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ANNALS OF
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IMMUNE RESPONSES TO EXTREME CHALLENGES

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KEY WORDS: Training, Psychological stress, Sleep, Environment, Nutrition

Numerous studies over the last 30 years indicate a decrease in immunity and an increase in upper respiratory infection (URI) symptoms in athletes and soldiers. Experts attribute these observations to the various stressors associated with both athletic training and competition (e.g. heavy exercise, nutritional deficits) and military training and field manoeuvres (e.g. sleep disruption and environmental stress)⁽¹⁸⁾. Psychological and physical stressors have long been known to influence the sympathetic-adrenal axis and pituitary-adrenal axis since the pioneering work of Walter B Cannon (coined ‘fight or flight’ response) and Hans Selye (coined term ‘stress’) in the 1930s. These common pathways and shared effector limbs for the body’s response to stress in its many forms give rise to increases in circulating catecholamines and glucocorticoid hormones; these hormones are widely acknowledged to have immunomodulatory effects. This presentation will provide new insights about, and recommendations for coping with, the effects of extreme challenges that athletes, soldiers and others encounter on immune health; including, the effects of heavy training stress, life stress, sleep disruption, environmental stress and nutritional deficits.

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HEAVY TRAINING STRESS

In athletes under heavy training both innate and acquired immunity are often observed to decrease after heavy exertion, typically 15–25%: prolonged heavy training sessions (> 90 min) and periods of overreaching and maladaptation in particular have been shown to decrease immunity (5, 13). Whether the observed changes in immunity with acute heavy exercise and heavy training are sufficient to increase URI susceptibility remains a point of contention. Recent work indicates that high level athletes are particularly susceptible to URI symptoms during periods of intensified training in the winter⁽⁹⁾. As such, when scheduling

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the training programmes of athletes and soldiers, coaches and commanders need to be mindful of the decrease in immunity associated with very prolonged exercise bouts, periods of high training load and when implementing increments in training load.

LIFE STRESS

Given the well-known and marked influence of psychological stress on immunity and infection resistance⁽⁴⁾, and the shared pathways and effector limbs for the body's response to various stressors (e.g. exercise, psychological stress) it stands to reason that psychological stress plays a role in the decrease in immunity with prolonged heavy exercise and heavy training^(15,19). Unfortunately, exercise immunologists rarely report measures of psychological stress in their studies and so there is little by way of empirical evidence to support this contention. It's quite conceivable, that psychosocial stress status in high level athletes and soldiers (related to life stress, competition or operations, injury, travel, sleep disruption, jet-lag etc.) accounts at least in part for the influence of acute exercise and heavy training on, immunity and host defence⁽¹⁹⁾. This presentation will make a call to exercise immunologists to account for psychological stress when examining the immune response to exercise; also, for coaches and support staff to monitor psychological wellbeing alongside more traditional physiological measures of training stress. Accordingly, very recent evidence highlights that aspects of mental health such as depression and psychological stress are important risk factors for illness in Olympic athletes⁽⁶⁾. Studies are required to demonstrate the utility of interventions to reduce psychological stress in athletes and soldiers experiencing high psychological stress in order to optimise immunity and host defence.

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SLEEP DISRUPTION

Like the other forms of stress discussed, sleep disturbances influence immunity via activation of the hypothalamic–pituitary–adrenal axis and the sympathetic nervous-system⁽¹⁴⁾. Chronic sleep disturbance and disruption to the normal circadian rhythm are associated with inflammation and desynchronization of rhythmic immune variables. These responses likely contribute to increased risk of infection, cardiovascular disease, and cancer in long-term shift workers. Not only do soldiers experience sleep disruption (e.g. during sustained operations), there is now evidence that athletes experience poor sleep patterns compared with non-athletes. This presentation will highlight what little we know about how sleep disturbance influences the immune responses to exercise. Compared with normal sleep, a disrupted night's sleep appears to prime the immune system and enhance immune-

surveillance by stimulating total lymphocytes, CD8⁺ T cells, NK cells, and $\gamma\delta$ T cells to leave the blood and migrate to potential sites of infection during the early recovery period after exercise⁽¹⁰⁾. By contrast, other studies indicate that a night without sleep does not influence leukocyte trafficking, neutrophil degranulation, or mucosal immunity at rest or after exercise⁽¹⁴⁾. Subtle immune changes have been observed after a night without sleep, including a shift toward a T helper 2 cytokine profile⁽¹¹⁾.

It is uncertain whether these subtle immune modifications with acute sleep loss are clinically meaningful for the athlete or soldier⁽¹⁴⁾. When considering the potential effects of poor sleep on immunity in athletes and soldiers, it is important to distinguish between acute and chronic sleep disturbance. Chronic sleep disturbance (12 nights, 50% sleep loss) increases the plasma inflammation markers C-reactive protein and IL-6⁽⁸⁾. However, intervening daytime naps can counter this apparent inflammatory response⁽¹⁷⁾. Short sleep duration (<7 h/night for 7 d) decreases the response to hepatitis B vaccination and the likelihood of clinical protection⁽¹⁶⁾. Similarly, a night of wakefulness after hepatitis A vaccination decreases the specific antibody response 2–4 months later⁽¹²⁾. People who experience poor quality sleep and/or regular sleep deprivation also have a 4–5-times greater risk of developing the common cold⁽³⁾. Continued research efforts should be directed towards monitoring and improving sleep in athletes and soldiers and understanding the implications for immune health.

ENVIRONMENTAL STRESS

This presentation will cover the controversial beliefs held by many athletes that breathing cold, dry air and getting a 'chill' through cooling of the skin cause the 'common cold'. Although controversial, some evidence shows that peripheral cooling of the nose and upper airways (and even the feet) can increase common cold symptoms, possibly by inhibiting immune cell trafficking and creating a suitable local environment for viral replication⁽⁷⁾. Although not entirely conclusive, evidence indicates that cold exposure often precedes, and is associated with increased incidence of, URIs including the common cold⁽¹⁹⁾. Other controversies discussed in this presentation include whether exposure to environmental extremes (e.g. heat acclimation, cryotherapy and hypoxic training) compromises immunity and increases URI in athletes and soldiers. With the exception of cell-mediated immunity that tends to be decreased, exercising in environmental extremes does not appear to provide an additional threat to immunity and host defence. Recent evidence suggests that immune health may actually be enhanced by regular intermittent exposures to environmental stress e.g. intermittent hypoxia training⁽²⁰⁾.

NUTRITIONAL DEFICITS

Nutrient availability can influence immunity directly because macro- and micro-nutrients are involved in a multitude of immune processes (e.g. as a fuel source) but also indirectly via increases in stress hormones during prolonged exercise e.g. when blood glucose falls. Athletes and soldiers either intentionally or non-intentionally experience deficits in energy intake (e.g. extreme weight-loss diets, restricted rations) and macronutrient intake (e.g. restricted carbohydrate). For example, soldiers on a 12-day training exercise in the tropics who received only half of their estimated energy intake in ration packs experienced decreases in both cellular and humoral immunity⁽²⁾.

Paradoxically, nutritional strategies currently adopted by endurance athletes, including training with low carbohydrate, may benefit training adaptations and performance at the expense of immunity; for example, carbohydrate restriction may increase the immunosuppressive stress hormone response to exercise⁽¹⁾. As such, the rather modest benefits studies show in terms of training adaptations and performance might, in the long term, be lost if the athlete gets sick more often. Studies are required to investigate whether the nutritional practices adopted by elite athletes impair immunity and increase infection; and, whether purported 'immune-boosting' supplements benefit immune health for athletes and soldiers without blunting the desired training adaptations.

This presentation highlights the effects of extreme challenges that athletes, soldiers and others encounter on immune health. Interested readers are directed to recent reviews on the topics covered in this presentation^(1,14,19).

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