Respiratory system physiology

sheet handout slides

Number	4
Doctor	Yanal
Done by	Abdulla Al-Zibdeh
corrected by	Husam Al-Jabiry

Introduction

Last time, we said that pulmonary diseases can be classified into 3 entities:

- Obstructive diseases: difficulty in exhalation; 70% of respiratory diseases.
- Restrictive diseases: difficulty in inhalation; difficulty in inflation 20-25%.
- Vascular: 5-10% of respiratory diseases; problem in oxygen diffusion across the respiratory membrane.

In this sheet, we will discuss the pathogenesis of COPD, the tests used to diagnose pulmonary diseases and the analysis of their results.

Pathogenesis of Obstructive Diseases

COPD has two forms; chronic bronchitis and emphysema. These two forms overlap; most chronic bronchitis patients have some emphysema, and vice versa. Remember that cigarette smoking is a major cause of COPD.

Pathogenesis of chronic bronchitis

Smoking involves the inhalation of tar. Mucous is secreted in response to the irritation of tar (which contains nicotine) to goblet cells and they start secreting more mucus. Furthermore, nicotine inhibits the cilia of the respiratory tract. The main role cilia play in the respiratory tract is the function of mucous escalation. So, with nicotine, this function is lost, resulting with the accumulation of mucous in the small airways, obstructing them. Mucous is a protein; it attracts bacteria, which results with recurrent infections. (Notice that the obstruction here is from inside.)

To diagnose chronic bronchitis patients, they have to have productive cough with sputum daily for 3 months, for 2 successive years. This disease is irreversible.

Pathogenesis of emphysema

Emphysema is also irreversible, involving obstruction caused externally. Nicotine plays a major role here, too. Normally, elastic fibers in the interstitial space keep the small bronchioles open by stretching them. Inhaled Nicotine inhibits anti-proteases (anti-proteases are good☺; anti-elastase is an example; proteases are bad☹; elastase is an example). This leads to the digestion of the elastic fibers, with the result of collapse (because they don't have cartilaginous support).

When inflating the normal lung, elastic fibers must be stretched, so inflation is easy in emphysema patients. However, deflation is passive normally, resulting from the recoil of elastic fibers, which, when absent, make it hard to exhale. (This is similar to what we discussed about the diaphragm movement previously; diaphragm contraction "and elastic fibers stretching" is active, while diaphragm relaxation "and fibers recoil" is passive.)

When inflation is easy, lung would be able to accommodate more air, resulting with a higher TLC. And when deflation is hard, VC gets smaller. And this is what is seen in COPD patients. Remember that stopping smoking stops further destruction, but it does *not* reverse the existing damage.

Pathogenesis of bronchial asthma

The wall of the bronchial tree contains small muscles and goblet cells. In bronchial asthma, the wall hypersensitivity renders it vulnerable to irritation, which results with smooth muscle contraction and increased goblet mucous secretion.

Bronchial asthma can be classified into:

- Extrinsic: irritant from outside
- Intrinsic: irritation produced inside
- Exercise-induced asthma

Bronchial asthma drugs

Asthmatic patients are given the following drugs (bronchodilators):

- β2 agonists: Salbutamol or Albuterol (Ventolin inhalers)
- Mucolytic drugs: because water is reabsorbed from the bronchial lumen, leaving dry mucous
- Antibiotics: prophylaxis
- Asthma emergencies: treated with subcutaneous adrenaline

Notice that cough suppressants are contraindicated for any productive coughing; including asthmatic patients. That is because coughing allows to get rid of mucous and sputum. (Cough suppressants are also contraindicated for children (always considered productive cough); they are only useful for dry cough.)

00:00 – 10:00

COPD and Cor pulmonale

Area of diffusion

In emphysema, the destruction of alveolar walls transforms the affected groups of alveoli from several small spheres to one big "ball". As a consequence, diffusion surface area decreases, resulting with decreased arterial oxygen (COPD and hypoxemia).

Vascular resistance

In addition to the destruction of the alveolar walls, capillary beds, which are present in the same area, also get destructed. This destruction reduces the total cross-sectional area of the capillaries. And because

vascular resistance is inversely proportional with (area) ^{2}, the resistance of the pulmonary circulation increases.

Pulmonary hypertension

Normal pulmonary systolic pressure = 25 mmHg
Normal pulmonary diastolic pressure = 8 mmHg
Mean pulmonary pressure = 1/3 systolic + 2/3 diastolic
= 14 mmHg

Remember that blood is ejected from the right ventricle into the pulmonary trunk, from which blood passes towards the pulmonary capillaries and then to the pulmonary veins. And because cardiac output (CO) is equal to the pressure difference over the resistance, increased pulmonary vascular resistance requires more pressure difference for CO to remain constant (CO = 5 normally). In this case, mean pulmonary artery pressure may reach 28 mmHg (normal is 14 mmHg). Now, the right ventricle has a bigger afterload; the elevated pulmonary pressure, to work against. (Afterload: load after the initiation of ventricular contraction; high pressure is bad and low pressure is also bad.)

Hypoxemia and vasoconstriction

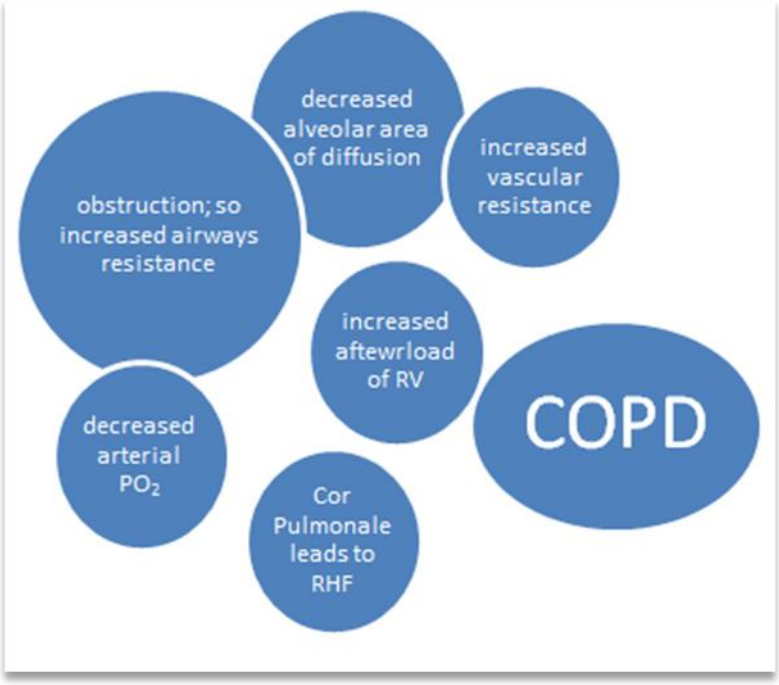
Hypoxemia in the systemic circulation leads to vasodilation (local vasodilators: increased PCO_2, decreased PO_2, increased $[H^+]$, adenosine secretion, increased [K], increased osmolarity of ECF , etc.). However, hypoxemia in the pulmonary circulation results with vasoconstriction. The physiological significance behind that is to not send blood to the obstructed area which has less oxygen. But the problem emerges when hypoxemia is everywhere. This vasoconstriction leads to pulmonary hypertension; even with no capillary bed destruction.

So, any lung disease that results in decreased oxygen PP results in vasoconstriction in the lung and Cor pulmonale.

To sum up, smoking results with antiproteases inhibition, and more action by proteases. Proteases destruct alveolar walls and capillary beds, decreasing capillary cross-sectional area and so increasing vascular resistance. To compensate, pulmonary artery pressure increases, which means increased the right ventricular afterload. The end result is Cor pulmonale; which is described as right ventricular dilatation with/without right ventricular failure due to pulmonary disease. Cor pulmonale is not restricted to obstructive diseases; any diseases that results with decreased oxygen partial pressure can end up in Cor pulmonale (hypoxemia and vasoconstriction). But since obstructive diseases are more common, Cor pulmonale is usually caused by them.

10:00 – 20:00

In this figure, we can notice the outcomes that are associated with cigarette smoking. Note that all these are irreversible. (Normal alveolar surface area = 50 – 100 m^2.)



Pulmonary Diseases; *tests and diagnosis*

Forced expiratory volume

For patients with deflation problems, we need to test their expiration. To do so, we do the following: After taking deep inspiration (from TLC; usually 6L), the person is asked to exhale forcefully to the end (to RV; 1L). Normally, 6 seconds are required to exhale all the TLC to RV.

TLC – RV = vital capacity (VC)

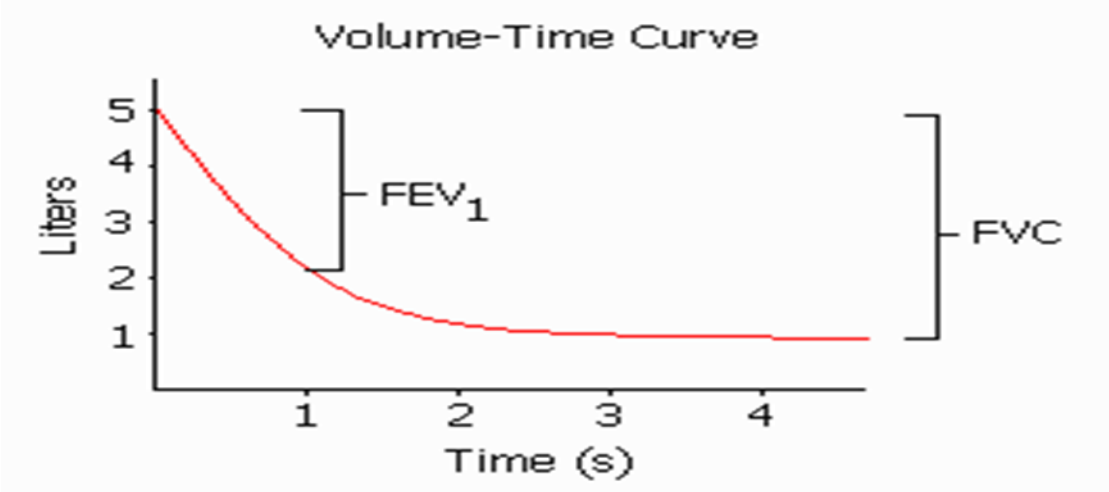
Normally: 6 – 1 = 5L

VC vs. FVC

In exhaling the vital capacity, the person exhales in a relaxed manner for longer time. On the other hand, to exhale the forced vital capacity, the person exhales as fast as possible. In healthy individuals, VC equals FVC, but in patients with obstructive diseases, some air trapping occurs beyond obstruction while exhaling FVC; in this case, VC is more than FVC.

$FEV_{1.0}$ results

Forced expiratory volume in the first second ($FEV_{1.0}$) is important for determining the degree of obstruction.

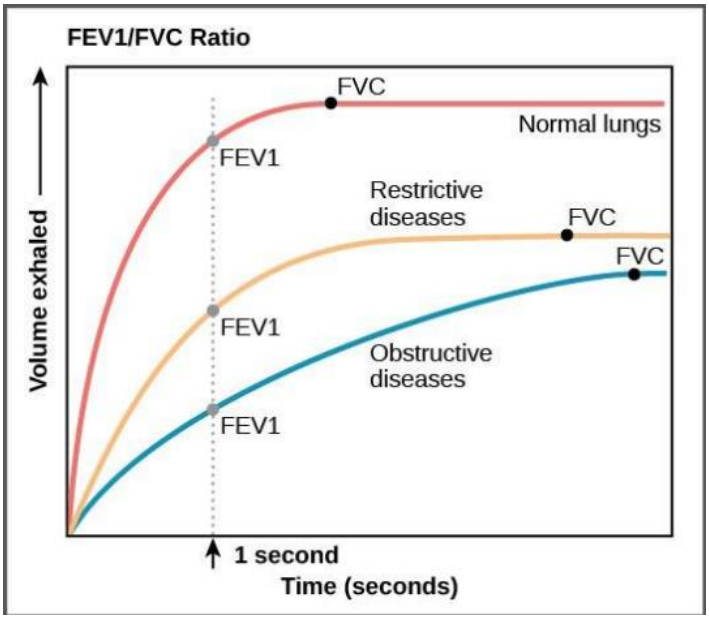


The normal or *predicted* value of $FEV_{1.0}$, like many other test standards, is determined according to the person's data, which include: age, weight, height and gender.

20:00 – 30:00

The observed $FEV_{1.0}$: predicted $FEV_{1.0}$ ratio of the total FVC can be analyzed as follows:

Percentage of predicted $FEV_{1.0}$	Description
80-100%	Normal
60-79%	Mild COPD
40-59%	Moderate COPD
<40%	Severe COPD



$FEV_{1.0}$/FVC ratio

- The normal person can exhale 80% of FVC in the first second (4 out of 5L), and 20% during the last 5 seconds.
- Mild COPD patients exhale 60% (3 out of 5L) in the first second (20% less than normal).
- Patients with restrictive diseases (such as fibrosis) cannot fully inflate the lung (decreased lung stretchability, stiffness and rigidity of the lung). In this case, TLC, VC, $FEV_{1.0}$, FRC and RV are all decreased (high tendency to collapase).

  Both $FEV_{1.0}$ and FVC are decreased so the ratio remains normal or above (≥ 80%).

- In obstruction cases, the curve is shifted to the right; $FEV_{1.0}$ is decreased, but FVC is normal, so the ratio is decreased.

Test Sensitivity

When the $FEV_{1.0}$:FVC ratio is 60%, then the difference from normal is 20%. But this 20% is not a good representative of the obstruction and the increased resistance in this case. That is because, if we assume that VC = 4L, then we will notice that:

- Exhalation of the first liter is easy for both the healthy individual and the diseased individual that has the obstruction
- Exhalation of the last liter is relatively hard for both the healthy individual and the diseased individual

So, in order to remove this "results diluents" and increase the test sensitivity, we remove the first and last liters of the 4 liters in our example. To generalize that, we take the middle 50% expiratory flow rate, which is also called forced expiratory flow 25–75% (FEF 25-75% or Mid-Expiratory flow rate). In our example, the FEF 25-75% = 50% of normal! This gives a pure image about the obstruction the patient has. A more sensitive test, the closing volume, will be explained later in the course.

30:00 – 40:00

Summary	
Obstructive disease	Restrictive disease
increased TLC	Decreased TLC
Low $FEV_{1.0}$ Because of the obstruction	Low $FEV_{1.0}$ Because the original volume is smaller
$\frac{FEV1.0}{FVC}$ Less than 80%	$\frac{FEV1.0}{FVC}$ More than or equal to 80% Because the decrease in FVC is more than the decrease in $FEV_{1.0}$ High tendency to collapse

Maximum expiratory flow rate

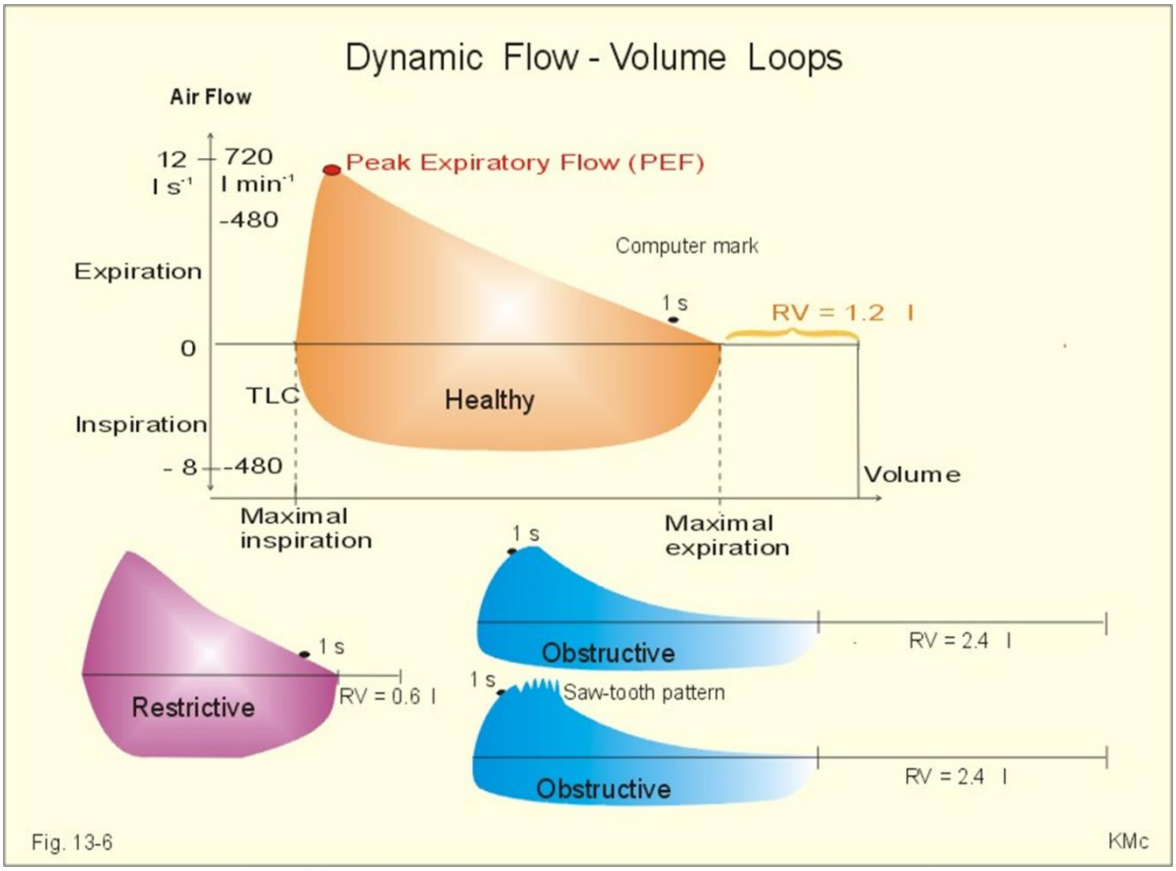
To test for peak or maximum expiratory flow rate, the person is asked to exhale forcefully after taking a deep inspiration, and then to inhale again, forcefully. Remember that:

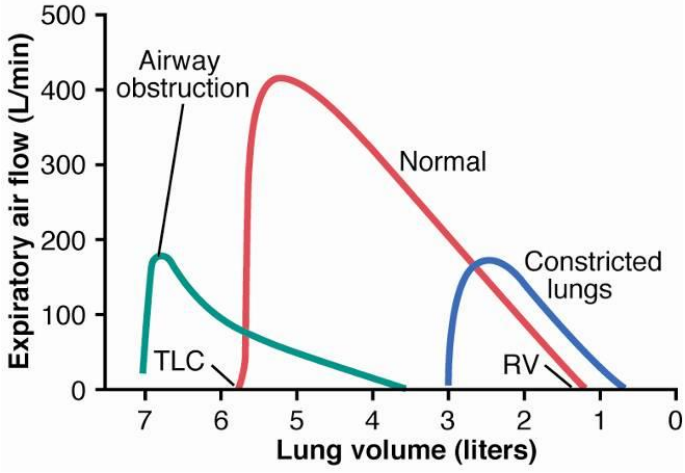
$$V_{max} = \frac{\Delta y}{\Delta x}$$; the maximum slope

The bigger the volume you start exhaling from, the faster the maximum expiratory rate. To reach that, the person takes a deep breath; filling the lungs to their maximum (TLC). Maximum flow rate can reach 8L per second.

Notice the figure bellow. In COPD patients, the maximum expiratory flow rate is lower than normal, and the TLC (starting point) is higher than normal; so the graph is shifted to the left. Note that the overall shape of the curve in this case differs than the normal curve.

In restriction, however, the starting point (TLC) is less than normal, and the peak is lower than normal; because the volume is less than normal (normal person has a higher V_{max} because he starts with a higher volume). Despite that, if the healthy person starts from the same starting point as the restrictive disease patient, the patient with restriction would have higher maximum expiratory rate (because of the huge collapsing force). So, with restriction, the curve shape resembles the normal curve, with less TLC (starting point), less RV (end point), lower peak and *higher-than-normal flow rate at comparable volumes*.





Notice that the x-axis values are in descending manner. Also notice that the starting x value is TLC, and the end x value is RV.

GOOD LUCK

… But I refuse to falter in what I believe