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## Airway remodeling and its reversibility in equine asthma

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### Abstract

Despite effective therapies for controlling its clinical manifestations, human asthma remains an incurable disease. It is now recognized that inflammation induced structural changes (remodeling) of the airways are responsible for the progressive loss of lung function in asthmatic patients. However, the peripheral airways, where most of the remodeling occurs in severe asthmatic patients, cannot be safely sampled in humans, and therefore, little is known of the effects of current therapies at reversing the established asthmatic remodeling, especially those occurring in the peripheral airways.

Animal models have been studied to unravel etiological, immunopathological, and genetic attributes leading to asthma. However, experiments in which the disease is artificially induced have been shown to have limited translational potential for humans. To the contrary, horses naturally suffer from an asthma-like condition which shares marked similarities with human asthma making this model unique to investigate the kinetics, reversibility, as well as the physiological consequences of tissue remodeling (Bullone and Lavoie 2015).

We reported an increased deposition of smooth muscle, collagen and elastic fibers in the peripheral airways of affected horses, which was correlated with the lung function (Herszberg et al., 2006; Setlakwe et al., 2014). The airway subepithelial collagen depositions were almost completely reversed with 6 to 12 months of treatment with either antigen avoidance or inhaled corticosteroids (ICS) administration, and there was a modest (30% on average) decrease in airway smooth muscle (Leclere et al., 2011). A recent study also found that ICS combined with long-acting  $\beta_2$ -agonists drugs (LABA) and ICS monotherapy similarly induced a 30% decrease of the airway smooth muscle mass at 3 months (Buollone, 2017). However, only ICS/LABA and antigen avoidance decreased airway luminal neutrophilia.

The findings indicate the enhance therapeutic effect of ICS/LABA over ICS monotherapy at controlling asthma exacerbations in humans may be due to their anti-remodeling and anti-inflammatory effects. However, airway smooth muscle remodeling is only partially reversible with current anti-asthma medications.

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