Respiratory system physiology

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A quick recap..

- **The work of Breathing (ATP consumption):**

  $W = \Delta P \times \Delta V$

  ✓ Normally 0.5 L (ΔV) X 5 cm H_2O (ΔP) = 0.25 J

  One Joule is equal to = 10 L X cm H_2O = J

  ✓ 50% of the work of breathing is used to expand the lungs and 50% to expand the chest wall.

- **The work of breathing is used to overcome:**

  1. Elastic forces (70% Contribution to the total work of breathing): They are under static (no-flow conditions). Two types:
     A) Elastic fibers (one third).
     B) Surface tension (two thirds).

     ✓ Basically, it's the work done to overcome lungs' tendency to collapse and to return to its resting position after being stretched during inspiration.

  2. Non elastic forces (30%) (Only present during the dynamic phase of breathing). Again, two types:
     A) 20% is attributed to tissue viscous resistance, which manifest only during tissue movement. This type of resistance, represented by frictional force (R), act against a change in shape and consistently opposes motion, whether during inspiration or expiration.
     B) 80% is due to air way resistance.

     So, the respiratory system's total pressure is comprised of:

$T_{Total} = P_{Elastic} + P_{Nonelastic}$

$P_{Elastic}$: elastic recoil P

$P_{Nonelastic}$: Is the pressure to overcome resistance to airflow.

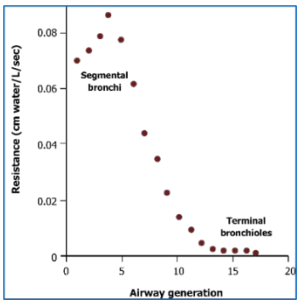
✓ Hence, we can conclude that when NO air movement takes place **$T_{Total} = E_{Elastic}$.**

• Airway resistance

– Ohm's law: Flow is **directly** proportional to the Driving force and **inversely** proportional to the Resistance.

Flow = pressure difference/ resistance = $\Delta P/R$

- ✓ ΔP: is the pressure difference between the two opposite ends of the airways: (P_{atm} - P_{alv}), and it's the driving force required to overcome the resistance.
- ✓ According to Poiseuille's law ($R = 8\eta l/\pi r^4$), Resistance is inversely proportional to the **fourth power of the radius** ($R=1/r^4$) meaning that a small change in "r" results in a significant change in R.
- ✓ Resistance is also inversely proportional to A^2 ($R=1/A^2$), where A^2 in this case represents the NET CROSS SECTIONAL AREA.
  - ➢ Resistance to airflow **is higher** in large airways despite their large radius due to less cross-sectional area compared to smaller airways (small radius) which tend to branch very extensively increasing their cross-sectional area. Thus, offering less resistance to air flow.



- ✓ **Variation** in total airway resistance primarily occurs in bronchioles, which can dilate (R↓) or constrict (↑R) under the influence of ANS, unlike large airways, why?
  - o lack of surrounding cartilage (collapsible), more smooth muscle cells.
  - o Small diameter makes them more prone to complete obstruction by any of the following:
    - Ciliary paralysis, irritation of smooth muscles and mucous accumulation (all are attributable to obstructive diseases and associated infections).
- ✓ R, when increased, is more evident during expiration rather than during inspiration.
  - ➢ That's why obstructive diseases (↑R) are often described as "hard to exhale conditions".

- Going back to ohm's low, when **resistance is increased** in a system, it leads to an **increase in the driving force** required. This **increases the demand for more ATP** to overcome the elevated resistance and maintain flow. Thus, **increasing the work**.
- If R is large then ΔP must be large too in order to keep airflow constant, and since V_T is constant, this eventually leads to increase in work.

This actually explains why systemic driving force (MAP) is greater than the pulmonary driving force, even if the blood flow is the same in both systems (5L)

- In systemic circulation, the blood has to overcome the resistance offered by the entire systemic vasculature (arteries, arterioles, capillaries, venules, veins), this extensive network of blood vessels results in higher overall resistance, which needs higher driving force =almost 100 at rest

$$\text{MAP} = \frac{2 * \text{DBP} + \text{SBP}}{3}$$

- In pulmonary circulation, the blood only needs to overcome the resistance of the pulmonary vasculature, resulting in a lower driving force (=14) and work requirement.

Note that;

- airway resistance is almost negligible constituting 1% of TPR.
- Pulmonary circulation is a low-pressure system with pressure values = 25/8 in comparison with the systemic circulation (120/80)
- systemic MAP = 7× pulmonary MAP.

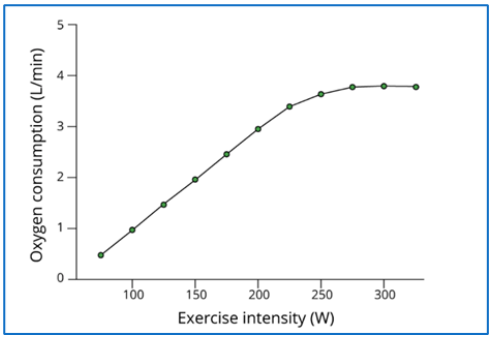
• ventilation, hyperventilation, hypoventilation

✓ ventilation = volume × frequency (respiratory rate)
- o if a person is breathing 500cc of air per breath and is taking 20 breath per minute, then their ventilation rate would be 10,000 CCS per minute.
- o **Alveolar ventilation** is useful for gas exchange (removes CO2, delivers O2), **Dead space ventilation** is wasted ventilation.

✓ Adequate ventilation ensures a sufficient supply of oxygen to alveoli, where oxygen is transferred to the bloodstream.
- o PaO2 is directly proportional to alveolar ventilation, and inversely proportional to oxygen consumption (VO2)

$PaO2 = V_A/VO2$

- ➢ VO2 = 250 ml at rest, =3000 ml during exercise and up to 5000ml in trained marathon runners.
- ➢ $VO2_{MAX}$ is represented by a plateau, and can be increased by increasing red muscle fibers, increasing lung capacity or diffusion capacity, allowing for higher levels of oxygen endurance.



✓ Efficient ventilation is responsible for removing CO2 produced by cellular metabolism, preventing the buildup of CO2 in the blood.
- o PaCO2 is directly proportional to rate of CO2 production (VCO2) and inversely proportional to alveolar ventilation (V_A)

$PaCO2 = VCO2 \times K / V_A$ (K is a constant= 0.863)

When VCO2= 200ml and V_A=4.2, PaCO2= 41mmHg

- What about PaCO2 and PaO2 during exercise?

Exercise demands a higher supply of oxygen to meet the increased metabolic needs of working muscles (VO2↑) and increases the CO2 production (VCO2↑)

So, a one can expect a significant change in ABGs and Alveolar composition during exercise.

What actually happens is that the body adapts to maintain a balance in ABGs, primarily driven by increased ventilation

The increased ventilation in rate and depth optimizes gas exchange in alveoli and efficiently eliminates CO2, preventing respiratory acidosis and maintaining normal or slightly decreased PaCO2 levels.

So, PACO2, PAO2, PaO2, PaCO2 remain normal during exercise.

- Respiratory exchange ratio (RER), Respiratory quotient (RQ)

✓ Is a parameter used to evaluate gas exchange efficiency during expiration, used in calculations for basal metabolic rate when estimated for CO2 production to O2 consumption.

✓ Calculated as the ratio of the volume of expired CO2 (VCO2) to the volume of O2 consumed (VO2) during a given period. RER = VCO2/VO2

✓ It's useful in assessing the substrate being metabolized for energy production, different substrates (carbohydrates, fats or proteins) have distinct RER values. For example;

- Carbohydrate metabolism: during complete oxidation the RER is close to 1
- Fat metabolism: RER is lower than 1
- Protein metabolism: RER can vary but is typically higher than fat metabolism

❖ **(this is a low yield topic, don't bother going into its details)**

Respiratory exchange ratio= VCO_2/VO_2; in carbohydrate diet=1

Fat= 0.7

Mixed diet=0.8 (200 mL CO_2 production)

- **Hyperventilation**

✓ an increase in ventilation beyond the body's metabolic needs
✓ leads to rapid removal of CO2 from the body. This causes a decrease PaCO2 below 41mmHg, and PACO2
✓ May lead to a slight increase in PaO2 due to enhanced gas exchange, but its main effect is on CO2 levels.
✓ The reduction in PaCO2 results in respiratory alkalosis, leading to an increase in blood pH.

- **Hypoventilation**

✓ A decrease in ventilation below body's metabolic needs.
✓ Causes buildup of CO2 in the body, increasing PaCO2, PACO2.
✓ May decrease PaO2 due to inadequate ventilation and gas exchange.
✓ The increase in PaCO2 results in respiratory acidosis, leading to a decrease in blood pH.

In hyperventilation, we are closer to air composition (more O_2, less CO_2) compared to hypoventilation where we're closer to mixed venous blood composition (less O_2, more CO_2).

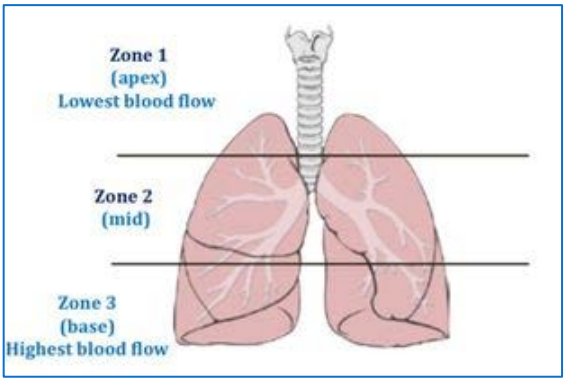
- **Ventilation to perfusion ratio V/Q**

✓ V/Q ratio: alveolar ventilation/ pulmonary blood flow
✓ is a measure used to assess **the matching** of ventilation (the amount of air reaching the alveoli) to prefusion (the blood flow reaching the alveoli) in the lungs, reflecting the harmony by which respiratory & cardiovascular systems are working.
✓ This ratio is crucial for efficient gas exchange, ensuring that oxygen is delivered to the blood and carbon dioxide is removed.
✓ Normal V/Q ratio = 1 and it yields normal PaO2 (100 mmHg) and PaCO2 (40 mmHg). So, if ventilation and perfusion become off, these numbers might not be achieved, also there might be wasted ventilation or perfusion if **they were mismatched**.

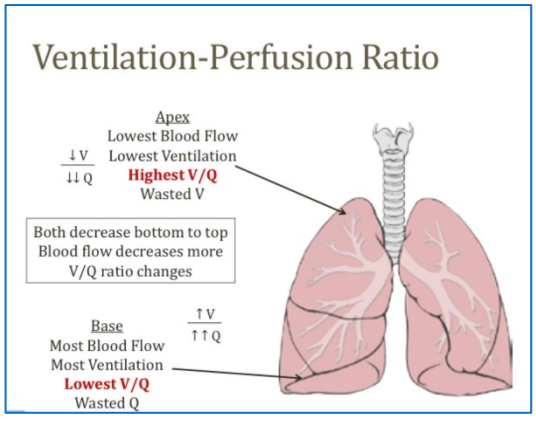
- ✓ Ventilation to perfusion mismatch (V/Q <1), happens when there's reduced ventilation relative to perfusion, and perfusion is wasted since blood is going where there's not enough O2 present. (this explains hypoxic vasoconstriction, explained in a minute)

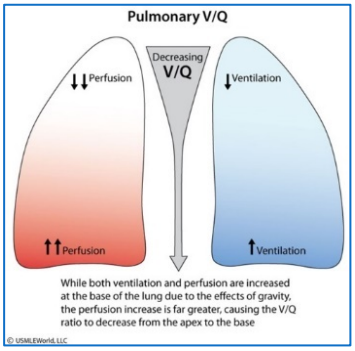
• Lung ventilation and perfusion

- ✓ In the upright position, blood flow distribution to lungs **is uneven** due to gravity. So, the lung is divided into 3 zones to describe perfusion;
  - o apex has the lowest blood flow
  - o base has the highest blood flow
- ✓ intrapleural pressure is **more negative in the apical region** (-8mmHg), causing increased lung expansion, making ventilation relatively lower.
- ✓ Intrapleural pressure **is less negative at the base**(-2mmHg), resulting in higher lung volume and better ventilation.
  - o apex has the lowest ventilation (alveoli are already inflated)
  - o base has the highest ventilation



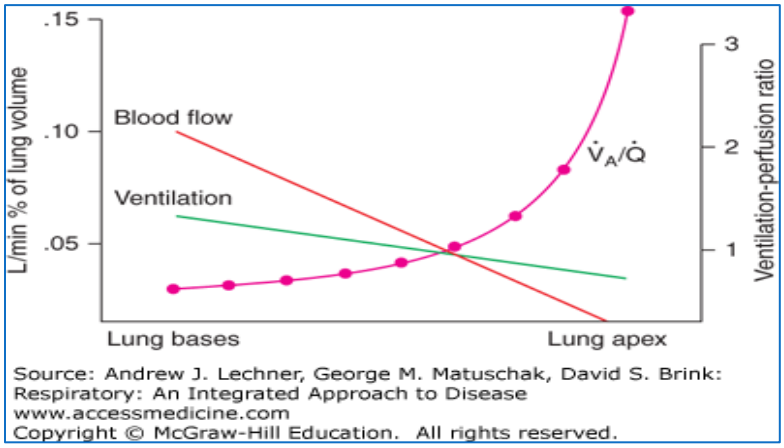
- ✓ just like ventilation and perfusion vary as you go from the base to the apex of the lung, so does the ventilation to perfusion ratio.
- ✓ While both ventilation and perfusion are increased at the base due to gravity, the perfusion increase is far greater, causing the V/Q ratio to decrease from the apex to the base.





To conclude:

- Basal ventilation is more than the apical one.
- Basal perfusion is higher than the apical.
- V/Q ratio is higher in the apical region (>1 in the apex, <1 in the base).



✓ Eventually, this will affect PO2 being the most at the apex (mixed expiratory air (130+90+90+90)/4=100mmHg).

✓ 130 mmHg from the apex while 90 mmHg from the base (1:3 contribution in expired air).

- **Control of Bronchiolar Diameter**

A. Nervous

✓ Sympathetic

o b_2 receptors dilate (mainly adrenaline).

✓ Parasympathetic

o Acetylcholine constricts bronchioles.

B. Humoral

✓ Histamine, acetylcholine >> Constrict.

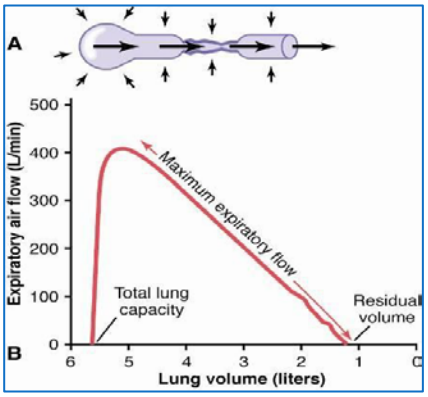
✓ Adrenergic (b_2 agonists) >> Relax.

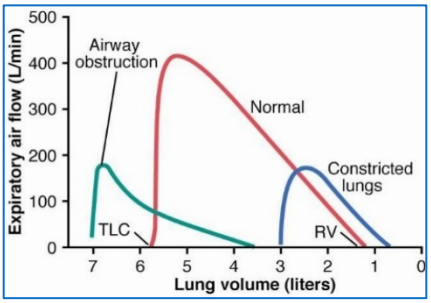
Adrenaline is secreted from the adrenal medulla which secretes 80% adrenaline and 20% noradrenaline.

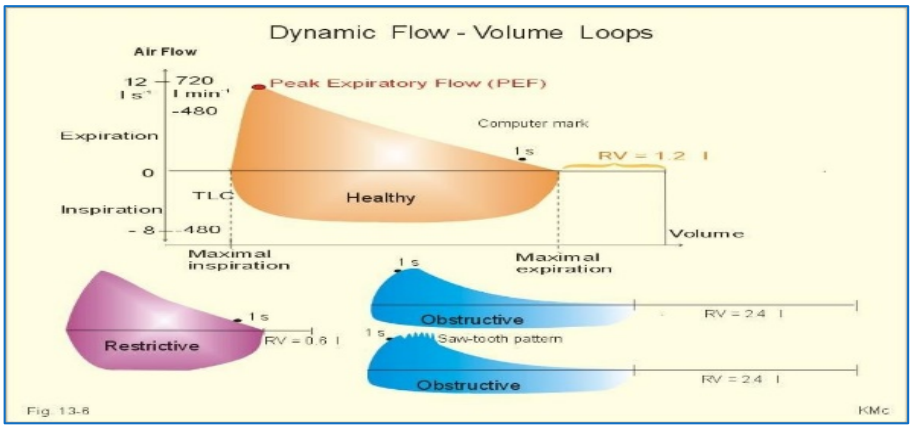
Pulmonary function tests

- We use these tests to diagnose, differentiate and determine the prognosis of different pulmonary diseases using a spirometry.
- Basically, you ask the patient to forcefully exhale and inhale and plot the results to measure the rate of airflow during **maximal expiratory effort**.

1. To assess Maximal Expiratory Flow Rate:
   - ✓ Normally, MEFR is 400L/min, at the beginning of expiration the flow rate is very high then it declines until it approaches zero.
   - ✓ **In COPDs**, TLC and RV is higher but the MEFR is lower (~200L/min); air faces more resistance in exhalation.
   - ✓ **In restrictive diseases**, the plot resembles the normal one with, except it's smaller and shifted more to the right;
     - ➢ A restrictive lung disease makes it hard for the patient to inhale so the TLC will be lower than normal, maximally 4L.
     - ➢ As forceful exhalation starts from a lower volume, the Maximum expiratory air flow will be less than normal and the RV will be also less.
     - ➢ Note that **at any volume the EFR will be higher than normal**, because the patient is still able to exhale air relatively quickly due to their lungs' high collapse tendency, but **it will never reach 400L/min as they cannot reach TLC in the first place**.

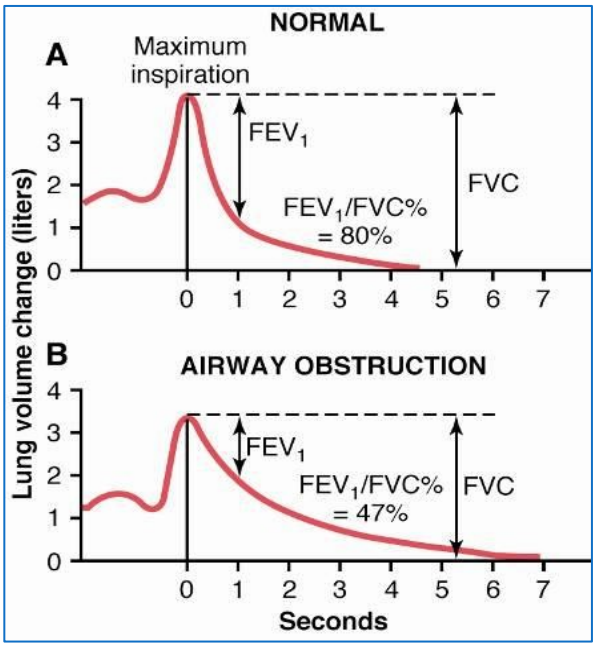






2. To compare **predicted** FEV_1, FVC and FEV_1/FVC ratio to **observed** ones:

- ✓ FEV_1: forced expiratory volume in 1 sec; the volume of air a person can forcefully exhale in the first second of a forced breath. And it's part of FVC
- ✓ FVC: forced vital capacity; the maximum amount of air you can forcibly exhale from your lungs after fully inhaling.
- ✓ Prediction is based on age, gender, height and race.
- ✓ Normally; FEV_1 is 4L and FEV_1/FVC ratio is 80% (theoretically fixing those numbers to easily compare with the observed ones).



- ✓ FEV_1 values (expressed as a percentage of predicted) may classify the severity of the COPD.

Stage	FEV_1 compared to predicted for age/ gender/ height
GOLD Stage I	$FEV_1 \geq 80\%$; normal
GOLD Stage II	$50\% \leq FEV_1 < 80\%$; mild
GOLD Stage III	$30\% \leq FEV_1 < 50\%$; moderate
GOLD Stage IV	$FEV_1 < 30\%$; severe

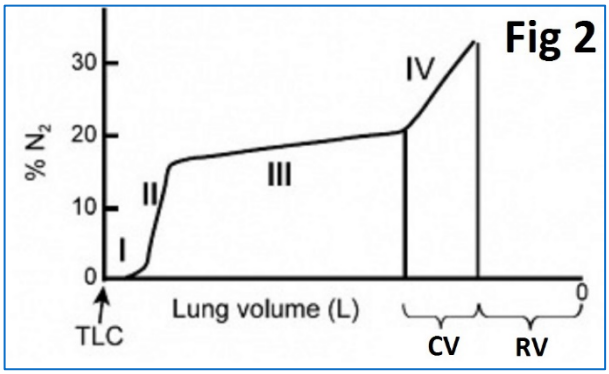
- ✓ The FEV_1/FVC ratio is used to differentiate between restrictive and obstructive diseases; >80% in restrictive diseases (normal exhalation) and <80% in obstructive ones.
  - o In obstructive diseases; lungs are unable to exhale properly so FEV_1 decreases and FVC also decreases, eventually, ratio will decrease significantly.
  - o While in restrictive ones; FVC decreases due to impaired inhalation and ratio will significantly increase.

- ✓ This test is also used to determine if the asthma is reversible or not; measurements are done before and after administration of bronchodilators (such as B_2 agonists). If 12% (200mL) improvement in FEV_1 occurs then it's reversible asthma. If not, we administer a glucocorticoid course and repeat the test to confirm irreversibility.

3. **More sensitive tests** may be performed, such as maximal mid expiratory flow, which is obtained by drawing a chord from the volume at 75% lung inflation to 25% inflation and dividing by the time. Mid expiratory flow is lower in obstructive diseases.
4. One last and **most sensitive test** is closing volume:

- ✓ Closing volume is the volume towards the end of a forced expiration, after which some airways have effectively closed and more of the expired gas comes from the relatively poorly ventilated regions of the lung (like the apex).
- ✓ So, it measures the volume of air remaining in the lungs after a slow, maximal exhalation.
- ✓ An elevated closing volume indicates that small airways closed prematurely during exhalation, and it's often associated with COPDs.

I. Zero PN_2; air from the ADS is pure oxygen (by this we can calculate ADS and it's called nitrogen washing technique).
II. Alveolar air begins to be expired.
III. ¾ of air is from the base and ¼ from the apex.
IV. Alveoli start closing and much of the air comes from the apex (high PN_2).



→ Earlier obstructions occur at the base thus leading to an increased CV.

Now, we're going to apply all this on pathology..

- ## Lung Diseases

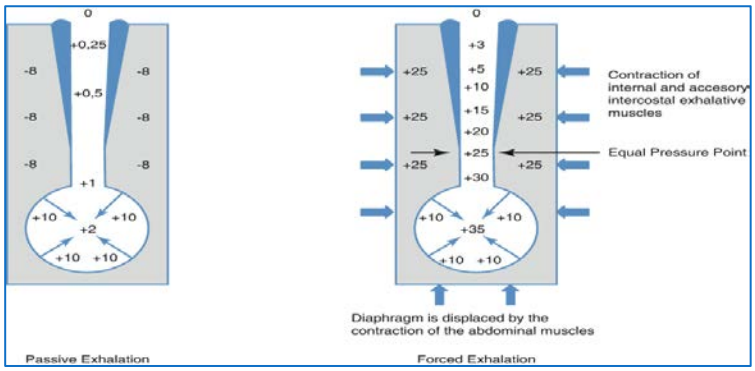
Prevalence of lung diseases depends on the population, but in general we have three families:

1. 70% Obstructive:
   - ✓ Obstructive Diseases: Increased resistance to flow; hard to exhale.
2. 20%-25% Restrictive such as pulmonary fibrosis and ARDS.
   - ✓ Restrictive Diseases: Decreased expansion of the lungs; hard to inhale.
3. 5-10% Vascular

– **COPDs (chronic obstructive pulmonary diseases)**

- ✓ Emphysema; physiological obstruction due to loss of elastic recoil.
- ✓ Chronic bronchitis; anatomical obstruction due to mucous plugging.
- ✓ Asthma (considered COPD only if chronic).

• Common pathology in obstructive diseases



- ✓ Obstructive respiratory diseases result in increased resistance to airflow.
- ✓ To overcome this resistance, the body exerts more pressure achieved by the contraction of muscles involved in breathing, including the diaphragm, intercostal muscles and accessory respiratory muscles.
- ✓ The increased contraction can inadvertently worsen the obstruction, and exacerbates the difficulty of moving air through the narrowed airways, creating a vicious cycle.

- ✓ As the obstruction increases, the Reynolds number also increases. A higher Reynolds number can lead to a transition from laminar flow to turbulent flow.
- ✓ Turbulent airflow contributes to audible sounds during expiration known as wheezing that can be heard during breathing. The severity of wheezing can vary, and it may be audible without the need for a stethoscope in more severe cases.

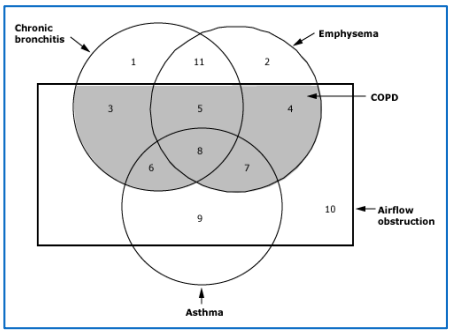
– **Emphysema; pathophysiology**

- ✓ Generally caused by dysfunction of a_1-antitrypsin (anti-elastase) either due to smoking (nicotine effect) or genetic mutations (a_1-antitrypsin deficiency).
- ✓ Imbalance between elastase (destructive force) and anti-elastase (protective force) activity→ alveolar and surrounding capillaries destruction.
- ✓ decreased alveolar area (after destruction) imposes higher resistance to blood flow and increases afterload →Cor pulmonale (right-sided HF) occurs.
- ✓ Decreased alveolar ventilation→ decreased P_AO_2 which induces vasoconstriction.
  - o Hypoxemia is a **systemic vasodilator** however it is a **pulmonary vasoconstrictor** as we need to keep V/Q ratio (ventilation to perfusion) without wasting energy.
  - o This is called hypoxic vasoconstriction; it shunts blood away from poorly ventilated areas to well-ventilated areas. Or else perfusion is wasted and V/Q is mismatched
- ✓ Pursed lip breathing.
  - o Pursed lip breathing deliberately creates a mild obstruction during the exhalation phase by pursing the lips together.
  - o The intentional pursing of the lips generates a back pressure within the airways which serves as a stenting effect, meaning it helps keep the airways open.
  - o By creating a gentle resistance to the outward flow of air, pursed lip breathing facilitates a slower and more controlled exhalation.

- The description emphasizes the importance of keeping the pressure applied by pursing the lips "minimal" or "gentle." Or else it could lead to fatigue and increased effort during breathing, counteracting the intended benefits.

✓ In emphysema, TLC and compliance are increased while FEV_1 and FVC are decreased.

✓ Generally, patients present with other COPDs such as chronic bronchitis.



• Pulmonary colloid and hydrostatic pressures

✓ In the Pulmonary circulation, as in other parts of the circulatory system, are forces that govern the movement of fluids across the capillary walls. Two key forces are colloid osmotic and hydrostatic pressure.

✓ Colloid osmotic pressure is primarily exerted by proteins, especially albumin, and it tends to draw fluid back into capillaries (it equals systemic colloid pressure =28)

✓ Hydrostatic pressure is generated by the force exerted by the blood against the walls of the capillaries, and it tends to push fluid out of the capillaries (pulmonary hydrostatic pressure is lower than the systemic)

➢ Because pulmonary capillary pressure = 7-10 mmHg (low)

Pulmonary pressures:

Systolic=25

Diastolic=8

Mean = 14 (one-seventh of TPR)

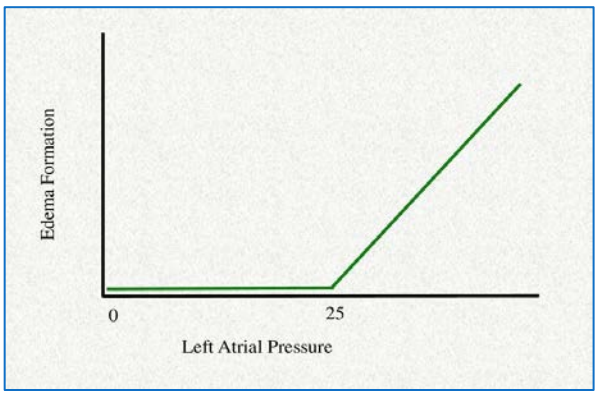
✓ **Differences between pulmonary capillary & that of systemic**

	Pulmonary capillary	*Systemic capillary*
Pc	10 mmHg	30 mmHg
∏c	28 mmHg	28 mmHg
Pi	-5 mmHg	Zero
∏i	14 mmHg	7 mmHg

Flow in thoracic duct= 100 mL/hr while 20 mL/hr in right lymphatic duct.

- lungs must be kept dry as pulmonary, laryngeal, cardiac and brain edemas are all life-threatening.
- 3 forces favor filtration in pulmonary circulation (Pi, ∏i and Pc= 29 mmHg) and one for reabsorption (∏c=28 mmHg) and the difference between the two is only +1 (towards infiltration).
- Lungs have numerous lymphatics to drain this excess infiltration (which ultimately drain into right lymphatic duct with the exception of apex of left lung that drains into the thoracic duct).

✓ Again, pulmonary edema is a very serious condition and for that the lungs have high capacity in draining excess fluid (lung lymphatics can drain up to 25L excess infiltration).



✓ Causes of pulmonary edema:

- Left heart failure; increased pressure in left ventricle, pulmonary veins and capillaries.
- Damage to pulmonary membrane: infection or noxious gas such as chlorine, sulfur dioxide.

- ✓ Safety factors:
  - o Negative interstitial pressure (*Pi).*
  - o Lymphatic pumping; if Pc increases to 28 mmHg, no edema occurs (net difference=+19; below maximal lymph capacity).

Pulmonary hypertension is what exceeds 25mmHg (at rest) and 30mmHg (at exercise)

V2

V3