CONFERENCE PAPER

Sports Med 2007; 37 (4-5): 412-415
0112-1642/07/0004-0412/$44.95/0

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Marathon Training and Immune Function

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Abstract

Many components of the immune system exhibit adverse change after marathon-type exertion. These immune changes occur in several compartments of the immune system and body (e.g. the skin, upper respiratory tract mucosal tissue, lung, peritoneal cavity, blood and muscle). Of all immune cells, natural killer (NK) cells, neutrophils and macrophages (of the innate immune system) exhibit the greatest changes in response to marathon competition, both in terms of numbers and function. Many mechanisms appear to be involved, including exercise-induced changes in stress hormone and cytokine concentrations, body temperature changes, increases in blood flow and dehydration. During this 'open window' of immune dysfunction (which may last between 3 and 72 hours, depending on the immune measure), viruses and bacteria may gain a foothold, increasing the risk of subclinical and clinical infection. Of the various nutritional and pharmacological countermeasures to marathon-induced immune perturbations that have been evaluated thus far, ingestion of carbohydrate beverages during intense and prolonged exercise has emerged as the most effective. However, carbohydrate ingestion during a marathon attenuates increases in plasma cytokines and stress hormones, but is largely ineffective against changes in other immune components including suppression of NK and T-cell function, and salivary IgA output. Other countermeasures, such as glutamine, antioxidant supplements and ibuprofen, have had disappointing results and thus the search for companion agents to carbohydrate continues.

One of the earliest studies in exercise immunology was published in 1902 by Larrabee[1] who reported a large increase in blood neutrophils among four athletes who ran the 1901 Boston Marathon. Larrabee observed "the exertion had gone far beyond physiological limits" and that changes in the white blood cell differential counts paralleled those seen in certain diseased and inflammatory conditions.

In the century since Larrabee's report, much has been learned about how marathon running influences the immune system and risk of upper respiratory tract infections (URTI) such as the common cold. Studies on marathon runners and other endurance athletes indicate that prolonged and intensive training, and competition cause numerous alterations in immunity, and, when combined with other stress factors, an increased risk of URTI.

1. Marathon Running and Immune Dysfunction

Many components of the immune system exhibit change after marathon-type exertion, reflecting the

physiological stress that the body is experiencing:[2,3]

- Neutrophilia and lymphopenia, including a steep drop in blood natural killer (NK) and T cells.
- Decrease in blood and spleen NK cell cytotoxic activity and T-cell function.
- Decrease in nasal neutrophil phagocytosis and mucociliary clearance.
- Decrease in nasal and salivary IgA concentration.
- Decrease in blood granulocyte oxidative burst activity.
- Decrease in the skin delayed-type hypersensitivity response.
- Blunted major histocompatibility complex II expression and antigen presentation in macrophages.
- Increase in pro- and anti-inflammatory cytokines and chemokines (e.g. interleukin [IL]-6, IL-1 receptor antagonist, IL-10, IL-8, granulocyte colony-stimulating factor, monocyte chemoattractant protein 1 and macrophage inflammatory protein 1-β).

Of all immune cells, NK cells, neutrophils and macrophages (of the innate immune system) exhibit the greatest changes in response to marathon competition, both in terms of numbers and function.[1,2] Several mechanisms appear to be involved, including exercise-induced changes in stress hormones, body temperature changes, increases in blood flow, lymphocyte apoptosis and dehydration. Following marathon competition, the concentration of serum cortisol is significantly elevated for several hours and has been related to many of the cell trafficking changes experienced during recovery.

During this 'open window' of altered immunity (which may last between 3 and 72 hours, depending on the immune measure), viruses and bacteria may gain a foothold, increasing the risk of subclinical and clinical infection (figure 1). Investigations are currently underway to determine whether or not athletes showing the most extreme immune suppression following heavy exertion are those that contract an infection during the following 1–2 weeks. This link must be established before the 'open window' theory can be wholly accepted in humans.

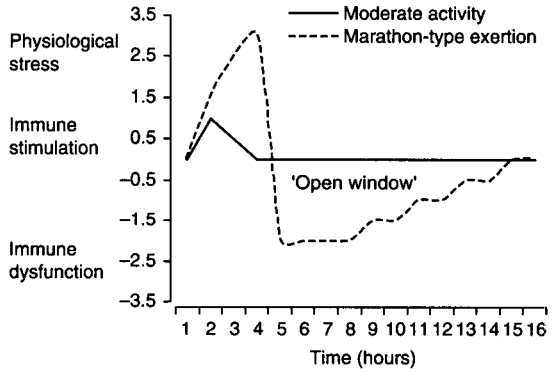

Fig. 1. The 'open window' theory. Moderate exercise causes mild immune changes; in contrast, prolonged, marathon-type exercise leads to immune dysfunction that increases the likelihood for opportunistic upper respiratory tract infections.

Attempts thus far to compare resting immune function in endurance athletes and non-athletes have failed to provide evidence that athletic endeavor is linked to clinically important changes in chronic, resting immunity.[4] Several studies indicate that the innate immune system responds differentially to the chronic stress of intensive exercise, with NK cell activity tending to be enhanced while neutrophil function is suppressed, but this is not a consistent finding.[4,5] The adaptive immune system (resting state), in general, seems to be largely unaffected by athletic endeavor. Thus, the magnitude of change in immunity that occurs after each marathon race bout may have more clinical significance than training-induced alterations in resting immunity.

2. Marathon Running and Risk of Upper Respiratory Tract Infections

A common perception among elite endurance athletes and coaches is that overtraining lowers resistance to URTI such as the common cold and sore throats.[6] Results of epidemiological studies generally support the belief that URTI risk is elevated during periods of heavy training and in the 1–2-week period following participation in competitive endurance races.[6-8]

However, it should be emphasised that the majority of endurance athletes do not report URTI after competitive race events. For example, only one in seven marathon runners reported an episode of UR-

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TI during the week following the March 1987 Los Angeles Marathon compared with 2 in 100 who did not compete.[7] URTI rates in marathon runners are even lower during the summer than winter/spring. In a study of 170 experienced marathon runners, only 3% reported an URTI during the week after a July marathon race event (own unpublished data, 1993). Even after competing in the 100-mile Western States Endurance Run, only one in four runners report URTI during the 2-week period following the race.[8]

When athletes train hard, but avoid overreaching and overtraining, URTI risk is typically unaltered. For example, in a cohort of 2300 marathon runners training for the Los Angeles Marathon, URTI risk was not elevated until training distances exceeded 100km a week.[7] Groups of marathon runners averaging 40–65km per week in training regularly report in surveys that they feel protected from URTI, but lose this protection following marathon race events.[6]

Together, these data indicate that there is a relationship between exercise workload and infection. Most endurance athletes should experience low to normal URTI risk during periods of regular training, with URTI risk rising during periods of overreaching/overtraining and competition. Other factors may amplify URTI risk for the marathon athlete, including exposure to novel pathogens, lack of sleep, severe mental stress, malnutrition and weight loss. A 1-year retrospective study of 852 German athletes showed that risk of URTI was highest in endurance athletes who also reported significant stress and sleep deprivation.[9] In other words, URTI risk is related to many factors that often converge during travel to and participation in important competitive events. Controlling these risk factors during critical training and competitive time periods is an important strategy for marathon athletes.

Athletes and fitness enthusiasts are often uncertain of whether they should exercise or rest during sickness. Human studies are lacking to provide definitive answers. However, animal studies generally support the finding that one or two periods of exhaustive exercise following injection of the animal with certain types of viruses or bacteria lead to a more frequent appearance of infection and more severe symptoms.[6] In general, if the marathon athlete has common cold symptoms (e.g. runny nose and sore throat without fever or general body aches and pains), intensive exercise training may be safely resumed a few days after the resolution of symptoms. Mild to moderate exercise training when sick with the common cold does not appear to be harmful. With symptoms of fever, extreme tiredness, muscle aches and swollen lymph glands, 2–4 weeks should probably be allowed before resumption of intensive training.

3. Countermeasures to Marathon-Induced Immune Dysfunction

The influence of nutritional supplements and drugs on the immune and infection response to marathon-type exertion is an active area of research by multiple investigators.[10] Supplements and drugs studied thus far in humans include zinc, dietary fat, plant sterols, antioxidants (e.g. vitamins C and E, β-carotene, N-acetylcysteine and butylated hydroxyanisole), amino acids, glutamine, carbohydrate, ginseng, echinacea, ibuprofen, probiotics, bovine colostrum and immunoferon. Except for carbohydrate beverages, none of these supplements have emerged as an effective countermeasure to exercise-induced immune suppression.[10] Antioxidants and glutamine have received much attention, but the data thus far do not support their role in negating immune changes after heavy exertion.

Of the various nutritional countermeasures that have been evaluated thus far for marathon athletes, ingestion of carbohydrate beverages during exercise has emerged as the most effective. However, carbohydrate supplementation decreases exercise-induced increases in plasma cytokines and stress hormones, but is largely ineffective against other immune components including NK cell function and salivary IgA, with an undetermined influence on URTI incidence. Ongoing research will determine the value of other nutritional components in countering immune dysfunction in marathon athletes.

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Acknowledgements

The author has indicated that he has no affiliation or financial interest in any organisation(s) that may have a direct interest in the subject matter of this article.

References

1. Larrabee RC. Leucocytosis after violent exercise. J Med Res 1902; 7: 76-82
2. Nieman DC. Immune response to heavy exertion. J Appl Physiol 1997; 82: 1385-94
3. Nieman DC. Special feature for the Olympics: effects of exercise on the immune system. Exercise effects on systemic immunity. Immunol Cell Biol 2000; 78: 496-501
4. Nieman DC, Buckley KS, Henson DA, et al. Immune function in marathon runners versus sedentary controls. Med Sci Sports Exerc 1995; 27: 986-92
5. Nieman DC, Nehlsen-Cannarella SL, Fagoaga OR, et al. Immune function in female elite rowers and non-athletes. Br J Sports Med 2000; 34: 181-7
6. Nieman DC. Is infection risk linked to exercise workload? Med Sci Sports Exerc 2000; 32 Suppl. 7: S406-11
7. Nieman DC, Johanssen LM, Lee JW, et al. Infectious episodes in runners before and after the Los Angeles Marathon. J Sports Med Phys Fitness 1990; 30: 316-28
8. Nieman DC, Henson DA, Dumke CL, et al. Relationship between salivary IgA secretion and upper respiratory tract infection following a 160-km race. J Sports Med Phys Fitness 2006; 46: 158-62
9. Konig D, Grathwohl D, Weinstock C, et al. Upper respiratory tract infection in athletes: influence of lifestyle, type of sport, training effort, and immunostimulant intake. Exerc Immunol Rev 2000; 6: 102-20
10. Nieman DC, Bishop NC. Nutritional strategies to counter stress to the immune system in athletes, with special reference to football. J Sports Sci 2006; 24: 763-72

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