ORIGINAL RESEARCH

Cardiovascular Deconditioning and Venous Air Embolism in Simulated Microgravity in the Rat

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Background: Astronauts conducting extravehicular activities undergo decompression to a lower ambient pressure, potentially resulting in gas bubble formation within the tissues and venous circulation. Additionally, exposure to microgravity produces fluid shifts within the body leading to cardiovascular deconditioning. A lower incidence of decompression illness in actual spaceflight compared with that in ground-based altitude chamber flights suggests that there is a possible interaction between microgravity exposure and decompression illness. *Hypothesis:* The purpose of this study was to evaluate the cardiovascular and pulmonary effects of simulated hypobaric decompression stress using a tail suspension (head-down tilt) model of microgravity to produce the fluid shifts associated with weightlessness in conscious, chronically instrumented rats. *Methods:* Venous bubble formation resulting from altitude decompression illness was simulated by a 3-h intravenous air infusion. Cardiovascular deconditioning was simulated by 96 h of head-down tilt. Heart rate, mean arterial blood pressure, central venous pressure, left ventricular wall thickening and cardiac output were continuously recorded. Lung studies were performed to evaluate edema formation and compliance measurement. Blood and pleural fluid were examined for changes in white cell counts and protein concentration. *Results:* Our data demonstrated that in tail-suspended rats subjected to venous air infusions, there was a reduction in pulmonary edema formation and less of a decrease in cardiac output than occurred following venous air infusion alone. Mean arterial blood pressure and myocardial wall thickening fractions were unchanged with either tail-suspension or venous air infusion. Heart rate decreased in both conditions while systemic vascular resistance increased. *Conclusions:* These differences may be due in part to a change or redistribution of pulmonary blood flow or to a diminished cellular response to the microvascular insult of the venous air embolization.

OPERATIONALLY IMPORTANT medical challenges of manned spaceflight include microgravity-induced cardiovascular deconditioning, total body calcium loss, and the risk of decompression illness (DCI) during extravehicular activity (EVA). Altitude DCI deserves particular attention because it is a preventable complication, but one that can have serious consequences if left unattended (26). Evaluation of the interaction between microgravity exposure and decompression illness is appropriate in view of plans for extended duration missions and an overall increase in the number of EVA's required for construction of the Space Station. It is intended that such investigation will lead to a better understanding of the interplay between DCI and the human cardiovascular system in a microgravity environment.

Decompression illness results from the formation and growth of gas bubbles within the tissues and venous blood; e.g., venous air emboli (VAE). Associated symptoms can range from mild skin itching or simple joint pain to central nervous system involvement and even cardiovascular collapse. The pathophysiology of DCI may also affect the lungs as the venous bubbles obstruct the pulmonary microcirculation (8,10) decreasing cardiac output (CO), increasing pulmonary vascular pressures and altering lung fluid balance. The preponderance of actual symptoms, however, involve limb pain that is presumably caused by extravascular bubbles.

The adaptation of the cardiovascular system to the microgravity environment (cardiovascular deconditioning) appears to be due in part to a cephalad fluid shift, and has been extensively studied in the conscious rat (22). Astronaut EVA's have brought into question the potential relationship between cardiovascular deconditioning and hypobaric DCI. Compared with careful ground-based studies conducted in hypobaric chambers, there is a lower incidence of DCI in space during the astronaut EVA's than would be predicted (25). These studies have established the predicted incidence of DCI expected, both in relation to the final altitude following a direct or staged decompression, and subsequent to washout of tissue inert gas (e.g., nitrogen) by oxygen prebreathing prior to decompression (14). In addition, other factors such as exercise, ambulation, time at altitude and individual susceptibility have been examined (1). The interaction between hypobaric decompression and the deconditioned cardiovascular system has not been previously evaluated. The purpose of this study was to assess pulmonary and hemodynamic effects of simulated microgravity and hypobaric decompression illness in the conscious rat.

METHODS

All experiments and procedures were approved by the Institutional Animal Care and Use Committee at The University of Texas Medical School at Houston. Six groups of rats were studied. Groups 1 and 2 were used to assess the hemodynamic effects of tail-suspension with and without venous air infusion, whereas groups 3–6 were used for biochemical analysis. Each animal served as its own control.

Cardiovascular Function (Groups 1–2)

Instrumentation: The rats were anesthetized with halothane, intubated and ventilated under isothermic conditions. A left parasternal thoracotomy was performed and the pericardium exposed and sectioned. A 20-MHz pulsed Doppler flow probe was then placed around the ascending aorta for cardiac output measurement. The displacement probe used to measure left ventricular wall thickening was sutured to the left ventricular wall and an 18-gauge thoracic drain was positioned until closure of the thorax.

The ultrasonic flow probe leads were tunneled to the dorsum of the neck for externalization and the surgical wounds closed. Polyvinyl catheters were placed into the abdominal aorta via the femoral artery and the jugular vein for measurement of arterial blood pressure and central venous pressure. The catheters were also tunneled to the neck dorsum. The lungs were reinflated under vacuum and the wounds were infiltrated with bupivacaine (0.5%) for post-operative analgesia. Antibiotic therapy (gentamycin 5 mg·kg⁻¹ IM) was initiated for a minimum of 5 ds. The animals were weighed daily and inspected for signs of infection.

The single-crystal pulsed Doppler technique for measurement of changes in myocardial wall thickening fraction has previously been described in detail (16). The displacement modules operated at a pulse repetition frequency of 8 KHz and an ultrasonic frequency of 20 MHz. The pulsed Doppler system measured displacement of myocardial tissue through a sample volume with the use of a single crystal that alternately serves as transmitter and receiver. Briefly, it operates by integrating the velocity of the various myocardial layers that pass back and forth through a range-gated sample volume located within the myocardium at a fixed distance from the epicardial surface where the crystal is attached to the myocardial wall. Thickening fraction is defined as the maximum excursion recorded during systole, divided by the sample volume depth. The range was set at a 2–3 mm depth near the endocardium.

The pulsed Doppler system for measurement of cardiac output in small animals has also been described in detail (17). Briefly, a linear relationship between true volume flow and Doppler frequency shift has previously been demonstrated in a variety of blood vessels with diameters ranging from 1–11 mm. At a pulse repetition frequency (PRF) of 125 KHz, the Doppler system resolves frequency shifts of up to 62.5 KHz (PRF/R) at a maximum range (R) from 0.6–6 mm and a spatial range of 0.3 mm. True blood flow was calculated from the maximum Doppler frequency shift using the standard relationship described by Ishida et al. (18). The Doppler flow probes were manufactured according to previously described techniques (16,17).

Hemodynamic measurements: All hemodynamic variables [e.g., heart rate (HR), mean arterial (MAP) and central venous pressure (CVP), left ventricular wall thickening (WT), and cardiac output (CO)] were processed with the multichannel pulsed Doppler flow/dimension system and were continuously displayed on a Gould physiograph. The wall thickening fraction (TF%) was calculated as $100 \times SE/R$ (SE, the systolic excursion and R, the range-gate depth). Systemic vascular resistance (SVR) was calculated as MAP/CO.

Experimental protocols: Group 1, (n = 8) designated VAE, was exposed to 3 h of venous air infusion. We elected to use VAE given as a continuous infusion to simulate the prolonged bubbling that is reported with hypobaric decompression exposures used to simulate an astronaut EVA. In these cases, VAE are detected with Doppler ultrasound probes for periods lasting several hours during the period of decompression. Injecting venous gas very slowly in the rat simulated that particular feature of decompression effects. Although this technique is well established for a number of species (8), little data are available for the rat. After hemodynamic parameters stabilized, rats received the venous air infusions into the central venous catheter at a rate of 0.015 ml·kg⁻¹·min⁻¹ for 180 min. Cardiovascular data were recorded at 15, 30, 45, 60, 120 and 180 min during venous air infusion and at 15, 30, 45, 60, and 120 min and 24 h post infusion.

Group 2 (n = 8), designated TS-VAE, experienced cardiovascular deconditioning by tail-suspension with a 30° head-down tilt. The tail suspension model has previously been described in detail (21) and is widely used by investigators to simulate the fluid shifts commonly observed upon exposure to microgravity. Briefly, rats were fitted with a flexible foam-tape cast applied to the proximal half of the tail. The cast was attached to a swivel and the rats were suspended in a 30° head-down tilt. This apparatus allowed the rats to rotate in a 360° arc using their forelimbs, and permitted free access to food and water in a light/dark cycled environment. Following 96 h tail-suspension, and while maintained in the suspended position, the animals were infused with venous air for 3 h as described above.

Pulmonary Measurements (Groups 3–6)

Group 3 consisted of normoactive controls; group 4, tail-suspension only; group 5, VAE only; and group 6, tail-suspension-VAE. The rats in groups 5 and 6 received venous air infusions, as described above. Immediately post infusion, the animals were anesthetized with pentobarbital sodium (50 mg IP). An arterial blood sample was collected anaerobically for blood gas and plasma protein analysis. The animals were euthanized by exsanguination and the lungs were removed for the following measurements.

Pulmonary edema measurement: The amount of blood-free extravascular fluid (edema) formation was measured using a modified method of Pearce (23) to account for the residual blood volume in the organ. The extravascular lung water (EVLW) was expressed as the extravascular fluid to dry weight ratio.
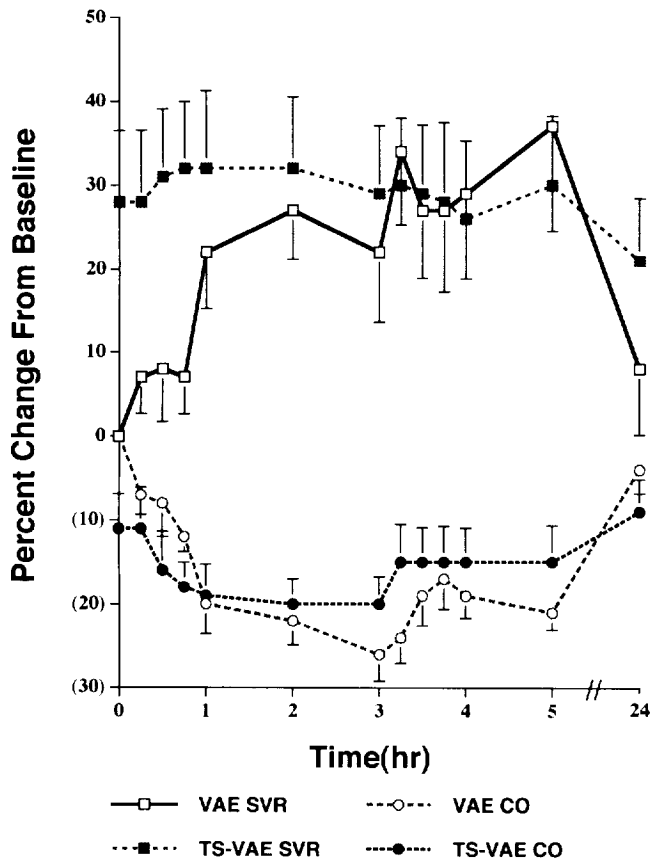
Fig. 1. Systemic vascular resistance (SVR) and cardiac output (CO) are plotted as percent change from baseline over time for the TS-VAE and VAE groups. Venous air infusion started at Time = 0 and continued until Time = 3 h TS-VAE SVR values were significantly elevated from the onset of tail-suspension and throughout the air infusion. SVR was also elevated in the VAE group during the air infusion and for 2 h recovery. Cardiac output was decreased significantly from baseline during the air infusion in both groups, and significantly different from each other at 180 min infusion.

Lung compliance: For quasi-static lung compliance measurement, the lungs were isolated, degassed under vacuum (29), placed in a heated humidified chamber and connected via a tracheal catheter to an infusion/withdrawal pump and an airway pressure transducer. The lungs were inflated to 30 cm H_2O at a rate of 20 ml·min^{-1}, and equilibrated for 15 min while maintaining 30 cm H_2O pressure. Inflation/deflation pressure-volume curves were then collected. The compliance measurements were taken from the deflation limb of the curve between 30% and 70% of total lung capacity.

Bronchoalveolar lavage (BAL): The trachea was cannulated and the airways were lavaged with 10 ml cold normal saline (5°C). This procedure was repeated 6 times for a total lavage volume of 60 ml. The BAL samples were pooled. Total BAL protein was assayed using the Lowry method with modification for the presence of lipid from the 60 ml pooled lavage (19). BAL hemoglobin levels were measured using a modified benzidine assay.

Cell counts: Total white cell counts were performed on BAL, pulmonary and arterial blood and pleural fluid using a Neubauer hemocytometer with EDTA stabilization. Differential cell counts were performed with microscopic survey using Wright-Geimsa stain.

Data Analysis

Data were analyzed using ANOVA with Dunnett's correction for the individual comparisons in the biochemistry studies. The cardiovascular data were analyzed using a 2-way ANOVA. Individual comparisons were analyzed using Student's *t*-test with Bonferroni correction. Significance was considered at $p < 0.05$.

RESULTS

Cardiovascular measurements: In the TS-VAE group, SVR increased significantly by 28% from the onset of tail-suspension and remained elevated throughout the venous air infusion (**Fig. 1**). In the VAE group, SVR increased significantly by 23% above baseline within 60 min of venous air infusion and remained elevated for 5 h. SVR in the VAE group returned to baseline within 6 h. CVP remained unchanged in both groups.

Cardiac output in the VAE group decreased by 26% by the end of the 180 min venous air infusion (Fig. 1). This was significantly greater than the TS-VAE group, whose CO decreased by 9%. In the TS-VAE group, however, tail suspension alone caused a 11% decrease (nonsignificant) in CO prior to the venous air infusion. Decreases in CO from baseline were significant at 1, 2 and 3 h of venous air infusion for both TS-VAE and VAE groups, versus control. CO returned to baseline within 24 h after venous air infusion. Arterial blood pressure was not significantly altered by either the tail-suspension or VAE. WT remained unchanged in response to tail-suspension or venous air infusion.

TS-VAE and VAE rats showed a similar response in
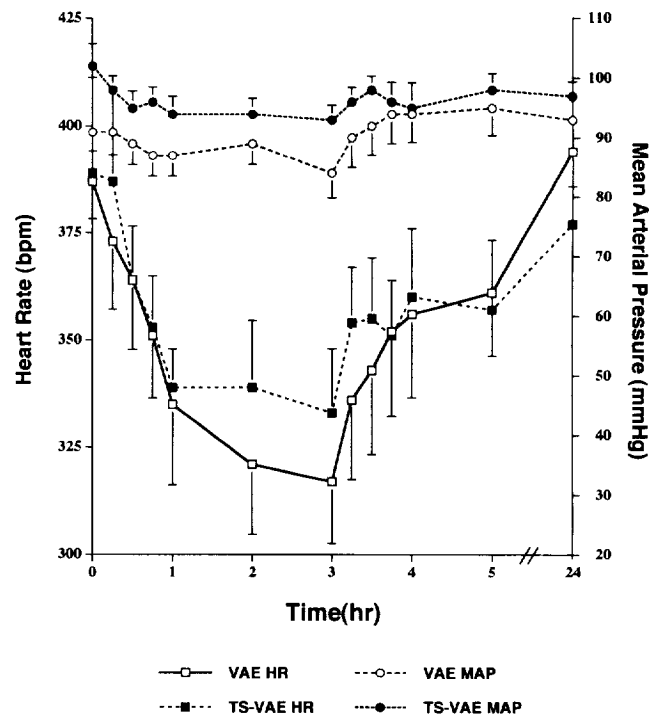
Fig. 2. Heart rate (HR) and mean arterial pressure (MAP) are plotted as a function of time. Venous air infusion started at Time = 0 and continued until Time = 3 h. MAP values were not significantly changed. HR decreased significantly in both groups during the air infusion.

TABLE I. LUNG EDEMA, COMPLIANCE AND BLOOD GAS DATA.

	Control	TS	VAE	TS-VAE
EVLW	4.18 ± 0.21	3.80 ± 0.41	6.02 ± 0.68*§	4.78 ± 0.73*
Compliance	2.20 ± 0.22	2.10 ± 0.21	2.00 ± 0.08	1.90 ± 0.17
Pa_{O_2} (mmHg)	89.90 ± 5.18	91.00 ± 8.83	77.20 ± 7.78	75.70 ± 16.86
Pa_{CO_2} (mmHg)	44.90 ± 2.35	50.30 ± 3.75	47.20 ± 2.33	47.50 ± 5.80
pH	7.35 ± 0.02	7.25 ± 0.02	7.24 ± 0.04	7.27 ± 0.03

Data are represented as mean ± S.D.
* $p < 0.05$ compared with control.
§ $p < 0.05$ compared with TS-VAE.
EVLW = extravascular lung water ratio.

heart rate to venous air infusion. HR decreased significantly by the first hour of air infusion and remained decreased until the end of the infusion. The differences between the two groups were not significant. In both groups, HR returned to baseline within 24 h (**Fig. 2**).

Pulmonary measurements: In the VAE group, lung wet-to-dry ratio was increased significantly as compared to the three other groups. TS-VAE rats also showed a significant increase in lung wet-to-dry ratio as compared to the control group. Tail suspension alone did not cause a significant increase in extravascular lung water. Arterial blood gas values, pH, Pa_{CO_2} and Pa_{O_2} were not different from control value in any experimental group, although the decrease in Pa_{O_2} and the increase in Pa_{CO_2} seen in the VAE and TS-VAE groups were consistent with the pathologic pulmonary changes reported with DCI. Pulmonary compliance was unchanged in all experimental groups (**Table I**).

Total arterial white blood cell counts (WBC) were unchanged in all experimental groups (**Table II**, top). Pulmonary arterial blood white cell counts were significantly increased, however, in the VAE group versus controls, but neither the TS or the TS-VAE groups showed significant differences from the control group. Pleural fluid white blood cell count was decreased in the VAE group versus the controls. This appeared to be a dilutional effect due to an increase in pleural fluid volume. BAL WBC counts were unchanged. Arterial blood neutrophil counts in both the TS-VAE and the VAE groups were significantly increased over control. Pulmonary and systemic arterial neutrophil counts were significantly increased in both the VAE and the TS-VAE groups versus the control group (Table II). Pleural fluid neutrophil counts were increased significantly in all experimental groups versus the control.

Pleural fluid protein concentration was increased in the VAE group versus the controls, but there was no significant change in either the TS or the TS-VAE groups. Plasma protein levels were unchanged (Table II, bottom). BAL protein was unchanged in both TS-VAE and in VAE rats (Table II).

DISCUSSION

Previous reports describing cardiopulmonary responses to significant decompression illness included hypotension, pulmonary hypertension, pulmonary edema, decreased lung compliance, hemoconcentration and hypoxemia (3,7,10,12,15). In similar conditions, Bove et al. observed increased systemic vascular resistance, tachycardia, increased central venous pressure and decreased cardiac output (3). Cardiovascular symptom expression and severity depend primarily on the extent of the decompression injury, and hence the degree of venous bubble formation. In our experimental design, the use of a venous air dose standardized by weight insured that the venous gas insult was uniform throughout the study population. Our findings demonstrate an attenuation in the response to both pulmonary edema formation and the decrease in cardiac output with simulated weightlessness and venous embolization (TS-VAE group).

TABLE II. CELL COUNTS AND PROTEIN DATA.

	Control	TS	VAE	TS-VAE
Total WBC (cells·mm⁻¹)				
Arterial	7920 ± 386	7831 ± 838	7975 ± 1448	6066 ± 1051
Pulmonary	7970 ± 427	8903 ± 1074	13139 ± 1242*	10457 ± 1840
BAL	674 ± 53	371 ± 61	638 ± 141	880 ± 185
Pleural	54462 ± 5050	60133 ± 9019	20539 ± 3005*	46169 ± 10354
Neutrophils (percentage of total WBC)				
Arterial	14.90 ± 1.34	29.60 ± 6.34	70.10 ± 2.99*	68.10 ± 6.28*
Pulmonary	11.27 ± 0.96	24.10 ± 5.17	55.10 ± 4.38*	52.95 ± 31*
BAL	0.68 ± 0.19	2.60 ± 1.66	3.20 ± 1.52	2.30 ± 0.75
Pleural	1.63 ± 0.24	4.60 ± 0.54*	11.40 ± 0.32*	10.60 ± 1.09*
Protein (mg·dl⁻¹)				
Plasma	48.30 ± 2.09	51.92 ± 1.66	50.45 ± 2.33	49.15 ± 2.85
BAL	7.08 ± 0.60	8.55 ± 0.50	20.06 ± 4.92	14.91 ± 8.72
Pleural	18.64 ± 1.14	16.25 ± 1.27	27.68 ± 0.97*	13.77 ± 2.81

WBC = white blood cells.
Data are represented as mean ± S.D.
* $p < 0.05$ compared with control.

Several mechanisms may be involved in the response of the deconditioned cardiopulmonary system to venous air embolization. The changes in cardiac output may be due either to fluid shifts or to a direct effect on myocardial function. The effects on the lungs include vascular distension, changes in volume, changes in ventilation to perfusion matching and potential changes in diffusing capacity (28). Additional factors may include mediator-induced changes in vascular tone and endothelial permeability (27), lymphatic recruitment (30), as well as hypoxic pulmonary vasoconstriction.

In the present study, there was a slight but non-significant decrease in cardiac output with tail suspension, a finding that in magnitude is consistent with other studies (4). This change could be expected to prolong recovery from a venous gas insult, possibly by decreasing pulmonary blood flow and thereby reducing the rate of gas embolus washout. However, venous air infusion produced an acute decrease in cardiac output in all animals, whereas in the TS-VAE group, the decrease in cardiac output was significantly less than the decrease experienced by the VAE alone group. It might therefore be inferred that even though both groups demonstrated approximately the same total decrease in cardiac output, the initial decrease experienced by the TS-VAE group occurred prior to the VAE and therefore may have allowed for compensatory changes to occur.

The result of a higher cardiac output in the TS-VAE group (after first hour of air infusion) relative to the VAE group may have allowed an increase in pulmonary perfusion enabling deeper penetration of the emboli into the pulmonary vascular tree. The emboli would thus block a smaller segment of the pulmonary vasculature and therefore obstruct less of the pulmonary blood flow. This could result in a lower pulmonary artery pressure and less edema formation. A higher cardiac output might also increase the diffusion of gas from the emboli into the surrounding blood by exposing the emboli to a greater volume of blood per unit time, resulting in a more rapid rate of resolution (20). This process might also be influenced by accumulation of protein and coagulation products at the blood-bubble interface (24). Measurement of left ventricular myocardial wall thickening fraction, an indicator of myocardial contractility, demonstrated no direct effects of either tail suspension or venous air emboli on the myocardium.

We observed that the systemic vascular resistance was increased initially in the TS-VAE group, in response to tail-suspension, with no further increase during venous air embolization. An analogous response in the pulmonary circulation, especially when venous bubbles obstruct pulmonary vessels, could result in a smaller increase in pulmonary artery pressure with venous air embolization than would be expected, leading to a decrease in pulmonary edema formation. Direct evidence for such a mechanism is unavailable.

The decrease (nonsignificant) in HR with the VAE in both groups was consistent with other reports of VAE or decompression in dogs (6,7). Possible mechanisms may include a bundle branch block if the insult was sufficient to cause myocardial ischemia (13) or a reflex-mediated response where the right heart chamber volumes are overwhelmed due to the venous gas challenges (5). Both

of these mechanisms are usually reported with large VAE doses, however, that are sufficient to cause systemic hypotension.

Simulated microgravity has been shown to improve ventilation to perfusion ratio via central fluid shifts (14). This might improve tolerance to pulmonary air emboli both by maximally recruiting the pulmonary vasculature and by optimizing the lung's ability to exchange gas, thereby eliminating the gas via the alveoli. This too could result in a decrease in pulmonary edema formation, as seen in our studies.

Indirect effects of venous air bubbles include neutrophil activation and mediator release (9,27) resulting in modification of vascular permeability and tone with consequent pulmonary edema formation. Evidence of this process was observed in all animals exposed to venous air infusion. Arterial, pleural and pulmonary arterial neutrophil percentages were increased in both the TS-VAE and the VAE groups, but only the VAE group showed significant changes in systemic arterial and pleural total white blood cell count, suggesting a possible mechanism for increased mediator activation in the VAE group as compared to the TS-VAE group. The decreased BAL and pleural protein values further suggest that the permeability of the microvascular and alveolar membranes were less affected in the tail-suspension VAE rats than the VAE alone.

Conclusions drawn from the present study are subject to certain limitations. It has been shown by other investigators that venous gas emboli will be distributed according to the gravity vector. However, Chang et al. reported that the size of the bubble, the speed of the blood flow and the size of the vessels do play a role. The authors found that, under most circumstances, the emboli followed the higher branch of a bifurcation (11). While the current model mimics the greater homogeneity in blood flow seen in microgravity, one would still expect a preponderance of emboli in the "upper" lobes. Additionally, the bubbles produced by venous air embolization are larger than DCI-induced bubbles, consequently some differences in pulmonary arterial occlusion patterns and possibly in surface-area dependent processes such as cellular activation and lung fluid balance might be expected. Although the results of the present study reflect some cardiopulmonary changes, clinical symptoms of DCI involving limb pain are usually attributed to extravascular gas.

Several theories have been reported to explain the observed low incidence of hypobaric decompression illness during EVA. A decrease in the formation of micronuclei due to reduced stress on the muscles, tendons and ligaments of the joints as a consequence of reduced activity (exposure) in the microgravity environment has been described (25). Additional reasons may involve actual reporting discrepancies related to operational factors such as crew motivation, redirected attention, masking of subtle pain, misinterpreting actual symptoms or actual reluctance to report DCI (2). The results of the present study do suggest, however, that more than one process may be responsible for the decreased incidence of DCI (at least in terms of cardiopulmonary effects), including an overall increase in tolerance to the combined effects of simulated microgravity and decompression.

REFERENCES

1. Arthur D, Margulies R. The pathophysiology, presentation, and triage of altitude-related decompression sickness associated with hypobaric chamber operation. Aviat Space Environ Med 1982; 53:489-94.
2. Bagian JP. Decompression sickness driven operational problems in space flight. In: Pilmanis AA, ed. USAF Special Report: Hypobaric Decompression Sickness. Brooks AFB, TX: Air Force Systems Command AL-SR-1992-0005 1992:329-32.
3. Bove A, Hallenbeck J, Elliott D. Circulatory responses to venous air embolism and decompression sickness in dogs. Undersea Biomed Res 1974; 1:207-20.
4. Brizzee B, Walker B. Altered baroreflex function after tail suspension in the conscious rat. J Appl Physiol 1990; 69:2091-6.
5. Brown AM. Cardiac reflexes. In: Berne RM, Sperelakis N, Geiger SR, eds. Handbook of physiology. The cardiovascular system. The heart. Bethesda, MD: American Physiology Society. 1979 Sect. 2, Vol I, chap. 19, pp. 677-98.
6. Butler BD. Cardiopulmonary effects of decompression bubbles: physiology of bubbles in the pulmonary and systemic circulation. USAF Special Report: Hypobaric Decompression Sickness. Pilmanis AA, ed. Brooks Air Force Base, TX: Air Force Systems Command, 1992; pp 53-82.
7. Butler BD, Kemper GB. Cardic pressure changes with venous gas embolism and decompression. Brooks Air Force Base, TX: Air Force Material Command, Armstrong Laboratory, U.S. Air Force Tech. Report. AL/AO-TR-0176; 1994; 1-24.
8. Butler B, Conkin J, Luehr S. Pulmonary hemodynamics, extravascular lung water and residual gas bubbles following low dose venous gas embolism in dogs. Aviat Space Environ Med 1989; 60:1178-82.
9. Butler BD, Little T. Effects of venous air embolism and decompression on thromboxane and leukotriene levels in dogs. Undersea Hyperbaric Med 1994; 215:21-2.
10. Catron P, Flynn E, Yaffe L, et al. Morphological and physiological responses of the lungs of dogs to acute decompression. J Appl Physiol 1984; 57:467-74.
11. Chang H, Delaunois L, Boileau R, Martin R. Redistribution of pulmonary blood flow during experimental air embolism. J Appl Physiol 1981; 51:211-7.
12. Davis J, Sheffield P, Schuknecht L, et al. Altitude decompression sickness: hyperbaric therapy result in 145 cases. Aviat Space Environ Med 1977; 48:722-30.
13. Durant TM, Long J, Oppenheimer MJ. Pulmonary (venous) air embolism. Am Heart J 1947; 33:269-81.
14. Engel L. Effect of microgravity on the respiratory system. J Appl Physiol 1991; 70:1907-11.
15. Fryer DL. Subatmospheric decompression sickness in man. Slough, UK: Technivision Services, 1969: AGARDograph No. 125, pp 37-57.
16. Hartley C, Lewis R, Ishida T, Chelly J, Entman ML. High frequency pulsed Doppler measurements of blood flow and myocardial dimensions in conscious animals. Proceedings of Working Conference on Applicability of New Technology to Biobehavioral Research. Bethesda, MD: NIH Publication #84-1654, 1984: 95-105.
17. Haywood J, Shaffer R, Fastenow C, Fink G, Brody M. Regional blood flow measurement with pulsed Doppler flowmeter in conscious rat. Am J Physiol 1981; 241:H273-8.
18. Ishida T, Lewis R, Hartley C, Entman M, Field J. Comparison of hepatic extraction of insulin and glucagon in conscious and anesthetized dogs. Endocrinology 1983; 112:1098-1109.
19. Lees M, Pasman S. Modification of the Lowry procedure for the analysis of proteolipid protein. Anal Biochem 1972; 47:184-92.
20. Martin RW, Ashleman B, Colley PS. Effects of cardiac output on the clearance of air emboli from the superior vena cava. Anesthesiology 1984; 60:580-6.
21. Morey E. Space flight and bone turnover: correlation with a new model of weightlessness. Bioscience 1979; 29:168-72.
22. Musacchia X, Steffen J, Dombrowski J. Rat cardiovascular responses to whole body suspension: head-down and non-head-down tilt. J Appl Physiol 1992; 73:1504-9.
23. Pearce M, Yamashita J, Beazell J. Measurement of pulmonary edema. Circ Res 1965; 16:483-8.
24. Philp R, Inwood M, Warren B. Interaction between gas bubbles and components of the blood: implications in decompression sickness. Aerosp Med 1972; 43:946-53.
25. Powell M, Norfleet W, Waligora J, Kumar K, Robinson R, Butler B. Modifications of physiological processes concerning extravehicular activity in microgravity. Warrendale, PA: SAE. SAE Technical Paper Series 9413334; 1994.
26. Rudge F, Shafer M. The effect of delay on treatment outcome in altitude-induced decompression sickness. Aviat Space Environ Med 1991; 62:687-90.
27. Seibert A, Thompson W, Taylor A, Wilborn W, Barnard J, Haynes J. Reversal of increased microvascular permeability associated with ischemia-reperfusion: role of cAMP. J Appl Physiol 1992; 72:389-95.
28. Staub N. Pulmonary edema due to increased microvascular permeability to fluid and protein. Circ Res 1978; 43:143-51.
29. Stengel P, Frazer D, Weger K. Lung degassing: an evaluation of two methods. J Appl Physiol 1980; 48:370-5.
30. Uhley H, Leeds S, Sampson J, Friedman M. Role of pulmonary lymphatics in chronic pulmonary edema. Circ Res 1962; 9:966-70.