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Exercise and immunity in sports horses

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Exercise is widely recognized as a physiological stressor that can influence immune responses mainly through the sympathetic nervous system (SNS) and/or the hypothalamic-pituitary-adrenal (HPA) axis. While physical activity is an intrinsic component of life, modern habits are associated with substantial decreases in daily activity levels, and human medicine recommends regular and moderate exercise as a "polypill" for the prevention and treatment of diverse diseases. Nonetheless, as any other medication, it can have side effects and the dose should be adjusted depending on the patient. Indeed, its effect is subject to inter-individual variability thus dependent on factors such as age, chronic stress, concomitant diseases, all of which influencing the basal inflammatory/homeostatic "set-point". Thus, the pro-inflammatory effect of exercise can benefit a healthy subject while it can exacerbate another's condition. Along the same line, its anti-inflammatory effect can control the acute inflammatory reaction occurring with intense exercise but can also compromise the immune response towards pathogens. Furthermore, exercise can have different effects on the immune system depending on its duration and intensity. Last decades have seen the rise of significant scientific literature describing the modifications induced by acute or repeated, moderate or strenuous exercise in humans, even though much still remains to be understood. The relationship between exercise and immunity may be assessed either through the study of different aspects of the immune response (functional parameters of immune cells, cellular response after stimulation, cell counting/identification etc.) or by epidemiological studies on individuals with different levels of physical activity. The collection of both epidemiological and experimental data in humans has led to the formulation of the "inverted J relationship" between the level of physical activity and immune function. According to

this hypothesis, moderate and regular physical activity, compared to a sedentary state, seems to boost immunity, reduce susceptibility to infections and protect against chronic inflammatory conditions. Experimentally, moderate exercise is associated with an increase in the activity of blood monocytes and granulocytes. In contrast, strenuous exercise seems to represent an immunological suppressant, as it has been shown to reduce the oxidative burst capacity of neutrophils and monocytes. Moreover, some Toll-like receptors (TLRs), which are conserved receptors of the innate immune system recognizing pathogen-associated molecular patterns and initiating inflammatory and immune responses, have been shown to be down-regulated after acute resistance exercise. Over the short-term, this phenomenon would entail in the short-term an increased risk for viral and bacterial infections. Over the long-term, this down-regulation could decrease the inflammatory capacity of leucocytes, thus preventing chronic inflammation. It is important to underline that the post-exercise period can be equally challenging for the immune system. Indeed, in human athletes, some immune changes (i.e. a reduction in the activity of natural killer cells, of T and B-cells, of airway neutrophils and a decrease in IgA salivary concentration) have been shown to happen and persist for up to 24 hours after strenuous exercise. In this period called "open-window", immune responses, especially in the upper respiratory tract, are impaired, increasing the risk of infections for the host. In horses, literature on the topic is still limited, but main findings are consistent with observations in humans, suggesting the possible beneficial effect of a moderate physical activity, the detrimental outcome of a strenuous exercise and the likely existence of a "window of vulnerability", where the risk of infections is increased. However, most of the equine studies have focused mainly on the exercise-induced modifications of the innate immune response in blood while only few have investigated pulmonary responses. Research on equine pulmonary macrophage function after exercise and training, together with research from our lab focusing on the stimulation of pulmonary, bronchial and blood cells with TLR ligands have supported the idea that intense training, more than acute exercise, would alter the local innate immune response in the lung and in the systemic circulation. It is important to note that a direct transposition of conclusions of human studies to horses should be avoided due to inter-species differences. For example, equines suffer frequently from lower airway inflammatory diseases while human athletes are more susceptible to upper airway infections. Furthermore, the main mechanisms

supposed to be central in the modulation of immune function during exercise in humans, as the pro-inflammatory role of adipose tissue, the secretion of IL-6 by skeletal muscle during exercise and the sensitivity to cortisol concentration may not have the same importance in horses. Moreover, the protective role of exercise against chronic inflammation in man does not seem consistent in racehorses where epidemiological data suggest that training seem to favor occurrence of inflammation rather than preventing it. Nonetheless, horses start racing at very young ages, when the immune system may still be immature, and exercise is generally intense. Last, but not least, exercise-induced pulmonary hemorrhage that has a very high incidence in racehorses, while very rare in humans, may also interfere with immune function due to impairment of pulmonary macrophage function. In conclusion, it is obvious that the interplay between exercise and immunity is a promising and still undisclosed field of research that definitely warrants further investigation in horses.

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