

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*

Philip E. Taylor, PhD; Richard Flagan, PhD;
Ann G. Miguel, PhD; Rudolf Valenta, MD; and
M. Michael Glovsky, MD

(*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 where asthma occurs. Over the past 20 years, studies showed that episodes of pollen-induced asthma occurred during the flowering season, especially after periods of rainfall or thunderstorm. Immunologic studies revealed that abundant quantities of micronic particles occur in the outdoor air, especially after rainfall, and they are loaded with birch pollen allergens. How these

*From the Division of Chemistry and Chemical Engineering (Drs. Taylor, Flagan, and Miguel), California Institute of Technology, Pasadena, CA; Asthma and Glovsky Center, Huntington Medical Research Institute (Dr. Glovsky), Pasadena, CA; and Department of Pathophysiology (Dr. Valenta), University of Vienna, Austria.

Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (e-mail: permissions@chestnet.org).

Correspondence to: Philip E. Taylor, PhD, Division of Chemistry and Chemical Engineering, 210-41, California Institute of Technology, Pasadena, CA 91125; e-mail: taylor@caltech.edu

respirable allergens were released into the air remained 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.¹ 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 submicronic particles, such as orbicules 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 800 nm are interorbicular structures. Particles of fragmented cytoplasm in the size range of 30 nm to 4.5 μ m 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

- 1 Taylor PE, Flagan RC, Valenta R, et al. Release of allergens as respirable aerosols: a link between grass pollen and asthma. *J Allergy Clin Immunol* 2002; 109:51–56

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

Rodolfo M. Pascual, MD; Bharat K. Awsare, MD;
Stephen A. Farber, PhD; Reynold A. Panettieri, Jr, MD;
Stephen P. Peters, MD, FCCP; and Raymond B. Penn, PhD

(*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)-1 β alone or in combination with serum or growth factors is known to induce cyclooxygenase (COX)-2 and prostaglandin E₂ synthesis, an effect presumably under-

*From the Department of Medicine, Jefferson Medical College, and Kimmel Cancer Center, Thomas Jefferson University, Philadelphia, PA.

Dr. Pascual is recipient of a Parker B. Francis Fellowship. This work was supported by grants HL-58506 and HL-67663. Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (e-mail: permissions@chestnet.org).

Correspondence to: Rodolfo M. Pascual, MD, Thomas Jefferson University, Division of Critical Care, Pulmonary Medicine, Allergic and Immunologic Diseases, Suite 805 College Bldg, 1025 Walnut St, Philadelphia, PA 19107; e-mail: Rodolfo.Pascual@mail.tju.edu

lying IL-1 β -mediated β_2 adrenergic receptor and epoprostanoid 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-1 β -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-1 β or growth factors. Treatment with IL-1 β induced a time-dependent increase in cPLA₂ protein levels (assessed by immunoblotting) with a twofold increase observed at 18 h. Epidermal growth factor had only a minimal effect on cPLA₂ induction, but cotreatment with IL-1 β 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-1 β 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 (D3803; Molecular Probes; Eugene, OR), was regulated by IL-1 β 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*

Lisa A. Miller, PhD; Dallas M. Hyde, PhD;
Laurel J. Gershwin, DVM, PhD; Edward S. Schelegle, PhD;
Michelle V. Fanucchi, PhD; Michael J. Evans, PhD;
Joan E. Gerriets, PhD; Lei F. Putney, MS; Mary Y. Stovall, BS;
Nancy K. Tyler, PhD; Jodie L. Usachenko, MS; and
Charles G. Plopper, BS

(*CHEST* 2003; 123:434S)

Abbreviation: HDM = house dust mite

*From the Center for Comparative Respiratory Biology and Medicine and the California Regional Primate Research Center, School of Veterinary Medicine, University of California, Davis, CA.

Supported by National Institute of Environmental Health Sciences grant ES-00628 and National Center for Research Resources grant RR000169.

Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (e-mail: permissions@chestnet.org).

Correspondence to: Lisa A. Miller, PhD, Department of Anatomy, Physiology and Cell Biology, School of Veterinary Medicine, One Shields Ave, University of California at Davis, Davis, CA 95616; e-mail: lmiller@ucdavis.edu

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 aeroallergens 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. Szeffler, 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

*From the Divisions of Clinical Pharmacology and Allergy and Immunology, Department of Pediatrics, National Jewish Medical and Research Center, Denver, CO.

Supported in part by Public Health Services research grants 1N01-HR-16048, HL36577, HL 51834, General Clinical Research Center grant 5 MO1 RR00051 from the Division of Research Resources, and NICHD Pediatric Pharmacology Research Unit Network grant 1-U01-HD37237.

Reproduction of this article is prohibited without written permission from the American College of Chest Physicians (e-mail: permissions@chestnet.org).

Correspondence to: Stanley J. Szeffler, MD, National Jewish Medical and Research Center, 1400 Jackson St, Room B121, Denver, CO 80206; e-mail: szefflers@njc.org