Overview of the Equine Respiratory System  (13-Mar-2002)

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Actions of Neurotransmitters and Inflammatory Mediators on Airway Smooth Muscle

When acetylcholine is released from parasympathetic nerves, it binds to specific receptors on the surface of airway smooth muscle. Activation of the M₃ receptor leads to release of calcium from the smooth endoplasmic reticulum. The resultant increase in the concentration of intracellular calcium leads to smooth muscle contraction. Acetylcholine can also activate M₂ receptors (see below).

When epinephrine binds to β₂-adrenoceptors, another important intracellular pathway is activated. Adenylyl cyclase is activated and this leads to an increase in the intracellular concentration of cAMP, resulting in relaxation of airway smooth muscle. Activation of M₂ receptors by acetylcholine has the opposite effect - it inhibits adenylyl cyclase, which leads to a decrease in the cAMP. Thus acetylcholine is a very effective spasmogen because it initiates contraction via the M₃ receptor and decreases relaxation via the M₂ receptor.

Mediators released by inflammatory cells and the airway epithelium also activate specific receptors on airway smooth muscle and initiate changes in the intracellular concentrations of calcium and cAMP. Histamine and leukotriene D₄ are examples of mediators that cause smooth muscle contraction via an increase in intracellular calcium concentration. Other mediators, for example PGE₂, initiate smooth muscle relaxation by increasing the intracellular concentration of cAMP. Some mediators can activate several types of receptors. For example, when histamine activates the H₁ receptor, intracellular calcium increases and contraction occurs. When it activates an H₂ receptor, cAMP increases and smooth muscle relaxes. The net effect of a single mediator depends on the number and type of each receptor on the smooth muscle cell.

Airway epithelium produces factors, such as nitric oxide and PGE₂, that can inhibit smooth muscle contraction [81] Nitric oxide does not bind to a specific receptor but rather diffuses into the smooth muscle where it activates guanylyl cyclase and causes an increase in the intracellular concentration of cGMP. This leads to smooth muscle relaxation. Damage to the endothelium by viruses may lead to alterations in the production of mediators and thereby affect smooth muscle tension.

During the inflammatory cascade, several mediators may be released or formed concurrently and these all act on their specific receptor(s) on both smooth muscle and nerves. Hence, during inflammation, the degree of smooth muscle tension is the result of interactions of several inflammatory mediators and neurotransmitters acting concurrently to determine the intracellular concentrations of calcium, cAMP, and cGMP [65,79].

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