Orthostatic intolerance remains an operational problem following spaceflight. In addition, there is growing evidence that cardiac dysrhythmias may pose a threat to the health of space travelers. At present, no effective countermeasures exist for orthostatic intolerance and for the probable increased risk of ventricular dysrhythmias. In the last six years, we have addressed the subject of renal, endocrine and volume-regulating function during head-down tilt bed rest. We have found that simulated microgravity induces changes in the volume-regulating systems and electrolyte excretion, and leads to changes in cardiac electrical stability. We have also found that using our tilt-test protocol, the pre-bed rest tilt-test tolerance was predictive of post-bed rest tilt-test tolerance. We propose now to conduct three double-blinded randomized trials to: 1) Investigate the use of a pre-bed rest tilt-test as a means to screen countermeasures against orthostatic intolerance, and investigate the influence of these countermeasures on the renal and
### Task Description:

1. Measure endocrine responses to orthostatic stress. 2) Develop effective interventions for the treatment of orthostatic intolerance in women since from our previous studies this complication of space travel appear to have a gender difference. 3) Investigate the effectiveness of individualized countermeasures identified during a pre-bed rest tilt-test in reducing post-bed rest orthostatic intolerance, as well as their influence on the renal and endocrine responses to orthostatic stress. 4) Investigate the effects of different countermeasures in reducing cardiac electrical instability, and to study the effects of these countermeasures on baseline orthostatic tolerance. 5) Investigate the effects of different countermeasures in reducing cardiac electrical instability after simulated microgravity, and to study the effects of these countermeasures on orthostatic tolerance and on the renal and endocrine responses to simulated microgravity. This grant interacts closely with a companion grant “Effects of Microgravity on Cardiovascular Function” Richard Cohen, M.D., Ph.D., principal investigator.

These studies have implications for the treatment and prevention of maladaptive hemodynamic responses experienced by astronauts particularly in women in flight and on return to Earth. They will provide an innovative way of testing “individualized countermeasures”. Finally, the results of these studies may help us better understand the pathophysiology of alterations in volume homeostatic mechanisms in cardiovascular diseases such as congestive heart failure, dysrhythmias and hypertension.

### Rationale for HRP Directed Research:

Orthostatic hypotension is an increasing medical problem. In some cases it is related to medications or disease. Often, however, it is related to structural changes in the individual’s life, e.g., prolong bed rest from an operation, injury or disease, and/or termed idiopathic. The latter condition affects nearly 1 million individuals in the USA and is more common in women of reproductive age. The current research will provide information concerning the relation of hormonal changes to the development of and background for orthostatic hypotension, thereby providing entée to specific treatment and preventive strategies. This work also has implications for the treatment and prevention of maladaptive hemodynamic responses to volume expansion and upright posture experienced in a variety of cardiovascular diseases such as congestive heart failure. Of interest, both of these conditions are more common and more severe in women than men. Our findings of gender differences in renal, hormonal and cardiovascular responses to simulated microgravity and upright tilt tolerance, may provide a mechanistic explanation for these differences and allow the development of more specific individualize preventive and treatment programs.

### Research Impact/Earth Benefits:

We have completed the initial studies in women and will finish the midodrine dose ranging study in them by March 25, 2006 (Specific Aim 2). We are currently enrolling other subjects into the study to complete Specific Aims 1 and 3.

### Task Progress:

We have completed the initial studies in women and will finish the midodrine dose ranging study in them by March 25, 2006 (Specific Aim 2). We are currently enrolling other subjects into the study to complete Specific Aims 1 and 3.

### Bibliography Type:

**Articles in Peer-reviewed Journals**


**Awards**

"Aerospace Medicine Student and Resident Organization- Scientific Paper Award 2005." Jan-2006

"Association des Medecins de langue francaise du Canada- Recognition Prize 2005." Jan-2006