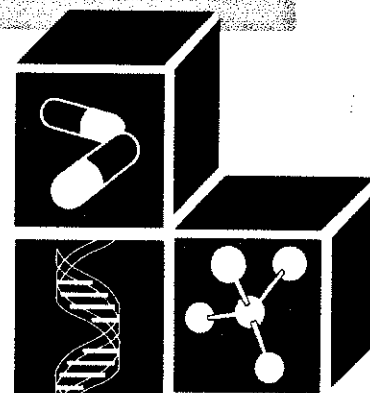


BACK TO BASICS



A review of
the scientific
foundations
of current
clinical practice

Diagnostic Tests of Lung Function

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Pulmonary function tests range from simple measurements of peak flow and pulse oximetry to complex evaluations of absolute lung volume and diffusing capacity. Objective measurement of pulmonary function can be useful in the diagnostic evaluation of children who have a cough, an exercise limitation, or other signs or symptoms referable to the respiratory system. However, pulmonary function testing more commonly is helpful in monitoring the current status or therapeutic response of a child who has a previously diagnosed condition such as bronchiolitis, asthma, or cystic fibrosis.

Objective measurements are only valuable if they are accurate and interpreted appropriately. Most pediatricians regularly rely on measurements of oxygen saturation, peak expiratory flow, and arterial blood gas tensions. Some pediatricians who follow patients who have asthma or cystic fibrosis also perform office spirometry. Those who use these measurements must be able to ascertain that the data are obtained and interpreted correctly. This review will focus on these common procedures. Measurements that require technical supervision and expertise generally available only in pediatric pulmonary function laboratories (eg, absolute lung volume and diffusing capacity determinations) will be covered in less de-

tail. This article is divided into two parts: individual tests and the use of pulmonary function testing in several common clinical situations.

Individual Lung Function Tests

Most pulmonary tests evaluate one or more of three major aspects of lung function: lung volume, airway function, and gas exchange.

The various lung volumes are diagrammed in Figure 1. The vital capacity (VC) is measured easily by simple spirometry; more complex techniques are necessary to measure the residual volume (RV) and, therefore, to calculate the total lung capacity (TLC). Measurements of lung volume are most helpful when evaluating and following children who have one of the restrictive processes: respiratory muscle weakness, chest wall deformity, or interstitial lung disease. Lung volumes also are characteristically altered in some patients who have airway obstruction.

Tests of airway function are particularly valuable because diseases characterized by airway obstruction (asthma and cystic fibrosis) are important pediatric conditions. The most useful tests of airway function are measurements of a maximal forced expiration. This is somewhat surprising in that forced expiration is an "unnatural" maneuver; normal individuals never achieve maximal flows during breathing, even with heavy exercise. Nonetheless, maximal expiration is a sensitive and specific measure of air-

way obstruction. The peak expiratory flow rate (PEF) and forced expiratory volume in 1 second (FEV₁) are the parameters used most commonly that are derived from the forced expiratory maneuver. Other tests of airway function, such as airway resistance, do not require forced expiration, but are more technically involved measurements and are more difficult to interpret.

Gas exchange (oxygen uptake and carbon dioxide elimination) is the primary objective of breathing, so it is natural that measurements of gas exchange are important tests of lung function. Arterial blood gas analysis

ABBREVIATIONS

ABG	Blood gas analysis
BDP	Bronchodilatory
CBV	Cardiac blood flow
CGP	Cardiac gas exchange
EMG	Electromyogram
FEV ₁	Forced expiratory volume in 1 second
PEF	Peak expiratory flow rate

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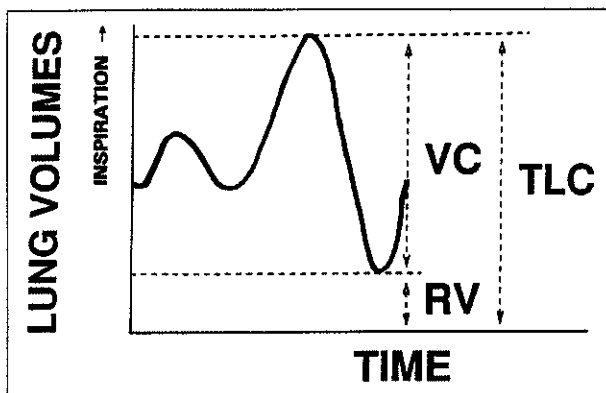


FIGURE 1. The volume of air present in the lung during a tidal breath followed by a maximal inhalation and expiration (vital capacity breath). Vital capacity (VC), residual volume (RV), and total lung capacity (TLC) are indicated. Only the VC can be measured by spirometry. Assessment of RV and TLC requires more sophisticated techniques.

has been the traditional gold standard, but pulse oximetry has become a powerful and efficient tool in pediatric practice. Venous bicarbonate levels, end-tidal carbon dioxide tension, and transcutaneous oxygen tension also are useful. The diffusing capacity is a complex test that is most valuable for monitoring patients at risk for interstitial fibrosis (eg, after chemotherapy or radiation therapy).

Correct interpretation of lung function tests requires an appreciation of normal values. In some cases (pulse oximetry), normal values are straightforward. In others (peak flow, FEV₁, lung volumes), normal values for individuals of the same height, age, and gender are available from predictive equations or tables. Results frequently are expressed as a percentage of the predicted value. Values within 2 standard deviations of the mean (often 80% to 120% of predicted) are considered within the normal range. Normal values vary as a function of racial group. For example, African-Americans tend to have smaller lung volumes than European-Americans of comparable heights; ethnicity, therefore, should be considered in the selection of the appropriate equation or table. There is more intra- and inter-individual variability for flow measurements than for volume measurements. This is reflected in the broader ranges of normal values for these parameters. It also is important to recognize that 5% to 10% of changes in flow measurements such as FEV₁

or FEF₂₅₋₇₅ (see section on spirometry) may represent measurement variability rather than significant changes in flows. Estimating normal values can be difficult for particular patients. For instance, the arm spans of patients who have scoliosis or other musculoskeletal deformities that affect stature may need to be substituted for height. Sequential measurements over time are more helpful than

isolated measurements, because 10% to 20% changes in many parameters in serial measurements can document a significant change in lung function, even when the values remain within the predicted normal range. In general, the physician responsible for interpretation should be familiar with appropriate predicted values, the normal variability of the measurement in question, and ways to compensate for idiosyncrasies of individual patients.

Tests of Lung Volume

VITAL CAPACITY (VC)

The VC or total volume of air that can be exhaled is measured easily by spirometry. After a full inspiration, the volume of either a relaxed (slow) or forced full exhalation is measured. Repeat VC measurements should agree within 5%. Forced vital capacity (FVC) and slow vital capacity (SVC) measurements should be similar, but in children who have airway obstruction, it is not unusual for the SVC, paradoxically, to be greater than the FVC. This is because forceful exhalation results in airway narrowing that may trap additional air in the lungs of an individual who has airway obstruction, thus increasing the RV and decreasing the FVC. VC is decreased in individuals who have restrictive lung disease, but also may be reduced in patients who have airway obstruction when RV is increased to a greater extent than TLC. Therefore, although the diagnosis of

restrictive lung disease is suggested by a decreased VC, this diagnosis should be confirmed by measurement of absolute lung volumes to document that RV is not increased.

ABSOLUTE LUNG VOLUMES

TLC, the volume of air in the chest at full inspiration, is the most objective estimate of lung size. Because TLC includes RV, techniques more complex than simple spirometry are necessary. Body plethysmography, helium dilution, and nitrogen washout are common methods for measuring TLC, each of which has advantages and drawbacks. Decreased TLC is the hallmark of restrictive processes; it may be increased in patients who have airway obstruction.

Tests of Airway Function

SPIROMETRY

Spirometry, the measurement of the volume and flow of inhaled and exhaled air, can be performed with any of a variety of instruments, some of which are suitable for the pediatric office. To assess airway function, the most useful spirometric parameters are those obtained during a maximal forced expiration. The person takes in a full inspiration and then exhales with maximum force in a single sustained effort for 6 seconds or until air flow ceases at RV. Most children 6 years of age or older can accomplish this maneuver, but coaching and some training often are necessary for people of any age. The most reliable indicator of acceptable performance is close reproduction of flows and volumes on repeated (usually three) efforts. Consistency of the shape of the flow volume curves (Fig. 2) is a particularly good indicator of maximal effort. Inadequate maneuvers usually represent failure to take a full inspiration, to form a tight seal around the mouthpiece, to breathe out with maximum effort from the very beginning of expiration, or to breathe out completely to RV. The last is most common. A major advantage of the forced expiratory maneuver is that achieving maximal flow does not require extreme effort after the initial 25% of the lung volume has been expired. Practical, detailed recom-

recommendations for performance, equipment, and interpretation of spirometry have been developed by the American Thoracic Society. These recommendations should be reviewed by anyone who interprets spirometry routinely.

Forced expiration can be represented either as a plot of volume versus time (a spirogram) or as flow versus exhaled volume (a flow-volume curve), as illustrated in Figure 2. Although both representations contain identical information, the reproducibility of the shape of the flow-volume curve is a useful indicator of adequate performance: Repeated tests should have identical shapes. The shape of the curve also is helpful diagnostically, especially when maximum inspiratory flow is recorded as well (Fig. 3). Parameters derived from the forced expiratory maneuver that commonly are used to characterize the degree of airway obstruction include the forced expiratory volume

in 1 second (FEV_1) and the forced expiratory flow between 25% and 75% of the vital capacity (FEF_{25-75} , previously called the maximal mid-expiratory flow rate or MMEFR).

Spirometry can be used to identify airway obstruction and to quantify the degree of obstruction. In general, the FEV_1 is the most specific and dependable measure of airway obstruction. It has been suggested that obstruction in peripheral airways can be discriminated from that in larger airways by a disproportionate decrease in the FEF_{25-75} , but the reliability of this interpretation has been questioned, primarily because of the large variability of this measurement. In a few patients who have airway hyperreactivity, the act of performing a maximal forced maneuver can precipitate airway obstruction (so-called "spirometry-induced bronchospasm"). Spirometry is of limited usefulness in such patients and can be detrimental.

In cooperative children who have a demonstrated ability to achieve reproducible measurements, PF measurements can be trusted to reflect the extent of acute changes in airway obstruction. PF is less suited than spirometry or a full pulmonary function evaluation to identify patients who have obstruction, in part because it represents only one point on the flow volume curve (Fig. 2). The value of PF testing is the ability to monitor changes in children who have established baseline values (ie, frequent, repeated measures over time). Tables of predicted values based on gender and height are supplied with the meters and vary between devices, but a knowledge of an individual's predicted value is less important than identification of that patient's best baseline value. This may require maximal therapy (sometimes including systemic steroids) for a brief interval (eg, 1 to 2 weeks) while measuring PF serially. PF maneuvers also can elicit spirometry-induced bronchospasm in susceptible individuals.

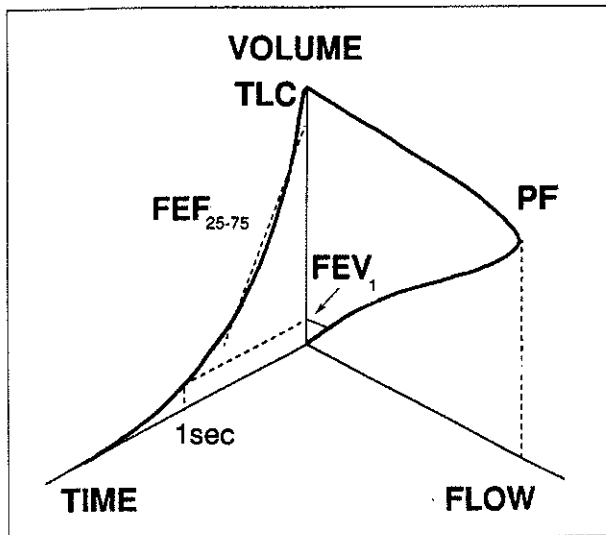


FIGURE 2. Maximal expiration in terms of lung volume, expiratory flow, and time. The left-hand curve represents the volume of air exhaled as a function of time of the exhalation (the spirogram). One second of exhalation is indicated on the time axis, and the corresponding volume (FEV_1) is easily read off the volume axis. The average flow over the middle 50% of lung volume (the forced expiratory flow between 25% and 75% of vital capacity [FEF_{25-75}]) also is measured easily from the spirogram, as indicated. Another depiction of the same information is the flow volume curve on the right, in which maximal expiratory flow is plotted as a function of lung volume. (The flow volume curve usually is represented with volume on the X axis and flow on the Y axis rather than in this form.) The peak flow (PF) or maximal flow rate obtained during the exhalation occurs early in the breath at a high lung volume. Although the curves contain identical information, each highlights different aspects of the maneuver.

PEAK EXPIRATORY FLOW (PF)

Longitudinal measurement of PF can be useful in the management of childhood asthma. Many patients older than 5 years can measure PF reliably by using one of several portable and inexpensive peak flow meters that now are widely available. The child inspires maximally to TLC, then exhales forcefully for a short period of time to obtain the highest value possible. Reproducibility depends on the patient's ability to take in a full breath and exhale rapidly with maximum force. Unlike the FEV_1 and other spirometric parameters, PF is exquisitely effort-depen-

AIRWAY RESISTANCE

The resistance of the airways to flow is a measurement of airway obstruction used less frequently than forced expiratory parameters because it is more difficult to measure and because important changes in the normally low-resistance intrapulmonary airways can be obscured by small changes in the high-resistance upper airway and larynx. Resistance (and its converse, conductance) can be measured plethysmographically or calculated when air flow and esophageal pressure, a technically challenging measurement, are monitored, as in the pediatric or neonatal intensive care unit.

AIRWAY CHALLENGE TESTING

Airway reactivity can be assessed by measuring airway function before and after bronchodilation or bronchoconstriction. The simplest challenge test involves spirometry or PF measurements before and 10 to 15 minutes after administration of an inhaled bronchodilator such as albuterol. An increase of more than 15% in FEV_1 confirms airway hyperreactivity, suggesting asthma. If a child who has

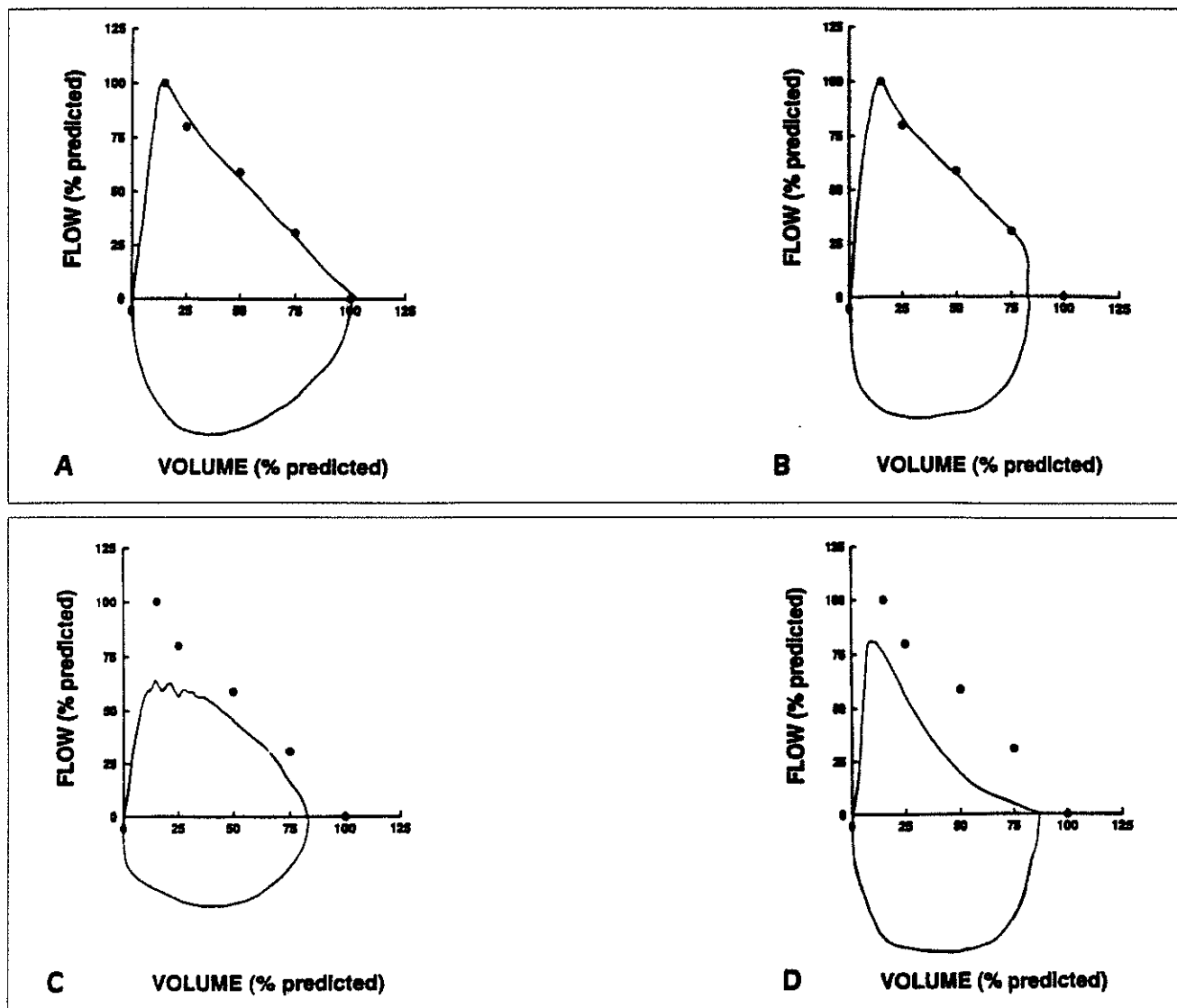


FIGURE 3. Typical flow volume curves demonstrating acceptable and unacceptable maneuvers and typical pathologic findings. **A:** Normal forced expiration. The curve is essentially a right triangle, with flows corresponding to predicted maximal flows (indicated by dots). Maximal inspiratory flow is similar to maximal expiratory flow. **B:** Premature termination of the exhalation. An unacceptable curve in which expiratory flow was discontinued prematurely, resulting in an abrupt drop in flow at low lung volumes. **C:** A submaximal effort. An unacceptable curve because of inadequate effort to reach maximal flow in the effort-dependent portion of the maneuver at high lung volumes. In repeated maneuvers, this maximum flow rate would vary dramatically. **D:** The typical curve of intrathoracic airway obstruction (asthma or cystic fibrosis lung disease). Maximal flows are lower than predicted values, and the curve sags toward the X axis. Inspiratory flows are normal.

asthma has no baseline obstruction, a more than 15% fall in FEV₁ immediately after a bronchoconstrictor challenge such as exercise (adequate to raise the heart rate to >80% of the predicted maximal heart rate for 5 minutes) also is diagnostic. The degree of airway hyperreactivity can be assessed with more sophisticated challenges that involve the inhalation of increasing concentrations of a bronchoconstrictor such as methacholine or histamine. The concentration

that results in a 20% drop in FEV₁ (Fig. 4) usually is used to quantify airway reactivity. Whatever the approach, bronchodilator therapy within the 24 hours prior to testing may mask hyperreactivity. Challenge testing generally is safe, but it does carry the risk of precipitating significant airway narrowing; therefore, it should be performed only by those familiar with the procedure in a setting in which airway constriction can be reversed.

Tests of Gas Exchange

BLOOD GASES

Arterial blood gases have been a gold standard for measurement of gas exchange. The arterial PCO₂ is an indicator of the adequacy of ventilation. An increase or decrease in alveolar ventilation results in a proportional decrease or increase in PCO₂ from the normal value of approximately 40 mm Hg. Acute changes in ventila-

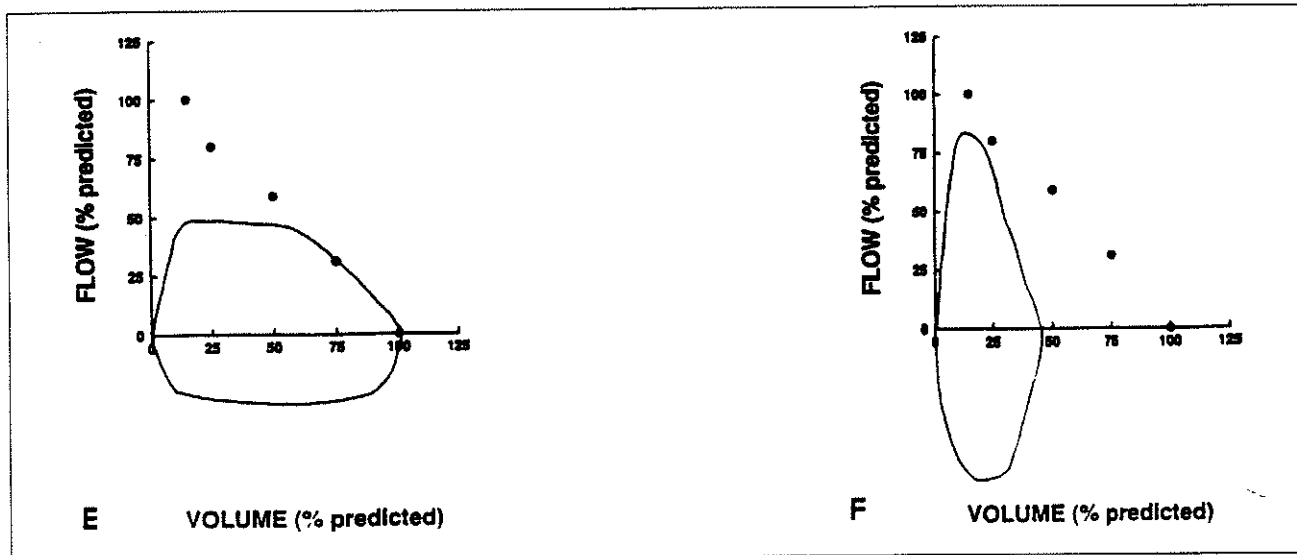


FIGURE 3. E: A curve typical of central airway obstruction. The curve is truncated but does not sag toward the X axis; and inspiratory flows also are lower than predicted. F: The curve of restrictive lung disease. Maximal flows are normal at high lung volumes, the curve does not sag, but vital capacity is reduced.

tion are associated with corresponding alterations in pH: An acute increase in PCO_2 of 10 mm Hg is associated with a decrease in pH of approximately 0.08 pH units. Chronic hypoventilation is associated with renal retention of bicarbonate, in-

creasing the serum bicarbonate and partially normalizing the pH. Therefore, in the absence of other metabolic disturbances, the pH indicates whether hypo- or hyperventilation is chronic or acute.

The arterial PO_2 is a sensitive indi-

cator of altered gas exchange.

Asthma, bronchiolitis, pneumonia, and the other common pulmonary disorders that disrupt the matching of ventilation and perfusion are associated with abnormal gas exchange and hypoxemia. Often these lung diseases do not result in an increase in carbon dioxide tension because patients simply increase the level of ventilation to compensate. However, increasing the level of ventilation does not increase the PO_2 to normal levels. Therefore, patients who have such conditions characteristically have a normal PCO_2 but a low PO_2 . Serial measurements of PO_2 can be used to monitor the severity of lung disease in such patients and are most helpful when the measurements are taken with the patient breathing room air. Right-to-left shunting of blood, as occurs in children who have cyanotic forms of congenital heart disease, also results in hypoxemia. Shunting can be discriminated from ventilation-perfusion mismatching because 100% oxygen breathing has relatively little effect on the hypoxemia caused by a pure shunt.

Arterial blood gas measurements are most reliable when drawn from an indwelling arterial cannula. Arterial puncture often is painful and may be associated with acute increases or decreases in the PO_2 , PCO_2 , and pH. When arterial puncture is performed in small or uncooperative infants,

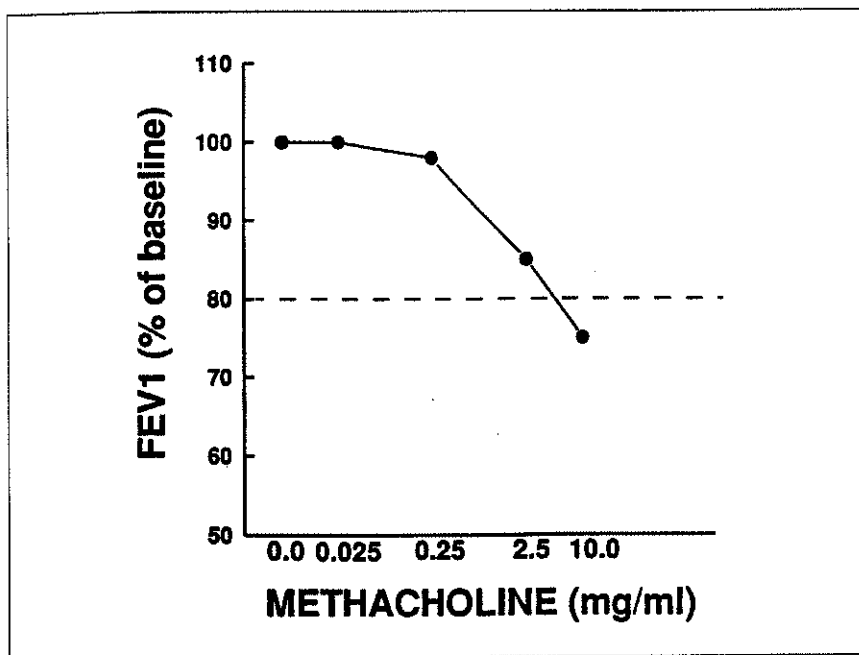


FIGURE 4. In the methacholine challenge, the doubling doses of methacholine are nebulized and inhaled. Spirometry is performed before the challenge is started and after each dose of methacholine. The FEV_1 as a percentage of the baseline value then is plotted at each dose of methacholine. The challenge is stopped when the FEV_1 falls below 80% of baseline. The concentration at which the FEV_1 reaches 80% is estimated from the point at which the curve crosses the 80% line on the plot. In this case, the concentration of methacholine causing a 20% fall in FEV_1 (PC_{20}) is approximately 5.0 mg/mL. Airway hyperreactivity can be defined as PC_{20} less than 10 mg/mL.

inadequate sample volume can result in dilution of the sample by the heparin solution and a spuriously low P_{CO_2} measurement. Measurement of the P_{O_2} and pH are affected less by dilution.

VENOUS BLOOD GASES

Venous samples sometimes are substituted by mistake for arterial blood for gas analysis or when arterial puncture is unsuccessful or impossible. Venous P_{CO_2} usually is 5 to 10 mm Hg higher than arterial, and venous pH is about 0.05 units lower than arterial; these differences increase when cardiac output is low. Significantly abnormal values should be confirmed with an arterial sample.

CAPILLARY BLOOD GASES

Measurement of capillary blood gases (CBGs) is an acceptable alternative to arterial gas measurements under

some circumstances, such as in a child who requires chronic blood gas monitoring. It is important that blood flow through the site of puncture (toe, finger, or heel) be "arterialized" by warming the extremity with a warm cloth, that the puncture achieve a rapid flow, and that the sample is kept on ice and analyzed promptly. The arterIALIZED capillary P_{CO_2} and pH are comparable to arterial values and are more reliable than the P_{O_2} . CBGs have certain advantages over arterial gases: Capillary sampling is easier and less painful than arterial puncture and may be associated with less of an acute change in the level of ventilation. Abnormal values of P_{CO_2} or pH may need to be confirmed with arterial puncture.

PULSE OXIMETRY

Reliable and economic pulse oximeters have been a major contribution

of biotechnology to pediatric practice. A light is shown through the ear or a distal extremity, and the differential light absorbance of saturated and unsaturated hemoglobin is used to calculate the hemoglobin oxygen saturation. Because most light is absorbed by tissue rather than by hemoglobin, it is important to verify that the oximeter is measuring the hemoglobin absorbance properly. In practice, a good arterial wave form that corresponds to the pulse rate indicates reliable values. Excluding environmental light can improve weak signals. When values seem inappropriately low, it is reassuring to measure the oximetry of a normal individual to document that the instrument is functioning correctly. Oximeters are standardized between 70% and 100% saturation; values below 70% suggest hypoxemia but are unlikely to be accurate. Other situations in which pulse oximetry may be inaccurate

TABLE 1. Limitations of Oximetry

PROBLEM	SPECIFIC	READING
Dark skin pigment		Inadequate signal
Decreased perfusion		Inadequate signal
Anemia		Inadequate signal
External light		Inadequate signal
Motion		Inadequate signal
Venous pulsations	Right heart failure Tricuspid regurgitation Tourniquet or blood pressure cuff above site	Low reading
Dyes and pigments	Methylene blue	Low reading
	Indocyanine green	Low reading
	Bilirubin	Usually accurate, but may be affected by coexisting carboxyhemoglobin*
Abnormal hemoglobin	Methemoglobin	Reading not reliable (tends to read 80% to 85% saturation regardless of actual saturation)
	Fetal hemoglobin	Usually reliable
	SS Hemoglobin	Saturation accurate but hemoglobin dissociation curve shifted to right
	Carboxyhemoglobin	Spuriously high saturation readings

*Children who have high bilirubin levels also may have high carboxyhemoglobin levels because carbon monoxide, like bilirubin, is a breakdown product of hemoglobin metabolism. In addition, some blood gas analyzers may read spuriously high levels of carboxyhemoglobin or methemoglobin because of overlap of bilirubin with the spectral analysis of hemoglobin. (see Veyckemans F et al, Suggested Readings).

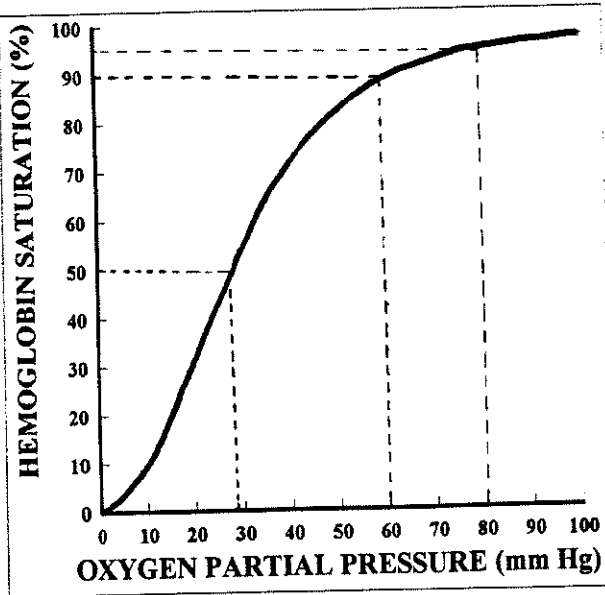


FIGURE 5. Hemoglobin saturation as a function of the partial pressure of oxygen. Note that normal hemoglobin is 90% saturated at a P_{O_2} of approximately 60 torr and is 50% saturated at a P_{O_2} of 27 torr.

include the presence of abnormal or carboxyhemoglobins and compromised light absorbance, such as in darkly pigmented individuals. Some situations influencing pulse oximetry readings are included in Table 1.

The pulse oximeter provides an unparalleled ability to measure and monitor the arterial hemoglobin saturation noninvasively and without the acute changes in gas exchange associated with arterial puncture. It is important to recognize that the oximeter measures arterial hemoglobin saturation and not arterial P_{O_2} . Figure 5 shows the relationship between P_{O_2} and hemoglobin saturation. Because of the shape of this relationship, the arterial oxygen tension (P_{O_2}) is a more sensitive indicator of mild degrees of lung disease: A P_{O_2} of 85 mm Hg or less is abnormal but may be associated with a saturation within the normal range (>95%). It also should be remembered that both P_{O_2} and oxygen saturation can remain high in the presence of inadequate oxygen delivery to tissues in severe anemia or carbon monoxide poisoning.

Pulse oximetry is useful in many clinical situations. In addition to identifying patients who have clinically significant hypoxemia, serial measurements are helpful in monitoring these patients. Serial measurements obtained while the patient is

breathing room air, with a clearly defined inspired oxygen concentration of 21%, are preferable to those with the patient breathing whatever oxygen concentration is indicated clinically. Brief periods of modest hypoxemia are not dangerous, and the value of room air oximetry readings justifies the temporary cessation of oxygen therapy while the oxygen saturation is being measured. In practice, oximetry is measured with the patient receiving added oxygen and

being monitored continuously as the oxygen is withdrawn. If the oximetry falls below 80%, oxygen is reintroduced. If not, the equilibrium value after 2 to 3 minutes is recorded as the room air oxygen saturation.

DIFFUSING CAPACITY

The lung's ability to take up oxygen can be estimated by having an individual inhale a single breath of a mixture of gases that includes a low concentration of carbon monoxide and measuring the amount of carbon monoxide absorbed. This measurement, called the single breath diffusing capacity, is decreased in patients who have interstitial fibrosis, is normal or paradoxically increased in patients who have asthma, and is increased in patients who have alveolar hemorrhage. Interpretation of the diffusing capacity is complicated by anemia. In pediatrics, this measurement most often is used to follow patients at risk for pulmonary fibrosis, such as oncology patients receiving radiation or chemotherapy.

Other Pulmonary Function Tests

RESPIRATORY MUSCLE STRENGTH

Inspiratory muscle strength can be evaluated by using a simple hand-

held manometer to measure the maximum negative pressure that can be developed after a full expiration. Expiratory muscle strength is tested by measuring the maximum positive pressure after a full inspiration. These tests are entirely effort-dependent and may be difficult or impossible in patients who have severe facial weakness. Most cooperative children can generate negative and positive pressures greater than 100 mm Hg. Clinical findings are unusual as long as negative and positive pressures are greater than 40 mm Hg. Respiratory muscle weakness results in decreased lung volumes and flows, but maximal pressure is a more sensitive measurement. Maximal pressures should be assessed in every patient who has low lung volumes because respiratory muscle weakness can be difficult to detect clinically and should be differentiated from other causes of lung restriction.

POLYSOMNOGRAPHY

Measurements of multiple physiologic parameters during sleep are used to investigate children whose sleep is disturbed, who snore excessively, and who have sleep apnea and other sleep-related problems. Simple continuous recordings of pulse oximetry, heart rate, and respirations during sleep sometimes can document hypoxemia or central sleep apneas. Drops in pulse oximetry readings during unattended periods should not be overinterpreted because movement artifacts can resemble drops in O_2 saturation and can be difficult to distinguish from episodes of true hypoxemia. It also is important to realize that obstructed breaths and other abnormalities may not be detected with such studies. Full evaluations, including measurements of end-tidal carbon dioxide, air flow, chest wall movements, electroencephalography, electromyography, and other parameters, are available in specialized sleep laboratories. Referrals for formal polysomnography usually are indicated for children who have atypical obstructive sleep apnea, unexplained pulmonary hypertension or right ventricular hypertrophy, and recurrent apparent life-threatening events or cyanosis.

EXERCISE STUDIES

Cardiopulmonary function during exercise can be evaluated to investigate the cause of exercise intolerance. In the usual exercise protocol, the person exercises on a stationary bicycle or treadmill for 10 to 15 minutes, gradually increasing his or her workload. Parameters such as pulse rate, respiratory rate, minute ventilation, electrocardiographic findings, carbon dioxide production, and oxygen consumption are monitored continuously. These data can be used to define a person's ability to exercise and to determine whether exercise is limited by cardiac and/or respiratory disease. This complex testing should not be confused with simple exercise challenge tests for bronchial reactivity that often are limited to spirometry before and after a period of exercise.

VENTILATION-PERFUSION SCANS

Underventilated or underperfused areas of lung as small as individual bronchopulmonary segments can be identified by using radionuclide scans. The chest is imaged with a gamma camera while the child breathes air containing a radioactive gas such as ¹³³xenon or receives an intravenous injection of a solution of a radioactive gas or a suspension of microscopic particles labeled with an isotope such as ⁹⁹technetium. The usual indication for ventilation-perfusion scans is suspected pulmonary embolus, a less common situation in pediatrics than in adult medicine. Lung scanning also can be an important part of the evaluation prior to lobectomy or pneumonectomy.

COMPLIANCE

The healthy respiratory system is remarkably compliant: The volume of the lung and thorax can be increased to take in a normal breath with a pressure change of only a few centimeters of water. Many different processes (airway obstruction, scoliosis, pulmonary edema, fibrosis, pneumonia) influence compliance, and the interpretation of acute or chronic changes in compliance can be difficult. In ventilated, sedated patients, respiratory system compliance can be calculated from airway pressure mea-

surements and tidal volume. The components of total respiratory system compliance, the compliance of the lung alone, and that of the chest wall alone can be measured individually by more involved methods. Outside of the intensive care setting, compliance is not measured frequently.

Pulmonary Function Tests in Specific Clinical Situations

ASTHMA

Although asthma often can be diagnosed and managed successfully without having objective pulmonary function measurements, pediatricians should be familiar with the indications for bronchial challenge testing, formal pulmonary function evaluations, and, particularly, for home peak flow monitoring.

The diagnosis of asthma usually is straightforward, but it can be difficult when a patient has atypical asthma symptoms (cough, chest tightness, bronchitis), responds poorly to asthma therapy, or has exercise intolerance of unclear etiology. Bronchial challenge testing can be used to identify airway hyperreactivity, supporting the diagnosis of asthma among individuals who have these atypical presentations. Although the presence of airway hyperreactivity increases the likelihood that asthma is the cause of a patient's respiratory symptoms, hyperreactivity can occur among individuals who do not have this diagnosis (especially following viral infections); conversely, some

individuals who have asthma can have normal airway reactivity for prolonged periods. Airway hyperreactivity can be quantified with formal inhalation challenge tests, which also are more sensitive than simple exercise challenge tests, but this rarely is necessary in clinical practice.

Formal pulmonary function tests, including spirometry, absolute lung volume determination, and, on rare occasions, diffusing capacity and muscle strength testing, can be useful in patients who have atypical features of asthma or symptoms that are particularly difficult to control. The primary purpose is to identify other processes that might be complicating or exacerbating the clinical picture. Most patients who have moderate-to-severe asthma have those pulmonary function abnormalities listed in Table 2. Identification of certain specific findings on pulmonary function testing suggests that other processes may be involved (Table 3). Atypical pulmonary function test findings suggest that further evaluation is indicated.

Home peak flow monitoring has become popular in the management of many children who have asthma. The potential advantages of peak flow testing include: 1) improved physician, patient, and parent appreciation of the level of airway obstruction so that exacerbations can be identified and treated earlier, 2) improved patient understanding of the disease, and 3) improved physician/patient communication. Despite these potential benefits, no studies have documented the extent to which peak

TABLE 2. Pulmonary Function Tests in Asthma

TEST	FINDINGS
Airway function	Decreased FEV ₁ , FEV ₂₅₋₇₅ Normal inspiratory flow rates 15% increase in FEV ₁ after bronchodilator has been given 15% fall in FEV ₁ after bronchoconstrictor has been given
Lung volumes	Slow VC > Forced VC Increased TLC Increased RV/TLC
Diffusing capacity	Normal to increased
Muscle strength	Normal

TABLE 3. Diagnoses Suggested by Atypical Pulmonary Function Test Results of Patients Suspected of Having Asthma

ATYPICAL TEST FINDING	POSSIBLE DIAGNOSIS
Small TLC	Restrictive process, allergic alveolitis, myopathy
Muscle weakness	Steroid myopathy
Flattened expiratory flow volume curve	Tracheal obstruction, mediastinal mass
Decreased inspiratory flows	Extrathoracic airway obstruction, laryngeal dysfunction

flow monitoring improves patient management, and most patients who have mild asthma can be managed easily without peak flow testing. Some patients who have more severe disease may adjust therapy successfully by using symptoms alone as an indicator of exacerbations. Long-term compliance may be a problem because many patients are unable or unwilling to conduct regular testing. Peak flow monitoring is most likely to be helpful for patients who have relatively poor symptom perception, those who have the gradual and subtle onset of exacerbations, those whose understanding of the asthmatic process is reinforced by regular testing, and those in whom communication with the physician is facilitated by quantification of airway obstruction.

When regular peak flow monitoring is undertaken, it is necessary to: 1) make sure that the measurements are technically adequate and that the maneuver is not associated with spirometry-induced bronchospasm, 2) identify the patient's best (unobstructed baseline, and 3) instruct the patient in the timing and recording of measurements. It is best to observe the patient by using the peak flow meter at regular visits. A period of intensive therapy, occasionally with a short course of systemic steroids, can be useful in identifying the patient's best baseline value. Once a child's baseline has been identified, the usual technique is to use a three-zone system in which therapeutic decisions are based on whether peak flow is near normal (>80% of baseline), moderately low (50% to 80% of baseline), or severely compromised (<50% of baseline). This schema is

illustrated in Figure 6 and has been described elsewhere in detail. Written records are important to document the baseline peak flow measurements as well as changes in response to "triggers" and therapeutic interventions. In the beginning, measurements can be obtained in the early morning and afternoon, both before and after bronchodilators are given. With experience, the physician and patient can decide together whether intermittent or regular measurements are necessary.

BRONCHIOLITIS IN INFANTS

The major abnormality in infants who have viral bronchiolitis is peripheral airway obstruction and hypoxemia due to the mismatching of ventilation and perfusion. Pulse oximetry is useful in monitoring the severity of bronchiolitis and in documenting the adequacy of oxygen therapy. Oximetry is most useful as a measure of disease severity when patients are breathing room air, as described previously. An oxygen saturation greater than 92% while the infant is receiving oxygen therapy indicates that therapy is adequate, but it is less useful as a measure of the disease process than a measurement taken when

the child is breathing room air. Arterial blood gas analysis seldom is necessary in a stable infant who has bronchiolitis and whose room air oxygen saturation is 88% or greater. Hypoxemia is such a constant finding in moderate-to-severe bronchiolitis that a normal room air oxygen saturation measurement in a distressed infant is an indication to consider another process, such as laryngeal or tracheal obstruction from a foreign body, subglottic stenosis, or vascular ring.

BRONCHOPULMONARY DYSPLASIA (BPD)

BPD, the chronic lung disease that can follow prolonged mechanical ventilation and oxygen use in the neonatal period, is characterized by disordered gas exchange and, often, reversible airway obstruction, both of which gradually improve over the first 2 or 3 years of life. Gas exchange can be assessed by oximetry and arterial/capillary blood gas analysis nearly as easily in infants as in older children. Measurements of lung volumes and airway function have been difficult in children younger than 5 or 6 years. Such measurements now are possible in infants and sedated toddlers in some centers, but the clinical utility of these techniques has not been established. Although infants who have BPD are followed at some centers via serial measurements of compliance and resistance,

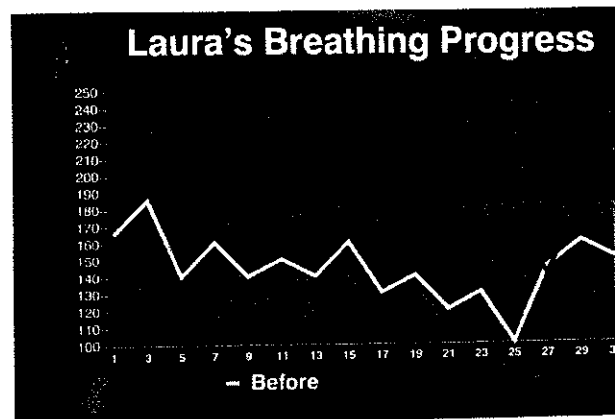


FIGURE 6. Sample peak flow record. This child's best peak flow measurements are 230 to 240 L/min. Measurements above 185 L/min (80% of the best) are in the well zone, those above 115 L/min (50% of the best) are in the intermediate zone, and those less than 115 L/min demonstrate a need for increased therapy. Peak flow was recorded daily, before and after bronchodilators were given.

Equipment Manufacturers and Suppliers

Peak Flow Meters

Allied Medical	1-800-645-2500
Armstrong Industries	1-800-323-4220
Dura	1-800-859-8586
Ferris Medical, Inc	1-800-724-7929
Healthscan	1-800-962-1266
Monaghan	1-800-833-9653
Multispiro	1-800-937-7476

Oximeters

Nellcor	1-800-635-5267
Novamatrix Medical Systems	1-800-533-3538
Ohmeda	1-800-345-2770

Spirometers

Collins	1-800-225-5157
Puritan Bennett	1-800-842-8023
Sensor Medics	1-800-231-2466
Vacumed	1-805-644-7461
Vitalograph, Inc	1-800-255-6626
Welch Allyn	1-315-685-4560

such tests generally are not available and have not been shown to be beneficial clinically.

Most infants who have BPD are monitored closely via pulse oximetry. Room air oximetry measurements help identify long-term improvements and short-term fluctuations associated with viral infections, fluid retention, or other processes. Oxygen therapy usually is adjusted to maintain oxygen saturation of greater than 92% and often can be discontinued when room air saturation exceeds this level consistently, even during feedings and sleeping. Oxygen saturation can be determined periodically on room air during office visits. If the saturation remains above 92% when the child is awake and playing or feeding during two or three readings obtained several weeks apart, it is reasonable to assume that oxygen saturation during sleep is adequate. However, if there is any question about oxygen saturation during sleep, overnight oximetry may be required.

When acute or chronic respiratory failure is suspected, blood gas analysis is indicated. Venous bicarbonate levels may be adequate to monitor respiratory compensation in more stable children. An elevated bicarbonate may be a sign of chronic respiratory compromise or of hypochloremia from diuretic therapy. Serial echocar-

diograms to visualize right ventricular wall thickness and estimates of pulmonary artery pressures may be helpful in children who have right ventricular hypertrophy.

Failure of any of these parameters (room air oximetry, serum bicarbonate, or right ventricular hypertrophy) to improve gradually with time is an indication for further investigation, particularly if overall growth is suboptimal. Although many children who have BPD become asymptomatic by the age of school entry, airway obstruction and hyperreactivity may persist, and a formal evaluation of pulmonary function should be considered at that time.

CYSTIC FIBROSIS (CF)

With the onset of lower respiratory symptoms, individuals who have CF have a gradual decrease of maximal flows (FEV₁, FEF₂₅₋₇₅) and an increase in RV and the ratio of RV to TLC. Spirometry and absolute lung volume measurements often are used to monitor the course of the lung disease. These measurements are particularly important in the identification of acute deteriorations related to respiratory exacerbations and in the monitoring of the response to therapy. Increased obstruction often accompanies an exacerbation that requires increased therapy, including antibiotics, bronchodilators, and increased chest physical therapy. Measurements at the end of a period of intensive treatment indicate the progression of the underlying chronic bronchiectasis. A baseline FEV₁ of less than 30% of the predicted value has been suggested to be an indication for considering lung transplantation in patients who have CF. Many patients who have CF also have significant airway hyperreactivity, which can be identified by using spirometry, with or without plethysmography, before and after bronchodilation or bronchoconstriction.

PULMONARY INTERSTITIAL FIBROSIS

Children who have pulmonary interstitial fibrosis may present with dyspnea or exercise intolerance. They usually have low absolute lung volumes, decreased diffusing capacity, and hypoxemia while exercising. Although children who have idiopathic fibrosis or fibrosis related to inhaled toxins or antigens are rare, a large number of children and adolescents treated with radiation or chemotherapy are at risk for developing severe progressive pulmonary fibrosis. Children who have received bleomycin, BCNU (carmustine), cyclophosphamide, busulfan, and methotrexate are at increased risk for pulmonary interstitial fibrosis, although other agents also have been implicated in this process. Lung function should be evaluated by spirometry, and absolute lung volumes and diffusing capacity should be measured at regular intervals during therapy, with treatment protocols modified if these values fall.

RESPIRATORY MUSCLE WEAKNESS

Objective measurements of lung function can be helpful in caring for children who have either acute or chronic respiratory muscle weakness. The most common cause of acute respiratory muscle weakness is the Guillain-Barré syndrome. Maximal pressures (which are measured easily at the bedside) and spirometric measurements of VC can be monitored as frequently as necessary. When pressures drop below 20 to 25 cm H₂O or the VC below 30 mL/kg of body weight, respiratory support should be considered. Serial peak flow measurements also may provide a convenient method of assessing progressive muscle weakness. Arterial or capillary blood gases can be monitored as well, but respiratory support is best initiated before the onset of carbon dioxide retention. Pharyngeal muscle weakness and the inability to handle oral secretions is an indication for intubation, even in the presence of adequate respiratory muscle strength.

Regular measurements of maximal pressures and lung function via spirometry can be useful among patients who have chronic muscle weakness.

such as muscular dystrophy. These patients are at risk of developing respiratory failure and chronic hypoxemia due to atelectasis; therefore, periodic monitoring of blood gases or serum bicarbonate levels and pulse oximetry also may be indicated. Respiratory failure often presents initially during a respiratory infection; thus, careful monitoring is particularly important in this clinical situation. During such illnesses, blood gas analysis should be considered. Because chronic hypoventilation may develop first during sleep, measurements during nighttime sleep may be useful. Clinical or echocardiographic evidence of chronic respiratory acidosis, right ventricular hypertrophy, and

hypoxemia all are relative indications for assisted ventilation.

Summary

Objective measurements of a wide variety of aspects of respiratory function can be useful in the evaluation and management of children and adolescents who have respiratory symptoms or disorders. Many of the tests described in this article can be performed reasonably in the pediatrician's office. Pediatricians can be comfortable in measuring and interpreting pulse oximetry, blood gas analysis, spirometry, and peak flow. They also should be familiar with the indications for the less common tests

of pulmonary function that now are widely available.

SUGGESTED READING

- Standardization of spirometry—1994 update. *Am J Respir Crit Care Med.* 1995;152:1107–1136 (Official statement of the American Thoracic Society, March 1987. This document is scheduled for revision.)
Clark NM, Evans D, Mellins RB. Patient use of peak flow monitoring. *Am Rev Respir Dis.* 1992;145:722–725
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Veyckemans F, Baele P, Guillaume JE, et al. Hyperbilirubinemia does not interfere with hemoglobin saturation measured by pulse oximetry. *Anesthesiology.* 1989;70:118–122

IN BRIEF

The Spectrum of Erythema Multiforme

Erythema Multiforme ("Minus" and "Maius") and Drug Intake. Fabbri P, Panconesi E. *Clin Dermatol.* 1993;11:479–489

The Many Faces of Erythema Multiforme. Cohen B. *Contemp Pediatr.* 1994;11:19–39
Management of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis in Children. Prendiville JS, Herbert AA, Greenwald MJ, Esterly NB. *J Pediatr.* 1989;115:881–887

Herpes Simplex Virus in Childhood Erythema Multiforme. Weston WL, Brice SL, Jester JD, Lane AT. *Pediatrics.* 1992;89:32–34

Erythema multiforme (EM) is an acute hypersensitivity reaction characterized by distinctive skin lesions and mucous membrane involvement that has a spectrum of severity. It occurs in two forms: the more common "minor" type and the more severe "major" type, also called Stevens-Johnson syndrome (SJS). Sometimes EM includes toxic epidermal necrolysis (TEN) or Lyell disease. EM minor first was described completely by von Hebra in 1866; Stevens and Johnson described the major variant in 1922. EM occurs more often in males, and 20% to 50% of cases occur in the pediatric age group, although rarely in those younger than age 3 years. A winter predominance is suggested.

The pathologic process responsible for EM is unknown. A review of the literature generates an extensive list of causative or inciting agents. Most frequently mentioned are sulfonamide

antibiotics and anticonvulsants, both used commonly in pediatric practice. Malignancies, radiotherapy, autoimmune diseases, and infectious agents such as mycoplasma also have been implicated as possible causes. In 1992, Weston et al described a high incidence of herpes simplex virus (HSV) in EM lesions among both adults and children with or without a preceding history of HSV infection.

Currently, the evidence suggests that EM is caused by an immune reaction. Histologically the lesions are similar to those seen with graft-versus-host disease reactions. Immune complexes have been demonstrated in the serum and lesions, but their role in the pathology is uncertain.

EM minor is characterized by a distinctive rash. Classically, the rash is an erythematous ring that has a dusky center—the target or iris lesion. The rash also may be macular, papular, and/or vesicular. Usually one type of lesion predominates. The lesions have a typical distribution: most commonly, the extensor surfaces of the extremities symmetrically, but sometimes the trunk and face are included. In addition, involvement of a single mucous membrane is possible. Oral lesions may be bullous or ulcer-like or the conjunctiva may be injected mildly. The lesions last 5 to 7 days and recur in

crosses over 2 to 4 weeks before finally resolving without any sequelae. The entire illness is preceded in one third of cases by a mild flu-like prodrome of 7 to 10 days.

In contrast, SJS typically is preceded by a serious prodrome consisting of fever, myalgias, arthralgias, sore throat, and abdominal complaints. This is followed by rapid (hours to days) and widespread bullous eruption involving the extremities, trunk, and at least two mucous membranes. The total body surface area involved can be extensive, possibly leading to fluid and electrolyte disturbances and secondary infection. Lesions of the mouth are more impressive than in EM minor and can be very painful. Severe, erosive conjunctivitis, keratitis, or uveitis may develop. Complications can include corneal ulceration, synechia, symblepharon (adhesion of the eyeball to the eyelid), and blindness. Genital, pulmonary, and gastrointestinal involvement are less common, but can be potentially severe. The overall complication rate is high, with a mortality rate of 5% to 25%.

The rash of TEN starts as a generalized sunburn-like erythema, which quickly progresses to full-thickness epidermal sloughing, sometimes secondary to trivial trauma (Nikolsky sign). Then extensive body surface involvement along with mucous mem-

brane involvement give rise to the same complications as seen in SJS.

EM is a clinical diagnosis. The classic symmetrically distributed, target-lesion rash usually confirms the diagnosis. In contrast to urticaria, EM is rarely pruritic and the duration of the rash is longer. Other annular lesions usually are not symmetric and spare the mucous membranes. Mucous membrane involvement and a toxic appearance differentiate SJS and TEN from other blistering syndromes.

The treatment for EM minor is supportive for the mild symptomatology. Any inciting agents should be discontinued or treated, if possible. Cohen suggests that cases secondary to HSV be treated with a 5-day course of acyclovir. Weston et al strongly discourage the use of steroids in EM minor because of the association with HSV. Children who have SJS and TEN need to be hospitalized, and the severity of skin in-

volvement may necessitate transfer to a burn unit. Careful attention to fluid and electrolyte levels, optimal nutritional support, and meticulous skin care are mandatory. Detection and treatment of infection can be lifesaving. Ophthalmologic attention should be on a daily basis. The use of steroids in SJS still is debated. Prendiville, et al state, "SJS is not a steroid-responsive dermatosis." Cohen reports on some studies that discourage steroid use and others that suggest that a short course might be useful.

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Comment: Although the efficacy of steroids in the treatment of children who have SJS may still be debatable, prudence argues against their

use as long as doubt remains; above all, do no harm. Steroids pose at least theoretic risks in the setting of SJS; they may retard wound healing and promote complicating infection. It also is possible, if not probable, that by the time most children are diagnosed with SJS, the immunologic cascade causing the damage has gone beyond the point where steroids can modulate the reaction. Managing affected patients as though they were suffering from burns, with meticulous attention to skin care, to fluid and electrolyte balance, to preventing secondary infections, and to providing appropriate nutritional support, has improved outcome dramatically for children and adults. We do best to focus where benefit clearly has been proven.

Henry M. Adam, MD
Associate Editor, In Brief