The advent of the Space Shuttle era elevated cardiovascular deconditioning from a research topic in gravitational physiology to a concern with operational consequences during critical space mission phases. NASA has identified three primary cardiovascular risks associated with short-duration (less than 18 d) spaceflight: orthostatic intolerance; decreased maximal oxygen uptake; and cardiac arrhythmias. Orthostatic hypotension (OH) was observed postflight in Mercury astronauts, studied in Gemini and Apollo astronauts, and tracked as it developed in-flight during Skylab missions. A putative hypotensive episode in the pilot during an early shuttle landing, and well-documented postflight hypotension in a quarter of crewmembers, catalyzed NASA's research effort to understand its mechanisms and develop countermeasures. Shuttle investigations documented the onset of OH, tested mechanistic hypotheses, and demonstrated countermeasures both simple and complex. Similarly, decreased aerobic capacity in-flight threatened both extravehicular activity and post-landing emergency egress. In one study, peak oxygen uptake and peak power were significantly decreased following flights. Other studies tested hardware and protocols for aerobic conditioning that undergird both current practice on long-duration International Space Station (ISS) missions and plans for interplanetary expeditions. Finally, several studies suggest that cardiac arrhythmias are of less concern during short-duration spaceflight than during long-duration spaceflight. Duration of the QT interval was unchanged and the frequency of premature atrial and ventricular contractions was actually shown to decrease during extravehicular activity. These investigations on short-duration Shuttle flights have paved the way for research aboard long-duration ISS missions and beyond. Efforts are already underway to study the effects of exploration class missions to asteroids and Mars.

**Learning Objectives:** Overview of the Space Shuttle Program research results related to cardiovascular risks, including the description the deleterious cardiovascular effects of short-duration spaceflight and a discussion of the development of countermeasures against the cardiovascular risks.

**Abstract for:** Panel on The Legacy of Biomedical Research during Space Shuttle: Lessons Learned, 83rd Annual Scientific Meeting of the Aerospace Medical Association, Atlanta, GA, May 13–17, 2012.