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COMPUTER SIMULATION OF PREFLIGHT BLOOD VOLUME REDUCTION AS A COUNTERMEASURE TO FLUID SHIFTS IN SPACEFLIGHT

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ABSTRACT

Fluid shifts in weightlessness may cause a central volume expansion, activating reflexes to reduce the blood volume. Computer simulation was used to test the hypothesis that preadaptation of the blood volume prior to exposure to weightlessness could counteract the central volume expansion due to fluid shifts and thereby attenuate the circulatory and renal responses resulting in large losses of fluid from body water compartments. We used the Guyton Model of Fluid, Electrolyte, and Circulatory Regulation, modified to simulate the six-degree head-down tilt that is frequently used as an experimental analog of weightlessness in bedrest studies. Simulation results show that preadaptation of the blood volume by a procedure resembling a blood donation immediately before head down bedrest is beneficial in damping the physiologic responses to fluid shifts and reducing body fluid losses. After ten hours of head down tilt, blood volume after preadaptation is higher than control for 20 to 30 days of bedrest. Preadaptation also produces potentially beneficial higher extracellular volume and total body water for 20 to 30 days of bedrest.

INTRODUCTION

The mechanisms causing an increased excretion of water and electrolytes in ground-based experiments simulating weightlessness by water immersion or head-down tilt are thought to be initiated by the headward redistribution of body fluids (Leach, 1979; Epstein et al., 1980). In weightlessness, circulatory changes include an early and rapid inflight elevation of hemoglobin concentration (Kimzey, 1977) coinciding with a loss of body mass that reflects a negative water balance. Most of the water loss occurs within the first three days, and a plateau is thought to be reached by 10 or 20 days of weightlessness (Thornton and Ord, 1977). Red cell mass may decrease by 15% after 2 or 3 weeks in space (Nicogossian and Parker, 1982).

The reduction of blood volume in weightlessness is considered to be an adaptation to the space environment (Cogoli, 1981; Leach et al., 1983; Ilyushin and Burkovskaya, 1980). Unfortunately this leaves astronauts maladapted to gravity when they return to earth; postflight orthostatic intolerance has been a problem that is now partially counteracted by oral rehydration before reentry (Bungo, 1989). It would be desirable to limit inflight body fluid losses if possible. There is also a possibility that fluid shifts play a role in space sickness etiology (Barrett and Lokhandwala, 1981; Leach, 1987; Kohl, 1985, 1987). Reducing the physiologic effects of fluid shifts might therefore help to ameliorate the space sickness problem.

The present study was undertaken to test the hypothesis that some of the major physiologic effects of a fluid shift could be counteracted by reducing the blood volume prior to the fluid shift. Blood volume reduction should decrease the central volume expansion due to fluid shifts and attenuate the circulatory, hormonal, and renal responses experimentally observed in water immersion and head-down tilt that are often used to model weightlessness. The net effects should be an attenuation of the physiologic responses to fluid shifts and decreased body fluid losses.

This hypothesis has previously been supported in two short-term water immersion experiments in human subjects (Simanonok and Bernauer, 1985; Simanonok, in review). For the present study we used a validated mathematical model of circulation to test the above hypothesis. Our purposes in employing mathematical modeling are 1) to extend the time period for testing the preflight blood volume reduction countermeasure beyond that possible in water immersion experiments, 2) to efficiently test different methods to optimize the countermeasure, and 3) to assist in the experimental design of further tests of the countermeasure using human subjects. This paper presents the initial results of our work toward those goals.

METHODS

The mathematical model used in this study was derived from the Guyton Model of Fluid, Electrolyte, and Circulatory Regulation (1972). It incorporates known relationships between physical, neural, and hormonal regulators of fluid balance and volume, pressure, and flow within the human circulatory system and fluid compartments (Fig. 1). The original model was modified for weightless simulation by head-down tilt by White (1974) and later improved for this purpose by Leonard and Grounds (1977). The model has been extensively validated through comparison with data from ground-based and flight experiments (Leonard et al., 1979, 1986). The present version of the model is coded in FORTRAN and runs on the IBM PC and compatibles. It required two changes for this simulation.

The first modification of the model was to enable it to reach a stable equilibrium at a reasonable reduced blood volume with a normal hematocrit after prolonged head-down tilt. The rationale for this change was based on the assumption that there is a final adapted state in weightlessness in which a new fluid equilibrium exists; after adaptation, the blood volume and other body fluid compartments should no longer continue to decrease. Present evidence suggests that the magnitudes of these adaptive changes in true weightlessness are somewhat greater than in bedrest (Leach and Johnson, 1984), but the model changes posture to simulate bedrest, not weightlessness. We used the experimental data from a bedrest study (Leach and Johnson, 1984) which was specifically designed to simulate the 10 day Spacelab 1 mission. The red cell mass reduction after 10 days of bedrest was -3.3% $\pm$ SEM 1.6% (n=6) as compared to the losses in the four Spacelab 1 astronauts of -9.3% $\pm$ SEM 1.6%. Obtaining a stable equilibrium with the model of a reduced blood volume including a red cell mass loss of -3.3% at 10 days required the replacement of the erythropoiesis block of the Guyton Model with a model of erythropoiesis developed by Leonard et al. (1981). The difference between the starting blood volume and the new blood volume at equilibrium was the preadaptation volume, the volume to remove to counteract fluid shifts.

The second change necessary was to enable simulation of bleeding. This required the addition of a BLEED RATE parameter allowing blood to be removed at any desired rate, with the removal of the constituents of blood (water, cells, salts, and protein) in proper proportions. From a previous test of the countermeasure in a water immersion study we had serial hematocrit data taken every two minutes during hemorrhages of 15% of blood volume in 8 supine subjects (unpublished data, Simanonok); two of these subjects had the same hemorrhage times of 18 minutes. We compared the data from these two subjects with a simulated bleed of 15% of blood volume in 18 minutes to validate the model's response to acute blood volume reduction.

To test our hypothesis that blood volume reduction would counteract fluid shifts, we simulated an acute blood volume reduction by the preadaptation volume over 18 minutes in the supine position immediately before a fluid shift induced by 6 degree head-down tilt. The control simulation was 6 degree head-down tilt alone.

RESULTS

The starting volume of blood before simulated head-down tilt was 5024 ml. After prolonged 6 degree head-down tilt (70+ simulated days), the equilibrium blood volume was 4490 ml. The difference, 534 ml, or about 11% of the starting blood volume, was the preadaptation volume to remove before head-down tilt to test the countermeasure.

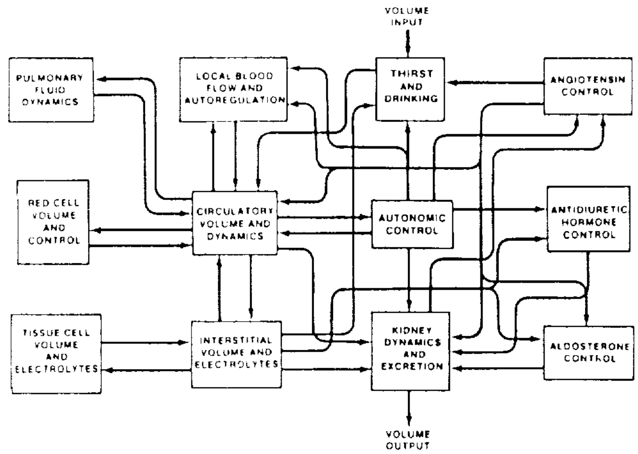

Fig. 1. Subsystems of the Guyton Model of Circulatory, Fluid, and Electrolyte Regulation.

The protective effects of preadapting the circulation to fluid shifts in maintaining blood volume, extracellular fluid volume, and total body water are shown in Figs. 2, 3, and 4, respectively. Of particular interest in Fig. 2 is that after ten hours of simulated head down tilt, the blood volume can be slightly better maintained for 20 to 30 days by a prior bleeding. The effects on urine flow are shown in Fig. 5. Data are plotted on a logarithmic time scale so that all phases of the experiment out to 70 days may be clearly distinguished.

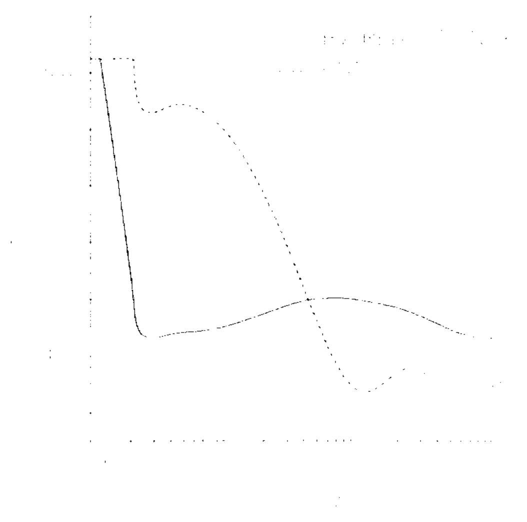

Fig. 2. BLOOD VOLUME. BV REDUCTION = acute reduction of blood volume by 534 ml in 18 minutes. HDT = head down tilt.

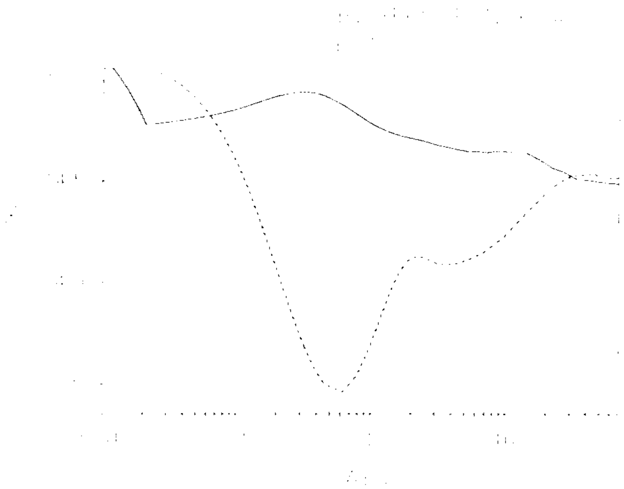

Fig. 3. EXTRACELLULAR FLUID VOLUME

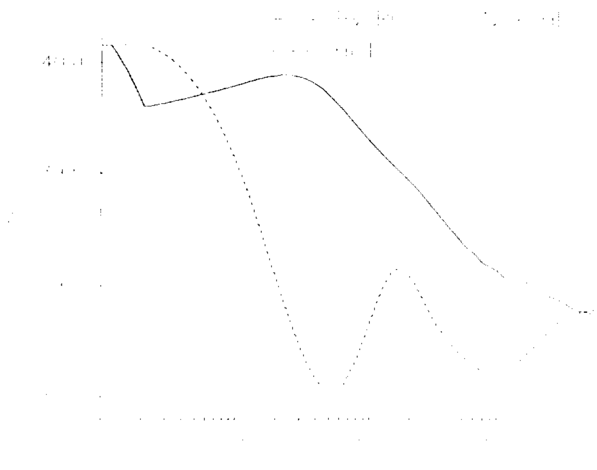

Fig. 4. TOTAL BODY WATER

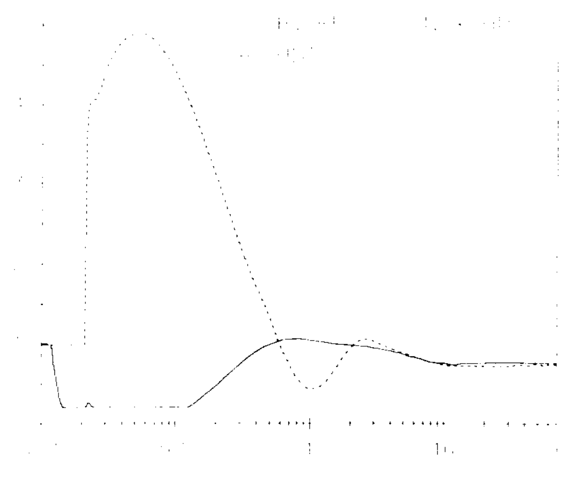

Fig. 5. URINE FLOW

DISCUSSION

The hypothesis that blood volume reduction before a headward fluid shift would counteract some of the major effects of that fluid shift was supported by the results of this computer simulation. These results are in agreement with two earlier water immersion studies (Simanonok and Bernauer, 1985; Simanonok, in review). Except for a short period of time after blood volume reduction during the first few hours of head down tilt, this simulation suggests that body fluid volumes would be better maintained for twenty to thirty days by preadapting the blood volume to headward fluid shifts. During the first few hours, loss of fluid by elevated urine flow (Fig. 5) in head-down tilt without the countermeasure rapidly met and surpassed the initial fluid loss due to a prior blood volume reduction.

In addition to attenuation of the volume losses, Figs. 2, 3, and 4 illustrate that the rates of change of the body fluid volumes during head down tilt are also decreased by prior blood volume reduction. Decreases in both the rates of change and the absolute magnitudes of the changes in body fluid volumes suggest that the physiologic stresses upon the simulated body were decreased. Homeostasis is the term applied to the physiologic tendency to maintain a constancy of the body's internal environment. Fluid shifts disturb the internal environment, invoking homeostatic responses that act to return the parameters of the internal environment to their normal operating range. Preadaptation of the blood volume may therefore reduce the magnitude of the homeostatic stresses accompanying adaptation to weightlessness.

The most unambiguous potential benefit of the countermeasure is that postflight orthostatic tolerance might be improved by the enhanced fluid retention for missions up to twenty or thirty days in length. There may also be other benefits. Head congestion, facial edema, and headaches in astronauts might be lessened. More important, if it is true that fluid shifts in some manner contribute to space sickness etiology (Barrett and Lokhandwala, 1981; Leach, 1987; Kohl, 1985, 1987), then it is possible that preadaptation of the circulation may be beneficial in ameliorating space sickness by reducing the physiologic impact of fluid shifts. Unfortunately, the mechanisms causing space sickness are only speculative and there are no nausea or motion sickness variables in the Guyton Model.

It is important to consider other ramifications of blood volume reduction that may be relevant to astronauts. We are not proposing that the optimum method to preadapt the circulation to weightlessness is by acute hemorrhage immediately preflight, in a procedure resembling a blood donation. This is because blood volume is usually restored within a day or two after an acute hemorrhage, although the restoration of plasma proteins and cells takes longer. Launch delays could easily ruin the effectiveness of that approach. A preflight regimen of diuretics, water immersion, or head-down tilt might effectively reduce the blood volume; at least one astronaut has slept in head-down tilt for about ten days before each of his three Shuttle missions to reduce his blood volume and ameliorate the effects of fluid shifts. He reports that he suffered none of the head congestion, facial edema, or headaches that astronauts commonly experience in weightlessness, and he never became space sick (Musgrave, personal communication).

Preflight orthostatic tolerance would if anything be decreased by blood volume reduction, so astronauts who were borderline in their orthostatic tolerance should probably not be preadapted unless their orthostatic tolerance could first be improved. Exercise capacity could be reduced somewhat by preflight blood volume reduction, and could conceivably affect an astronaut's performance in the event of a preflight emergency egress. These concerns must be thoroughly addressed before preflight blood volume reduction can be seriously considered for astronauts. Further computer simulations may be useful in answering some of these questions.

The utility of computer simulation in planning and designing experimental studies is amply demonstrated by this and previous simulation studies. Simulation is a highly cost-effective method for initial hypothesis testing and experimental design optimization, especially when investigating the physiology of human adaptation to weightlessness.

This computer simulation extends earlier work which suggests that preflight blood volume reduction on the order of magnitude of an ordinary blood donation could be beneficial to astronauts by damping their physiologic responses to fluid shifts and reducing body fluid losses. These results suggest that this countermeasure to fluid shifts could possibly improve postflight orthostatic tolerance for missions of 20 to 30 days in duration, and could ameliorate some of the head congestion, facial edema, and headaches that afflict many astronauts. To the extent that fluid shifts contribute to the problem, an effective countermeasure to fluid shifts could also be beneficial against space sickness.

REFERENCES

Barrett RJ, Lokhandwala MF. Circulatory and vestibular implications of central angiotensin mechanisms in physiological adaptation to weightlessness. Medical Hypotheses 1981; 7:1415-9.

Bungo MW. The cardiopulmonary system. In: Nicogossian AE, Huntoon CL, Pool SL, eds. Space Physiology and Medicine, 2nd ed. Lea & Febiger, Philadelphia, 1989:179-201.

Cogoli A. Hematological and immunological changes during space flight. Acta Astronaut. 1981; 8:995-1002.

Epstein M, DeNunzio AG, M Ramachandran. Characterization of renal response to prolonged immersion in normal man. J. Appl. Physiol. 1980; 49:184-8.

Guyton AC, Coleman TG, Granger HJ. Circulation: overall regulation. Ann. Rev. Physiol. 1972; 34:13.

Ilyushin AV, Burkovskaya T Ye. Cytokinetic evaluation of erythropoiesis during long-term orbital flights. USSR Report: Space Biology and Aerospace Medicine 1981; 15:60-4.

Kimzey SL. Hematology and immunology studies. In: Johnson RS, Dietlin LF, eds. Biomedical Results from Skylab. NASA SP-377, Sup. of Documents, Washington, DC, 1977:249-82.

Kohl RL. Endocrine correlates of susceptibility to motion sickness. Aviat. Space Environ. Med. 1985; 56:1158-65.

Kohl RL. Hormonal responses of metoclopramide-treated subjects experiencing nausea or emesis during parabolic flight. Aviat. Space Environ. Med. 1987; 58:A266-9.

Leach CS. A review of the consequences of fluid and electrolyte shifts in weightlessness. Acta Astronaut. 1979; 6:1123-35.

Leach CS. Fluid control mechanisms in weightlessness. Aviat. Space Environ. Med. 1987; 58:A74-9.

Leach CS, Johnson PC. Influence of spaceflight on erythrokinetics in man. Science 1984; 225:216-8.

Leach CS, Johnson PC, Suki WN. Current concepts of space flight induced changes in hormonal control of fluid and electrolyte metabolism. The Physiologist 1983; 26:S24-7.

Leonard JI, Grounds DJ. Modification of the Long Term Circulatory Model for the Simulation of Bed Rest. NASA Contractor Report (NASA CR-160186), Washington, D.C., 1977.

Leonard JI, Kimzey SL, Dunn CDR. Dynamic regulation or erythropoesis: A computer model of general applicability. Exp. Hematol. 1981; 9:355-78.

Leonard JI, Rummel JA, Leach CS. Computer simulations of postural change, water immersion and bed rest: an integrated approach for understanding the spaceflight response. The Physiologist, 22:S32-2, 1979.

Leonard JI, White RJ, Rummel JA. Math modelling as a complement to the scientific inquiry of physiological adaptation to space flight: fluid, endocrine and circulatory regulation. In: Hunt J, ed. Proc. of 2nd Intl. Conf. on Space Physiology, Toulouse, France, 20-22 Nov. 1985, European Space Agency publication no. SP-237, Paris, 1986:233-44.

Nicogossian AE, Parker JF Jr. Space Physiology and Medicine. NASA SP-447, Sup. of Documents, Washington, D.C., 1982:129.

Simanonok KE. Effects of hypovolemia on the responses to water immersion in men. In review.

Simanonok KE. Bernauer EM. Hemorrhage as a countermeasure to fluid shifts in water immersion. (abstract) The Physiologist 1985; 28:285.

Thornton WE, Ord J. Physiological mass measurements in Skylab. In: Johnson RS, Dietlin LF, eds. Biomedical Results from Skylab. NASA SP-377, Sup. of Documents, Washington, D.C., 1977:175-90.

White RJ. A Long-term Model Of Circulation: Final Report. NASA Contractor Report (NASA CR-147674), Washington, D.C., 1974.