Eosinophilic Bronchitis as a Cause of Cough

To the Editor:

I read with interest the valuable article by Pratter et al (November 1999), regarding the role of sinus imaging in the management of chronic cough. Figure 2 in this article contains a useful algorithm for investigation and treatment of chronic cough. Unfortunately, one potentially important cause of cough will be missed by following this algorithm.

Eosinophilic bronchitis is a recently described syndrome. Subjects with eosinophilic bronchitis have cough with eosinophilic airway inflammation characteristic of that seen in asthma; however, these patients have normal lung function, negative methacholine challenges, and no evidence of variable airflow obstruction. The cough in this condition responds nicely to inhaled corticosteroids. This syndrome would appear to be a precursor to (or perhaps the very mildest form of) symptomatic asthma. While the “purists” would not include this within the umbrella of the label asthma, it seems reasonable to consider that this is a variant of the syndrome known as cough-variant asthma.

In a recent study, corticosteroid responsive eosinophilic bronchitis with negative methacholine challenge was shown to be present in 13% of subjects with chronic cough. The authors have pointed out the poor predictive value of a positive methacholine challenge in predicting response to asthma therapy. The relative common prevalence of eosinophilic bronchitis as a cause of cough underscores that a negative methacholine challenge is also a poor predictor of nonresponse to inhaled corticosteroids.

There are two important messages. First, this questions the value of the routine use of methacholine challenges in the evaluation and management of chronic cough. It is possible that a brief diagnostic trial of high-dose inhaled corticosteroids might be a preferable tool at step 2 of the cough algorithm. Second, it suggests the potential value for standardized evaluation of sputum for inflammatory cells, particularly eosinophils, in arriving at a diagnosis and the management plan for cough.

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Propofol and Too Much Sulfite?

To the Editor:

It was with great interest that we read the letter from Dr. Langevin (October 1999) regarding the sulfite content of propofol. Dr. Langevin states that when the generic formulation of propofol (Genus; Irvine, CA) is given at the maximum labeled dosage of 50 μg/kg/min, the sodium metabisulfite (SMBS) exposure approaches the median lethal dose for rats (125 mg/kg). Assuming that a 70-kg patient receives 50 μg/kg/min of the generic propofol for 24 h, the actual exposure to the patient of SMBS would be a total of 126 mg/d. This dosage of 126 mg/d of SMBS would actually only be 1.8 mg/kg, 70 times less than reported by Dr. Langevin. This level of sulfite exposure would seem to support the conclusion of the US Food and Drug Administration (FDA) that “the substitution of sodium metabisulfite for EDTA [ethylenediaminetetraacetic acid] as an excipient in propofol injection emulsion does not effect the safety profile of the product.”

If the total amount of sulfite exposure is of concern, there are several amino acid preparations, utilized in total parenteral nutrition solutions, that provide a much higher level of sulfite. Examples of such products would range from Novamine (Chlnice Nutrition; Deerfield, IL), which provides SMBS at approximately 450 mg/d (6.4 mg/kg for a 70-kg patient), to Amionsyn-PF (Abbott; Abbott Park, IL), which provides sodium hydrosulfite at 3,450 mg/d (49 mg/kg for a 70-kg patient).

Dr. Langevin also states that there are only two agents currently being used by anesthesiologists that are sulfite-containing products. In actuality, there are several more sulfite-containing products, including meperidine injection (Elkins-Sinn; Philadelphia, PA), norepinephrine injection (Levophed; Sanofi-Winthrop; New York, NY), and phenylephrine injection (Neo-Synephrine; Sanofi-Winthrop), that are commonly used by anesthesiologists.

The issue of whether SMBS should be used as an excipient in pharmaceutical products is unclear. Until the FDA makes a definitive decision, the actual exposure from replacement products that contain sulfite should be assessed based on appropriate estimations of exposure and compared with currently available products that are being utilized frequently.

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