REVIEW ARTICLE

Immune Responses to Exercising in a Cold Environment

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Cold temperature and exercise independently impose stress on the human body that can lead to circulatory and metabolic changes, and depress the immune system. Multiple stressors applied together may amplify this immunodepression, causing greater immune impairment and heightened infection risk than with either stressor alone. As such, winter athletes and other persons who work or physically exert themselves in cold temperatures may have greater levels of stress-induced immune impairment than would be expected under mild temperatures. This review examines the literature regarding changes to physiological and immunological parameters arising from exposure to cold temperatures and to exercise. Even brief exposure to cold leads to increased levels of norepinephrine and cortisol, lymphocytosis, decreased lymphoproliferative responses, decreased levels of TH1 cytokines and salivary IgA, and increased lactate levels during exercise. Whether these changes lead to increased susceptibility to infection, as suggested by some epidemiological reports, remains to be determined. Although there is some evidence that exercising in temperatures near 5°C leads to greater immune impairment compared to exercising in milder temperatures, there is a need to explore the effects of exercise on immunity in the subfreezing conditions typically encountered by winter athletes. This is required to fully determine the extent to which performing vigorous exercise in subfreezing temperatures amplifies exercise-induced immune impairment and infection risk.

Key words: cold temperature, NK-cell activity, exercise, immunology, upper respiratory tract infection

Introduction

Exercise presents multiple stressors to the human body that lead to physiological and immunological changes. This is a hormetic effect, where moderate exercise seems to improve some areas of immunity, and vigorous exercise leads to depressed immune function. Exposure to environmental extremes is also physiologically stressful and can affect immunity. It may be that a combination of both exercise and environmental stressors will increase the degree of observed physiological changes above what is observed with either stressor alone. For example, an additive effect has been observed with vigorous exercise in a hot environment, where the combination of these 2 physiological stressors depresses the immune system further than what has been shown to result from the exercise stress on its own.^{1–3} An additive effect on the immune system may also occur with exercise in a

cold environment. Winter athletes, long-distance swimmers, military personnel, and individuals in some occupations must maintain high levels of physical performance in cold conditions; increased susceptibility to infection and disease would place this performance at risk. By reviewing existing literature, this article seeks to determine if exercising in cold temperatures leads to greater impairment in immune function and increased infection risk compared to exercising in mild temperatures.

Natural-killer cells (NK cells) are cytotoxic effectors of the innate immune system, and are one cell population affected by exercise and exposure to extreme temperatures. Natural-killer cells are large, granular lymphocytes that constitute 10% to 15% of peripheral blood mononuclear cells (PBMC) and play a pivotal role in preventing the replication of cancerous and viral-infected cells by causing them to undergo apoptosis. Natural-killer cells express adrenergic receptors, rendering them responsive to catecholamines secreted in response to stress; in fact, a large portion of the exercise-induced leukocytosis is composed of NK cells. The ability of NK cells to kill infected or cancerous cells is often measured as an index

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of innate immune function, which is referred to as NK cell activity (NKCA). Natural-killer cells also have the ability to produce both Type 1 and Type 2 cytokines, and thus help direct further immune responses. Type 1 (Th1) responses are primarily responsible for clearing intracellular pathogens, whereas Type 2 (Th2) responses are responsible for extracellular pathogens. A decreased number or decreased function of circulating NK cells could, therefore, have important implications for infection risk.

The PubMed database was searched for papers published in English through September 2010 with the key words "cold temperature," "immunology," and/or "exercise." The majority of the exercise studies reviewed here used an acute bout of aerobic exercise. Cold temperatures were considered to be air temperatures less than 12°C or water temperatures less than 20°C. The results of the literature review are presented in 3 sections outlining the reported infection risks of winter athletes, the physiological and immunological changes observed following passive exposure to cold temperatures and, finally, the physiological and immunological changes following exercise in cold temperatures. The literature shows exposure to cold temperature on its own is a stress, causing release of norepinephrine, vasoconstriction, lymphocytosis, an increase in stress hormones, and a decrease in cytokine production. The addition of exercise stress on top of cold stress, despite exercise-related thermogenesis, also leads to the release of norepinephrine and increased secretion of stress hormones.

Winter Athletes and Infections

It is commonly believed that cold exposure increases the risk of developing infections, such as an upper respiratory tract infection (URTI); the term for the common "cold" reflects this belief.⁴ However, a direct causal relation between cold exposure and the development of infection in humans remains to be established. There are some reports that vigorous exercise in cold temperatures is associated with increased susceptibility to URTI.^{5,6} Epidemiological studies of cross-country skiers have found that infectious disease, especially URTI, explains the bulk of medical absence from training, and that these infectious incidences are highest during the winter months and at the peak of competition.⁵ Canadian military patrols in the Arctic undergoing vigorous activity have similarly reported an increase in symptoms of URTI.⁷

A limitation of these studies is the reliance on self-reported symptoms of URTI, which may not reflect true infection incidence.⁸ Breathing cold air can itself elicit symptoms similar to these types of infections, such as

bronchospasms and rhinitis.^{9,10} Even healthy individuals exhibit shortness of breath during exercise in cold temperatures.¹¹ It may be that cold weather exercise does negatively impact the respiratory system, but independently of changes in immunity. Asthmatic symptoms are more common in cross-country skiers than in athletes that do not regularly compete in subfreezing temperatures, although a causal link between exercise in the cold and these symptoms has not been established.¹² It has, therefore, been suggested that physicians consider both infectious and noninfectious causes when treating athletes complaining of URTI symptoms.⁸

Another possibility is that winter athletes who report increased incidence of illness may be at a higher risk of infection because they have increased exposure to pathogens. Cold air facilitates the proliferation of some microorganisms, and ailments other than URTI have been reported to increase in cold conditions.¹³ For example, the incidence and severity of poliomyelitis infection increases with chilling and exhausting exercise.¹⁴ Also, it has been shown that an encounter with influenza virus is more likely to result in infection in the winter months than summer months; differences in host susceptibility to infection may be one explanation.¹⁵

Passive Exposure to Cold Environments

PHYSIOLOGICAL RESPONSES

The physiological adjustments that are made by the human body to maintain core temperature when exposed to cold are brought about by the stimulation of the sympathetic nervous system and the hypothalamic-pituitary-adrenal (HPA) axis. These adjustments include shivering thermogenesis and increased peripheral vasoconstriction. Vasoconstriction helps maintain body temperature by constricting blood flow to the skin; this lowers skin temperature, thereby decreasing the thermal gradient between the skin and the environment. This constriction also limits blood flow to underlying muscle and redistributes blood to the core, leading to increased stroke volume and cardiac output, and increased metabolic thermogenesis.¹⁶ The increase in intrathoracic blood volume also causes diuresis and hypertension.¹⁷ This last effect might partly explain the increased incidence in myocardial infarction during cold winter months.¹⁸

Stimulation of the sympathetic nervous system and HPA axis also causes hormone release, including the catecholamines epinephrine and norepinephrine, the stress hormone cortisol, and aldosterone. Changes in thyroid hormones are also noted after exposure to subfreezing air temperatures, with a decrease in thyroid hormone binding capacity and an increase in free thyroid

hormone levels.¹⁹ Norepinephrine seems to be the most responsive catecholamine to cold stimulation. Elevated levels of norepinephrine are observed following cooling of either core body temperature or skin temperature alone.²⁰ Even partial exposure to cold temperatures, such as hand or foot immersion in 0°C- to 10°C water, will cause an increase in norepinephrine, as well as cortisol and aldosterone.^{21,22} The cold-stimulated catecholamine secretion is reported to be a likely explanation of observed changes to metabolism, where cold exposure leads to an increase in lipid and glucose metabolism.²³ It appears that a certain degree of cold stress must be reached to cause the norepinephrine and cortisol responses, as no changes in levels of these hormones were observed following body immersion to midchest in 23°C water.³

IMMUNE RESPONSES

Exposure to cold temperatures affects the physical, cellular, and molecular defenses against pathogens in both humans and animals. Table 1 summarizes the findings of studies examining immunity in humans following passive cold exposure. Cold temperatures can damage normal physical barriers to infection, such as increased mucus viscosity and decreased ciliary action in the upper respiratory system.^{10,13} Cutaneous barrier function is also disrupted upon cold exposure, even without the occurrence of frostnip or frostbite.²⁴

The increased production of corticosteroids and catecholamines following cold exposure impacts immune cell function. These hormones can induce leukocytosis, reduce

the production of inflammatory mediators, decrease the expression of adhesion molecules on inflammatory cells, and are associated with a decrease in mitogen-stimulated lymphocyte proliferation. The lymphoproliferative response is a measure of immune function, as it assesses the ability of T cells to replicate in response to an antigen. Norepinephrine especially seems to be involved in many of the physiological and immunological changes observed with cold temperature. Passive exposure to 5°C air for 2 hours leads to a norepinephrine-mediated mobilization of demarginated leukocytes.²⁵ Similar results have been observed following 1 hour of exposure to 14°C water.²⁶ Subjects that sat for 30 minutes in 4°C had a decreased lymphoproliferative response to the mitogen phytohemagglutinin (PHA). As this decreased response was accompanied by an increase in plasma norepinephrine, but not any other hormones measured, the authors suggest a relationship between the decreased proliferative response and the increase in norepinephrine.²⁷ A reduced lymphocyte proliferative response has also been observed following a drop of 1°C in core temperature during induced perioperative hypothermia. The reduction in lymphocyte proliferation lasted up to 48 hours and was accompanied by reduced IL-2 production.²⁸ This reduction in lymphocyte function was not observed in normothermic patients who also underwent surgery.

Norepinephrine down-regulates NKCA through binding of β_2 -adrenergic receptors and the down-regulation of IL-12 receptors.²⁹ Therefore, a cold-induced increase in norepinephrine would be expected to result in a decrease in NKCA. Nonetheless, some researchers have found that acute exposure to cold temperature (4°C and

Table 1. Effects of passive exposure to cold on stress hormone levels and immunity in humans

Reference	Subjects	Protocol	Results (compared to room temperature conditions)
3	9 men (27.3 $\pm$ 6 yr)	80 min immersion to midchest in 23°C water	$\leftrightarrow$ cortisol, NE
20	6 men (35.5 $\pm$ 8.1 yr)	1h immersion in 10°C water	$\uparrow$ NE
21	9 men, 8 women (mean: 26.6 yr)	6 min immersion of foot in 5 °C water	$\uparrow$ NE, cortisol, aldosterone
22	20 men, 14 women (mean: 23 yr)	Seated 1h in 4°C, wearing summer clothing; or 10 min immersion of hands in 0°C water	$\uparrow$ NE, cortisol
25	7 men (24 $\pm$ 1.9yr)	Seated, 2h in 5°C air, wearing shorts and socks	Leukocytosis, $\leftrightarrow$ in NKCA
26	10 men (mean: 22yr)	1h immersion in 14°C water	$\uparrow$ NE, leukocytosis, $\downarrow$ IL-6
27	8 men (25 $\pm$ 5 yr)	Seated, 30 min in 4°C air, wearing swimming suit	$\uparrow$ NE, $\downarrow$ lymphoproliferative response to PHA
28	30 patients undergoing abdominal surgery	Perioperative hypothermia (-1°C below normal body temperature)	$\downarrow$ lymphocyte proliferation, $\downarrow$ IL-2 production
31	8 men (10–26 yr)	Standing, 30 min in 4°C, nude: body temperature decrease by -0.45°C	$\uparrow$ NE, $\uparrow$ NKCA, $\leftrightarrow$ in interferon levels

NKCA, natural killer cell activity; NE, norepinephrine.

8°C air) leads to an increase in NKCA, while others have reported no change in NKCA in 5°C air when expressed as lytic activity per NK cell.^{25,30,31} It could be that these temperatures are not cold enough to induce a stress response. Leukocytosis is also not observed after 40 minutes of exposure to 23°C water, but is present after exposure to 14°C water.^{3,26} This suggests that, similar to physiological changes, changes in immunological parameters are dependent on the severity of the cold exposure.

The temperatures used in these studies are warmer than those often encountered in the winter months in the Northern Hemisphere, and so the current findings may have limited relevance. The 30-year average January temperature in the 31 US states north of the 35th parallel is -5.1°C, whereas most researchers have used air temperatures ranging from 4°C to 9°C.³² However, an important consideration is that most subjects in laboratory studies are not dressed in cold weather clothing, but are often wearing minimal clothing. Male athletes at rest wearing shorts and a vest will lose heat to the surrounding environment in air temperatures lower than 24°C and water temperatures lower than 32°C.³³ This also limits the applicability of the current findings to “real world” scenarios. Studies measuring immune responses in subjects exposed to subfreezing air or cold (< 10°C) water wearing common winter clothing are needed to more fully understand immune responses related to cold exposure.

Several animal models have been used to study cold stress. Most of these indicate that cold temperatures induce a state of immunodepression. A lowered core body temperature in rats significantly reduces splenic antigen-binding and the number of antigen-producing cells.³⁴ Mice exposed to cold temperatures exhibit increased adrenal cortisol concentration, decreased NK cell numbers, and cytotoxicity.^{35–37} Interestingly, blocking norepinephrine receptors can restore NKCA, again indicating a large role for norepinephrine.^{37,38} Cold stress has been shown to increase the viremia and neuroinvasiveness of arboviruses in mice.³⁹ These data suggest decreased immune function and increased susceptibility to infection in rodents exposed to cold temperatures. In contrast, a recent study found that rats housed at 5°C for 7 weeks had upregulated IL-6 and TNF- α expression as well as macrophage and T-cell infiltration into various tissues, suggesting that the cold induced an inflammatory state in these animals.⁴⁰

Exercise in Cold Environments

PHYSIOLOGICAL RESPONSES

There are physiological differences between exercise in cold temperatures and exercise in warmer temperatures.

In instances where the skeletal muscle is cooled, contractile force and time to fatigue are decreased.⁴¹ Muscle strength and dynamic power are decreased by 50% at 23°C.^{42,43} Some researchers report increased glycolysis and higher blood lactate concentrations during exercise in cold temperatures (-2°C air or 18°C water) compared to milder conditions (24°C air or 28°C water).^{44,45} The increased rate of glycolysis leads to an increased reliance on muscle glycogen. In one study, light exercise (50W–65W) lasting 30 minutes in 9°C air decreased glycogen concentrations in the vastus lateralis by 23%, whereas little change in glycogen stores were seen following light exercise in 21°C air.⁴⁶

Exercise performed at a sufficient intensity may provide protection against reductions in body core temperature due to surface heat loss following exposure to cold air.⁴⁷ As a result, some of the metabolic changes observed following passive exposure to cold temperatures are attenuated. For example, no differences in glycogen depletion were found between cycling in 9°C and 21°C air at workloads of 85W to 120W, indicating a potential protective effect of exercise-related thermogenesis at the higher workload.⁴⁶ However, higher workloads may not be able to provide a protective effect at even lower temperatures. Exercise time to exhaustion is lower during cycling at 70% of $\text{VO}_{2\text{max}}$ at air temperatures of 4°C than 11°C.⁴⁸

Heart rate at a given workload in cold air or water is lower than in mild temperatures. This is likely due to the redistribution of blood to the core caused by peripheral vasoconstriction.⁴⁹ Some researchers also report an increase in VO_2 at a given submaximal workload in cold temperatures compared to mild temperatures.⁴⁵ Oxygen costs of swimming increase with a decrease in water temperature, perhaps because of the work devoted to shivering.⁵⁰ Not all research supports the idea of increased VO_2 in cold temperatures.⁴⁶ Leaner individuals tend to have a higher exercise VO_2 in the cold than do subjects with greater body fat.⁵¹ Differences in VO_2 due to temperature decrease as the exercise intensity increases.⁵² This suggests that increased VO_2 is related to the amount of metabolic heat needed to maintain core body temperature.

Catecholamine and cortisol secretion is increased during exercise in cold temperatures, compared to the same exercise in warmer temperatures. Incremental exercise in -2°C air leads to an increase in norepinephrine levels compared to the same exercise at 24°C.⁴⁴ Cycling for 1 hour at 65% $\text{VO}_{2\text{max}}$ in 5°C air leads to significantly higher cortisol levels than cycling in 21°C air.⁵³ A longer exercise bout of 90 minutes at 5°C causes increased levels of both epinephrine and norepinephrine, as well as cortisol, compared to similar exercise in both 20°C and

30°C.⁵⁴ In this study, the cold temperature elicited a larger stress hormone response than exercise in the hot (30°C) temperature; no measures of the immune system were taken.

IMMUNE RESPONSES TO EXERCISE IN THE COLD

Exercise itself, without additional sources of stress, has long been known to influence the immune system. Experimental data generally support anecdotal and epidemiological reports that the intensity and duration of exercise decides the outcome of immune responses, with moderate exercise yielding increased immune function and vigorous exercise leading to immunodepression.^{13,55} Physical activity in room temperature conditions leads to leukocytosis and the release of stress hormones, the degree of which is dependent on the intensity and duration of the exercise.⁵⁶ Natural-killer cells are some of the most responsive cells to exercise, although there are conflicting reports in the literature in both the magnitude and direction of exercise-induced changes in NK cell function.^{55,57,58} These discrepancies (ie, large or small increases or decreases in NKCA) likely arise from differences in the time of sample collection following exercise, the use of trained athletes or sedentary subjects, differences in exercise bouts (type, mode, intensity, and duration), the methods of measuring NKCA, and different methods of reporting activity. One meta-analysis of exercise-induced changes in NKCA has found that most studies using a sustained aerobic exercise protocol (> 50% aerobic power) report increased NK cell counts and activity immediately after exercise, followed by depressed cell counts and function for several hours after exercise.⁵⁹ This temporary suppression of the immune system has been shown to be a possible contributing factor for the reported increase in infection rates among athletes in vigorous training programs.^{6,60–62}

There have not been many studies that have specifically examined the effect of exercise in cold temperatures on the immune system. The available evidence indicates that cold weather exercise increases stress hormone production compared to exercise in mild temperatures. However, the data are mixed regarding the impact on immunity, as there are results suggesting both a suppressive effect as well as no effect of exercise in cold temperatures, compared to exercise in mild temperatures. Table 2 summarizes the results of studies that examine immunity in humans following exercise in cold temperatures.

Reductions in inflammatory cytokine production have been reported following exercise in cold temperatures. Walking for 4 hours in 5°C into a headwind down-regulates pro-inflammatory Th1 cytokines, without a significant increase in anti-inflammatory Th2 cytokines.⁴ A brief swim (0–5 min) in ice-cold water has been shown to reduce the lipopolysaccharide (LPS)-stimulated release of IL-1 β and IL-6 in whole blood and PBMC culture in subjects unaccustomed to the activity.⁶³ This might indicate a decrease in the ability of this branch of immunity to respond to bacterial infections. A decreased Th1 cytokine response has also been seen in horses running while breathing cold air, who exhibit a shift towards anti-inflammatory Th2 cytokine responses, compared to responses seen to similar exercise in room temperature conditions.⁶⁴ Not all research has shown differences in cytokine production between exercising in cold or mild temperatures. Levels of plasma IL-6 did not differ between cycling for 1 hour at 70% $\text{VO}_{2\text{max}}$ in 20°C or 0°C conditions.⁶⁵

Some researchers have suggested that a decrease in mucosal immune function might explain increases in URTI in winter athletes. It has been noted that vigorous cross-country skiing leads to a significant loss of nasal fluid, which could potentially decrease the protective effect of antibodies located on the mucosal surface.⁶ Tomasi et al found that secretory IgA levels in elite cross-country skiers were significantly lower than age-matched controls, and that these levels decline further following a long-distance cross-country ski race.⁶ However, other researchers have shown similar or even increased s-IA secretion following exercise in cold temperatures compared to mild temperatures.^{66,67} Other changes noted with exercise in cold temperatures include decreased lymphocytosis following 1 hour of cycling at 60% $\text{VO}_{2\text{max}}$ in 8°C air compared to 38°C air, but no difference in NKCA.³⁰

Repeated bouts of exercise in cold temperatures result in adaptations that moderate the stress response to cold stimuli. Subjects who regularly performed ice water swims had an increase in LPS-stimulated production of cytokines, compared to a decreased response in subjects who were unused to ice water swimming.⁶³ Speed skaters that cycled for 1 hour at 65% $\text{VO}_{2\text{max}}$ in 5°C air had significantly lower cortisol levels compared to cycling in 21°C air, whereas inline skaters unused to exercising in cold temperatures had increased cortisol levels.⁵³ These data suggest that adaptations do occur, which may be especially important to consider when designing research studies or applying existing data to winter athletes.

Table 2. Effect of exercise in cold temperatures on stress hormone levels and immunity

<i>Reference</i>	<i>Subjects</i>	<i>Protocol</i>	<i>Results (compared to room temperature conditions)</i>
4	9 men (24.6 $\pm$ 3.8 yr)	Walking, $\leq$ 6h into wind in 5°C, wetted, US Army uniform	↓ TH1 cytokines
6	Nationally ranked Nordic skiers: 5 men, 3 women (mean: 23.5 yr)	50/20 km ski race (men/women)	↓ salivary IgA
30	10 men (25.56 $\pm$ 1.67yr)	1h cycling at 60%VO _{2max} in 8°C air, 50% RH	↓ lymphocytosis, ↔ in NKCA
44	8 men (mean: 26.7 yr)	Incremental cycling to exhaustion in -2°C	↑ VO ₂ , lactate, FFA, NE
53	22 short track or inline skater men (25.7 $\pm$ 5.1 yr)	1h cycling 65% VO _{2max} in 5°C air	↑ cortisol
54	8 men (27.88 $\pm$ 0.32 yr)	1.5h cycling at 65% VO _{2max} in 5°C, wearing shorts	↑ lactate, E, NE, cortisol, ↓ RE
63	9 men (mean: 44 yr) 11 women (mean: 38.7yr)	Swimming 0–5 minutes in ice water, nude	↑ cortisol, ADH, prolactin; ↓ in LPS-stimulated release of IL-1 β and IL-6 in cell culture (nonadapted subjects)
65	8 men	1h cycling, 70% VO _{2max} , 0°C	↑ plasma IL-6, ↔ soluble IL-6 receptor
66	15 cyclist men (29 $\pm$ 2)	2h cycling, 70% VO _{2max} in -6.4°C and 19.8°C air	↓ salivary IgA in both conditions
67	16 recreationally active women (23.4 $\pm$ 6.8 yr)	30 min run, 71% heart rate reserve, in 1°C and 24°C air	↑ plasma IL-6 in 1°C compared to 24°C

NKCA, natural killer cell activity; NE, norepinephrine; E, epinephrine; FFA, free fatty acid; RE, respiratory equivalent; ADH, antidiuretic hormone; RH, relative humidity.

Summary and Conclusions

Exposure to cold temperatures causes secretion of the stress hormones norepinephrine and cortisol, lymphocytosis, decreased lymphoproliferative responses, and altered cytokine levels. Exercise in cold temperatures decreases the time to exhaustion and increases levels of lactate, norepinephrine, and cortisol. Some, but not all, researchers have found decreased lymphoproliferative responses, decreased inflammatory cytokine production, and decreased salivary IgA levels following exercise in cold temperatures. The disagreement in results between different studies highlights the need for more research that examines the effects of exercising in cold temperatures on the immune system.

One limitation of most of the existing work is that researchers have not used temperatures as cold as those routinely encountered during the winter months for much of the world, meaning that the cold stress may not be the same as that experienced by winter athletes. Just as the effects on immune function by moderate exercise are not the same as the effects resulting from vigorous exercise, the effects of exercise in moderately cold temperatures may not be the same as those in extremely cold temper-

atures. There is some evidence in the current literature that illustrates this “dose” response. Subjects cycling in 18°C water have attenuated rises in cortisol, epinephrine, and norepinephrine, and they have a blunted NKCA response compared to exercise in warmer water.²⁵ Likewise, passive exposure to 23°C water does not result in stress hormone secretion, while exposure to 0°C to 10°C water and 5°C air does elevate cortisol and the catecholamines.^{3,20–22,53,54} This suggests that the degree of change from baseline physiologic and immunologic values is dependent on the severity of the cold stress. Other limitations that should be considered in future research include using clothing that is commonly used by winter athletes, and using subjects who are adapted and not adapted to cold temperatures.

Few studies have measured immunological markers following exercise in very cold temperatures. As such, it is not yet certain what immunological changes winter athletes undergo during routine training and competition in the winter months, and a direct casual relationship between infection and cold exposure has not been demonstrated. Still, because both exercise and exposure to very cold temperatures have been

shown to be potentially immunosuppressive, it may be that the combination of vigorous exercise in subfreezing temperatures does decrease immunity, and leads to increased risk of infection. The mechanism behind immune perturbations may be increased corticosteroids or norepinephrine levels caused by both cold and exercise stress. The metabolic responses to an absolute workload are also greater at colder temperatures. This is suggested by the decreased time to exhaustion and increased blood lactate levels in exercise in cold temperatures compared to exercise in mild temperatures. However, without controlled laboratory studies examining the immunological effects of exercise in conditions below 0°C, the degree, duration, and nature of the effect on the immune system remain unknown. Such research would further our understanding of potential mechanisms of immune dysfunction, as well as infection risk, among winter athletes.

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