

UNIVERSITY OF JORDAN
DEPT. OF PHYSIOLOGY & BIOCHEMISTRY
RESPIRATORY PHYSIOLOGY
MEDICAL STUDENTS
FALL 2014/2015
(lecture 1)

Textbook of medical physiology, by A.C. Guyton and John E, Hall, Twelfth Edition, 2010.

In general the **11** lectures will cover the following Respiratory Physiology Topics:

1. Overview and Mechanics of Breathing (Lung Ventilation)...1 lectures.
2. Lung Compliance...2 lectures.
3. Airway Resistance...2 lectures.
4. Ventilation-Perfusion Ratio...1 lecture.
5. Gas Exchange and Transport...2 lectures
6. Regulation of Lung Ventilation, high altitude, exercise etc...2 lectures.
7. Pulmonary Function Test and Pathophysiology (lung Diseases) and Clinical Applications...1 lecture.

- **Potential Causes of Hypoxia...from your first lecture**

INTRODUCTION

Respiration is the process by which the body takes in and utilizes oxygen and gets rid of CO₂.

Three determinants of respiration

Respiration depends on three things: the lungs, the blood, and the tissues.

The lungs:

The lungs must be adequately ventilated and be capable of adequate gas exchange.

Ventilation: is determined by the activity of the control system (respiratory system), the adequacy of the feedback control systems (neural and hormonal), and the efficiency of the effector system (muscles of respiration).

Gas exchange: depends on the patency of the airways, the pressure gradient across the alveolar-capillary membrane, the diffusability of individual gases and the area and thickness of the exchange membrane.

The Blood:

The blood must pick up, carry and deliver O₂ and CO₂ in amounts that are appropriate to the body's need. It depends in the presence of adequate amount of the correct type of Hb, the cardiac output, and local perfusion.

The Tissues:

Individual cells must be capable of taking up and utilizing O₂ properly.

Respiratory failure can therefore result from a fault at any point along this lungs-blood-tissue chain.

PULMONARY VENTILATION (pulmo- means lung)
(lecture 2)

Lecture Outline:

- I. Overview of the Respiratory Physiology.
- II. Functional Anatomy of the Lung
- III. Alveolar Ventilation
- IV. Respiratory Muscles
- V. Lung Volumes & Capacities.

OBJECTIVES: After attending the lecture, the student should be able to perform the following tasks

1. Understand the participation of the respiratory system in homeostasis. 4
2. The non-respiratory functions of the respiratory system (Note: *These non-respiratory functions of the lungs will not be covered in this course*):
 - Aids in venous return
 - Acid base balance
 - Pulmonary capillary remove any air bubble which might otherwise reach systemic circulation
 - Airways remove airborne particles
 - Ventilation contribute to heat loss and water loss
 - Important reservoir of blood
 - Phonation
 - Metabolic functions such as:
 - Conversion of angiotensin I to AII
 - Synthesis and removal of bradykinin and PGs
 - Storage and release of serotonin and histamine
 - inactivation of noradrenaline and adrenaline
 - synthesis of peptides like substance P and opiates
 - secretion of heparin by mast cells
 - secretion of immunoglobulins in the bronchial mucus
3. Identify the structure of the respiratory system. 472-473
4. Explain the structure of the alveolar-capillary (respiratory) membrane. Name the 5 layers 489-490. Are these layers going to affect the diffusion of O₂ and CO₂? WHY?
4. Describe the tracheobronchial tree and list its functional characteristics. At what branch no more cartilage? 472-473
5. Describe how the structure of the respiratory tube changes as branches become finer. 472-473
6. Define the anatomic and physiologic dead space. 471-472
7. Explain why some fresh air arriving in the respiratory unit might be Considered as a "wasted" volume. The V/Q ratio 471-472, 492-493

8. Explain how unwanted particles are prevented from entering the respiratory unit. 25, 472-473
9. Define respiratory minute ventilation, alveolar ventilation, dead space ventilation, and maximal voluntary ventilation. 471-472
10. Describe the respiratory unit and state its functional characteristics.
11. Write the equation relating air flow, air resistance and driving pressure.

12. Give a general account of how we normally breath (inspiration =inflow and expiration=outflow). 465-466

13. Explain how forced inspiration and forced expiration are accomplished.

14. List the major muscles of inspiration and expiration and indicate their functional significance(from your anatomy course).

15. Draw a spirometry tracing that illustrates the lung volume and capacities which can be measured with a spirometer. Define those volumes and capacities which cannot be measured using Spirometer. How we measure them? 469-470

LUNG COMPLIANCE

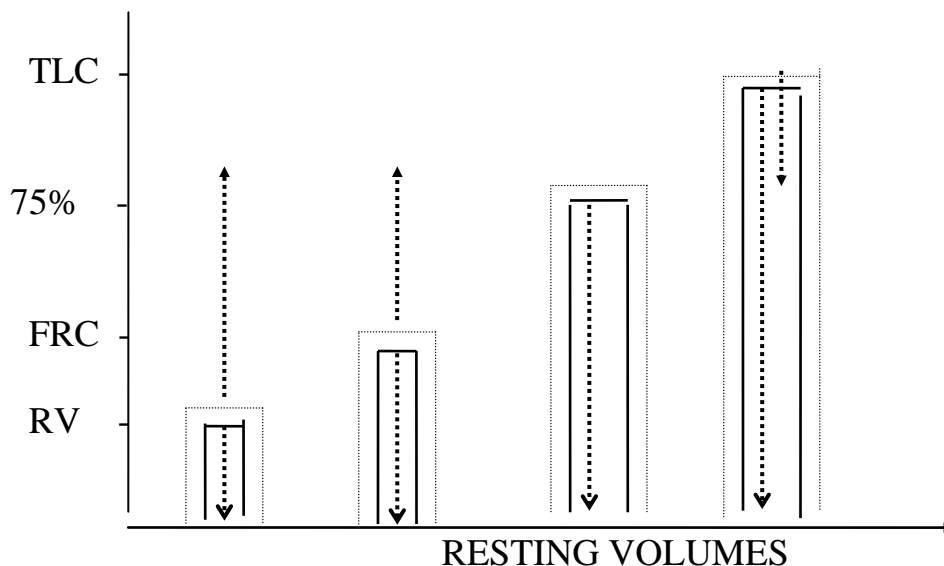
(Lectures 3 + 4)

Lecture Outline:

- I. Binding Between Lung And Thorax (Resting Volumes)
 - A. Lung
 - B. Chest wall
 - C. Chest-lung system
- II. Elastic properties of the respiratory system
 - A. The relaxation curve
 - B. lung and chest compliance curve
- III. Pathological changes in lung compliance
 - A. Emphysema & asthma
 - B. Fibrosis & RDS
- IV. Surface Tension forces
 - A. Influence of surfactant
 - B. Role of alveolar interdependency

OBJECTIVES: After attending the lecture, the student should be able to perform the following tasks

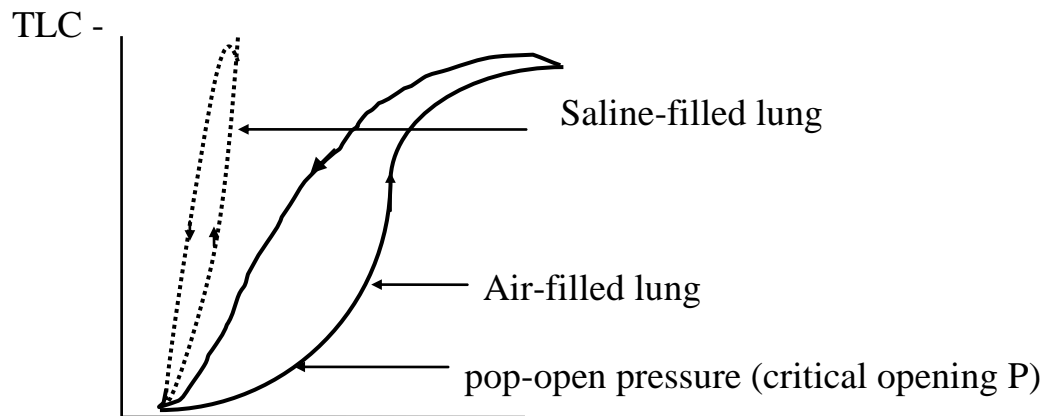
1. Describe the coupling between lungs and thorax. 466
2. Compare the functional residual capacity (FRC) with the separate resting volumes of the lung and thorax.



volumes of the lung and thorax.

3. Explain the information summarized by the compliance curves for the lung. 467-468
4. Explain how changes in lung compliance will alter lung volumes.
5. The Pressure Volume Curve. Draw an inspiratory and expiratory compliance curve of air-filled and saline-filled lung (Hysteresis). Know why lung compliance is increased by filling the lung with saline. 467

6. The Pressure Volume Curve. Draw an inspiratory and expiratory compliance curve of air-filled and saline-filled lung (Hysteresis). Know why lung compliance is increased by filling the lung with saline.



7. Define compliance and hysteresis. Draw compliance curves describing elastic characteristics of the lung, chest wall, and the intact chest lung system
- Understand the mathematical relationship between lungs, chest wall, and total lung compliances.
 - Explain how lung compliance depends on the size and gas volume of the lung.
8. The Collapsing Forces of the Lungs. Define surface tension, and explain how it aids the breathing mechanism. Explain how expiration can be passive with no muscular activity occurring.
9. Explain the role of surface tension and surfactant molecules on the elastic properties of the lungs. 468, 519, 1021-2, 1026
10. Write and understand Laplace's law. 468
11. Define "alveolar stability" and explain the role of surfactant and alveolar dependency (alveolar traction) in alveolar stability.

AIRWAY RESISTANCE

(Lectures 5-6)

Lecture Outline:

- I. Resistance to air flow
 - A. Airway resistance
 - B. Tissue viscous resistance
- II. Positive and negative pressure breathing
- III. Intra-alveolar pressure during inspiration & expiration
- IV. Intra-pleural pressure during inspiration & expiration

OBJECTIVES: After attending the lecture, the student should be able to perform the following tasks

1. List the forces of non-elastic resistance associated with the respiratory system. 469
2. Define airway resistance and know the importance of the radius of a tube in determining its resistance. 163-164, 471-472
3. Describe the distribution of resistance in the respiratory tract.
4. Explain the difference between positive and negative pressure breathing. 522-523
5. Know why airway resistance is a dynamic property. Contrast airway resistance during inspiration & expiration and explain the difference. 518-519
6. Describe intra-alveolar pressure changes during inspiration & expiration and relate those changes to airway resistance. (Fig. 37-2)
7. Describe intra-pleural pressure changes during inspiration & expiration and relate those changes to lung compliance and airway resistance. (Fig. 37-2).
8. Using lung compliance curves combined with dynamic intra- pleural pressure loops, describe the changes in lung compliance, lung volumes and airway resistance associated with: 516- 520
 - A. Asthma
 - B. Emphysema
 - C. Fibrosis
 - D. RDS.
9. Interpret the following:
 - Obstructive disorders affect the ability to exhale.
 - Restrictive disorders affect the ability to inhale.

VENTILATION-PERFUSION RATIOS

(Lecture 7)

Lecture Outline

- A. Distribution of ventilation & perfusion.
- B. Hypoxemia resulting from ventilation-perfusion inequalities

OBJECTIVES: After attending the lecture, the student should be able to perform the following tasks

1. List the functional components contributing to venous admixture. 492-494 and Fig. 40-2
2. Describe & explain normal difference in ventilation & perfusion between the apex & base of the lungs. 477- 480, 492- 494
3. Explain how ventilation-perfusion inequalities will affect the composition of alveolar gases, thus generating hypoxemia.
4. Draw & explain the PO_2 - PCO_2 , V/Q diagram. Show the following points at the curve (PO_2 & PCO_2). (Fig. 39-11)
 - Normal V/Q = 0.8 (4 lit per min/5 lit per min)
 - V/Q = Zero (normal perfusion occurs without ventilation) ... *Shunt unit*.
 - Physiologic shunted blood (lung base and venous admixture).
 - V/Q = ∞ (normal ventilation occurs without perfusion) *dead space unit*.
 - Physiologic dead space (lung apex).
 - Severe hemorrhage.
 - Pulmonary embolism. 459
 - Physiologic Dead Space
 - *Silent unit*...no ventilation and no perfusion.

Accordingly, lung disorders are classified into two categories: 1. Shunt-producing disease (V/Q less than 0.8) or 2. dead-space- producing disease (V/Q greater than 0.8).

5. Understand the origin of these two equations:

- Physiological dead space (V_D):

$$V_D = \left[\frac{PACO_2 - PECO_2}{PACO_2} \right] * V_T$$

- Physiologic shunted blood (Q_{ps}) :

$$Q_{ps}/Q_t = (C_{iO_2} - C_{aO_2}) / (C_{iO_2} - C_{vO_2})$$

6. Explain why there is normally no difference between the partial pressure of carbon dioxide in alveolar air & arterial blood (why PaO_2 is affected & not $PaCO_2$)? 495-504.
7. Explain what is meant by oxygen is perfusion-limited.

GAS EXCHANGE

(Lecture 8)

Chapter 39

Lecture Outline:

- I. Explanation of total and partial pressures
- II. Partial pressures of gases in inspired, alveolar, expired, arterial, interstitial fluid and mixed venous blood
- III. Changes in alveolar composition with hyper-and hypoventilation.
- IV. Respiratory gas exchange ratio (respiratory quotient)
- V. Diffusion capacity of the lung.

OBJECTIVES: After attending the lecture, the student should be able to perform the following tasks

1. Explain what is meant by the partial pressure of a gas in a gaseous mixture, how it is calculated?
2. Write Henry's law.
3. Write the equation relating flow of gas across a respiratory membrane, driving force (gas partial pressure difference), and permeability.
4. Write the equation relating diffusion coefficient of a gas, solubility of a gas and molecular weight of a gas.
5. Fill the following.

	<u>Gas</u>	<u>Solubility</u>	<u>Diffusion Coefficient</u>
--	------------	-------------------	------------------------------

- | | | | |
|----|-----------------|--|--|
| 1. | O ₂ | | |
| 2. | CO ₂ | | |
| 3. | CO | | |

6. List the partial pressures of O₂, CO₂ in: (Table 39-1, Fig. 39-6).
 - A. Dry atmospheric air
 - B. Humidified inspired air
 - C. Anatomic Dead Space at The End of Inspiration.
 - D. Alveolar air
 - E. Mixed expired air
 - F. Anatomic Dead Space at The End of Expiration
 - G. Arterial blood
 - H. Peripheral tissue interstitial fluid
 - I. Intracellular fluids.
 - J. Mixed venous blood
7. Describe the changes in alveolar, expired, and arterial partial pressures of O₂ and CO₂ during:
 - A. Hyperventilation.

B. Hypoventilation.

8. Draw the alveolar ventilation- PO_2 alveolar curve. (Fig 39-4).
9. Draw the alveolar ventilation- PCO_2 alveolar curve. (Fig 39-5).
10. Write the equation relating the alveolar P_{ACO_2} , CO_2 production per minute, V_{CO_2} production and alveolar ventilation... (Fig. 39-5)...
$$P_{ACO_2} = (V_{CO_2}/V_A)$$
11. Write the equation relating the alveolar P_{AO_2} , O_2 consumption per minute, and alveolar ventilation... $P_{AO_2} = P_{IO_2} - (V_{O_2}/V_A)$.
12. Explain how gas tensions in mixed arterial blood come about, taking in consideration the variation in VA/Q in individual pulmonary sections and venous admixture.
13. Describe the structure (histology) of the alveolar-capillary (respiratory) membrane.
14. Define diffusion capacity of the lung (D_L) for O_2 (D_{LO_2}).
15. Write the equation relating flow of gas across a respiratory membrane, D_L , and a gas partial pressure difference.
16. State the different factors affecting D_L (diffusion coef, area, thickness ...etc).
17. Define and contrast the diffusion capacity of the lung for O_2 , CO_2 , and CO . Understand why only CO can be used to calculate such capacities.

GAS TRANSPORT

(Lecture 9)

Chapter 40

Lecture Outline

- I. Oxygen transport
 - Oxygen carrying capacity
 - Oxygen dissociation curve
 - Changes in affinity of hemoglobin for oxygen
 - Carboxyhemoglobin
 - Dissolved Oxygen
- II. Carbon Dioxide Transport
 - Reaction involving carbon dioxide
 - Means of transporting carbon dioxide
 - Bicarbonate
 - Carbamino compounds
 - Dissolved carbon dioxide
 - Chloride shift
 - Carbon dioxide dissociation curve

OBJECTIVES: After attending the lecture, the student should be able to perform the following tasks

1. Understand the factors affecting the exchange of gases between blood and other compartments such as lungs and tissues. Figs. 40(1-7).
2. What are the physiological advantages of Hb being inside RBCs and not in plasma. 413
3. Describe the structure of hemoglobin. What is meant by; hemoglobin is an allosteric protein. 417-418 (+ biochemistry course).
4. List the means by which O₂ is transported in the blood. Which is the major transport form for O₂? (Fig 40-9).
5. Calculate the arterio-venous difference of the dissolved O₂.
6. Define oxygen carrying capacity, saturation, and content of blood.
7. Draw and understand the relationship between saturation, O₂ content, and O₂ tension (PO₂) of blood. Figs. 40 (8-9).
8. Discuss the significance of the "plateau" portion versus the "steep" portion of the oxyhemoglobin dissociation curve. (Fig.40-8).

9. Describe and explain the effect of pH, PCO_2 , temperature, and 2,3 DPG on the oxyhemoglobin dissociation curve (Bohr effect). (Fig. 40-10).
10. Explain the significance of the differences in adult and fetal hemoglobin. 1005-1007.
11. Discuss the oxygen therapy in the different types of hypoxia 520-521.
12. Understand why O_2 excess can be toxic, and why CO poisoning can be lethal? 536-537, 1027
13. List the three ways that CO_2 can be transported in the blood. Which is the major transport form for CO_2 ?
14. Calculate the venous-arterial difference of the dissolved CO_2 .
15. State the location and function of carbon anhydrase.
16. Plot CO_2 concentration as a function of PCO_2 (CO_2 dissociation curve and the Haldane effect). (Fig. 40-15).
17. Describe the chloride shift.
18. Draw a diagram illustrating the uptake of CO_2 and the liberation of O_2 in systemic capillaries. (Fig.40.5).

The affinity of Hb is defined by the PO_2 required to produce 50% saturation (P_{50}) and is measured in modern laboratories. Normal P_{50} is 27 mmHg. Shift of Hb- O_2 curve to the right increases P_{50} and Shift of Hb- O_2 curve to the left decreases P_{50} .

CONTROL OF BREATHING

(lecture 10)

Chapter 41

Lecture Outline

- I. The respiratory "controller"
- II. Respiratory centers
Medullary dorsal and ventral respiratory groups
Pneumotaxic and apneustic center.
- III. Spinal cord integration
- IV. Pulmonary receptors
Stretch receptors of the Hering-Breuer reflex.
Irritant receptors.
- V. Other peripheral input
Proprioceptors
Baroreceptors
- VI. Peripheral and central chemoreceptors
- VIII. Ventilatory responses to altered PO_2 , PCO_2 , and pH.
- IX. Ventilation during exercise.
- X. Ventilation at high altitude.

OBJECTIVES: After attending the lecture, the student should be able to perform the following tasks

1. Describe the functional characteristics of the different respiratory centers in the medulla and pons (briefly).
2. Describe the ventilatory response to changes in arterial PO_2 , PCO_2 , or pH. Indicate the sensitivity of the respiratory system to such changes.
3. Under normal physiological conditions, which is more important in controlling the respiratory system...is it the PO_2 or the PCO_2 and why ?
4. Describe the Hering-Breuer "inflation reflex" and the influence of irritant receptors on ventilation.
5. In COPD patient, administration of pure oxygen is dangerous !!!?
6. State the mechanisms stimulating ventilation during a week of altitude acclimatization. Compare the immediate and chronic changes when reaching a high altitude. 527-530
7. Understand how O_2 consumption changes with exercise. (Figs. 20-2, 41-9, 41-10)
8. Speculate on the likely mechanisms driving ventilation during exercise. 1036-1037.
9. Draw the interstitial fluid PO_2 -Blood flow curve, under normal, low, and high O_2 consumption. (Fig. 40-4)
10. Draw the interstitial fluid PCO_2 -Blood flow curve, under normal, low, and high metabolism. (Fig. 40-7)
11. What is maximum oxygen consumption (VO_{2max}).
What limits VO_{2max} ? 1036-9
12. What is O_2 debt. 861.

LECTURE 11
Pulmonary Function Tests (PFT) And Its
Application To Respiratory Physiology
(Lecture 11)

- PFT: cannot make diagnosis but the effect of the disease.

LECTURE OUTLINE

1. Why we do pulmonary function tests (PFT)?
2. What are the major categories of PFT (e.g. ventilatory & gas analysis)?
3. List the ventilatory function tests used to detect increases in airway resistance.
4. Describe and explain the relationship between maximal expiratory flow rate (Peak Flow Rate) and lung volumes.
5. Again, understand the origin of this equation
- Physiologic shunted blood (Qps) :
$$Qps/Q_t = (C_{iO_2} - C_{aO_2}) / (C_{iO_2} - C_{vO_2})$$
6. Example of PFT in two major pathophysiological disorders affecting the respiratory system:

HINTS:

Why to do PFT?

1. Aid in diagnosis of lung disease.
2. Monitor the progress of lung disease (mine workers).
3. Response to treatment.

Categories:

1. Ventilatory functions (mechanicals).
 - Volumes under static of dynamic conditions.
 - Different pressures.
2. Gas Exchange:
Gas analysis in:
 - Expired air
 - Blood (P_{aO_2} , PCO_2 , pH)

Spirometry:

Spirometry is used to measure the rate of airflow during maximal expiratory effort after maximal inhalation. It can be useful in differentiating between obstructive and restrictive lung disorders. In asthma (an obstructive lung disorder) the forced expiratory volume in 1 second (FEV1) is usually decreased, the forced vital capacity (FVC) is usually normal and the ratio FEV1/FVC is decreased. In restrictive disorders the FEV1 and FVC are both decreased, leaving a normal FEV1/FVC.

Spirometry measurements are usually done before and after administration of a β_2 agonist. Reversibility with the use of a bronchodilator is

defined as an increase in FEV1 of 12% or 200 ml. Patients with severe asthma may need a short course of oral steroid therapy before they demonstrate reversibility.

	<u>Obstructive Pattern</u> affect the ability to exhale	<u>Restrictive Pattern</u> affect the ability to inhale.
RV	↑	↓
FRC	↑	↓
TLC	N ↑	↓
VC	N ↓	↓
*FVC	N ↓	↓
FEV _{1.0}	↓	N ↓
FEV _{1.0} /FVC	↓	N ↑
MMFR	↓	N ↓
CV	↑	-
P _a O ₂	↓	N ↓ (Exercise)
P _a CO ₂	↑	N ↓
pH	↓	N ↑

***FVC (Forced Vital Capacity)** -- This is the total volume of air expired after a full inspiration. Patients with obstructive lung disease usually have a normal or only slightly decreased vital capacity. Patients with restrictive lung disease have a decreased vital capacity.

FEV1 (Forced Expiratory Volume in 1 Second) -- This is the volume of air expired in the first second during maximal expiratory effort. The FEV1 is reduced in both obstructive and restrictive lung disease. The FEV1 is reduced in obstructive lung disease because of increased airway resistance. It is reduced in restrictive lung disease because of the low vital capacity.

FEV1/FVC -- This is the percentage of the vital capacity which is expired in the first second of maximal expiration. In healthy patients the FEV1/FVC is usually around 70%. In patients with obstructive lung disease FEV1/FVC decreases and can be as low as 20-30% in severe obstructive airway disease. Restrictive disorders have a near normal FEV1/FVC.

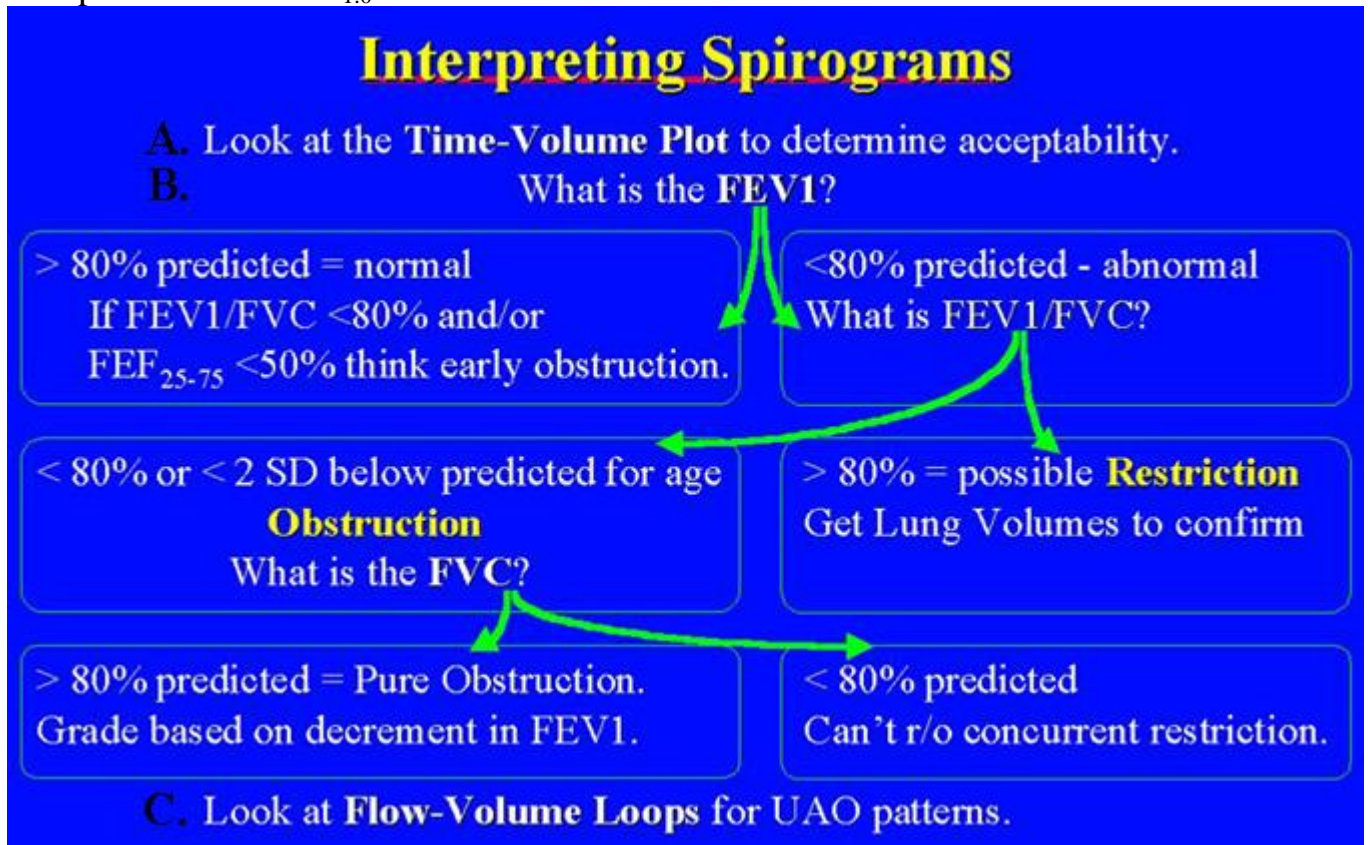
FEF25-75% (Forced Midexpiratory Flow Rate) -- This is the average rate of airflow during the midportion of the forced vital capacity. This is reduced in both obstructive and restrictive disorders.

DLCO (Diffusing Capacity of the Lung for Carbon Monoxide) -- Carbon monoxide can be used to measure the diffusing capacity of the lung. The diffusing capacity of the lung is decreased in parenchymal lung disease and COPD (especially emphysema) but is normal in asthma.

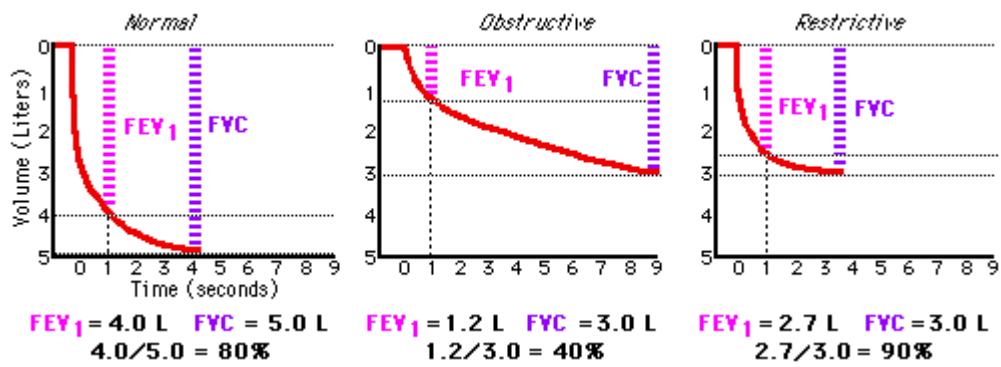
Closing volume (CV) is the volume of air that can be exhaled after the gravitationally dependent airways have closed down. The point at which the closure begins during expiration is called the closing point which is normally reached near to residual volume. If its reached before the end of normal V_T , then the V/Q ratio falls sharply. By the mid-forties, CV equals FRC in the lying position and by the mid-sixties it equals FRC in the erect position. It increases in smokers, pulmonary congestion, pulmonary edema, chronic bronchitis, and excessive bronchial secretions. Any condition which interfere with diaphragmatic movement such as, tight clothing, obesity, pregnancy, ascites, phrenic paralysis, obesity, pneumothorax.

Examples:

Interpretation of $FEV_{1.0}$



In an obstructive condition, however, such as asthma, bronchitis or emphysema, the forced vital capacity is not only reduced, but the rate of expiratory flow is also reduced. Thus, an individual with an obstructive defect might have a forced vital capacity of only 3.0 liters, and in the first second of forced expiration, exhale only 1.5 liters, giving a $FEV1/FVC$ of 50%. With a restrictive disease, such as fibrosis, forced vital capacity is also compromised. However, due to the low compliance of the lung in such conditions, and the high recoil, the $FEV1/FVC$ ratio may be normal or even greater than normal. For example, a patient with a restrictive condition might have a FVC of 3.0 liters, as was seen in the obstructive cases, but the FEV1 might be as high as 2.7 liters, giving a $FEV1/FVC$ ratio of 90%.



FEV₁ values (expressed as a percentage of predicted) may classify the severity of the COPD

60% - 79% predicted: MILD COPD
40% - 59% predicted: MODERATE COPD
Less than 40% predicted: SEVERE COPD

Dr. Yanal Shafagoj