Reprint
Publishers: S. Karger, Basel
Printed in Switzerland

Gravity – Diving

Dejours (ed.), Comparative Physiology of Environmental Adaptations, vol. 2. 8th ESCP Conf., Strasbourg 1986, pp. 15–26 (Karger, Basel 1987)

Gravitational Force and the Cardiovascular System[1]

D.R. Pendergast, A.J. Olszowka, M.A. Rokitka, L.E. Farhi

Hermann Rahn Laboratory of Environmental Physiology, Department of Physiology, State University of New York at Buffalo, Buffalo, N.Y., USA

Over millions of years man has evolved from a water breather in a weightless environment to an air breather in a 1-G environment. This gradual evolution allowed the development of structural and functional changes in both the respiratory and cardiovascular control mechanisms that allow man to cope with specific stresses in his normal habitat. In the area of cardiovascular performance, we have come to rely heavily on complex feedback responses to cope with postural changes, which alter the body axis along which gravitational forces act. The activities of daily living evoke these reflexes as we stand, sit, lie down, or become immersed. Over the past several years, many individuals have 'returned' to a weightless state during space missions whose duration has ranged from a few hours to several months. Missions related to space are likely to increase the time of exposure to the weightless condition. However, some of the mechanisms that are operative at 1-G appear to 'fail' when the 1-G load is reapplied following exposure to a period of weightlessness. There is indisputable evidence that, in some cases, the space environment, by relieving gravitational stresses, has permitted adaptive mechanisms to lapse, causing serious problems upon return to the 1-G condition. If man is to function in a space environment on a periodic basis, he must be able to adjust not only to weightlessness but also to the effects of the earth's gravity upon re-entry and, with a view to the future, to the gravitational fields of other planets that may eventually be reached.

[1] This work was supported by National Aeronautics and Space Administration Contract NAS9-16042.

Successful adaptation to the space environment as we know it requires man to perform work. Cardiovascular feedback mechanisms must cope with two stresses, often combined: postural changes combined with changes in gravitational forces, and physical exercise. Appropriate responses to these stresses may be more difficult to achieve after adaptation to the weightlessness of space; in fact, man may not be able to fully adjust to the stress of gravity unless appropriate feedback responses are reinforced continuously during flight. Although many studies have been conducted prior to, during, and after space flight, due to logistic constraints, information to address the problems stated above is insufficient. To compensate for this lack of information, ground-based simulation studies have been conducted by us and others in an attempt to add insight into the problems of the cardiovascular adaptation to alterations in gravitational force.

The purpose of the present paper is to consider cardiovascular responses to changes in gravitational force. Man is ideally suited to his 1-G environment. Although cardiovascular adjustments are required to accommodate to postural changes and exercise, these are fully acomplished for short periods (min). More challenging stresses are those of short-term microgravity (h) and long-term microgravity (days) and of gravitational forces greater than that of earth. The latter can be simulated in the laboratory and quantitative studies can be conducted.

Weightlessness

Acute Exposure

When a person is standing in air, a large volume of blood is pooled in the periphery. This does not present a problem insofar as venous return (VR) is generally sufficient to maintain a stroke volume (SV) which, when combined with increased heart rate (HR), positive inotropic tone and venomotor tone, result in a cardiac output ($\dot{Q}$) that is sufficient to perfuse tissue to supply needed nutrients as well as to maintain mean arterial blood pressure. These cardiovascular responses are regulated by complex feedback mechanisms that meet the existing demands as well as the imposed stress of physical exercise. A decrease in the gravitational force results in less peripheral pooling, causing a cephalad shift of blood. This occurs when we assume the supine position or in the head down tilt position (HDT) and results in translocation of 200–500 ml of blood to the thorax. A further shift of blood can be accomplished by applying a graded differential pressure

either from below the diaphragm (lower body positive pressure, LBPP) or a graded differential pressure from distal to proximal (water immersion in water of thermoneutral temperature, WI).

During WI to the neck, ~800 ml of blood are translocated to the thorax [1]. The result of these graded increases in thoracic volume are increases in central venous pressure (CVP), right atrial pressure (P_{RA}) and end diastolic volume (EDV); typically heart rate and cardiac contractility remain unchanged. The outcome of these primary changes is an increase in stroke volume and cardiac output. An increase in $\dot{Q}$ could result in an increase in mean arterial pressure ($\bar{P}a$); however, this is not usually observed during weightlessness. $\bar{P}a$ does not increase because of a drop in total peripheral resistance (TPR) that is proportional to the increased $\dot{Q}$. The decrease in TPR is the result of increased blood flow to many vascular beds including skeletal muscle [3, 19].

One of the most striking responses to WI is the development of a diuresis and natriuresis [12]. The diuresis develops rapidly (with 2 h of WI) while the natriuresis develops more slowly, reaching a peak in 3–4 h. An increase in free water clearance is more marked in normally hydrated subjects as compared to hydropenic subjects [4] with little change in glomerular filtration rate or renal blood flow [12].

Gauer and co-workers [14–16] postulated that the diuresis is due to the inhibition of antidiuretic hormone (ADH), induced by stimulation of the left atrial volume receptors resulting from cardiac stretch (increased pressure and volume). The consequences of the diuresis were postulated to be a reduction in plasma volume (PV) and consequently decreased thoracic blood volume and SV. Initial studies supported this postulate [12]; however, recent studies clearly demonstrate that the cardio-renal coupling is not necessarily as tight as once thought [7, 17].

Data for HDT experiments from several investigators are presented in table I along with our data collected in the supine position and during WI. As indicated in table I, CVP, $\dot{Q}$ and SV increased initially during HDT while HR and $\bar{P}a$ were not changed significantly. After these initial changes, CVP, $\dot{Q}$ and SV decreased along with HR while $\bar{P}a$ did not change significantly. Although the magnitude of these changes in the supine position was less (~5%) and during WI greater (~15%), the overall pattern of the responses was similar in the three conditions. Most importantly, the initial increase in $\dot{Q}$ is offset by a decrease in TPR as $\bar{P}a$ did not change. Over the first 2–3 h of either HDT (6 °) or WI, HR and SV decreased, the result being a decrease in $\dot{Q}$. During HDT the CVP decreased to control levels after 5 h, which could

Table I. Cardiovascular responses to head down tilt (HDT), supine (S), and water immersion (WI)

		Time							
		0 h (seated)	1 h	2 h	3 h	4 h	5 h	6 h	7 h
CVP, mm Hg	HDT	3.9	3.6	4.6	4.4	–	3.8	–	3.8
$\dot{Q}$, liters · min^{-1}	HDT	6.5	7.9	7.8	7.2	–	6.9	–	6.9
	S	6.7	7.6	7.1	6.9	7.0	6.7	6.6	6.9
	WI	6.8	8.8	7.4	7.2	7.0	7.0	7.2	7.1
SV, ml	HDT	94	114	116	110	–	106	–	106
	S	93	106	101	101	107	105	101	104
	WI	92	122	107	109	105	107	109	107
HR, beats · min^{-1}	HDT	69	69	67	65	–	65	–	65
	S	72	72	70	68	66	64	65	66
	WI	74	72	69	66	67	65	66	66
$\bar{P}a$, mm Hg	HDT	97	95	101	98	–	94	–	96
	S	89	86	89	87	88	86	87	88
	WI	88	89	90	88	87	86	87	86
PV, %	HDT	100	101	104	106	105	103	104	101
	S	100	101	102	101	100	99	99	99
	WI	100	104	103	100	100	99	99	98

account for the decreases in SV. During HDT, however, Echt has shown that CVP remains elevated for at least 4 h while SV decreases [11]. During WI, the decreased SV must be due to decreased cardiac contractility, presumably due to a decrease in sympathetic tone. Furthermore, PV, after an initial hemodilution, was not significantly less after 7 h of HDT, S or WI.

All three simulated microgravity experiments resulted in increases in cardiac stretch, urine flow and sodium excretion which were accompanied by a lower plasma renin, aldosterone, and ADH; a careful examination of the results indicate that these changes do not necessarily take place in a parallel manner. For instance, in sedentary subjects, the $\dot{Q}$ increases 35–40% during WI with an increased SV; however, within 2 h of WI it returns to control levels. On the other hand, both the diuresis and natriuresis are sustained for 2–4 h during WI. This dissociation between cardio-renal responses to WI was most dramatically demonstrated in endurance-trained athletes. In these subjects, WI initiates a greater increase in $\dot{Q}$ than in sedentary subjects; furthermore, it is sustained longer. Despite the cardiac

response, the renal responses to WI (both diuretic and natriuretic) were markedly attenuated in trained subjects [7]. The latter finding was accompanied by the lack of an ADH response; plasma-renin-angiotensin (PRA) and aldosterone responses remained normal. The dissociation of cardio-renal responses can be further demonstrated by the nocturnal attenuation of renal responses to WI; cardiac responses are unaltered [27]. The lack of a tight coupling of the cardiac-renal-endocrine responses to WI strongly suggests that while the Gauer-Henry mechanisms may play an important role in eliciting renal-endocrine responses to WI, other mechanisms must contribute to the overall outcome. Furthermore, the renal-endocrine responses do not alter PV over 8 h of WI while SV is decreasing to control levels.

Chronic Exposure

In spite of the absence of changes in PV over an 8-hour period, CVP continued to decrease to only 20% of the pre-HDT values during a 6-day HDT study; $\dot{Q}$ and SV did not decrease further [18, 22]. This finding during HDT agrees with data collected over 2–3 days of space flight where CVP and $\dot{Q}$ were not elevated over control levels; there was, however, a significant diuresis and PV decrease [21, 26, 29]. These 'second phase responses' to microgravity apparently contribute to the cardiovascular deconditioning observed after space flights. The exact mechanism of these responses needs further investigation. Apparently after 7 h of microgravity, CVP and $\dot{Q}$ as well as $\bar{P}a$ and PV are not elevated above 1-G levels. The question remains as to cause of the second phase of responses to microgravity. A partial explanation may be advanced that is related to the hydration state of the subjects during the 2 to 7-day experiments. The hydration state of these subjects is not well-explained; however, in our supine and WI experiments water loss was not repleted. In previous experiments in which water loss was repleted [4, 12], $\dot{Q}$ remained elevated, and the diuresis persisted over a 4-hour period. In these experiments $\dot{Q}$ was sustained at a high level during WI in spite of a decrease in SV. The effect of partial rehydration during microgravity might be to support the cardiac stretch which could lead to the continuation of the diuresis. Assuming that this tissue fluid loss is maximal, the second phase diuresis could result in a net loss of PV. This postulate needs further investigation; however, there is indisputable evidence that in some cases a microgravity environment, by relieving the stresses of gravity, allows adaptive mechanisms to lapse, resulting in what has been termed cardiovascular deconditioning.

Table II. Resting cardiovascular response to increased G_z

		+1 G_z	+2 G_z	+3 G_z
$\dot{V}_{O_2}$, liters · min^{-1}	a	0.29	0.32	0.35
	b	0.25	0.29	0.40
$\dot{Q}$, liters · min^{-1}	a	7.3	5.9	5.6
	b	5.3	4.4	4.3
SV, ml	a	105	66	50
	b	70	47	46
HR, beats · min^{-1}	a	68	89	115
	b	76	98	115
$\bar{P}a$, mm Hg	a	95	107	115
	b	–	–	–
$(Ca–\bar{C}v)_{O_2}$, liters O_2 · l_b^{-1}	a	4.1	5.4	8.1
	b	4.8	7.1	8.4

a = Average data from refs 6, 13, 20, 23, and 25; b = average data from our laboratory for the erect posture.

Increased Gravitational Force (+G_z)

When going from the supine to erect posture, gravity pulls 200–500 ml of blood into the dependent limbs, resulting in a decrease in $\dot{Q}$ and $\bar{P}a$ and an increase in HR. Under normal conditions, the drop in $\bar{P}a$ is not sufficient to lead to orthostatic intolerance. If an individual has a pathological condition or altered cardiovascular reflexes as occurs in the adaptation to microgravity, the effect of gravity may lead to orthostatic intolerance. To this end, studying normal subjects in an increased G_z environment may provide insight into the feedback mechanisms involved in the prevention of or tolerance to orthostatic hypotension. Many studies of G_z tolerance have been conducted; however, relatively few have measured cardiovascular variables during steady state adjustment to increased G_z [6, 13, 20, 23, 25]. Data from these studies are combined with data from our studies in table II. Inasmuch as man can only sustain 3 G_z when unassisted by a G-suit or straining, only data at 1, 2 and 3 G_z are presented.

As indicated in table II, there is an increase in $\dot{V}_{O_2}$ with increasing G-load; this increase is most dramatic at 3 G_z. SV is markedly reduced at 2 and 3 G_z when compared to 1 G_z; this results in a decreased $\dot{Q}$ in spite of the dramatic increase in HR. The decreased $\dot{Q}$ is offset by a dramatic increase in TPR as $\bar{P}a$ actually increases at 2 and 3 G_z when compared to 1 G_z and the

Table III. Resting cardiovascular responses to prolonged exposure to $+G_z$

Variable	$+G_z$	Exposure time				
		4 min	12 min	20 min	28 min	32 min
$\dot{V}_{O_2}$, liters · min^{-1}	2	0.24	0.26	0.28	0.29	–
	3	0.41	0.49	0.61	–	–
$\dot{Q}$, liters · min^{-1}	2	4.4	4.5	4.4	4.4	–
	3	5.6	5.0	4.6	–	–
SV, ml	2	51	48	44	51	–
	3	47	35	32	–	–
HR, beats · min^{-1}	2	87	94	99	86	–
	3	120	142	140	–	–
$(Ca–C\bar{v})_{O_2}$, liters O_2 · l_b^{-1}	2	5.4	5.8	5.2	6.6	–
	3	7.3	9.8	13.3	–	–

arterio-venous oxygen difference $(Ca\text{-}C\bar{v})_{O_2}$ is much greater to meet the metabolic demands. At first glance, body position at $+G_z$ did not make a difference; however, the decrease in SV or $\dot{Q}$ and increase in HR are greater in the erect than in the seated position. This difference is presumably due to the greater degree of venous pooling in the erect than in the seated position. The cardiovascular adjustment to 2 and 3 G_z can apparently overcome the increased stress of gravity as the cardiovascular system appears to be in steady state with the only compromise being a reduced cardiovascular reserve. This reduced reserve could become a limitation when the subject is asked to exercise.

In spite of the apparent adjustment to increased G_z discussed above, it is well known that subjects cannot sustain $+G_z$ for very long. We attempted to expose 6 subjects to 32 min resting experiments at 1 and 3 G_z. The data from these experiments are presented in table III. The $+2$ G_z protocol was tolerated for 20–28 min, while $+3$ G_z was tolerated for only 12–20 min by which time the subjects developed narrowing peripheral vision. The subjects appeared to maintain their initial adaptations to $+G_z$. Resting $\dot{V}_{O_2}$ increased with exposure time, especially at 3 G_z, while $\dot{Q}$ was sustained at a level lower than that at 1 G_z until just prior to the decompensation when $\dot{Q}$ decreased ($\sim$20%). HR increased as a function of G_z exposure time up to near maximal exposure time when it decreased. Linnarsson [20] has shown that $\bar{P}a$ is increased at $+G_z$ initially; however, as exposure time increases, there is a decrease of $\bar{P}a$ resulting in an inability of the circulatory system to

support the heart-brain pressure gradient, resulting in inadequate brain perfusion. There is a progressive fall in SV and increase in HR during $+G_z$; however, the decrease in $\bar{P}a$ is much greater than would be expected from the decreased $\dot{Q}$ alone. This suggests that the initial increase in TPR cannot be sustained at either 2 or 3 G_z.

A possible countermeasure to the initial and/or progressive decrease in SV during $+G_z$ exposures could be the muscle-pumping action to increase the VR and therefore SV. In early studies [6, 23], it was suggested that low levels of exercise supported the cardiovascular system during increased G_z; it was already well known that straining maneuvers assist G_z tolerance [2, 10, 17]. No studies, however, follow the cardiovascular variables over a period of constant G_z. We used low levels of exercise ($\dot{V}_{O_2}$ = 0.6–1.0 liters · min^{-1}) during 32 min of 2 and 3 G_z. All 6 subjects completed 32 min at 2 and 3 G_z. with a $\dot{Q}$ that was 10–15% above rest and a HR not significantly different from rest at $+G_z$. Both HR and $\dot{Q}$, and presumably $\bar{P}a$, were maintained for the entire 32 min. It would appear that muscle and abdominal/thoracic pumping assisted VR sufficiently to increase $\dot{Q}$ and maintain the increased value for the exposure period.

Adaptation to Work

Although low levels of exercise during $+G_z$ experiments might be useful, their effectiveness during weightlessness remains to be investigated. In addition, the balance between increased VR due to muscle pumping and the increased demand for muscle blood flow and $\dot{Q}$ at increased and decreased G_z should be examined at higher workloads. Data are presented in table IV for the cardiovascular responses to exercise at 0-G (supine), +1 and 3 G_z.

Under 1 G_z conditions, $\dot{Q}$, HR and $\bar{P}a$ increase linearly with $\dot{V}_{O_2}$ until their maximal values are reached. Under simulated 0 G_z (supine), resting is higher than 1 G_z, HR is lower and $\bar{P}a$ is similar. As $\dot{V}_{O_2}$ rises, $\dot{Q}$, HR and $\bar{P}a$ increase in the 0 G_z condition; however, the differences between 0 and 1 G_z disappear at exercise levels of ~2.0 liters $O_2 \cdot min^{-1}$. When compared to 1-G_z values, $\dot{Q}$ is lower at rest and at all levels of exercise at 3 G_z, while HR is significantly greater; $\bar{P}a$ is also elevated. The delivery of O_2 to tissues is increased in all G_z conditions by increased SV and HR; however, under $+G_z$ conditions, HR dominates while under 0 G_z, SV plays a greater role. The subjects appear to adapt to exercise under all G_z conditions, but the

Table IV. Cardiovascular responses to exercise at 0 G, +1 G_z and +3 G_z for seated exercise from the literature (a) and for our erect exercise data (b)

Variable	$\dot{V}_{O_2}$, liters · min^{-1}			
	G_z	rest	1.0	2.0
$\dot{Q}$, liters · min^{-1}	0	7.3	12	15
	1	6.3	11	16
	3a	5.6	10	–
	3b	4.8	8	13
HR, beats · min^{-1}	0	68	90	137
	1	72	99	134
	3a	115	150	–
	3b	115	148	172
$\bar{P}a$, mm Hg	0	94	106	122
	1	95	105	125
	3a	115	125	–
	3b	–	–	–

mechanisms of the adjustments are different. For example, at a $\dot{V}_{O_2}$ of 1.0 liters · min^{-1}, the $(Ca\text{-}C\bar{v})_{O_2}$ is 8, 9.1, and 12 liters O_2/1 blood for 0, 1, and 3 G_z, respectively. At the higher workload $(Ca\text{-}C\bar{v})_{O_2}$ was 13, 13, and 15 for 0, 1 and 3 G_z, respectively. As higher workloads are achieved, the increased VR due to the supine posture is no longer evident, while on the other hand, the decreased VR due to $+G_z$ becomes a major limitation to $\dot{Q}$. The limit to the adjustment of the cardiovascular system can be considered to be the maximal aerobic power. Previous work has shown that the $\dot{V}_{O_2}$ max in the supine position is 10–15% lower than in the erect position in spite of the greater SV at lower workloads [5, 24, 28].

On the other hand, it is obvious from table IV that the maximal $\dot{V}_{O_2}$ at 3 G_z is significantly lower than at 1 G_z (~40%). In spite of the limitations of increased G_z on the cardiovascular system, exercise can be carried out at least at modest workloads while the response of the cardiovascular system at 0 G_z is not appreciably different than at 1 G_z. It should be noted, however, that at low exercise levels ($\dot{V}_{O_2} < 1.0$ liters · min^{-1}) 3 G_z can be tolerated for 30–45 min while at higher workloads ($\dot{V}_{O_2} > 1.0$ liters · min^{-1}), G_z tolerance time is reduced to 16–24 min. This would suggest that the cardiovascular system is not in a true steady state. Further investigation into this area is needed.

Adapation to the space environment requires first the adjustment to weightlessness and then re-adaptation to gravity. Astronauts will be required to perform work in both a weightless environment and under increased gravitational force. The ability to adapt to exercise over time is critical to successful adaptation. Exercise during weightlessness is apparently not limited at submaximal levels. As discussed above, under increased G_z conditions, there is an initial adjustment of the cardiovascular system; however, in a relatively short period of time, the cardiovascular system cannot meet the demands of G_z plus exercise. It is not apparent that these observations could be applied to a 1 G_z environment following adaptation to weightlessness; however, the response to 1 G_z after adaptation to weightlessness seen as cardiovascular deconditioning would appear similar to that made in going from 0 to 1 G_z. In studies by Convertino [8, 9], exercise performance after 10 days of HDT or bed rest (0 G_z) demonstrated that $\dot{V}_{O_2}$ max was lower (~8%), submaximal HR was greater (~5%), and the anaerobic threshold lower. This author concluded that PV lost during adaptation to weightlessness resulted in the observed cardiovascular deconditioning. Interestingly, Convertino's findings are qualitatively similar to the data where 2 G_z is compared to 1 G_z.

In summary, it appears that man is capable of adapting to a weightless environment. Although the application of the Gauer-Henry hypothesis to this adjustment needs to be reconsidered, there appears to be a decrease in PV as well as in sympathetic tone after 2–3 days of 0 G_z. The role of the hydration state of the subjects needs further investigation, as there appears to be complete adjustment to 0 G_z within 8 h without a decrease in PV (when subjects are allowed to dehydrate mildly). In actual space flight, space motion sickness is experienced at least mildly by most astronauts. This may alter the hydration state for the first few days, and once relieved by rehydration, may lead to the decrease in PV that is typically reported. Hydration changes account for the inability to re-adapt to gravity upon return to earth and may lead to the inability to function when landing on other planets. Apparently exercise, per se, does not serve as an effective countermeasure. Even though $+G_z$ tolerance was improved, it did not persist long enough to maintain the steady state.

Given sufficient adjustment time, man can re-adapt to gravity; however, the dynamics of the adjustments of the cardiovascular system need further investigation. It is clear that, if man is to successfully adapt to the space environment and return from it, we must prevent cardiovascular deconditioning that develops during the weightless period by either uncov-

ering and interfering with the mechanism that causes it or by developing effective countermeasures. These could presumably be used not only during weightlessness but also during re-entry. By identifying and using such countermeasures, we may be able to effectively extend man's interplanetary initiatives as he learns to cope with gravitational force in much the same way as he deals with other environmental variables.

References

1 Arborelius, M.J.; Balldin, U.I.; Lilja, B.; Lundgren, C.E.: Hemodynamic changes in man during immersion with head above water. Aerospace Med. *43:* 592–598 (1972).

2 Balldin, U.I.: Physical training and +Gz tolerance. Aviat. Space envir. Med. *55:* 991–992 (1984).

3 Balldin, U.I.; Lundgren, C.E.G.; Lundvall, J.; Mellander, S.: Changes in the elimination of ^{133}xenon from the anterior tibial muscle in man induced by immersion in water and by shifts in body position. Aerospace Med. *42:* 489–493 (1971).

4 Begin, R.; Epstein, M.; Sackner, M.; Levinson, R.; Dougherty, R.; Duncan, D.: Effects of water immersion to the neck on pulmonary circulation and tissue volume in man. J. appl. Physiol. *40:* 293–299 (1976).

5 Bevegard, S.; Holmgren, A.; Jonsson, B.: Circulatory studies in well-trained athletes at rest and during heavy exercise, with special reference to stroke volume and the influence of body position. Acta physiol. scand. *57:* 26–50 (1963).

6 Bjurstedt, H.; Rosenhamer, G.; Wigertz, O.: High-G environment and response to graded exercise. J. appl. Physiol. *25:* 713–719 (1968).

7 Claybaugh, J.R.; Pendergast, D.R.; Davis, J.E.; Akiba, C.; Pazik, M.; Hong, S.K.: Fluid conservation in athletes. Responses to water intake, supine posture and immersion, J. appl. Physiol. *61:* 7–15 (1986).

8 Convertino, V.A.; Goldwater, D.J.; Sandler, H.: Effect of orthostatic stresses on exercise performance after bedrest. Aviat. Space envir. Med. *53:* 652–657 (1982).

9 Convertino, V.A.; Montgomery, L.D.; Greenleaf, J.E.: Cardiovascular responses during orthostatics. Effect of an increase in V_{O_2} max. Aviat. Space envir. Med. *55:* 702–708 (1984).

10 Cooper, K.H.; Leverett, S.: Physical conditioning versus +Gz tolerance. Aerospace Med. *37:* 462–465 (1966).

11 Echt, M.; Lange, L.; Gauer, O.H.: Changes of peripheral venous tone and central transmural venous pressure during immersion in a thermoneutral bath. Pflügers Arch. *352:* 211–217 (1974).

12 Epstein, M.: Renal effects of head-out water immersion in man. Implications for an understanding of volume homeostasis. Physiol. Rev. *58:* 529–581 (1978).

13 Farhi, L.E.; Linnarsson, D.: Gravity, exercise and cardiac output. Proc. int. Union Physiol. Sci. *XII:* 715 (1977).

14 Gauer, O.H.: In Graybiel, Recent advances in the physiology of whole body immersion in basic environmental problems of man in space, pp. 31–39 (Pergamon Press, New York 1976).

15 Gauer, O.H.; Henry, J.P.: Neurohormonal control of plasma volume; in Guyton, Cowley, Int. Rev. Physiol. Cardiovascular Physiology II, pp. 145–190 (University Park Press, Baltimore 1976).
16 Gauer, O.H.; Henry, J.P.; Behn, C.: The regulation of extracellular fluid volume. A. Rev. Physiol. *32:* 547–595 (1979).
17 Greenleaf, J.E.; Morse, J.T.; Barnes, P.R.; Silver, J.; Keil, L.C.: Hypervolemia and plasma vasopressin response during water immersion in man. J. appl. Physiol. *55:* 1688–1693 (1983).
18 Katkov, V.E.; Chestukhin, V.V.; Nikolayenko, E.M.; Rumgantser, V.V.; Crozdev, S.V.: Central circulation of a normal man during 7 day head down tilt and decompression of various body parts. Aviat. Space envir. Med. *54:* 524–530 (1983).
19 Krasney, J.A.; Pendergast, D.R.; Powell, E.; McDonald, B.W.; Plewes, J.L.: Regional circulatory responses to head-out water immersion in anesthetized dog. J. appl. Physiol. *53:* 1625–1633 (1982).
20 Linnarsson, D.: Exercise and arterial pressure during simulated increase of gravity. Acta physiol. scand. *74:* 50–57 (1968).
21 Michel, E.L.; Rummel, J.A.; Sawin, C.F.; Buderer, M.C.; Lem, J.D.: Results of Skylab medical experiment M 171-metabolic activity; in Johnston, Dietlein, Biomedial results from Skylab; NASA SP-377, pp. 372–387 (National Aeronautics and Space Administration, Washington 1977).
22 Nixon, J.V.; Murray, G.; Bryant, C.; Johnson, R.L.; Mitchell, H.J.; Holland, B.; Golez-Savcher, C.; Verane-Marini, P.; Blomqvist, G.: Early cardiovascular adaptation to simulated zero gravity. J. appl. Physiol. *46:* 541–548 (1979).
23 Nunneley, S.A.: Gas exchange in man during combined $+G_z$ acceleration and exercise. J. appl. Physiol. *40:* 491–495 (1976).
24 Pendergast, D.; Shindell, D.; Cerretelli, P.; Rennie, D.W.: Role of central and peripheral adjustments in oxygen transport at the onset of exercise. Int. J. Sports Med. *14:* 160–170 (1980).
25 Rosenhamer, G.: Influence of increased gravitational stress on the adaptation of cardiovascular and pulmonary function to exercise. Acta physiol. scand. *276:* 61–82 (1967).
26 Sandler, H.: Cardiovascular responses to weightlessness and ground-based simulations; in Proc. of the Workshop of the European Space Agency, Toulouse 1982, ESA SP-180, pp. 107–146.
27 Shiraki, K.; Konda, N.; Sagawa, S.; Claybaugh, J.A.; Hong, S.K.: Cardiorenal-endocrine responses to head-out immersion. J. appl. Physiol. *60:* 176–183 (1986).
28 Stenberg, J.; Astrand, P.O.; Ehbolm, B.; Royce, J.; Saltin, B.: Hemodynamic response to work with different muscle groups, sitting and supine. J. appl. Physiol. *1967:* 61–70.
29 Thornton, W.E.; Hoffler, G.W.; Rummel, J.A.: Anthropometric changes and fluid shifts under weightlessness; in Johnston, Dietlein, Biomedical results from Skylab; NASA SP-377, pp. 330–338 (National Aeronautics and Space Administration, Washington 1977).

D.R. Pendergast, Ed.d., Department of Physiology, 124 Sherman Hall,
State University of New York at Buffalo, Buffalo, NY 14214 (USA)