Risk of Upper Respiratory Tract Infection in Athletes: An Epidemiologic and Immunologic Perspective

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Objective: The chronic and acute immune responses to both heavy and moderate exercise are reviewed, with guidelines provided for the prevention and management of upper respiratory tract infection (URTI) in athletes.

Data Sources: Epidemiologic and experimental exercise immunology research data were used. The MEDLINE database was searched for the years 1970 to 1997 with the terms "exercise," "immune," "infection," "lymphocyte," and "neutrophil."

Data Synthesis: A descriptive review with summary figures and one table.

Conclusions/Recommendations: The epidemiologic data suggest that endurance athletes are at increased risk for URTI during periods of heavy training and the 1- to 2-week period after marathon-type race events. Several researchers have reported a diminished neutrophil function in athletes during periods of intense and heavy training. Following each bout of prolonged heavy endurance exercise, several components of the immune system appear to demonstrate suppressed function for several hours. This has led to the concept of the "open window," described as the 3- to 12-hour time period after prolonged endurance exercise when host defense is decreased and the risk of URTI is elevated. There is sufficient evidence for sports medicine professionals to encourage athletes to practice various hygienic measures to lower their risk of URTI and to avoid heavy exertion during systemic illness.

Key Words: immune system, exertion, lymphocyte, neutrophil, common cold

Among elite athletes and their coaches, a common perception is that heavy exertion lowers resistance and is a predisposing factor to upper respiratory tract infections (URTI).[1–3] Many elite athletes, including Sebastian Coe, Uta Pippig, Liz McColgan, Michelle Akers-Stahl, Alberto Salazar, and Steve Spence, have reported significant bouts with infections that have interfered with their ability to compete and train.[1]

On the other hand, there is also a common belief among many individuals that regular exercise confers resistance against infection. For example, a 1989 *Runner's World* subscriber survey revealed that 61% of 700 runners reported fewer colds since beginning to run, while only 4% felt they had experienced more colds (*Runner's World.* April 1990:77). A survey of 750 masters athletes (ranging in age from 40 to 81 years) showed that 76% perceived themselves as less vulnerable to viral illnesses than their sedentary peers.[4] Among 170 nonelite marathon runners (personal best time, average of 3 hours, 25 minutes) who had been training for and participating in marathons for an average of 12 years, 90% reported that they definitely or mostly agreed with the statement that they "rarely get sick" (D.C.N., unpublished data, 1993).

The National Center for Health Statistics reports that acute respiratory conditions (primarily the common cold and influenza) have an annual incidence rate of 90 per 100 persons, imposing substantial morbidity and economic burden upon families.[5] The common cold is probably the most frequently occurring illness in humans worldwide. More than 200 different viruses cause colds, and rhinoviruses and coronaviruses are the culprits 25 to 60% of the time. Rhinoviruses often attack during the fall and spring seasons, while the coronavirus is common during the winter.[1] The average adult has two or three respiratory infections each year, with young children suffering six to seven infections.[1,6]

Understanding the relationship between exercise and infection has potential implications for public health. Illness may cause the athlete to perform at a subpar level or miss an event altogether.[1] The relationship between exercise and URTI[1] may be modeled in the form of a "J" curve (Figure). This model suggests that although when one engages in moderate exercise training the risk of URTI may decrease below that of a sedentary individual, risk may rise above average during periods of excessive amounts of high-intensity exercise.

UPPER RESPIRATORY TRACT INFECTION

Heavy Exertion and URTI: Epidemiologic Evidence

Several epidemiologic reports suggest that athletes engaging in marathon-type events and/or very heavy training are at increased risk of URTI (Table). Nieman et al[6] researched the incidence of URTI in a group of 2,311 marathon runners who varied widely in running ability and training habits. Runners retrospectively self-reported demographic, training, and URTI episode and symptom data for the 2-month period (January, February) before and the 1-week period immediately after the 1987 Los Angeles Marathon. During the week following the race, 12.9% of the marathoners reported a URTI, compared with only 2.2% of control runners who did not participate (odds ratio, 5.9). Forty percent of the runners reported at least one URTI episode during the 2-month winter period before the Marathon.

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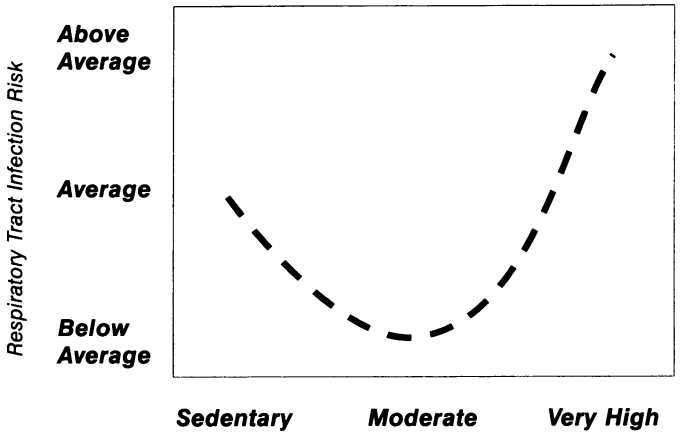

"J"-shaped model of relationship between varying amounts of exercise and risk of URTI. This model suggests that moderate exercise may lower risk of URTI while excessive amounts may increase the risk.

Controlling for various confounders, it was determined that runners training more than 96 km/wk doubled their odds for sickness compared with those training less than 32 km/wk.

Other epidemiologic data support these findings. Linde[7] studied URTI in a group of 44 elite orienteers and 44 nonathletes of the same age, sex, and occupational distribution during a 1-year period. The orienteers experienced significantly more URTI episodes during the year in comparison with the control group (2.5 versus 1.7 episodes, respectively).

Peters and Bateman[8] studied the incidence of URTI in 150 randomly selected runners who took part in a 56-km Cape Town race and compared them with matched controls who did not run. Symptoms of URTI occurred in 33.3% of runners, compared with 15.3% of controls during the 2-week period after the race, and were most common in those who achieved the faster race times. Two subsequent studies from Peters et al[9,10] have confirmed this initial finding. In one study, 28.7% of the 108 subjects who completed the 56-km Milo Korkie Ultramarathon in Pretoria, South Africa, reported nonallergy-derived URTI symptoms during the 2-week period afterward, as compared with 12.9% of controls.[10] In another study, 68% of runners reported the development of URTI symptoms within 2 weeks after the 90-km Comrades Ultramarathon.[9] Using a double-blind placebo research design, it was determined that only 33% of runners taking a 600-mg vitamin C supplement daily for 3 weeks before the race developed URTI symptoms. The authors suggested that because heavy exertion enhances the production of free oxygen radicals, vitamin C, which has antioxidant properties, may be required in increased quantities.

URTI risk following a race may depend on the distance, with an increased incidence conspicuous only after marathon or ultramarathon events. For example, Nieman et al[11] were unable to establish any increased prevalence of URTI in 273 recreational runners during the week after 5-km, 10-km, and 21.1-km events as compared with the week before. URTI incidence was also measured during the 2 winter months before the three races. Twenty-five percent of those running 25 or more km/wk (average of 42 km/wk) reported at least one URTI episode, as did 34% of those training fewer than 25 km/wk (average of 12 km/wk) ($p = .09$). These findings suggest that, in recreational running, an average weekly distance of 42 km versus 12 km is associated with either no change in, or even a slight reduction of, URTI incidence and that racing 5 to 21.1 km is not related to an increased risk of sickness during the ensuing week.

Together, these epidemiologic studies imply that heavy acute or chronic exercise may be associated with an increased

Epidemiologic and clinical research on the relationship between exercise and URTI

Investigators	Subjects	Method of Determining URTI	Major Finding
Peters and Bateman[8] (1983)	150 South African marathon runners vs 124 controls who lived with them	2-wk recall of URTI incidence and duration after 56-km race	URTI incidence twice as high in runners (33.3%) vs controls (15.3%) after 56-km race
Linde[7] (1987)	44 Danish elite orienteers vs 44 matched nonathletes	URTI symptoms self-recorded in daily log for 1 y	Orienteers had 2.5 URTIs vs controls' 1.7 URTIs during year
Nieman, Johanssen, & Lee[11] (1989)	273 California runners training for race	2-mo recall of URTI incidence; 1-wk recall after March 5-, 10-, and 21-km races	Training 42 vs. 12 km/wk associated with fewer URTIs; no effect of race participation on URTI
Peters[10] (1990)	108 South African marathon runners vs 108 controls who lived with them	2-wk recall of URTI incidence and duration after 56-km race	URTI incidence: 28.7% in runners vs 12.9% in controls after 56-km race
Nieman et al[6] (1990)	2,311 Los Angeles marathon runners	2-mo recall of URTI incidence during training for marathon; 1-wk recall after March race	Runners training ≥97 vs <32 km/wk at higher URTI risk; odds ratio 5.9 for participants vs nonparticipants 1 wk after 42.2-km race
Nieman et al[13] (1990)	36 mildly obese, inactive California women	Daily logs using self-reported, precoded URTI symptoms	Walking group reported fewer days with URTI symptoms than controls (5.1 vs 10.8)
Heath et al[12] (1991)	530 South Carolina runners	1-y daily log using self-reported, precoded symptoms	Increase in running distance positively related to increased URTI risk
Peters et al[9] (1993)	84 South African marathon runners vs 73 nonrunner controls	2-wk recall of URTI incidence and duration after 90-km race	URTI incidence: 68% in runners vs 45% in controls after 56-km race, 33% in runners using vitamin C vs 53% of controls
Nieman et al[14] (1993)	42 elderly North Carolina women (30 inactive, 12 athletes)	Daily logs using self-reported, precoded URTI symptoms	Incidence of URTI: 8% in athletes; with inactives randomized to 12-wk walking vs controls, 21% in walkers, 50% in sedentary controls

risk of URTI.[1,12] The risk appears to be especially high during the 1- or 2-week period after marathon-type races. Among runners varying widely in training habits, the risk for URTI is slightly elevated for the longest distance runners, but only when confounding factors (eg, training and demographic variables) are controlled.

Moderate Exertion and URTI

What about the common belief that moderate physical activity is beneficial in decreasing URTI risk? At present, there are no published epidemiologic reports that have retrospectively or prospectively compared the incidence of URTI in large groups of moderately active and sedentary individuals.

Two randomized experimental trials using small numbers of subjects have provided important preliminary data in support of the viewpoint that moderate physical activity may reduce URTI symptomatology[13,14] (Table). In one randomized, controlled study of 36 women (mean age, 35 years), exercise subjects walked briskly for 45 minutes, 5 days a week, and experienced one-half the number of days with URTI symptoms during the 15-week period compared with that of the sedentary control group (5.1 ± 1.2 vs 10.8 ± 2.3 days, $p = .039$).[13]

In a second study, the incidence of the common cold in a population of elderly women during a 12-week period was found to be lowest in highly conditioned, lean subjects who exercised moderately each day for about 1.5 hours (8%). Subjects who walked 40 minutes, 5 times per week, had an incidence of 21%, compared with 50% for the sedentary control group ($\chi^2 = 6.36$, $p = .042$).[14] These data suggest that elderly women not engaging in cardiorespiratory exercise are more likely than those who do exercise regularly to experience a URTI during the fall season.

EFFECTS OF EXERCISE ON THE IMMUNE SYSTEM

If heavy and fatiguing exertion leads to an increased risk of URTI, it follows that various measures of immune function should be negatively affected. Conversely, if moderate exercise decreases URTI risk, there should be some aspect of immune function that is chronically or at least transiently improved.

Resting Immunity in Endurance Athletes Versus Nonathletes

In this section, data currently available on cross-sectional comparisons of human endurance athletes and nonathletes for natural killer cell activity (NKCA),[15–19] neutrophil function (phagocytosis and oxidative burst),[20–29] and lymphocyte proliferative response (T-cell function)[14,16,17,19,20,30–32] will be reviewed.

Natural Killer Cell Activity

Natural killer (NK) cells are large granular lymphocytes that can mediate non-major histocompatibility complex (MHC)-restricted cytolytic reactions against a variety of neoplastic and virus- or bacteria-infected cells.[33] NK cells also exhibit key non-cytolytic functions and can inhibit microbial colonization and growth of certain viruses, bacteria, fungi, and parasites.

Most cross-sectional studies support the finding of enhanced NKCA in athletes when compared with nonathletes, in both younger and older groups.[15–19] NKCA data comparing 22 experienced marathon runners and 18 sedentary controls indicated higher NKCA in the marathon runners (373 ± 38 versus 237 ± 41 total lytic units, $p = .02$).[17] Tvede et al[19] also observed a higher NKCA in elite cyclists during the summer months (intensive training period) when compared with the winter (light training period).

However, several prospective studies with subjects exercising moderately for 8 to 15 weeks reported no significant elevation in NKCA relative to sedentary controls.[14,34,35] Together, data from these studies imply that endurance exercise may have to be intensive and prolonged (ie, at athletic levels) before NKCA is chronically elevated.

Neutrophil Function

Neutrophils are an important component of the innate immune system, aiding in the phagocytosis and killing (ie, through an oxidative burst) of many bacterial and viral pathogens and the release of immunomodulatory cytokines.[25] The neutrophil function cross-sectional data appear to contrast with those for NKCA. No researcher has reported an elevation in neutrophil function (ie, both phagocytic and oxidative burst activity) among endurance athletes when compared with nonathletes.[20–29] Instead, during periods of high-intensity training, neutrophil function has been reported to be suppressed in athletes. This is especially apparent in studies by Hack et al[23] and Baj et al,[20] demonstrating that neutrophil function in athletes was similar to controls during periods of light training workloads but significantly suppressed during the summer months of intensive training. Pyne et al[27] reported that elite swimmers undertaking intensive training have significantly lower neutrophil oxidative activity at rest than do age- and sex-matched sedentary individuals and that function is further suppressed during periods of strenuous training before national-level competition.

Neutrophils are considered the body's best phagocytes. Suppression of neutrophil function during periods of heavy training is probably a significant factor explaining the increased URTI risk among athletes. Muns[29] has reported that neutrophils in the upper airway passages of athletes have a decreased phagocytic capacity when compared with those of nonathletes and that, following heavy exertion, a further suppression is experienced for 1 to 3 days afterward. Repeated cycles of heavy exertion may thus put athletes at increased risk of URTI.

Lymphocyte Proliferative Response

T and B cells are a part of the adaptive immune system, taking several days to divide and secrete various chemicals in response to foreign antigens. Determination of the proliferative response of human lymphocytes upon stimulation with various mitogens (eg, phytohemagglutinin or concanavalin A) in vitro

is a well-established test to evaluate the functional capacity of T and B lymphocytes. Mitogen stimulation of lymphocytes in vitro using optimal and suboptimal doses is believed to mimic events that occur after antigen stimulation of lymphocytes in vivo. Data on the lymphocyte proliferative response to athletic endeavor are less clear than for NK cells and neutrophils but generally support no significant difference between athletes and nonathletes.[14,16,17,19,20,30–32]

Among highly conditioned elderly women in a state of rest, phytohemagglutinin-induced lymphocyte proliferative response was reported to be 56% higher than among sedentary controls.[14] Data from Japan also support enhanced T-cell function among trained elderly men versus untrained controls.[32] These data are interesting because T-cell function tends to diminish with age. However, moderate exercise training for 12 weeks failed to alter T-cell function in elderly women, indicating that higher levels of vigorous exercise may be necessary over greater time periods before an effect on T-cell function can be measured in the elderly population.[14]

Salivary Immunoglobulin A (IgA)

The secretory immune system of the mucosal tissues of the upper respiratory tract is considered the first barrier to colonization by pathogens, with IgA the major effector of host defense.[36] Secretory IgA inhibits the attachment and replication of pathogens, preventing their entry into the body. While several studies have shown that salivary IgA concentration decreases after a single bout of intense endurance exercise, further research is needed to determine the overall chronic effect.[36–38] Tomasi et al[39] reported that resting salivary IgA levels were lower in elite cross-country skiers than in age-matched controls, but this was not confirmed by a follow-up study of elite cyclists.[37]

Together these data support the concept that the immune system responds differentially to the chronic stress of intensive exercise, with NKCA tending to be enhanced, while neutrophil function is suppressed. The decrease in neutrophil function may be of more importance when considering host protection against foreign pathogens. T and B cells seem to be largely unaffected by athletic endeavor, although the research data at present are mixed. Further study is needed with larger groups of athletes to allow a more definitive comparison.

THE ACUTE IMMUNE RESPONSE TO AEROBIC EXERCISE

As reviewed earlier, epidemiologic studies suggest that marathon and ultramarathon race events are associated with a significant increase in risk of URTI during the 1- to 2-week recovery period. In light of the mixed results regarding the effect of chronic, intensive training on resting immune function, several authors have posited that prolonged cardiorespiratory endurance exercise (defined in the present article as longer than 2 hours) leads to transient but significant perturbations in immunity and host defense, providing a physiologic rationale for the epidemiologic data.[1,36,40]

For example, NKCA,[41–48] mitogen-induced lymphocyte proliferation,[45,49–54] upper airway neutrophil phagocytosis and blood neutrophil oxidative burst,[29,55,56] and salivary IgA concentration[36–39,57] have all been reported to be suppressed for at least several hours during recovery from prolonged, intense endurance exercise. During this "window of decreased host protection," viruses and bacteria may gain a foothold, increasing the risk of subclinical and clinical infection. This may be especially apparent when the athlete goes through repeated cycles of heavy exertion.

Natural Killer Cell Activity

NKCA is decreased 45 to 62% for at least 6 hours after 2.5 to 3 hours of high-intensity running.[41,43] The drop in NKCA has been related to a loss of natural killer cells from the blood compartment, which probably reduces host protection against viruses and bacteria for a short time period.[43]

Lymphocyte Proliferative Response

The mitogen-induced lymphocyte proliferative response (T-cell function) after 2.5 hours of running at high intensity is suppressed for several hours relative to control levels.[49,50,52] Additionally, after 2.5 hours of running at high intensity, serum cortisol concentrations are significantly elevated above control levels for several hours.[43] There is evidence that elevation of serum cortisol and plasma epinephrine both inhibit mitogen-induced lymphocyte proliferation.[51–53] Various monocyte functions are inhibited in the presence of cortisol, and since monocytes are important as accessory cells in many T and B lymphocyte responses, cortisol-induced inhibition of monocyte function indirectly contributes to the decrement in ability of T-cells to proliferate in response to concanavalin.[58]

Taken together, these data suggest that the immune system is suppressed and stressed following prolonged endurance exercise, decreasing host protection against viruses and bacteria. More research, however, is needed to link these immune changes to the increased risk of URTI suggested by epidemiologic data. In a small study of elite squash and hockey athletes, Mackinnon et al[59] have demonstrated that low salivary IgA concentrations precede URTI. However, exercise training-induced changes in T-cell or neutrophil function have not been related to URTI.[27,59,60]

MANAGEMENT OF THE ATHLETE DURING INFECTION

Endurance athletes are often uncertain of whether they should exercise or rest during an infectious episode. There are few data available in humans to provide definitive answers. Most clinical authorities in this area recommend that if the athlete has symptoms of a common cold with no systemic involvement, then regular training may be safely resumed a few days after the resolution of symptoms.[61–64] Mild exercise during sickness with a common cold does not appear to be contraindicated, but there is insufficient evidence at present to say one way or the other. However, if there are symptoms or

signs of systemic involvement (fever, extreme tiredness, muscle aches, swollen lymph glands, etc), then 2 to 4 weeks should probably be allowed before resumption of intensive training.[1,61–64]

These recommendations are speculative, however, and are primarily based on animal studies and some case reports among humans who died following bouts of vigorous exercise during an acute viral illness.[1] Depending on the pathogen (with some more affected by exercise than others), animal studies generally support the finding that one or two periods of exhaustive exercise following inoculation of the animal leads to a more frequent appearance of infection and a higher fatality rate.[65] It is well established that various measures of physical performance capability are reduced during an infectious episode.[63,65–69] Although causes are debated, muscle protein catabolism, circulatory deregulation, and mitochondrial abnormalities have been reported.[68,70,71] Several case histories have been published demonstrating that sudden and unexplained deterioration in athletic performance can in some individuals be traced to either recent URTI or subclinical viral infections that run a protracted course.[61–64] In some athletes, a viral infection may lead to a severely debilitating state known as "post-viral fatigue syndrome."[70,71] The symptoms can persist for several months and include lethargy, atypical depression, excessive sleep, night sweats, easy fatiguability (made worse by exercise), and myalgia.

For athletes who may be undergoing heavy exercise stress in preparation for competition, several precautions may help to reduce their risk of URTI:[1]

1. Eat a well-balanced diet to keep vitamin and mineral pools in the body at optimal levels.[72] Although there is insufficient evidence to recommend nutrient supplements, ultramarathon runners may benefit by taking vitamin C supplements before ultramarathon races.
2. Keep other life stresses to a minimum. Mental stress in and of itself has been linked to an increased risk of URTI.[73]
3. Avoid overtraining (ie, training beyond what the body can recover and adjust to) and chronic fatigue.[6,12,19,20,27,59]
4. Avoid rapid weight loss (eg, more than 1% of body weight per week, which has also been linked to negative immune changes, especially T-cell suppression).[74]
5. Avoid putting hands to the eyes and nose (a primary route of introducing viruses into the body).[75] Before important race events, avoid sick people and large crowds when possible.
6. For athletes competing during the winter months, flu shots are recommended.[1]
7. Obtain adequate sleep on a regular schedule. Sleep disruption has been linked to suppressed immunity.[76]
8. Use carbohydrate beverages before, during, and after marathon-type race events or unusually heavy training bouts. These may lower the impact of stress hormones on the immune system.[77,78]

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