Adenosine Helps Differentiate Asthma, COPD

One's response to AMP could help monitor airway inflammation and response to treatment.

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MIAMI BEACH — Measuring airway responsiveness to inhaled adenosine helps discriminate between a diagnosis of asthma and chronic obstructive pulmonary disease.

It's also a valuable clinical tool for monitoring airway inflammation and response to anti-inflammatory treatment in asthma, Dr. Riccardo Polosa reported at the annual meeting of the American Academy of Allergy, Asthma, and Immunology. "AMP challenge is noninvasive, non–time consuming, low cost, has good reproducibility and patient acceptability, and safety is optimal," he said.

Adenosine 5'-monophosphate (AMP) is a proinflammatory mediator that induces bronchoconstriction in patients with inflammatory lung diseases. Response to AMP is determined by measuring the concentration of inhaled AMP causing the forced expiratory volume in 1 second (FEV_1) to decrease by 20%. The exact cutoff point between normal and abnormal PC20 AMP, as it is known, remains somewhat unclear. But a cutoff of 160 mg/mL has been used successfully to discriminate between asthmatics and healthy controls. AAAAI is considering standardizing and writing protocols for AMP and other indirect challenges, said session moderator Dr. Richard A. Nicklas, of George Washington University, Washington.

Dr. Polosa and his colleagues at the University of Catania (Italy) have shown that airway responsiveness to inhaled AMP is closely related to the number of eosinophils in the airways of atopic patients, whereas no association was observed with methacholine, an agent commonly used to assess bronchial hyperresponsiveness (Eur. Respir. J. 2000;15:30-5). Dr. Polosa and other researchers from the university also showed that PC20 AMP could detect inflammatory changes as early as the first week of treatment with inhaled budesonide 0.8 mg per day in mild to moderate asthmatics, while methacholine responsiveness and changes in the percentage of sputum eosinophils could be observed only by the fourth week (J. Allergy Clin. Immunol. 2002;110:855-61).

Investigators at King's College, London, were able to demonstrate in three consecutive studies that a single dose of intranasal fluticasone propionate 100-1,000 mcg inhibited an asthmatic response to AMP in just 2 hours in patients with mild, stable asthma. A single inhalation of fluticasone 1,000 mcg had no effect on airway responsiveness to histamine (J. Allergy Clin. Immunol. 2002;110:603-6).

But when Dr. Polosa's team performed a similarly designed randomized, double-blind study using a single inhalation of fluticasone 1,000 mcg in 14 patients with chronic obstructive pulmonary disease (COPD) and 13 with mild asthma, there was a change in response in only one of the COPD patients, he said. The experiment was repeated with similar results in 10 patients with a clear history of asthma and 10 patients with COPD and comparable fixed airway obstruction. "This tells me very nicely that AMP challenge can be used as a strong discriminator for COPD and asthma," he said of the unpublished findings.

AMP also has been used to assess the nonsteroidal anti-inflammatory potential of several therapeutic agents including allergen immunotherapy (Clin. Exp. Allergy. 2003;33:873-81), the leukotriene receptor antagonist montelukast (Am. J. Respir. Crit. Care Med. 2003;167:1232-8), and the humanized monoclonal anti-IgE antibody omalizumab (Int. Arch. Allergy Immunol. 2006;139:122-31).

AMP may be a more useful and sensitive tool than methacholine and histamine because of its mechanism of action, Dr. Polosa said. Histamine and methacholine have a direct spasmogenic effect on airway smooth muscle cells. AMP acts indirectly via the secondary release of mediators. Inhaled AMP is rapidly converted to adenosine and mainly induces mast cell degranulation and release of mediators such as histamine, prostanoids, and eicosanoids that cause smooth muscle constriction and mucosal edema, resulting in bronchoconstriction. ■

Mouse Allergen in Dust Triggers Asthma in Preschool Children

MIAMI BEACH — Exposure to mouse allergen in the home is a risk factor for asthma morbidity in early childhood, according to the findings of two prospective studies presented at the annual meeting of the American Academy of Allergy, Asthma, and Immunology.

Occupational exposure to mouse allergen is known to contribute to asthma morbidity. But there are no published studies evaluating the role of early mouse allergen exposure in the home in the development of wheezing, asthma, and atopy later in life.

In a study in which dust samples were collected at baseline, 3 months, and 6 months from the bedrooms of 127 preschool children with asthma from inner-city Baltimore, patients were stratified by exposure and sensitization status into four groups at each visit. Higher exposure was defined as a level of mouse allergen of more than 0.5 mcg/g of dust.

Skin testing revealed that 68% of the patients were atopic and 26% were sensitized to mouse, Dr. Elizabeth Matsui and her colleagues at Johns Hopkins University, Baltimore, wrote in a poster. At baseline, there were 8 children (6.3%) in the positive sensitization/lower-exposure group; 25 (19.7%) in the positive sensitization/higher-exposure group; 22 (17.3%) in the negative sensitization/lower-exposure group; and 72 (56.7%) in the negative sensitization/higher-exposure group.

In longitudinal analyses, mouse-sensitized children exposed to higher levels of mouse allergen were three times more likely to have an unscheduled doctor's visit and more than twice as likely to have had an emergency department visit for asthma in the previous 3 months. Nine of the 10 hospitalizations that occurred during the study period were among children in this group.

Exposed and sensitized children also were more likely to report more days of symptoms (odds ratio 1.5), more days of cough (OR 1.6), more nighttime symptoms (OR 1.3), and more use of rescue medications (OR 1.8) in the previous 2 weeks. The findings persisted after adjustment for age, sex, atopy, and cockroach allergen sensitization and exposure.

"Clinicians have to think about skin testing or obtaining RASTs [radioallergosorbent tests] on patients we see in the clinic to determine their mouse sensitization status, and then talk to them about exposure and what they can do," Dr. Matsui said in an interview. Parents can help reduce exposure by sealing cracks and holes in walls or doors, disposing of all leftover food, and having pest exterminators treat their home.

In a second poster presented at the meeting, the Home Allergens and Asthma Study—a prospective birth cohort study of children in metropolitan Boston—followed 505 infants from 498 families with a history of asthma or atopy. House dust samples collected when children were age 2 months and 3 months were analyzed for mouse urinary protein. Skin testing or allergen-specific IgE testing was performed at age 7 years.

After adjustment for sex, household income, and other confounding factors, multivariate analysis revealed that infants who were exposed to mouse allergen had twice the odds of developing any atopy by age 7, Dr. Wanda Phipatanakul and colleagues at Harvard Medical School, Boston, wrote. Increasing levels of mouse allergen exposure didn't substantially increase the risk of developing recurrent wheezing, asthma, allergic rhinitis, or eczema later on.

Infants with detectable mouse allergen exposure at 2-3 months also had an increased risk of wheezing in early life, but this effect was not significant by age 7. "We think that the effect attenuates over time," Dr. Phipatanakul said in an interview.

Although mouse allergen exposure is considered an inner-city problem, the cohort included suburban households, suggesting that clinicians consider mouse allergen exposure when evaluating any child for asthma. A national study showed that 82% of American homes had detectable levels of mouse allergens (J. Allergy Clin. Immunol. 2004;113:1167-71). ■

Fatal Asthma Shifting to the Elderly, Declining Overall

MIAMI BEACH — Preliminary data from a fatal asthma registry suggest that asthma deaths continue to fall and are more common in the elderly, Dr. Carlos Camargo Jr. said at the annual meeting of the American Academy of Allergy, Asthma, and Immunology.

Dr. Camargo and colleagues at Massachusetts General Hospital, Boston, developed a standard protocol for contacting next of kin that was submitted to institutional review boards in four states: Arkansas, Missouri, Ohio, and Massachusetts. So far they have identified 222 possible asthma fatalities, a much lower number than would have been predicted in the late 1990s when asthma rates were climbing, he said. Estimates vary, but 5,500 asthma deaths occurred annually in the early 1990s compared with about 4,300 today.

An analysis of the first 20 deaths in Massachusetts showed that half occurred in patients older than 80 years. In almost two-thirds of the 20 fatalities, families reported that the patient who died had a history of anxiety or depression in the previous 12 months. Most of the 20 deaths occurred in the hospital, and almost half in patients who had visited an emergency department in the previous 12 months.

"There have been some reports in recent years on how deaths are occurring more in the elderly, but I think it's getting more dramatic," said Dr. Camargo, chair of the academy's asthma mortality committee.

The most common triggers of death were allergens or cold weather. Nearly 75% of the 20 patients who died had reported frequent night awakening due to their asthma prior to their deaths, consistent with a more persistent affliction. The study was funded by an unrestricted grant from GlaxoSmithKline.

The finding of increasing asthma deaths in the elderly has sparked efforts to create the Veterans Affairs Fatal Asthma Project, which will match cases of asthma deaths with age-matched controls living with asthma, and which aims to evaluate their health care utilization. Veterans Affairs centers in Ohio, Wisconsin, Massachusetts, and Arizona are enrolled, but Dr. Camargo urged audience members who work in the VA to contact him to broaden participation.

Efforts to create this registry have been hampered by the Health Insurance Portability and Accountability Act and different internal review board interpretations that preclude a standard approach for contacting next of kin, he said (J. Asthma 2006;43:19-23). ■