

Correspondence

Methacholine test and the diagnosis of asthma

To the Editor:

Airway hyperresponsiveness (AHR) is a defining feature of the disease we call asthma. The report by Sumino et al¹ documenting that 20% of treated asthmatic patients had a potentially false-negative methacholine challenge ($PC_{20} > 16$ mg/mL) is counter-intuitive and requires some commentary. There are several nonmutually exclusive possible explanations for this apparent loss of diagnostic sensitivity.

Perhaps the most important issue is the bronchoprotective effect of deep inhalations² associated with the dosimeter method of delivering methacholine as recommended by the American Thoracic Society.³ Our data document that almost a quarter of asthmatic patients with tidal breathing PC_{20} of less than 16 mg/mL had a negative dosimeter challenge; this increased to almost 50% in those with milder AHR (PC_{20} 2-16 mg/mL). This issue is discussed in the article, but we suspect that the magnitude of this effect is underappreciated. This is a critical issue in asthmatic subjects with *mild AHR*, which does not equate exactly with *mild asthma* as stated in the article.¹

A second important consideration is the clinical currency of the patient's symptoms. In untreated asthmatic patients, lack of symptoms and relevant exposures (allergen, sensitizer, viral respiratory infection) for even a few days can lead to a normalization of methacholine AHR.⁴ It is also possible that effective doses of inhaled corticosteroids could normalize the methacholine challenge⁵; this would be true only in those with symptom resolution. Thus, the measurement properties of a test such as AHR need to be interpreted in terms of "current asthma" as opposed to "ever asthma."

A third concern, as always, is that the symptoms or some of the symptoms might not be due to asthma, always a concern even in treated *doctor-diagnosed asthma*.⁶ This, in fact, would be the most important reason to perform methacholine challenge in treated asthmatic patients, namely, as a diagnostic test in those persistent clinically current (as noted above) symptoms that are responding inadequately to therapy. In this context, a negative nondeep inhalation challenge should suggest alternate or additional mechanisms to explain the patient's symptoms. The only other potential clinical rationale for methacholine challenge in

treated asthmatic patients would be to monitor treatment⁷ with the goal of documenting improvement or even normalization as suggested above.

A final and, we suspect, less likely possibility is the accidental use of potent functional (long-acting beta agonist in particular) or specific (anticholinergic) antagonist prior to challenge. This is important to check in patients whose methacholine test result is unexpectedly negative.

In summary, we remain convinced that with infrequent exceptions (high-intensity athletes for example) a negative nondeep inhalation protocol methacholine test effectively excludes that clinically current respiratory symptoms are due to variable airflow obstruction.

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