



# NEWS Beyond Our Pages

*Marc E. Rothenberg, MD, PhD, and Harold S. Nelson, MD, Editors*

## **Asthma after World Trade Center dust exposure**

*JAMA* has published the results of a follow-up survey conducted in 2006 and 2007 of more than 46,000 persons exposed to dust resulting from the terrorist attack on the World Trade Center on September 11, 2001 (Brackbill et al. *JAMA* 2009;302:502-16). Participants included rescue/recovery workers, passersby, and residents and office workers in the vicinity. Of those who had no history of asthma before exposure, 10.2% reported new onset of physician-diagnosed asthma at follow-up. The highest incidence was in rescue/recovery workers (20.5% of those on the pile on September 11) and next highest in passersby on September 11 (8.6%). Incidence was related to intense dust cloud exposure that was reported by 39% of those with incident asthma. Risk was also increased with damage to the home or office and with a heavy coating of dust in the home or office. Although new asthma continued to be diagnosed over the follow-up period, the highest rate of development of asthma, 3%, was in the remaining months of 2001, and by 2003, incidence rates had stabilized. It was concluded that both acute and prolonged exposure to dust from the World Trade Center attack constituted a risk for development of asthma.

## **The best of both responses**

Schmitz and coauthors (*J Exp Med* 10.1084/jem.20090199) presented an exciting possibility that might essentially cure cat dander allergy one day. They engineered a recombinant molecule



made from bacteriophage-derived, virus-like particles (VLPs) coupled to Fel d 1, the major cat allergen, and tested both its immunogenicity and reactogenicity in mice. The authors reported that VLP-coupled Fel d 1 enhanced antigen-specific IgG1 and IgG2 but not antigen-specific IgE levels;

*... This approach might replace traditional immunotherapy*

thus immunized mice were nonresponsive to allergen rechallenge, as well as being protected from IgE- and IgG-mediated anaphylaxis. Additionally, *in vitro* tests with human basophils demonstrated inhibition of basophil degranulation.

The authors determined that vaccination with VLP-coupled Fel d 1 inhibited the type I allergic response through IgG–Fel d 1 complexes bound to the low-affinity IgG receptor (FcγRIIb). They also suggested that this approach might replace traditional immunotherapy with other allergens.

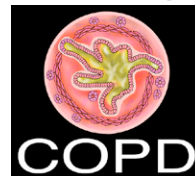
## **The right measures**

When treating chronic illnesses, it is no longer enough to demonstrate effectiveness and safety in the short-term; patients and their physicians want information about how therapy will affect their disease, functionality, and quality of life. This requires observations over an extended period of therapy. Sinha et al (*PLoS ONE*, doi:10.1371/journal.pone.0006276) examined clinical trial literature on inhaled corticosteroid therapy for asthma published between 1988 and 2007. Not surprisingly, they reported that the majority of clinical trial results were published by the pharmaceutical industry, with clinically objective measures (FEV<sub>1</sub> and

*... How therapy will affect their disease, functionality, and quality of life*

peak expiratory flow rate) and adverse events as primary outcomes. Mean duration was 3 to 6 months, and no study measured long-term disease status or quality of life. The authors reported that end points were similar between industry-funded and federally funded studies, although pharmaceutical studies reported more adverse events. Sinha et al concluded that published clinical trial outcomes were dictated largely by drug regulatory requirements, which are not the outcomes most relevant to patients and physicians.

## **Defining the efficacy of roflumilast in chronic obstructive pulmonary disease**



There is need for improvement in chronic obstructive pulmonary disease (COPD) pharmacotherapy. Animal studies with phosphodiesterase IV (PDE-4) antagonists have shown promise, but until recently, this has not translated into similar

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beneficial results in studies in human subjects. In a recent issue of the Lancet devoted to COPD, results of 4 large studies with the PDE-4 antagonist roflumilast are reported. The first 2 were identical studies with more than 3,000 subjects selected for severe COPD and history of an exacerbation in the previous year. Half the subjects were taking long-acting  $\beta$ -agonists, but none was taking inhaled corticosteroids. Subjects received roflumilast, 500 mg/d, or placebo for 1 year. Mean prebronchodilator FEV<sub>1</sub> increased by about 50 mL, and exacerbations, defined by use of oral corticosteroids, hospitalization, or death, were decreased 17% in the roflumilast group.

The second 2 studies, which included more than 1,600 subjects, examined the addition of roflumilast to either salmeterol or tiotropium in subjects with moderate-to-severe asthma. Again, no inhaled corticosteroids were allowed. Addition of 500 mg of roflumilast each day improved prebronchodilator FEV<sub>1</sub> by a mean of 49 mL in subjects receiving salmeterol and 80 mL in those receiving tiotropium. Other outcomes were generally better with roflumilast in subjects receiving background tiotropium, and there were improvements in the occurrence of exacerbations in both groups with roflumilast.

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**... Four large studies with PDE-4 antagonist roflumilast**

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because of side effects in the roflumilast groups.

Overall, results were modest, yet the calculation that 1 moderate-to-severe COPD exacerbation per year will be prevented by treating 3.6 to 5.3 subjects with roflumilast suggests that this would be a worthwhile addition to COPD treatment options.

In all 4 studies, expected side effects of roflumilast (ie, diarrhea, nausea, and headache) were observed, and there were more discontinuations

(Fabbri et al. Lancet 2009;374:695-703; Calverley et al. Lancet 2009;374:685-94).

**Tobacco smoking is only one cause of COPD**

A review of the epidemiology of COPD reveals that worldwide perhaps only 50% of COPD cases are caused by smoking tobacco. Although tobacco smoking is a well-established cause of COPD, there are about 1 billion tobacco smokers compared with 3 billion who are exposed to another major hazard, the use of biomass fuel, especially for cooking. Even in developed countries, such as the United States, perhaps a quarter of patients with COPD have never smoked. In these countries occupational exposures might account for 15% of COPD cases. Occupational risks include toxic gases, dusts, and fumes in factories, farming, mining, and construction. In some countries tuberculosis or asthma contribute to a picture resembling COPD, but the

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**... Only 50% of COPD is caused by smoking tobacco**

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pathology and perhaps prognosis differ with these diseases. The challenge for the future is to study the patients with non-tobacco smoke-induced COPD to determine the pathophysiology, prognosis, and response to treatment in this diverse group of patients. (Salvi and Barnes. Lancet 2009;374:733-43).

*Editor's note: Our November issue will feature several reviews on persistent airway obstruction, including a review on the management of COPD.*

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*Most news items are written by Sherri Gabbert, PhD.*

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