session consisted of 90 min. For the first 30 min, the subjects breathed with no inspiratory load present. In the last 60 min, the load varied according to group assignment: group 1, no inspiratory load; group 2, low inspiratory load (1.3 cm H₂O/L/s); or group 3, medium inspiratory load (3.4 cm H₂O/L/s); or group 4, heavy inspiratory load (14.1 cm H₂O/L/s). Trials were repeated on 3 consecutive days for the first three groups and for 4 days for the fourth group. Borg scores were obtained at the beginning and the end of the first 30 min, and at the beginning of loaded breathing and every 30 min thereafter. Anxiety was measured using the State-Trait Anxiety Inventory.

We found that dyspnea was significantly greater in subjects exposed to the heavy load, when compared to the control subjects and low-load group (Tukey-Kramer multiple comparison). We further investigated subjects exposed to the heavy-loaded group for a fourth day. We found that dyspnea was significantly improved in the heavy-loaded subjects on this fourth day. Anxiety did not change significantly throughout the protocol.

These findings indicate that there is a threshold of inspiratory loading where normal subjects experience dyspnea, and that normal subjects are able to overcome this dyspnea. This compensation occurs over days and represents learning.

Identification of Birch Pollen Respirable Particles*

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(CHEST 2003; 123:433S)

Trees in the birch family, including alder, hazel, and birch, have wind-pollinated flowers that produce copious amounts of pollen and are a major cause of allergic rhinitis. How their pollen allergens cause asthma has been a mystery because pollen grains are too large to be inhaled into the airways. How these allergens are released into the air remains unknown. Recently, we have shown that for flowering grasses, pollen remains on the open anthers in the absence of wind or other disturbances. If wetted, pollen can rupture within minutes. Fragmented cytoplasm is emitted through the pore region of the pollen grain. Drying winds release this cytoplasmic debris as a respirable allergen-loaded aerosol.

A similar mechanism results in the release of respirable allergen-loaded aerosol from birch flowers. However, birch pollen requires at least 3 h of wetting, and may germinate within the anther, prior to rupture. Other submicron particles, such as oribules and interorbicular structures, are also released from the anther surface; however, immunoblots show that they are not loaded with birch pollen allergens. Less than 5% of particles released in the size range of 30 to 500 nm are interorbicular structures. Particles of fragmented cytoplasm in the size range of 30 nm to 4.5 µm are released from birch pollen grains and emitted into the air. The small size of these particles suggests that they can readily deposit in the lower airways.

Reference


Regulation of Phospholipase A₂ by Interleukin-1 in Human Airway Smooth Muscle*

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(CHEST 2003; 123:433S–434S)

Abbreviations: COX = cyclooxygenase; cPLA₂ = cytosolic phospholipase A₂; HASM = human airway smooth muscle; IL = interleukin; PLA₂ = phospholipase A₂

Treatment of human airway smooth muscle (HASM) with interleukin (IL)-1β alone or in combination with serum or growth factors is known to induce cyclooxygenase (COX)-2 and prostaglandin E₂ synthesis, an effect presumably under-

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lying IL-1β–mediated β2 adrenergic receptor and epoprostenol receptor desensitization and inhibition of mitogen-stimulated cell growth in HASM. Although COX-2 induction is clearly required and COX-2 activity is believed to be limiting in IL-1β-stimulated prostaglandin E2 synthesis, the role of phospholipase A2 (PLA2) in this process is unclear. We therefore assessed potential alterations in the following: (1) cytosolic PLA2 (cPLA2) protein levels, (2) cPLA2 phosphorylation state, and (3) PLA2 activity in growth-arrested HASM cultures treated with IL-1β or growth factors. Treatment with IL-1β induced a time-dependent increase in cPLA2 protein levels (assessed by immuno blotting) with a twofold increase observed at 18 h. Epidermal growth factor had a minimal effect on cPLA2 induction, but cotreatment with IL-1β plus endothelial growth factor was synergistic, resulting in a greater than fourfold induction. cPLA2 induction was partially inhibited by the p38 inhibitor SB203580 and the classical protein kinase C inhibitor Bis I. IL-1β induced a rapid phosphorylation of cPLA2, which peaked at approximately 1 h and then waned toward basal levels by 18 h. Lastly, PLA2 activity in cultured HASM, characterized by cleavage of a phospholipid analog conjugated to a BODIPY fluorophore (D3953; Molecular Probes; Eugene, OR), was regulated by IL-1β but occurred against a background of high basal PLA2 activity in cell culture medium, suggesting an important role for secretory PLA2 in HASM arachidonate metabolism. These data suggest that regulation of HASM PLA2 activity may be important in cytokine- and growth factor-mediated eicosanoid synthesis and associated functional consequences.

**The Effect of House Dust Mite Aeroallergen and Air Pollutant Exposures During Infancy**

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**Abbreviation:** HDM = house dust mite

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**Indoor allergens such as house dust mite (HDM) are a contributing factor to the development of allergy and asthma in children. There is increasing evidence that air pollutants such as ozone may affect the initiation or severity of atopic diseases. We have previously established that experimental exposure of adult rhesus monkeys to HDM produces a clinical and pathologic syndrome similar to that of human asthmatics. In order to understand the combined effects of ozone and HDM aerollenrgens during a period of pulmonary and immune system development, we exposed infant rhesus monkeys for 22 weeks to one of four regimens: (1) filtered air, (2) priming doses of HDM plus adjuvant parenterally followed by biweekly aerosolized HDM, (3) ozone at 0.5 ppm for 8 h/d 5 days on and 9 days off, or (4) HDM plus ozone. In response to HDM exposure, epithelial and mesenchymal components of the airway wall were altered in association with elevated baseline airway obstruction. Exposure to ozone exacerbated the remodeling changes associated with HDM exposure. Similarly, peripheral blood and lavage T-helper cell activation was enhanced in response to HDM and ozone exposures. Within specific airway generations, the abundance of activated T lymphocytes, dendritic cells, and eosinophils were also affected by HDM and ozone exposure regimens. Our cumulative findings indicate that air pollutants have a modulatory effect on the pulmonary and systemic response to allergens.**

**Pediatric Asthma**

**An Approach to Pharmacogenetics Analysis**

Stanley J. Szefler, MD

(CHEST 2003; 123:434S–438S)

**Abbreviations:** IL = interleukin; NHLBI = National Heart, Lung, and Blood Institute; PC20 = provocative concentration of methacholine causing a 20% fall in FEV1

Numerous studies have clearly demonstrated that inhaled glucocorticoids alleviate clinical symptoms, improve pulmonary function, and reduce airway inflammation; there is some evidence that they may alter disease

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