Bronchial Provocation Challenges

by Susan Blonshine BS, RRT, RPFT

Asthma is a chronic inflammatory disease of the airways that affects individuals at all ages. The bronchial hyperreactivity and reversible airflow obstruction lead to multiple symptoms. Hyperresponsiveness is associated with the presence and severity of disease. It is imperative that objective measurements such as spirometry, airway mechanics, and bronchoprovocation are used to establish the diagnosis and evaluate the effectiveness of interventions.

Bronchial challenge testing is the accepted method to evaluate airway hyperresponsiveness in those individuals who have nonspecific or unclear symptoms. This includes people with symptoms of asthma, normal spirometry, and no response to a bronchodilator, as defined by the American Thoracic Society (ATS).

Multiple agents and methods are used for a bronchial challenge testing. These include, but are not limited to, aerosolized nonspecific pharmacological agents such as methacholine or histamine, exercise, isocapnic hyperventilation with cold air, and specific antigens found in occupational settings.1

Other methods of bronchial challenge testing continue to be explored in the literature. The most common method is methacholine challenge testing.2 It has been well characterized and is a safe procedure. The American Association for Respiratory Care published a Clinical Practice Guideline in 1992 addressing methacholine and/or histamine challenges. The ATS is also developing a guideline for bronchial challenge testing. Although there has been significant standardization of bronchoprovocation tests, controversy continues to exist around aspects of the methodology.

Patient preparation

The first critical step in performing bronchial provocation tests is preparation of the patient. Medications that may affect the results of the testing should be withheld from the patient for the appropriate length of time prior to testing. These include all medications that could affect airway caliber or act as an antagonist to the challenge agent.

Other variables that may warrant control on the day of the test are the consumption of coffee, tea, cola drinks, and chocolate. The patient should also refrain from smoking. Recent illness, such as viral infections, may also preclude performance...
of the challenge because infections may increase the hyperresponsiveness of the airways for several weeks post-infection. It may also be important to avoid specific antigens related to occupational exposure. Challenge testing may be performed while a patient is on specific medications to assess the effectiveness of the treatment.

**Methacholine preparation**

Regardless of the method selected, careful attention to the mixing, storage, and delivery of the agent must be observed. The effect of pH on the stability of methacholine in solution has been studied at the National Center for Immunology in Denver, CO. Methacholine chloride solutions rapidly decompose if the pH is greater than 6, and the decomposition increases as the pH increases.

The buffers also influence the stability of the solution. The buffer varies the rate of deterioration over time and the different absolute amounts of methacholine hydrolyzed. The Denver study emphasizes the need to prepare methacholine chloride in the proper buffers and verify the pH to provide accurate assessment of airway hyperresponsiveness. Manufacturer recommendations should be followed for methacholine storage.

**Delivery methods**

The specific delivery method and protocol the respiratory therapist selects will determine the concentrations of the agent delivered. Generally, a saline solution is inhaled as the baseline or diluent level. Studies continue to debate the necessity of the saline level, but it remains as the preferred method. A fall in FEV1 (forced expiratory volume after one second) greater than or equal to 10 percent after the diluent level may be considered a positive test.

The two delivery options commonly employed are the dosimeter or two-minute tidal-volume breathing techniques. Limiting variability in the technique and equipment is critical to meaningful interpretation of the results. The nebulizer output and particle size must be controlled. In addition, the technologist should control the volume inhaled, the length of the breath-hold, and the inspiratory flowrate. Variance in any of these factors can influence the test results.

**What is measured?**

Testing includes spirometry, lung volumes, and airway mechanics before and after the inhalation of increasing concentrations of an agonist. The addition of the measurement of airway resistance (Raw) and specific conductance (sGaw) increases the sensitivity of the test procedure. One study suggests that the addition of sGaw and thoracic gas volume (TGV) increases the sensitivity of methacholine challenges from 60 percent to 97 percent.

In younger children, wheezing on pulmonary auscultation has been studied. The appearance of wheezing determines the provocative concentration of methacholine.

**Evaluating the test results**

A positive methacholine response is considered a fall in the FEV1 of 20 percent and a decrease in sGaw of 35 percent at less than 8 mg/mL. This is referred to as the provocative dose. Producing a 20 percent in FEV1 (PD20FEV1) or PD35sGaw. Discriminating the asthmatic from the nonasthmatic has a sensitivity of approximately 60 percent and a specificity of 90 percent. The positive and negative predictive values are 86 percent and 69 percent, respectively, when the prevalence of asthma is high and 40 percent and 95 percent when the prevalence of asthma is low, such as in population studies.

The positive predictive value of methacholine challenge in diagnosing cough due to asthma varies from 60 percent to 82 percent. In a 1997 study at the University of Massachusetts Medical School, this was also
found to have a high correlation with metaproterenol treatment in the same group.\(^6\)

The airways of geriatric patients are as sensitive and responsive to methacholine provocation as those of the younger patients.\(^9\) Regardless of age, the goal remains to determine the dose-response characteristics of the airways.\(^5\)

It is important to realize that a negative test does not necessarily mean that an individual does not have asthma. This is due to the variability of the triggers and disease process. An individual may respond to provocative agents differently as well. A challenge may also be interpreted as a false-negative when only FEV\(_1\) is measured or the inspiratory curve is not appropriately evaluated. Upper airway processes may be reflected in a truncation of the inspiratory curve on the flow volume loop. A positive test in a symptomatic individual has prognostic value as well as probable therapeutic value. A positive test in an asymptomatic individual probably carries potential predictive value.\(^6\) The “challenge” in bronchial provocation testing may still remain in the interpretation of the data.

**Looking ahead**

Methods, delivery options, antigens, and dosing schedules for bronchoprovocation studies continue to be investigated. Although methacholine is the most widely accepted method at this point, it may be replaced as the search for methods with greater sensitivity and specificity expands. Bradykinin and adenosine have been studied, and some researchers claim it is a better method to differentiate the asthmatic from the normal person. At this point, the cost of bradykinin is extremely high, and neither method has achieved wide usage. Another example of a possible challenge method, proposed in Australia, is the study of the inhalation of a dry powder of mannitol.

It is important to evaluate the parameters measured so that they will lead to a greater understanding of changes in airway caliber and possible therapeutic interventions. The effect of the test on patients in relation to test administration and time requirements will be a factor as new testing methods emerge.

Assessment of airway responsiveness is a significant factor in the diagnosis and treatment of asthma. Asthma is the only pulmonary disease that can be diagnosed objectively on the basis of pulmonary function tests alone.\(^6\)

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**references**


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**additional reading**