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Title: The innate immune response in the airways and in blood is altered by training in horses

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Body: Lower airway diseases are common problems in sports and racing horses. In humans, exercise has been associated with upper respiratory tract infections due to down-regulated expression of Toll-like receptors (TLRs), costimulatory and antigen-presenting molecules on monocytes. The objectives of this study were 1) to examine the expression of TLRs in equine bronchial epithelial cells (EBEC) and blood monocytes in untrained and trained horses; 2) to stimulate EBEC and monocytes in vitro with TLR ligands, in order to mimic bacterial/viral infections; 3) to compare the cytokine production of EBEC and monocytes in untrained and trained horses. Bronchial biopsies were taken from 8 horses during lower airway endoscopy at rest and 24 hours after a standardized exercise test (SET). Bronchial epithelial cells were grown in vitro and activated with TLR ligands. Blood monocytes were collected at rest and after the SET. TLR1-TLR9 expression was evaluated via real-time PCR and cytokine production was measured via ELISA. TLR3 and TLR4 expression was modified by training. The expression of TLR2, TLR7 and TLR8 was modified only by strenuous exercise in trained horses. Training had local immuno-suppressive effects shown by a decreased production of TNF-alpha and IFN-beta in EBEC in response to TLR2 and TLR3 ligands. Training also caused a systemic pro-inflammatory response evidenced by increased production of TNF-alpha in monocytes in response to TLR2 and TLR4 ligands. These findings suggest that training and strenuous exercise in trained subjects may result in an increased susceptibility of the lower airway to infections associated with systemic inflammation.