Clinical Management of Immuno-Suppression in Athletes Associated with Exercise Training: Sports Medicine Considerations

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Abstract- The Overtraining Syndrome (OTS) is a physically debilitating medical condition that results in athletes being totally compromised in their capacity to perform and compete. Many physiological systems are affected by the process of overtraining and the development of the OTS which results from it; but one system in particular, the immune, is highly susceptible to degradation resulting in a reduction in overall health and physical performance. The aim of this paper is to review; 1) the evidence-based proactive steps and actions to take to greatly reduce the risk of development of an infection or a compromised immune system in athletes; and 2) the course of action for clinicians to take when they are dealing with an athlete displaying overt signs of an infection and, or inflammation. Evidenced reported here within support that it is essential for clinicians to take practical preventative and management steps – actions with athletes (involved in intensive exercise training) in order to help preserve and maintain a healthy and robust immune system if they are going to perform optimally.

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Introduction

The focus of an athlete's exercise training program is to improve their physical performance capacity in select sporting events. In attempting to enhance physical performance and cause positive physiological adaptations, competitive athletes perform a remarkable amount of exercise on a systematic basis. If the exercise training regimen stresses are excessive (involving working at too great an intensity, and/or containing too great a volume of work), or an athlete has too many additional life stresses (*e.g.*, emotional worry, financial concerns) during training, it is possible for physiological mal-adaptations to occur. Such physiological mal-adaptations can lead to physical performance declines. In the field of exercise physiology this process of applying excessive training stress is referred to as overtraining (1-3). If overtraining is persistently applied to an athlete, then there is the potential for the medical condition called the Overtraining Syndrome to develop in the athlete (4-6).

The Overtraining Syndrome (OTS) is a physically debilitating medical condition that results in an athlete being totally compromised in their capacity to perform and compete in sporting events. Table 1 presents some of the most commonly reported signs and symptoms associated with overtraining and the development of the OTS. The information in table 1 indicates that a multitude of physiological systems can affected by the OTS. Recent research evidence points to one system in particular being profoundly affected by overtraining; that system is the immune system. Findings point to a compromise of the immune system when exercise training becomes excessive and it is well documented that a compromised immunological function can impact greatly on many aspects of an athlete's health. To this end, the intent of this paper is to provide a brief overview of recommended steps for sports medicine clinicians toward the management and care to prevent and, or treat some of the health consequences of overtraining and OTS as related to the immune system established using current evidence-based research findings.

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Background immuno-suppression

The actions of the immune system can be divided into what are referred to as the *Innate* and *Adaptive* immune responses. In general the innate responses are the first line of immunological defense and are viewed as indiscriminately attacking pathogens, while the adaptive responses (which typically follow those of the innate) tend to target specific pathogens and have an antigen-specific memory of such pathogens (7). Figure 1 gives a schematic overview of the broad-spectrum aspects of these components to the immune system. Both the innate and adaptive immune responses are associated with the production of cytokines (see reference 7 for an extensive overview of cytokine type and function). There are a large number of cytokines that can be produced, and they are typically classified as either pro-inflammatory or anti-inflammatory in function; although, some cytokines have both pro- and anti-inflammatory actions (7). Research by Smith and colleagues indicates intensive exercise training resulting in skeletal muscle tissue trauma (7). This tissue trauma from exercise (if excessive) results in the production of an abundance of pro-inflammatory cytokines, which then leads to the development of a sickness response or a chronic fatigue-like behavior in an athlete (8-11). Smith and associates have proposed this be called the "cytokine tissue trauma hypothesis" of overtraining (7). The key pro-inflammatory cytokines most associated with this trauma events are; interleukin-1 beta (IL-1β), interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α) (8). Research by several other investigators has produced findings that substantiate the role of pro-inflammatory cytokines, especially IL-6, as being key physiological mediator and modulator for development of many of the symptoms associated with OTS (Table 1) (10-11).

Additionally, research evidence points to the production of pro-inflammatory cytokines facilitating the up-regulation of humoral immunity and the suppression of the cell-mediated immunity components of the adaptive immune responses (7). Because of its immune system role, development of cell-mediated immuno-suppression increases the risk of illness or illness-like symptoms such as upper respiratory symptoms (URS) and infections (URI). The development of such an illness or illness-like symptoms can be further associated with compromises in physical performance capacity in athletes – that is, they find exercise training or competition difficult or impossible under such conditions (12,13).

These phenomena of cell-mediated immuno-suppression and increased URS-URI risk are in-line with what are referred to as the "Open Window" and "J-Curve Response" concepts which are related to exercise training and illness developmental state as proposed by several eminent health researchers (14-16).

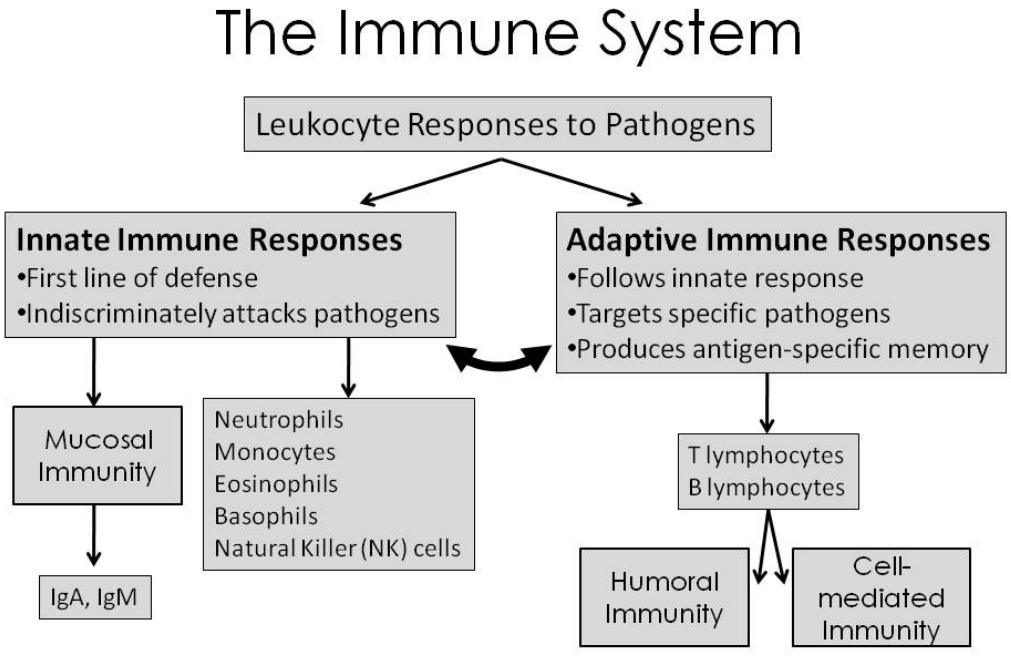

Figure 1. A schematic overview of the basic components of the immune system (abbreviations: IgA=Immunoglobulin A; IgM=immunoglobulin M.

Table 1. A listing of some of the major signs and symptoms of overtraining and the Overtraining Syndrome as reported by athletes.

Physiological Function:
Decreased competitive performance
Decreased muscular strength
Increased muscular soreness
Chronic fatigue
Reduced tolerance to training overload
Sleep-wake cycle abnormalities
Gastrointestinal disturbances
Reduced testosterone levels
Reduced thyroid hormone levels
Elevated cortisol levels
Elevated creatine kinase
Altered lactate responses to exercise
Reduced sexual drive and libido
Altered heart rate responses to exercise
Suppressed immunological function
Psychological Function:
Increased feelings of depression
Lethargy and apathy
Emotional abnormalities
Loss of appetite
Lack of competitive drive
Restlessness
Difficulty in concentrating

The open window concept entails that after an intensive exercise session there is a period of time (typically 3-72 hours) in which there is an increased susceptibility to illnesses, such as URI. If there is insufficient daily rest then there can be a cumulative effect of consecutive days of intensive training (*i.e*., the "window" staying open for a longer period of time). This notion of a period of increased susceptibility to illness following exercise has been linked to the occurrence of Natural Killer cell inhibition (part of the innate immune responses [immune-suppression]) that can happen after an exercise session brought on by the increased levels of cortisol, catecholamines, pro-inflammatory cytokines, and increased prostaglandins (from monocytes) in response to the exercise session (15,17-19). The Natural Killer cell suppression in turn seems to assist in the aspects of the greater adaptive immune responses and the up-regulation of humoral immunity and down-regulation of cell-mediated immunity (8,9). Interestingly, Natural Killer cell suppression is especially associated with and found following prolonged-duration endurance (aerobic) forms of exercise activities (*e.g*., marathon training) which have some of the highest incidences of OTS development (5,11,20,21). In a similar fashion, the J-curve response concept states that the risk of URI development initially goes down as a sedentary individual gets involved with light to moderate exercise training for health and fitness, but the prevalence substantially increases as the individual advances their training to higher levels of volume and/or intensity such as occurs in individuals wanting to compete in sporting activities; Figures 2 and 3 display diagrammatic depictions of these concepts.

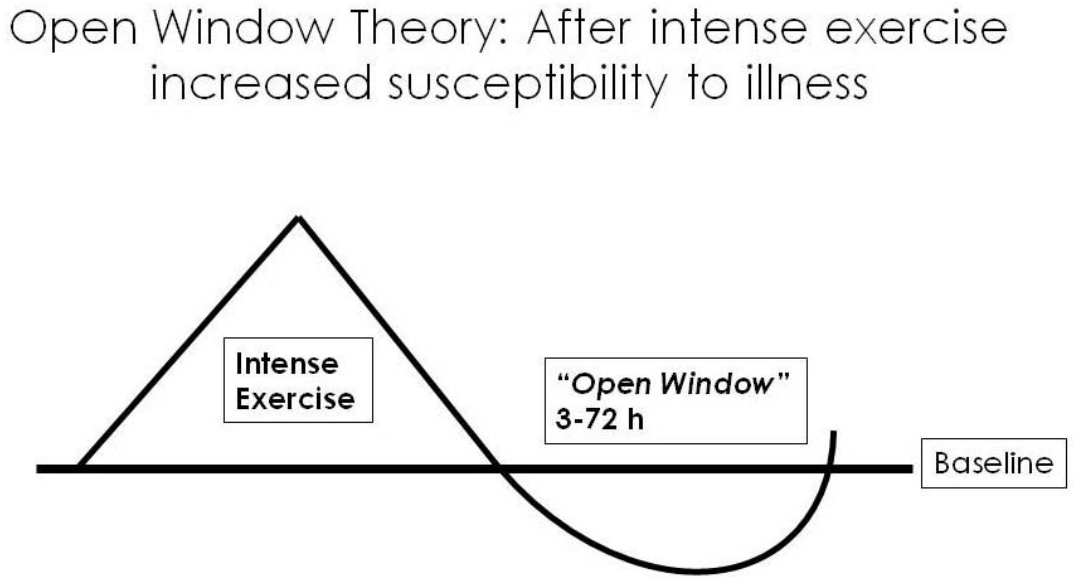

Figure 2. The "Open Window" theoretical concept associated with immune responses to acute exercise (abbreviation: h = hours).

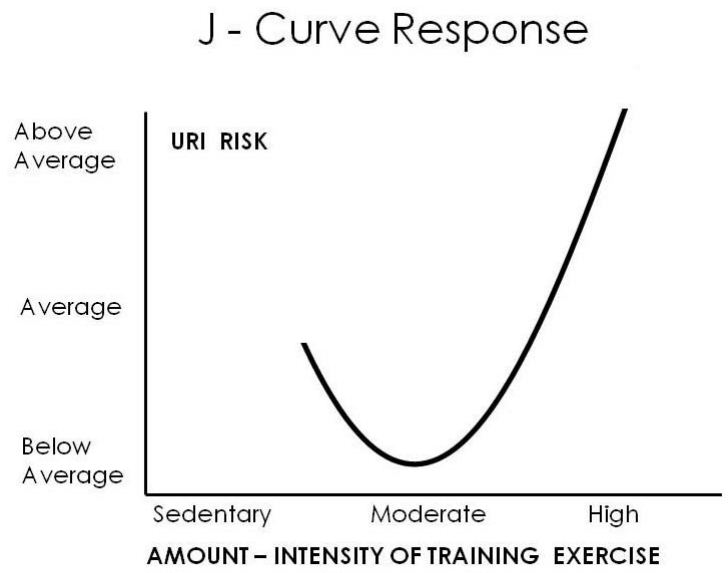

Figure 3. The "J-Curve" response concept associated with the immune responses to exercise training (abbreviation: URI = upper respiratory infections).

Practical aspects of dealing with immuno-suppression

As noted above, the evidence supports that the development of exercise training induced immuno-suppression is associated with compromised physical performance (12,15). Furthermore, development of an infection of any type, for any reason, in an athlete can lead to an inability to exercise train or compete at an optimal level (12,16). Therefore, it is important for sports medicine clinicians to take and recognize preventative - treatment steps and actions to allow for maintenance of appropriate immune function and health in athletes (22). What follows are the recommendations for such steps – actions based upon the current research literature.

Prevention

As with nearly all medical and health conditions, prevention is far superior to treatment in providing for a more successful overall maintenance of the athlete's training regimen and physical performance capacity. Research findings support that there are several proactive steps and actions that athletes and sports medicine clinicians can take to greatly reduce the risk of development of an infection or a compromised immune system (12,23). These steps – actions include such items as the athlete should;

- Keep vaccine(s) administration updated
- Attempt to minimize contact with people who have a known infection or are sick
- Wash hands frequently throughout the day
- Limit mouth/nose contact when with infection symptoms (*i.e*., URS)
- Do not share drinks with other athletes
- Do not share towels or washcloths with other athletes
- Isolate team members from others if displaying infection symptoms
- Protect airway from very cold or dry air with performing strenuous exercise
- Maintain adequate daily dietary carbohydrate intake (~60% daily caloric intake)
- Wear proper clothing for weather conditions and avoid getting cold-wet after exercise
- Attempt to get a minimum of 7 hours sleep a night
- Avoid rapid weight loss and "crash" dieting approaches to weight loss
- Wear clothing to prevent unnecessary hazardous dermatological exposures (*e.g*., shower shoes)
- Whenever possible minimize other life stressors

Evidence-based findings support that following these steps can significantly decrease the risk of infections developing in athletes (7,12). Obviously, though it may not be completely realistic to incorporate all of the above into the daily behaviors and life-styles of every athlete.

Treatment

Even with compliance to all of the abovementioned preventative steps and actions there is always a strong likelihood that an athlete will develop an infection of

some type. This occurrence would be apparent if they display such symptoms as; sore throat, coughing, runny/congested nose, muscle/joint pain - edema, headache, fever, malaise, diarrhea and/or vomiting (7). Recently, a collection of leading exercise immunologists recommended the following course of action when sports medicine clinicians are dealing with an athlete displaying overt signs of an infection and, or inflammation (12,23).

- Day 1 of Illness – No strenuous exercise or competition; the ill athlete should drink plenty fluids; keep from getting wet/cold; minimize life-stress. If feverish – induce nasal drainage, and use decongestants-analgesics.
- Day 2 of Illness – If symptoms worsen – no exercise, rest. If no fever or worsening of symptoms; then light-easy exercise (30-45 minutes) allowed.
- Day 3 of Illness – If fever, symptoms persist consult physician. If no fever or worsening of symptoms; then light-moderate exercise (45-60 minutes) allowed.
- Day 4 of Illness – If no symptom relief, no exercise – continued rest; have an office visit with a physician. If relief (1st day of improved symptoms), and no fever, then light-easy exercise (as noted above). Use the same number days as off to return and step up to normal training; monitor tolerance to gradually increasing exercise intensity, take additional days off if poor tolerance (if necessary).

Finally, in order to optimize the treatment regimen, it is critical that all members of the health-care team treating the athlete have good communication with one another concerning the progression and responses of the athlete if symptoms develop or persist (24-26). In conclusion, competitive athletes subject themselves to a high level of exercise training stress in order to enhance their physical performance capacity. This training stress, as well as the other stresses of life that athletes encounter, places them at a great risk for developing the OTS. The "cytokine tissue-trauma" hypothesis of OTS proposes that undue pro-inflammatory cytokine responses to excessive exercise training (overtraining) creates a "sickness behavior" response, development of immuno-suppression, and ultimately leads to a decline in physical performance capacity of the athlete.

It is critical that sports medicine clinicians take steps to prevent and reduce the risk of infection by helping athletes to foster and develop appropriate behaviors and actions as recommended above. Likewise, once an infection – inflammation response is manifested in the athlete it is critical for these same clinicians to take the actions to mitigate the severity and impact of the illness development through the recommended intervention steps. By doing so, the clinician can promote a more rapid return to normal health and exercise training level in the athlete.

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