## GRAVELINE DE, MCCALLY M. *Body fluid distribution: implications for zero gravity.* Aerosp. Med. 1962; 33:1281.

This Classic paper was one of the first to recognize in detail the cardiovascular problems of spaceflight. The first prediction that there would be significant alteration of cardiovascular function in weightlessness was probably the one by Gauer and Haber published in 1948 (1). In a previously reviewed Classic paper, only minor changes in cardiovascular parameters were observed in monkeys on suborbital flights in 1952 (5). The authors believed that bed rest and water immersion were analogues of weightlessness because those techniques minimized gravity's hydrostatic pressure effects on body fluids (2, 3). It had previously been found in bed rest studies that 11% of blood volume (600 ml) was shifted from the lower extremities and redistributed to the thorax where atrial cardiac volume receptors were activated (by the then recently discovered Henry-Gauer reflex). In both analogues this reflex resulted in a pronounced compensatory diuresis which subsided after 72 h, resulting in a relative dehydration on return to the upright position in the 1-G environment. In this Classic paper, the authors predicted that the same effect would occur during spaceflight. They presented the data from the recent Mercury-Atlas flights of Schirra (MA-8) and Cooper (MA-9) both of which showed a significant decrease in body weight, fluid output exceeding intake, and the excretion of a large amount of very dilute urine (2360 cc, specific gravity of 1.003 on MA-9). Moderate reductions in orthostatic tolerance were noted postflight, but were not operationally significant. These findings were more pronounced with the 22-orbit flight of MA-9 than with the 6-orbit flight of MA-8. The authors pointed out that in the analogue studies, exercise had an inconsistent anti-diuretic effect and had demonstrated that intermittent venous occlusion with extremity tourniquets during water immersion was effective in maintaining cardiovascular adaptability by simulating hydrostatic pressure effects (4). He also suggested the use of anti-diuretic hormone (ADH) in future research to prevent diuresis and fluid loading prior to re-entry as a countermeasure.

### *Background*

Duane Graveline, M.D., was a U.S. Air Force flight surgeon who had completed residency in Aerospace Medicine and was assigned as a research scientist first at the Aerospace Medical Research Laboratory (AMRL) with Michael McCally, M.D., and later at the USAF School of Aerospace Medicine (USAFSAM). As part of his research at AMRL, Graveline spent 7 days continuously immersed in water from his neck down. He was involved in the development of lower body negative pressure (LBNP) hardware at USAFSAM and was later a Flight Controller and Medical Monitor for the Mercury and Gemini programs. He was one of six scientists to be selected into the 1965 astronaut group, but left the program before having flown in space. His application of lower extremity occlusion as a countermeasure was evaluated on two Gemini flights with ambiguous results, but has subsequently been used in a limited fashion by Soviet (and now Russian) space station crewmembers as the "Braslet" device to slow the redistribution of body fluids during initial adaptation to weightlessness.

Dr. McCally remained at AMRL and continued to pursue research related to spaceflight, including not only simulation of microgravity but also LBNP, acceleration tolerance, and the effects of 100% gradient acceleration on a short-arm centrifuge. In 1968 McCally published in book form a collection of papers, "Hypodynamics and Hypogravics- The Physiology of Inactivity and Weightlessness." Soon thereafter, McCally moved on to other areas of medicine.

The possible adverse effects of spaceflight presented in this Classic were not initially accepted by the space medicine community, and a 1965 paper stated, "It has not been proved that weightlessness has an adverse influence upon the cardiovascular system," citing prolonged immobilization, emotional stress, fatigue, and thermal stress as responsible for the orthostatic intolerance seen on the Mercury flights (6). The authors of that paper were concerned that misconceptions regarding cardiovascular adaptability in spaceflight would adversely affect the planning for future missions. However, subsequent studies confirmed the implications of this paper: tilt table tests on Gemini astronauts showed consistently elevated heart rates, reduced pulse pressures, and increased pooling of fluids in the lower extremities in the early postflight period which returned to normal after 50 h. Volumetric studies of the lower extremities on Skylab confirmed the fluid shift as predicted by Graveline and at the volumes observed on the analogue studies. It is now known that there are other cardiovascular alterations during exposure to what is now termed "microgravity," including baroreceptor insensitivity and direct cardiac deconditioning with loss of stroke volume. Exercise is used as a countermeasure for cardiac deconditioning and anti-G garments are used during re-entry to counteract the immediate orthostatic effects. However, one of the most effective orthostatic countermeasures has been found to be fluid loading prior to re-entry as first suggested in this article by Dr. Graveline.

### *Commentary by Dr. Graveline*

In 1960, when I was assigned to the AMRL, I could do just about anything that I wanted to. If I wanted a room filled with 95º F water with a viewing port in the wall for water immersion research, I was able to obtain it, together with a rubber suit connected via a neck seal to a partial-pressure helmet as well as instrumentation to record EEG and EKG. I also obtained a small-animal centrifuge for my "2-G Supermice." I was in paradise; research in today's highly regulated environment would drive me crazy with frustration.

The use of anti-diuretic hormone (ADH) as a countermeasure during water immersion was logical and worked well for me at the AMRL. I have told NASA that they should consider administering ADH during re-entry as a way to enhance orthostatic tolerance, since 80% of the station astronauts still show orthostatic intolerance to such a degree that it would compromise unassisted recovery. I also wish that I could sell the concept of doing away with all in-flight countermeasures, allow complete adaptation to zero gravity for the duration of the mission, and return to Earth in a hydropod with postlanding gravity readaptation in a water immersion facility back on Earth.

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