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A COMPARISON OF THE MECHANISMS OF COLD- AND MICROGRAVITY-INDUCED FLUID LOSS

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The physiological mechanisms involved in the diuresis and overall fluid loss associated with exposure to cold or microgravity environments are compared. Although the data available to thoroughly describe these responses are yet unavailable, some similarities in the changes caused by these different stimuli are apparent. The central mechanism common to the physiological responses to both these environments is an increase in central blood volume. The common endpoint of a net loss in body fluids and electrolytes is also clear. Differences in the response patterns also exist. The differences are evaluated, and the value of additional research in both areas, with potentially mutually beneficial results, is considered. Keywords: Low temperature;

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SUMMARY PAGE

THE PROBLEM

Thermal stress can degrade performance and health of naval and Marine Corps personnel under operational conditions in cold weather. One problem related to this degradation is dehydration associated with cold-induced diuresis. Fluid loss is also a significant problem in the microgravity environment of space flight. The possibility that these two entirely different environmental changes or stresses might have common pathways in their physiological effects was suggested as a comparative study to foster better understanding of both mechanisms.

FINDINGS

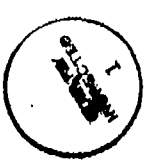
A literature review of fluid loss in these two diverse environments revealed several significant similarities in the physiological responses leading to the common endpoint of fluid and electrolyte loss through diuresis and natriuresis. Differences in the responses were also noted, although the data necessary to thoroughly describe these mechanisms are not yet available.

RECOMMENDATIONS

The advantages of using the cold-exposed model in future research to better understand the responses to both environments was considered. Open communication and exchange of data among the investigators concerned with these fluid-loss mechanisms is recommended.

Acknowledgments

We are indebted to CAPT J.O. Houghton, MC, USN, for the suggestion to consider the similarities in the physiology of fluid loss in these environments.



INTRODUCTION

The possibility that two entirely different environmental changes or stresses--namely cold temperatures and the microgravity of space flight--might have common pathways in their physiological effects was suggested as a comparative study to foster better understanding of both mechanisms (J.O. Houghton, CAPT, MC, USN, personal communication, 1987). A review of the literature confirmed the similarities of the physiological reactions and adaptation to these stresses and also suggested some interesting differences (1-3).

This report summarizes the mechanisms of fluid loss due to cold or microgravity exposure and highlights points of comparison. Relevant questions include the role of hydrostatic fluid factors, arginine vasopressin (AVP, previously known as antidiuretic hormone or ADH), and renin-angiotensin system changes, as well as the possible role of natriuretic peptides. Although our current interest is in dry, cold environments, coldwater immersion may involve similar effects, as the buoyancy of water immersion is a partial analogue of microgravity (4).

The validity of a hypothesis that cold- and microgravity-induced diuresis might share a common mechanism was partially tested in 1952 by Bader and his associates (5). They found that cold-induced diuresis was significantly greater in human subjects when supine as compared to standing. The diuresis was reduced after physical exercise, presumably because of a redistribution of blood to the muscles from the central volume. Although a change in hormonal secretion by the pituitary was postulated as a mechanism, the recently discovered role of atrial natriuretic factor (ANF) in fluid balance suggests a more complex, multifaceted endocrine involvement in the cold-induced fluid loss. To elucidate the mechanism involved, we have begun to investigate the multiple hormonal interrelationships in primates exposed to acute, dry cold. In the case of microgravity, data from space crewmembers may yield an understanding of a common physiological reaction to these quite different environmental stresses.

THEORY OF COLD-INDUCED FLUID LOSS

One of the early events in human reaction to cold exposure is a constriction of the peripheral vasculature and a resultant increase in central blood volume. The latter may stimulate carotid and cardiac pressoreceptors with the possible increase in ANF and the suppression of vasopressin secretion leading to diuresis. Peripheral vasoconstriction is under the control of both central and peripheral effector mechanisms. Circulating catecholamine levels increase in cold-exposed subjects (6,7) and appear to play an important role in fluid losses that remains to be fully defined. In rats, 6-hydroxydopamine prevents both the increase in mean arterial pressure and the diuresis that results from cold exposure (8). This suggests that the cold-induced diuresis can be eliminated by blocking the sympathetic nerve responses involving norepinephrine.

Although very little data are available on ANF, plasma renin activity (PRA), angiotensin, or aldosterone during cold exposure, a strong consensus of early studies (9-11) and more recent ones (8,12,13) indicates that cold exposure reduces circulating levels of AVP. The stimulus for these changes in AVP secretion may be fluid shifts, or it may be osmolality changes that result from the fluid loss. Morgan et al. (8) reported a water diuresis in the rat that was independent of solute excretion but

mediated by suppression of vasopressin. Their results supported the hypothesis that this reduction in AVP secretion by the pituitary was due to changes in blood pressure (8), but other studies have suggested that AVP secretion during cold exposure may depend on changes in blood osmolality (14) or involve direct effects of blood temperature on neurons in the brain as well (12,13).

Based on the limited data available, the physiological events leading to cold-induced diuresis may be summarized to include the following:

1) peripheral vasoconstriction
2) increased central blood volume
3) stimulation of atrial and carotid pressure receptors
4) suppression of AVP release from the neurohypophysis
5) changes in other factors such as:
   - increased metabolic clearance rate of AVP
   - increased excretion of sodium (natriuresis)
   - activity of renin-angiotensin-aldosterone system
   - secretion of ANF (increase or decrease ?)
   - increased secretion of catecholamines.

Although the physiology of ANF has been examined intensively, its possible role in cold- or microgravity-induced diuresis, which is a logical hypothesis given the increase in central blood volume, has received very little study. The ANF has important effects on both kidney function and blood pressure control (15). It has multiple interactions with the other fluid-balance controlling hormones, particularly the renin-angiotensin-aldosterone system, and is thought to modulate the secretion of vasopressin (15). In fact, ANF and the renin-angiotensin-aldosterone system may act in opposition or function in a negative feedback manner in their effects on renal function and blood pressure control (16). Further, ANF has a number of significant vasoactive properties, which include causing peripheral vasodilation and decreasing mean arterial blood pressure (15). These vasoactive properties may be even more physiologically important than the natriuretic properties of this atrial peptide in the endocrine response to cold or microgravity exposure. A recent study measured the effects of enhanced venous return on ANF secretion and the activity of the renin-angiotensin-aldosterone system during exercise and postural changes (17). The results suggest that ANF release during exercise may be influenced by factors other than hemodynamic stimuli. During exercise, PRA was altered more than ANF by blood volume displacement, and ANF increases did not inhibit aldosterone secretion.

Water immersion (WI) of subjects has been used as a model to study fluid and hormonal shifts that result from increases in central blood volume. In both human and animal subjects, WI markedly increases ANF and decreases PRA, aldosterone, and vasopressin (18). Another model used to test the physiological responses to increased central blood volume is volume loading, either with hypotonic, isotonic, or hypertonic solutions. The effects of volume loading on ANF and the renin-angiotensin-aldosterone system are similar to those of WI, but the effect differs depending on the osmolality of the infused solution (14). Even as ANF levels change in association with the natriuresis of acute volume expansion (19), changes in ANF alone do not appear to account for the natriuresis resulting from volume expansion (20).

In dealing with cold exposure, one recent study reported a decrease in ANF and an increase in aldosterone in rats exposed to acute, dry cold (21). These data were actually in contrast to the anticipated result that increased central blood volume would cause an increase in ANF and a decrease in activity of the renin-angiotensin-aldosterone system. Thus, the hormonal involvement in cold- or microgravity-induced fluid loss is likely to be complex.

THEORY OF MICROGRAVITY-INDUCED FLUID LOSS

In 1979, Alvioli et al. (22) listed key events in the physiology of fluid shift in space:

1) reflex peripheral vasodilation
2) suppression of the renin-angiotensin-aldosterone system
3) suppression of antidiuretic hormone (ADH)
4) increased secretion of humoral natriuretic substances
5) reduced thirst.

Leach described the body's reaction to the cephalad shift of fluid as a response by the stretch receptors in the left atrium as though this fluid shift represented an increase in total blood volume. The result is a compensatory loss of water, sodium, and potassium from the renal tubules (3,23-25). The mechanism is thought to be neural, humoral, and hydrostatic in nature. The initiation of the mechanism of fluid loss in microgravity is thought to be hydrostatic, as reported by Norsk in studies of central venous pressure increases during short periods of weightlessness (1). Leach reports the hormonal aspects of the mechanism of fluid loss in both Skylab and Space shuttle crewmembers (1,3,23,24,26). She also discusses the possible importance in fluid loss of the decreases in catecholamine production by the sympathetic nervous system that were observed during space flight (3,23). The physiological mass measurements on Skylab tend to add credence to this hypothesis. A rapid weight loss during the first few days in space is quickly reversed postflight, suggesting fluid loss as the mechanism (26). An increase in ADH in blood and urine after return to Earth supports this hypothesis nicely.

Early diuresis, predicted by the above theory, has been measured in bedrest studies (27,28), which model the microgravity environment. The mechanism in space, however, has been unclear due to the difficulty in obtaining early data, a marked reduction in water intake, and possible masking by early motion sickness experienced by many crew members (26). Leach and Rambaut reported that the nine Skylab crewmen decreased water intake by 700 ml/day during the first 6 days in flight (27). Urine volume decreased 400 ml/day during the same period resulting in a net loss of fluid. Reporting on a 175-day flight of the Salyut-6-Soyuz, Egorov observed in-flight increases in urinary output of sodium, potassium, chloride, an in-flight decrease in ADH, and a reduced postflight excretion of sodium (29).

Additional observations that verify fluid shift include photographic evidence of periorbital puffiness, facial edema, and thickening of the eyelids. Other indications include a fullness of veins in the head and neck (26) and an in-flight decrement in calf girth up to 30% that rapidly reverts to preflight values upon return to Earth (30). Leach describes the response to microgravity as having on early dynamic phase leading to a resetting of set points and a stable adaptive stage (25). The magnitude of the fluid shift is thought to be 1.5-2 liters from the lower extremities. The rate peaks within

24 h and reaches a plateau within 3-5 days. Soviet data have a similar pattern. Gasenko reports a plateau on the 12th in-flight day but describes fluctuations in leg volume with a wavelike course of loss and recovery over 140-, 175-, and 185-day missions (28).

SIMILARITIES AND DIFFERENCES IN THE MECHANISMS

Table 1 lists the comparative qualities of the physiological mechanisms involved in microgravity- and cold-induced fluid loss.

Table 1. Comparative Features of Cold- and Microgravity-induced Fluid Loss.

Physiological action	Cold-induced diuresis	Microgravity-induced diuresis
Reflex peripheral vasodilation	no	yes
Peripheral vasoconstriction	yes	no
Increased central blood volume	yes	yes
Suppression of renin-angiotensin aldosterone system	?	yes
Suppression of ADH	yes	yes
Increased secretion of humoral natriuretic substances	?	?
Reduced thirst	?	yes
Role of catecholamines	?	?

Body fluid is redistributed, and the end result is a loss of both water and electrolytes during exposure to cold or microgravity environments. The central mechanism common to the physiological responses to both these environments is an increase in central blood volume. Whether or not intermediate physiological responses to the two different environments are also similar remains to be seen. Further analysis of these hormone concentrations in cold and microgravity environments is necessary to resolve questions about their relative roles. Experiments are planned to further investigate the role of ANF in the fluid dynamics of crew response to microgravity in space. We have an experimental effort in progress to determine the role of ANF and other hormones in the mammalian response to cold, dry temperatures in a monkey model. Our approach is to determine the basic patterns and interrelationships of fluid-balance hormones and fluid-loss characteristics during cold exposure. Following a determination of these responses, the mechanism of these changes will be explored by altering the baseline physiological conditions through infusion of hormones, or volume loading, or by other pharmacological means. The information gained from this approach will be helpful in developing countermeasures to cold-induced fluid loss and in understanding the similar response in space.

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