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PULMONARY FUNCTION IN INFANTS AND CHILDREN

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Respiratory diseases represent the most common cause of death in infants worldwide.[7] Advances in neonatal medicine have led to the survival of many premature infants with chronic lung disease. Asthma may afflict as many as 3.2 million American children.[2] These patients, especially the younger child and infant with their developing respiratory systems, represent a challenge for the clinician. Much of our decision making must rely on clinical assessment without the benefit of objective measures of pulmonary function. The technical difficulties inherent in pulmonary function testing of infants and young children are obstacles to the development of simple, clinically relevant procedures for assessment. Methodologies differ as the patient matures and is able to cooperate voluntarily with the process. Standardization of testing procedures is a developing science in pediatric pulmonary medicine, and familiarization with testing strategies and techniques is important if useful information is to be obtained. Though many of the tests currently available are found only in specialized centers, development of these methods is a growing area of interest and will add greatly to understanding of the growth and development of the respiratory system.[7] The ability to measure pulmonary function provides a tool that can confirm a clinical diagnosis, monitor response to therapy, and follow progression of disease. This article gives an overview of lung function testing in childhood,

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including testing in infants. A summary of the more commonly used methods is presented with some background into the physiologic variables that are measured. It also reviews the advantages inherent in certain testing modalities as well as their limitations.

LUNG FUNCTION TESTING IN OLDER CHILDREN

Lung Volume Measurement

Total lung capacity (TLC) is the volume of gas in fully inflated lungs. Its subdivisions represent a set of variables by which the type(s) of disease that occur can be understood. Figure 1 shows tidal volume (TV) as the amount of gas exchanged with normal, quiet breathing. Functional residual capacity (FRC) is the lung volume at the end of a tidal breath. Residual volume (RV) is the lung volume at the end of a complete expiration and together with expiratory reserve volume (ERV) equals FRC. It may be helpful to remember that capacities are always the sum of volumes. Note that the sum of TV, inspiratory reserve volume (IRV), and ERV is vital capacity (VC).

Direct measurement of lung volumes is usually made by either body plethysmography or by gas dilution techniques.[11] These methods are used to determine absolute lung volume, usually at FRC. With FRC known, the standard lung volumes can be computed by adding or subtracting the appropriate measured volumes that are obtained from expiratory or inspiratory maneuvers. Gas dilution methods have the advantage of being fairly easy to perform and are relatively inexpensive. They are useful in children and infants without obstructive disease[37]; however, when gas trapping is present due to airway obstruction, gas dilution methods may underestimate true thoracic gas volume. Conversely, plethysmography may tend to overestimate this volume in obstructive disease. RV is also one of the most variable measurements of lung function

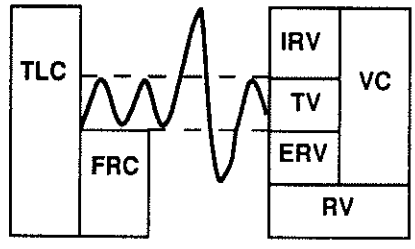

Figure 1. Total lung capacity and its component parts; displayed with spirogram tracing. TLC = Total lung capacity, FRC = functional residual capacity, TV = tidal volume, RV = residual volume, IRV = inspiratory reserve volume, ERV = expiratory reserve volume, VC = vital capacity.

in children and must be interpreted with caution.[47] Measuring lung volume allows determination of the RV/TLC ratio which will increase with gas trapping from obstructive disease. Lung volume measurement also will help to define the process when spirometry does not distinguish between obstructive and restrictive disease. Finally, with restrictive processes, such as interstitial lung disease, chemotherapy, or scoliosis, the FRC, TLC, and RV should be followed to assess the progression of illness which diminishes these values.

Spirometry

Spirometry measures the volume of air exhaled from the lungs during a maximal expiratory maneuver (Fig. 2). Forced vital capacity (FVC) is the total volume of air that can be exhaled. Note that forced expiration is begun at TLC after a full inflation and ends at RV, usually taking fewer than 3 seconds. In patients with obstructive disease, however, it may take as many as 6 seconds to reach RV. Forced expiratory volume in 1 second (FEV_1) is the volume of air forcefully expired from full inflation in the first second. Both FVC and FEV_1 are recorded in liters. Healthy individuals are able to exhale more than three quarters of their FVC in the first second. There is a trend for the FEV_1/FVC ratio to decrease slightly after early adulthood.[27]

The rate at which a volume of gas is exhaled is flow, and it is recorded as liters per second (L/sec) or liters per minute (L/min). The peak expiratory flow rate (PEFR) occurs early in expiration and is dependent on large airways' resistance and on effort by the patient. In contrast,

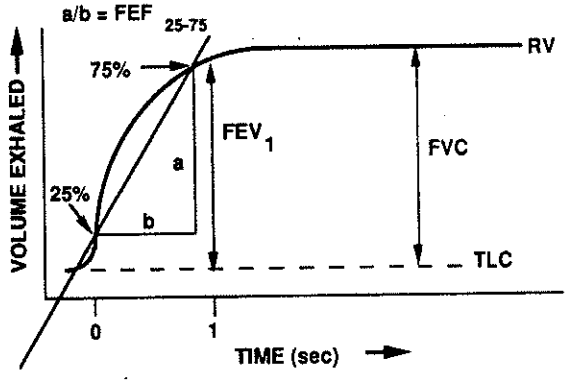

Figure 2. Volume-time plot demonstrates the measurement of forced vital capacity (FVC), forced expiratory volume in 1 second (FEV_1), and forced expiratory flow at 25%-75% of forced vital capacity (FEF_{25-75}). Residual volume (RV) and total lung capacity (TLC) are also indicated.

the resistance of the smaller airways is believed to have a greater effect on flow at lower lung volumes.[61] To study flow at lower lung volumes, graphically average flow over the mid-portion of lung volume. Picking the points at which 25% and 75% of the FVC have been exhaled, define a line across the mid-portion of the curve (see Fig. 2). The slope of this line is called the *forced expiratory flow* from 25% to 75% of FVC (FEF_{25-75}) and averages the rate of flow over the mid-portion of the tracing.

An important principle of spirometry should be mentioned. A maximal flow rate at any given lung volume can be achieved with moderate effort. Once reached, this maximal flow becomes independent of effort. In other words, no matter how hard the subject blows, only a certain maximal flow will be obtained at a given lung volume. This is termed *flow limitation*. At flow limitation, the determinants of flow are believed to be resistance from intrathoracic airways and driving pressure from the elastic recoil of the lung. Maximal flow will be proportional to recoil (driving pressure) and inversely related to airways' resistance. Thus, spirometric measurement of maximal forced expiration allows us to study disease processes as they affect the parenchyma and airways of the lung in a noninvasive manner.

The Testing Environment

Obtaining adequate spirometry requires patient cooperation and coordination. Generally, however, most 5-year-old children can produce an acceptable curve with adequate coaching. Guidelines have been described by the GAP. Conference published in 1980,[53] and by the American Thoracic Society Statement on Spirometry in 1987.[14] Recommendations regarding the testing environment are summarized in Table 1. Just as important as having the proper equipment is having a technician who is sensitive to the needs of children.[30] Many younger patients can be uncooperative because of distractions in the environment, apprehension about the technician, and fear that testing will hurt. Sensitivity to these issues will result in a more pleasant environment for the patient and technician. The patient can master the necessary techniques beforehand through practice. First, the child is asked to practice a slow inspiration with a breath hold for 1 to 2 seconds at full inflation. Then, a maximal expiratory maneuver is practiced. The last demonstration is the maximal vital capacity maneuver. The child is asked to take a slow breath to full inflation, followed by a brief hold, and then a maximal forced exhalation for at least 3 seconds.[30] This maneuver can be performed by asking the child to pretend to "blow out all the candles on the birthday cake in one breath." An example of such coaching might be, ". . .take a deep breath, more, more, more. Now blow, blow, blow, more, more, squeeze, squeeze. . .good! Now, let's see if we can do even better." The practice

Table 1. STANDARDS FOR THE PATIENT TESTING ENVIRONMENT DURING SPIROMETRY IN CHILDREN

The child's torso and head should be erect throughout testing in either a sitting or standing posture.
A nose clip should be used.
Special training is required for those administering testing to children.
Spirometry used for diagnostic studies should produce a hard copy for ready analysis by the tester. Follow-up studies can be done without hard copy capability.
All reports of lung function should include date of birth, date of test, standardized height (without shoes), weight, sex, race, absolute values of all measurements with percent of predicted values, and conditions of the tests (e.g., baseline, postexercise, postbronchodilator).
The vital capacity should be reported as the largest volume obtained from any of the respiratory maneuvers.
Older children and adolescents should have the best of three tests taken as the "truest" measure of lung function.
Younger children may require more than three tests to obtain one which is adequate. The "best" test is the one with the greatest sum of FEV_1 and FVC.

Data from Taussig LM, Chernick V, Wood R, et al: Standardization of lung function testing in children. J Pediatr 97:668–676, 1980.

can be done with the mouthpiece in place before connecting the spirometer or with a party favor. Most children will master the skills necessary for adequate testing after 4 to 5 minutes of practice. For those younger than 6 years, this may take longer. Again, the importance of a calm, success-oriented environment with an experienced tester cannot be overemphasized.

Interpreting Spirometry

Spirometry not only allows the characterization of a patient's lung function against reference values[27] but also can define the disease class. Most lung diseases can be classified as obstructive, restrictive, or mixed-type processes. To understand these processes, again divide TLC into its component parts as in Figure 1, now shown in Figure 3. An obstructive

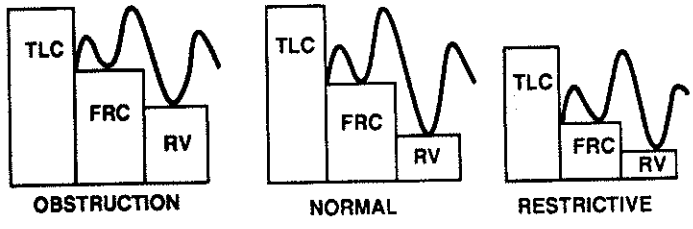

Figure 3. Effect of disease state on components of total lung capacity (TLC). Notice the small residual volume (RV) in restrictive disease and the expanded functional residual capacity (FRC) and RV in obstructive disease.

process limits flow during exhalation as in asthma or cystic fibrosis. The VC is decreased in both obstructive and restrictive disease so the RV is used to help differentiate these processes. The RV is increased due to airway closure with gas trapping in obstructive disease, which results in an increased RV/TLC ratio. Because the rate of flow is slowed, the volume of gas exhaled in the first second is reduced which results in depression of the FEV_1/FVC ratio (less than 0.75). In restrictive disease the FVC, RV, and TLC are all reduced, but the ratio of FEV_1/FVC is normal (greater than 0.75). Thus, the FEV_1/FVC ratio usually allows disease classification without the need to measure lung volumes. Note also from Figure 3 that FRC is decreased in restrictive disease. The configuration of the flow-volume and volume-time curves when taken from a maximal forced expiration can provide valuable information about the disease class when compared with the normal curve (Fig. 4). In obstructive disease, flow decreases rapidly as gas is exhaled, giving a flow-volume curve which is convex towards the volume axis. In restrictive disease, the curve shape is generally normal but smaller than the normal curve because of the reduced vital capacity.

Interpreting spirometric results begins with an assessment of the quality of the study. Criteria for acceptable spirometry in children are offered in Table 2. Examples of inadequate expiratory flow-volume tracings shown in Figure 5 problems are often related to poor patient effort or coughing. The problem can usually be corrected with additional instruction, incentives, or allowing the patient to rest for a moment. To illustrate the problem with inadequate testing, use the example of inadequate patient effort. As noted previously, FVC will be diminished in both obstructive and restrictive disease. In restrictive disease, the FEV_1 also may be low, but the FEV_1/FVC ratio is normal or high, as flow is unimpeded. In obstructive disease, however, flow is reduced because of increased airway resistance resulting in a decreased FEV_1 and FEV_1/FVC ratio. If the patient quits prior to the end of the forced expiratory maneuver, FVC may be underestimated, and the FEV_1/FVC may be falsely normalized, thus leading the examiner to conclude erroneously that the patient has a restrictive rather than obstructive disease.

Forced expiratory flow at 25% to 75% of FVC (FEF_{25-75}) is a more

Table 2. CRITERIA FOR ACCEPTABLE MAXIMAL EXPIRATORY VITAL CAPACITY

Appropriate curve shape: Artifact-free results (no coughing, premature termination, or delayed onset).
Sustained expiration for at least 3 seconds.
At least three forced vital capacities within 10% of the best effort (except in the very young child where the "best" effort may not be reproducible).
Satisfactory effort as observed by the tester.

Adapted from Lemen RJ: Pulmonary function testing in the office, clinic, and home. In Chernick (ed): Disorders of the Respiratory Tract in Children, ed 5. Philadelphia, WB Saunders Co, 1990, pp 147–154.

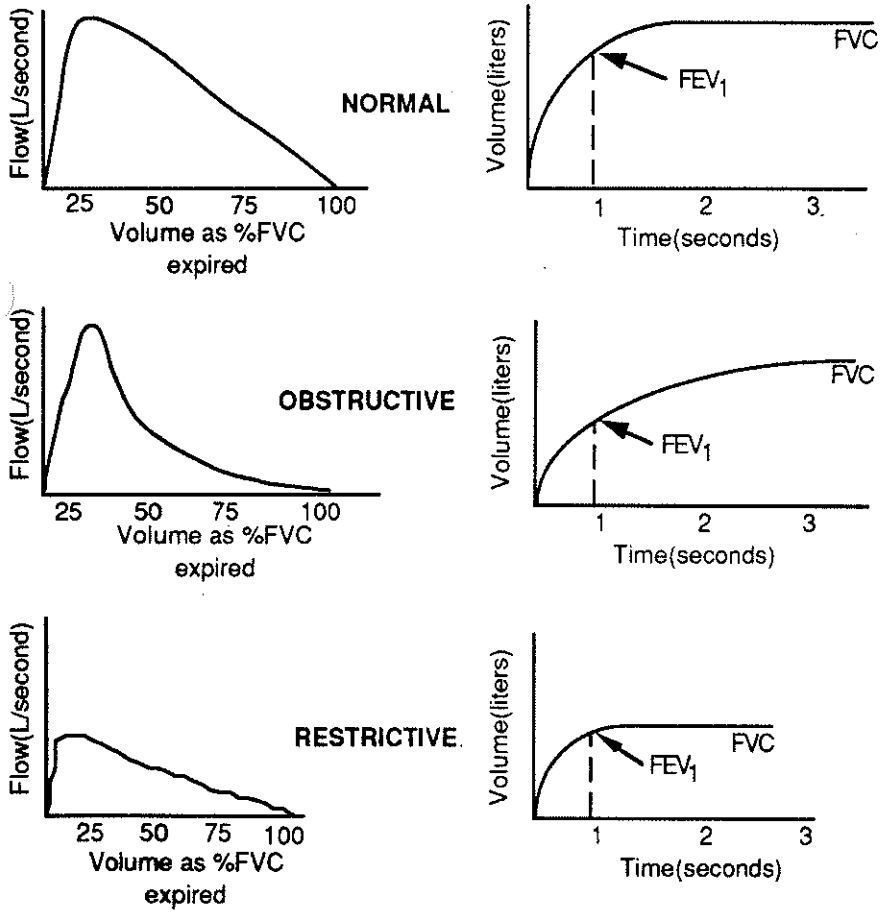

Figure 4. Comparison of flow-volume and volume-time plots in normal versus disease states. Note the usual high ratio of FEV_1/FVC for normals and in restrictive disease. In obstructive disease the FEV_1/FVC ratio is seen to be reduced.

sensitive indicator of mild small airways obstruction than FEV_1. It may, therefore, be a better measure for following disease in children whose other tests are normal. Its disadvantage lies in a wide range of normal, with one standard deviation from the mean (SD) equal to 11.3% to 32.9%.[45] Some caution must be used in interpreting FEF_{25-75} results from patients with moderate to severe obstruction. In this case, an improvement in FVC in response to therapy may be accompanied by a decrease in RV. When this happens, flow over the mid-portion of the flow-volume curve will occur at a lower overall lung volume. The result may be that no change in FEF_{25-75} occurs, or a decrease may be observed, despite the fact that airways obstruction has improved and FVC increased. For the reasons mentioned, it is necessary to interpret measures of small airways' flow, such as FEF_{25-75}, at the same lung volume when repeating tests. When measurements of absolute lung volume are not available, the volume exhaled below TLC is used as an acceptable constant against which small airways' flow can be standardized. Measuring flows at the same lung volume below TLC will also avoid errors introduced by changes in residual volume during bronchial provocation.

ASSESSING THE PATIENT WITH AN ANATOMIC OBSTRUCTION

When an anatomic obstruction is present in the large, central airways, the configuration of the maximal flow-volume plot can help identify the location or type of obstruction.[30] In Figure 6*A* flow is limited in both the inspiratory and expiratory limb of the flow-volume curve. This limitation can occur from a fixed, extrathoracic obstruction such as post-extubation tracheal stenosis, or a fixed intrathoracic obstruction such as a tumor. Figure 6*B* and *C* show variable obstruction. In variable extrathoracic obstruction (Fig. 6*B*), expiration has a near-normal configuration; inspiratory flows, however, are dramatically decreased. In variable intrathoracic obstruction (Fig. 6*C*) the reverse happens. Inspiratory flow is normal, and there is reduced flow with a plateau in the mid-portion of expiration. To quantify variable obstruction in the laboratory, use the ratio of expiratory flow to inspiratory flow at mid-vital capacity ($\dot{V}max_{50\%}/MIF_{50\%}$). In the normal patient, the value is equal to 1. Note that in a variable, extrathoracic obstruction (Fig. 6*B*) the ratio is greater than 1 as $MIF_{50\%}$ is reduced. In variable intrathoracic obstruction (Fig. 6*C*), the ratio is less than 1 as the $\dot{V}max_{50\%}$ is decreased.

ASSESSING THE PATIENT WITH REACTIVE AIRWAYS DISEASE

Spirometry

The most commonly asked question in the pulmonary clinic is whether a child's airways are hyperresponsive. Testing with bronchocon-

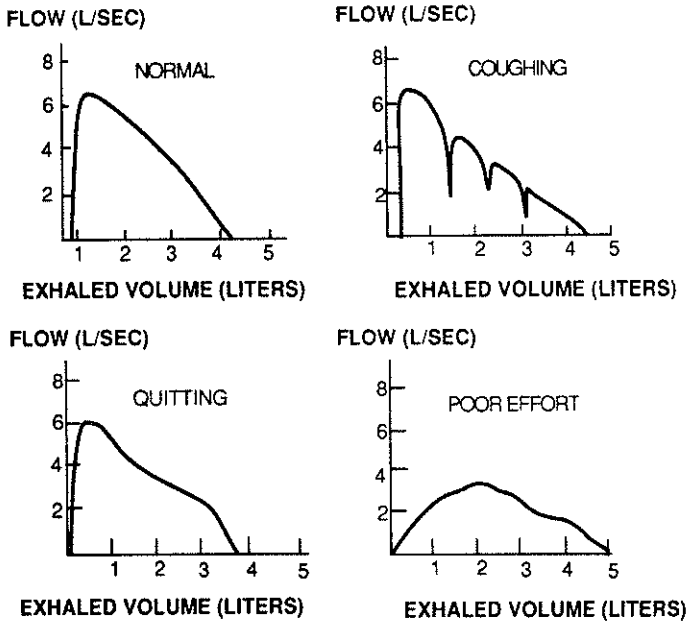

Figure 5. Normal versus inadequate spirometry tracings. The value of pattern recognition cannot be overemphasized in the interpretation of spirometry results.

stricting stimuli, such as histamine, or with bronchodilators can help answer this question. Spirograms provide a way of comparing results both before and after such medication. The normal person responds on average with less than a 5% increase in FEV_1 after isoproterenol is inhaled (Table 3).[4] When patients with a clinical history of asthma demonstrate an increase in FEV_1 greater than 10%, the diagnosis of asthma is

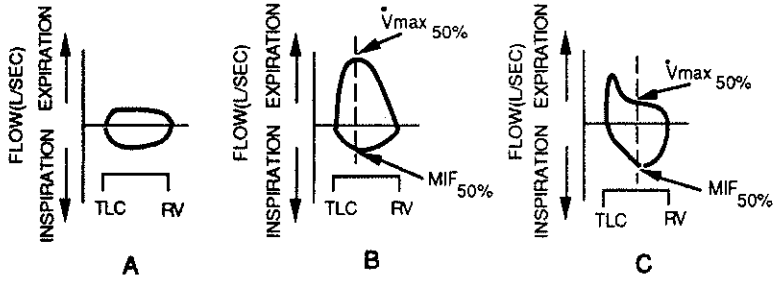

Figure 6. Examples of flow-volume loops in *A*, fixed airway obstruction, *B*, variable, extrathoracic obstruction ($\dot{V}max_{50\%}/MIF_{50\%} > 1$), and *C*, variable, intrathoracic obstruction ($\dot{V}max_{50\%}/MIF_{50\%} < 1$). (*Adapted from* Lemen RJ: Pulmonary function testing in the office, clinic, and home. *In* Chernick (ed): Disorders of the Respiratory Tract in Children, ed 5. Philadelphia, WB Saunders Co, 1990, pp 147–154.)

Table 3. AIRWAY RESPONSE TO ISOPROTERENOL IN NORMALS

FEV_1(L)	+3.6% ($P< 0.001$)
VC(L)	+1.4% (NS)
PEFR(L/sec)	+2.6% (NS)
$\dot{V}_{max}50\%$(L/sec)	+9.0% ($P< 0.001$)
SGaw(L/sec)	+34.7% ($P< 0.001$)

Average response of normal individuals to a bronchodilator challenge (isoproterenol) for forced expiratory volume (FEV_1), vital capacity (VC), peak expiratory flow rate (PEFR), flow maximum at 50% of vital capacity ($\dot{V}_{max}50\%$), and specific airways conductance (SGaw). Probability (P) expressed parenthetically. A nonsignificant (NS) change is designated.

Data from Bouhuys A, van de Woestijine KP: Mechanical consequences of airway smooth muscle relaxation. J Appl Physiol 30:670, 1971.

supported. Restoration of pulmonary function to normal helps to define adequate therapy. Other bronchodilators, such as albuterol and metaproterenol, also are used for airway bronchodilator studies. Provocation of airways obstruction in patients with suspected airways' hyperresponsiveness can be performed by inhalation of methacholine chloride, histamine, or by exercise. Bronchial provocation challenges should be performed in specialized centers with staff experienced in handling the complications of acute airways' obstruction. Equipment for treating bronchoconstriction must be readily available. Exercise provocation can usually be accomplished safely by using a treadmill, a bicycle ergometer, or free running (provided the exercise is quantified). A drop in FEV_1 of 10% or more is taken as a positive test.[26, 37] Measuring other parameters of obstruction, such as peak flow, FVC, or FEF_{25-75} adds to the sensitivity of the test. All positive tests are based on a change from baseline of two intrasubject standard deviations for that test; normals have been compiled for reference.[45] The interpretation of aerosol challenge techniques is substantially more complex and requires specific expertise. Response to drugs with slower responses than methacholine or albuterol, such as cromolyn or steroids, can be assessed longitudinally with serial spirometry, which can often be done in the clinic setting. There are a number of inexpensive machines that are appropriate for office use (reviewed by Enright[12]). Indeed, the primary issue is not equipment but adequate training, dedication of personnel, and the development of an organized quality assurance program.

Peak Expiratory Flow Rate

Peak expiratory flow rate (PEFR) is easily measured and values are reduced in obstructive disease. The variety of durable, inexpensive devices for measuring peak flow rates make it a valuable tool for monitoring airways' disease in the office or home.[29] In the management of

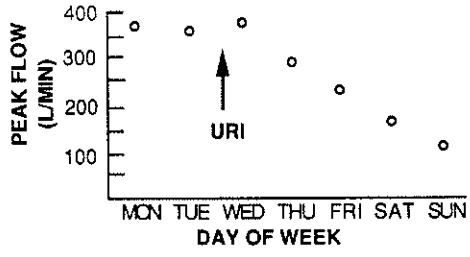

Figure 7. Peak flow diary in an asthmatic child. Note the persistent fall in flows after onset of an upper respiratory tract infection (URI). This may indicate a need for additional therapeutic intervention.

asthma, PEFR can be measured by the patient at home. With proper instruction the results can be used to monitor improvement, intercept early worsening, and measure response to therapy. The peak flow meter is especially useful in managing asthma "attacks" when performing full spirometry could cause worsening of bronchoconstriction. A peak flow diary can offer the clinician a longitudinal record by which to evaluate disease activity or therapeutic efficacy (Fig. 7). Measuring peak flow in the morning and afternoon also can detect increased airway lability. A variation of greater than 20% of baseline may indicate increased reactivity. It must be kept in mind that the PEFR is also a reflection of muscle strength and effort. In obstructive disease, flow transients may produce normal values at high lung volumes. Therefore, normal values do not rule out mild or moderate airways disease. Most peak flow meters for home use provide a chart for comparison of test results against population determined normal values. Useful tables for peak flow values are available from the recently published data of Sanz and colleagues.[46]

Airway Resistance

Measuring airway resistance (R_{aw}) in older children is usually performed using the body plethysmograph.[43] This procedure is limited to specialized laboratories because it requires constant attention to technical detail and the use of expensive equipment. As much as half of the total airway resistance in children may be from the upper airway (pharynx and glottis), so direct measurement of R_{aw} may not clearly represent resistance in the pulmonary airways. For these reasons, the more commonly applied test for assessing airway obstruction in children is the forced expiratory maneuver. Respiratory system resistance (R_{rs}) includes resistance from the airways, lung, and chest wall. It can be measured by applying small pressure changes (forced oscillations) at the mouth during quiet breathing.[48] This technique is applicable in smaller children as it requires little patient cooperation but, again, includes more than just pulmonary airways in the measurement of resistance, and it may be insensitive to small changes. Resistance is usually converted to its recip-

rocal, airway conductance (G_{aw}), because this value is linearly related to lung volume. Conductance can then be normalized for increases in lung volume with growth by dividing it by FRC to calculate the specific conductance (SG_{aw}). Although it may decrease in early infancy, SG_{aw} changes little during childhood in normals.[5]

Considering the complexity of studying airway resistance, one may wonder why it is measured instead of relying on spirometry alone. Airway resistance is measured because spirometry only assesses the combined interaction of lung recoil and airway resistance and cannot distinguish which of these has resulted in a given change in lung function. To do this, either resistance or elastic recoil needs to be measured. In most clinical situations, however, children can be managed without measurement of R_{aw} as decreased flow is rarely due to abnormal elastance.

STANDARDIZING LUNG FUNCTION IN INFANTS AND CHILDREN

Infants and children are in a constant state of change because of growth. There is a problem inherent in testing lung function in these patients as their absolute values change with somatic growth. The task of developing reference values for lung function measures has been undertaken through population studies. Referenced by age, sex, standing height and arm-span,[49] sitting height,[8] and even ethnicity,[39] we have the ability to evaluate a patient's performance against reference values taken from a similar population, which is called *referenced testing*. A patient's performance, when tested against their own past performance, is referred to as *longitudinal testing*. Both are valuable methods of following disease progression and response to therapy, as shown in Figures 7 and 8.

The difficulty of following a large population of patients from infancy into adulthood leaves us dependent on cross-sectional data for most lung function standards. Such studies, however, have established some consistencies in lung function standards between different populations. A good example is the consistent finding of tidal volume per kilogram body weight (TV/kg) in infants of 7 to 9 mL/kg between numerous investigators.[15, 55, 58] When testing Black or Hispanic patients, results must be compared with standards from comparable populations as there are differences between ethnic groups.[22]

In longitudinal testing, a patient's pulmonary function is followed over time, compared with the patient's usual results. The value of this comparison becomes clear when observing a positive response to treatment or confirming progression of disease (see Fig. 8). The authors use

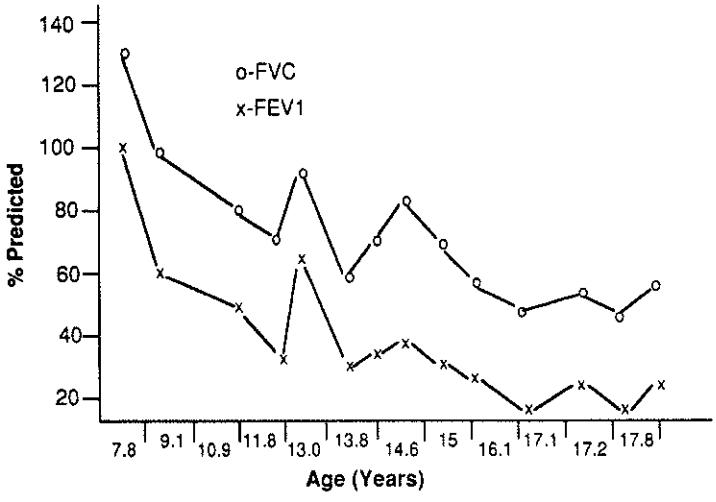

Figure 8. Longitudinal record of spirometry in a male cystic fibrosis patient demonstrating average lung function at age 8 years with a progressive decline through adolescence.

short-term longitudinal testing when performing a provocative challenge for bronchoreactivity. Only by knowing the patient's baseline FEV_1 can a significant drop be appreciated once the airways are exposed to a stimulus (i.e., greater than 10% of baseline FEV_1), although the variability is greater in obstructive disease than in normal subjects.[42]

LUNG FUNCTION IN INFANTS AND SMALL CHILDREN

Many methods have evolved to assess the pulmonary physiology of infants and toddlers who cannot cooperate with sophisticated testing methods. Indeed, no cooperation can be expected of such subjects. Noninvasive methods are of paramount importance to avoid disturbing the physiology being studied and to ensure patient and parent acceptance.

Respiratory System Measurement

The compliance of the lung (C_L) is a measure inversely related to lung "stiffness," and it is expressed as volume divided by pressure:

$$C_L = \Delta V(mL)/\Delta P(cm\ H_2O)$$

When measured during active breathing, it is called dynamic compliance (C_{dyn}). Compliance is decreased in diseases such as respiratory distress syndrome of the newborn (RDS)[6] and bronchopulmonary dysplasia

(BPD).[50] Compliance of the respiratory system as a whole (C_{rs}) also can be measured noninvasively by using a well-fitted mask connected to a water-filled spirometer. After a normal tidal tracing is obtained a weight is added to the spirometer to give a continuous positive airway pressure. The $C_{rs}(\Delta V/\Delta P)$ is calculated by dividing the change in tidal baseline by the pressure generated in the circuit.[57, 60] In the presence of significant obstruction, the pressure applied to the circuit will be less able to distend already hyperinflated lungs, and compliance may be underestimated or may open airways and overestimate compliance. Weighted spirometry can be used in this situation with certain adaptations. By using a series of differing weights, a slope can be derived for changes at different levels of continuous positive airway pressure, thus minimizing the problems in underestimating compliance in patients with airways obstruction.

Pulmonary resistance (R_L) includes both airway resistance and the viscous or tissue resistance of the lung and is expressed as pressure divided by flow:

$$R_L = \Delta P(\text{cm } H_2O)/\Delta V(\text{mL/sec})$$

Resistance is increased in airways obstructive disease such as BPD,[62] bronchiolitis, and asthma. R_L has been used as a means of following response to bronchodilator therapy in infants with asthma or bronchiolitis.[40] Respiratory system resistance also can be measured in infancy using forced oscillation, although such studies have been limited. Airway resistance and specific airway conductance also can be measured in infants using a body plethysmograph.[28] This technique has been used to study airway conductance in both normals and infants with lung disease. Unfortunately, in infants with obstructive lung disease, the assumption that pressure is evenly distributed between the alveoli and the mouth during airway occlusion may not be valid leading to inaccurate estimation of airway resistance.

Respiratory system mechanics also can be measured using the passive deflation technique described by LeSouef and colleagues.[32] The Hering-Breuer reflex can be invoked in infants to relax the respiratory muscles if an airway occlusive pressure is applied at end inspiration. This passive deflation technique, referred to as the single breath occlusion technique (SBT), uses a face mask and a pneumotachygraph. A simple slide valve in the circuit is used to occlude the airway and pressure is measured at the mouth. The volume exhaled is related to pressure at end-inspiration to give the static compliance of the respiratory system(C_{rs}). The slope of the flow-volume curve relates inversely to the resistance $\times$ compliance and allows calculation of resistance. The SBT is noninvasive and has been used to measure respiratory mechanics in normal infants as well as the intubated and paralyzed child.[7, 32] A variation of this technique using multiple occlusions (MOT) has been developed and has been shown to have equal utility in determining C_{rs} in

healthy preterm infants, provided complete relaxation occurs with no expiratory braking.[10, 13]

The ability to measure compliance and resistance in the lung of infants has added to the understanding of the natural history of diseases that afflict them. In critical care and neonatal medicine, the study of pulmonary mechanics has aided in the development of treatment methods by providing an objective way of assessing outcome. The measurement of pulmonary mechanics requires the relation of the pressures generated during breathing to the flows and volumes achieved. By placing a water-filled catheter tip or soft rubber balloon in the lower third of the esophagus, intrathoracic pressure changes can be measured.[40] The transpulmonary pressure (P_L) can then be obtained by referencing the esophageal pressure to the pressure measured at the mouth. Flow is measured with a pneumotachygraph connected to a face mask or an endotracheal tube, and volume is calculated by integrating the flow signal. At any given point in the respiratory cycle, the following is true.

$$P_L = \text{flow} \times \text{resistance} + \text{volume/compliance}$$

By measuring a series of reproducible breaths, the resistance and dynamic compliance of the lung (R_L and C_L) can be calculated for both inspiration and expiration using either a graphic technique[38, 44] or a least squares regression calculated by a computer.[3] The use of an esophageal catheter or balloon has some limitations. The most important one is that the pressure in the esophagus may not represent global pleural pressure when there is chest wall distortion.[33] Further, it is critical to ensure that the balloon is placed appropriately and inflated to an ideal working pressure. To ensure pressure is accurately measured, the changes in intraesophageal catheter pressure and mouth pressure must be within 5% of each other when there is no flow. These can be measured simultaneously with output from the pneumotachygraph displayed on an oscilloscope or computer monitor[19] during occlusion of the airway for a few seconds to prevent flow. Mouth pressure should be approximately equal to alveolar pressure under these conditions.

Volume Measurements

Whole body plethysmography has been used to determine thoracic gas volume (TGV) since 1956 when first described in adults by DuBois and colleagues.[11] With the infant's body in a sealed box and breathing through a shutter which is closed at a predetermined point in the respiratory cycle, change in alveolar pressure can be measured at the mouthpiece and related to the simultaneous change in the volume of gas in the lungs. From these data a measurement of TGV can be made. There are some problems with this technique as the accurate calculation of TGV is

variable at different phases of the respiratory cycle. As the infant expires dynamic collapse of the airways may occur, especially in patients with obstructive disease.[40] In this setting the TGV will be overestimated because mouth pressure does not equal alveolus pressure when the airway is occluded. Lanteri et al[28] found that by measuring TGV at end-inspiration (TGV_{ei}) rather than at end-expiration (TGV_{ee}) the measurements were more accurate. As noted above, one advantage of body plethysmography is that airway conductance can be measured simultaneously with TGV and corrected by TGV to calculate the specific conductance.[51]

Another way of measuring functional residual capacity (FRC) is by gas dilution. One gas dilution method involves breathing a known concentration of helium from a reservoir. Once a new equilibrium for helium concentration is reached, FRC is calculated as the additional volume into which the helium has diffused. To compensate for oxygen consumption during the 1.5 to 2 minutes of equilibration, oxygen must be added to the circuit during the test. A carbon dioxide absorber prevents carbon dioxide (CO_2) from accumulating. Helium dilution has been used in normal infants[58] and infants with lung disease.[6, 59] The helium dilution method tends to underestimate lung volumes in infants with airways' obstruction due to slow equilibration of helium with areas of gas trapping.

Partial Expiratory Flow-Volume Measures

Small children will not inspire voluntarily to TLC and therefore they must have flows tested by other means than the maximal forced expiratory flow method. Over a quarter of a century elapsed between the first report of flow rates from maximal expiratory flow-volume plots by Dayman[9] and the description of partial expiratory flow-volume loops for young children by Taussig[54] in 1977. From partial expiratory flow-volume (PEFV) curves produced by a forced exhalation, flow can be measured at functional residual capacity to obtain the $\dot{V}_{max}FRC$, which is a maximal flow at a relatively low lung volume (FRC is approximately 40% of TLC). Taussig[54] demonstrated that these flows could be obtained reliably in young children and he showed that males have lower specific or volume corrected flows than females. In 1978 Adler and Wohl[1] expanded the application of partial expiratory flow-volume loops and used rapid thoracic compression to generate PEFV curves in infants. By this method, they were able to demonstrate forced flows that were higher than those obtained during tidal expiration. Partial expiratory flow-volume curves have now been applied to the study of the smallest of infants to determine normal lung growth and development, effects of disease on early lung function, and airway responsiveness.[41] To understand how this is possible let us first look at the partial flow-volume plot (Fig. 9).

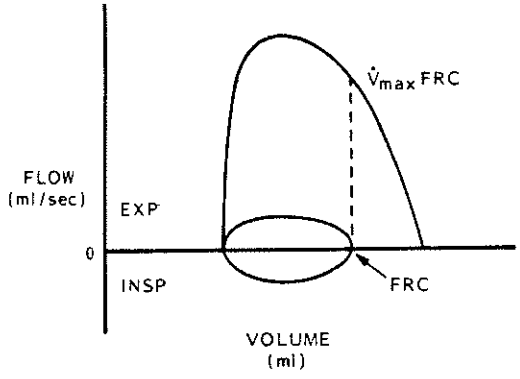

Figure 9. Normal partial expiratory flow volume loop showing $\dot{V}_{max}$FRC. (*From* Tepper RS, Morgan WJ, Cota K, et al: Physiologic growth and development of the lung during the first year of life. Am Rev Respir Dis 134:513–519, 1986; with permission.)

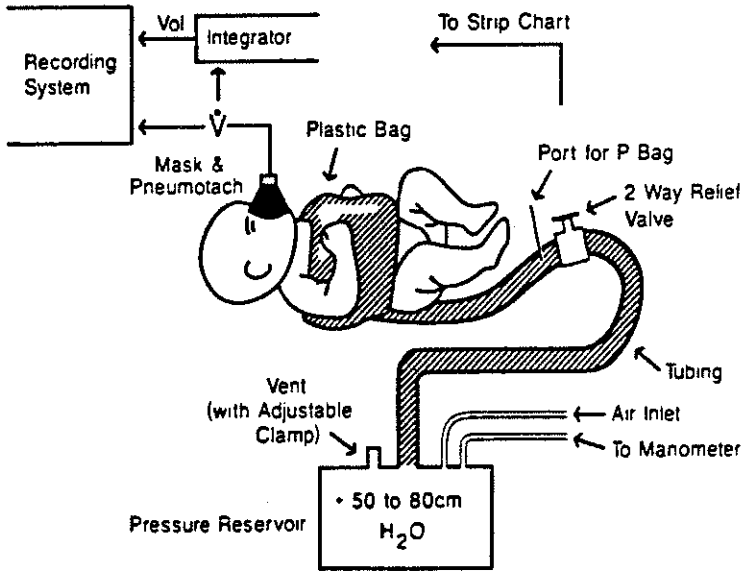

Figure 10. Schematic diagram of the rapid thoracoabdominal compression apparatus used to produce PEFV curves in infants. The compressive cuff (plastic bag) should encircle the infant's trunk from the axillae to the anterior superior iliac spines. (*From* Morgan WJ, Geller DE, Tepper RS, et al: Partial expiratory flow-volume curves in infants and young children. Pediatr Pulmonol 5:232–243, 1988; with permission, copyright © 1988 Wiley-Liss, A Division John Wiley and Sons, Inc.)

From this we see that flow can be measured on the forced expiratory curve at functional residual capacity (FRC). In the young child, aged 3 to 5 years, this can be done with a nose clip and mouthpiece attached to a pneumotachygraph. In the infant this technique has been modified by Taussig et al[52] and Tepper et al[58] to include a face mask with a pneumotachometer and by rapidly applying a positive pressure over the infant's chest and abdomen using an inflatable bag[16] (Fig. 10). First, the infant is allowed to breathe at rest until a reproducible tidal flow-volume loop is established. Testing is performed in the supine position 15 to 20 minutes after falling asleep either spontaneously or after 50 to 75 mg/kg of orally administered chloral hydrate. The bag encircles the infant and an initial positive pressure of 30 to 40 cm H_2O is applied to the bag from a reservoir at end inspiration to give a forced exhalation. By using a small bag which encircles only the chest and abdomen a rapid response time is obtained (<100 ms).[58] Using a reservoir which is at least ten times the bag volume ensures that a relatively constant pressure is applied throughout the maneuver.[41] This method is now referred to as the rapid thoracoabdominal compression technique (RTC).

To obtain the maximal flow at functional residual capacity ($\dot{V}_{max}$FRC) during RTC it is necessary to perform repeated tests at increasing reservoir pressure, usually from 20 to 80 cm H_2O, until the maximal flow is reported. Using too much pressure has been found to give submaximal flows in some infants, probably due to dynamic airway compression. The value reported as $\dot{V}_{max}$FRC is the best obtained, rather than the average of all flows. The mean intrasubject coefficient of variation (COV), when taken from the three highest measures of flow at FRC ($\dot{V}$FRC) during a single testing session, has been found to be 11 ± 7%.[58] The amount of intersubject COV in $\dot{V}_{max}$FRC in the first year of life is 37%, a value similar to that obtained in older children and adults for flows at low lung volumes.[41] To allow for effects of patient size on flow at FRC the results can be standardized by referencing again to FRC ($\dot{V}_{max}$FRC/FRC). FRC can be determined from the helium dilution technique described previously.

To understand the clinical utility of partial expiratory flow-volume curves (PEFV) by the rapid compression technique, a relatively new method of lung function testing in infancy and young children, let us review some of the work done so far in infants and add to this the work done using partial flow-volume curves. Younger infants (newborns and prematures) have the highest size-corrected flows in infancy.[58] This suggests that airway size may be larger relative to lung size in the very young. Infant females have higher size-corrected flows than similar sized male infants.[58] This is an interesting finding since males tend to have more severe wheezing illness than females. In infants older than 2 months, $\dot{V}_{max}$FRC/FRC has been found to be fairly constant for the first 12 months of life supporting the concept of isotropic lung growth.[36]

Longitudinal testing has given strong support to the concept that infants with low $\dot{V}_{max}$FRC values as newborns may actually be the group at highest risk for having subsequent wheezing illnesses in the first years of life.[34, 35] While newborns with cystic fibrosis have normal lungs at birth, cystic fibrosis infants requiring hospitalization for pulmonary problems have persistently lower flows than do controls and show improved flow with in-patient therapy.[20] Infants with bronchopulmonary dysplasia have been shown to have lower $\dot{V}_{max}$FRC versus body length than controls and no evidence of catch-up growth with respect to flows compared to normal infants.[59] Infants with BPD respond to both theophylline and diuretics with increased $\dot{V}_{max}$FRC.[25] Infants having pertussis were found to have decreased $\dot{V}_{max}$FRC, FRC, and compliance of the respiratory system (C_{rs}) but showed recovery to normal within 5 months.[21] The noted recovery of pulmonary function supports the findings of Johnston et al[24] who reported normal pulmonary function in school-aged children who had had pertussis. Thus, PEFV curves in infancy have allowed the study of both normal growth in lung function and alterations with disease.

Evaluating infants for bronchial responsiveness using the partial expiratory flow volume (PEFV) maneuver has revealed some interesting, if controversial, findings. A large percentage of cystic fibrosis infants were found to have a greater than 30% increase in $\dot{V}_{max}$FRC/FRC after bronchodilator.[20] A curious finding in infants with bronchiolitis has been a drop in $\dot{V}_{max}$FRC in response to a bronchodilator (albuterol),[23] which may be due to a decrease in bronchomotor tone after bronchodilator treatment and a resultant tendency to dynamic airway collapse. Recovered "wheezy bronchitis" infants also were found to respond with decreased $\dot{V}_{max}$FRC in response to histamine. Infants have been identified by PEFV maneuvers to respond with bronchoconstriction to both methacholine, a β-agonist, and cold air challenge.[16, 56] Unfortunately, the meaning of this response is unclear because it is effectively impossible to compare bronchial challenge doses in infants with those used in older children and adults.[31]

Although the applicability of the PEFV maneuver offers great potential in evaluating infant pulmonary function, several problems need to be addressed. Only two centers have published standards for $\dot{V}_{max}$FRC by the RTC technique, and some of their data conflict in later infancy.[17, 58] Infants have been observed to make a reflex inspiratory effort in response to chest compression which may prevent adequate measurement of $\dot{V}_{max}$FRC. This inspiratory effort may prevent flow limitation from being reached. Reflex glottic closure has been observed in lambs undergoing chest compression[18] and has been suggested to occur in infants. Care also must be taken to prevent upper airway narrowing by improper head positioning or nasal compression. End-expiratory volume may be dy-

namically maintained and vary with alterations in lung function. It remains to be established what the best criteria will be for determining a reliable study. The most challenging problem of all is that PEFV maneuvers in healthy infants may not achieve flow limitation. Although some have suggested that flow limitation is achieved, no investigator has convincingly demonstrated that true effort independence is achieved.[7,41]

It seems likely that rapid thoracoabdominal compression to obtain partial expiratory flow-volume curves will have a valuable place in evaluating infant pulmonary function once the previously mentioned concerns are solved. Its application gives the ability to assess airway reactivity and track the progression of lung growth and development through infancy and into childhood. Its role in evaluating the relationship between initial lung function and lower respiratory tract illness in the development of subsequent chronic lung disease may be no less important.

CONCLUSION

Measures of lung function will continue to be valuable tools by which the pediatric pulmonary patient can be assessed. Currently, there are multiple methods of lung function testing that can be used and some have been surveyed in this article. In all cases, it is critical that attention be given to obtaining accurate and reliable results, which means attention to detail and careful interpretation of the results in light of the phenomenon being measured and the limitations of the method being used. Tests should be chosen to be age appropriate and as noninvasive as possible. Adequate standards for test performance and reference norms need to be developed for many new techniques such as PEFV measurement in infancy. The clinical use of some of these methods is still being defined, and continued development in this field promises to further elucidate the understanding of normal lung growth and development and their alteration by disease.

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