To the Editor:

I appreciate the comments by Dr. Zalman and his colleagues in relation to our article (Chest 1993; 104:362-65). In general, I agree with them that PCR sequencing is time-consuming and laborious and that ELISA assay would be suitable as a routine clinical test. However, before it is used as a routine test, the following questions should be answered.

(1) Does the presence of anti-p53 antibody perfectly correspond with the presence of p53 mutations? Are there some classes of mutations that are somewhat more antigenic than the other?

(2) Does the presence of the anti-p53 antibody reflect the immunologic response of the host to the cancer cells? It would be worth testing if patients with cancer with positive anti-p53 antibody have a better prognosis than those without this humoral response? If this is proven, then this test would be of a prognostic value rather than of a diagnostic value.

(3) Are a small number of cancer cells that can be cured by conventional therapy enough to evoke an antigenic response?

In relation to the third question, we were impressed that two patients with anti-p53 antibody who had been originally referred for benign pulmonary diseases later developed lung cancer.

Dr. Zalman’s work is worthy to be tested by many other laboratories to establish clinical usefulness. We would also like to examine the anti-p53 antibody in our cohorts, when we have a chance.

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Simpler Is Not Always Better

To the Editor:

We read with interest the comprehensive literature review by Torén et al entitled “Asthma and Asthma-Like Symptoms in Adults Assessed by Questionnaires” in the August 1993 issue of Chest.1 We disagree with one of the conclusions of the review, ie, that questions about “self-reported” asthma, especially “physician-diagnosed” asthma are to be preferred. These questions have a high specificity, ie, identify mostly true asthmatic subjects. Not surprisingly, the validity of such questions relative to a gold standard chosen to be “physician’s diagnosis” is usually good.

If we were to use only those questions, then we would miss many asthmatic patients who have atypical symptoms, ie, have a low sensitivity. British general practice audit2-5 have convincingly shown that diagnosis of asthma is usually overlooked in children with recurrent wheezy episodes. One study6 showed that 16 to 20 consultations were needed before a diagnosis of asthma was performed! Using a questionnaire including “self-reported” asthma or “physician-diagnosed” asthma would not identify such asthmatic children. Patients with chronic dry cough would also not be identified as asthmatics. Clinical evaluation proved that bronchial hyperreactivity could be shown in up to 30 percent of those patients.1 Exercise-induced asthma is also largely underdiagnosed. A study performed on high school athletes showed that two-thirds of adolescents with exercise-induced asthma were not aware of having asthma.5 In like manner, among 1,997 airmen referred to rule out asthma, primarily because of respiratory symptoms with exercise, only 45 percent had been previously diagnosed as asthmatics.

The reducing approach supported by Torén et al offers the advantage of simplifying comparison of prevalence rates obtained in surveys performed in different places. It may be justified in a situation where identification of typical asthmatic patients is needed. In an epidemiologic setting, however, such an approach would miss asthma-like symptoms, which are very common in children and adolescents. Thus, before genetic studies could provide us indisputable markers of asthma, we have to admit that life is not easy and to go on using several questions on respiratory symptoms to identify asthma in epidemiologic studies.

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REFERENCES

1 Torén K, Brisman J, Järvelm B. Asthma and asthma-like symptoms in adults assessed by questionnaires: a literature review. Chest 1993; 104:600-08
3 Levy M, Bell M. General practice audit of asthma in childhood. BMJ 1984; 289:1115-16

To the Editor:

We agree with Denis Charpin and Daniel Verloot that preferring a gold standard when validating asthma-related questions is a problem. As we pointed out in our review, future studies of validations must be performed against clearly stated definitions of asthma, including both clinical physiologic findings and a history.1 A simple question like “physician-diagnosed” asthma will have rather low sensitivity. There are, of course, situations where high sensitivity is preferred, for instance when different work places are screened with the intention of identifying as many subjects as possible with occupational asthma. In such situations, the use of “physician-diagnosed” asthma is inappropriate.

In studies of the etiology of a rare disease such as asthma, however, high specificity is (≥99 percent) crucial. Low specificity (<99 percent) generates a large number of false-positives, ie, the positive predictive value will be low. This will underestimate the risk-estimates.