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The combination of cold exposure and exercise performed in this environment elicits profound physiological responses. These include increases in metabolic heat production and vasoconstriction in order to maintain body temperature, changes in fluid balance, and changes in substrate mobilization in order to fuel increased metabolic activity. Many of these physiological responses are associated with endocrine secretion and concentration changes. It is acknowledged that differences in plasma levels as a result of cold exposure could be due to secretion, clearance, and volume of distribution that cannot be differentiated in these studies. Most of the studies examining the role of cold exposure on hormone responses have been completed during resting exposure and these are still relatively few in number. The interaction of exercise and cold on the endocrine system is even less studied. The primary purpose of this chapter is to survey the endocrine responses to exercise-cold stress in humans. Animal studies will not be considered. Sedentary cold exposure responses are also reviewed to provide background information and for use as a point of comparison to exercise studies. Table 1 presents the hormones that will be discussed and presents a general overview of the changes caused by resting and exercise-cold stress.

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Chapter 33

Human Endocrine Responses to Exercise–Cold Stress

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Introduction

The combination of cold exposure and exercise performed in this environment elicits profound physiological responses. These include increases in metabolic heat production and vasoconstriction in order to maintain body temperature, changes in fluid balance and changes in substrate mobilization in order to fuel increased metabolic activity. Many of these physiological responses are associated with endocrine secretion and concentration changes. It is acknowledged that differences in plasma levels as a result of cold exposure could be due to secretion, clearance and volume of distribution that cannot be differentiated in these studies. Most of the studies examining the role of cold exposure on hormone responses have been completed during resting exposure and these are still relatively few in number. The interaction of exercise and cold on the endocrine system is even less studied. The primary purpose of this chapter is to survey the endocrine responses to exercise–cold stress in humans. Animal studies will not be considered. Sedentary cold exposure responses are also reviewed to provide background information and for use as a point of comparison to exercise studies. Table 33.1 presents the hormones that will be discussed and presents a general overview of the changes caused by resting and exercise–cold stress.

Catecholamines

When people are exposed to the cold, metabolic heat production increases via shivering thermogenesis and cutaneous blood flow is decreased, limiting heat loss to the environment. These physiological responses are mediated by the sympathetic nervous system (SNS) in order to defend against a drop in body temperature. Plasma norepinephrine (NE) concentrations are used as an acute marker of SNS activity since NE is released from peripheral nerve endings during acute cold exposure. NE exerts its thermoregulatory effects via β-adrenergic receptors on skeletal muscle (metabolic heat production) and α-adrenergic receptors on smooth muscle (vasoconstriction). Plasma NE increases two to sixfold during sedentary cold exposure (Wilkerson *et al.* 1974; Johnson *et al.* 1977; O'Malley *et al.* 1984; Wang *et al.* 1987; Weiß *et al.* 1988; Frank *et al.* 1997; Armstrong 1998; Castellani *et al.* 1998, 1999a, 1999b) and also increases urinary NE excretion (Arnett & Watts 1960; Lamke *et al.* 1972), a 24-h marker of SNS activity. The weighting/contribution factor of core and skin temperature for the NE response to resting cold exposure is ~ 2 : 1, that is ~ 67% of the increase in NE is due to decreases in core temperature and 33% is due to the fall in skin temperature (Frank *et al.* 1999).

NE concentrations increase during exercise–cold stress (Castellani *et al.* 2001), not surprisingly, but the responses between cold and temperate environments are likely dependent on whether core temperature declines. When high intensity exercise (~ 60% $\dot{V}O_{2max}$) was performed for 2 h, plasma NE was not different between a dry, 15°C environment and a wet, windy, 5°C environment (Weller *et al.* 1997a). However, as soon as the intensity was lowered to less than 30% $\dot{V}O_{2max}$, and core temperature subsequently fell, NE concentrations were 240% higher in

Table 33.1 Summary of hormone responses during exercise–cold stress.

Hormone	Physiological effects	Response to resting cold exposure	Response to exercise–cold stress	Other observations
Catecholamines	↑ Cutaneous vasoconstriction ↑ Heat production ↑ Glycogenolysis ↑ Lipolysis	↑ 2–6-fold	↑ At exercise intensities below 40% $\dot{V}o_{2max}$ compared to temperate; ↑ Epinephrine during long duration exercise (> 6 h)	
T_3 & T_4	↑ Metabolism vasodilator	↓ In 30 min to 3-h exposures	↑ Levels after 6–9 h at 30% $\dot{V}o_{2max}$	
Plasma renin activity	Converts angiotensinogen to angiotensin I	↓ Or no change	↓ Following graded exhaustive exercise	
Arginine vasopressin	↑ Water conservation	↓ In water or air	No change with graded exercise	
Atrial natriuretic peptide	↓ Sodium reabsorption	No change	↑ After graded exercise to exhaustion	
Cortisol	Catabolic hormone; promotes lipolysis vasoconstriction	↑ Or no change	↑ After 5-h cold–wet exposure at 30% $\dot{V}o_{2max}$; ↓ After 1-h swimming at 68% $\dot{V}o_{2max}$	Responses may be related to time of day & intensity-duration interaction
Insulin	Anabolic hormone; promotes glucose uptake	No change when core temperature does not fall; ↓ when core temperature ↓ by 1°C	↓ With cold-water exercise but not different from temperate; no change during cold-air exercise	
Glucagon	Catabolic hormone; ↑ glycogenolysis ↑ gluconeogenesis ↑ lipolysis	No change	No change	
Growth hormone	Anabolic hormone; ↑ free fatty acid mobilization ↑ gluconeogenesis	No change	No change after 1-h swimming at 68% $\dot{V}o_{2max}$	β_2-Adrenergic stimulation may suppress GH levels; released in pulsatile manner
Prolactin	Lactation	↓ During and after exposure	Small increase with exercise–cold stress but lower than exercise–heat stress	Possible marker of cold acclimation
Testosterone	Anabolic hormone; spermatogenesis	No change	Variable responses depending on exercise stress	
Luteinizing hormone	Promotes testosterone estrogen & progesterone secretion	Chronic exposure to cold lowers basal values	No effect from acute exercise	

T_3, triiodothyronine; T_4, thyroxine.

the cold environment. However, if the exercise intensity is relatively high (60% $\dot{V}O_{2max}$) but performed over an extended duration (4 h) that causes core temperature to fall, plasma NE concentrations are 45% higher in a cold–wet environment. Galbo *et al.* (1979) found that swimming in 21°C water for 1 h (rectal temperature decreased by 0.8°C) increased NE concentrations 87% above that compared to swimming in 27°C. As well, when both core and skin temperatures are low during submaximal and maximal exercise, absolute NE responses are the greatest (Bergh *et al.* 1979).

The interaction between skin temperature and exercise intensity may also influence plasma NE concentrations during exercise–cold stress when there are no differences in core temperature. Plasma NE is doubled in 5°C air (versus 21°C) during cycle ergometry at 50 W but not at 150 W (Stevens *et al.* 1987). Furthermore, Weller *et al.* (1997b) found that when exercise initially begins at a low intensity (30% $\dot{V}O_{2max}$) in a cold–wet environment, plasma NE concentrations are three-times higher after 2 h even though rectal temperature is not different compared to dry–temperate conditions. Skin temperatures in these low intensity studies were 5–8°C lower in the cold. However, when cycle exercise is performed at 50–100% $\dot{V}O_{2max}$, there are no differences in NE concentrations between temperate and cold environments (Quirion *et al.* 1989; Anderson & Hickey 1994).

The effect of cold exposure on epinephrine (EPI) is less clear. In contrast to NE, plasma EPI responses do not appear to increase during resting cold-water immersion (Weiß *et al.* 1988), cold-saline infusion (Frank *et al.* 1997) and cold-air exposure (Wang *et al.* 1987; Armstrong 1998). However, Frank *et al.* (2002) found that EPI levels increased when the core temperature decreased by 1.0°C using cold-saline infusion (skin temperature remained normal). That study did not collect peripheral venous (antecubital) blood but instead sampled central venous blood and suggested this source is closer to the site of EPI release and is not affected by clearance. They suggest that the lack of an EPI response in other studies is due to the sampling methodology. If EPI is increased during cold exposure, it likely would increase shivering thermogenesis and fat mobilization via β-adrenergic receptors.

Plasma EPI concentrations during exercise–cold stress, compared to temperate conditions, are elevated if core temperature falls, similar to plasma NE. EPI levels were elevated after 4–6 h of cold–wet exposure, compared to a 15°C dry condition when the rectal temperature difference was 0.4°C (Weller *et al.* 1997b). Likewise, Galbo *et al.* (1979) observed 71% higher EPI levels after swimming in 21°C water versus 27°C. On the other hand, if core temperatures are not different between cold and temperate environments, EPI concentrations are the same (Weller *et al.* 1997a, 1997b) or lower (Parkin *et al.* 1999).

It is important for the reader to be aware that cold acclimatization might influence the NE response to exercise–cold stress, although no studies have directly tested this. However, there have been several studies that have examined the effect of cold acclimation on NE levels during resting cold exposure.

There are three distinct types of cold acclimation: habituation, metabolic and insulative acclimation (Young 1996). Cold habituation, characterized by blunted shivering and vasoconstrictor responses, typically occurs after cold exposures not severe enough to elicit falls in body core temperature. Metabolic acclimatization is defined as a higher metabolic activity. This has been observed in one study and occurred after moderate cold exposure for 6 weeks. Insulative acclimatization is induced by repeatedly lowering the body core temperature, which causes greater peripheral vasoconstriction, lower skin temperatures and perhaps a shift in the onset of shivering thermogenesis so that shivering does not begin until a lower mean body temperature is reached. When multiple cold-air exposures were used to induce cold habituation (with little fall −0.5°C in core temperature), plasma NE values declined during standardized cold air tests (Hesslink *et al.* 1992; Leppäluoto *et al.* 2001). On the other hand, when 25 cold-water immersions (18°C water) were used for acclimating subjects (causing significant falls in core temperature −1°C) that led to an insulative acclimation (lower core and skin temperatures), plasma NE was significantly higher after acclimation, compared to preacclimation, during a standardized cold-air exposure (Young *et al.* 1986).

Thyroid hormones

The thyroid hormones, triiodothyronine (T_3) and thyroxine (T_4), are very important for maintaining basal metabolism and thermogenesis. The calorogenic effect of these hormones is believed to be caused by increasing energy consumption of the sodium–potassium pump. Also, thyroid hormones have been shown to be vasodilators. Thus, these hormones may affect peripheral heat loss during cold exposure.

Sedentary cold-air exposure (4–10°C) from 30 min to 3 h has no effect on plasma thyroid-stimulating hormone (TSH), T_3 and T_4 levels (Hershman *et al.* 1970; Wilson *et al.* 1970; Nagata *et al.* 1976; Tuomisto *et al.* 1976; Leppäluoto *et al.* 1988). In contrast, several authors (Golstein-Golaire *et al.* 1970; O'Malley *et al.* 1984) have noted increases in these hormones after short-term resting cold exposure whereas others (Solter & Misjak 1989) found that TSH, total T_3, reverse T_3 and total T_4 were all lower following an 8-h work day in a cold environment. Short-term cold stress should not bring about large increases or decreases in plasma concentrations because most of the hormone is bound to plasma proteins that provides a substantial reservoir of thyroid hormone (Goodman 1994).

Only a few studies have examined thyroid hormone responses during controlled exercise–cold stress experiments. The response pattern could be related to a number of factors including exercise duration or intensity. T_4 is elevated following 6–9 h of cold–wet exposure during low intensity exercise (Dulac *et al.* 1987; Castellani *et al.* 2002) whereas T_3 responses did not change or increased. Thyroid hormones likely increased during prolonged exercise–cold stress to support lipid metabolism, since it amplifies β-adrenergic responses of the SNS. Core temperature was not a likely mediator of this effect since it reached only 36.9°C in one study (Castellani *et al.* 2002). TSH was not elevated during these low intensity exercise studies, but increased by 90% during a 30-min moderate intensity performance swim in 20°C water (Deligiannis *et al.* 1993). Likewise, free T_4 levels increased by 46% during cold-water swimming. Whether this effect was a result of central (core) or peripheral (skin) input is not known since these values were not reported. The elevated T_3 and T_4 following long duration exercise–cold stress is more likely due to the exercise stimulus per se, rather than the cold exposure, since acute cold exposure has little effect on these hormones.

Since cold habituation leads to blunted shivering and higher skin temperatures, thyroid hormones could also change since they are involved in thermogenic and vasodilatory responses. Hesslink *et al.* (1992) exposed subjects to 4.4°C air for 30 min twice a day for 8 weeks (80 total exposures). They also supplemented a group of subjects with T_3 to artificially suppress TSH and T_4 levels in order to determine the relative importance of these hormones for inducing cold acclimation. The repeated cold exposure program did indeed induce habituation as demonstrated by reductions in oxygen uptake, mean arterial pressure and plasma NE values subsequent to acute cold exposure. No differences were observed between the supplemental T_3 group (low TSH and T_4) and the non-supplemented group and there were no changes in thyroid hormone concentrations. Similarly, Leppäluoto *et al.* (2001) exposed subjects for 11 straight days for 2 h·day^{-1} in 10°C air and found no changes in T_3, T_4 and TSH, even though skin temperatures were higher after acclimation. Savourey *et al.* (1994) studied eight men who underwent a 1°C cold-air test for 2 h before and after cold acclimation. Acclimation was induced by 20 ice-water immersions to the thigh over a 1-month period and resulted in lower rectal temperatures during cold-air exposure after acclimation, compared to preacclimation. T_3, T_4 and TSH were not different after the acclimation period. These studies demonstrate that thyroid hormones do not have a role in cold acclimation induced over a short-time period.

The pattern observed in fairly short acclimation studies is somewhat different than that seen in personnel over-wintering in Antarctica for 8–12 months. Reed *et al.* (1986, 1988, 1990) characterized that Antarctica residence leads to an elevated TSH response subsequent to thyroid-releasing hormone stimulation, lower T_3 levels and no changes in T_4. Sawhney *et al.* (1995) related lower T_3 values to the period of the Antarctic summer when physical activity levels are high and observed higher T_3 in the

winter, when is was extremely cold and dark. Interestingly, if personnel from Antarctica are given supplemental T_4, declines in cognitive performance are attenuated (Reed *et al.* 2001). Likewise feelings of fatigue and confusion are lessened in the supplemental group. The reader should be aware that Antarctic sojourners are exposed to a multitude of factors including low ambient temperature, extreme light conditions, highly variable physical activity levels, high electromagnetic radiation and isolation. Thus, it is difficult from these studies to discern if the cold per se has an effect on thyroid levels or if it is due to the combination of all these environmental factors.

Thyroid status is classically linked to cold sensitivity, i.e. people with thyroid insufficiency typically complain about feeling cold (Larsen *et al.* 1998). Nagashima *et al.* (2002) recently showed that T_4 concentrations were 29% lower in women who complained about feeling cold, compared to matched controls. Associated with this increased cold feelings were lower finger temperatures and metabolic rates. However, the relative importance of thyroid hormones during acute cold exposure in humans is still not well understood. Surprisingly, there are little data (one subject, Thompson *et al.* 1971) on acute thermoregulatory responses during cold exposure in people who are hypothyroid. After T_4 administration, this subject exhibited a higher oxygen consumption, but a blunted fall in skin temperature, so that the core temperature response was about the same after 2 h in 10°C air. Thus, thyroid hormones appear to have little effect on thermal balance as it simultaneously increases heat production and heat loss.

Fluid regulation

Fluid balance is regulated by several hormones, including renin–angiotensin–aldosterone, atrial natriuretic peptide (ANP) and arginine vasopressin (AVP). These hormones monitor blood volume and plasma osmolality in order to precisely regulate water and electrolyte losses to maintain normal levels. Angiotensin and aldosterone are regulated by the enzyme renin, which is released from the juxtaglomerular cells in the kidney. Renin is regulated by decreased pressure (volume) and decreased sodium and chloride flux in the kidney. Higher angiotensin and aldosterone levels increase sodium and water retention. ANP is released from right-atrium cardiac myocytes in response to high central blood pressure/volume and causes greater sodium and water excretion from the kidney. AVP is released from the posterior pituitary in response to increased plasma osmolality as well as decreases in blood volume sensed by high-pressure (carotid) and low-pressure (right atrium) receptors. AVP directly increases water reabsorption in the collecting duct of the kidney.

Exposure to cold temperatures lowers total body water levels via several mechanisms including cold-induced diuresis (CID), sweating, respiratory water loss, blunted thirst, poor water availability and conscious under-drinking (O'Brien *et al.* 1998). These body water losses are associated with changes in plasma volume and electrolyte concentrations that can have a profound effect on fluid regulatory hormones. Cold exposure also increases central blood volume and right atrial pressure. Exercise causes profound changes in plasma volume and electrolytes. However, relatively few studies have examined fluid regulatory hormones during rest in cold environments, and only one study has examined these responses during exercise.

The most commonly studied effect of cold exposure on body fluid balance is CID. Over 50 years ago, Bader *et al.* (1952) suggested that CID is caused by a fall in AVP levels, subsequent to higher central blood volumes. Administering pitressin, an AVP analog, abolished the higher urine flows observed in the cold, without affecting the glomerular filtration rate, although this has not always been observed (Lennquist 1972). If cold exposure causes an essential water diuresis then plasma tonicity should go up, but it does not. A series of studies (Lennquist *et al.* 1974; Wallenberg & Granberg 1974; Atterhog *et al.* 1975; Knight & Horvath 1985; Deuster *et al.* 1989) demonstrated that urine electrolyte excretion is also elevated with cold exposure suggesting that CID is due to an isosmotic fluid loss. What is not known is whether an elevated renal solute excretion (primarily sodium) leads to water loss, or if cold increases both sodium and water

excretion via mechanisms independent of each other. Some evidence supports that salt losses are primary in CID. When NaCl supplementation was used during a 48-h field exercise (Rogers *et al.* 1964) in extreme cold, 30% less urine was secreted compared to a non-NaCl group even though both groups drank the same amount of water.

Resting studies that have examined fluid-regulatory hormone responses during cold exposure (Segar & Moore 1968; Hiramatsu *et al.* 1984; Hassi *et al.* 1991; Wittert *et al.* 1992; Hynynen *et al.* 1993; Nakamitsu *et al.* 1994; Jansky *et al.* 1996; Arjamaa *et al.* 1999, 2001; Sramek *et al.* 2000) commonly find that plasma renin activity either does not change or falls, plasma aldosterone and ANP are not changed and AVP levels decrease. Urinary sodium excretion was elevated in these studies. Cold-induced natriuresis was not mediated via changes in aldosterone or ANP, but possibly through the paracrine influence of urodilatin, an ANP-like compound secreted from the kidney (Nakamitsu *et al.* 1994; Bestle *et al.* 1999). Lower AVP concentrations lead to increased water excretion, secondary to increases in central blood volume and right atrial pressure.

Only one study has examined fluid-regulatory hormones during exercise–cold stress. Therminarias *et al.* (1992) found lower plasma renin activity and higher ANP levels during graded exercise to exhaustion in 10°C air, compared to 30°C air. No differences were observed for AVP. The higher ANP and lower plasma renin activity levels in 10°C air were due to greater cardiac filling caused by a central redistribution of blood volume.

Cortisol

Plasma cortisol modulates many physiological processes that are important for responding to cold exposure. These include increasing resting energy expenditure, inhibiting vasodilation, increasing free fatty acid availability for substrate utilization, and functioning of the SNS. Cortisol secretion is regulated by adrenocorticotrophic hormone (ACTH), which is secreted by the anterior pituitary. Plasma cortisol concentrations are lowest in the evening hours and highest just before awakening. This point is important as stress-related changes in cortisol concentrations are blunted when plasma levels are highest in the morning.

The effects of resting cold exposure on plasma cortisol concentrations are equivocal as both increases (Suzuki *et al.* 1967; Wilkerson *et al.* 1974; Kauppinen *et al.* 1989; Hennig *et al.* 1993; Tikuisis *et al.* 1999) and no change (Golstein-Golaire *et al.* 1970; Wilson *et al.* 1970; Ohno *et al.* 1987; Wittert *et al.* 1992; Frank *et al.* 1997; Marino *et al.* 1998) have been observed.

Exercise–cold stress studies, as with resting studies, show both increases and decreases. Potential reasons include the exercise duration and the time of day. Galbo *et al.* (1979) studied swimming exercise, whereas McMurray *et al.* (1994) and Castellani *et al.* (2002) used cycle ergometry and walking, respectively. Only one study corrected for changes in plasma volume and reported the use of standardized blood draws controlling for factors such as arm position and posture (Castellani *et al.* 2002). Differences in the change in core temperature between Galbo *et al.* (1979) (–0.8°C) and McMurray (1994) (0°C) could explain why cortisol declined in the swimming study but not following cycling. However, Castellani *et al.* (2002) also observed a fall in core temperature (0.2–0.5°C) and found that exercise–cold stress increased cortisol concentrations. Perhaps the long duration cold exposure (~ 5 h) combined with moderate intensity exercise (50% $\dot{V}O_{2max}$) leads to a greater stress response compared to high intensity, short duration exercise bouts (Galbo *et al.* 1979). Pandolf *et al.* (1992) also did not find any changes in cortisol after exercising in cold water for 50 min at 50% $\dot{V}O_{2max}$. Interestingly, in Castellani *et al.* (2002), cortisol increases occurred in the absence of an ACTH response suggesting that cortisol secretion during prolonged exercise–cold stress is ACTH-independent.

Time of day may be the most important factor in determining whether plasma cortisol changes as a result of exercise–cold stress. Castellani *et al.* (2002) studied their subjects in the late afternoon/early evening when cortisol levels are typically lower and stress responses are discriminated easier, whereas other studies exercised their subjects in the morning, when cortisol levels are high. Also, if exercise studies are initiated in the morning and are fairly

long and not intense (Ainslie *et al.* 2002), lower cortisol concentrations post-cold exposure could just reflect the normal diurnal rhythm. Utilization of proper control groups will allow for correct interpretation of exercise–cold stress studies.

Insulin and glucagon

Insulin and glucagon are the two primary fuel regulatory hormones. Insulin is an anabolic hormone that promotes fuel storage throughout the body whereas glucagon acts on the liver to secrete glucose and β-hydroxybutyrate. Since moderate sedentary cold exposure increases plasma glucose oxidation by 138%, muscle glycogen oxidation by 109% and lipid oxidation by 376% (Haman *et al.* 2002), it would appear that these hormones would have a role in mobilizing substrates to fuel shivering thermogenesis.

Plasma insulin does not appear to change as a result of acute cold exposure where there are minimal changes in core temperature (Martineau & Jacobs 1989; Vallerand *et al.* 1995; Tipton *et al.* 1997; Haman *et al.* 2002; Koska *et al.* 2002), but during a 10°C cold-water immersion that elicited a 1°C decline in core temperature and higher metabolic rates, Jacobs *et al.* (1984) found a 32% decline in insulin concentrations. Cold-air exposure does appear to enhance insulin sensitivity or insulin responsiveness in skeletal muscle. Following an intravenous glucose tolerance test, plasma glucose falls more rapidly with lower plasma insulin concentrations in 10°C air compared to a temperate environment (Vallerand *et al.* 1988).

Exercise–cold stress studies are difficult to interpret due to different research designs, exercise modes and intensities. It appears that, unlike rest, lower insulin levels are not related to lower core temperatures during exercise (Galbo *et al.* 1979) and that the response is not mediated via β-adrenergic receptors (Lehtonen *et al.* 1984). Ten weeks of cold-water exposure causes insulin to fall during light intensity cold-water swimming (Hermanussen *et al.* 1995). It is unclear if this is related to changes in body temperatures or to the higher basal insulin concentrations. The catabolic state also may influence the insulin response. Following a 36-h fast, insulin was significantly lower at baseline, but exercise–cold stress caused no further decline in serum insulin levels after fasting whereas insulin fell 68% in the non-fasting trial (Weller *et al.* 1998). Similarly, 5 h of exhaustive exercise lowers baseline insulin levels and remains low during subsequent cold–wet exposure (Tikuisis *et al.* 1999).

Glucagon concentrations have been shown to both increase and decrease as a result of resting cold exposure. In the two studies that found increased levels (Seitz *et al.* 1981; Tikuisis *et al.* 1999), plasma hormone values were not corrected for plasma volume changes (decreased by 9–10%), which could account for the higher values. In the other studies, conducted either in cold water or cold air, glucagon did not change as a result of cold exposure (Jacobs *et al.* 1984; Martineau & Jacobs 1989; Vallerand *et al.* 1995).

There are limited data on the response of glucagon to exercise–cold stress. During moderate intensity swimming in cold water (21°C) that elicited a 0.8°C decline in core temperature (Galbo *et al.* 1979), glucagon levels did not change during or after exercise, while the same exercise elicited an increase in glucagon in warm water. These findings suggest that either cold-water exercise suppresses glucagon release or that a threshold core temperature needs to be reached before glucagon secretion occurs. Free fatty acids levels rose throughout the exercise period and during recovery, but the same response was observed during swimming in 27° and 33°C water, arguing against cold exposure increasing the need for fat metabolism. In a study of diabetic patients (Ronnemaa *et al.* 1991), glucagon levels did not change during exercise in either warm (30°C) or cold (10°C) conditions. Exercise was limited to three 15-min bouts of cycle ergometry at 60% $\dot{V}O_{2max}$. Considering that the magnitude of the glucagon response is dependent on the intensity and duration of exercise, the lack of a glucagon response is not surprising.

Growth hormone

Growth hormone (GH) is secreted by the anterior pituitary and defends glucose concentrations by sustaining lipolysis and inhibiting glucose metabolism.

Therefore, it may be important for regulating fuel homeostasis during prolonged exercise–cold stress. For example, by defending glucose concentrations and preventing hypoglycemia, GH may have a role in maintaining shivering thermogenesis.

GH has been studied using various methodologies to induce cold stress, including cold-air exposure, ice ingestion and cool-water immersion combined with ice ingestion. The findings from these studies are highly variable. Sitting in cold air for 2-h has been shown to either cause no change (4°C air, Golstein-Golaire *et al.* 1970) or lower GH concentrations (10°C, Leppäluoto *et al.* 1988), with transient increases 30 min following exposure (Okada *et al.* 1970). Ice-water ingestion that lowered tympanic temperatures by 0.5–0.8°C demonstrated either no change (Berg *et al.* 1966) or a significant decrease (Weeke & Gundersen 1983). The reader must be cognizant that many of these studies did not employ a control group and also are measuring GH at one point in time. This is important because GH is secreted in a pulsatile fashion and depending when the sample is taken, GH can be relatively high or be undetectable. Serial sampling over many hours has not been done using repeated subjects designs during or after cold exposure.

Only three studies have examined GH responses during or after exercise–cold stress. Galbo *et al.* (1979) found that exercising in 21°C water (decreased rectal temperature by 0.8°C) for 60-min elicited no change in GH, whereas GH was elevated following exercise in 27°C and 33°C water. These data suggest that lower body core temperatures suppress GH release or that a core temperature threshold is needed before plasma GH levels rise. Lehtonen *et al.* (1984) exercised subjects for 1 h at –3°C at a heart rate of 140–150 b·min^{-1} on one of three treatments: placebo, atenolol (β_1-adrenergic blocker) and pindolol (blocks β_1 and β_2). They found that GH was significantly higher during the pindolol trial compared to placebo, suggesting that β_2-adrenergic receptors modulate GH responses to exercise–cold stress. Studies (Hermanussen *et al.* 1995) also show that GH does not change in the post-exercise period after swimming in 2–7°C water for 1.5–15.0 min. Since these studies only provide a 'snapshot' in time, it is unknown how the normal pulsatility of GH release is affected by the interaction of exercise and cold stress and what these changes mean for overall fuel metabolism.

Reproductive hormones

Brain serotonin is linked to temperature regulation; increases in brain serotonin levels are associated with feelings of sleepiness and lethargy; and there is evidence implicating serotonin in producing central fatigue during exercise (Cheuvront & Sawka 2001). Since central serotonin levels in humans cannot be measured, plasma prolactin (PRL) concentrations are an accepted marker for brain serotonergic activity (Cheuvront & Sawka 2001) due to anatomical relationships within the brain as well as the finding that plasma PRL concentrations change in response to serotonin agonists and antagonists. Thus PRL changes during exercise–cold stress may be indicative of changes in temperature regulation or useful as a marker of fatigue.

Resting cold exposure significantly decreases prolactin concentrations during and up to 90 min post-exposure (Mills & Robertshaw 1981; O'Malley *et al.* 1984; Leppäluoto *et al.* 1988), although the studies varied slightly in exposure temperature and duration.

The literature is equivocal concerning exercise–cold stress and acute changes in PRL, and there appears to be influences of both exercise and cold-stress intensity. No clear relationship exists between PRL changes and temperature regulation. One study (Frewin *et al.* 1976) found no change in PRL levels during moderate intensity treadmill exercise in 10°C air, but an increase when the same exercise was performed in 40°C air. Another study (Ronnemaa *et al.* 1991) reported an increase in PRL during exercise in 10°C air in patients with diabetes, but, again, the PRL response at 10°C was lower compared to exercise at 30°C in these patients. The increase in PRL during 10°C exercise in diabetics may be due to the subject population, although PRL is lower in type I diabetics compared to healthy subjects (Ramires *et al.* 1993). A third study reported a decrease in PRL during an 8-h shift in meat-processing plant workers exposed to –20°C to –40°C temperatures (Solter & Misjak 1989). Other research

suggests that PRL levels only increase during exercise when core temperature increases above 38°C (Cheuvront & Sawka 2001). Therefore, PRL as a sensitive marker of temperature regulation or fatigue during exercise–cold stress is not supported by the literature.

There is evidence, however, that PRL may be a marker of cold acclimation. Ten weeks of a winter swimming program (2–7°C water) doubled the baseline PRL compared to preswimming concentrations while non-exercise control group PRL levels did not change, indicating the possibility of seasonal variation (Hermanussen *et al.* 1995).

Testosterone is an anabolic hormone that is responsible for growth and development of tissues that characterize males, including skeletal muscle growth. With respect to cold environments, this hormone has been studied in relation to sperm production. McConnell and Sinning (1984) found exercise–cold stress (running at 80% maximal heart rate in 6.2°C air for 5 consecutive days) had no effect on sperm count, semen sample volume, or total sperm per sample. They also found testosterone increased on days 4 and 5 compared to baseline following daily cold-air exercise. However, the same response was found whether the exercise was conducted in warm and hot conditions, indicating that the testosterone results are caused by exercise and not cold stress. On the other hand, resting cold exposure does not change testosterone concentrations (Leppäluoto *et al.* 1988) and other exercise–cold stress studies suggest testosterone decreases. During 10 days of outdoor military training in the winter (Hackney & Hodgdon 1991), subjects who slept in tents at night had a lower testosterone on day 5 compared to subjects who slept in warmer barracks at night. Testosterone in the outdoor-sleeping group returned to normal on day 10. Testosterone decreased after an 8-h shift in meat processing plant workers, but only in the group exposed to the lowest ambient temperatures (Solter & Misjak 1989). This group was the only one who experienced intermittent exposure and the effect of the alternating 1-h work and 1-h rest (in normal room temperature conditions) is not known. Core temperature was not reported during this study, but it is likely that it did not change due to clothing worn by the workers. In a 42-day field study (Johansen & Norman 1991), three of the four male subjects gained total body mass and lean mass and lost body fat during a period of severe testosterone deficiency (the authors remarked that testosterone values during the last 22 days were in the 'female range'). This is in contrast to the remaining subject, who lost a significant amount of total body mass, lean mass and body fat yet had a similar testosterone profile during the trek. The authors speculated that GH may have been elevated during the trek and was responsible for the increased lean mass, but they present no data to support this hypothesis.

Luteinizing hormone (LH) stimulates Leydig cells in the testes to synthesize and secrete testosterone. Sedentary exposure for 2 h to 10°C air does not change blood LH values (Leppäluoto *et al.* 1988). The exercise studies are difficult to interpret due to environmental/field conditions and methodologies and there is no clear linkage to testosterone. Several minutes of swimming in ice water has no effect on plasma LH (Hermanussen *et al.* 1995). Solter and Misjak (1989) studied meat-processing workers who were exposed to ambient temperatures between –40°C and –20°C for 3.5 $h \cdot day^{-1}$ and compared them to workers either exposed to less severe cold (4–8°C) or normal room temperature. No acute changes were observed in LH in any group, although workers chronically exposed to extreme cold had lower basal LH values. LH decreased over time during a 500-km ski-trek (6 weeks) in Greenland, reaching a nadir during the 4th week, and then increasing during the final 2 weeks (Johansen & Norman 1991).

Menstrual cycle status affects thermoregulatory responses in cold environments. During the luteal phase, when endogenous levels of estrogen and progesterone are high, shivering is lower at any given mean body temperature and there is also higher heat flux from the body (Gonzalez & Blanchard 1998). Hessemer and Brück (1985) found that the temperature onset for shivering was ~ 0.5°C higher in the luteal phase, paralleling the rise in core temperature observed during this phase. Likewise, Charkoudian and Johnson (1999) also demonstrated that the onset of cutaneous vasoconstriction began at a higher internal temperature during the luteal

phase. These studies demonstrate that reproductive hormones influence thermoregulatory effector responses in the cold. However, it is less clear what effect cold exposure has on estrogen and progesterone secretion. There are no studies describing how cold exposure impacts these reproductive hormones.

Summary

Information on the effect of exercise–cold stress on endocrine responses is limited. Because there have been relatively few studies completed and these have used a variety of experimental approaches, it is difficult to discern if the changes are due to the interaction of exercise–cold stress or if they are due to the independent effects of exercise or cold exposure. Future studies need to systematically examine the interaction of exercise duration, mode and intensity with cold exposure to determine endocrine responses and, more importantly, the role of the endocrine system in maintaining physiological homeostasis. Whether the changes in hormone levels as a result of cold exposure have important physiological or performance consequences is unknown. An example is the role of thyroid hormones during acute cold exposure. What happens if a person with hypothyroidism exercises in a cold environment? Are they worse off or does it not matter? This question cannot be answered at this point. The use of patients with clinical endocrine disease may further our understanding of the physiological role of specific hormones during exercise–cold stress.

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