Mechanisms and Biomarkers of Exercise-Induced Bronchoconstriction

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KEYWORDS

• Hyperpnea • Water loss • Osmolarity • Epithelium • Mast cells • Eosinophils • Eicosanoids • Sensory nerves

KEY POINTS

- The conditioning of inhaled air during exercise-hyperpnea initiates osmotic and vascular events that lead, in susceptible individuals, to airway narrowing.
- A loss of physical barrier integrity and impairment in signaling and secretory functions of the airway epithelium increases the susceptibility to exercise-induced bronchoconstriction.
- Airway smooth muscle contraction and mucin release in individuals with exercise-induced bronchoconstriction are mediated predominantly by release of inflammatory mediators with associated activation of neural pathways.
- Cysteinyl leukotrienes and prostaglandin D_2 are the primary inflammatory mediators released into the airways from mast cells and eosinophils during exercise-induced bronchoconstriction.

INTRODUCTION

The underlying basis for exercise-induced bronchoconstriction (EIB) is becoming increasingly understood. Initial work starting in the 1970s revealed the major determinants of EIB in susceptible individuals. The aims of this review are to examine the respective roles of evaporative water loss and thermal changes as stimuli to EIB;

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provide evidence that loss of physical barrier functions of the epithelium during exercise-induced hyperpnea is associated with the development of bronchoconstriction in susceptible individuals; discuss the central role of leukocyte activation and the associated generation of lipid mediators and release of neuropeptides that sustain bronchoconstriction during EIB; and consider the role that regional airway closure may play in the development of EIB.

CONDITIONING THE AIR INSPIRED DURING EXERCISE

Under most conditions of exercise, the air inspired needs to be heated and humidified to body conditions (37°C, 100% relative humidity, or 44 mg H_2O/L) before it enters the alveoli. As a result, heat and water are lost from the airway surface during inspiration. The number of generations involved in conditioning depends on the level of ventilation reached and sustained during exercise, and the temperature and water content of the inspired air.[1]

Heat Loss as a Stimulus to Airway Narrowing

Cooling of the airways, from heat lost through vaporization of water and from heating the inspired air, was initially identified as a potential stimulus for EIB.[2] The proposal was subsequently extended to include a rewarming of the airways after exercise[3] (**Fig. 1**). This hypothesis suggested that cooling initiated vasoconstriction during exercise, followed by a reactive (or rebound) hyperemia at the end of exercise.[3] These vascular events are most significant when air of subzero temperature is inspired during intense exercise of 4 minutes or more[4] and when the smaller airways are recruited into the conditioning process, but are unlikely to occur in temperate or hot environments. These vascular events may be relevant to anyone performing vigorous exercise in cold conditions and may serve to amplify airway narrowing in individuals with asthma who may have a more rapid and exaggerated vascular response than non-asthmatics.[5,6]

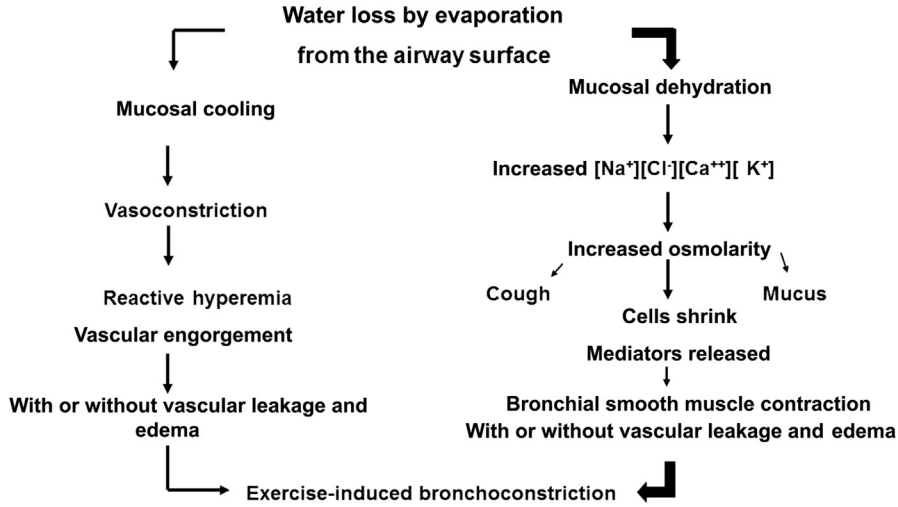

Fig. 1. Both airway cooling and mucosal dehydration occur in response to evaporative water loss from the airway surface. These events lead to exercise-induced bronchoconstriction. (*From* Rundell KW, Anderson SD, Sue-Chu M, et al. Air quality and temperature effects on exercise-induced bronchoconstriction. Compr Physiol 2015;5(2):581; with permission.)