tients have a wide range of vascular endothelial growth factor (VEGF) levels in our study. The lowest and highest levels that we observed were 202 pg/mL and 1,538 pg/mL, respectively. We have five patients with VEGF levels > 1,000 pg/mL. All of these patients have bilateral infiltration in their chest radiographs. A significant correlation (p < 0.05) was observed between VEGF levels and fever in active pulmonary tuberculosis patients. However, there was not any other correlation between VEGF levels and clinical or laboratory data.

Metallothionein may be an interesting marker since the imbalance between oxidants and the antioxidant defense system is an important issue in both tuberculosis and other inflammatory diseases. The investigations to determine a marker for the active form of tuberculosis will continue in the future.

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References

What About Add-On Second-Line Controller Therapy?

To the Editor:

The review by Roland et al (July 2004) in CHEST has provided a timely reminder of the local adverse consequences of the use of inhaled corticosteroids in treating asthma. However, while playing an integral role in the management of inflammatory airways disease, inhaled corticosteroids are effective when used in smaller doses in combination with additional second-line controller therapy. This is especially pertinent, and indeed is advised, in patients with mild-to-moderate disease whose conditions are suboptimally controlled with low-dose inhaled corticosteroids.

In their article, the authors do not mention the use of concomitant nonsteroidal antiinflammatory therapy with leukotriene receptor antagonists or long-acting β2-agonists. Using these agents would obviously permit a lower inhaled corticosteroid dose to be used, while maintaining or even improving asthma control. In turn, this would reduce the dose of corticosteroid delivered to both the oropharynx and endobronchial tree, minimizing the risk of both troublesome local and serious systemic sequelae. Common sense tells us that we should continue to advise patients to use a spacer device, rinse their mouths, and gargle after using an inhaled corticosteroid. Moreover, clinicians should be aware that the addition of second-line controller therapy with a concomitant reduction of inhaled corticosteroid dose should be considered when dealing with a patient with oropharyngeal candidiasis and dysphonia. Indeed, encountering an asthmatic patient with such problems provides an ideal opportunity to consider adjusting the burden of inhaled antiinflammatory therapy.

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To the Editor:

We read the letter from Dr. Currie with interest, and we agree with the issues raised in the letter.

Our article was primarily written to bring to everyone’s attention the side effects of corticosteroids in the upper airway. We think that these quite distressing symptoms are often ignored.

The basic thrust of the article was to describe the side effects and to discuss what can be done for those patients who need therapy with inhaled steroids to control their symptoms. The assumption was that there are a large number of patients who are receiving full asthma treatment according to the various guidelines, which clearly state that long-acting β2-agonists are an integral part of asthma management when the dose of inhaled steroids is getting above 800 µg/d (British Thoracic Society guidelines). The latest British Thoracic Society guidelines also have introduced add-on therapy at an earlier stage on the basic assumption that this provides better control and will have some steroid-sparing effect. In addition, there is now increasing evidence that doubling the dose of inhaled corticosteroids during an exacerbation is probably not very effective.

Leukotriene antagonists do seem to have some steroid-sparing effect for inhaled steroids (the effect for oral steroids is much more controversial). However, there is still considerable debate about the stage at which they should be used.

Thus, we agree with Dr. Currie that everything possible should be done to provide good asthma control, including the case of add-on therapies. However, even when all this is done, many
patients will still be complaining of upper airway side effects resulting from their use of inhaled corticosteroids.

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Diagnosing Tubercular Pleural Effusions

To the Editor:

We read with interest the article by Hikari et al (March 2004) comparing the markers of tuberculosis in pleural effusions. We wish to express our disagreement with their statement that interferon (IFN)-γ should be measured routinely in all suspected cases of pleural tuberculosis. They have based their conclusion on the basis of a perfect area under the curve of 1.000 on receiver operator characteristic analysis for IFN-γ as compared to 0.958 for adenosine deaminase (ADA). The authors have failed to adequately review the fairly large body of literature on biological markers of tubercular pleural effusion.

ADA has been reported with perfect values in the literature (100% sensitivity,2–5 and also 100% specificity, positive predictive value, and negative predictive value)3 in studies with larger sample sizes (n = 221, 48 tuberculous; n = 405, 91 tuberculous2; n = 350, 76 tuberculous3; and n = 138, and 61 tuberculous4) than the present study (n = 55, 20 tuberculous).1 Valdes et al,3 using simultaneous measurement in the same set of patients (n = 405), reported a higher sensitivity for ADA (100%) than IFN-γ (94.2%) and a higher specificity (95%) for ADA and 91.5% for IFN-γ. Villegas et al5 compared ADA and IFN-γ (along with polymerase chain reaction [PCR]) simultaneously in 140 patients with 42 confirmed TB cases and reported a higher sensitivity (88.1% for ADA vs 85.7% for IFN-γ) and better negative predictive value than IFN in the whole prevalence range. Valdes et al6 reported that 253 of a total of 254 tuberculous pleurisy patients had ADA levels >40 IU/mL, and in the 82 patients in whom both ADA and IFN-γ were done, the sensitivity of IFN was 89% (73 of 82 patients) against at least 98.78% (81 of 82 patients) for ADA.

Studies comparing ADA and IFN-γ simultaneously in the same set of patients have reported both ADA better than IFN-γ5–7 and IFN-γ better than ADA8–10 as diagnostic markers. In fact, a meta-analysis by Greco et al10 regarding the diagnostic accuracy of ADA vs IFN-γ included 31 studies in favor of ADA (total, n = 4,738) and 13 studies in favor of IFN-γ (total, n = 1,189). Using summary receiver operating characteristic curve, they found only a marginal difference in overall sensitivity and specificity: 93% for ADA, and 96% for IFN-γ. Using Bayes theorem, the posttest probability of a negative test result was calculated. The minute difference in posttest probabilities (ADA vs IFN-γ, 0.4% vs 0.2%, 2.4% vs 1.2%, and 24% vs 17%) was maintained over a wide prevalence range of 5 to 85%. The authors concluded that "ADA and IFN-γ appear to be reasonably accurate at detecting TB pleurisy." Virtually similar sensitivity and specificity coupled with lower cost should favor the use of ADA as a diagnostic tool compared to IFN-γ.

Lastly, the authors suggest that PCR should be compared with IFN, etc. Such a study comparing PCR, IFN, and ADA simultaneously in pleural effusion patients has already been published in CHEST.6

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To the Editor:

We are confused by the comments by Drs. Gupta and Chhabra concerning our article.1 Indeed, high concentrations of adenosine deaminase (ADA) in the pleural fluid of patients with tuberculous pleuritis have been confirmed by many studies. However, the statement that the use of ADA has been reported with perfect values for sensitivity and specificity in the literature is overstated. Perez-Rodriguez and Castro2 summarized the results of 11 studies and reported the sensitivity and specificity for ADA are 77 to 100% (average, 93.3%) and 81 to 97% (average, 91.3%), respectively. Chen et al3 summarized the results of eight studies and reported the sensitivity and specificity for ADA as 79 to 100% (average, 86.6%) and 80.5 to 96% (average, 85.4%), respectively. A meta-analysis including 40 articles conducted by Goto et al4 showed that the sensitivity of ADA ranged from 47.1% to 100% and the specificity from 50.0% to 100%. However, these studies4–6 also showed that the false-positive rate is relatively high. In a meta-