Annotation

Bronchial provocation tests

Asthma occupies an honoured position in medical history having appeared in many ancient medical texts. The Ebers Papyrus,¹ written about 1550 bc contains an extensive list of remedies for asthma, including the use of inhalations. Early physicians recognized that among the variety of factors that could precipitate wheezing, exposure to dust and feathers sometimes initiated an attack². It was Charles Harrison Blackley,³ however, who unlocked the Pandora's box on allergic asthma, when he performed skin, nasal, conjunctival, and even bronchial challenges on himself using pollen grains.

Herkheimer⁴ and Colldahl⁵ (1952) resurrected the use of bronchial provocation tests (BPTs) as an aid to allergy diagnosis in asthma. Many authors have asserted that clinical history and prick skin tests were unreliable methods of specific allergy diagnosis;⁶⁻¹⁰ despite this, few paediatricians considered BPTs necessary in the investigation of childhood asthma.

Safety

There are doubts about the safety of the procedure,¹¹ but Aas,¹² with extensive experience of inhalation tests in children, has encountered no problems. Most authors conclude that the test is safe in experienced hands.

Specificity

Nonspecific airways lability is a frequent problem in asthma¹³. Therefore, it is essential that the allergen preparations used for BPT are purified by extraction of nonspecific irritants.⁸ The significance of a reaction can be enhanced if tolerance and sensitivity to other allergens can also be shown.⁹ In this way most studies have satisfactorily confirmed the specificity of reactions.^{9, 12, 14} Nevertheless, Killian *et al.*¹⁵ showed an inverse correlation between the intensity of allergic reaction required to produce an airways response and the level of nonspecific bronchial reactivity, as assessed by histamine challenge. This suggests that asthma is more easily provoked by inhaled allergens if there is greater nonspecific bronchial reactivity. It may explain the failure of most authors to find a correlation between the degree of specific bronchial sensitivity with BPT and the severity of asthma clinically.

Reproducibility

It has been suggested that BPTs could increase⁴ or decrease¹⁶ subsequent bronchial sensitivity to the allergen tested. However, other authors have shown a reasonable consistency of response.^{7, 17, 18}

Techniques

There are almost as many variations in the technique of bronchial challenge and methods of monitoring response as there are papers on the subject. Efforts have been made to standardize the procedure,¹⁹ but all can be criticized as they do not mimic the situation that occurs during natural allergen exposure. BPTs utilize soluble rather than particulate allergen, and the duration of exposure is limited rather than prolonged or repeated. It is impossible to calculate how much allergen reaches the airways during BPT as this will depend on the mode of delivery, temperature, particle size, and the degree of pre-existing airways obstruction. Furthermore, the other nonspecific factors such as emotion, atmospheric changes, and viral infections, which combine to produce spontaneous asthma cannot be reproduced in the laboratory.

Doubts

Thus it is not surprising that recent re-evaluation of BPTs suggest that they are rarely necessary and that clinical history and skin tests are sufficient.^{18, 20} The careful use of prick skin tests with more dilute allergen preparations, and observation for late skin reactions may give reliable allergy diagnoses.²¹ The advent of the less invasive serum IgE antibody measurements have made BPT superfluous in many situations.^{22, 23} However, even allergen-specific IgE assays may not offer any major diagnostic advantage over skin tests.^{24, 25} This appears to leave allergy diagnosis in a state of complete confusion and little advanced since the work of Blackley over a century ago.³

Late reactions

Renewed interest in BPTs has come from the study of late bronchial reactions which sometimes occur

after BPT. The immediate airways obstruction that occurs within minutes of the bronchial challenge is of short duration, resolving spontaneously, and completely corrected by bronchodilators. Many asthmatics, however, also have a late airways obstruction beginning 4 to 6 hours after inhalation. This reaction is more prolonged and more severe than the immediate reaction. The changes in lung mechanics during the late reaction are similar to those found in severe exacerbations of asthma and are poorly responsive to bronchodilators. Late reactions occurred in nearly three-quarters of perennial asthmatic children who were allergic to the house-dust mite, and there was a significant association between more severe clinical asthma and the presence of a late reaction on BPT.²¹ As late reactions are being observed with equal frequency to other allergens,²⁶ BPT responses probably have a much greater significance in relation to naturally occurring asthma than has formerly been appreciated.

Indications

BPTs are still the final arbiter in the diagnosis of a bronchial allergy. They are necessary as research tools to clarify the relevance of skin test responses and IgE antibody measurements. The late bronchial reactions form an ideal model for studying the pathophysiology of asthma and the efficacy of anti-asthma therapy. BPTs continue to be used where accurate allergy diagnosis is considered important, as for selection of patients for hyposensitization trials or where drastic allergen avoidance is to be recommended such as getting rid of the cherished family pet. Finally, BPTs are occasionally useful in the rare instance where the diagnosis of asthma in an allergic child is in doubt. In the routine clinical situation, however, BPTs have only marginally more to offer than a well-taken clinical history, prick skin tests, and possibly IgE antibody measurements.

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