

**THE EDITORIALIST REPLIES:** Gleich is correct that a body of evidence supports a pathogenic role of eosinophils in asthma. However, I respectfully disagree with his suggestions concerning the breadth and scope of their effect. Eosinophils (in tissue, sputum, and blood) were largely absent in the subjects who received anti-interleukin-5 monoclonal antibodies. Yet there was no effect on chronic symptoms, the forced expiratory volume in 1 second, or the patient's perception that he or she was receiving active treatment. This lack of effect does not mirror the more global effects of corticosteroids and suggests that broader approaches to reducing eosinophils will have little further effect on these rather important outcomes.

Finally, although eosinophilic inflammation may be present in 50% of patients who have well-characterized, severe asthma, many of whom require oral corticosteroids for symptom control, in large populations of patients with difficult-to-treat asthma, the percentage is likely to be much lower. Thus, from a drug-development standpoint, the cost-effective use of treatment with anti-interleukin-5 monoclonal antibodies (or perhaps any targeted eosinophilic approach) will probably be limited to a small fraction of the population of patients with asthma.

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## Drug Therapy for Asthma

**TO THE EDITOR:** In his review of drug therapy for asthma, Fanta (March 5 issue)<sup>1</sup> begins by reviewing the dramatic increase in morbidity associated with asthma in the United States during the 1970s and 1980s and the more recent improvement in asthma outcomes. However, there was no mention of the marked racial, ethnic, and socioeconomic disparities in asthma outcomes that are partly related to drug-treatment barriers.

Asthma outcomes are worse in minority and low-income populations than in nonminority and middle- and high-income populations.<sup>2</sup> The underuse of controller medications in children receiving Medicaid is much more common among Hispanic children (44%) and black children (34%) than among white children (22%),<sup>3</sup> for example. In one study,<sup>4</sup> one third of physicians (35%) reported that the cost of medication was a considerable barrier to prescribing effective medications for asthma. For example, treatment with inhaled corticosteroids is associated with a significant reduction in asthmatic exacerbations and hospitalizations,<sup>5</sup> but they are not available in the so-called \$4 formulary of large pharmacy chains. Inhaled corticosteroids now cost at least \$70 per month. Even among the insured, cost sharing is associated with decreased use of maintenance medicines.<sup>6</sup> Eliminating cost barriers could improve outcomes and reduce disparities.

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**TO THE EDITOR:** Fanta does not mention the role of oral corticosteroids in the management of bronchial asthma. The British Thoracic Society guideline for the management of asthma<sup>1</sup> recommends the use of the lowest effective dose of oral corticosteroids in patients who remain symptomatic despite the use of 2000  $\mu$ g of an inhaled corticosteroid daily, long-acting  $\beta$ -agonist stimulant inhalers, and leukotriene modifiers (step 5 in the stepped-care approach to asthma treatment). Early oral corticosteroid therapy is also recommended for the management of acute exacerbations of asthma.

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1. British guideline on the management of asthma. *Thorax* 2008; 63:Suppl 4:iv1-iv121. (Also available at [http://www.brit-thoracic.org.uk/Portals/0/Clinical%20Information/Asthma/Guidelines/asthma\\_final2008.pdf](http://www.brit-thoracic.org.uk/Portals/0/Clinical%20Information/Asthma/Guidelines/asthma_final2008.pdf))

**TO THE EDITOR:** Hydration is the first rule in the treatment of asthma, yet it is not mentioned in the article by Fanta. In my experience, patients with asthma do not like to drink water, but they should be informed about the need to drink water and encouraged to drink a sufficient amount to promote a dilute urine. Theophylline treatment is not well described in this review, and ephedrine is not mentioned.

Thus, this article does not mention the importance of hydration or two historically used medicines (theophylline and ephedrine), nor does it mention the possible benefits of expectorants. It does mention all of the more expensive but, in my view, not necessarily more beneficial treatments.

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**THE AUTHOR REPLIES:** Although asthma-related morbidity and mortality have decreased over the past decade among both whites and nonwhites, large disparities in asthma-related health outcomes persist. For example, the age-adjusted rate of death from asthma in the black population is three times that in the white population, and the rate of hospital discharges may likewise be as many as three times higher among blacks than among whites.<sup>1</sup> There are probably multiple causes of these disparities, reflecting differences in biology, environmental exposures, utilization of health care services, health care beliefs, and socioeconomic resources. In terms of drug therapy for asthma, there are documented racial and socioeconomic differences in the use of controller therapies (especially inhaled corticosteroids) as compared with quick-relief bronchodilators, with associated poorer outcomes when the ratio of prescribed inhaled corticosteroids to inhaled short-acting  $\beta$ -agonist bronchodilators is low.<sup>2</sup> Rust rightly points out that in the United States, medication costs probably contribute to the underprescription and underuse of effective controller therapy for asthma among the economically disadvantaged. His observation is particularly relevant in the current global economic downturn.

Systemic corticosteroids are a crucial compo-

ment of the treatment of severe asthmatic attacks. As Hilmy points out, some ambulatory patients with severe, persistent asthma continue to have troublesome symptoms despite optimal medical therapy, and they may require daily or alternate-day orally administered corticosteroids in order to maintain adequate control. All such patients should be referred for consultation with a specialist to explore irritant or allergenic stimuli that make the patient's asthma unusually difficult to control, coexisting conditions (e.g., aspiration, chronic rhinosinusitis, and allergic bronchopulmonary aspergillosis), noncompliance with medication, alternative diagnoses mimicking asthma, and new asthma therapies that may obviate the need for the long-term use of systemic corticosteroids.<sup>3</sup>

In the early 1980s, when I began to practice pulmonary medicine, virtually all of my patients who had asthma that was more than mild were treated with a slow-release theophylline preparation. Like Farel, I found that many patients were helped by this class of medication. We adjusted their theophylline doses according to side effects (e.g., jitteriness, nausea, diarrhea, headache, tachycardia, and insomnia) and the results of periodic measurements of the blood theophylline level, and occasionally, we treated in the intensive care unit their seizures or cardiac arrhythmias due to medication overdoses. However, since the introduction of inhaled long-acting  $\beta$ -agonist bronchodilators, my prescriptions of theophylline to treat asthma have dwindled to almost none. The long-acting  $\beta$ -agonists are more effective,<sup>4</sup> and despite concerns about potential severe asthmatic events, they have fewer side effects, do not require blood-level monitoring, are not associated with medication and food interactions, and have not been associated with toxic overdoses.

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