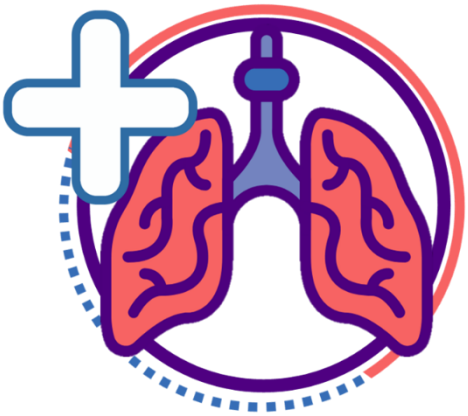

RESPIRATORY SYSTEM

Physiology

Sheet Slide

Number:	-4
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Hypoxemia is an abnormally low level of oxygen in the blood ,which might be due:

1. Airway resistance is greater than normal
2. Lung is rigid (stiff) can't be inflated
3. The membrane is thick due to pneumonia or other causes like in the case of Respiratory Distress Syndrome

The work of breathing

-Muscles utilize 2%-3% (approximately 5%) of total ATP in our bodies ,this utilized ATP helps the muscles such as the diaphragm and the intercostal muscles to contract which in turn leads to inhalation . On the other hand, expiration requires relaxation of the muscle, which doesn't require ATP utilization.

-Work of breathing is how much ATP is utilized to inflate the thorax and the lung because we are talking about two balloons over here it's not just inflating the lung, but we also have to inflate the thorax, and this requires more energy than inflating one balloon. So, the work of breathing is 50% to inflate the thorax and 50% to inflate the lung for example.

Work= $\Delta p \times \Delta v$ = difference in pressure x difference in volume

Δp is small, about -1 mmHg is enough

Δv is about 0.5 liters

If Δp became -10 mmHg just to inhale air, this indicated a problem in breathing especially that the patient is unable to exhale the air as well, in this case expiration requires +10mmHg and becomes an active process that requires ATP. The work of breathing increases because we need to overcome to two types of forces:

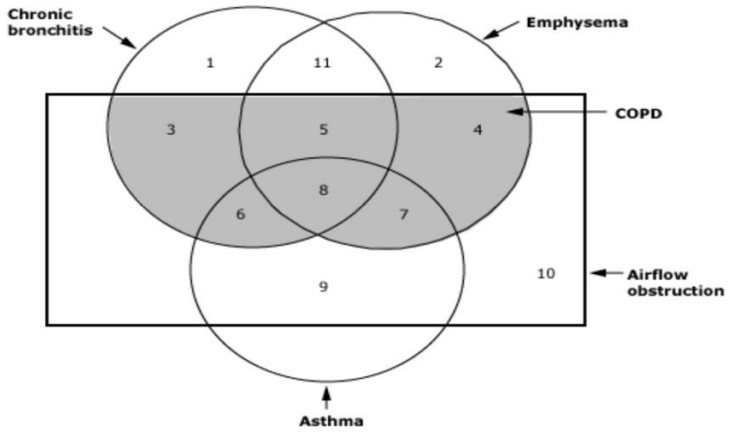
1. **Elastic forces (static force):** to keep a balloon inflated you need to do some work otherwise it will deflate.
   70% of the total work of breathing is devoted to overcome elastic forces.
   elastic forces are of two types:
   A) 1/3 (30%): to overcome elastic forces exerted by elastic fibers, you need to stretch them.
   B) 2/3 (70%):to overcome surface tension, collapsing force.
2. **Non-elastic forces (dynamic):** these forces manifest only during the movement of air.
   30% of the total work of breathing is devoted to overcome non-elastic forces.
   note: if there is no air moving then the total work of breathing is devoted to only overcoming elastic forces.
   For example: in this example the muscle contraction is similar to work of breathing. If you want to move an object you have to overcome its weight plus the friction. The friction is only manifested if there is movement. If there is no movement there is no friction.
   So, if there is inhalation or expiration
   non-elastic forces are two types:
   A)80%: airway resistance seen only when air is moving during breathing
   B)20%: tissue viscose resistance.
   For example if you have a putty since it's not elastic if you stretch it would require work and to compress it will require work as well. So, during inspiration you would spend energy to overcome tissue viscosity resistance and airway resistance, you would also require work during expiration as well since it's not elastic.

AIRWAY RESISTANCE

- Airway resistance is negligible, and the proof is that we only require 1mmHg driving force. To inhale 5 liters, you require a driving force of -1mmHg in 1 minute. On the other hand, in the vascular system we required a difference in pressure of 100 because the total peripheral vascular resistance is 100 times more than the airway resistance.
  The main contributor of airway resistance is small airways because:
  1. they have small lumen.
  2. they lack cartilage support.
  3. they are easily obstructed.
  4. their smooth muscles might contract and cause bronchoconstriction.
  5. the wall becomes thick due to chronic inflammation.
  6. Occurrence of edematous changes here due to inflammatory process in the respiratory epithelium
- Obstructive airway diseases cause the airways to become narrowed or blocked making it difficult to expel air from the lungs .This results in an abnormally high volume of air being trapped in the lung after expiration which in turn leads to trapping of air and hyperinflation of lungs ; increasing the total lung capacity from 6 to 7 .
- If the patient is facing obstruction, he would mainly face it during expiration which becomes more difficult due to the increase in the intrapleural pressure which is a collapsing force .

3 diseases are going to be discussed :

1. Emphysema
2. Chronic bronchitis
3. Bronchial asthma



Most patients who have emphysema also suffer from chronic bronchitis and vice versa.
Most asthma are reversible (90%) unlike emphysema and chronic bronchitis which are irreversible in most cases and both are due to cigarette smoking.

Emphysema

Smoking nicotine will stimulate macrophages which will release digestive enzymes, elastase which will digest elastin.
In Alveoli, the cell membrane is made of 50% lipids and 50% protein so proteases released will digest proteins and you will have hyperinflated regions in the lung which have decreased surface area and the alveolar capillary bed which will decrease the routes for blood to go from the arterial side to the veins and therefore you increase vascular resistance. Since the resistance is inversely proportional to cross sectional area ; when capillary cross-sectional area decreases, vascular resistance increases.
So pulmonary vascular resistance increases due to:

1. Destruction of capillaries
2. Hypoxemia causes pulmonary artery vasoconstriction which will increase pressure

Further explanation : the blood flow=V/R; now resistance (R) increased cause there is destruction to the capillary bed. so, the heart has to put more force to pump blood, so the right ventricle will dilate and then fails this is called cor pulmonale.
cor pulmonale: abnormal enlargement of the right side of the heart as a result of disease of the lungs or the pulmonary blood vessels.

So, in emphysema we have:

1. Increased airway resistance
2. Pulmonary hypertension
3. cor pulmonale
4. decreased surface area for diffusion this causes decreased Po_2 and later increased Pco_2 arterial

To diagnose emphysema

1. pulmonary function test
2. biopsy to see destruction and know what type of emphysema it is
3. x-ray, CT scan
4. history + physical examination where you will hear wheezes.
   Note: obstruction in the upper airways you will hear stridor.
   In the lower airways you will hear wheezes.

Quick note on CVS

- resistance is a vague concept
- Poiseuille's Law measures resistance and resistance=$(8nl)/(3.141xR^4)$

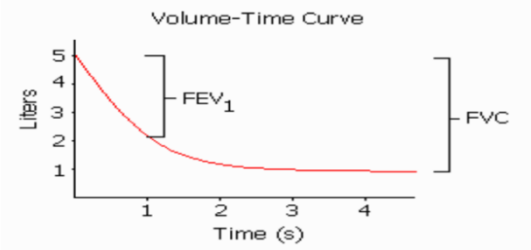
There are three conditions that should be met before you use this rule:
1) Laminar flow not turbulent, tendency of turbulence is Reynolds number.Not all areas in our bodies have laminar flow
Laminar flow means parabolic flow meaning layers low friction highest velocity in the center and lowest near the vessel wall
Laminar flow is silent, turbulent flow is noisy
Laminar changes to turbulent when there is obstruction (hits the wall)
2) Non-pulsatile so that systole flow isn't higher than diastole flow this isn't true in our body
3) Homogenous solution ex. Plasma, water. Blood isn't homogenous.

- So in conclusion we can't measure resistance we can get a hint of how high or low resistance is

Pulmonary function test

So, if a patient has a problem in expiration, he/she will be asked to fill his lungs (inhale) as much as he/she can, and this will be his/her total lung capacity (TLC=6 liters)
And then you ask him/her to empty their lungs as forcefully as they can (use all their expiratory muscle ex. abdominal muscle) and he empties 5 liters this is known as forced lung capacity.
In normal people forced lung capacity and vital lung capacity are equal, however in those who suffer from obstructive lung diseases (higher airway resistance) this is not the case since there is air trapping in the lung, so the forced lung capacity is less than vital capacity.

As you can see in this diagram in the first 1 second during forced vital capacity/forced lung capacity (forced expiration) is about 4 liters (6-2=4)
So, Forced Expiratory Volume in the first second (FEV1) is 4 liters and the rest of the volume is expired in the next 3-4 seconds.
There is a predicted FEV1 that depends on ethnicity, gender, age, weight, height… so let's say that the predicted is 4L and when tested the observed FEV1 was 4L then
observed FEV1 / predicted FEV1=100%
The observed might be less or more than the predicted, but the patient who suffers from obstruction is going to have a less observed FEV1 than predicted it can't be more.



Ranges of the ratio between observed FEV1 / predicted FEV1.
if it is more than 80% then its normal
If its 60%-79% mild COPD
If its 40%-59% moderate COPD
If it's less than 40% sever COPD

So, the pulmonary function test tells me:

1. If the patient has COPD
2. What stage is he in if COPD is present?

However pulmonary function test isn't diagnostic, you can't tell from the result that the patient has emphysema or chronic bronchitis or asthma.
After we figured out the patient has COPD (low FEV1) with pulmonary function test ,the patient is given a bronchodilator to diagnose asthma for example. The smooth muscles of bronchioles have B2 receptors which induce relaxation by epinephrine and nor epinephrine and induce contraction by acetylcholine, leukotrienes and histamine. We don't give epinephrine to test for asthma since it has wide spectrum of activity, instead we give salbutamol or albuterol which are b2 agonists after he receives these inhalers, we repeat the test and if FEV1 increased by 200 ml (or 12% increase of FEV1) this indicates reversibility. If FEV1 didn't increase, we don't say its irreversible obstruction could be due to something else like inflammation in the bronchial tree so we give him cortisone inhalers and then we retest the patient if this

didn't increase FEV1 we might start thinking that this is irreversible

Important note a patient with emphysema and chronic bronchitis is called COPD patient with reversible asthma is not a COPD patient since its more of acute attacks rather than continuous obstruction.
That's why sometimes we have to provoke asthma during the test if we don't find wheezes and FEV1 is normal FEV1/Vital Capacity is normal, but he suffers from dyspnea, it might be exercise induced asthma. So, we give him something to cause asthma for example tmt (treadmill test) similar to ischemia test we took in CVS.

Note: when you force inhale (fill the lung to the maximum) and start the exhale the first quarter (FEV1) is going to be easy in both patients with obstructive disease and normal patients and the last quarter exhaled is going to be difficult in both too. With that in mind let's say you got FEV1/FVC= 70% you might say it's not that far from normal (80%). But in reality, this patient has 2X the airway resistance of normal person so the test you did isn't sensitive so in order to get a sensitive test you have to cancel the first 25% and the last 25% and just measure the middle 50% of the vital capacity (mid expiratory rate) here you will notice that its ½ the normal. Those tests will be discussed in the next lecture.

RESTRICTIVE LUNG DISORDER

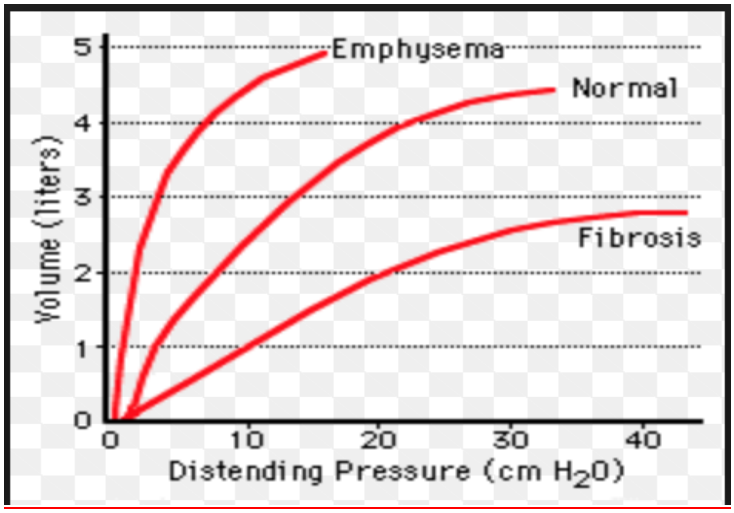
Some patients don't have problem in the airways, they have a problem in the lung itself were the lung isn't inflating , the lung is collapsing so the TLC reaches only 4L instead of 6L.
Note: in obstructive diseases we have discussed none of them affect lung capacity/ inflation they can fill their lungs with 6L.

A little comparison between obstructive and restrictive lung disorders:

	obstructive	restrictive
FEV1	3Ldue to obstruction in exhale	3Ldue to less lung capacity (no air)
FVC	4.5L	3.5L
FEV1/FVC	66% low	85% normal or high

Lung diseases are divided into 3 main types
1. Obstructive (70%)
2. Restrictive (20%-25%)
3. Vascular (5%-10%) (pulmonary hypertension)

Compliance is the change in volume per unite change in pressure
So, in a **complaint tissue** little pressure change will cause a huge volume change
In a **noncompliant tissue** a huge pressure change will cause little volume change



In emphysema, the elastic fibers which need to be stretched during inhalation, while during exhalation due to their elastic properties they regain their shape . If those elastic fibers are destroyed it becomes easy to inflate (compliance is high) but deflation is harder, so you can't empty the lung that's why they have more air left in their lungs so the curve is shifted to the left. On the other hand, those with fibrosis have hard time inflating the lung and require huge pressure change to inflate and this shifts the curve to the right

When compliance increases the lungs can't deflate while when compliance decrease the lungs can't inflate .