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An Assessment of the Circulatory Problem of Weightlessness in Prolonged Space Flight

LAWRENCE E. LAMB, M. D.

IT HAS LONG BEEN thought that prolonged weightlessness during space flight would result in significant deterioration of fundamental cardiovascular dynamics.[11, 12, 15, 16] Gauer and Haber postulated that susceptibility to circulatory collapse might occur due to elimination of presso receptor tonus similar to that observed after prolonged confinement at bed rest. While less concern has been expressed over short-term flights, there has been considerable concern that prolonged space flights might cause cardiovascular deconditioning making the space crewman susceptible to syncope or circulatory collapse during re-entry or return to earth. The circulatory area and the metabolic area in reference to mobilization of calcium, have received the greatest attention. Studies designed to simulate weightlessness by different investigators have shown cardiovascular deconditioning leading to increased susceptibility to syncopal episodes and calcium mobilization.[4, 13, 14]

Interest in the problem of weightlessness relative to the circulatory system received added impetus due to observations made after the orbital flights of Walter M. Schirra, Jr. and Gordon Leroy Cooper. Published postflight observations indicate that on Schirra there was an increased lability of blood pressure and pulse rate. On assuming the upright position there was some evidence of orthostatic intolerance. The heart rate increased from an average level of 70 beats per minute to 100 beats per minute or greater. There was also a slight drop in systolic blood pressure with decreased pulse pressure. It was reported that these minor observations were noted as long as 24 hours after the six-orbit flight.[3]

Following Cooper's flight of 22 orbits, representing approximately 33 hours of space flight, orthostatic intolerance was again noted.[4]

Little is really known or understood about the influence of absence of a gravitational field since it is not possible to create a prolonged gravity-free environment on earth. If the influence of the absence of gravitational field were thoroughly understood, its role in the production of these observed phenomena would be easier to establish. Absence of such data causes the problem to be somewhat complex. Confining one's self to the facts, the observations noted were simply orthostatic intolerance. In its extreme degree, orthostatic intolerance leads to syncope or simple fainting secondary to cerebral ischemia. The alterations in cardiovascular physiology that lead to temporary orthostatic intolerance or syncope can and frequently are induced by a host of different factors.[7, 8, 15] Individuals who have studied syncope are well aware of the wide range of different factors which can lead to such circulatory phenomena. The assumption that evidence of orthostatic intolerance noted after two space flights is due to absence of g force during orbiting can and should be seriously questioned because of the many other factors which could significantly contribute to such episodes. Many factors which are known to cause syncopal episodes in normal healthy people were components of both missions. It is important to establish that temporary orthostatic intolerance or simple fainting is not a rare event in healthy flying personnel.[17] Incidence of syncope studies on the flying population have clearly demonstrated the frequent occurrence of such events due to a multitude of factors.

In its proper perspective, in view of the limited data known at this time, an analysis of the likelihood of orthostatic intolerance after space flights requires careful analysis of the factors related to simple syncope. Insofar as circulatory function is concerned, the basic problem is one of preventing transitory orthostatic intolerance

From the USAF School of Aerospace Medicine, Aerospace Medical Division, Brooks Air Force Base, Texas.
Dr. Lamb is Professor of Internal Medicine Chief, Clinical Sciences Division.

or syncope at the critical time of re-entry or following completion of the space flight. This report will review the more pertinent features of circulatory physiology that may be altered to influence orthostatic intolerance. It will further critically review the analysis of orthostatic intolerance as observed during the two space flights mentioned above based on published data, and review the complexities of evaluating experimental procedures currently in widespread use, thought by many to simulate the problems of weightlessness.

The importance of a clearer definition of this problem can hardly be overemphasized. If, indeed, syncopal-like episodes can result at a critical time secondary to prolonged weightlessness, this must be recognized and efforts made to prevent or control it. If such transitory orthostatic intolerance is related to factors other than relative weightlessness, these factors must be identified before appropriate preventative measures can be included for future manned space flights.

CIRCULATORY MECHANISMS

There are two general categories of circulatory mechanisms which can be altered to cause relative cerebral anemia manifested by syncope, (1) regulation of the vascular bed (distribution) and (2) cardiac output. Alteration of the circulating blood and changes in muscle tone may also influence the occurrence of syncope.

Vascular. The caliber of the large arteries and smaller blood vessels is controlled by contraction of smooth muscle within the vessel walls. The larger arteries can only be partially closed by contraction of their smooth muscle wall. The smaller arteries and arterioles can be closed completely by the smooth muscle contraction in the vessel wall. The endothelial cells form to completely plug the lumen. The arterioles then branch into arteriovenous capillaries (A-V capillaries). These shunt directly to the venous bed and are considered as a main thoroughfare between arterial and venous systems. These A-V capillaries are abundantly supplied at the arterial end with smooth muscle. The smooth muscle is more diffuse near the venous end. Another type of capillary really forms a capillary loop or detour originating from the A-V capillary and terminating at another region of the A-V capillary. The origin of the true capillary has a small, sphincter-like cuff of smooth muscle at its base. This sphincter is capable of closing off the true capillary. There is no other smooth muscle in the wall of the true capillary. Some of the true capillaries are open and others are closed. There is a continuous gradual process of opening and closing of the capillary bed. In this manner the flow through the capillary bed is constantly changing. By muscular action at diffuse areas in the large arteries, small arteries and arterioles, A-V capillaries and the origin of true capillaries, the distribution of blood flow locally or more generally can be controlled.[25]

Vasodepressor syncope or orthostatic intolerance really involves an unsatisfactory distribution of cardiac output resulting in cerebral anemia. Distribution of cardiac output is controlled by the caliber of the various components of the vascular system. It is generally accepted that smooth muscles within the vascular tree are innervated by nerve fibers which terminate within the smooth muscle itself. In certain instances the smooth muscle may be innervated by both constrictor and dilator fibers.[20] Vascular smooth muscle that is not significantly innervated apparently responds readily to the influences of epinephrine and acetylcholine. In addition to autonomic nerve regulation of the circulatory system, chemical activities also influence peripheral vascular function.

When cardiac output is acceptable and decreased cerebral blood flow results from shunting the cardiac output away from the brain, the vascular areas most commonly involved are in the skeletal muscle, skin, and splanchnic bed. The smooth muscle within the vessel walls of skeletal muscle receive efferent fibers which act on alpha receptors to cause smooth muscle constriction. These efferent fibers pass through the sympathetic chain from a region in the thoracic segment of the spinal cord. Stimulation of these efferent nerves cause peripheral vascular constriction to the blood flow in the skeletal muscle thereby elevating blood pressure and proportionately diminishing blood flow through the skeletal muscle. The sympathetic constrictor fibers may be considered as adrenergic fibers. Sympathetic efferent fibers coursing the same route to the vessels as skeletal muscle can be dilator fibers. These fibers are actually cholinergic fibers even though anatomically they come from the sympathetic system.[33] They act on gamma receptors within the smooth muscle wall and effectively dilate the peripheral vascular bed. When this occurs decreased resistance to blood flow in the skeletal muscle permits a greater proportion of cardiac output to go to these regions and this can result in significant decrease in cerebral blood flow. The efferent constrictor fibers originating from the thoracic spine are supervised by higher centers in the brain stem. These are called the vasopressor and vasodepressor centers. These are diffuse areas and stimulation of the pressor center results in the relay of the signal through the efferent constrictor fibers to the peripheral vessels. Stimulation of the depressor center tends to inhibit pressor action and through such inhibition of the vasopressor center prevents peripheral efferent constriction. The carotid sinus reflex is thought to act by afferent stimuli resulting in inhibition of the vasopresor center.

A direct communication from the central nervous system bypassing the vasomotor centers results in stimulation of the efferent dilator cholinergic fibers. An area within the motor cortex relays its signal to the hypothalmous, bypassing the medullary centers, and results in efferent dilatation. This mechanism can be prevented by administration of atropine.[10]

In addition to the autonomic control of the vascular beds of skeletal muscle described above humoral action can contribute to the control of the peripheral vascular bed. Humoral action is normally not thought to have as important a role on control of the peripheral vascular bed as the autonomic mechanisms described above.[25] Norepinephrine chiefly stimulates the alpha receptors resulting in vascular constriction. L-epinephrine, if it stimulates the alpha receptors, likewise will result in peripheral vascular constriction in the skeletal muscles. If beta receptors are stimulated it causes dila-

tation. Thus the action of l-epinephrine is not entirely predictable in its action on the vascular bed of skeletal muscle. The gamma receptors respond to cholinergic drugs, producing vascular dilatation.

Any time blood supply to a skeletal muscle is diminished, for example by occlusion, when the occlusion is removed there is a period of relative hyperemia.[24] Increased blood flow has also been noted for prolonged periods after exertion. These factors point to the presence of an unidentified vasodilator substance (s). This may occur during development of relative hypoxia following exertion or in any other situation in which inadequate blood supply to the skeletal muscles exists for a period of time. This substance has not been clearly identified although a number of different products have been studied. It is not likely that it is serotonin or histamine.[25] This represents one of the unidentified enigmas associated with the control of vascular tone.

There are four ways in which the vascular bed of the skeletal muscle area can be dilated, these include (1) inhibition of sympathetic constrictor mechanism, for example, sympathectomy, or by carotid sinus stimulation, (2) activation of the sympathetic (cholinergic) vasodilator fibers, (3) chemical stimulation of the beta effectors, and (4) the action of unidentified vasodilator substances.

Control of the vascular bed of the gastrointestinal tract is similar to that of skeletal muscle except that at present there is no evidence of sympathetic vasodilator fibers. There are gamma receptors, but apparently these respond to humoral action. Dilatation of the splanchnic bed then, is achieved prinicipally by inhibition of sympathetic constrictor fibers or through humoral mechanisms. Control of the volume of blood within the splanchnic area can have a major influence on blood pressure or orthostatic tolerance. Regulation of the blood flow to the skeletal muscle and splanchnic area is commonly a major factor in vasodepressor syncope or orthostatic intolerance.

Cerebral blood flow in man is commonly thought to be more susceptible to chemical influences than it is to neurogenic factors.[29, 19, 28] Cerebral blood flow is usually controlled by extracranial factors, arterial blood pressure and cardiac output, while cerebral vascular tone is chiefly influenced by chemical factors.[27] Increased oxygen tension causes constriction of the cerebral vascular bed while increased carbon dioxide levels tend to cause cerebral vascular dilatation. Other than these chemical influences, it is difficult to change the cerebral vascular blood flow.

There are important reflex mechanisms which influence the blood flow to other organs, notably the kidney, spleen, and skin. Reflex mechanisms originating from vessels and from other areas of the body may eventually, through complex pathways, produce efferent impulses which cause peripheral vascular dilatation leading to transitory orthostatic intolerance or vasodepressor syncope. Reflexes of this type may originate from almost any part of the vascular tree, or, indeed, any part of the body, or even secondary to emotional or psychic factors. Powerful reflex mechanisms may originate from the lungs such as those noted during pulmonary embolism and various breathing maneuvers. Pulmonary blood flow may be impeded mechanically with sufficiently elevated positive pressure breathing which can either produce reflex changes or increase the load upon the right heart circulation.

Skeletal muscle activity or contraction significantly compresses the peripheral vascular bed and during contraction significantly prevents flow. Muscular contraction, however, has a powerful affect on the transport of venous blood. Even in the presence of peripheral constriction with an external tourniquet, venous pooling can be significantly prevented by muscular contraction.[2]

Cardiac. Syncopal episodes are not limited to vasodepressor mechanisms which are chiefly related to the vascular bed. Efferent action of the simple carotid sinus reflex, for example, may ultimately produce either peripheral vascular dilatation, or cardioinhibitory responses, or both. Peripheral vascular mechanisms which ultimately result in cerebral anemia, may be associated with decreased cardiac output, and in certain instances, this may be the dominant factor. Whenever the heart, as a pump, fails to maintain adequate cardiac output, unless sufficient compensatory mechanisms are induced elsewhere, inadequate cerebral blood flow will occur. In an extreme degree, simple cardiac arrest with no cardiac output may manifest itself by sudden simple syncope.[7, 8] Experience has shown in studies in large numbers of flying personnel with a reported syncopal episode that cardioinhibitory responses are a relatively common component of simple syncope. These may be induced during common breathing maneuvers of the type that commonly occur during flight. These are frequently a significant component of syncope following orthostatic stressing, such as noted during simple standing or tilt table procedures. Numerous examples of straightforward cardiac arrest terminated by assuming the recumbent position have been noted during simple orthostatic testing with the tilt table. Cardioinhibitory responses may be overlooked when drugs are used in conjunction with studies of syncope. The use of atropine tends to block cardioinhibitory responses and any drug, such as the nitrites that induce a generalized sympathetic response tend to prevent cardioinhibitory responses. Simple cardiac standstill on a reflex basis can commonly be induced during simple experimental conditions such as an ordinary tilt table without any additional stress factors. They have also been noted during breathholding, venipunctures, fright, cold pressor tests, and a host of other procedures. The occurrence of cardioinhibitory responses during orthostatic stress testing in young healthy pilots is of particular importance since it implies that attention must be given to the question of cardioinhibitory responses during any syncopal episode as well as vasodepressor mechanisms. During a number of significant cardiac arrhythmias including rapid heart rates with irregularities, the stroke volume of the heart may be significantly compromised and cardiac output significantly decreased. This, in turn, can induce syncopal responses.

Circulatory Blood. Changes in the blood may contribute to syncopal episodes. If the blood volume is significantly decreased, such as during blood loss or dehydration, circulatory dynamics may be sufficiently compromised causing an inadequate cerebral blood

flow with orthostatic intolerance or syncopal-like reactions. Toxins, such as carbon monoxide may render the blood incompetent of adequate oxygen transport, causing syncope. Hypoglycemia, anemia, and a host of other factors contributing to changes, either quantitatively or qualitatively, may either induce or contribute to loss of consciousness.

Muscular Tone. Decreased muscle tone has been demonstrated to be a contributory factor in syncope.[22] The increase in venous pressure associated with assuming the upright position is not adequately counterbalanced by associated significant increase in intramuscular pressure. The intramuscular pressure is directly affected by the tonus of the muscle fibers. Thus, absence of muscular tone contributes to decrease in orthostatic tolerance.

ORTHOSTATIC INFLUENCES

It should be emphasized that transitory orthostatic intolerance or syncope in the upright position is not analogous to the stresses of re-entry generally envisioned during manned space flight. Orthostatic intolerance during standing or on tilt table procedures involves inability to adapt to vertical positive g ($+G_z$). The g load during re-entry profiles is essentially transverse g ($+$ Gx). The demonstration of orthostatic intolerance, either on standing or during tilt table procedures, does not necessarily have any relationship to tolerance to transverse g. While it is possible that an inappropriate angle of the spacecraft could induce certain amounts of vertical g, most flight plans, if followed, would not involve significant amounts of either positive or negative vertical g. The demonstration, within the laboratory, then, or after orbital flight, of orthostatic intolerance to vertical positive g should not be acceped as conclusive evidence that a significant problem will occur during re-entry with the entirely different situation of exposure to transverse g.

Immediately on assuming the upright position a number of dynamic changes occur within the circulation. These are chiefly due to the influence of hydrostatic pressure or vertical g ($+G_z$). Changes in blood pressure within the arterial and venous column are affected. Compared to the blood pressure at heart level, there is an increase in blood pressure below heart level and decrease in blood pressure above the heart level. Blood flow depends upon a difference in pressure between the arterial and venous pressure. Hydrostatic or gravitational influences affect both the venous and arterial column. The A-V pressure gradient, then, may be essentially maintained despite the actual differences in pressure measurements. In the average adult male there is an increase in the pressure at the foot level of 86 mm. Hg and a decrease in pressure at the level of the base of the skull of approximately 24 mm. Hg. There is a fall in right atrial pressure and there is venous pressure collapse in the superior vena cava just above the right atrium. The extramuscular pressure, in the normal well-conditioned individual, below the heart is increased.

There is a redistribution of the blood volume upon standing. As much as 15 per cent of the total blood volume pools in the legs. With prolonged standing or orthostasis 10 per cent of the plasma volume is lost to the tissues after 20 to 30 minutes of prolonged standing or simple orthostasis. These changes result in a decreased central venous reservoir with a loss of available circulation blood volume.[32] Commonly, there is a slight decrease in cardiac output,[30] whereas the normal adult male in the recumbent position may have a cardiac output slightly in excess of 5 liters per minute, on standing this may drop to approximately 4 liters per minute. The decreased cardiac output in the normal individual on standing is usually between 10 and 20 per cent. The stroke volume slightly decreases. In the recumbent position it may be approximately 70 cc. and in the standing position it may be 60 cc. or less per minute. The stroke volume decrease with the decrease in venous return to the heart is commonly conpensated for, by an increased heart rate. Other vascular reservoirs contract to help augment or maintain adequate circulation. This is seen in the contraction of the cardiac volume. In the recumbent resting position the heart is usually at maximum volume during diastole and it may retain approximately half of its volume at the end of systole. This systolic reserve diminishes on standing. This is reflected in a decreased volume of the heart.

Simple standing or orthostasis also has a significant influence upon blood flow distribution. There is approximately a 20 per cent decrease in cerebral blood flow. The brain compensates for this by increased oxygen and glucose extraction.[26] The coronary blood flow normally may remain relatively unchanged. Renal blood flow is diminished. The liver and splanchnic areas have as much as 60 per cent decrease in blood flow.[6] A significant change occurs in the arteries of the skeletal muscles in the leg. On assuming the upright position the arterial portion of the peripheral vascular bed significantly contracts. It is this mechanism which prevents a sudden runoff from the arterial pressure into the venous reservoir. The blood flow to the lower extremities may diminish to 50 per cent of their value in the recumbent state.[21] In order to maintain adequate oxygen delivery to the skeletal muscles the A-V oxygen difference is increased to two times its value noted in the recumbent state.

These are all relatively significant changes in circulation produced by the simple physiological maneuver of assuming the upright position. When these complex mechanisms fail to function adequately, further decrease in cerebral blood flow occurs and susceptibility to syncope or orthostatic intolerance follows.

In addition to the simple mechanics of circulation, failure of the various reflex mechanisms can and do result in cardioinhibitory responses which influence the heart's ability to maintain adequate cardiac output.

ASSESSMENT OF IN-FLIGHT EXPERIENCES

Although findings suggestive of orthostatic intolerance have been reported following manned orbital space flight, it does not appear to be possible at this time to assess accurately whether or not these changes were due to temporary absence of a gravitational field. The more prolonged the space flight, and the more intricate it is, the more likely that it will be associated with

fatigue. It is well established that significant degrees of fatigue tend to increase susceptibility of orthostatic intolerance. It is difficult to state that the observations reported were not influenced by the fatigue factor. A number of other environmental factors which influence man in his ability to maintain adequate circulation were also present. The cabin pressure was at 5 P.S.I. with 100 per cent oxygen, thus, there was a change in the environmental factor of oxygen and a change in the environmental factor of barometric pressure. Temperature may also have been a contributing factor. There were also alterations in fluids and blood volume. Finally, it must be emphasized that in the Mercury Project, both on the Schirra and Cooper flights, the astronaut was relatively immobilized. The capsule was physically small and room for significant motion or activity was nonexistent. Most normal subjects studied for orthostatic tolerance undergo normal daily activity. The occurrence of immobilization in itself or inactivity can significantly influence muscle tone which can contribute significantly to orthostatic intolerance. Immobilization has characteristically been studied during bed rest experiments. Thus, immobilization without absence of vertical positive g has not been sufficiently studied to say that it was not a significant or major factor in the evidence of orthostatic intolerance noted in both flights.

It must also be considered that particularly after a prolonged flight that such an experience is indeed a major emotional event. After the success of such a major achievement the natural post-mission letdown is an expected physiological occurrence. What impact these factors have had upon the occurrence of manifestations of transitory orthostatic intolerance is difficult to judge.

ASSESSMENT OF EXPERIMENTAL METHODS

A number of problems exist in attempting to evaluate the influence of weightlessness within the earth laboratory. None of the studies that have been done to date can clearly be defended as truly representing the influences of weightlessness because of the multiple change in factors associated with the experiments.

Immobilization. Almost all studies done directed toward learning on earth the influence of weightlessness have involved immobilization. The early work done by all bed rest experiments have automatically resulted in relative immobilization or inactivity. The fact that the subject is transverse and perpendicular to the vertical g field does indeed permit an assumption that vertical positive g is essentially absent, however, the absence of vertical positive g is not the only environmental change which is effected with this experiment. At the time of this writing the study of the influence of significant inactivity or immobilization on individuals still exposed to vertical g has not been carried out, as a satisfactory control to evaluate the influence of the absence of vertical g. The work done by Taylor on six healthy men between the ages of 20 and 33 involved bed rest.[31] The studies carried out by Dietrick, et al.,[9, 34] involved immobilization to the extent that bivalved body casts were utilized. Subsequent experiments using water immersion and bed rest all are subjects to the same criticism since in none of these experiments is there a clear-cut differentiation between the influences of inactivity or immobilization and the influences of the absence of vertical g.[13, 14] Unless adequate differentiation can be made, no conclusion is valid that these studies indicate that weightlessness will indeed be a problem for manned space flights. All studies done on bed rest following surgical procedures or other illnesses are subject to the same critical analysis, namely, that conditions evaluate inactivity and immobilization as well as any possible influences that the orientation of the g environment could have upon physiological mechanisms. It is interesting to note, however, that in these hypodynamic states decreased blood volume has been observed.[9] A decrease in hemoglobin and hematocrit has also been reported.[4] This is of some significance concerning the mechanisms of orthostatic intolerance.

Instrumentation Problems. To understand the influences of altered environmental factors it is desirable to obtain as many suitable measurements as possible. Unfortunately, instrumentation and complex procedures all contribute to the problem of orthostatic intolerance. Simple venipuncture can result in fainting or orthostatic intolerance.[1] Experience demonstrates that a subject's first introduction to a tilt table, unless he is carefully prepared, may raise his level of anxiety and contribute to susceptibility to orthostatic intolerance. If one is to measure the influence of a hypodynamic environment, it is desirable to exclude all other factors which may contribute to alteration of results. An individual placed on the tilt table alone with no further instrumentation may be properly sudied for orthostatic intolerance complicated by the subject's own reaction to the tilt table. If the subject is given a venipuncture during the procedure the study actually includes an evaluation of the subject's reaction to the tilt table, the subject's response to the venipuncture, and the subject's orthostatic tolerance. Any one of these three can result in syncope. If an arterial puncture is added to the venous puncture procedure, the additional insult offers one more opportunity to complicate the procedure. Thus, complex instrumentation which may be threatening to the patient, venipunctures, arterial punctures, cardiac catheterizations, dye dilution studies, or any other such procedures, nullify the experimental design. When these procedures are carried out, one can no longer state that the subject's orthostatic tolerance is being studied. Almost every experiment that has been carried out in this area needs critical review to be certain that the experimentation itself has not distorted the significance of the results.

Orthostatic Tolerance. The measurement of orthostatic tolerance by the tilt table procedures cannot be equated to the individual's tolerance to re-entry transverse g forces. The use of tilt table procedures or standing measurements all evaluate the subject's ability to withstand vertical positive g force. This is entirely different to the application of transverse g force. The direct equating of orthostatic tolerance measurements to the inflight re-entry circumstance is a totally invalid concept for these purposes.

COMMENTS

Since a portion of the original studies on orthostatic tolerance was directed toward bed rest subjects, early thinking tended to equate bed rest as being analogous or comparable in some manner to the problems of weightlessness. It is true that bed rest and weightlessness both have an absence of vertical positive g stimulus; at this point this similarity ends. Very little attempt has been made to study the influence of immobilization or inactivity on orthostatic intolerance without the subjects being at bed rest; thus, no clear-cut distinction between the influences of hypogravics and hypodynamics is possible at this date. The changes described in bed rest experiments in healthy subjects, in patients, the changes noted with water immersion experiments and other similar procedures, are all an evaluation of multiple stress factors. This is also true in evaluating the results of presently available manned space flights in which immobilization associated with inactivity, changes in atmosphere, dehydration, temperature, and multiple other factors complicate any reasonable definitive conclusion. *At this date it has not been proved that weightlessness has an adverse influence upon the circulatory system.* The reflex and humoral mechanisms in control of the vascular system and cardiac response are highly complex. It has been pointed out by Peterson that a number of the reflex mechanisms called pressor receptors are not due to pressure at all, but are related to stretch receptors.[23] Accepting the fact that many of the reflex mechanisms involved in the regulation of circulatory tone are stimulated by vessel stretching and accepting the fact that the vessel wall itself plays a prominent role in the physiological mechanisms, many of the postural adaptations, such as decrease in blood flow to the extremity on standing, may be more causally related to stretching secondary to distribution changes induced by g force. If one accepts that neuro regulation is related to stretching as opposed to pressure, it becomes less certain that changes in the gravitational force would significantly influence neuro regulation of the peripheral vascular bed. It is the presence of gravity which gives weight to blood and it is this influence which creates pressure. If, indeed, these were pressor receptors, as commonly expressed, a better theoretical case might be offered for the probability that weightlessness would result in deterioration of autonomic control of the vascular bed. Since they are not pressor receptors, such theories are based on less solid grounds. They have not been further augmented by objective facts at this date.

A clear incisive view of this problem is now a national necessity. A misconception that adverse circulatory responses occur secondary to weightlessness or prolonged space environments could seriously deter utilization of man in prolonged space flight missions. The circulatory problems relative to space flight are most likely to be satisfactorily managed if their cause is clearly understood. If transitory orthostatic intolerance occurs due to confinement and inactivity, measures should be directed to maintain appropriate activity thus preventing such effects. If these factors are related to other environmental factors, such as cabin atmosphere, this must clearly be defined so that appropriate atmospheric environment can be designed into future spacecraft for prolonged manned space missions. In order to learn the true influence of weightlessness on man the influence of the other environmental factors associated with the mission must be known or eliminated. Unless observations are obtained under circumstances that permit such a separation, manned space flights will not provide any real information relative to the influence of prolonged weightlessness on man's metabolic, cardiovascular, or hematological systems.

SUMMARY

The problem of the circulatory aspects of weightlessness has been discussed. It has been emphasized that most observations to date have been directed toward orthostatic intolerance. For this reason, a review of the more important basic mechanisms associated with simple syncope or orthostatic intolerance has been included.

It has been emphasized that it has not at this date been proved that weightlessness associated with space flight is responsible for orthostatic intolerance. The report includes a critical analysis of the multiple factors associated with manned space flight. It is emphasized that the flights to date have also been associated with significant immobilization and inactivity of the space crewman. It is also emphasized that other environmental factors have been changed, including the gaseous environment and barometric pressure. It has been pointed up that orthostatic intolerance or syncope is a symptom which can originate from multiple factors. The observation of transitory orthostatic symptoms in itself frequently does not permit a definitive answer relative to etiology.

This report has pointed out that the majority of experimental work done to date has involved changes in multiple environmental factors. Because bed rest experiments, water immersion experiments, and all other experiments of this type have essentially involved immobilization and inactivity as well as relative absence of vertical g stimulation, the relative influences of these multiple environmental changes on the incidence of subsequent syncope cannot be determined.

It has been emphasized that multiple instrumentation procedures used during experimental studies complicates the experimental design and nullifies interpretation. These procedures are useful in studying syncope but artificially destroy the experimental design in the study of orthostatic tolerance.

It has been emphasized that orthostatic tolerance tests in tilt table procedures are in no way analogous to transverse g tolerance required for re-entry for most planned manned space missions.

Having laid this background of clarification of some of the facets of the problem of space flight relative to the circulatory system, subsequent articles in this series will report experiments relative to the assessment of the problems encompassed in prolonged manned space flight.

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