CHAPTER 8
Common Office Procedures

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INTRODUCTION

The purpose of this chapter is to provide an overview of the common procedures that are performed in the allergist’s office. We assume that the physician already possesses sufficient knowledge and familiarity with these procedures. Therefore, our purpose primarily is to help educate office staff by focusing on goals, methodology, training, equipment and documentation associated with these procedures. In many cases, there are multiple accepted and valid methods of performing these tests. This chapter is not meant to be the final word, but rather a quick reference guide.

PULMONARY FUNCTION TESTING

Spirometry

Spirometry is a basic pulmonary function test which measures the volume of air inspired or expired as a function of time. It allows easy and direct measurement of FEV₁, FVC and FEV₁/FVC ratio. Spirometry cannot, however, measure lung volumes. Thus, information about FRC and lung volumes computed from FRC, such as total lung capacity and residual volume, require body plethysmography or gas dilution. The youngest age to perform spirometry with reproducible results varies between 5 and 7 years.

Healthy young children may reach FVC in a few seconds, but it can take older patients much longer, especially those with airflow obstruction. In such case, sustaining a maximal expiratory effort until achieving FVC may cause lightheadedness. In adults, FEV₆ has been shown to be a reliable substitute.

Procedures. Calibration with a 3-L syringe should be performed each day of testing. Calibration should be repeated when the room temperature changes, when the equipment is disassembled and reassembled or when the equipment has been performing frequent tests for four hours. American Thoracic Society (ATS) standards state that calibration should be performed by discharging the calibration syringe at least three
times with a low, medium and high flow varying between 0.5 and 12 L/s. If the calibration is not within ±3.5% of the syringe volume, it should be repeated.

All patients performing spirometry should be given instructions prior to the test. The patient should maintain a good posture and remain upright until the test is completed. For safety reasons, the ATS recommends that patients be allowed to sit during the procedure. If you choose to have patients stand, it is a good idea to have a chair behind them so that they may sit during the test if they begin to feel lightheaded. Regardless of the position you choose, it is important that the position remain consistent from test to test and visit to visit, as patients may have slightly lower lung functions when sitting than they would when standing.

There are two techniques for performing the FVC test: the open method and the closed method. In the open method, the patient begins by inhaling completely. The patient places the mouthpiece in his or her mouth and immediately exhales forcefully and rapidly. The patient continues to exhale until no more air can be expelled, followed by a full inspiratory effort. This maneuver is repeated at least three times, with a maximum of eight attempts to meet reproducibility and acceptability criteria.

In the closed method, the patient first places the mouthpiece in the mouth, ensuring a good seal. He or she then inhales completely and rapidly, and immediately exhales forcefully and rapidly until no more air can be expelled, followed by a full inspiratory effort. This maneuver is repeated at least three times, with a maximum of eight attempts to meet reproducibility and acceptability criteria.

Depending on the particular software that you are using, the patient may be required to breathe tidally into the spirometer prior to taking the initial forceful inhalation.

Reversibility is the process of determining the patient’s response to a bronchodilator. It is technically defined by an increase in FEV₁ of at least 12% compared to baseline and a 200-mL improvement in FEV₁. Current ATS guidelines recommend administering four puffs of albuterol (90 μg/puff) at 30-second intervals via a spacer device. When evaluating reversibility, the ATS recommends that the patient abstain from using short-acting β₂-agonists for four hours before the test, and from long-acting β₂-agonists for 12 hours prior to testing. Smoking should be avoided for one hour prior to the test.

Acceptability of a Test

Any of following criteria make a spirometry effort unacceptable:

- Poor start
- Poor end
- Cough during the first second
- A Valsalva maneuver or hesitation
- An air leak at the mouth
- Obstruction of the mouthpiece

A poor start occurs when the patient hesitates between maximal inhalation and exhalation. The delay before maximal exhalation may be calculated into the FEV₁ and result in an inaccurate measurement. A poor end occurs when the patient does not blow long enough, resulting in a falsely low FVC. Technicians should instruct patients to
completely exhale through energetic coaching. The ATS recommends an exhalation time of six seconds. However, some patients may not be able to meet this criterion in spite of multiple attempts. For these patients, an obvious plateau on the time/volume graph will demonstrate an acceptable end.

A cough during the first second of an effort will result in an unacceptable effort because of the potential effect on the FEV$_1$. A Valsalva maneuver prematurely stops airflow, influencing FEV$_1$ or FVC. A good seal around the mouthpiece is needed to prevent air leaks during the procedure. If a patient is breathing through his or her nose during the test, nose clips can be used to obstruct the nasal passages. The mouthpiece should be clear of obstruction. Technicians should instruct patients not to occlude the mouthpiece with their tongue or teeth, and chewing gum should be discarded prior to testing.

Spirometry efforts are considered acceptable only if they meet all of the following criteria:

- They are free of artifact.
- There is a rapid start.
- There is an acceptable end (six seconds or an obvious plateau).
- The two highest FVC values are within 0.15 L of each other.
- The two highest FEV$_1$ values are within 0.15 L of each other.

**Documentation.** When performing spirometry, keep proper documentation of the equipment. This documentation should include calibration procedures.

According to the National Heart, Lung, and Blood Institute (NHLBI) asthma guidelines, a spirometry is recommended at the initial assessment and after treatment is initiated and symptoms have stabilized. It also is recommended during a period of progressive or prolonged loss of asthma control. Finally, spirometric assessment is recommended at least every 1-2 years to assess the maintenance of lung function.

**Equipment.** There are many available choices of spirometry equipment, and no one system is best for everyone. When deciding which system to invest in, consider the set-up of your office and how you would like to utilize the equipment. Do you want to have a hand-held unit that can go into patient rooms or will you have a dedicated procedure room?

Manufacturers of spirometry equipment should be able to provide you with documentation that the system meets ATS requirements. In addition, if you plan to participate in clinical trials, you should ensure that the system meets the requirements of 21 CFR 11, the federal regulations regarding electronic records in clinical trials.

Built-in quality control aids can be helpful in obtaining good spirometry results. The use of incentives can encourage patients, particularly children, to blow out longer and faster than they otherwise would. Alerts can be helpful in detecting potential errors in technique and pointing them out to the technician. Finally, a reminder message from the equipment if calibration has not been performed will help ensure that test results are reliable.
Exercise Challenge

The exercise challenge is used to evaluate exercise-induced bronchoconstriction, both for the purpose of diagnosis and to evaluate the effectiveness of treatment. Exercise challenge testing also can be used to rule out other causes of exercise-induced shortness of breath, such as vocal cord dysfunction (VCD). The ATS recommendations for performing exercise challenges are summarized here. Contraindications for this test include unstable cardiac conditions and orthopedic limitations.

Procedures. The patient should be instructed to wear comfortable running clothes. If possible, medications that can alter bronchial responsiveness, including antihistamines, should be withheld (see table 8.1). In addition, prior exercise should be avoided for at least four hours before testing, as it can exert a protective effect. A baseline spirometry should be performed immediately prior to exercise for comparison to post-test results.

The treadmill is the preferred method for performing the exercise challenge. The patient’s heart rate should be monitored by EKG. Alternatively, a pulse oximeter may be used. Testing should be done at a temperature < 25°C and a relative humidity <50%.

The exercise portion of the procedure consists of exercising vigorously to quickly achieve a target heart rate between 80% and 90% of the patient’s maximum predicted heart rate, which is calculated with the following equation:

Maximum predicted heart rate = \[ \frac{220 - \text{age in years}}{ } \times 35 \]

Once the target heart rate is reached, the patient should maintain that heart rate for four to six minutes. The test is concluded when the patient has completed at least four minutes of exercise at the target heart rate, or when the patient becomes too symptomatic to continue. Alternatively, ventilation rather than heart rate can be used to monitor exercise intensity. Ventilation should reach 40-60% of the predicted maximum voluntary ventilation (MVV), calculated as \( \text{FEV}_1 \times 35 \). Although not always accurate during exercise, estimation of arterial \( \text{O}_2 \) saturation by pulse oximetry is recommended both during and after exercise.

### TABLE 8.1. RECOMMENDED WITHHOLDS PRIOR TO EXERCISE CHALLENGE TESTING

<table>
<thead>
<tr>
<th>Exercise</th>
<th>Withhold</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antihistamines</td>
<td>48 hours</td>
</tr>
<tr>
<td>Short-acting bronchodilators</td>
<td>8 hours</td>
</tr>
<tr>
<td>Ipratropium</td>
<td>24 hours</td>
</tr>
<tr>
<td>Long-acting bronchodilators</td>
<td>48 hours</td>
</tr>
<tr>
<td>Theophylline</td>
<td>12-48 hours</td>
</tr>
<tr>
<td>Cromolyn sodium</td>
<td>8 hours</td>
</tr>
<tr>
<td>Nedocromil</td>
<td>48 hours</td>
</tr>
<tr>
<td>Leukotriene modifiers</td>
<td>24 hours</td>
</tr>
<tr>
<td>Caffeine</td>
<td>Day of the test</td>
</tr>
</tbody>
</table>
Serial spirometries are performed at 5, 10, 15, 20, and 30 minutes after cessation of exercise. At least two acceptable tests should be obtained at each time interval. A decrease in FEV₁ ≥10% compared to baseline is considered a positive challenge, although some authors suggest a cut-off value of 15% or greater. A significant decline in FEV₁ also can be seen in VCD, but usually it is associated with flattening of the inspiratory phase of the flow-volume curve.

**Technician Training.** The technician performing the exercise challenge should be skilled in pulmonary function testing and be able to recognize signs of respiratory and cardiac distress. For high-risk patients, it is recommended that the physician personally monitor the entire procedure.

**Equipment.** Necessary equipment to perform an exercise challenge includes:
- Crash cart
- Pulse oximeter
- Sphygmomanometer
- Treadmill or exercise bicycle
- Air temperature and humidity monitor

**Documentation.** All documentation recommended in the spirometry section of this chapter also applies to the exercise challenge. In addition, a log should be kept detailing the temperature and humidity of the testing room.

**Eucapnic Voluntary Hyperpnea (EVH)**

A number of surrogates for exercise testing have been developed that may be easier to implement than an exercise challenge. These include eucapnic voluntary hyperpnea (EVH) of dry air and inhalation of hyperosmolar aerosols, such as 4.5% saline or dry powder mannitol. Of these, the most widely recognized is EVH. In fact, EVH is now the gold standard of the International Olympic Committee to identify athletes with exercise-induced asthma who may legitimately be allowed to use bronchodilators before competition. With EVH, the patient voluntarily, without exercising, rapidly breathes dry air enriched with 5% CO₂ for six minutes. As with exercise, a ≥10% decline in FEV₁ from baseline is consistent with exercise-induced bronchoconstriction.

**Methacholine Challenge**

Methacholine challenge testing often is performed when asthma is a diagnostic possibility but traditional methods such as pre- and post-bronchodilator spirometry and fractional exhaled nitric oxide measurement are inconclusive. The test is more suited to rule out the diagnosis of asthma due to its high sensitivity and high negative predictive value. It is less well suited to confirm the diagnosis of asthma because of its moderate specificity and low positive predictive value. Indeed, increased bronchial hyperresponsiveness also can be seen in COPD, congestive heart failure, cystic fibrosis, bronchitis and allergic rhinitis. Contraindications for testing are listed in Table 8.2.

Drugs that may decrease bronchial responsiveness ideally should be withheld prior to testing (see Table 8.3). In addition, coffee, tea, cola drinks and chocolate should be withheld the day of the study. Finally, patients should be free of respiratory tract infections prior to testing, as they may increase bronchial responsiveness.
**Technician Training.** The technician performing the test should:

1) Be familiar with the guidelines and be knowledgeable about specific test procedures.

2) Be capable of managing the equipment, including set-up, verification of proper function, maintenance and cleaning.

3) Be proficient at spirometry.

4) Know the contraindications to methacholine challenge testing.

5) Be familiar with safety and emergency procedures.

6) Know when to abort testing.

7) Be proficient in the administration of bronchodilators and evaluation of the response to them.

Inhaled methacholine causes bronchoconstriction. Technicians with asthma are at increased risk of bronchospasm during testing and should take extra precautions to minimize their exposure.

**Procedure.** Methacholine is the agent of choice for nonspecific bronchoprovocation challenge testing. It is FDA-approved and available in 100-mg vials as a dry powder. Normal saline is the recommended diluent. There are different published dilution schemes that depend on the dosing protocol used. Both two-minute tidal breathing and five-breath dosimeter protocols are available. Refer to the ATS guidelines for specifics on dilutions and dosing schemes (ATS 2000). In general, baseline spirometry is obtained. If the baseline FEV₁ is <60%, albuterol is administered and the spirometry is repeated. The first dose of methacholine is given, followed by spirometry at the

**TABLE 8.2. CONTRAINDICATIONS FOR METHACHOLINE CHALLENGE TESTING**

<table>
<thead>
<tr>
<th>Absolute:</th>
<th>Relative:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Severe airflow limitation (FEV₁ &lt;50% predicted or &lt;1.0 L)</td>
<td>• Moderate airflow limitation (FEV₁ &lt;60% predicted or &lt;1.5 L)</td>
</tr>
<tr>
<td>• Heart attack or stroke in the last three months</td>
<td>• Inability to perform acceptable-quality spirometry</td>
</tr>
<tr>
<td>• Uncontrolled hypertension (systolic BP &gt;200 mm Hg or diastolic BP &gt;100 mm Hg)</td>
<td>• Pregnancy</td>
</tr>
<tr>
<td>• Aortic aneurysm</td>
<td>• Nursing mothers</td>
</tr>
<tr>
<td></td>
<td>• Cholinesterase inhibitors (for myasthenia gravis)</td>
</tr>
</tbody>
</table>

**TABLE 8.3. DRUGS THAT DECREASE BRONCHIAL RESPONSIVENESS**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short-acting bronchodilator (albuterol)</td>
<td>8 hours</td>
</tr>
<tr>
<td>Long-acting bronchodilator (salmeterol)</td>
<td>48 hours</td>
</tr>
<tr>
<td>Ipratropium</td>
<td>24 hours</td>
</tr>
<tr>
<td>Intermediate-acting theophylline</td>
<td>24 hours</td>
</tr>
<tr>
<td>Leukotriene modifiers</td>
<td>24 hours</td>
</tr>
<tr>
<td>Antihistamines</td>
<td>3 days</td>
</tr>
<tr>
<td>Corticosteroids (inhaled, oral)</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>
appropriate time interval. If the drop in FEV\textsubscript{1} is <20% from baseline, testing proceeds to the next dose. If at any point the change in FEV\textsubscript{1} is >20% from baseline, testing is stopped, signs and symptoms are recorded, albuterol is given and spirometry is performed 10 minutes later. If the highest dose of methacholine is given and the decline in FEV\textsubscript{1} is <20% from baseline, the test is complete. A sample methacholine challenge test report form is available in Appendix C of the ATS guidelines (2000).

**Fractional Exhaled Nitric Oxide Measurement**

Measurement of fractional nitric oxide in exhaled breath (FENO) is a noninvasive, simple and safe method of measuring eosinophilic airway inflammation. The ATS recently released guidelines regarding the interpretation of FENO in the clinical setting (Dweik 2011). Unlike conventional spirometry or methacholine challenge, FENO offers added advantages, including (1) detecting eosinophilic airway inflammation, (2) determining the likelihood of corticosteroid responsiveness, (3) monitoring airway inflammation and (4) monitoring adherence to corticosteroid therapy. The CPT code 95012 was established in 2007 to describe nitric oxide expired gas determination. Reimbursement by insurance, however, currently remains variable. The physician is encouraged to check with the patient's insurance provider before proceeding.

**Procedure.** As opposed to pulmonary function testing, the exhalation maneuver for FENO is slow and steady, with a desired optimal flow rate of 50 mL/s over six seconds. A mouthpiece filter is used to provide enough resistance to close the soft palate on exhalation and prevent contamination of exhaled nitric oxide from the nasal passages.

Spirometry may transiently affect FENO results; therefore, it is more accurate to assess FENO prior to spirometry. Patients should avoid nitrate-rich foods one hour before FENO testing. Likewise, alcohol may alter FENO levels and should be avoided. Smoking may reduce FENO levels, and therefore patients should not smoke for one hour prior. Finally, URIs can increase FENO levels, and such infections should be documented along with the test.

Calibration of the machine varies by manufacturer. Some require daily calibration by a healthy control volunteer. Others use bottled nitrous oxide of a known quantity. Familiarity with calibration and control measures is important for accurate results.

FENO is an indirect measure of eosinophilic inflammation. Interpretation of findings is beyond the scope of this chapter. Cut-off values recently have been published to help determine which patients likely will respond to inhaled corticosteroids (>50 ppb in adults and >35 ppb in children) and those who are less likely to respond (<25 ppb in adults and <20 ppb in children) (Dweik 2011). Following values longitudinally in an individual also can help fine-tune his or her dose of inhaled corticosteroid and monitor for adherence.

**Technician Training.** Staff should be educated on proper FENO technique. The test is less dependent on patient effort than spirometry. An effort will be deemed either adequate or inadequate by the machine with little need for interpretation by staff. If calibration is required by a healthy control, staff volunteers should
be taught the proper methods. Having more than one healthy control may be advantageous to avoid problems if a single control is absent.

**Documentation.** When performing FENO in your office, keep proper documentation of the equipment. Manuals should be easily accessible to staff in case of error codes or malfunction. Calibration logs, if necessary, should be kept as well. Record FENO measurements for each patient in a manner that easily can be tracked over time.

**Equipment.** There currently is at least one portable FENO measurement device available (NIOX MINO, Aerocrine), along with a full-sized device that is more appropriate for research and academic centers. These devices are better utilized if kept in a central location rather than moving them from room to room. When deciding which device to purchase, consider how many tests you likely will perform in a month, as the sensors for each device expire after a certain number of tests or a specified time period. Consider the cost per test for disposable equipment. Does the machine itself need to be replaced after a set number of tests? What control measures are needed? Does the machine lock you out if you do not perform controls? Does the software interface with your electronic medical record system? Consider these questions before deciding on a particular device.

**ALLERGEN SKIN TESTING**

**Skin Prick Testing**

Skin testing is a bioassay which detects the presence of allergen-specific IgE on a patient’s mast cells. When allergen is introduced into the skin of a patient during skin testing, it comes into contact with cutaneous mast cells. Binding of the allergen occurs if the patient’s mast cells are coated with IgE to the specific allergen. If both IgE and allergen are present in sufficient quantities, adjacent allergen-specific IgE molecules become cross-linked on the mast cell surface, resulting in a positive skin test.

Skin prick tests can be used to diagnose sensitivity to aeroallergens, foods, venoms and selected drugs and chemicals. A number of commercial devices may be used, although studies to date have not shown a clear-cut advantage for any single or multi-test device. Optimal results hinge on properly training the staff and performing quality assurance.

To prepare for skin prick testing, you will need to assemble a tray of antigens for testing purposes. There are commercially available products with wells that can be filled with antigens. An alternative is small dropper bottles that can be used to apply the antigen to the patient’s skin. The testing procedure will be most efficient if the tray is arranged in such a way that the bottles of antigen stay in the correct order (such as a board with half-inch-deep holes that are the size of the bottles). This will allow the technician to anticipate the order of the bottles and quickly find the antigen.

The number of skin tests and the allergens selected should be based on the patient’s age and clinical history, and should take into consideration local aerobiologic data and pollen cross-allergenicity. The indiscriminate use of a large number of skin tests is cost-inefficient and strongly discouraged.
**Procedure.** The procedure that will be reviewed here is the use of a single needle to prick the skin. Note, however, that most allergists use multi-test devices to save time and minimize the risk of an accidental needle stick. These devices will therefore be discussed as well.

Prior to skin testing, assess whether the patient inadvertently has taken medications that may suppress wheal-and-flare responses. In the affirmative, you can check a histamine control and still proceed with skin testing if it is adequately positive. A list of common medications and their recommended withhold periods is found in Table 8.4. The suggested withhold period for second-generation antihistamines has been revised in light of data from a recent retrospective study in which all 97 patients who had discontinued second generation antihistamines three days before testing had strong positive histamine control responses (Shah 2010). The same study also suggested that selective serotonin reuptake inhibitors, selective norepinephrine reuptake inhibitors and proton pump inhibitors did not significantly interfere with skin testing. H₂-antagonists alone are unlikely to interfere with skin testing, but if taken with other agents, may need to be withheld for up to 48 hours.

The first step is to gather supplies and prepare the patient. Skin testing can be performed on the patient’s upper back or the volar surface of the forearm. The back is generally preferred because it is more reactive than the forearm and offers a greater surface area to work with. Skin testing should not be performed in areas of active dermatitis or if dermatographia is present.

Begin by cleaning the skin with an alcohol wipe and allowing the area to dry. Using a washable marker, designate the areas for each antigen. This can be done in a code that is standardized for your clinic. For example, the code may be the first letter of the antigen in a standardized order. For a group of
similar antigens such as molds, an “M” can be put above a series of dots or numbers to keep track of the antigen to be placed in the designated area. Rows of antigens should be at least two inches apart and two inches lateral from the spine.

Prior to skin testing, a positive and a negative control should be placed. Some offices choose to check the controls prior to skin testing, whereas others perform allergen testing concurrently with the controls. For the positive control, a 10-mg/mL histamine dihydrochloride control is placed on the skin and pricked with a needle. The positive histamine control must have a wheal ≥3 mm surrounded by erythema for it to be considered valid. A 50% glycerinated human serum albumin-saline solution is generally used for the negative control.

Place a small drop of each antigen on the patient’s skin. Using a small needle, lightly prick the skin at a 45 to 60-degree angle. The skin is then gently lifted, creating a small break in the epidermis through which the allergen solution penetrates. The prick does not need to be deep and should not cause bleeding. To avoid cross-contamination of the testing sites, the needle should be cleaned between pricks. This can be done by wiping the needle with a 2-inch × 2-inch gauze pad containing alcohol. Once all of the antigens have been placed and pricked, wait for 15 minutes before assessing reactivity.

To read the tests, use a small ruler with millimeter markings. Using a cotton ball, wipe off each antigen individually. The size of both the wheal and flare should be recorded. This method enables objective interpretation of the results and easier comparison among physicians. Moreover, specific cutoff levels may obviate the necessity for confirmatory challenge tests to certain foods. The old qualitative scoring (0 to 4) method is discouraged because of inter-physician variability. A positive skin test is defined as a wheal >3 mm in diameter compared to the negative control, and accompanied by surrounding erythema.

After the tests have been read, thoroughly wipe the testing site. If desired by the patient, apply a topical corticosteroid or other anti-itch cream. An oral antihistamine can also be administered. Prepare the patient to see the physician by instructing him or her to get dressed.

If using a Multi-Test® or QUINTEST® device, the procedure is very similar. After cleaning the skin, the antigen-loaded testing device is placed on the patient’s back. Use a slight rocking motion to ensure that each antigen has penetrated the skin. On removal of the device, the pattern of the device should be seen. The device is then discarded in a sharps container. After 15 minutes, the test results are measured and recorded in the same manner as described previously.

The DermaPIK® and Duotip-Test® devices have wells that can be filled with antigen. The patient is prepared in the same manner as with the single needle except that the testing device will already have antigen on it, and the prick will cause that antigen to be introduced to the skin.

**Technician Training.** To ensure quality control, skin test proficiency should be periodically assessed. The target coefficient variation (CV) should be less than 30%. Refer to Table 3 of the Allergy Diagnostic Testing Practice Parameter for more details. (Bernstein 2008)
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**Equipment.** Equipment needed to perform skin prick testing will vary depending on the device chosen. Examples of available devices include the Multi-Test®, the DermaPIK®, the QUINTEST®, the Duotip-Test® and single needles. In addition, you will need to determine which antigens you will be testing after carefully considering your geographic location. Antigen suppliers are listed in Appendix B.

Cotton balls or 2-inch × 2-inch pads, alcohol wipes, and a marker are required. It also is necessary to have the appropriate emergency medications on hand in the rare event of a systemic reaction. You will need a refrigerator to store the antigens when not in use.

**Documentation.** Results of skin prick testing must be documented in the patient’s medical record. A sample skin test template is available for download at www.aaaai.org. Office-specific information, such as location and the antigens that you commonly use, can be added to the template.

**Intradermal Testing**

Intradermal (ID) tests generally are done when increased sensitivity is needed (i.e. when the prick test is negative despite a very convincing history). In addition, sensitivity to low-potency allergenic extracts may best be evaluated by this method. ID tests are especially useful in the diagnosis of drug and venom sensitivity. However, because of very high false-positive rates and potential risks for anaphylaxis, ID testing to foods is not recommended.

**Procedure.** ID testing is performed by injecting a small amount of diluted antigen into the intradermal space. ID testing should be performed using disposable 0.5- or 1.0-mL syringes. Begin by cleaning the forearms and marking the testing locations. Always wear gloves while performing ID testing. To perform an ID test, hold the skin taut. With the bevel of the needle up, insert the needle almost parallel to the skin. When the bevel is just into the skin, inject 0.02-0.05 mL of diluted antigen, forming a small wheal on the skin. Both positive and negative controls should also be placed. The tests are read 15-20 minutes after injection, and both wheal and flare (in millimeters) should be recorded.

Unlike the interpretation of skin prick tests, there is no consensus as to what constitutes a positive intradermal test. Most allergists, however, use the criterion of 3 mm above the negative control.

After the tests have been read, thoroughly wipe the testing site. If desired by the patient, apply a topical steroid or other anti-itch cream. An oral antihistamine can also be administered. Prepare the patient to see the physician by instructing him or her to get dressed.

**Technician Training.** All considerations for skin prick testing also apply to ID testing. It is important that the technician be well trained in the correct technique so that antigens are not accidentally injected into the subcutaneous tissue or muscle.

**Equipment.** An ID testing tray should be available. The antigens used for ID testing should be 500- to 1000-fold more dilute than the concentration used for prick testing. The histamine control dilution should be 0.1 mg/mL. The technician always should wear gloves to minimize the risk of a needle stick. Emergency medications should be readily available, as systemic reactions are more common with ID tests.
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Documentation. Document the results of the ID testing in the allergy testing record.

Local anesthetic testing

Most adverse reactions to local anesthetics are not due to IgE-mediated mechanisms but rather nonallergic factors such as vasovagal responses, anxiety, or toxic reactions related to epinephrine. Nonetheless, to exclude the rare possibility of an IgE-mediated reaction to local anesthetics, skin testing and graded challenge can be performed in patients with a convincing history.

Local anesthetics are divided into two groups based upon their chemical structure:

- **Group I**: The benzoic acid ester agents, which include benzocaine, procaine, and tetracaine
- **Group II**: The amide agents, which include bupivacaine, lidocaine, and mepivacaine

There is evidence for cross-reactivity among group II agents and a lack of cross-reactivity between group I and II agents.

Procedure. Skin prick tests are first performed with the undiluted anesthetic. The anesthetic should not contain epinephrine to avoid vasoconstriction. If the result is negative, successive subcutaneous injections of 0.1 mL at 1:100, 1:10 and full-strength solutions are given at 15-minute intervals. If no reactions are encountered, 0.5 to 1 mL of full-strength anesthetic is injected subcutaneously.

Penicillin testing

Skin testing is the most rapid, sensitive, and cost-effective testing modality for evaluating patients with suspected penicillin allergy. However, it has no role in the diagnosis of exfoliative skin reactions, such as Stevens-Johnson syndrome or toxic epidermal necrolysis.

Procedure. Penicillin skin testing involves at least two steps. Skin prick test should be performed first, and, if negative, intradermal tests should follow. Skin testing should not be performed for at least four weeks following anaphylaxis to allow enough time for the cutaneous mast cell population to replenish.

Penicillin skin testing is performed with the following reagents:

- The major determinant: penicilloyl-polylysine (Pre-Pen)
- The minor determinant: penicillin G (10,000 units/mL)
- Ampicillin (2.5 mg/mL) and/or amoxicillin (3 mg/mL) if relevant to the patient’s situation

Aminopenicillins, such as amoxicillin and ampicillin, should be included in patients who report an immediate systemic reaction to these drugs. These patients can form IgE antibodies to the R-group side chain rather than the penicilloyl determinant. Therefore, they would not necessarily react to Pre-Pen or penicillin G.

Each test solution may be applied single or in duplicate. However, if a single intradermal test result is equivocal, it should be repeated in duplicate. Furthermore, both a positive and negative control should be applied to verify that the patient’s skin is normally responsive.
Interpretation of results

Skin prick tests are read 15 minutes after application.
- A positive response is a wheal that is 3 mm or greater in mean diameter than the negative control.
- A negative response is no reaction at the prick site or erythema alone without a wheal.

Intradermal skin tests are read 15-20 minutes after application:
- A positive response is a wheal that has increased in size from the original bleb and is 3 mm or greater in mean diameter than the negative control.
- A negative response is no increase in the size of the original bleb and no wheal greater than the control site.

Confirmatory challenge

The negative predictive value for penicillin skin testing with a combination of Pre-Pen and penicillin G is high, but not 100 percent. For this reason, negative testing should be confirmed by an oral challenge followed by a two-hour observational period. If possible, the patient should be challenged to the same specific penicillin to which he or she reacted. For inpatients with a current need for a particular penicillin product, the challenge procedure can be incorporated into the first parenteral dose by administering one-tenth the normal dose, observing for one hour, and then if there is no adverse reaction, administering the remaining nine-tenths of the dose and observing for another hour.

Hymenoptera venom testing

Patients older than 16 years of age who have experienced a systemic reaction to a suspected Hymenoptera insect should be venom tested, as they are potential candidates for venom immunotherapy. This includes older adults in whom the stinging event and systemic reaction occurred decades earlier, because the risk of another reaction can persist. On the other hand, skin testing generally is not indicated in patients younger than 16 years of age who have had systemic reactions limited to the skin (i.e. urticaria/angioedema), as these patients have only a 10% chance of a future systemic reaction.

Timing of testing

If the sting event was recent, wait at least four weeks before skin testing to allow enough time for the cutaneous mast cell population to replenish.

Choice of venoms

In the United States, purified, standardized venom extracts exist for honeybee, yellow jacket, yellow hornet, white-faced hornet and wasp. Due to the difficulty in correctly identifying the insect that caused the sting, testing is generally performed with all five venoms. In addition, clinicians in areas inhabited by imported red fire ants should consider fire ant venom testing.

Procedure. In patients who have experienced severe anaphylaxis, start with a skin prick test at a concentration of 0.1 mg/ml. Otherwise, proceed directly to intradermal testing. The recommended starting concentration is either 0.001 or 0.01 mg/ml (depending on the likelihood of a positive test).
The concentration is subsequently increased by 10-fold increments until a positive skin test response occurs or a maximum concentration of 1.0 mg/mL is reached.

For imported red fire ant venom testing, whole-body extract is used, available as 1:10 weight/volume stock solution. Start with a skin prick test at a concentration of 1:100 w/v, followed by intradermal testing at a concentration of 1:1,000,000 w/v. The concentration is then increased in 10-fold increments until a positive skin test response occurs or a maximum concentration of 1:500 or 1:1000 w/v is reached.

**Patch Testing**

Patch testing is the gold standard for identification of a contact allergen. Although many contact allergens have been identified and reported, fewer than 40 allergens are responsible for the majority of cases of allergic contact dermatitis. The T.R.U.E. TEST® is an FDA-approved test to screen for contactant allergens. The test is preloaded with 35 common contactants and a negative vehicle control. In certain situations, supplementary patch test series may be required based on specific occupations (e.g., hairdressers, machinists) or exposures (e.g., shoes, plants, photoallergens).

**Procedure.** Before patch testing, verify that the skin site where the patch tests will be placed has been free of topical corticosteroids and calcineurin inhibitors (Elidel® or Protopic®) for at least seven days prior to testing. Also, note that oral corticosteroids in moderate doses (>20 mg/d of prednisone or its equivalent) may result in diminished reactivity, although lower doses are generally safe. Oral antihistamines and leukotriene modifiers do not interfere with patch test reactivity. Patch testing a patient with significant atopic dermatitis can result in an “angry back” reaction, resulting in a false-positive reading.

The T.R.U.E. TEST is composed of three panels. Peel open the foil sleeve and remove the first test panel from its protective plastic cover, being careful not to touch the test substances. Position the panel on the patient’s upper back, approximately 2.5 cm lateral to the mid-spine. Select an area that is rash-free. The panel should be smoothed out from the center to ensure that each of the allergen windows is in contact with the skin. While the panel is in place, a marker can be used to mark the test location at the notches found on the panel. Repeat the above steps for the second and third panels. Once completed, secure the edges of the panels with adhesive tape to ensure that they remain firmly on the patient’s back. Instruct the patient to keep the back dry until the patches are removed. Showering, bathing (except for sponge baths) and swimming should be avoided. If any of the patches begins to peel loose, ask the patient to reinforce them with adhesive tape.

Patch tests should be kept in place for 48 hours, then removed for interpretation. After the first reading (at 48 hours), an additional reading at 72-96 hours is recommended to reduce false-positives (i.e. positive at first reading but negative at second reading) and false negatives (i.e. negative at first reading but positive at second reading). Approximately 30% of relevant allergens that are negative at the 48-hour reading become positive at 72-96 hours. Conversely, irritant reactions at 48 hours tend to disappear by 72-96 hours. For weak sensitizers such as neomycin
or p-phenylenediamine, additional readings at 5-7 days may be necessary.

Interpretation. Tests may need to be read 30 minutes after removal of the patches to allow resolution of erythema due to occluding pressure. Interpret reactions using the descriptive scale developed and validated by the International Contact Dermatitis Research Group (Table 8.6).

With positive reactions of clinical relevance, counsel patients on avoidance. A patient education handout on each contactant is available from the manufacturer.

**Atopy patch testing**

Atopy patch testing (APT) is a variant of traditional patch testing used for the diagnosis of non-IgE cell-mediated immune responses. In the United States, it has been used primarily as an adjuvant to skin prick tests in the investigation of foods sensitivities associated with eosinophilic esophagitis. However, the lack of standardized test materials and methodology is an important limitation. Reimbursement by insurance also may be problematic, as most carriers consider it to be investigational.

**Procedure.** APTs for foods are usually prepared with 2 g of dried foods mixed with 2 mL of isotonic saline. The mixtures are placed in 8- or 12-mm Finn Chambers® mounted on Scanpor® tape, and placed on the patient’s back. Undiluted samples of commercially prepared single-ingredient foods may be placed directly in the Finn Chambers. The patches are removed at 48 hours but interpreted at 72 hours.

**ALLERGEN IMMUNOTHERAPY**

Allergen immunotherapy is a cornerstone of the allergist’s practice. Our focus in this section will be on

### TABLE 8.6.

<table>
<thead>
<tr>
<th>No.</th>
<th>Grade</th>
<th>Meaning/appearance</th>
<th>Clinical relevance*</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>-</td>
<td>Negative reaction</td>
<td>Excludes ACD. If ACD is still suspected, recheck technique or do ROAT.</td>
</tr>
<tr>
<td>2</td>
<td>R</td>
<td>Irritant reaction</td>
<td>Controls show similar response or there was an excited skin response.</td>
</tr>
<tr>
<td>3</td>
<td>± + or ?</td>
<td>Doubtful reaction</td>
<td>Negative test result. Repeat readings at 3, 4, and 7 days after patch removed. If ACD still suspected, recheck technique or do ROAT.</td>
</tr>
<tr>
<td>4</td>
<td>1+</td>
<td>Light erythema, non vesicular</td>
<td>Equivocal test result. Could either be negative or indicative of waning prior sensitization. False-positive test result or excited skin syndrome must be ruled out by test in control subject. Repeat steps in 3.</td>
</tr>
<tr>
<td>5</td>
<td>2+</td>
<td>Edema, erythema, discrete vesicles</td>
<td>Positive test result. Indicative of prior or current sensitization. Should correlate with history and physical findings. False-positive test result or excited skin syndrome must be ruled out by test in control subject.</td>
</tr>
<tr>
<td>6</td>
<td>3+</td>
<td>Coalescing vesiculobullos papules</td>
<td>Strongly positive result. Same conditions in 5 apply.</td>
</tr>
</tbody>
</table>

Abbreviations: ACD, allergic contact dermatitis; ROAT, repeat open application test.

*Clinical relevance is based on the Joint Task Force’s appraisal of current literature
subcutaneous allergen immunotherapy. Although an increasing number of studies have demonstrated the efficacy of sublingual immunotherapy (SLIT), FDA-approved formulations are still lacking in the United States; therefore, SLIT will not be discussed. Similarly, oral immunotherapy for food hypersensitivity is considered investigational at this juncture, and will not be discussed either.

Subcutaneous allergen immunotherapy is a method of employing subcutaneous injections of gradually increasing doses of antigenic materials for the purpose of inducing immune tolerance in allergic patients. This chapter will focus on immunotherapy administration. Guidelines for immunotherapy extract preparation are discussed in Chapter 9.

**Procedures**

**Injection Procedure.** The nurse completes the following steps when administering immunotherapy:

1. The nurse or receptionist pulls the shot chart or accesses the electronic patient shot record.
2. The shot chart is compared with the check-in slip to verify full name and identification number.
3. The nurse checks the date the patient last received an immunotherapy injection and follows the standing order protocol for the dose to be given. The nurse documents the date and initials the chart.
4. The patient is questioned about any previous large local or systemic reaction. The patient also is asked about potential contraindications, particularly poorly controlled asthma, recent start of a β-blocker, and pregnancy. If pre-
5. The dose to be given is documented in the shot record. If more than one injection is to be administered, perform each step individually, as all vials may not be at the same dose level.
6. The proper vials for the patient are retrieved. Take care to ensure that the correct vials are administered to the correct patient. Double-check labels to ensure patient safety.
7. Draw up the serum as documented in the chart. Take your time.
8. Call the patient by his/her complete name and re-verify his/her identity.
9. The injection is given subcutaneously at a 45- or 90-degree angle in the upper arm. Prior to injecting, ensure that you aspirate for blood. If blood appears, the needle is in a vein. Remove the needle immediately without giving the shot. Discard the needle and serum into a sharps container and begin the process of drawing up a new dose.
10. The patient should sit in the waiting area for at least 30 minutes.

**Post-injection Care.** All patients are to wait for at least 30 minutes after their injection(s). In high-risk patients, the wait time can be extended at the physician’s discretion. The patient may choose to place ice packs over the injection site(s) if susceptible to large local reactions. If the patient does not wait, document it in the patient’s chart and follow your clinic’s procedures. Most clinics elect to issue a warning for the first offense but discontinue immunotherapy after the second or third offense.
Bear in mind that the physician ultimately is liable for any immunotherapy-related adverse reactions that may occur.

After the patient's designated waiting period, check the arms for any local reaction. Document the size of any induration or erythema. Large local reactions are not predictive of systemic reactions, and usually can be prevented by pretreatment with oral antihistamines and application of ice. Nonetheless, some physicians prefer to reduce the dose. In such case, the treating physician should formulate an easy-to-follow dose-adjustment protocol.

**Treatment of Large Local Reactions.** For local reactions that are 2.5-3 cm in size, apply ice and have the patient wait an additional five minutes. For a reaction >3 cm, apply ice and administer an additional antihistamine. Oral corticosteroids are generally not necessary.

**Treatment of Systemic Reactions.** The diagnosis and treatment of anaphylaxis is beyond the scope of this chapter, and so will be discussed only briefly. For a more detailed discussion, please refer to the 2010 Joint Task Force Practice Parameter on the diagnosis and management of anaphylaxis (Lieberman, 2010).

**Systemic Reaction Protocol**

- Notify the physician immediately, and transfer the patient to an exam room if safe to do so.
- In some clinics, the clinical staff may be authorized to administer epinephrine even before the patient is seen by the physician. In other clinics, the protocol calls for epinephrine to be drawn up but not administered. Note that antihistamines and corticosteroids are secondary medications that should never replace epinephrine in the treatment of anaphylaxis.
- Assess airway, breathing, circulation, and mental status. Record vital signs, including $O_2$ saturation, on an emergency flow sheet.
- Place the patient in a supine position and elevate the lower extremities, particularly when there is concern for hemodynamic compromise.
- Administer oxygen. Titrate to keep $O_2$ saturation > 92%.
- Administer an IV saline bolus in patients who remain hypotensive in spite of epinephrine.
- For patients who develop bronchospasm, administer nebulized beta-2 agonists.
- If the patient's condition does not improve in spite of administration of an adequate dose of epinephrine, consider prompt transfer to the emergency department.
- Once the patient has stabilized, antihistamines and corticosteroids can be administered as ancillary measures.
- Inform the treating allergist of the systemic reaction, and note the dose adjustment in the shot chart.
- Patients with systemic reactions should carry an epinephrine auto-injector. The auto-injector also is useful for delayed systemic reactions that have occurred after the patient has left the physician's office.

**Technician Training.** Staff who administer allergen immunotherapy must be thoroughly trained to recognize the symptoms of anaphylaxis, particularly in children, who may not be able to verbalize symptoms. Staff should regularly run mock drills.
simulating shot reactions, and should possess at least Basic Life Support certification.

**Immunotherapy Dosing Schedule.** Allergy injections are conventionally given once or twice a week during the build-up phase. Once a patient reaches a maintenance dose, the interval between injections can be progressively increased, as tolerated, up to an interval of four weeks for inhalant allergens and up to eight weeks for venom. Accelerated schedules such as cluster or rush immunotherapy, where several sets of injections are administered per visit, allow patients to achieve a maintenance dose much more rapidly. In these situations, the risk of both local and systemic reactions is greatly increased. Pre-medication is strongly recommended, and patients should remain in the office for a longer period after their injections (up to three hours).

Although there is no published evidence to support modification of immunotherapy doses due to treatment gaps during the build-up or maintenance phases, it is customary to reduce the dose when the interval between injections is prolonged. One suggestion is to reduce the previous dose by 25% 14-21 days after the missed scheduled injection and by 50% 21-28 days after the missed scheduled injection (Cox 2011). A similar dose-reduction protocol may be used for gaps in maintenance immunotherapy.

As previously mentioned, large local reactions are not predictive of subsequent systemic reactions. However, some allergists feel more comfortable decreasing the dose. Similarly, some allergists reduce the dose during high-pollen season, although several published studies have not found an association between pollen counts and systemic reactions. Finally, some authorities advocate reducing the dose when starting a patient on a new maintenance vial.

A pregnant patient may continue allergen immunotherapy, but her dose should not be increased until after delivery because of fetal risk in the event of a systemic reaction. If a pregnant patient’s dose is decreased for any reason (e.g., new vial, large local reaction), her dose should be held at the decreased level until after delivery.

**Contra-indications.** Staff should be aware of certain situations that would dictate withholding immunotherapy. In particular, asthmatic patients whose asthma is poorly controlled should not receive their allergy injections due to a high risk of anaphylaxis. For that reason, some allergists advocate measuring peak expiratory flow readings in all asthmatics and withholding injections if the reading is less than 70% of predicted. Additional situations that dictate withholding immunotherapy include a patient who is experiencing fever or is acutely ill; is unable to wait for the entire waiting period; has skipped prior waiting periods; appears intoxicated or impaired; or recently has started beta-blocker therapy without the allergist’s prior knowledge.

**Equipment.** The equipment necessary to perform immunotherapy includes syringes, cotton balls, alcohol prep pads, individualized allergen extracts, emergency equipment including epinephrine, oxygen, nebulizer machine, IV saline, and an automated external defibrillator (AED). An easy-to-understand written anaphylaxis protocol that has been thoroughly reviewed and practiced with the staff is of critical importance.
**Documentation.** Prior to initiating allergen immunotherapy, inform patients of the clinic’s immunotherapy procedures, including the mandatory 30-minute wait time. Asthmatic patients in particular should be reminded not to discontinue their maintenance asthma medications without their physician’s permission and to defer immunotherapy if their asthma is not well controlled. Review potential adverse reactions, including both local and systemic reactions. Have all patients sign an informed consent form prior to receiving their first injection. If the clinic’s protocol requires carrying an epinephrine auto-injector, give a prescription to the patient with a reminder to carry it each time he or she comes in for an allergy injection.

**ORAL FOOD CHALLENGE**

An oral food challenge provides the most definitive means to diagnose food allergy. It is used to identify, confirm or rule out a suspected food allergy, and may prevent unnecessary food restrictions. An oral food challenge in the outpatient setting should be performed only if the benefit to the patient of a negative result is greater than the risk of the testing, and only if previous skin prick or in vitro tests have concluded a high probability of a negative result. The Food Allergy & Anaphylaxis Network has published *A Health Professional’s Guide to Food Challenges*, which provides detailed information on conducting oral food challenges (Mofidi 2004).

**Procedure.** Testing can be an open, single-blind or double-blind challenge. Open challenges are the simplest to perform and the less time-consuming. They are ideal for situations where multiple foods are in question. However, as open challenges are prone to patient bias, view positive results with caution. Foods that result in symptoms should be further investigated in a blinded controlled challenge.

As opposed to an open challenge, the single-blind challenge helps eliminate patient bias. Single-blind challenges are technically easier to perform, because they do not involve an additional un-blinded participant to prepare the placebo and active doses. Single-blind challenges have more flexibility in design, such as the addition of multiple initial placebo doses. This can be particularly helpful in patients in whom food reactions are not causally related to foods.

The double-blind placebo-controlled food challenge remains the gold standard for the diagnosis of food allergy. Although the single-blind challenge helps eliminate patient bias, the individual performing the food challenge has the potential to be biased in the interpretation of the results. Nevertheless, double-blind placebo-controlled food challenges are usually not necessary in most clinical situations.

Food challenges may be performed in the office, in the hospital or, in rare circumstances, at home. The setting is dependent on the patient’s history and likelihood of a positive challenge.

Consider an oral food challenge after a negative skin prick test to the suspected food or low food-specific IgE antibodies. Foods that are identified by positive IgE tests with no clinical history of reactivity, or those that are unlikely to provoke a reaction, may be screened with open food challenges.

Perry et al. (2004) describe the following standardized procedure. The challenge is performed
over a 90-minute period. The total amount of food protein to be administered is 4 g for children \( \leq 4 \) years of age and 8 g for those \( \geq 5 \) years of age. Doses are administered at 15-minute intervals. The amount of food is increased with each dose, beginning with 5% of the total dose and increasing by 5% increments with each subsequent dose, with the final two doses being 25% of the total amount to administer (see Table 8.7).

**TABLE 8.7. ORAL FOOD CHALLENGE PROCEDURE**

<table>
<thead>
<tr>
<th>Example: Total of 8 grams to administer</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>5%</td>
<td>0.4 g</td>
</tr>
<tr>
<td>10%</td>
<td>0.8 g</td>
</tr>
<tr>
<td>15%</td>
<td>1.2 g</td>
</tr>
<tr>
<td>20%</td>
<td>1.6 g</td>
</tr>
<tr>
<td>25%</td>
<td>2.0 g</td>
</tr>
<tr>
<td>25%</td>
<td>2.0 g</td>
</tr>
<tr>
<td>Total</td>
<td>8.0 g</td>
</tr>
</tbody>
</table>

Sicherer (1999) described a similar procedure for the oral food challenge. In his procedure, 8-10 g of dry food or 100 mL of wet food are administered on an incremental basis, with a doubling of the amount over 10-15 minutes for a total of 90 minutes. Details on how to prepare an oral food challenge, including challenge substances, placebos and vehicles, are given in the above-referenced article on oral food challenges.

**Technician Training.** Technicians who are assisting with the oral food challenge should be well versed in recognizing and treating anaphylaxis. At the first sign of an IgE-mediated reaction, immediately stop the challenge and give appropriate treatment. Symptoms to watch for include hives, flushing, cough, difficulty breathing and vomiting. A physician should be present during the entire procedure.

Emergency medications and supplies need to be readily available prior to beginning the challenge. The following is a sample listing of medication and supplies to have on hand:

- Epinephrine solution 1:1000
- Normal saline
- Diphenhydramine
- Albuterol sulfate
- Nebulizer machine
- Methylprednisolone sodium succinate (Solu-Medrol)
- Prednisolone sodium phosphate (Orapred)
- Glucagon
- Oxygen
- Large-bore catheter
- Peak flow meter
- Pulse oximeter
- Sphygmometer
- Automated external defibrillator (AED)

For patients at high risk for anaphylaxis, consider performing the food challenge in an inpatient setting where highly-skilled personnel are available to promptly intervene.

**Documentation.** Document the oral food challenge in the patient's medical record, along with the reason for performing the challenge. Be sure to fully document the details of the challenge, including the time and amount of each dose and any reactions that
were observed. All patients should sign an informed consent form prior to the challenge.

ASPIRIN DESENSITIZATION

Aspirin desensitization is indicated for patients who have aspirin-exacerbated respiratory disease (AERD) and whose asthma and/or rhinosinusitis is suboptimally controlled. It also is indicated for cardiac patients who require aspirin for antiplatelet therapy. Additionally, aspirin desensitization may be offered to individuals without AERD but with a history of urticaria/angioedema to aspirin or NSAIDs. However, it is generally not offered to patients who have experienced systemic reactions. Similar to other drug desensitizations, tolerance is maintained only as long as aspirin is continuously taken. Loss of tolerance generally occurs in 2-4 days after discontinuation of therapy.

Reactions to aspirin and NSAIDs can be categorized as either pseudoallergic or allergic. Pseudoallergic reactions are related to COX-1 inhibition and are elicited by aspirin and multiple NSAIDs. These typically occur in patients with AERD or chronic urticaria. Allergic reactions, on the other hand, are IgE-mediated reactions that are elicited by either aspirin or a single NSAID.

Desensitization protocol for AERD

In general, patients are treated with increasing incremental doses of aspirin over set time intervals. After a positive response to aspirin and subsequent recovery, the dose at which the response occurred is repeated until no reaction occurs and the dose is increased until a maximum dose is reached. The most commonly cited protocol, from the Scripps Clinic, involves incremental oral administration of aspirin during 2-day course starting at 30 mg and finishing at 650 mg (Table 8.8).

Alternatively, the Joint Task Force recently published (Solensky et al, 2010) a shorter protocol with a starting dose of 20.25 mg and a final dose of 325 mg (Table 8.9). Note that both protocols recommend starting a leukotriene modifier prior to desensitization to diminish the likelihood of lower airway symptoms. Once patients are desensitized, daily administration of 325-650 mg of aspirin is recommended to maintain tolerance. At that dose, universal cross-reactivity with all NSAIDs also is achieved.

Desensitization protocol for aspirin-induced urticaria/angioedema

Desensitization protocols for aspirin-induced urticaria/angioedema are typically shorter, but they start at a lower dose of aspirin. They often are used in patients in urgent need of aspirin in the context of an acute coronary syndrome or a coronary stent placement. An example of a protocol is highlighted in Table 8.10. Although their aggregate success rate exceeds 90%, no confirmatory challenge studies were ever performed to determine whether these patients were truly aspirin sensitive.
CHAPTER 8—Common Office Procedures

TABLE 8.8

**Aspirin Induction of Drug Tolerance Scripps Protocol**

<table>
<thead>
<tr>
<th>Assessment and premedication (1-7 days before procedure)</th>
<th>FEV$_1$, &gt;60% predicted (&gt;1.5L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start or continue treatment with montelukast, 10 mg daily</td>
<td>Start or continue treatment with inhaled corticosteroid and long-acting β-agonist</td>
</tr>
<tr>
<td>Systemic steroid burst if low FEV$_1$ or bronchial instability</td>
<td></td>
</tr>
</tbody>
</table>

### Protocol

<table>
<thead>
<tr>
<th>Time</th>
<th>Aspirin Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1: 0</td>
<td>30 mg</td>
</tr>
<tr>
<td>Day 1: 3 hours</td>
<td>60 mg</td>
</tr>
<tr>
<td>Day 1: 6 hours</td>
<td>100 mg</td>
</tr>
<tr>
<td>Day 2: 0</td>
<td>150 mg</td>
</tr>
<tr>
<td>Day 2: 3 hours</td>
<td>325 mg</td>
</tr>
<tr>
<td>Day 2: 6 hours</td>
<td>650 mg</td>
</tr>
</tbody>
</table>

Start intravenous catheter with heparin lock (keep in for 2-3 days).
FEV, and clinical assessment every hour and with symptoms.
Reactions typically occur with a provoking dose of 20-101 mg. Treat with medication described below. Chance of reaction to repeated threshold dose is small, but if occurs, repeat dose until reactions cease and then proceed.
After patient completely stabilized, provoking dose can be repeated (assuming another 3 hours of observation time), otherwise start with provoking dose on day 2.
If nasal, gastrointestinal, or cutaneous reactions occur on day 1, pretreat with histamine$_1$ and histamine$_2$ receptor antagonists for remainder of procedure.

### Medications for treatment of aspirin-induced reactions

<table>
<thead>
<tr>
<th>Ocular</th>
<th>Topical antihistamines</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasal</td>
<td>Antihistamine, topical decongestant</td>
</tr>
<tr>
<td>Laryngeal</td>
<td>Racemic epinephrine nebulization</td>
</tr>
<tr>
<td>Bronchial</td>
<td>β-Agonists</td>
</tr>
<tr>
<td>Gastrointestinal</td>
<td>Histamine$_2$-receptor antagonists</td>
</tr>
<tr>
<td>Urticaria/angioedema</td>
<td>Antihistamine</td>
</tr>
<tr>
<td>Hypotension</td>
<td>Epinephrine</td>
</tr>
</tbody>
</table>

Abbreviation: FEV$_1$, forced expiratory volume in 1 second.
Aspirin Induction of Drug Tolerance, Aspirin Desensitization Joint Task Force Recommendations*

Assessment and premedication (within 1 week before procedure) FEV \(_1\) >70% predicted
- Consider starting or continuing leukotriene modifier therapy
- Start or continue treatment with high-dose inhaled corticosteroid and long-acting \(\beta\)-agonist if poorly controlled asthma
- Systemic steroid burst if low FEV \(_1\) or bronchial instability
- If receiving maintenance systemic steroids, consider doubling daily dose (if on alternate day steroids change to daily dose)

<table>
<thead>
<tr>
<th>Protocol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>90 min</td>
</tr>
<tr>
<td>180 min</td>
</tr>
<tr>
<td>270 min</td>
</tr>
<tr>
<td>360 min</td>
</tr>
</tbody>
</table>

Document informed consent and advise patient it may take several days to complete (most will take 2 days).

Establish intravenous access.

FEV \(_1\) and clinical assessment every 90 minutes and with symptoms.

Dosing interval may be extended to 3 hours based on individual patient characteristics.

Reactions will likely occur with early doses, usually 81 mg.

Treat reactions as indicated below.

After patient completely stabilized (but not less than 3 hours after the last dose), the provoking dose can be repeated. A persistent >15% decrease in FEV \(_1\), with or without associated symptoms, lasting longer than 3 hours despite therapy, is an indication to discontinue the desensitization process for the day.

If nasal, gastrointestinal, or cutaneous reactions occur on day 1, pretreat with histamine \(_1\) and histamine \(_2\) receptor antagonists for remainder of procedure.

**Medications for treatment of aspirin-induced reactions**

- **Ocular**
  - Oral antihistamines

- **Nasal**
  - Oral antihistamine, topical decongestant

- **Laryngeal**
  - Racemic epinephrine nebulization and/or intramuscular epinephrine

- **Brochial**
  - \(\beta\)-Agonists

- **Urticaria/angioedema**
  - Oral or intravenous antihistamines

- **Hypotension**
  - Parenteral epinephrine

Abbreviation: FEV \(_1\), forced expiratory volume in 1 second.

This recommended protocol is intended to be more practical, using doses based on commercially available 81 mg aspirin products and a shorter dosing interval. There are no data on safety and efficacy of this protocol.
TABLE 8.10
Rapid Aspirin Challenge/Desensitization Protocol for Patients With Coronary Artery Disease Requiring Aspirin

<table>
<thead>
<tr>
<th>Time</th>
<th>Aspirin dose, mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0.1</td>
</tr>
<tr>
<td>15</td>
<td>0.3</td>
</tr>
<tr>
<td>30</td>
<td>1</td>
</tr>
<tr>
<td>45</td>
<td>3</td>
</tr>
<tr>
<td>60</td>
<td>10</td>
</tr>
<tr>
<td>75</td>
<td>20</td>
</tr>
<tr>
<td>90</td>
<td>40</td>
</tr>
<tr>
<td>105</td>
<td>81</td>
</tr>
<tr>
<td>120</td>
<td>162</td>
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<td>135</td>
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Dosing interval shown is 15 minutes but may also dose every 20 minutes with premedication with oral antihistamine.

XOLAIR

Omalizumab (Xolair), a humanized monoclonal IgG anti-IgE antibody, has been used for more than a decade to treat allergic asthma. Xolair first received FDA approval in 2003 for the treatment of moderate to severe allergic asthma in patients 12 years and older. In March 2014, it received an FDA indication for the treatment of chronic idiopathic urticaria in patients 12 years and older who remain symptomatic despite H1 antihistamine treatment. There are currently several ongoing clinical trials investigating its potential use in other disorders, including seasonal and perennial allergic rhinitis, peanut allergy, latex allergy, atopic dermatitis, idiopathic anaphylaxis, mastocytosis, eosinophilic gastroenteritis, and nasal polyps.

Dosing

Xolair is administered subcutaneously every 4 weeks (150 or 300 mg per dose) or every 2 weeks (225, 300, or 375 mg per dose) based on pretreatment serum IgE level and body weight. Please refer to the manufacturer’s dosing table for details at www.xolair.com/pdf/dosingtables.pdf.

Storage

Prior to reconstitution, Xolair should be stored under refrigerated conditions (36-46°F).

Preparation and Administration

The following section contains simplified step-by-step instructions on how to prepare and administer Xolair in the office. Please refer to the manufacturer’s website for more detailed instructions (http://www.xolair.com/hcp/how-to-prepare-and-administer-xolair.html).

Supplies needed

1. Xolair vial
2. Diluent vial (sterile water for injection)
3. Two 3-cc syringes
4. Two one-inch, 18-gauge needles (for reconstitution)
5. One 25-gauge needle (for subcutaneous injection)
6. Alcohol swabs

Preparing the vials

Step 1: Remove the plastic caps from the Xolair and diluent vials.

Step 2: Using an alcohol swab, wipe the rubber stopper of the Xolair and diluent vials.
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Reconstituting the dose

Step 1: Draw 1.4 mL of sterile water into a 3-cc syringe equipped with a one-inch, 18-gauge needle.

Step 2: Place the Xolair vial upright on a flat surface and, using standard aseptic technique, insert the needle and inject the sterile water. Remove the syringe and needle from the vial.

Step 3: Keeping the Xolair vial upright, gently swirl the vial for 1 minute to evenly wet the powder. Do not shake.

Step 4: After completing step 3, gently swirl the vial for five-10 seconds approximately every five minutes to dissolve any remaining solids. There should be no visible gel-like particles in the solution. Note that some vials may take longer than 20 minutes to dissolve completely.

Stability after reconstitution

The solution should be used for subcutaneous administration within eight hours following reconstitution if refrigerated (36-46°F) or within four hours if stored at room temperature. Reconstituted Xolair vials should be protected from sunlight.

Injection Preparation

Step 1: Invert the vial for 15 seconds to allow the solution to drain toward the stopper. Using a new 3-cc syringe equipped with a one-inch, 18-gauge needle, insert the needle into the inverted vial. Position the needle tip at the very bottom of the solution just beyond the vial stopper when drawing the solution into the syringe. Before removing the needle from the vial, pull the plunger all the way back to the end of the syringe barrel to remove all of the solution from the inverted vial.

Step 2: Replace the 18-gauge needle with a 25-gauge needle for subcutaneous injection.

Step 3: Expel air, large bubbles, and any excess solution to obtain the required 1.2-mL dose (150 mg). For a 75-mg dose, draw up 0.6 mL into the syringe and discard the remaining product.

Injection administration

Step 1: Prepare the injection site with alcohol and administer Xolair subcutaneously. Because the solution is viscous, the injection may take 5-10 seconds to administer.

Step 2: When finished with administration, immediately discard syringes, needles, and remaining solution (if any) in a container designated for medical waste disposal.

For patients requiring more than one injection per administration, choose a different injection site for each injection. This ensures that injections are limited to not more than 150 mg per site.

Post-injection monitoring

Anaphylaxis has been reported after administration of Xolair. According to the Omalizumab Joint Task Force, the overall incidence is estimated at 0.09%, with the majority of reactions occurring within the first two hours after the first three injections. A two-hour wait period is therefore recommended for the first three injections, followed by a 30-minute wait period with subsequent injections. In addition, all patients should be prescribed an epinephrine auto-injector.
NEBULIZED AEROSOL TREATMENTS

Nebulized aerosol treatments frequently are given in the allergist’s office to treat an acute asthma exacerbation. It is therefore advisable to always have enough supplies available.

**Procedure.** Begin by gathering the needed equipment. As with the administration of any medication, the staff should ensure that the right patient is being treated with the correct medication and dose. Nebulization is generally done with a compressor device, but if the patient is hypoxemic, nebulization can be performed with oxygen and a flowmeter.

To use the nebulizer with oxygen, connect the oxygen tubing to the nebulizer with a flowmeter in place. Place the ordered medication in the nebulizer cup, and set the oxygen rate to 4-6 L/min. If a portable compressor is used, attach the tubing to the cup and assemble per the manufacturer’s instructions. Continue nebulization for the prescribed time or until all of the medication has been given.

During nebulization, instruct the patient to sit upright and breathe deeply through the mouth at a normal rate. Take care to prevent hyperventilation. Record details of the treatment, along with any adverse reactions, in the patient’s chart.

**Technician Training.** The technician administering the treatment must be skilled at detecting adverse reactions to bronchodilators. The following adverse reactions may occur:

- **Increase in pulse rate.** Bronchodilators may cause a significant increase in pulse rate. In some clinics, pulse rates are checked regularly and treatment is discontinued if the pulse rate increases by 50% from baseline. In such case, note the reason for discontinuing aerosol therapy and notify the physician.

- **Chest pain.** If the patient complains of sudden chest pain during aerosol therapy, stop the treatment immediately, listen for bilateral breath sounds, monitor pulse for rate and regularity and report your findings to the physician.

- **Cardiac or respiratory arrest.** If the patient experiences cardiac or respiratory arrest during treatment, immediately call the physician, begin cardiopulmonary resuscitation and summon assistance to call 911.

**Equipment.** To perform nebulization in your office, use either oxygen with a flowmeter or a portable compressor. There are many choices of nebulizers, but if you plan to administer nebulized budesonide, ultrasonic nebulizers are not recommended. It is a good idea to have a variety of nebulized medications on hand so you have a choice of which medication to use.

**Documentation.** Document any nebulized treatment in the medical record. This includes the name of the medication, the route, the dose and the time given. In addition, document any adverse reactions.

RHINOSCOPY

Fiberoptic rhinopharyngolaryngoscopy (commonly known as rhinoscopy) is a procedure that increasingly is performed in the allergist’s office. The procedure is conducted with a rhinoscope, a device used to view anatomic structures in the nasal passages, sinuses,
pharynx and larynx. The rhinoscope can be used in the
diagnosis of diseases of the upper airway, including
sinusitis, nasal polyps, and vocal cord dysfunction.
In the diagnosis of sinusitis, rhinoscopy has been
shown to be more sensitive than sinus X-rays, but
less so than a CT scan or MRI. On the other hand,
in-office rhinoscopy is far less expensive compared
to the latter. Moreover, it is useful in monitoring
disease progression and response to therapy.

Procedure. Briefly explain to the patient the
procedure and obtain written consent. Ensure that
he or she is seated comfortably. The procedure
is performed most easily in a chair that has an
adjustable height and is equipped with a headrest.

Administer a topical nasal decongestant (either 1%
epinephrine or 1% ephedrine) via a nasal atomizer.
Alternatively, administer an over-the-counter
dehcongestant spray, such as oxymetazoline, using a
nasal speculum to preserve sterility of the applicator.
Warn the patient that the decongestant solution
may drip down the back of the throat and impart an
unpleasant taste.

Administer topical anesthesia in the form of 4%
lidocaine solution in a spray bottle or 4% viscous
lidocaine on a sterile swab applied between the nasal
septum and the middle and inferior nasal turbinates
for five minutes. When using lidocaine, ensure that
the administered dose is safe. The adult dosing for
lidocaine is 0.3-1.5 mg/kg. Lidocaine solution is self-
administered from a primed atomizer. Instruct the
patient to sniff gently. Ideally, administer two sprays
on each side and wait one to two minutes. Assess the
patient for numbness, then repeat administration
until the patient is sufficiently numb or the maximum
dosage is reached. Viscous lidocaine can be added to
the tip of the scope as an adjuvant to the anesthesia
and to lubricate the insertion. If using lidocaine,
instruct the patient not to have any food or drink for
one hour afterward to reduce the risk of aspiration
resulting from numbness.

The physician should stand in front of the patient
and look directly into the eyepiece if a camera is
not attached to the scope. If the scope has video
capability, ensure that the monitor is in a position
that allows for comfortable viewing by the physician.
Position the chair so that the patient is eye-to-eye.

When choosing a method for performing rhinoscopy,
some find it helpful to always scope the most patent
nare first, whereas others always start with their
preference of the left or right nare. Ensure that the
light source or battery attachment on the scope is
in the “on” position and adjusted to the appropriate
brightness. Ensure that the optical focus is adjusted
properly. If the angulation control has a locking
mechanism, ensure that the lock is disengaged
so that the scope moves freely. Use the minimum
illumination necessary for adequate viewing to avoid
mucosal burns to the patient, as the distal end of the
endoscope may get hot.

Systematically insert the scope to view the anatomic
features. While inserting the scope, instruct the patient
to open his or her mouth and breathe. Warming the
tip of the scope with warm water prior to insertion
can help prevent fogging of the view. In patients with
suspected sinusitis, take care around the osteomeatal
complex, as this area can be quite painful when
touched with the distal end of the scope.
If assessing the patient for vocal cord dysfunction, you can combine the procedure above with the exercise challenge procedure to view the vocal cords after exercise. Complete patient preparation steps prior to exercise so the scope can be inserted immediately following the challenge. When the true vocal cords are viewed, instruct the patient to perform high- and low-pitch phonation, normal respiration and forced expiration to induce paradoxical vocal fold motion. Davis, Brugman and Larsen (2007) performed a combination exercise and laryngoscopy procedure with video recording. The video clips can be seen by viewing their article online.

After the procedure, clean the scope with soap and water and sterilize it with either ethylene oxide or 2%-3% glutaraldehyde solution. Use care to follow the manufacturer’s recommended cleaning and sterilization procedures, as a stronger solution may harm the scope.

**Equipment.** Several manufacturers produce high-quality rhinoscopes. Prior to purchasing a scope, be sure that the desired functionality is present. Consider whether you will want multiple light sources of varying intensity, video capability and comfort for the subject based on scope diameter. Light sources may be incorporated or provided in a separate unit. Both flexible and rigid scopes are available. Although a rigid scope allows visualization of airway areas that are not accessible with a flexible scope, the procedure is significantly less comfortable for the patient. The serviceability of the scope is another consideration prior to purchasing your equipment, as the scope may become damaged and need repair.

**Documentation.** Documentation in the medical record should include the indication for rhinoscopy, patient consent, pre-procedure and post-procedure diagnosis, list of medications used, significant findings on exam, and the patient’s tolerance of the procedure.

**REFERENCES**


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