INTRODUCTION - Exercise accelerates inert gas elimination during oxygen breathing prior to decompression (prebreathe), but may also promote bubble formation and increase the risk of decompression sickness (DCS). The timing, pattern and intensity of exercise are likely critical to the net effect. The NASA Prebreathe Reduction Program (PRP) combined oxygen prebreathe and exercise preceding a 4.3 psi exposure in non-ambulatory subjects (a microgravity analog) to produce two protocols now used by astronauts preparing for extravehicular activity (CEVIS and ISLE). Additional work is required to investigate whether exercise normal to 1 G environments increases the risk of DCS over microgravity simulation. METHODS - The CEVIS protocol was replicated with one exception. Our subjects completed controlled ambulation (walking in place with fixed cadence and step height) during both preflight and at 4.3 psi instead of remaining non-ambulatory throughout. Decompression stress was graded with aural Doppler (Spencer 0-IV scale). Two-dimensional echocardiographic imaging was used to look for left heart gas emboli (the presence of which prompted test termination). Venous blood was collected at three points to correlate Doppler measures of decompression stress with microparticle (cell fragment) accumulation. Fisher Exact Tests compared test and control groups. Trial suspension would occur when DCS risk >15% or grade IV venous gas emboli (VGE) risk >20% (at 70% confidence). RESULTS - Eleven person-trials were completed (9 male, 2 female) when DCS prompted suspension. DCS was greater than in CEVIS trials (3/11 [27%] vs. 0/45 [0%], respectively, p=0.03). Statistical significance was not reached for peak grade IV VGE (2/11 [18%] vs. 3/45 [7%], p=0.149) or cumulative grade IV VGE observations per subject-trial (8/128 [6%] vs. 26/630 [4%], p=0.151). Microparticle data were collected for 5/11 trials (3 with DCS outcomes), with widely varying patterns that could not be resolved statistically. CONCLUSION - We did find that ambulation increases decompression stress. Additional trials would improve the statistical power to assess differences in VGE and to evaluate the relationship between decompression stress and microparticles.