; i.e., ordinary MS. These subjects all had continuing symptoms of SMS.

Subjective relief is common afterward. In the absence of eating or drinking, these events, which produce clear vomitus, may be repeated from one to several times, usually with hours between events. Vomiting is not prolonged, there are no dry heaves, nor frequent bouts. Typically all significant amounts of ingested food or drink will be lost, usually within 30 min to 1 h or more. The majority of subjects deny nausea, but, in some, this is a major symptom or may be a presenting symptom. This nausea may wax or wane, but in the first author's experience it is not related to other activity, although some motions and situations will be avoided. Loss of appetite is almost universal. A variety of non-specific epigastric symptoms have been reported, the most common being a "knot in the stomach." This may occur in individuals with and without SMS, usually early inflight. Lower bowel functions, as judged by flatus and defecation, seem normal.

There have been attempts to link the vomiting to either visual or motion inputs. Such inputs may trigger an impending event, but ingestion of food seems to be the only certain way to induce it.

Sweating and Pallor: There is virtually no incidence of sweating, and flushing is more common than pallor. The absence of sweating cannot be attributed to the "cool, dry environment of Spacelab" (32), since it is the same environment as most test labs on Earth.

Other Symptoms: Malaise, lack of initiative, and irritability are near universal during this time. Headache is common, usually mild, non-specific and with various locations in different individuals. Malaise typically increases during the first few hours and then plateaus. Somnolence is very common and may cause brief periods of sleep given the slightest opportunity. This is frequently a symptom which develops early and persists until resolution. It may be complicated by lack of usual sleep.

Effects of Activities: Anecdotes abound in this area so only the most consistent are offered. Demanding activities such as the Commander's duties, responsibility for satellite launch or RMS (remote manipulator system) operations appear to reduce the perceived discomfort, if not the actual level of SMS. Another common report is that excessive movement early on orbit may precipitate or increase the symptoms. In any event, cessation of activity, even sleeping, may decrease the discomfort, but does not cure the problem.

Incidence

Two interrelated questions are the incidence of SMS and the overlap of symptoms in those affected vs. those unaffected. The presence of symptoms from other causes must also be considered. Incidence depends upon the observer's criteria and has been placed by some investigators at 50% or more. Statistics from informal questioning of the astronauts show approximately 40%. To this date there has been no comprehensive objective study of incidence.

The obvious difference between those with and those without SMS is impressive. While there are variations in severity with some mildly affected, there is a distinct clustering of well vs. sick subjects. In some cases without frank SMS, some features of the sopite syndrome are present. There is also ample stimulus available for ordinary motion sickness, e.g., vertical launch and visually inverted flight with up to 3.5 G and −0.6 Gz terminating in weightlessness, plus a host of other new sensations. Consequently, diagnosis of SMS must be made with some care.

Objective Studies

Because of the unique relation between eye motion and the greater vestibular system (1,16,20), electro-oculography (EOG) was the most intensively studied of all investigations (Fig. 1) (25). Horizontal and vertical EOG were recorded during launch on one flight and during entry on two flights with three subjects. Horizontal EOG and head motion were monitored during three ascents and entries with a total of four subjects.

Conventional calibration, electrode configurations and equipment standards were employed (2,30). Standardized voluntary head oscillations with eyes open and fixed on a target, and with vision, occluded by opaque, tightly fitted goggles were made before, during, and after ascent and entry. Continuous recordings were made during launch and entry (Fig. 2). No abnormalities were seen, not even brief nystagmus.

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

Again conventional standards were adhered to, although the equipment had to be designed to fit the situation. Some 41 records were made on orbit, 7 during SMS, with 57 preflight and 19 postflight controls. This series can be summarized succinctly as "clinically normal" (25). Two isolated records contained distortion during the head oscillation which seemed most likely to be artifactual.

Another major effort was documentation of autonomic

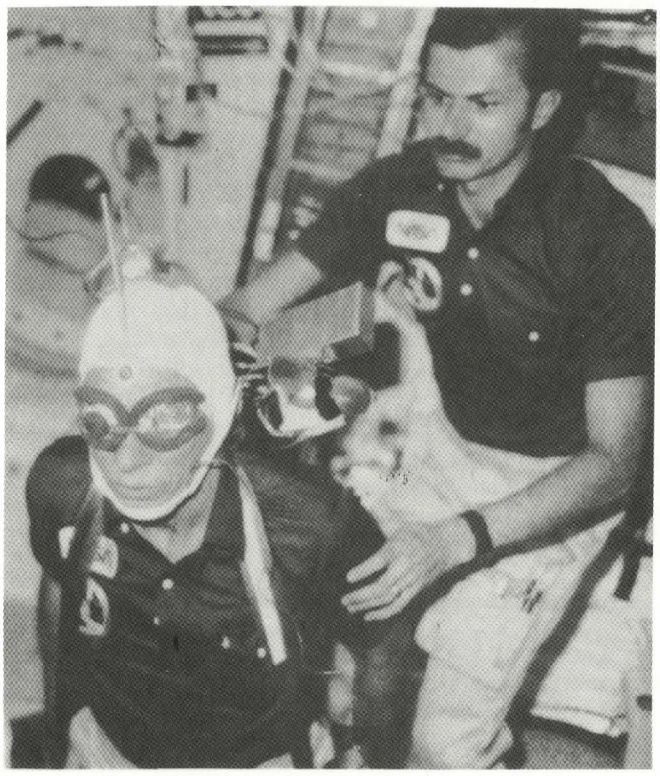

Fig. 1. Author during EOG study with sinusoidal rotation on STS-8. A two-axis gyroscope is mounted on the head.

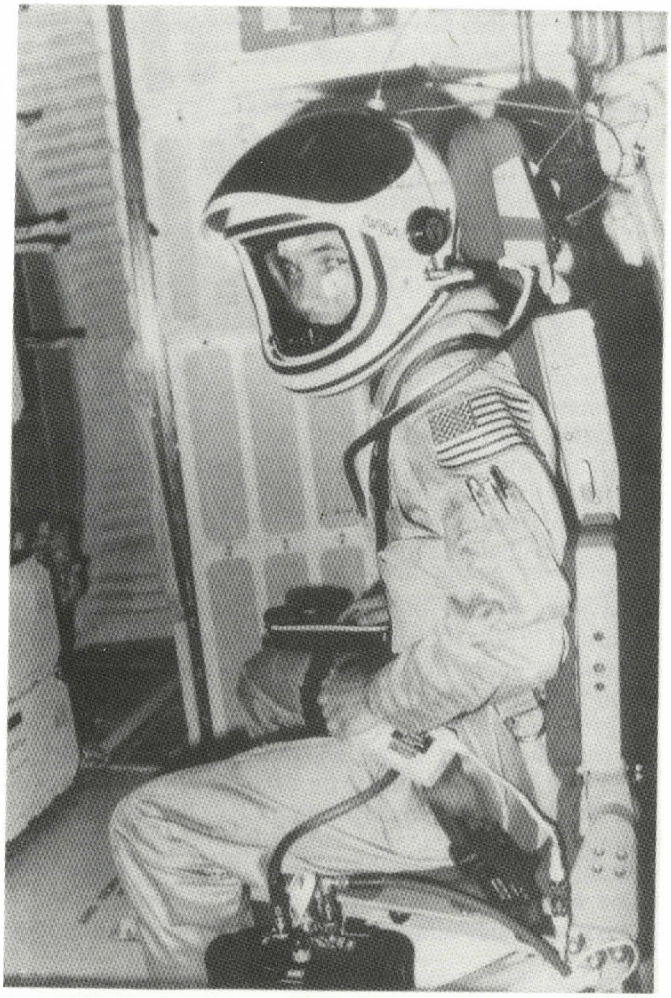

Fig. 2. Crewman instrumented for EOG and recording of head position prior to launch. Data was recorded or transmitted continuously during launch and entry.

TABLE II. ON-ORBIT EOG PROTOCOL AND NUMBER OF PARTICIPATING SUBJECTS.

Procedure	Total subjects	(Subjects with SMS)
Gaze, Eyes open and closed, Horizontal 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)

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 we do not have an adequate statistical sample to date, however, attempts continue. Objective studies of pupillary size are made by macrophotography under light controlled and measured conditions. Pallor-flushing studies are also done by photography with color control. They are analyzed by chromatic microdensitometry. This work and analysis is in progress. As noted, depending upon the individual, observation shows pallor or flushing with apparently normal pupillary size. Ambulatory heart rate and blood pressure recording from one subject showed them to become remarkably low as the symptoms plateaued the first day (29). Ambulatory heart rate from a subject during recovery from SMS showed a significant increase in basal heart rate.

Gastrointestinal motility studies, while difficult, have been most valuable. Dr. Thagard observed, as part of our studies on STS-7, that bowel sounds were absent during the course of SMS and this finding has been subsequently confirmed by auscultation in every case observed[b], and in all those studied objectively (27).

Objective studies consist of recording sounds from right and left upper quadrant preflight and during and after SMS in parallel with unaffected controls. The records are semi-quantitatively scored by counting the rate of audible events by standard criteria. Weightlessness does not greatly alter the rate or quality of bowel sounds in those unaffected although some individuals may be hyperactive the first day on orbit. Conversely, SMS greatly depresses or even virtually eliminates sounds during the course of the syndrome. There is some evidence for rebound activity for the first hours after recovery followed by normal activity. To date, this phenomenon is the only symptom which bears a constant relation to the presence of this syndrome.

Performance During SMS: This, as always, is the most difficult evaluation to make. Even under normal circumstances, tests of performance are, at best, difficult to use as objective criteria.

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. There have been two precautionary delays of scheduled EVA's. It isn't necessarily easy, nor do people affected seek extra duties during the period; i.e., there is a lack of initiative, but tasks trained for and scheduled are done and done well. Many of these require concentration as well as good neuromuscular and eye-hand coordination. Individuals with less-extensive preflight training have occasionally been 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 from it with visual clues, and manual tracking of a visual target on a linear scale which moved in a series of regular and aperiodic functions. A second study uses the relatively common Sternberg complex reaction time test. This consists 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 cases we have been able to examine to date.

Temporal Profile of Symptoms: As noted, with an exception that will be treated later, onset of symptoms (e.g., usually, awareness of motion sensitivity by occasionally

[b] Since writing this, at least one cause of hyperactive sounds during SMS with nausea and vomiting has been seen. It is possible that this hyperactivity was antiperistaltic duodenal activity which has been seen with nausea.

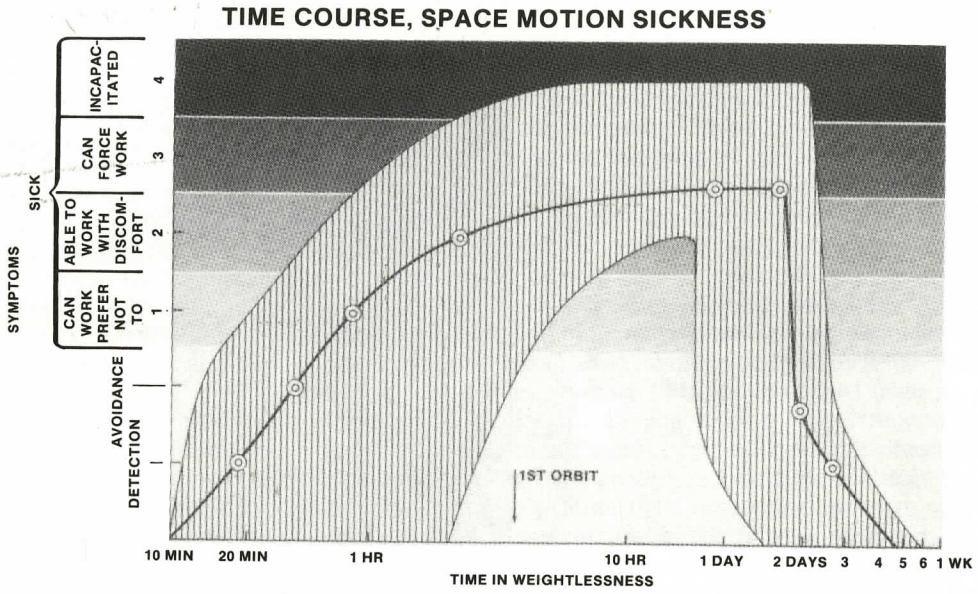

Fig. 3. Time course of symptoms of SMS. The range of symptoms that have been recorded on Shuttle crewmembers is shown in the shaded area. Note that the time scale is logarithmic.

vomiting) occurs within minutes to 1–2 h of exposure to weightlessness (Fig. 3). This progresses in intensity over a period of hours to a plateau, which, for a given condition remains stable. There are typically both head (motion sensitivity, malaise, somnolence, lethargy, etc.) and gut (anorexia, vomiting, nausea) symptoms, although one or the other may predominate. In some subjects, the gut symptoms may be the only ones recognized, but in every case the gut remains quiet. Episodes of vomiting are often more frequent at the beginning, but are usually separated by 1–3 h or more. In some cases, after one or two episodes, it may not recur in the absence of intake.

The resolution of symptoms is typically sudden and dramatic and most frequently occurs between 30 to 48 h, but has been as short as 12 h, and possibly as long as 72 h. During and after resolution there is a marked change in attitude, loss of malaise, return of stomach activity and usually appetite, and marked decrease in motion sensitivity. This typically occurs in a matter of hours or less. There may be some residual motion sensitivity which decreases to normal over the next 2 to 3 d. With determined effort this sensitivity can be aggravated (32), but is not a problem with normal movement. Anorexia may remain also, but hunger is more common. At this time or in the days immediately following, resistance to all forms of motion sickness develops. This includes 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 four crewmen who had significantly delayed onset of symptoms, one for 48+ h. One such crewman was observed by the first author, and he was very active and symptom-free for the first 2 d, yet developed a moderate case of SMS which persisted for 24+ h. All four had medication with scopalamine/dexedrine and all experienced onset of symptoms after discontinuation of the medication. This is the most convincing evidence seen for efficacy of any drug, but it represents only a small number of subjects having taken this medication. It seems significant that symptoms were not prevented, only delayed.

Reentry and Postflight: In the American Shuttle Program, there has been no recurrence of symptoms after landing, although this is reported to be common in the Russian Program (17). During reentry and for hours thereafter head turns may provoke a sense of disequilibrium in some subjects, including those not affected by SMS, but never with the sense of unpleasantness experienced by those with SMS inflight (Fig. 4). One subject without SMS claims to have developed motion sickness on reentry while doing vigorous head motions as part of an investigation. A few subjects have noted an illusion of translation on head turns after reexposure for some hours after return to 1 G and this is under investigation by other workers (22). Such phenomena could not be elicited inflight from any subject including one excellent observer 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 with minimum tactile stimulation.

While several changes in sensation are transiently present postflight, none can in any way be characterized as sickness. Most striking of these postflight changes is resistance to all forms of motion sickness[c] or even disequilibrium. This has not been properly studied. There have been anecdotes of such increased postflight resistance to unpleasant motion sensations and motion sickness, especially in aircraft, including crewmen who did not experience space motion sickness. In the first author's experience, at 19 d after his first flight, repetitions of every maneuver possible in the T-38 aircraft elicited nothing. Two astronauts 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 weeks but is one of many questions which need quantitative answers.

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 violent repetitive maneuvers in the

[c] One exception to this was the sea sickness which developed in one Skylab crewman during the recovery period. However, this was consistent with my experience immediately postflight on the Coriolis chair. This crewman was also resistant to effects of the Coriolis chair by the time of testing postflight.

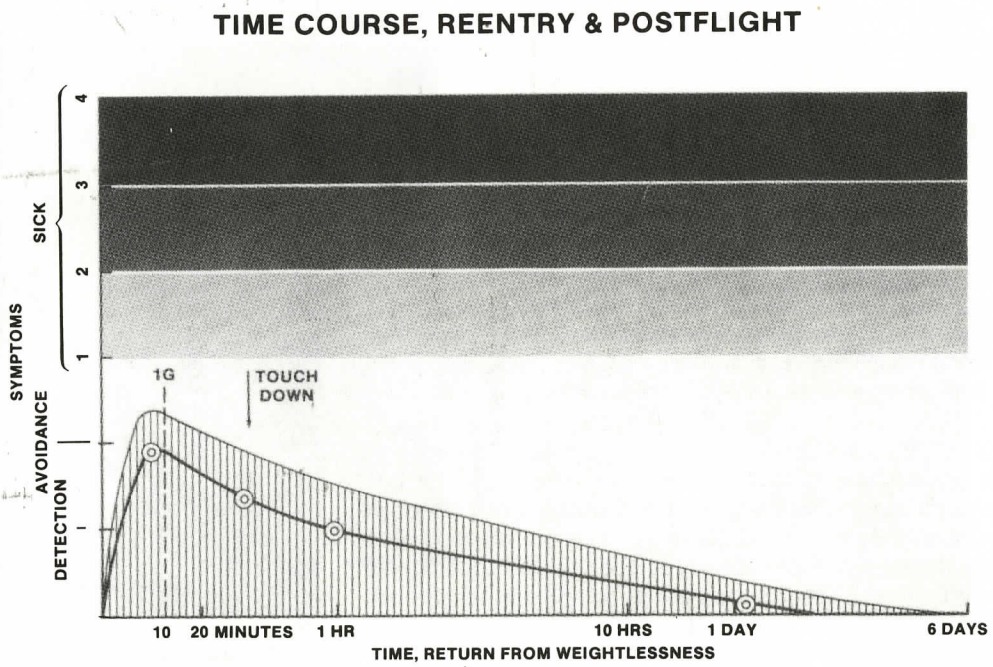

Fig. 4. Time course of symptoms during neurological readaptation upon return to Earth.

T-38 and in some cases prolonged sessions in the spinning chair. Some of the subjects most resistant to motion sickness from 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 in reflown individuals. 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 is wide individual variation with some showing relatively small change in sensitivity even with flights as recent as 7 months, while another was symptom free on his second flight after a delay of 2+ years. In some there is no reduction in symptoms but a reduction in duration, while in others there is 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 in our experience, has there been redevelopment of symptoms once resolved.

Etiology

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

We have also seen significant differences between SMS symptoms and those of classic motion sickness. There are other factors to consider in SMS such as the large and rapid cephalad fluid shifts on exposure to weightlessness (21,26,28). Taking 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 this inflight investigation was started and without

TABLE III. POSSIBLE ETIOLOGIES OF SMS.

Disordered Function	Anomalous Signals
Vestibular Hydrops	Visual
Increased Intracranial Pressure	Vestibular
Cervical Vertigo	Semicircular Canals
	Statolith Organs
	Somatosensory
	Visceral

the previously described data and experience, the following possible causes had to be considered and investigated (Table III). They were based on clinical experience and a word of explanation may be in order for each.

Vestibular hydrops, or in this case pseudo Meniere's disease, could result from a sudden shift of labyrinthine fluid pressure or composition (31). In the same way changes in intracranial pressure or fluid composition were also possible. It was known that in weightlessness with the absence of hydrostatic pressures, several liters of fluid are shifted from legs alone and that part of it was retained as edema in facial tissue and in mucous membranes (26). 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 (24,26). There is also a change in the carrying angle of the head in weightlessness (26). These two factors could conceivably produce distortion in cervical sensors and their 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 somatosensory signals will 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.

An investigational program was designed to study as many potential etiologies as possible with minimum resources. For example, EOG provided information on several of the above categories. Because of its nature, determination of etiology was not possible with techniques currently available to us, rather it was feasible to reasonably exclude most of the possibilities 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.

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 audioevoked potentials between those affected and unaffected (13), and there was no significant difference in volume of fluid shifted from legs in those with and without SMS (21).

Increased CNS Pressure: Illusions and other neurological disturbances were denied; clinical neurological exam was normal; no changes in fundus were noted; 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 in fluid volume shifted from legs in those with and without SMS (21) was found.

Cervical Vertigo: Illusions and other neurological disturbances were denied; clinical neurological exam was normal; EOG was normal; no difference in height increases in those with and without SMS were found; and cervical loading was without effect in one subject.

In summary, there was no positive evidence for altered sensory or CNS function. When the potential role of various sensory inputs is examined there is less hard evidence, and subjective symptoms are open to many interpretations.

Visual Disturbances: Visual disturbances were denied; visual acuity and extraocular motion were normal, as were reflexes to light and accommodation. Visual tracking function for saccadic, pursuit, and nystagmoid motion was normal, as was optokinetic nystagmus; i.e., the purely visual inputs were normal by routine test procedures. Absence of oscillopsia, or pathological nystagmus, and 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 small, individual changes in VOR gain, as determined from eyes-occluded head oscillation, the differences appear random in time and between subjects. Overall, there appears to be no change in VOR gain. The strongest evidence for the role of vestibular inputs is the overwhelming conscious sensations that occur with angular motions. In many, the pitch plane is most sensitive, while in others it is yaw; but in any event it is a potent, albeit poorly characterized, sensation. There is no such obvious argument for the static components (defined here as the mean operating point without acceleration) of the otolith organ signals except by allowing *a priori* that this is a cause of SMS. If this is allowed, then one can argue that the static component must be affected, for there are several documented examples of individuals' vomiting on orbit before appreciable body or head motion occurred. Also severely restricting movement may cause some improvement in feeling, but it does not cure SMS, as evidenced from gastrointestinal studies. Restricting motion only temporarily reduces the unpleasant sensations and has 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 study of this system was 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: We had no way to study this, and, other than the gastric symptoms noted, visceral sensation did not reach consciousness.

In summary, we have 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 do not appear to be 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 not obvious.

There are known pathways through nuclei connecting the end organs to the one area which is consistently affected by SMS, the upper gastrointestinal tract (24,28). It may be significant that the vestibular nuclei, the nuclei which control the digestive tract, the CTZ, and the emesis center are in very close proximity around and under the 4th ventricle.

Summary

In general, our current problem is an ignorance of basic mechanisms. Though we speak of "conflicts," in fact, we don't know the different pathways or the nature of the signals which cause our problems—the ileus of the upper gastrointestinal tract or the head symptoms. There are two basic possibilities: neurological transmission and/or humoral transmission. The question of cerebral spinal fluid as a pathway has been raised by one set of experiments, and this certainly deserves consideration.

It may be a decade or more before we cure or prevent

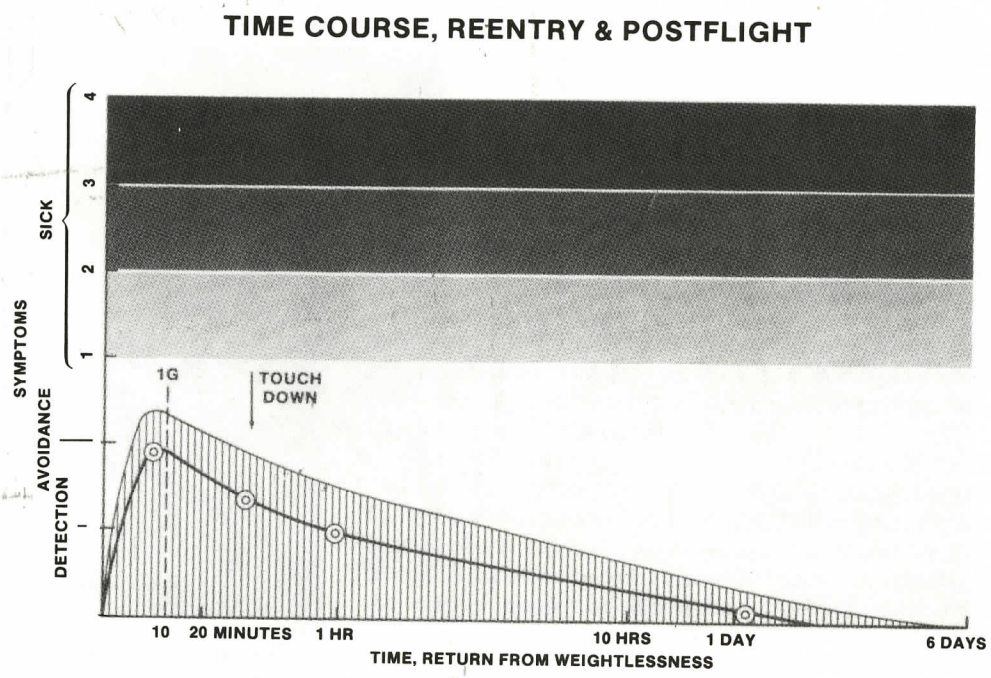

Fig. 4. Time course of symptoms during neurological readaptation upon return to Earth.

T-38 and in some cases prolonged sessions in the spinning chair. Some of the subjects most resistant to motion sickness from 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 in reflown individuals. 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 is wide individual variation with some showing relatively small change in sensitivity even with flights as recent as 7 months, while another was symptom free on his second flight after a delay of 2+ years. In some there is no reduction in symptoms but a reduction in duration, while in others there is 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 in our experience, has there been redevelopment of symptoms once resolved.

Etiology

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

We have also seen significant differences between SMS symptoms and those of classic motion sickness. There are other factors to consider in SMS such as the large and rapid cephalad fluid shifts on exposure to weightlessness (21,26,28). Taking 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 this inflight investigation was started and without the previously described data and experience, the following possible causes had to be considered and investigated (Table III). They were based on clinical experience and a word of explanation may be in order for each.

TABLE III. POSSIBLE ETIOLOGIES OF SMS.

Disordered Function	Anomalous Signals
Vestibular Hydrops	Visual
Increased Intracranial Pressure	Vestibular
Cervical Vertigo	Semicircular Canals
	Statolith Organs
	Somatosensory
	Visceral

Vestibular hydrops, or in this case pseudo Meniere's disease, could result from a sudden shift of labyrinthine fluid pressure or composition (31). In the same way changes in intracranial pressure or fluid composition were also possible. It was known that in weightlessness with the absence of hydrostatic pressures, several liters of fluid are shifted from legs alone and that part of it was retained as edema in facial tissue and in mucous membranes (26). 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 (24,26). There is also a change in the carrying angle of the head in weightlessness (26). These two factors could conceivably produce distortion in cervical sensors and their 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 somatosensory signals will 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.

An investigational program was designed to study as many potential etiologies as possible with minimum resources. For example, EOG provided information on several of the above categories. Because of its nature, determination of etiology was not possible with techniques currently available to us, rather it was feasible to reasonably exclude most of the possibilities 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.

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 audioevoked potentials between those affected and unaffected (13), and there was no significant difference in volume of fluid shifted from legs in those with and without SMS (21).

Increased CNS Pressure: Illusions and other neurological disturbances were denied; clinical neurological exam was normal; no changes in fundus were noted; 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 in fluid volume shifted from legs in those with and without SMS (21) was found.

Cervical Vertigo: Illusions and other neurological disturbances were denied; clinical neurological exam was normal; EOG was normal; no difference in height increases in those with and without SMS were found; and cervical loading was without effect in one subject.

In summary, there was no positive evidence for altered sensory or CNS function. When the potential role of various sensory inputs is examined there is less hard evidence, and subjective symptoms are open to many interpretations.

Visual Disturbances: Visual disturbances were denied; visual acuity and extraocular motion were normal, as were reflexes to light and accommodation. Visual tracking function for saccadic, pursuit, and nystagmoid motion was normal, as was optokinetic nystagmus; i.e., the purely visual inputs were normal by routine test procedures. Absence of oscillopsia, or pathological nystagmus, and 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 small, individual changes in VOR gain, as determined from eyes-occluded head oscillation, the differences appear random in time and between subjects. Overall, there appears to be no change in VOR gain. The strongest evidence for the role of vestibular inputs is the overwhelming conscious sensations that occur with angular motions. In many, the pitch plane is most sensitive, while in others it is yaw; but in any event it is a potent, albeit poorly characterized, sensation. There is no such obvious argument for the static components (defined here as the mean operating point without acceleration) of the otolith organ signals except by allowing *a priori* that this is a cause of SMS. If this is allowed, then one can argue that the static component must be affected, for there are several documented examples of individuals' vomiting on orbit before appreciable body or head motion occurred. Also severely restricting movement may cause some improvement in feeling, but it does not cure SMS, as evidenced from gastrointestinal studies. Restricting motion only temporarily reduces the unpleasant sensations and has 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 study of this system was 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: We had no way to study this, and, other than the gastric symptoms noted, visceral sensation did not reach consciousness.

In summary, we have 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 do not appear to be 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 not obvious.

There are known pathways through nuclei connecting the end organs to the one area which is consistently affected by SMS, the upper gastrointestinal tract (24,28). It may be significant that the vestibular nuclei, the nuclei which control the digestive tract, the CTZ, and the emesis center are in very close proximity around and under the 4th ventricle.

Summary

In general, our current problem is an ignorance of basic mechanisms. Though we speak of "conflicts," in fact, we don't know the different pathways or the nature of the signals which cause our problems—the ileus of the upper gastrointestinal tract or the head symptoms. There are two basic possibilities: neurological transmission and/or humoral transmission. The question of cerebral spinal fluid as a pathway has been raised by one set of experiments, and this certainly deserves consideration.

It may be a decade or more before we cure or prevent

either ordinary motion sickness or space motion sickness; it will depend upon an understanding of fundamental processes at the neuronal and molecular level; and this will be done primarily in labs on Earth.

A most important aspect of our investigation was the demonstration that useful objective data can be gathered quickly and with minimum resources during operational missions. Neither technical problems, nor astronaut recalcitrance need be limiting factors.

Finally, scientific evidence is determined by scientists, their techniques and interpretations. The life blood of science is diversity and disagreement. It is present in various investigations with striking differences in American and Russian experience, as well as large areas of common experience. Only the caustic of time and experience is adequate to prove the correct view, and these few observations and studies are submitted to that process.

ACKNOWLEDGMENTS

This was a special project supported by the Office of Manned Space Flight, NASA HQ and a joint effort between individuals in the Astronaut Office and Medical Sciences Division, Johnson Space Center. There were too many individuals who made significant contributions to list but special thanks are due to Gen. Abrahamson who made the project possible, to many of the astronauts and payload specialists who acted as both subjects and co-investigators, to Dr. Norman Thagard who was the inflight investigator on STS-7, to Mr. Hugh Harrington, and others for technical aid, Mr. Henry Whitmore for fabrication of many flight hardware items and to Ms. Pam Thompson for editorial aid.

REFERENCES

1. Baloh RW, Honrubia V. Clinical neurophysiology of the vestibular system. Philadelphia: F. A. Davis Co, 1979.
2. Barber HO, Stockwell CW. Manual of electronystagmography, 2nd ed. St. Louis: C. V. Mosby Co, 1980.
3. Berry CA. President's Page. Aerospace Med. 1969; 40:793.
4. Billingham J. Russian experience of problems in vestibular physiology related to the space environment. In: The role of the vestibular organs in space exploration. Second Symposium. Washington, DC: NASA, 1966 (NASA-SP-115).
5. de Jong PTVM, de Jong JMBV, Cohen B, Johnkees LBW. Ataxia and nystagmus induced by injection of local anesthetics in the neck. Ann. Neurol. 1977; 1:240–6.
6. Graybiel A. Oculogravic illusion. AMA Arch. Opthalmol. 1952; 48:605–15.
7. Graybiel A, Clark B, Zarriello JJ. Observations on human subjects living in a "slow rotation room" for periods of two days. Arch. Neurol. 1960; 3:55–73.
8. Graybiel A, Guedry FE, Johnson WH, Kennedy RS. Adaptation to bizarre stimulation of the semicircular canals as indicated by the oculogyral illusion. Aerospace Med. 1961; 32:321–7.
9. Graybiel A, Hupp DI. The oculogyral illusion. A form of apparent motion which may be observed following stimulation of the semicircular canals. J. Aviat. Med. 1946; 17:3–27.
10. Graybiel A, Knepton J. Sopite syndrome: a sometimes sole manifestation of motion sickness. Aviat. Space Environ. Med. 1978; 47:873–82.
11. Graybiel A, Miller EF II, Homick JL. Experiment M131. Human vestibular function: susceptibility to motion sickness. In: Johnston RS, Dietlein LF, eds. Biomedical results from Skylab. Washington, DC: NASA, 1977:74–103 (NASA SP-377).
12. Graybiel A, Wood CD, Miller EF II, Cramer DB. Diagnostic criteria for grading the severity of acute motion sickness. Aerospace Med. 1968; 39:453–5.
13. Homick JL. Validation of predictive tests and countermeasures for space motion sickness. In: Pool SL, Johnson PC, Mason JA, eds. STS-2 medical report. Houston, TX: NASA, 1982:8 (NASA TM-58245).
14. Homick JL. Validation of predictive tests and countermeasures for space motion sickness. In: Pool SL, Johnson PC, Mason JA, eds. STS-3 medical report. Houston, TX: NASA, 1982:8 (NASA TM-58247).
15. Homick JL, Miller EF. Apollo flight crew vestibular assessment. In: Johnston RS, Dietlein LF, Berry CA, eds. Biomedical results of Apollo. Washington, DC: NASA, 1975:323–40 (NASA SP-368).
16. Honrubia V, Brazier MAB, eds. Nystagmus and vertigo: clinical approaches to the patient and dizziness. UCLA Forum in Medical Sciences, No. 24. London: Academic Press, 1982.
17. Kornilova LN, *et al.* Vestibular dysfunction in cosmonauts during adaptation to zero-G and readaptation to 1G. Physiologist 1983; 36(Suppl):S35–6.
18. Lackner JR, Graybiel A. Parabolic flight: loss of sense of orientation. Science 1979; 206:1105–8.
19. Lansberg MP. A primer of space medicine. Amsterdam: Elsevier, 1960.
20. Leigh RJ, Zee DS. The neurology of eye movements. Philadelphia: F. A. Davis, 1983:281.
21. Moore TP, Thornton WE. Space Shuttle inflight and postflight fluid shifts measured by leg volume changes. Aviat. Space Environ. Med. 1987; 58(9, Suppl.):A91–6.
22. Parker DE, Reschke MS, Arrot AP, Homick JL, Lichtenberg BK. Otolith, tilt-translate reinterpretation following prolonged weightlessness: implications for preflight training period. Aviat. Space Environ. Med. 1985; 56:601–6.
23. Reason JT, Brand JJ. Motion sickness. London: Academic Press, 1975.
24. Thornton WE. Anthropometric changes in weightlessness. In: Webb Associates, eds. Anthropometric source book. Volume I: Anthropometry for designers. NASA RP-1024, 1978:1–82.
25. Thornton WE, Biggers WP, Pool SL, Thomas WG, Thagard NE. Electronystagmography and audio potentials in space flight. Laryngoscope 1985; 95:924–32.
26. Thornton WE, Hoffler GW, Rummel JA. Anthropometric changes and fluid shifts. In: Johnston RS, Dietlein LF, eds. Biomedical results from Skylab. Washington, DC: NASA, 1977:330-8 (NASA SP-377).
27. Thornton WE, Linder BJ, Moore TP, Pool SL. Gastrointestinal motility in space motion sickness. Aviat. Space Environ. Med. 1987; 58(9, Suppl.):A16–21.
28. Thornton WE, Moore TP, Pool SL. Fluid shifts in weightlessness. Aviat. Space Environ. Med. 1987; 58(9, Suppl.):A86–90.
29. Thornton WE, Wallace JW. Aerospace applications of blood pressure monitoring. In: Ambulatory blood pressure monitoring. New York: Pergamon Press, 1985:95–104.
30. Toglia JU. Electronystagmography: technical aspects and atlas. Springfield, IL: Charles C. Thomas Co, 1976.
31. Wolfson RE. The vestibular system and its diseases. Philadelphia: Univ. of PA Press, 1966:159, 180, 375.
32. Young LR, Oman CM, Watt DGD, Money KE, Lichtenberg BK. Spatial orientation in weightlessness and readaptation to Earth's gravity. Science 1984; 225:206.