Respiratory Physiology & Neurobiology 169S (2009) S30–S33

Contents lists available at ScienceDirect

Respiratory Physiology & Neurobiology

journal homepage: www.elsevier.com/locate/resphysiol

Cardiovascular adaptations, fluid shifts, and countermeasures related to space flight☆

Alan R. Hargens[a,*], Sara Richardson[b]

[a] Department of Orthopaedic Surgery, University of California, UCSD Medical Center, 350 Dickinson Street, Suite 121, Mail Code 8894, San Diego, CA 92103-8894, United States
[b] Department of Bioengineering, University of California, San Diego, United States

ARTICLE INFO

Article history:
Accepted 2 July 2009

Keywords:
Cardiovascular adaptations
Fluid shifts
Countermeasures
Microgravity
Weightlessness
Exercise
Orthostatic intolerance
Vascular smooth muscle
Lower body negative pressure
Gender
Transcapillary fluid flow

ABSTRACT

Significant progress has been made related to understanding cardiovascular adaptations to microgravity and development of countermeasures to improve crew re-adaptation to gravity. The primary ongoing issues are orthostatic intolerance after flight, reduced exercise capacity, the effect of vascular-smooth muscle loss on other physiologic systems, development of efficient and low-cost countermeasures to counteract these losses, and an understanding of fluid shift mechanisms. Previous animal studies of cardiovascular adaptations offer evidence that prolonged microgravity remodels walls of blood vessels, which in turn, is important for deconditioning of the cardiovascular system and other functions of the body. Over the past 10 years, our studies have documented that treadmill exercise within lower body negative pressure counteracts most physiologic decrements with bed rest in both women and men. Future studies should improve hardware and protocols to protect crew members during prolonged missions. Finally, it is proposed that transcapillary fluid shifts in microgravity may be related to the loss of tissue weight and external compression of blood vessels.

1. Introduction

It is well known that both bed rest and microgravity lower orthostatic tolerance and exercise capacity. When astronauts return to Earth, even after relatively short-duration exposures to microgravity, Earth's gravity can reduce brain blood flow and cause fainting in some crew members (Watenpaugh and Hargens, 1996). During microgravity exposure, exercise countermeasures are used to maintain crew health and fitness and to ensure adequate physical capacity for extravehicular activity and emergency egress upon landing. The type and amount of exercise required to preserve functional capacity during prolonged space flight is unknown, but probably requires both aerobic and resistive modalities (Schneider et al., 2009). High intensity aerobic exercise maintains aerobic capacity ($\dot{V}_{O_2}$ peak), while resistive exercise maintains muscle mass and strength. Both orthostatic intolerance and reduced exercise capacity constitute post-flight cardiovascular deconditioning, which delays return to normal upright activities on Earth from hours to days.

Reduced blood volume is a documented contributor to post-flight orthostatic intolerance. Some investigators postulate that reduced stroke volume due to hypovolemia causes cardiac remodeling and atrophy, which in turn contributes to intolerance (Levine et al., 1997). The arterial cardiac-chronotropic baroreflex appears to function appropriately in response to post-flight hypovolemia because all astronauts exhibit accentuated postural tachycardia after flight (Watenpaugh and Hargens, 1996). Leg compliance does not increase during space flight, but some evidence suggests that problems with the vascular efferent baroreflex arm contribute to post-flight orthostatic intolerance (Whitson et al., 1995). In microgravity, gravitational pressure gradients do not exist in the circulation, so cerebral blood flow is actually aided by a higher than normal blood pressure (Fig. 1), and baroreflexive vasoconstriction is chronically under-stimulated (Watenpaugh et al., 2007). Also, chronic lack of gravitational pressures in the lower body circulation may compromise local arteriolar structure and function (Watenpaugh and Hargens, 1996; Delp, 1999; Zhang, 2001; Wilkerson et al., 2005). In this paper we review recent progress to develop an integrated, physiologic countermeasure for prolonged space flight and propose a unified theory for transcapillary fluid shifts related to microgravity.

2. Cardiovascular and musculoskeletal structure and function

Recent studies indicate that cardiovascular and musculoskeletal structure and function depend importantly on weight bearing

☆ This paper is part of a supplement entitled "Cardio-Respiratory Physiology in Space", guest-edited by P. Norsk and D. Linnarsson.

* Corresponding author. Tel.: +1 619 543 6805; fax: +1 619 543 2540.
E-mail address: ahargens@ucsd.edu (A.R. Hargens).

1569-9048/$ – see front matter © 2009 Elsevier B.V. All rights reserved.
doi:10.1016/j.resp.2009.07.005

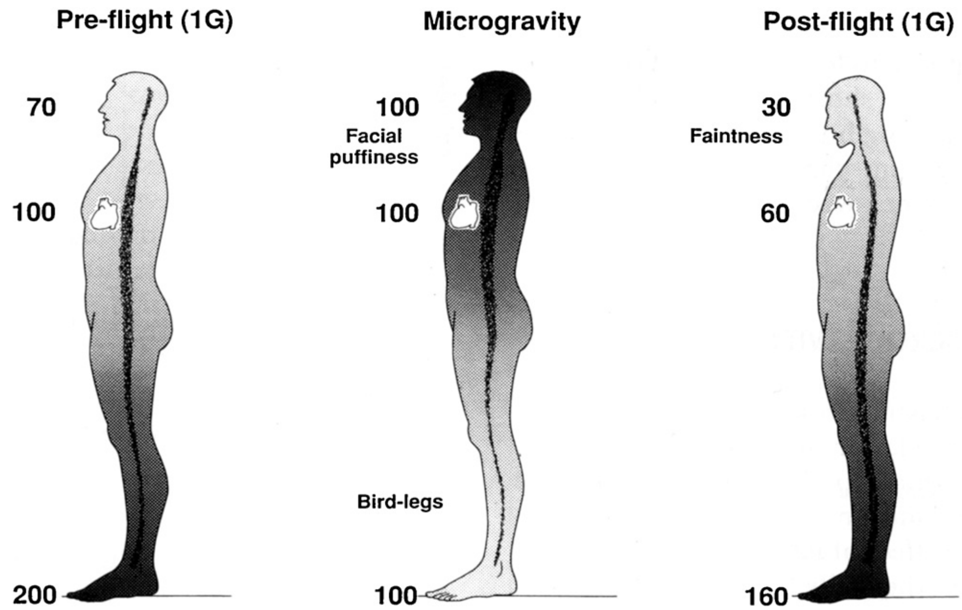

Fig. 1. Hypothesized mean arterial blood pressures due to gravity and loss of gravity before, during and after microgravity exposure (from Watenpaugh and Hargens, 1996).

as well as gravitational blood pressures and flows within the body (Watenpaugh and Hargens, 1996; Delp, 1999, 2007; Colleran et al., 2000; Zhang, 2001). Furthermore, preservation of neuromotor control and sensory feedback during microgravity for normal post-flight ambulation may require walking and running against artificial gravity in space. These factors may explain why existing exercise countermeasures for prolonged microgravity have failed to protect bone, muscle, orthostatic tolerance and fitness fully. There are various options for exercising in a microgravity environment. For example, bungee cord-assisted treadmill exercise in microgravity is restricted to low impact forces due to harness discomfort and is greatly limited by the absence of gravitational blood pressures. Human centrifuges are available to generate 1-G, but it is very difficult to ambulate normally in a rotating environment. Exercise within lower body negative pressure (LBNP) is a desirable concept because weight bearing as well as gravitational blood pressures within the body is generated to simulate various gravity environments. These conditions are not possible with bungee cord-assisted treadmill exercise or with human centrifuges as discussed above. Moreover, we can use supine treadmill exercise within LBNP to simulate lunar EVA work, perform 1-G equivalent countermeasures and test aerobic capacity periodically during bed rest analog studies.

3. LBNP provides load bearing independent of gravity

Exercise countermeasures for astronauts in space are still unresolved, although recent calculations suggest that all exercise in space to date has lacked sufficient loads to maintain pre-flight bone mass. Although Russian cosmonauts walk and run on a treadmill for 2–3 h per day in an attempt to prevent bone loss, their bungee-cord loading apparatus is uncomfortable at loads over 70% body weight (Watenpaugh and Hargens, 1996). Furthermore, blood pressure stimuli at their feet are abnormally low because gravitational blood pressures are absent with their treadmill hardware. Most literature indicates that exercise training during bed rest does not protect orthostatic tolerance. However, based on mechanisms identified above, we previously theorized that addition of a gravity-like stress such as supine exercise within LBNP may be effective. In our bed-rest simulations of microgravity for 15-, 30- and 60-day, we hypothesized that supine treadmill exercise within LBNP maintains orthostatic tolerance and exercise capacity in women and men. Over time our countermeasure protocol has evolved to include 5–10 min of resting LBNP immediately following the 40-min period of LBNP treadmill exercise (Lee et al., 1997, 2007; Watenpaugh et al., 2000; Schneider et al., 2002, 2009; Guinet et al., 2009). With a hypothesis of using LBNP to create Earth-like musculoskeletal and vascular loads during exercise in microgravity, we predicted and then directly measured the foot-ward forces generated during upright-standing and supine LBNP (Hargens et al., 1991). These forces are borne by the feet, legs and spine (using shoulder straps). Examples of the “weighting” effect of LBNP exercise are illustrated in our website: http://bones.ucsd.edu. Reduced musculoskeletal loads and loss of gravitational blood pressures on orbit may explain the 1–2% bone loss per month experienced in microgravity. Our HDT bed rest studies of identical twins document that our LBNP treadmill exercise protects against bone loss, while maintaining muscle strength, exercise capacity, and to a lesser degree, orthostatic tolerance (Smith et al., 2003; Lee et al., 2007; Watenpaugh et al., 2007).

4. Gravitational hemodynamics on Earth and during microgravity

Adult humans spend about two-thirds of their existence in upright, sitting and standing postures. During upright posture on Earth, blood pressures are greater in the feet than at heart or head levels due to gravity’s effects on columns of blood in the body, so-called hydrostatic or gravitational pressures (Watenpaugh and Hargens, 1996). For example, mean arterial pressure at heart level is normally about 100 mm Hg (Fig. 1), whereas that in the head is slightly lower (e.g. 70 mm Hg) and that in the feet is much greater (about 200 mm Hg). During exposure to microgravity, all gravitational blood pressure gradients (arterial, venous and microcirculatory) are lost so that blood immediately shifts to chest and head tissues. Prior work indicates that the structure and function of blood vessels is maintained by transmural stresses associated with local blood pressures (Delp, 1999, 2007); and that decreased aortic compliance occurs in both orthostatically tolerant astronauts and head-down tilted rats (Tuday et al., 2007). Presently, there is no exercise hardware available for space flight to provide additional (gravitational) blood pressure to tissues of the lower body. Recent findings in the hindlimb-suspended rat model indicate that maintenance of bone also depends on gravity-