Cardiovascular Function Discipline Report on Countermeasures

I. Nature of the Problem

Evidence from spaceflight missions and ground based analog experiments indicates that prolonged exposure to microgravity induces a variety of adaptations in the function of the cardiovascular system that significantly compromise orthostatic tolerance and physical work performance upon return to earth's 1G environment. Reduced orthostatic and work capacities are associated with alterations in cardiac and vascular functions that appear to include the following characteristics:

1) Significant reductions in circulating blood volume as a result of a rapid decrease in plasma volume followed by a more gradual loss of red blood cell mass.

2) Reductions in stroke volume and cardiac output with little evidence of compromise in normal ventricular function.

3) Possible increased occurrence of cardiac arrythmias.

4) Alterations in peripheral vascular function that include increased venous compliance of the lower extremities, reduced muscle blood flow, and limited capacity for increasing peripheral resistance in response to standing on return to 1-g.

5) Changes in autonomic nervous system function, including both afferent and efferent limbs of reflexes.

6) Altered baroreflex function that is associated with attenuated tachycardia and decreased vasoconstrictive response to hypotensive stimuli.

7) Possible reduction in cardiac mass.

8) Reduction in central venous pressure, as compared to head-down posture pre-launch in 1-g.

Together, the above listed adaptations in cardiovascular function may result from underlying mechanisms that contribute to the well-documented profile of orthostatic intolerance and lower aerobic capacity following spaceflight. Combinations of these functional deficits has the potential to deleteriously affect an astronaut’s ability to egress the space vehicle following reentry in the case of an emergency situation upon landing.

II. Countermeasures to the Problem

The development of a countermeasure program designed to maintain normal cardiovascular function should continue to focus on two primary operational functions and include the following approaches:

1) Protection of orthostatic tolerance

    a. Countermeasures in use include:

        a.1. Astronauts consume an isotonic saline 'load' consisting of 8 salt tablets (1 g NaCl per tablet) with about 960 ml fluid approximately 2 hours before re-entry in an attempt to restore plasma and blood volume.

        a.2. Use of an anti-G suit inflated to approximately 1 psi during re-entry and landing that provides protection against blood pooling in the lower extremities. (The standard Air Force CSU-13B/P anti-G suit is currently used during landing).

        a.3. A specially-designed full coverage Liquid Cooling Garment (LCG) with a network of plastic tubing that allows for the circulation of water across the body surface is worn under the Landing and Reentry Suit (LES) to provide conductive cooling of the astronaut in an effort to minimize the peripheral vasodilatory effect of body heating and improve comfort.

        a.4. A reconfiguration of the seats in the middeck of the Space Shuttle allows astronauts to lie on their backs in an attempt to minimize the +Gz orthostatic impact on the cardiovascular system of crewmembers during reentry from orbit, after long-duration space flight on Mir and, in the future, on the International Space Station.

    b. Countermeasures that have been attempted in flight and are no longer being pursued, but could be, if new evidence indicates they have promise:

        b.1. Exposing astronauts to 4 hours of lower body negative pressure (LBNP) at 30mmHg decompression with consumption of the standard oral fluid load during the early part of the exposure. This LBNP/Saline 'Soak' is performed 24 hours before landing.

        b.2. A single-bladder Re-entry Anti-G Suit (REAGS) that provides protection against blood pooling in the lower extremities without covering the abdominal area, knees, or the buttock, inflated to approximately 1 psi during re-entry.

        b.3. An acute graded cycle exercise protocol designed to elicit maximal effort (maximal oxygen uptake) performed within 24 hours of reentry from orbit which might restore blood volume, autonomic function, and orthostatic tolerance.

    c. Potential countermeasures that have not been tried include:

c.1. Resistive exercise designed to prevent muscle atrophy might minimize blood pooling in the lower extremities during standing. Also, reflexes associated with autonomic regulation of blood pressure could be maintained or protected by resistive exercise designed to defend normal motor unit recruitment.

c.2. Periodic exercise during flight within a lower-body negative pressure (LBNP) device might maintain orthostatic function as well as aerobic capacity.

c.3. The use of various pharmacological countermeasures, such as adrenergic agonists and antagonists might prove effective in enhancement of autonomic responses to orthostatic challenges postflight.

c.4. The use of a small-arm centrifuge (artificial gravity) might replace the physiological stimuli to the cardiovascular system naturally provided in earth's environment, and forces greater than 1G might be used to minimize the time required for countermeasure application.

c.5. Since variations in fluid-electrolyte balance (e.g., hyponatremia, potassium deficiency) can impact cardiovascular function, the application of standards for dietary intake during spaceflight could prove to be an important nutrition countermeasure.

c.6. Periodic application of negative pressure to the carotid baroreceptors with the use of a neck pressure chamber might provide a pressure loading stimulus in an attempt to maintain normal baroreflex control of cardiac function (Note: this is speculative and unlikely to be acceptable).

2) Protection of aerobic capacity

   a) Dynamic physical exercise of moderate intensity and long duration designed to provide endurance profiles has been performed during spaceflight using cycle ergometer, rower, and treadmill devices. No set prescription has yet been determined; hence, currently, the amount of exercise (frequency, duration, intensity) is variable.

   b) An elasticized garment (Penguin Suit) with rubber bands woven into the fabric, extending from the shoulders to the waist and from the waist to the lower extremities, provides continuous tension (exercise) for antigravity muscles. The benefit derived from its application has not been systematically evaluated.

   c) A Human-Powered Centrifuge is a potential countermeasure designed to simultaneously apply cycle exercise (endurance) with head-to-foot gravity (+Gz) acceleration by using a short-arm (<3 m), dual cycle, human-powered centrifuge.

The induced acceleration may potentiate the beneficial effects of exercise and other countermeasures on cardiovascular function after return from spaceflight.

d) Exercise within an LBNP device (See 1.c.2., above).

III. Concerns

The use of ground-based analogs for the study of long-term exposure to microgravity and its effects on the human cardiovascular system is justified by numerous similarities in the physiological adaptations caused by both actual and simulated microgravity. However, numerous dissimilarities that were presented in our discussions raised the concern that ground-based models may not be adequate and perhaps some microgravity effects cannot be studied on the ground. Unfortunately, a significant use of pharmacological agents and lack of control over experimental conditions such as sleeping, eating (nutrition) and scheduled mission activities significantly limits our ability to interpret how much of the observed differences between spaceflight and ground-based experiments is actually the result of the environments and how much is due to these numerous confounding factors.

The identification and use of tests designed to monitor the effectiveness of a countermeasure are critical to the success of any countermeasure program. Many pre- and post-flight tests are developed as a result of constraints in mission schedules and medical operations. There is concern that some tests such as the 10-minute stand test or submaximal exercise used for cardiovascular assessment do not have sensitivity great enough to measure the effectiveness of the countermeasures being tested.

The observations from SLS-1 and SLS-2 that peak VO2 in spaceflight was not reduced from pre-flight values, but was reduced by 22% upon return to Earth, raises concern regarding the ability to predict effectiveness of cardiovascular countermeasures with measurements made during spaceflight.

There is compelling evidence that the vestibular system has pronounced influence through the central nervous system on autonomic control of cardiovascular reflex mechanisms associated with blood pressure regulation. It is our recommendation that expertise be recruited to examine potential countermeasures for vestibular dysfunctions that may contribute to the treatment of compromised orthostatic tolerance post flight.

IV. Recommendations

1) A basic approach to assure a countermeasure program that will enhance 'health' and function during long-duration spaceflight should include several actions that are associated with data collection and medical monitoring of the cardiovascular system. These activities should include, but not be limited to:

a. Cardiac rate and rhythm monitoring should be done in an optimal manner during flight, e.g., one day biweekly, with periodic downlinkage.

b. Testing suits, like the penguin suit, with detection and recording of exogenous loads they provide.
c. Collecting data to assess any relationships between microgravity exposure, the use of physical countermeasures and drugs, and the frequency and severity of arrhythmias.
d. Using data to correlate external physical loads from countermeasure devices (e.g., penguin suit, resistive exercise devices, cycle ergometer, etc.) with inflight and post-flight cardiovascular performance (e.g., aerobic capacity, orthostatic tolerance, autonomic function).
e. Observing cardiovascular structure and performance in-flight, if technology becomes available, and immediately post-flight.
f. Initiating a program for testing, and determining pharmacokinetics and pharmacodynamics of pharmacologic agents likely to benefit cardiovascular function.
g. Defining the relation between diet and metabolic balance data previously obtained in microgravity; from diet logs, relate dietary intake to cardiovascular performance and rhythm.

2) Continue research to identify the optimal exercise prescription(s) (i.e., minimal amount of exercise intensity, duration, frequency, and mode) required to produce the greatest cardiovascular benefits associated with physical and orthostatic functions. Also, there is a need to identify at what point in the mission exercise countermeasures should be applied. Continued ground research to evaluate and validate exercise countermeasure protocols should be conducted prior to space flight.

3) Research is needed to identify countermeasure procedures that will acutely increase central venous pressure operational setpoint and plasma albumin. Fluid loading should be combined with such countermeasure techniques. (Acute exercise designed to elicit maximal aerobic effort restored plasma volume in bedrest subjects; the combination of fluid loading and acute maximal exercise may be effective to enhance restoration of vascular volume).

4) The use of inflight exercise within the LBNP chamber as a countermeasure should be examined. While members of the Committee questioned its relevance for supporting orthostatic tolerance, the fact that this technique does support aerobic capacity indicates additional research should be done to further define its possible use for improving cardiovascular homeostasis.

5) NASA should continue to develop the Liquid Cooling Garment (LCG) as a countermeasure, but continue development and testing of an upper torso LCG designed with greater cooling tube density to provide adequate total cooling capacity.

6) NASA should continue to develop an anti-G suit that can be comfortably inflated and worn in combination with the LCG to provide maximum protection against orthostatic compromise during re-entry and landing.

7) There are numerous approaches that have not been specifically tested in the U.S. space program, but hold potential as countermeasures that NASA should consider. These include the 'Penguin' suit, resistive exercise, pharmacological agents, and a human-powered centrifuge. These 'potential' countermeasures may be worthy of support for future ground and spaceflight experiments in order to investigate and define their impact on cardiovascular functions.

8) The LBNP/Saline “Soak" procedure has not proven effective in ameliorating cardiovascular stress during post-flight stand tests and should therefore be discontinued as a countermeasure. However, use of LBNP for evaluation of other cardiovascular countermeasures and functions during a space mission should continue.

V. Overarching Issues

One goal of countermeasure programs for maintaining astronaut health and fitness during long duration spaceflight is to assure that each crew person has sufficient power, strength, and endurance to conduct daily tasks and sufficient reserve and functional capacity to perform emergency functions. To accomplish this, a strong scientific base will be required, as well as careful operational validation and testing. An understanding of the basic physiology of spaceflight and mechanisms involved in adaptation to microgravity is needed to provide the most efficient and effective countermeasures. This important knowledge will require a scientific approach and not a trial-and-error approach. The development of a systematic approach to investigation of the effects of long duration exposure to spaceflight on the cardiovascular system will include the integration of three basic issues: 1) identification and quantification of physiological adaptations; 2) determination of underlying mechanisms; and 3) identification of the physiological stimulus required to maintain normal function in 1G (on earth). Once basic research investigations have identified the physiological stimulus required to maintain normal function in 1G (on earth), operational research can be directed to testing the application of 'treatments' that provide similar stimuli to the cardiovascular system and assess their effectiveness on orthostatic and exercise performance.

The success of this approach will depend upon an organization that can oversee and coordinate the numerous issues and subsequent investigations to assure optimal integration of all activities and knowledge.

Use of exercise as an effective countermeasure will depend on a thorough understanding of operant mechanisms of physiological adaptation to microgravity and how they are affected by the stimulus of specific intensities, durations, frequencies, and modes of exercise and other treatments that have yet to be clearly defined. Present practices appear to be excessively costly in terms of both time and money. Better countermeasure should be identified and tested on the ground and during spaceflight. Data from both ground and inflight investigations have suggested several findings and strategies that can be used for development of exercise and other countermeasures for training before, during, and after spaceflight:

1. It is clear that no one current countermeasure applied during exposure to microgravity has been completely successful in maintaining or restoring impaired cardiovascular function. Research on the development of countermeasures for cardiovascular (and other physiological) functions should include tests for combinations of countermeasure prescriptions.

2. Ground-based models should be used to develop information and understanding of basic mechanisms that underlie deleterious physiological adaptation to microgravity. Head-down tilt bedrest is one model that has been used effectively investigate some of the alterations in physiological functions induced by exposure of crews to microgravity. This model provides a controlled laboratory environment to conduct experiments for later inflight testing.

3. In addition to exercise alone, some degree of gravity loading with acceleration may be required to provide optimum effects.

4. Future inflight exercise-training programs will probably require a mix of dynamic and resistance modes to maintain both anatomical structure and physiological function. Each of these modes of exercise with varying profiles of intensity, frequency and duration provide specific stimuli to the cardiovascular system. For optimum countermeasure effects, it is important to determine which types of exercise provide beneficial as opposed to detrimental alterations in cardiovascular function

Development of flight countermeasure prescriptions must include consideration of equipment that meets feasible and effective operational requirements. The equipment must be convenient to use so it will promote optimum crewmember compliance. Devices should be small; easy to handle, setup, and stow; and function with minimal external power requirement.

Finally, research efforts should help in the identification of minimal countermeasure application (e.g., time, workload, etc.) required for maintaining health, safety and productivity of crewmembers[1]. This approach can be successful only if specific criteria are well defined through systematic analysis of the physical and physiological requirements for adequate accomplishment of flight-operational tasks.

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[1] Prolonged daily exercise presently used during spaceflight is costly and drains life support materials which are expensive to place and maintain in orbit. For instance, the average daily exercise metabolic cost of 725 kcal during Russian missions represent about 25% of the total caloric intake of 3,150 kcal. If exercise time and ensuing energy costs could be halved, the saving over a 6-month mission would be enough to supply another crewperson with an additional 27 days of food, 23 days of water, and 13 days of oxygen. This issue will become more critical on longer interplanetary missions.