Exercise-Induced Bronchoconstriction and the Air We Breathe

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KEYWORDS

• Air pollution • Particulate matter • Ozone • Trichloramines • Nitrogen dioxide • Sulfur dioxide • Exercise-induced bronchoconstriction • Asthma

KEY POINTS

- Environmental factors that influence mediator release and airway pathology include ambient air humidity and airborne pollutants, including chemical irritants and particulate matter.
- The high ventilatory demands of exercise exacerbates total exposure to noxious stimuli and allows particulate matter to deposit at deeper levels within the lungs.
- Subjects with and without respiratory pathologies may present respiratory symptoms in polluted environments or cold, dry air.
- The prevalence of exercise-induced bronchoconstriction and asthma in competitive athletes is attributed to training and competing in adverse environmental conditions.
- New-onset asthma from chronic inhalation of pollutants and the acute exercise-induced bronchoconstriction response is a major health concern for individuals training, competing, working, and recreating in high pollution environments.

INTRODUCTION

Exercise-induced bronchoconstriction (EIB) is defined as the transient abnormal constriction of the airways in response to vigorous exercise.[1] Key mediators in this response are histamine, leukotrienes, and prostaglandins that are released from mast cells, eosinophils and neutrophils in the airways.[2,3] These mediators are released in response to the airway mucosa being exposed to various triggers related to air

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quality. Environmental factors that influence mediator release include ambient air humidity and airborne pollutants, including chemical irritants and particulate matter (PM).[4,5] The high ventilatory demands of exercise exacerbates total exposure to these noxious stimuli, while also allowing PM to deposit at deeper levels within the lungs.[6]

Although acute exposure to these environmental triggers is capable of initiating an EIB event, chronic exposure is epidemiologically linked to the development of asthma and other allergic/immunologic conditions. The prevalence of EIB and asthma in competitive athletes exceeds that found in the recreational athlete, and has been attributed to training and competing in adverse environmental conditions,[1] such as the high pollution conditions found in ice rinks, indoor swimming pools, and high vehicular traffic areas.[7] New-onset asthma from the chronic inhalation of pollutants and the acute EIB response present a major health concern for individuals training, competing, working, and recreating in these high pollutant environments. Thus, this paper aims to explore the relationship between EIB and asthma with specific environmental exposures commonly encountered during exercise, in the hopes that a greater understanding of these associations can lead to improved prevention and clinical management of airway disease.

GENERAL PATHOGENESIS OF POLLUTION-INDUCED AIRWAY DYSFUNCTION

Oxidative Stress

There is increasing evidence supporting the notion that oxidative stress caused by the inhalation of environmental pollutants during exercise promotes the development of asthma and enhances the EIB response.[8–12] Oxidative stress is a key feature in the pathogenesis of asthma[13] and is likely involved in the production and release of inflammatory mediators in the EIB response.[14] The oxidative stress in the airways includes the increase in reactive oxygen/nitrogen species (RONS) concomitant with a decrease in resident antioxidants. Increased concentrations of 8-isoprostane, a marker of airway oxidative stress, in exhaled breath condensate are associated with EIB.[14] Additionally, plasma and exhaled breath condensate concentrations of biomarkers associated with lipid peroxidation, such as malondialdehyde, are increased after exercise in athletes with EIB.[15]

Inflammation

The biologic response to the inhalation of air pollution has been shown to stimulate airway inflammation through oxidative stress and is characterized by an increase in airway inflammatory cells and inflammatory mediators (**Fig. 1**). Pollution exposure (fine particles, particles <2.5 μm and >0.1 μm in diameter, [$PM_{2.5}$], diesel exhaust, ozone) has been associated with increased neutrophils, eosinophils, eosinophil cationic protein, interleukin (IL)-8, and IL-33 in nasal lavage, in vitro animal studies, and human bronchial lavage samples.[16–19] Increases in myeloperoxidase, neutrophils, mast cells, $CD4^+$ and $CD8^+$ T lymphocytes, and the upregulation of adhesion molecules (eg, intercellular adhesion molecule-1 and vascular cell adhesion molecule-1) have been associated with ultrafine particle exposure,[20,21] supporting neutrophilic inflammation in the airways.[18,22,23]

Glutathione Depletion

Reduced glutathione (GSH) plays a central role in protection against airway oxidative stress and has been shown to decrease in asthmatics[24] and after PM exposure in airway epithelial cells in vitro.[25] Conversely, GSH may increase in healthy subjects after exposure to mild levels of diesel exhaust, indicating that the air–lung interface in