PULMONARY FUNCTION TESTING ESSENTIALS

Michael Grippi

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Abbreviation list

~	approximately
Δ	change in...
η	Eta
≠	not equal to
π	Pi
α	represents quantities such as angles—Fick's law
A	area—Fick's law
ABG	arterial blood pH and gas tension
Cdyn	dynamic compliance
cmH_2O	centimeters of water
CO	carbon monoxide
COPD	chronic obstructive pulmonary disease
CO_2	carbon dioxide
CPET	cardiopulmonary exercise test
C_{st}	static compliance
D_L	diffusing capacity
D_LCO	lung CO-diffusing capacity
ERV	expiratory reserve volume
f	respiratory frequency
F_ACO_2	fractional volume of alveolar carbon dioxide
F_EHe	fractional concentration of helium expired
F_EN_2	fractional concentration of nitrogen expired
F_ECO_2	fractional concentration of carbon dioxide in expired gas
F_EO_2	fractional concentration of oxygen expired
FEV_1	forced expiratory volume in 1 s
F_ICO	fractional concentration of carbon monoxide inspired

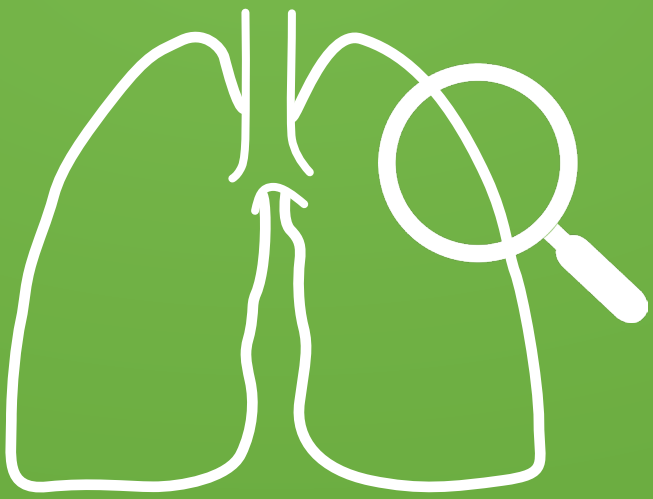
F_IHe	fractional concentration of helium inspired
F_IN_2	fractional concentration of nitrogen inspired
F_IO_2	fractional concentration of oxygen inspired
FIVC	forced inspiratory vital capacity
FVC	forced vital capacity
FRC	functional residual capacity (aka resting lung volume)
GOLD	Global Initiative for Obstructive Lung Disease
HAST	high altitude simulation test
He	helium
HIT	hypoxia inhalation test
IC	inspiratory capacity
ILD	interstitial lung disease
IRV	inspiratory reserve volume
l	length
k	constant—Boyle's law
LLN	lower limit of normal
mEq	milliequivalent
mmHg	millimeter of mercury
MVV	maximal voluntary ventilation
MW	molecular weight—Fick's law
NHANES	National Health and Nutrition Examination Survey
NO	nitric oxide
N_2	nitrogen
O_2	oxygen
P	pressure—Boyle's law
ΔP	pressure difference driving airflow
P_1, P_2	pressure gradient across alveolar-capillary membrane —Fick's law

P_A	alveolar pressure
P_A	partial pressure of a gas component—Dalton's law (aka P_1)
P_ACO	alveolar partial pressure of carbon monoxide
P_ACO_2	alveolar partial pressure of carbon dioxide
P_aCO_2	arterial partial pressure of carbon dioxide
P_aO_2	arterial partial pressure of oxygen
P_{alv}	alveolar pressure
P_B	partial pressure of a gas component—Dalton's law (aka P_2)
$P_{barometric}$	total air pressure
P_{bs}	body surface pressure
Pbx	box pressure
P_C	partial pressure of a gas component—Dalton's law (aka P_3)
P_C	driving pressure of gas across capillary membrane
P_CO_2	partial pressure of oxygen in capillary blood
P_CCO	partial pressure of carbon monoxide in pulmonary capillaries
PD20	provocative dose 20
P_ECO_2	expired partial pressure of carbon dioxide
PEmax	peak or maximal expiratory pressure
PImax	peak or maximal inspiratory pressure
P_L	transpulmonary pressure
PO_2	partial pressure of oxygen
Pm	mouth pressure
P_{pl}	pleural pressure, or intrapleural pressure
$P_{rs, dyn}$	distending pressure driving gas down airways during inflation
$P_{rs, st}$	distending pressure maintaining lung inflation
P_{total}	total pressure—Dalton's law
Ptp	transpulmonary pressure
Q	flow rate
r	radius

R	respiratory exchange ratio
Raw	resistance of the airway or airway resistance
Rw	resistance of chest wall
RQ	respiratory quotient
Rrs	respiratory system resistance
rs	respiratory system
Rti	tissue resistance
RV	residual volume
Sol	solubility—Fick's law
SpO_2	oxygen saturation levels
SVC	superior vena cava
T	thickness—Fick's law
TLC	total lung capacity
TV	tidal volume
V	volume—Boyle's law
$\dot{V}$	flow or ventilation
ΔV	volume difference driving airflow
V_A	alveolar ventilation / space
VC	vital capacity
$\dot{V}CO$	carbon monoxide production per unit of time
$\dot{V}CO_2$	carbon dioxide production per unit of time
V_D	dead space
$\dot{V}_E$	minute ventilation
$\dot{V}_{gas}$	flow of gas—Fick's law
$\dot{V}_I$	volume of gas inspired
$V_{iso}\dot{V}$	volume at which flow rates become identical (aka iso-flow or Iso)
$\Delta\dot{V}_{max}$	maximal expiratory flow
$\dot{V}O_2$	Oxygen uptake or consumption
V_T	tidal volume

Chapter 1

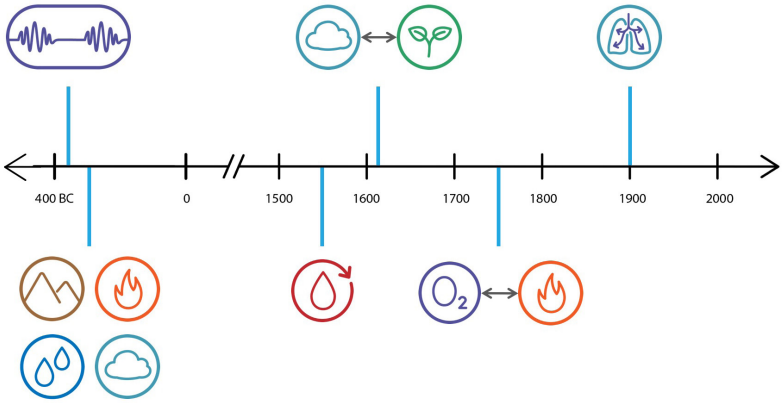
THE BACKGROUND



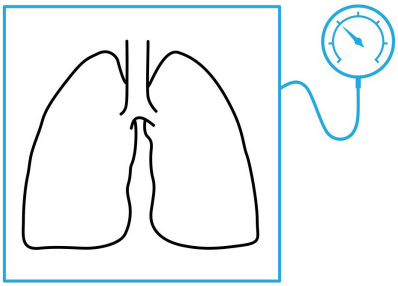
1.1 REVIEWING KEY HISTORICAL MILESTONES

Respiratory physiology and clinical assessment of lung function have evolved over 2000 years.

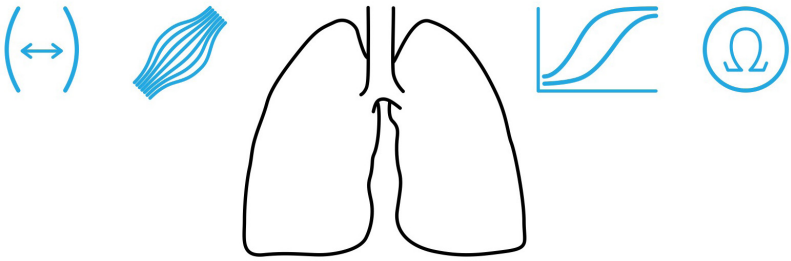
- Progress was slow until the 16th and early 17th centuries, when William Harvey described the circulation of blood, and the *Oxford physiologists*, including Robert Boyle, described the necessity of air for life.
- In the 18th Century, Joseph Priestley discovered oxygen.



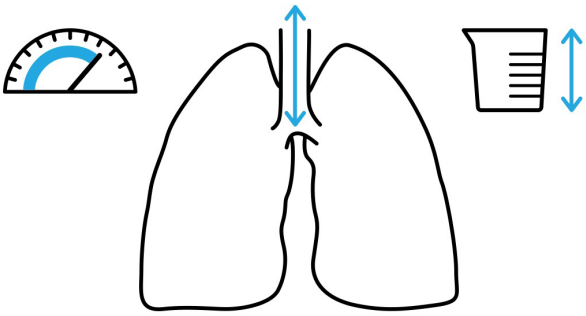
- In the early 20th century, the Kroghs described diffusion of oxygen.
- In the mid-20th century, body plethysmography, a method by which lung volumes can be measured by assessing changes in pressure in a closed system and applying Boyle's Law, was developed.



- In the 20th century, the study of lung mechanics, including the elastic properties of the lung and chest wall, the role of the respiratory muscles, and analysis of pressure-volume curves became central to understanding respiratory physiology and function. Additionally, measurement of airway resistance became part of routine pulmonary function testing.

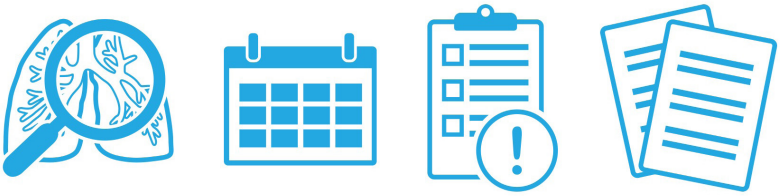


- Use of the Fleisch pneumotachograph to measure airflow in the mid-1950's constituted an additional critical development.



1.2 IDENTIFYING INDICATIONS FOR PULMONARY FUNCTION TESTING

In general, broad indications for pulmonary function testing include



- Evaluating suspected or known underlying lung disease.
- Monitoring the course of lung disease or its response to treatment.
- Performing preoperative risk assessment, including preoperative assessment of those undergoing lung resection.
- Performing epidemiologic and clinical research studies.

- Elucidating respiratory symptoms.
- Clarifying signs of potential pulmonary disease, including auscultatory findings in the chest or thoracic cage deformities (e.g., kyphoscoliosis).

- Explaining laboratory abnormalities, e.g., low P_aO_2 or oxygen saturation, elevated P_aCO_2, or an unexplained elevation in hemoglobin.
- Screening for lung disease in smokers, in those with workplace-related exposures, or in patients undergoing drug trials.

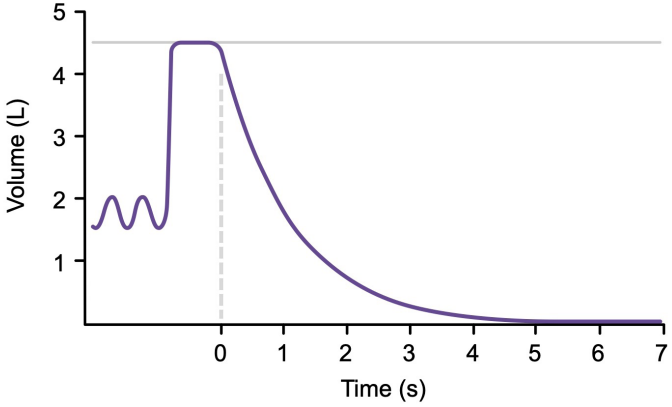
- Assessing the response to therapy, including bronchodilators, corticosteroids, or therapy for a variety of interstitial lung diseases.
- Following the pulmonary response to treatment of an underlying neuromuscular disease affecting the thorax, including the diaphragm.
- Assessing the impact of occupational exposures.

1.3 RECOGNIZING PULMONARY FUNCTION TEST CATEGORIES

Pulmonary function testing can be broadly categorized as consisting of spirometry, lung volume measurements, determination of diffusing capacity, and other *specialized* tests. While spirometry can be performed using small, portable devices in physician's offices, the other tests require more specialized equipment and technical expertise.

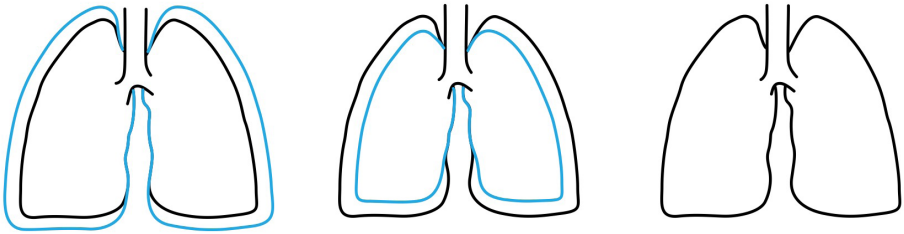
Spirometry

The cornerstone of pulmonary function testing is spirometry, a test which measures the change in lung volume over time during maximal inspiration or expiration. A maximal expiratory effort from the maximal achievable lung volume, total lung capacity or TLC, defines the expiratory vital capacity, while a maximal inspiratory effort from the minimal achievable lung volume, residual volume or RV, defines the inspiratory vital capacity. These maneuvers can be done slowly or with maximal speed, constituting so-called slow and forced vital capacity maneuvers, respectively.



Lung volumes

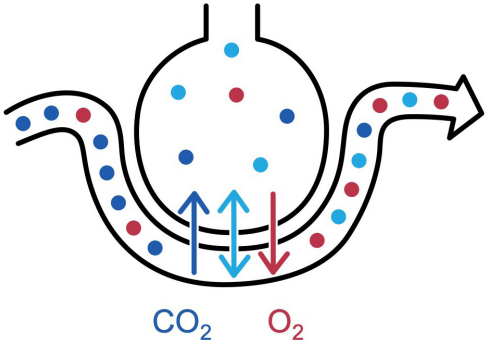
Lung volumes, including TLC, RV, and functional residual capacity or FRC, are measured using body plethysmography or helium dilution methods. Measurement of lung volumes is complementary to spirometry in the assessment of lung function.



TLC RV FRC

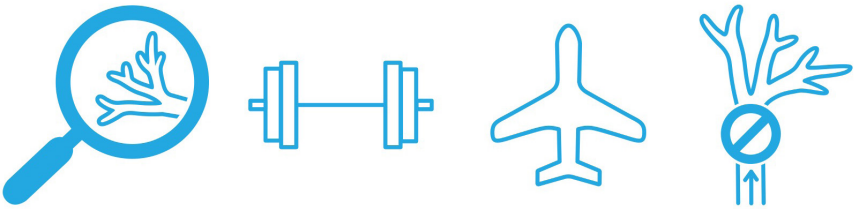
Diffusing capacity

Evaluation of the lung's gas transfer function by measurement of diffusing capacity is based upon determination of the efficiency of a test gas's movement across the alveolar-capillary membrane. Diffusing capacity is a very sensitive, albeit nonspecific, measurement of the underlying pathophysiologic effects of a wide variety of diseases on the lung.



Specialized tests

A multitude of pulmonary function tests can be considered more specialized in nature. These include tests to assess small airways function, tests to evaluate the respiratory response to exercise, and tests to predict changes in arterial oxygen levels during commercial air flight. Additionally, airway response to inhaled agents can be used to determine bronchial reactivity in assessing symptoms of unclear etiology or in suspected asthma.



Further reading

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Krogh, M. 1915. The diffusion of gases through the lungs of man. *J Physiol.* **49**: 271–300. https://www.ncbi.nlm.nih.gov/pubmed/16993296

Chapter 2

THE BASIC TECHNIQUES

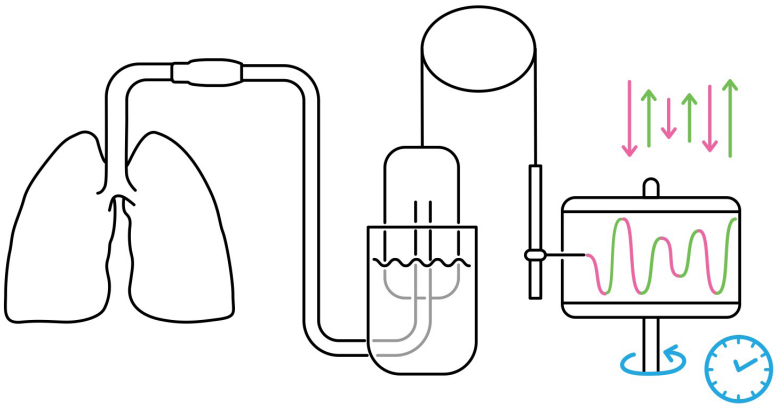
2.1 APPRECIATING TESTING INGENUITY

Spirometers

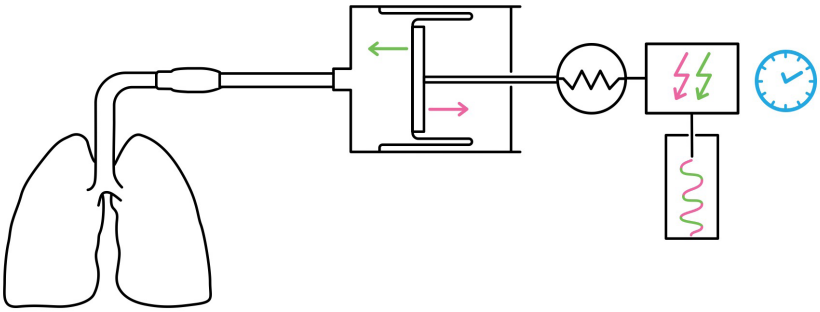
Measurement of airflow in and out of the lungs is made using a spirometer. Traditional spirometers include water-sealed and dry rolling-sealed varieties. Pneumotachographs electronically detect air flow rates.

The basis for operation of a water-sealed spirometer is the interface between the spirometer bell and a rotating drum that incorporates calibrated paper to measure flow versus time.

The rolling-sealed spirometer makes use of a piston which moves with inspiration and expiration, creating a voltage signal which is proportional to inhaled or exhaled volume.



Water-sealed spirometer

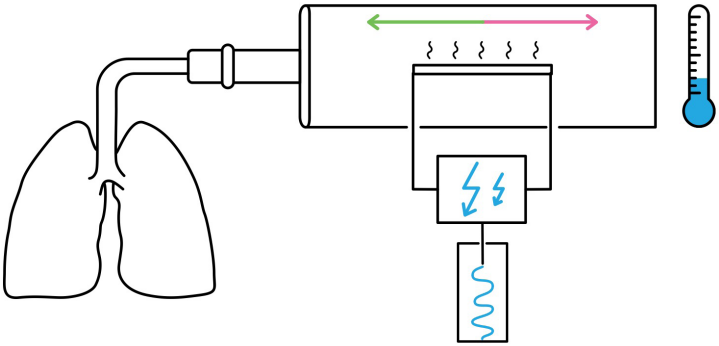


Dry rolling-seal spirometer

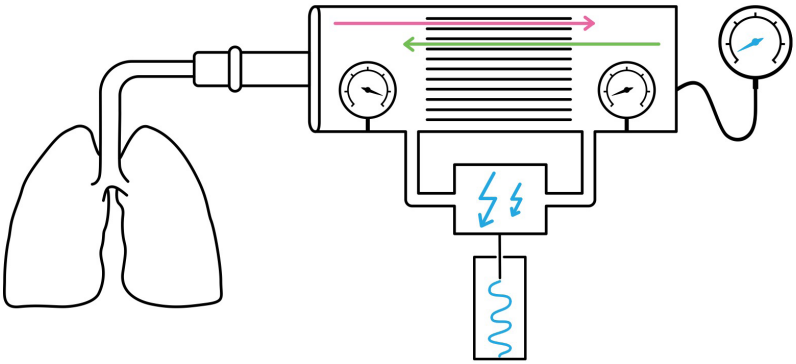
Pneumotachographs

Pneumotachographs, include hot wire and flow-resistive types. The former incorporates a hot wire, which is cooled during airflow; the change in temperature is proportional to the rate of airflow. In the flow-resistive type, a pressure gradient is created across a resistive element within the spirometer; the magnitude of the pressure drop across the element creates an electronic signal proportional to flow.

With either type of pneumotachograph, the electronic signal generated provides a measure of the flow rate, which, if integrated over time, provides a measurement of inhaled or exhaled volume.



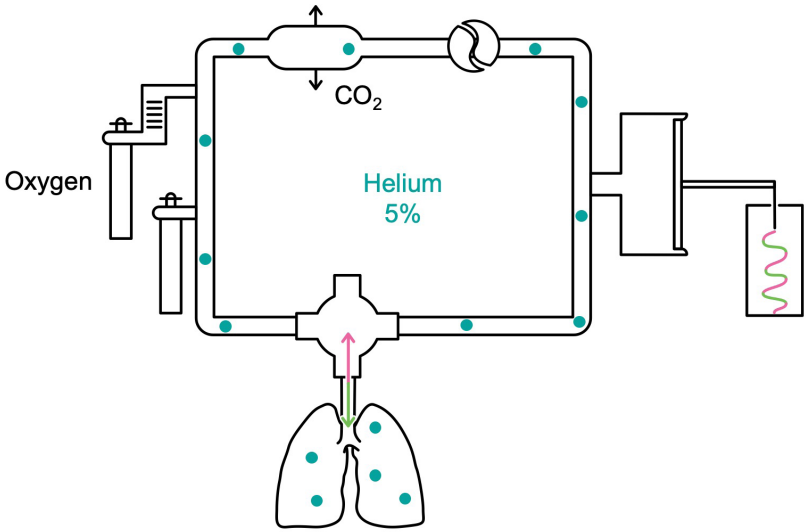
Hot wire pneumotachograph



Flow-resistive pneumotachograph

2.2 HELIUM DILUTION TECHNIQUE

Resting lung volume can be measured using gas dilution techniques, the most common of which is helium dilution.

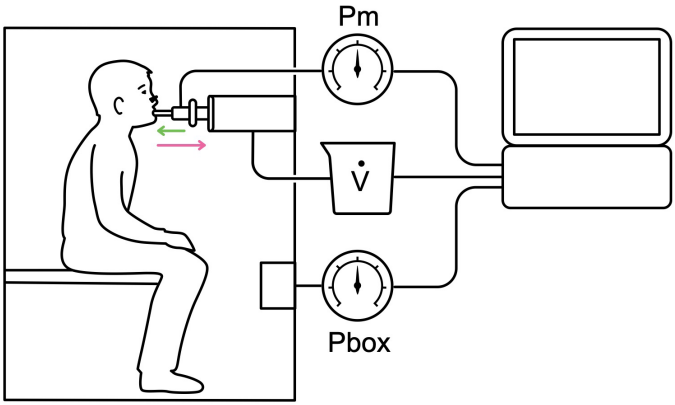


During testing, the seated patient breathes in a circuit containing an initial concentration of helium. After sufficient time for full equilibration of gas, contained within the subject's lungs and that within the circuit, the magnitude of the dilution of the helium provides a measure of the incremental volume added to the circuit (i.e., the patient's resting lung volume).

2.3 USING BODY PLETHYSMOGRAPHY

Plethymography

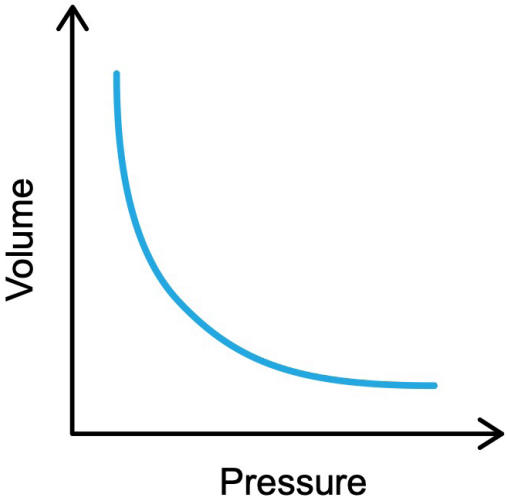
Lung volumes may also be measured using plethysmography, which is based on measurement of changes in pressure in a closed system (the plethysmograph or *body box*) as a reflection of enlargement of the subject's thorax with inspiration. The underlying basis for translating the change in pressure to the change in volume is Boyle's Law.



Boyle's law

According to Boyle's Law, within a contained system, the volume of a gas and its pressure are inversely related. When a patient, seated in the body box, inspires, the lungs enlarge, increasing the pressure in the box. Conversely, when the patient exhales, air surrounding the chest within

the box is rarefied, reducing box pressure. By calibrating the change in pressure and change in volume with inspiratory and expiratory maneuvers, the resting volume of the lungs can be calculated.

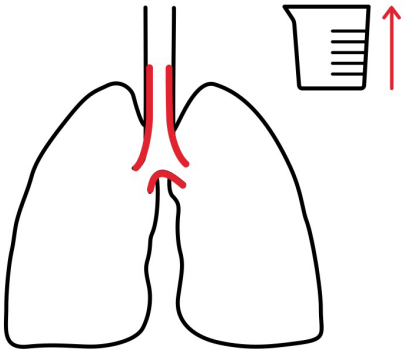


Boyle's law

2.4 APPRECIATING DIFFERENCES BETWEEN VARIOUS METHODS

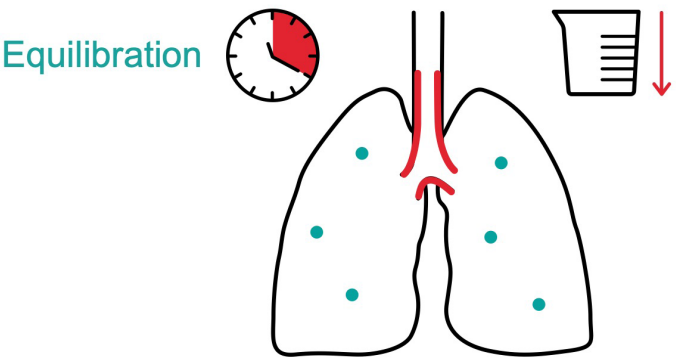
Body Plethysmography

In the setting of obstructive lung disease, the body box technique may provide an artificially elevated measurement of functional residual capacity. This is due to incomplete equilibration between the pressure measured at the mouth and that in the alveoli, as airways obstruction leads to mouth pressure underestimating alveolar pressure. This, in turn, translates into underestimation of the change in alveolar pressure with breathing and an increase in the lung volume measured.



Body Plethysmography

With the helium dilution technique, poorly ventilated areas of the lung, as seen, for example, in obstructive airways disease, limits full equilibration of the helium throughout the lungs and breathing circuit, resulting in underestimation of lung volume relative to body box measurements.



Helium dilution

Further reading

Grippi, MA, Elias, JA, Fishman, JA, et al. 2015. *Pulmonary Diseases and Disorders*. 5th edition. New York: McGraw-Hill. (Grippi, Tino 2015, 502–536)

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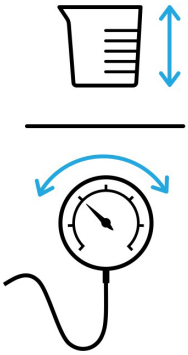
Chapter 3

EVALUATING THE LUNGS AT REST

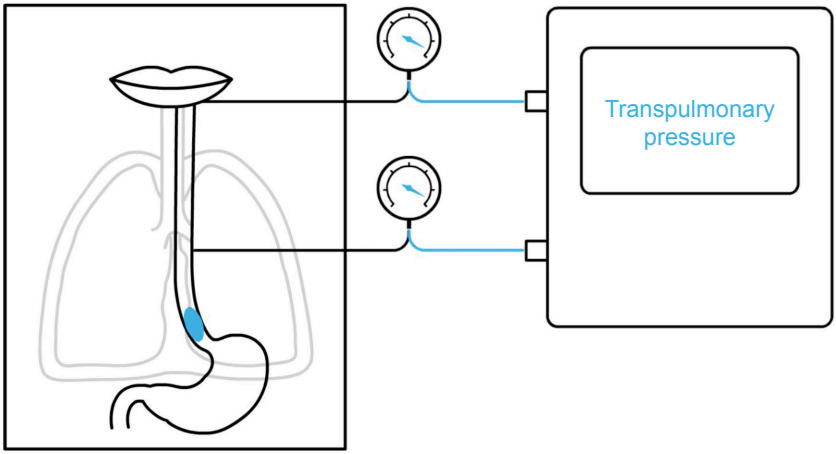
3.1 MEASURING RESPIRATORY SYSTEM COMPLIANCE

The lungs and chest wall are elastic structures. Their degree of elasticity or distensibility provides insight into their functional status. A physiologically and clinically useful term reflecting lung and chest wall distensibility is compliance, defined as the change in lung or thoracic volume relative to the change in recoil force or distending pressure.

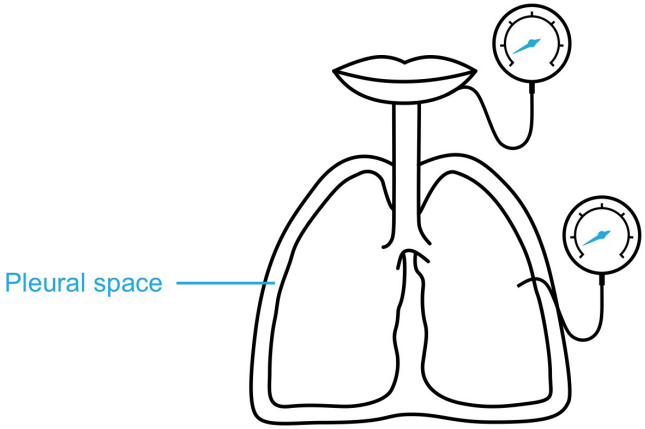


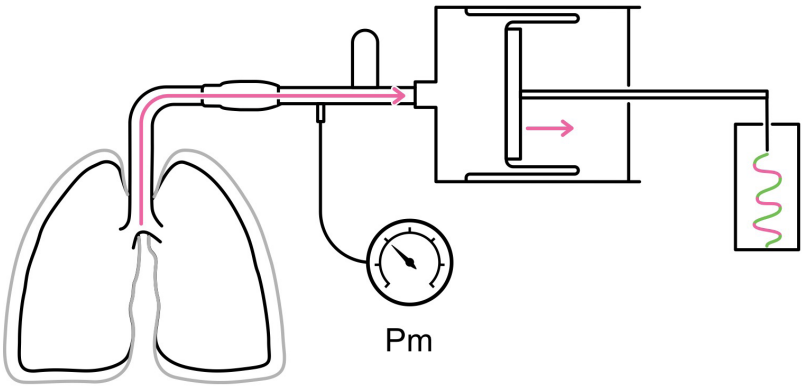
Lung compliance

If the distending pressure across the lung is measured (as opposed to the pressure across the chest wall or intact respiratory system), then the change in lung volume relative to the change in pressure, known as transpulmonary pressure (i.e., pressure across the lung) reflects lung compliance.



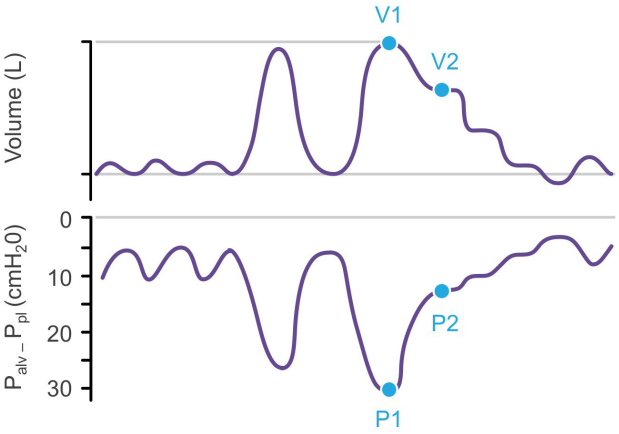
On the other hand, if the pressure across the entire thorax is measured, that is, across both the lung and the chest wall, the compliance determined is the compliance of the intact respiratory system.

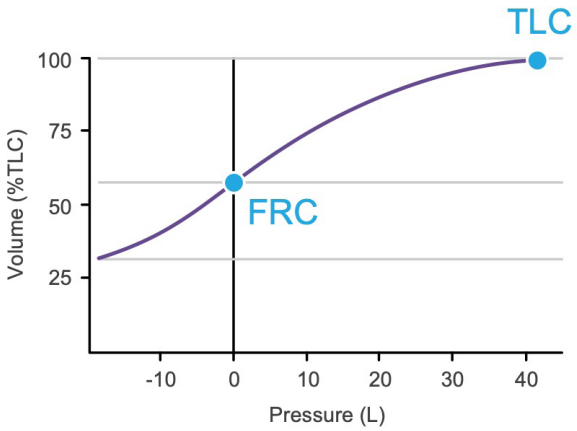


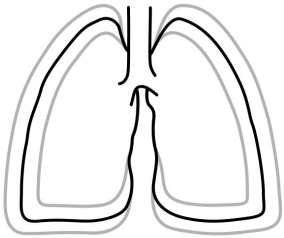


Relaxation technique

Measurement of compliance of the intact respiratory system is based on the so-called relaxation technique. The subject breathes through a spirometer, which incorporates a shutter in the system, enabling periodic occlusion of the patient's expiratory effort. When the subject breathes to maximal lung capacity (i.e., TLC) and then relaxes the inspiratory muscles, to allow passive exhalation, intermittent closure of the valve momentarily eliminates flow and allows measurement of pressure in the alveoli relative to atmosphere, as well as measurement of the exhaled volume. Consequently, the change in volume relative to the change in pressure reflects compliance of the intact respiratory system.

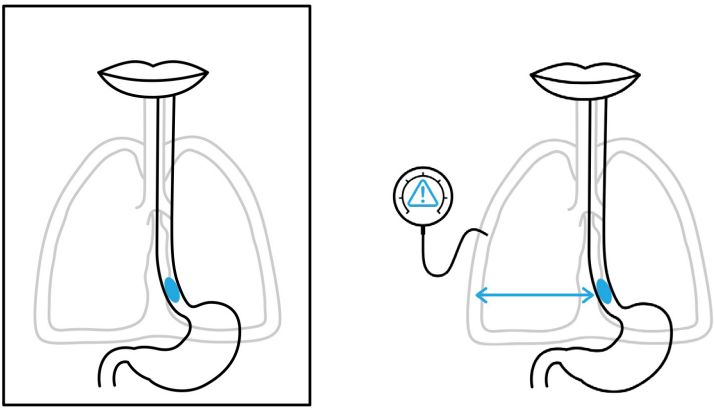

V1
V2
Volume (L)
0
10
20
30
$P_{alv} - P_{pl}$ (cmH_2O)
P2
P1


TLC
100
75
50
25
Volume (%TLC)
FRC
-10
0
10
20
30
40
Pressure (L)



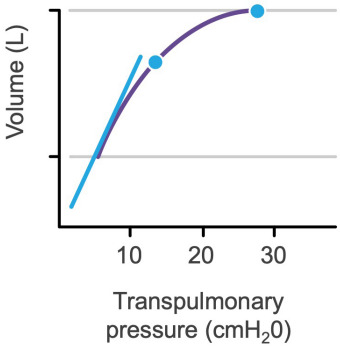
3.2 MEASURING STATIC LUNG COMPLIANCE

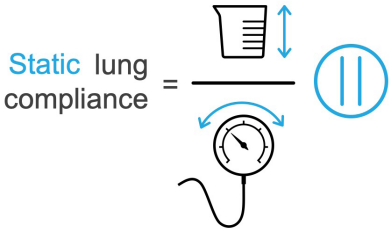
Measurement of pressure across the lung can be determined using body plethysmography and an intra-esophageal balloon. When an intra-esophageal balloon is placed in the lower third of the esophagus, intra-esophageal pressure measurement closely reflects pleural pressure, thereby enabling measurement of the pressure gradient across the lung (the difference between alveolar and pleural pressures). Lung volume changes measured using the plethysmograph, can then be related to the pressure gradient across the lung, to determine lung compliance.



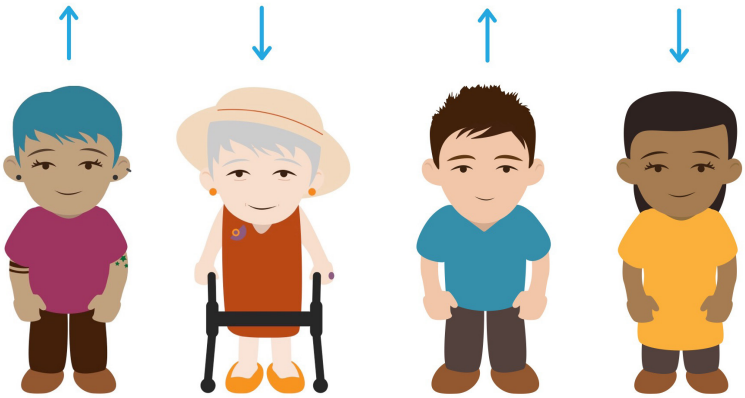
Diseases may selectively affect the elastic properties of the lungs, chest wall, or both.

Static lung compliance is measured over the linear portion of the pressure-volume curve of the isolated lung.

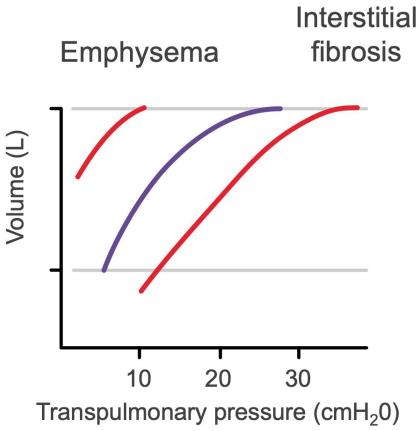




A range of normal values has been established. Static lung compliance decreases with age.

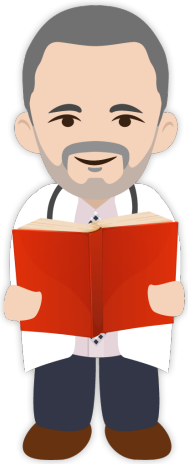


A variety of acute and chronic diseases may alter static lung compliance; for example, pulmonary fibrosis results in decreasing compliance, while emphysema is associated with an increase in static lung compliance.


Emphysema
Interstitial fibrosis
Volume (L)
10
20
30
Transpulmonary pressure (cmH20)

3.3 MEASURING STATIC CHEST WALL COMPLIANCE

To measure isolated *chest wall compliance*, one can first determine the compliance of the intact respiratory system, as described below, and then subtract the lung component, based on measurement of transpulmonary pressure, as previously described.



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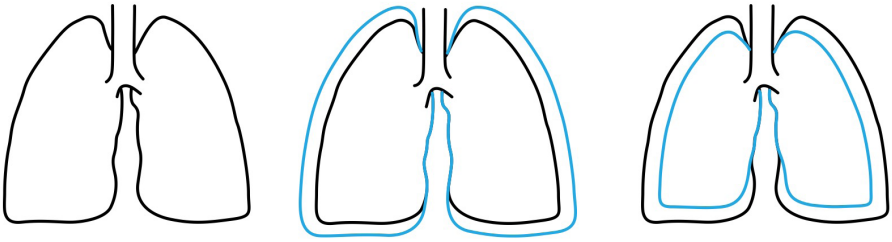
Chapter 4

ASSESSING BREATHING

4.1 MEASURING FORCED VITAL CAPACITIES

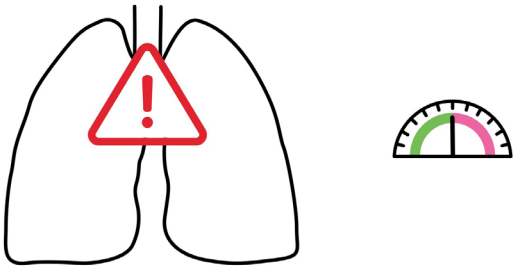
Measurement of forced expiratory and inspiratory vital capacities constitutes an important element in assessment of lung function.

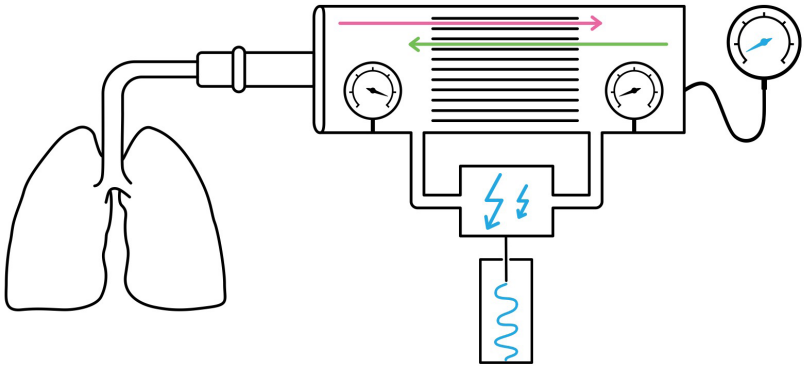
Many pulmonary diseases affect the volume of air in the thorax at resting lung volume, known as functional residual capacity (FRC); the maximal lung volume achievable, known as total lung capacity (TLC); or the minimal achievable lung volume, known as residual volume (RV).



FRC TLC RV

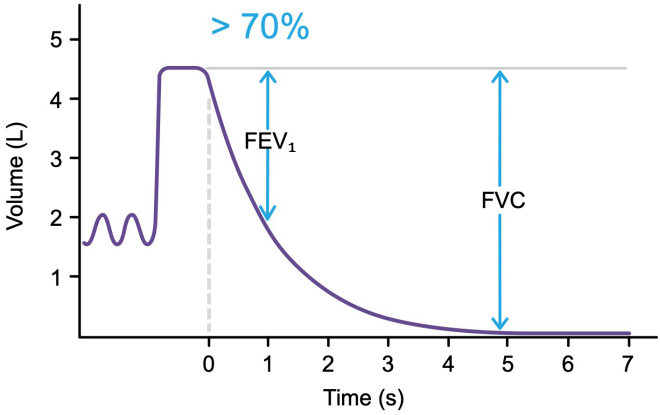
Diseases also affect the rate of expiratory or inspiratory gas flow, measurement of which is made using a spirometer or pneumotachograph.





Flow-resistive pneumotachograph

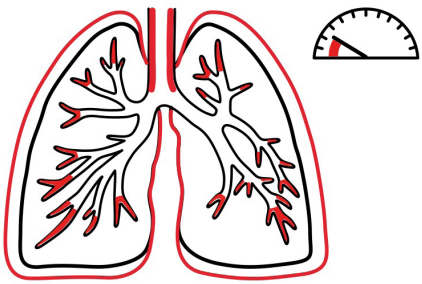
In performing spirometry, the subject performs a series of normal tidal breaths from resting lung volume and then makes a maximal inspiratory effort to total lung capacity, followed by a maximal expiratory effort to residual volume. The difference between maximal and minimal lung volumes is vital capacity, which can be measured during inspiration or expiration. When the measurement is done, with the patient making a maximal effort and as rapidly as possible, the measurement is known as forced vital capacity (FVC).



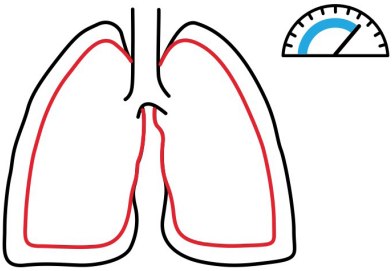
A normal spirogram is characterized by > 70% of the total exhaled volume (exhaled within the first second), a measurement known as the forced expiratory volume in one second ($FEV_{1)}$.

Patterns of abnormal spirometry

Application of spirometry, to evaluation of known or suspected respiratory disease, is based on classification of the physiologic disturbance produced by the disease, into either an obstructive or restrictive category.



Obstructive



Restrictive

Obstructive disease

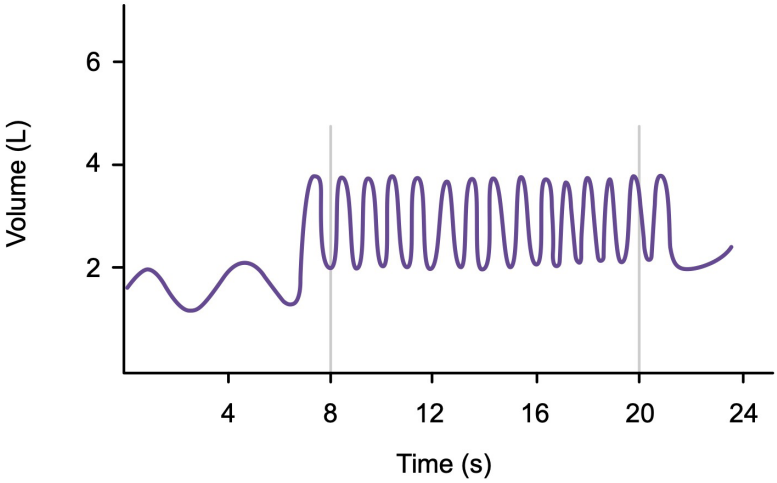
Obstructive diseases, for example, asthma, are characterized by airway narrowing and resulting reduction in the rate of expiratory gas flow.

Restrictive disease

On the other hand, restrictive disorders, for example, pulmonary fibrosis, are characterized by limited lung inflation and a decrease in the total volume of gas available for expiration; gas flow rates are preserved.

4.2 MEASURING MAXIMAL VOLUNTARY VENTILATION

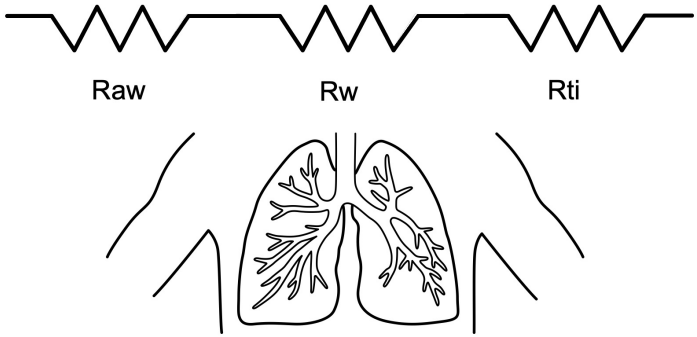
Maximal voluntary ventilation (MVV), constitutes an overall measure of respiratory performance, including performance of the respiratory muscles, as well as ventilation. To measure MVV, the patient makes maximal inspiratory and expiratory efforts over the course of 12 seconds. The total volume of gas exhaled during the 12-second measurement is extrapolated to one minute.



MVV provides an overall assessment of effort, respiratory muscle strength, and the elastic and flow-resistive properties of the lung and chest wall.

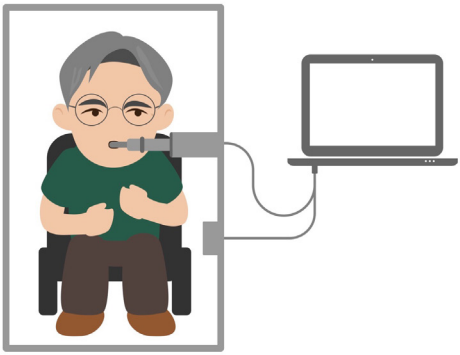
4.3 ASSESSING AIRWAY RESISTANCE AND CONDUCTANCE

Total respiratory resistance is the sum of the resistances offered to airflow by the airways, expansion of the chest wall, and stretching of lung tissue.

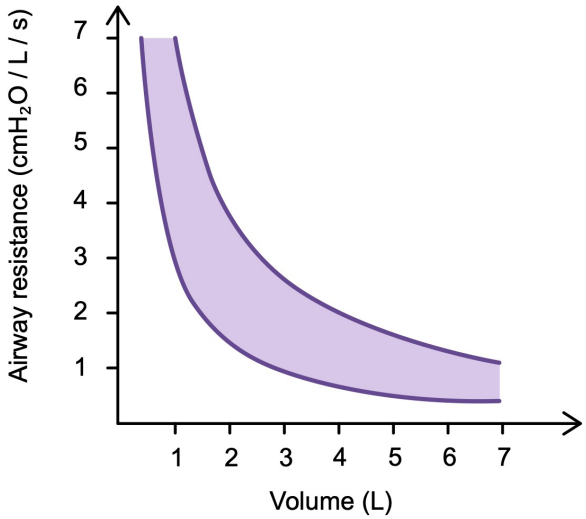


Respiratory resistance (Rrs)

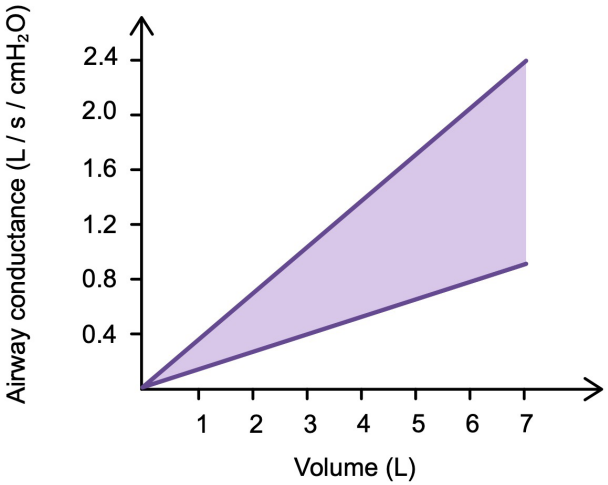
Overall airway resistance is calculated as the pressure differential along the airways during airflow, divided by the rate of airflow. Air flow rates and driving pressure can be calculated using body plethysmography.



Airway resistance varies with lung volume, increasing curvilinearly with decreases in lung volume, as airway diameters decrease due to reduction in radial traction on the airways by the elastic lung parenchyma.



The reciprocal of airway resistance is known as airway conductance. Airway conductance falls linearly with decreases in lung volume.



4.4 DETECTING AIRWAY INFLAMMATION

An additional clinically useful measurement of airway constriction, in the setting of diseases like asthma, is exhaled nitric oxide (NO). NO is a marker of airway inflammation. During asthma exacerbations, concentrations of exhaled NO increase. Levels of NO in expired gas may be elevated, in asymptomatic patients with normal spirometry.

Further reading

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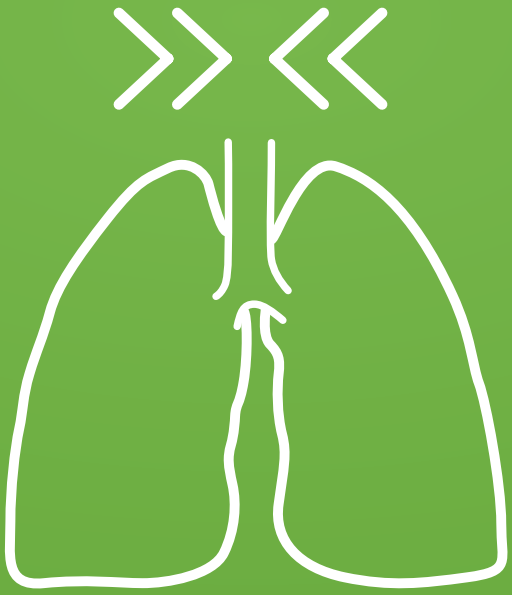
Chapter 5

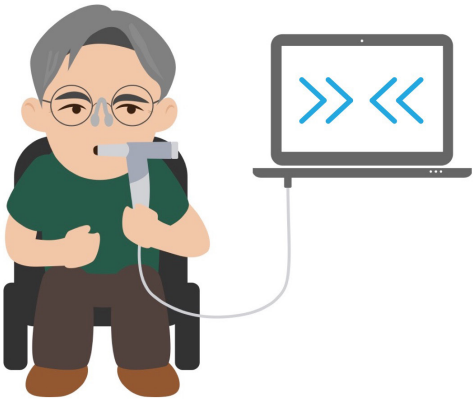
CHALLENGING THE AIRWAYS



5.1 PERFORMING THE METHACHOLINE CHALLENGE TEST

Bronchoprovocation testing refers to assessment of bronchial reactivity in response to administration of selected stimuli, either pharmacologic or environmental.

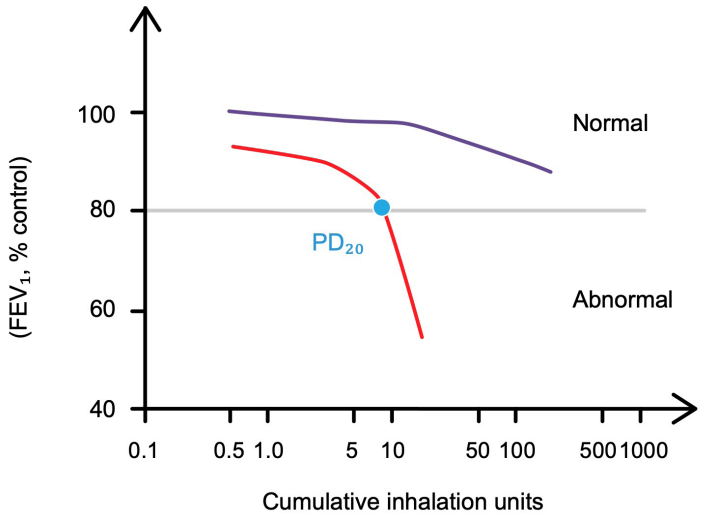
The most common form of bronchoprovocation testing is the methacholine challenge. Methacholine is a synthetic cholinergic agent that invokes airway smooth muscle contraction.



In performing the test, baseline spirometry is performed and then repeated after inhalation of a standard solution of a methacholine aerosol. Various concentrations of the methacholine solution are prepared, and each is administered sequentially as post-administration FEV_1 is measured.

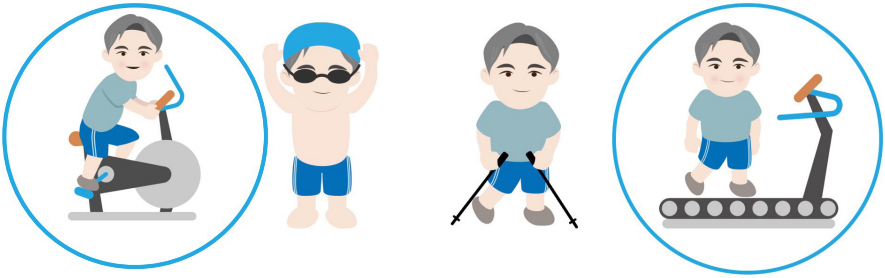
The cumulative dose of methacholine delivered is expressed in *inhalation units*, where one inhalation unit equals a single inhalation of methacholine at 1 mg / mL. The test is stopped if the baseline FEV_1 drops below 80%, or if the patient develops a cough or chest tightness.

Results are plotted as FEV_1, expressed as a percentage of control, versus the cumulative dose of methacholine. The dose that produces a 20% drop in the baseline FEV_1 is known as the PD_{20}, or provocative dose.

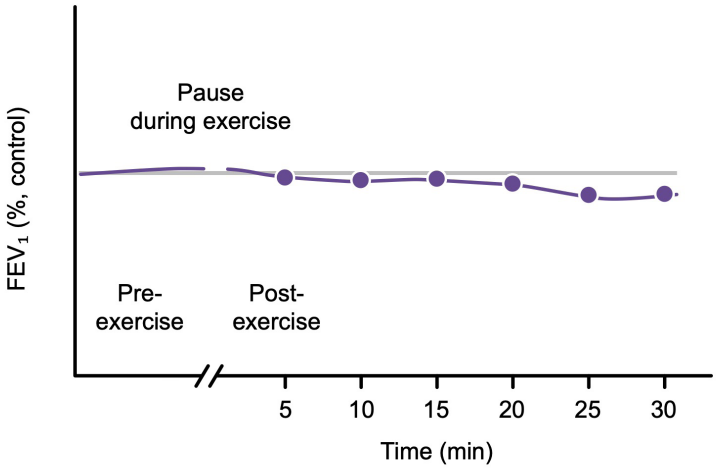


5.2 USING THE EXERCISE TEST

Another form of challenge testing is *exercise*, utilized primarily in the context of evaluating patients for exercise-induced asthma.



Typically, either a treadmill or bicycle ergometer is used. FEV_1 is measured at baseline and then at 5-minute intervals, for up to 30 minutes following cessation of exercise, which is typically performed for 4–8 minutes.

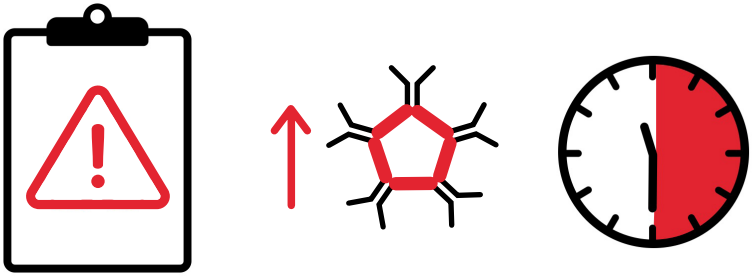


5.3 ADMINISTERING THE INHALATIONAL CHALLENGE TEST

A variety of inhalational agents may also be used, to evaluate for hyper-reactive airways disease, in the context of occupational asthma. These include agents that are found in the patient's workplace.

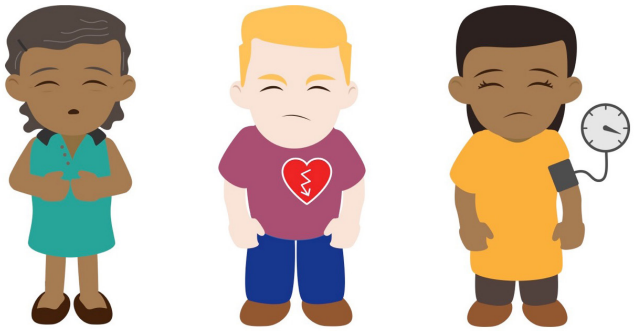
The tests can be dangerous and should be performed only by experienced personnel.

Particular attention must be paid to the so-called *late response*, which may develop six hours or more following agent administration.



5.4 TAKING PRECAUTIONS WITH BRONCHOPROVOCATION TESTING

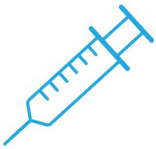
Absolute contraindications to performing any form of bronchoprovocation testing include significant reductions in the baseline FEV_1 (e.g., FEV_1 < 50% predicted), recent myocardial infarction or stroke, or poorly controlled hypertension.



Relative contraindications include mild reduction in FEV_1 (> 50% predicted), pregnancy, lactation, or use of a cholinesterase inhibitor.

Testing should not be performed in the setting of a recent upper respiratory tract infection, recent caffeine ingestion, or following bronchodilator administration. Exercise and inhalation of cold air should be avoided prior to testing.

6 weeks



8 weeks

6 hours

6 hours

Caveats

Further reading

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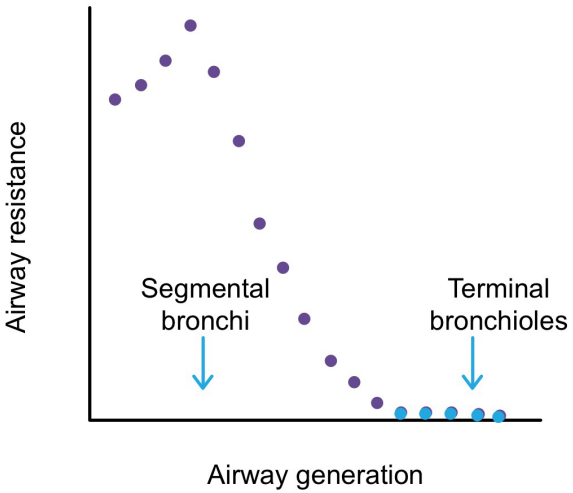
Chapter 6

CHECKING SMALL AIRWAYS FUNCTION

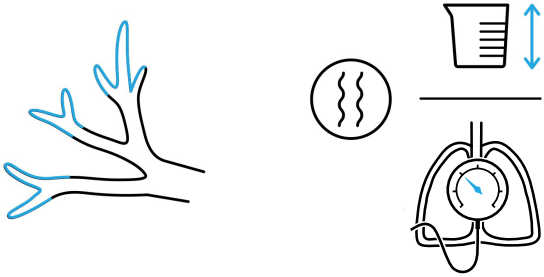
6.1 MEASURING DYNAMIC COMPLIANCE

Diseases isolated to the small airways (those < 2 mm in diameter) may not be manifest early in their course, using routine pulmonary function tests. The small airways contribute less than one third to total airways resistance, so disease initially confined to small airways may not be demonstrated in routine spirometry.



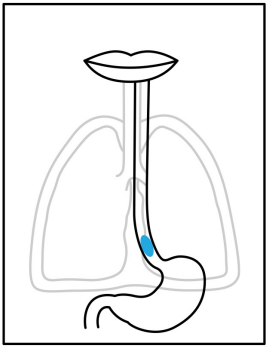
One test of small airways function is frequency dependency of dynamic compliance. Dynamic compliance is defined as the change in lung volume, during airflow produced by a given change in transpulmonary pressure.

Dynamic Compliance (Cdyn)

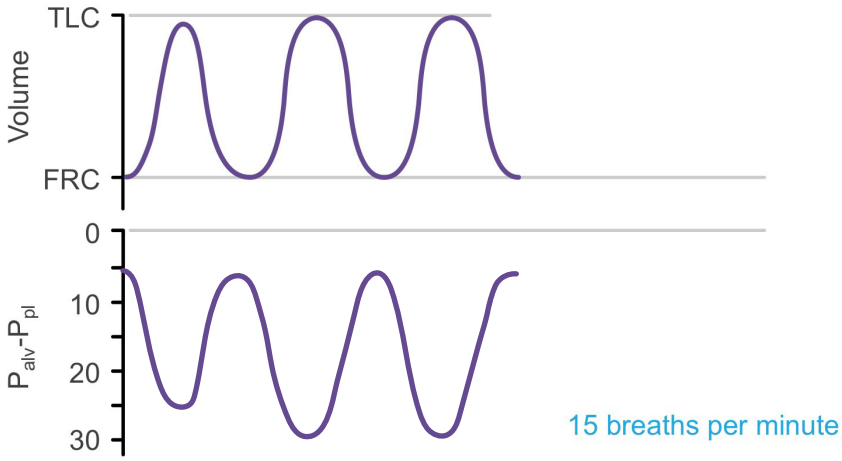


Normally, this measurement does not change in response to changes in breathing frequency. However, if ventilation throughout the lung is not uniform because of heterogeneous small airways disease, dynamic compliance may become frequency-dependent.

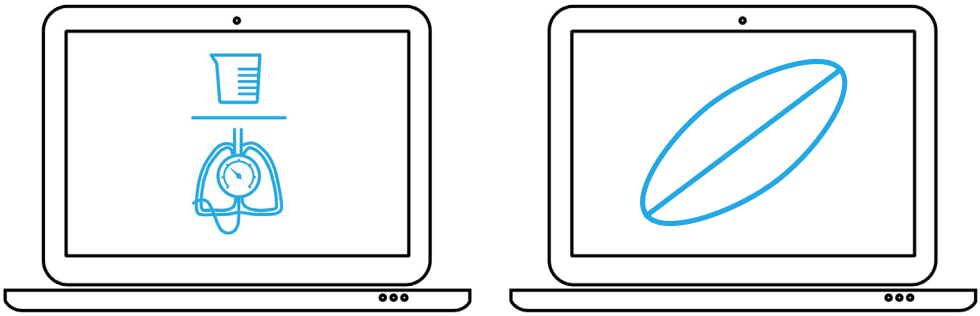
To measure frequency dependence of dynamic compliance, the patient sits in a body box with an intra-esophageal balloon inserted, to enable measurement of transpulmonary pressure.



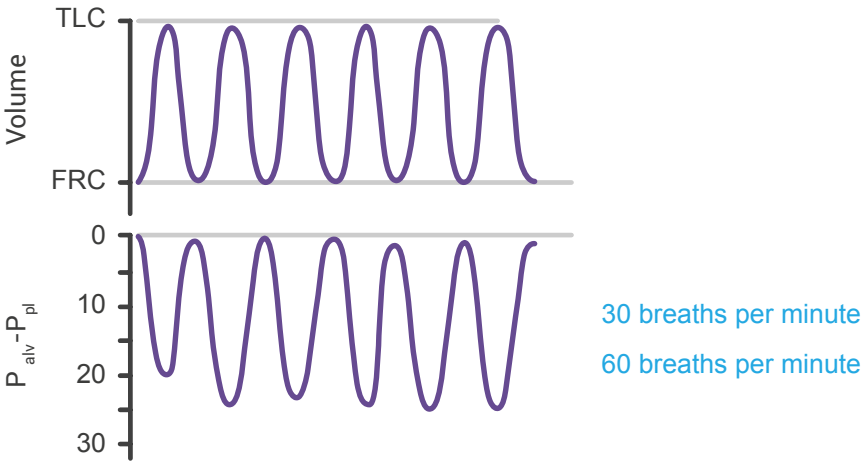
Measurement of tidal volume versus transpulmonary pressure is plotted at a respiratory rate of 15 breaths per minute.



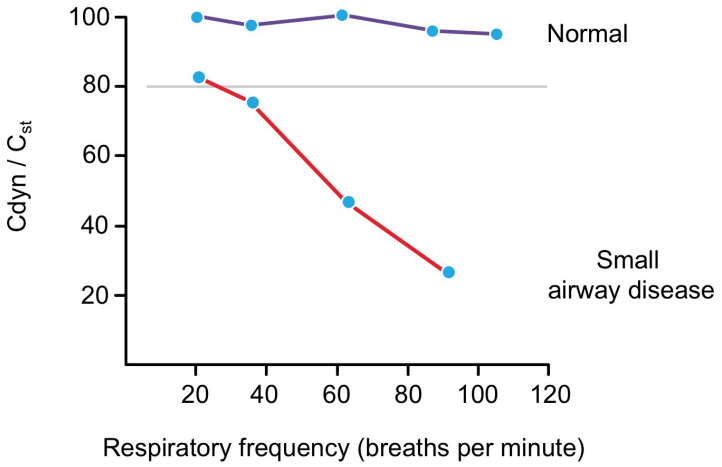
On another screen, tidal volume and transpulmonary pressure are plotted against one another, generating a loop. The slope of the line represents dynamic compliance.



The subject then repeats the measurement at respiratory rates of 30 breaths per minute and 60 breaths per minute.



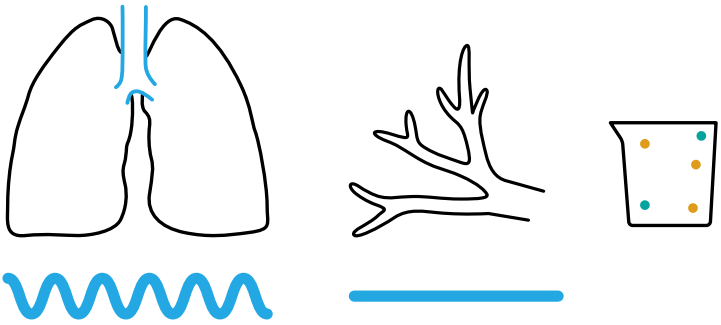
Normally, dynamic compliance is expressed as a percentage of static compliance and remains constant, despite variations in respiratory frequency. With small airways disease, the ratio falls with increasing respiratory rates. The basis for the fall is that isolated small airways disease results in over-inflation of distal alveoli (through ball-valve physiology), with smaller changes in volume per breath with increasing respiratory rate because of inadequate alveolar deflation.



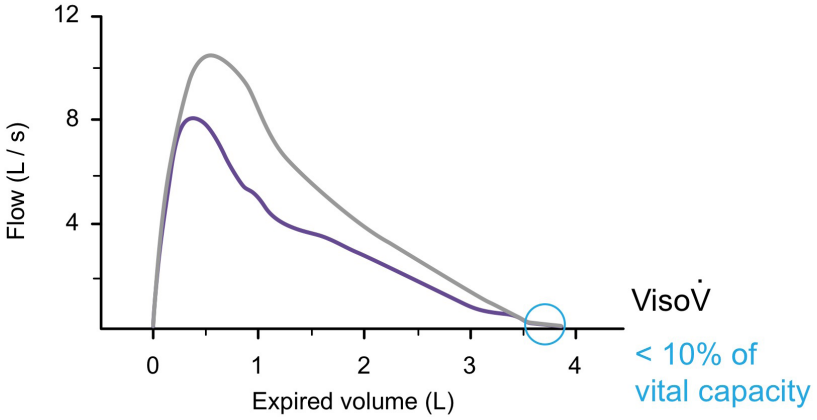
6.2 INTERPRETING HELIUM–OXYGEN FLOW VOLUME CURVES

Another test of small airways function is the *helium–oxygen flow volume curve*. The test is based on the principle that in distal, small airways, airflow patterns are laminar and, therefore, independent of gas density.

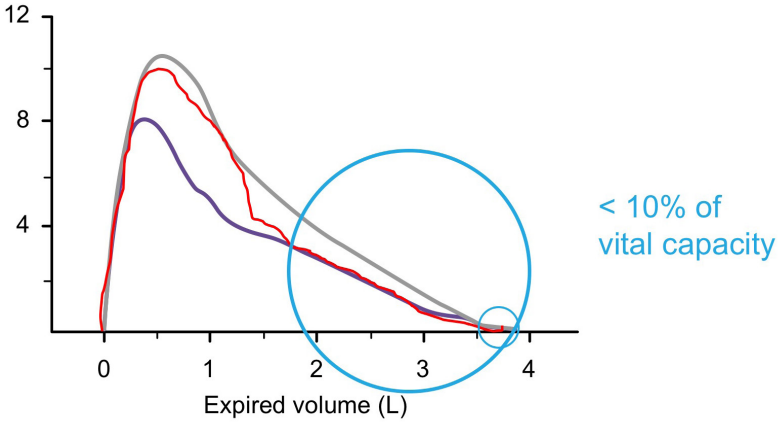
However, with development of small airways disease, airflow in the distal airways becomes more turbulent. Since turbulent airflow is density-dependent, the presence of small airways disease is reflected in improvement in gas flow when a gas mixture of lower density, a helium-oxygen mixture, is used.



In performing the helium–oxygen flow volume curve, vital capacity breaths performed, while breathing room air, are followed by breaths of a helium–oxygen mixture. Expiratory flow volume curves are compared at 50% of the vital capacity and at the point where the curves coincide.

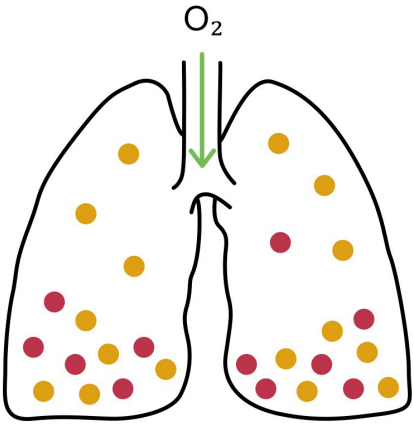


Normally, the volume of isoflow, the lung volume at which the curves coincide, is < 10% of vital capacity. If isoflow occurs at a higher lung volume, small airways disease is diagnosed. The increase in expiratory flow at 50% vital capacity is also increased under these circumstances.

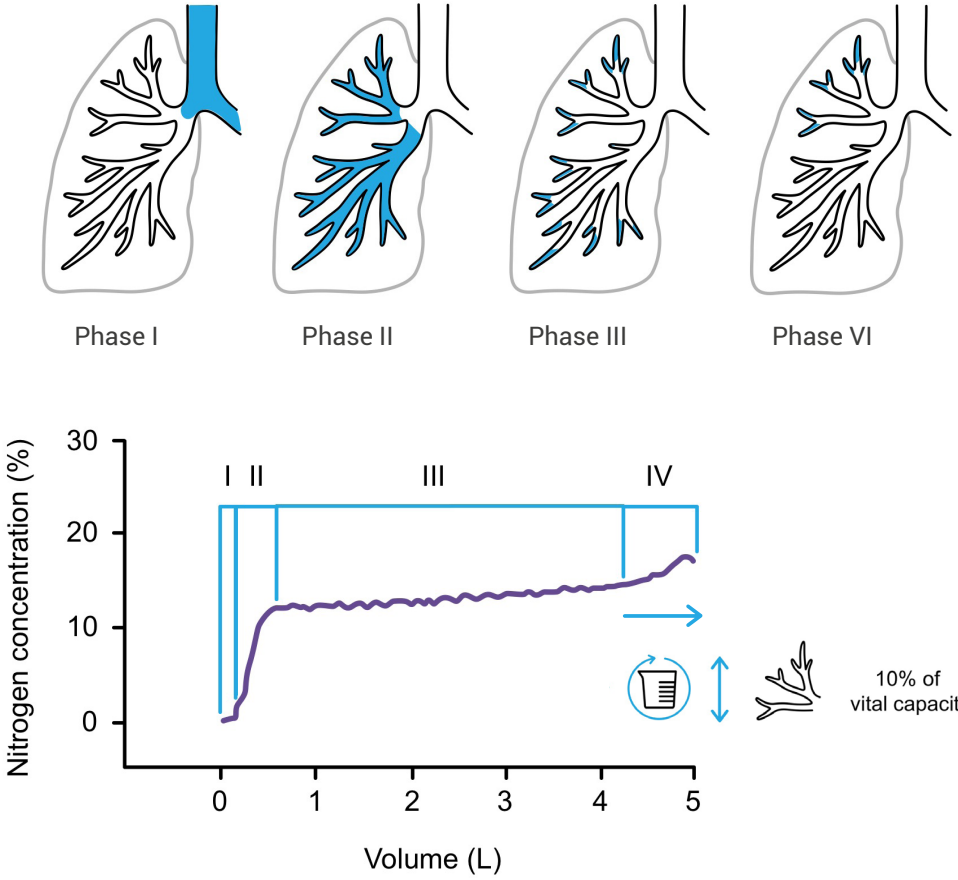


6.3 USING THE NITROGEN WASHOUT TEST

One additional test of small airways function utilizes measurement of exhaled gas concentrations throughout an expiratory maneuver. The test is based on the observation that inspired gas is heterogeneously distributed throughout the lung during inspiration.



Consequently, measurement throughout expiration of the concentration of the predominant gas resident in the lung, nitrogen, provides insight into the presence of small airways disease and constitutes the nitrogen washout test.



The subject takes two breaths of air followed by a single maximal breath of pure oxygen, before exhaling into a circuit, while the concentration of nitrogen is measured throughout expiration. An initial plateau (Phase I), characterized by a low nitrogen concentration, reflects the anatomic dead space of the central airways, which were filled with pure oxygen during the prior inhalation. A subsequent rise (Phase II) represents a mixture of gases from both dead space and alveoli. There-

after, is seen a long plateau (Phase III), representing a mixture of gases from the lung apices, mid-zones, and bases. The final phase (Phase IV) represents the closing volume (the point at which small airways in the lung bases close), resulting in enrichment in the contribution of apical lung regions, to expired gas concentrations. If the closing volume is > 10% of vital capacity, small airways disease, reflected in premature airway closure, is diagnosed.

Further reading

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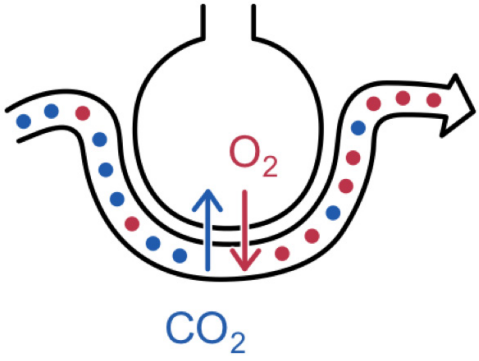
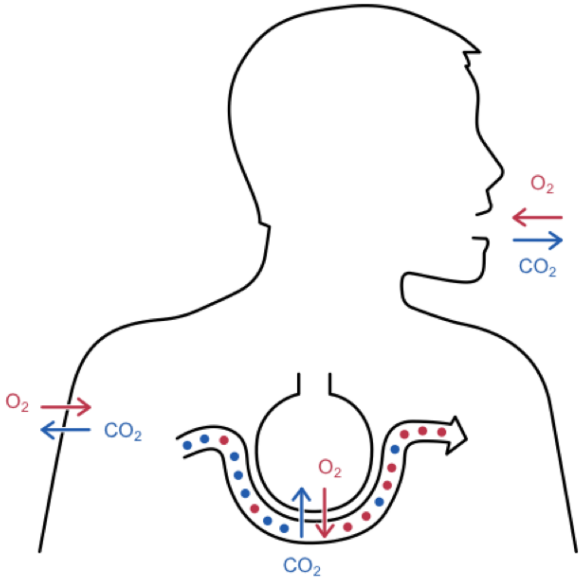
Chapter 7

ANALYZING GAS EXCHANGE

7.1 MASTERING THE PHYSIOLOGY OF VENTILATION

Primary functions of the lung include oxygen uptake and carbon dioxide elimination. Under steady-state conditions, oxygen uptake and carbon dioxide elimination across the lungs equal, oxygen uptake and carbon dioxide production at the tissue level.





The total volume of air breathed per minute is minute ventilation ($\dot{V}_{E)}$, which is equal to the product of tidal volume (V_T), and respiratory rate (f). Normal resting $\dot{V}_E$ is 6–8 L / m and V_T is 0.4–0.6 L.

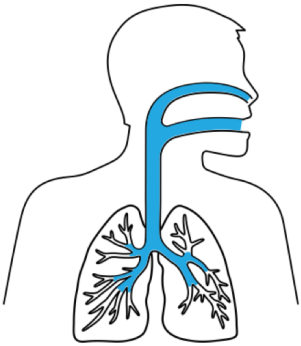
As the concentration of carbon dioxide in inspired gas is negligible, the amount of carbon dioxide produced per minute can be calculated as, $\dot{V}_E$ x F_ECO_2, were F_ECO_2 is the concentration of carbon dioxide in expired gas.

Oxygen uptake is calculated as the difference between the amount of oxygen in inspired gas and the amount of oxygen in expired gas: ($\dot{V}_I$ x F_IO_2) – ($\dot{V}_E$ x F_EO_2).

In a normal, fasting, resting subject, the ratio of carbon dioxide output to oxygen uptake is known as the respiratory exchange ratio (R), which is normally 0.8. Under steady-state conditions, measurement of R can be used to estimate the respiratory quotient, the ratio of carbon dioxide production to oxygen utilization at the tissue level.

Dead space

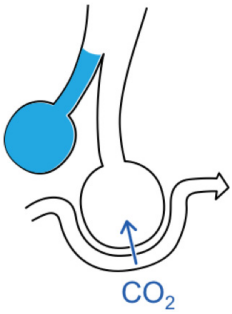
Within the lungs, not all inspired gas participates in gas exchange. The nose, mouth, and airways down to the level of the terminal bronchioles do not contain alveoli and, hence, do not participate in CO_2 elimination. These areas constitute so-called anatomic dead space, estimated at 1 mL per pound of body weight.



Anatomic dead space

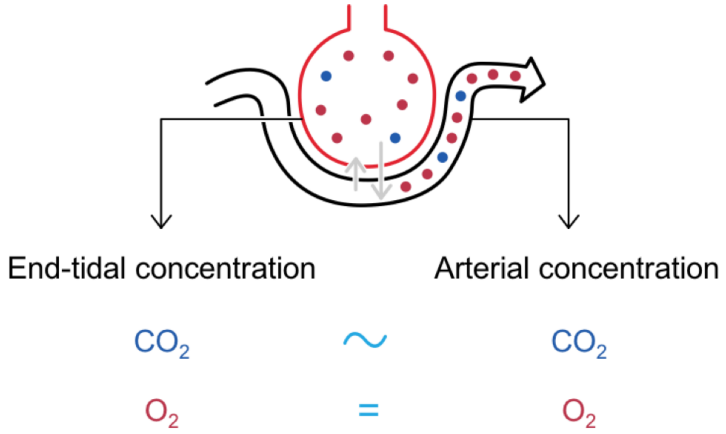
In diseased regions of the lung, alveoli may not have pulmonary capillary blood flow. As a result, carbon dioxide elimination across diseased alveolar capillary walls may not occur, resulting in physiologic dead space. The total amount of dead space relative to the tidal volume, expressed as V_D / V_T (dead space-to-tidal volume ratio), can be determined by sampling expired gas (to measure mixed expired CO_2 concentration, P_ECO_2) and a concurrent arterial blood gas specimen: V_D / V_T = (P_aCO_2 - P_ECO_2) / P_aCO_2.

Physiologic dead space

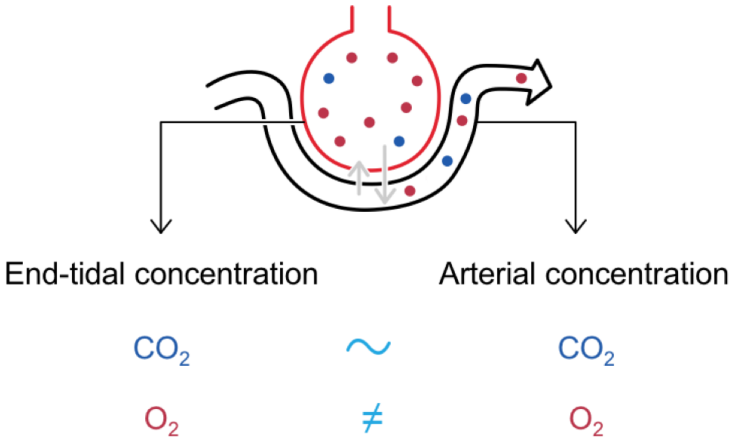


7.2 ANALYZING ALVEOLAR GAS COMPOSITION

Normally, the concentrations of oxygen and carbon dioxide in exhaled gas at the very end of a breath, end-tidal concentrations, approximate mean arterial values.



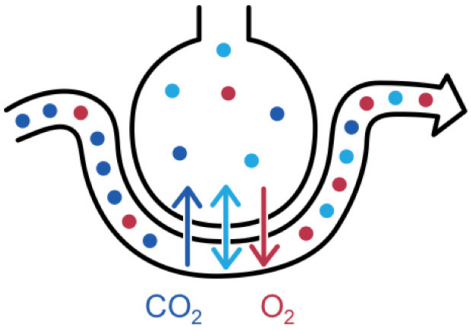
In the presence of structural lung disease, imbalances in the relationship between ventilation and perfusion translate into a disconnect between end-tidal and alveolar oxygen concentrations.



On the other hand, carbon dioxide is so highly diffusible, that even in the presence of significant structural lung disease, the gas readily diffuses across the alveolar-capillary membrane into pulmonary capillary blood.

Mean alveolar PO_2 (P_AO_2) is calculated using the alveolar gas equation: $P_AO_2 = P_IO_2 - P_ACO_2 (F_IO_2 + (1 + F_IO_2 / R))$.

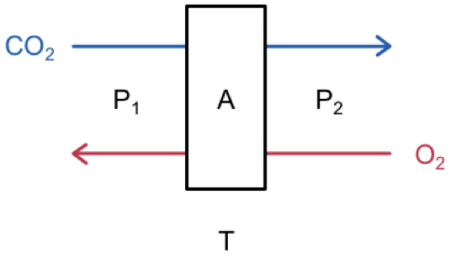
7.3 MEASURING DIFFUSING CAPACITY



Diffusing capacity measures the efficiency with which a test gas moves across the alveolar-capillary membrane. Diffusing capacity, represented as D_LCO, is a nonspecific, but highly sensitive test used to assess lung function in a wide array of circumstances.

The underlying physiologic basis for measuring D_LCO is Fick's Law, which states that the movement of gas across the alveolar-capillary membrane is directly proportional to the area of the membrane, the diffusibility of the gas, the solubility of the gas, and the concentration gradient of the gas across the membrane; gas movement is inversely proportional to the thickness of the alveolar-capillary membrane and the molecular weight of the gas.

$$\dot{V}_{gas} \alpha \frac{A}{T}\left(\frac{Sol}{\sqrt{MW}}\right) \times (P_1 - P_2)$$



Carbon monoxide, because of its great affinity for hemoglobin, has emerged as the most commonly employed test gas for measuring diffusing capacity of the lung. D_LCO is calculated as $V_A \times 60 / P_{barometric} - 47) \times \ln (F_ACO_{initial} / F_ACO_{final})$, where V_A is alveolar volume, measured using the body box or helium dilution technique.

Interstitial lung disease, COPD, pulmonary hypertension, and anemia result in a decline in diffusing capacity, while polycythemia and alveolar hemorrhage increase the diffusing capacity.

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Chapter 8

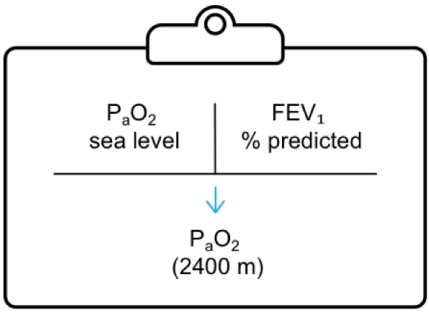
USING SPECIALIZED LUNG FUNCTION TESTS

A variety of less commonly performed, but, nonetheless, informative tests can be employed in evaluating patients for lung disease.

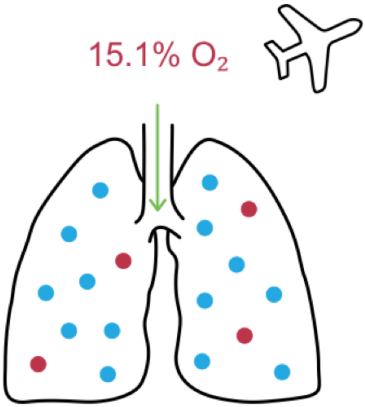
8.1 USING THE HIGH ALTITUDE SIMULATION TEST (HAST)

Assessment of a patient with underlying lung disease, for safety during commercial air flight, is based on one of two methods: application of a predictive nomogram or the high altitude simulation test (HAST).

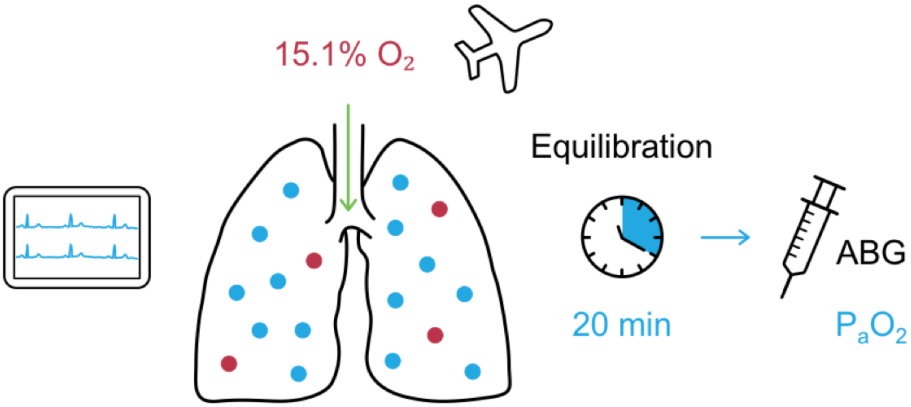
The nomogram-based approach predicts the patient's arterial oxygen tension, during a commercial flight in a partially pressurized cabin (equivalent altitude of 1800–2400 meters above sea level). The tool incorporates the patient's known P_aO_2 at sea level and FEV_1% predicted.



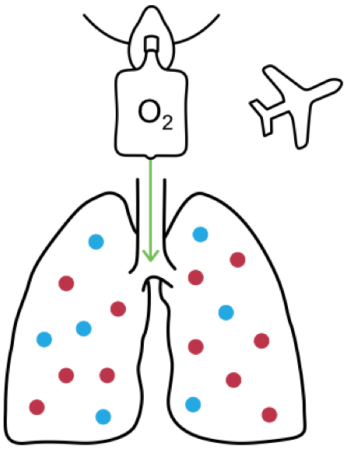
In conducting the HAST, the patient is administered a hypoxic gas mixture of 15.1% oxygen.



An arterial blood gas is obtained following equilibration, which generally takes about 20 minutes.



Supplemental oxygen is then provided to mitigate the drop in oxygen saturation and determine the appropriate oxygen flow rate during flight.

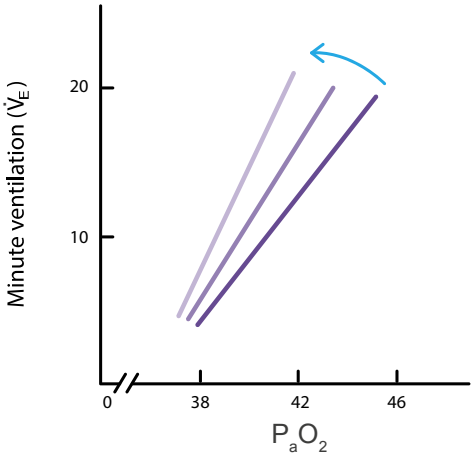


8.2 EVALUATING VENTILATORY RESPONSES TO HYPOXEMIA AND HYPERCAPNIA

Unlike assessment of oxygen during flight in patients with lung disease, evaluation of a patient's response to progressive hypercapnia or hypoxemia is uncommonly performed.

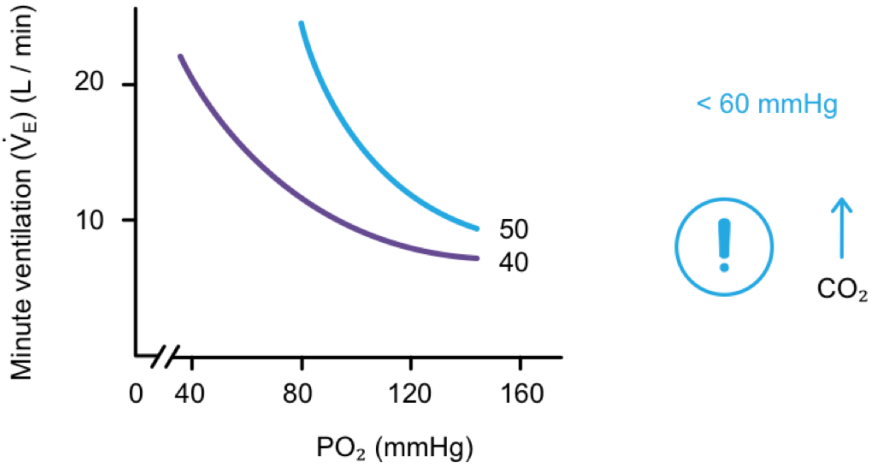
Hypercapnia

In assessing the response to hypercapnia, the patient breathes CO_2-enriched gas at two or more concentrations and time is allowed for equilibration with arterial blood. The patient's level of minute ventilation at each level of arterial P_cO_2 is determined; the slope of the line of minute ventilation versus arterial P_cO_2 defines the hypercapnic response. The response is steeper at lower levels of P_aO_2. The rebreathing method measures the same ventilatory response, but is based upon continuous rebreathing of a CO_2-enriched gas mixture, rather than measurement at discrete CO_2 levels.



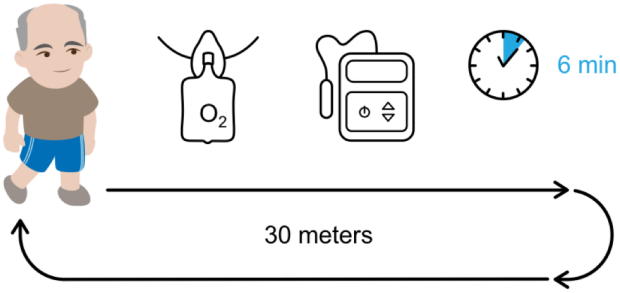
Hypoxemia

In assessing the response to hypoxemia, the patient breathes a hypoxic gas mixture and the ventilatory response measured. The response to decreasing oxygen tension is curvilinear. Higher prevailing levels of carbon dioxide accentuate the ventilatory response to hypoxemia. Both steady state and non-steady state techniques have been developed.



8.3 PERFORMING THE SIX-MINUTE WALK TEST

Finally, a commonly employed test to assess a patient's overall cardio-pulmonary performance is the six-minute walk test. The patient walks a measured course of 30 m, back and forth, in a linear fashion, with supplemental oxygen administered, as needed. Pulse oximetry is continuously measured.

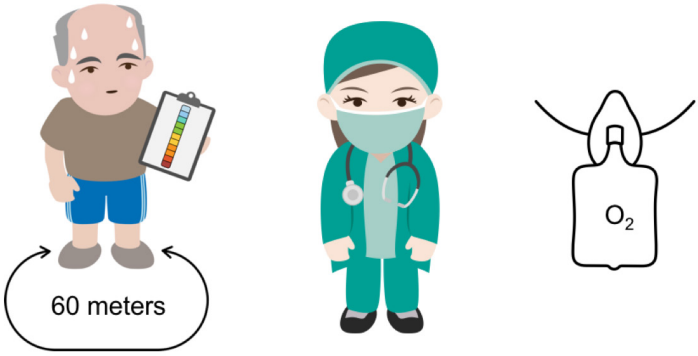


A Borg scale is used to quantitate the patient's level of dyspnea. The total distance walked and the associated symptom level are recorded after six minutes of activity.

0	Rest
1	Really easy
2	Easy
3	Moderate
4	Sort of hard
5	Hard
6	
7	Really hard
8	
9	Really, really hard
10	Maximal: Just like my hardest race

The test is not performed in patients with recent myocardial infarction, angina, tachycardia, or poorly controlled hypertension.

Indications for stopping the test include development of chest pain, diaphoresis, refractory desaturation, or unrelenting dyspnea. Test results can be used to stratify patients awaiting lung transplantation or to determine candidacy for volume reduction surgery.



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Chapter 9

DIAGNOSING RESPIRATORY DISORDERS

9.1 INTERPRETING ABNORMAL PATTERNS

The traditional method of pulmonary function test interpretation is based on a normal value for FEV / FVC% as > 70%, and normal values for other parameters (e.g., lung volumes), as > 80% predicted.

In patients with FEV_1 / FVC < 0.70

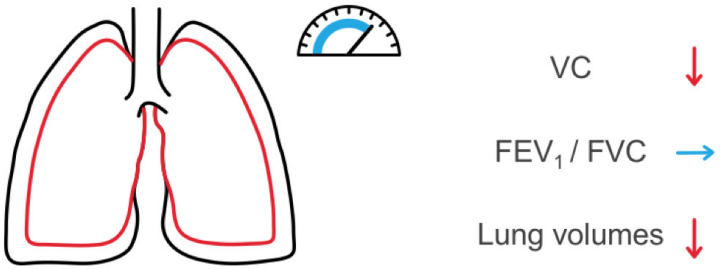
GOLD 1	Mild	$FEV_1 \geq 80\%$ predicted
GOLD 2	Moderate	$50\% \leq FEV_1 < 80\%$ predicted
GOLD 3	Severe	$30\% \leq FEV_1 < 50\%$ predicted
GOLD 4	Very severe	$FEV_1 < 30\%$ predicted

Such methodology has been useful and practical in managing patients, but it lacks statistical validation.

According to the historical scheme, FEV_1 / FVC% < 70% is considered evidence of obstruction; the magnitude of the obstructive defect is predicated upon the magnitude of the reduction in FEV_1 (below 80% of predicted).

Obstructive disease

Similarly, reductions in lung volumes, particularly a TLC below 80% predicted, suggests restriction.

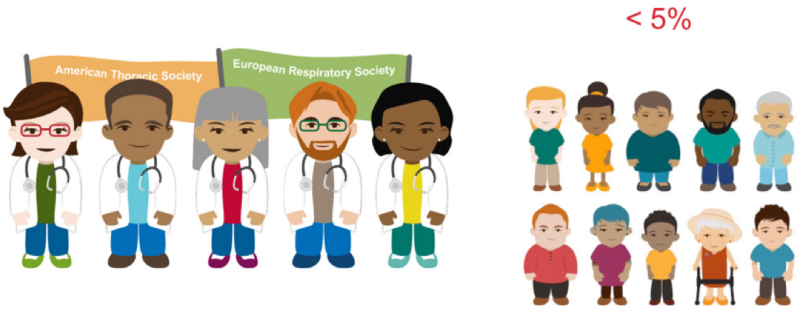


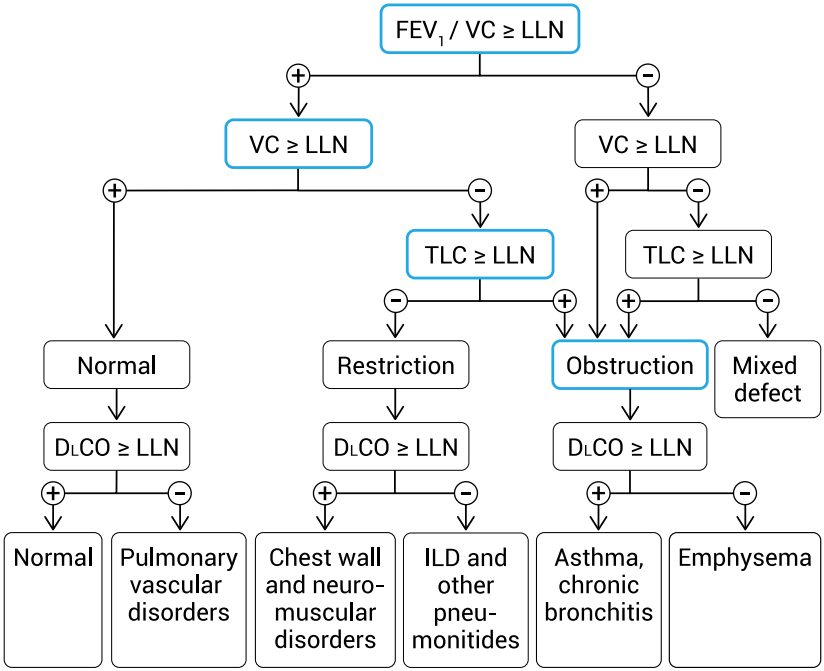
Restrictive disease

Isolated or concurrent reductions in D_LCO < 80% predicted indicate gas transfer abnormalities. Lung volume elevations > 120% predicted, particularly in the setting of a reduced FEV_1 / FVC%, are consistent with hyperinflation, most commonly seen in the setting of obstructive airways disease.

9.2 ADHERING TO INTERPRETATION GUIDELINES

The current interpretation scheme, as recommended by the American Thoracic Society and European Respiratory Society, bases the diagnosis of test abnormality on results below the 5th percentile of the frequency distribution of values in the reference population.





The contemporary classification scheme begins with review of FEV_1 / VC. In this case, VC includes forced vital capacity (FVC), VC (so-called, slow vital capacity) or FIVC (forced inspiratory vital capacity), whichever result is greatest.

- If FEV_1 / VC is < 5th percentile and VC > 5th percentile, the pattern is obstructive. Distinctions among asthma, chronic bronchitis, and emphysema are made on the basis of whether the D_LCO is normal (asthma and chronic bronchitis) or reduced (emphysema). Additionally, in this setting, if TLC is < 5th percentile, concurrent restriction, (i.e., a mixed pattern), is present.

- If FEV_1 / VC is > 5th percentile and VC < 5th percentile, a reduced TLC implies restriction. A normal D_LCO in this setting suggests possible underlying neuromuscular disease as the basis for the restriction. A concurrent reduction in D_LCO suggests underlying pulmonary parenchymal disease, for example, ILD, or pulmonary vascular disease.

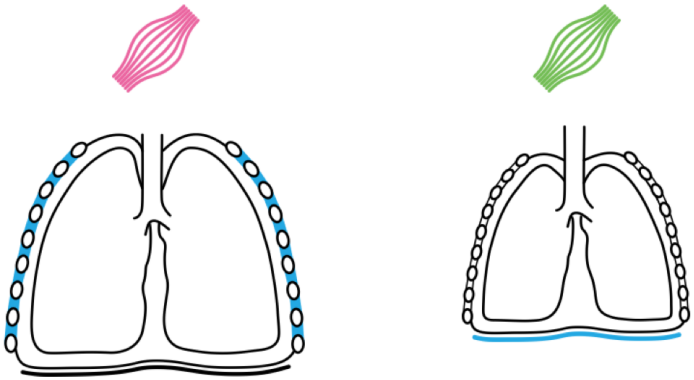
- According to this scheme, obstruction can be diagnosed with a normal FEV_1 / VC if VC is reduced and TLC is normal or elevated.

- When FVC / VC is > 5th percentile and VC is > 5th percentile, (i.e., when spirometry is normal), a reduced D_LCO may indicate underlying pulmonary vascular disease.

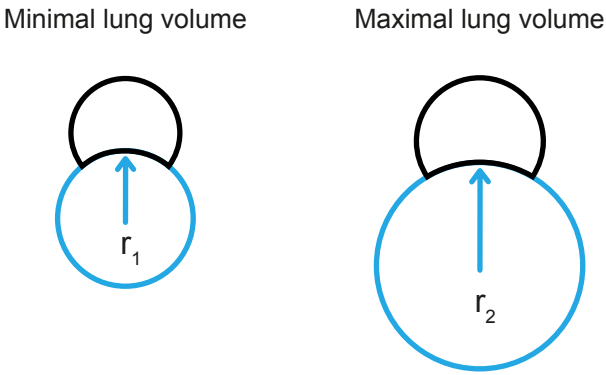
Over diagnosis of obstruction

9.3 ASSESSING PHYSIOLOGICAL DETERMINANTS

Respiratory muscle strength, an important determinant of respiratory performance, is measured as peak inspiratory (PImax) and peak expiratory (PEmax) pressures under static conditions. Since the length-tension relationship for expiratory muscles is optimized at maximal lung volume, TLC, PEmax is measured at this lung volume.

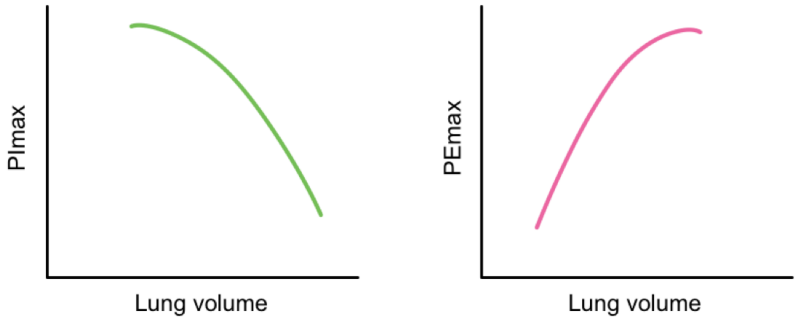


For the principal inspiratory muscle, the diaphragm, the length-tension relationship is optimized at minimal lung volume, RV. Furthermore, the diaphragm is curved, and the curvature is maximal at RV. Application of Laplace's Law reveals that maximal diaphragm strength is achieved at this lung volume.



P = surface tension / radius. At constant surface tension, P is inversely proportional to r (i.e., lung volume).

Diseases which affect lung volume can change the length of inspiratory or expiratory muscles, resulting in changes in inspiratory or expiratory pressures. Diseases which increase lung volume flatten the diaphragm and reduce the operating length of the muscle, thereby reducing maximal inspiratory pressure generation. Conversely, diseases which result in smaller lung volumes decrease expiratory muscle length and decrease maximal expiratory pressure.



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