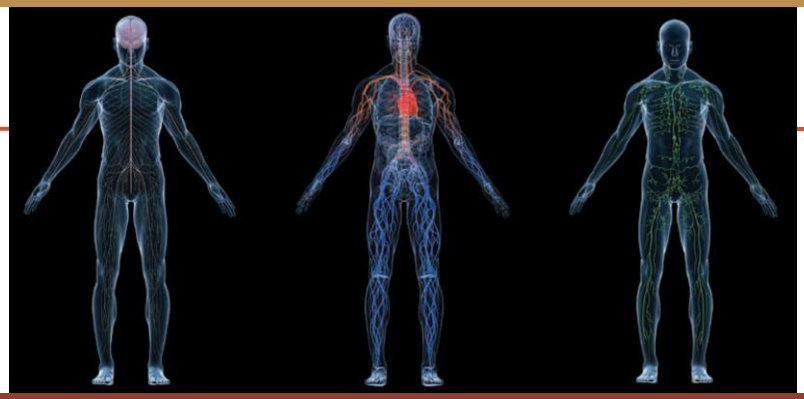
UNIT VII

GUYTON AND HALL *Textbook of*

Medical Physiology

TWELFTH EDITION



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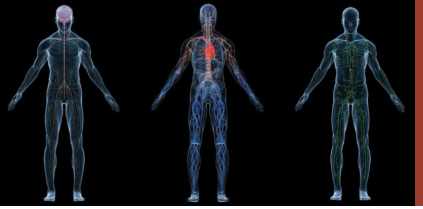
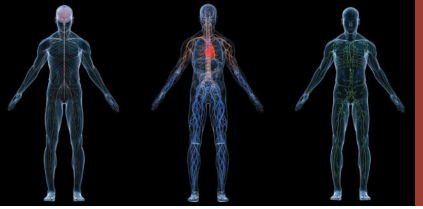
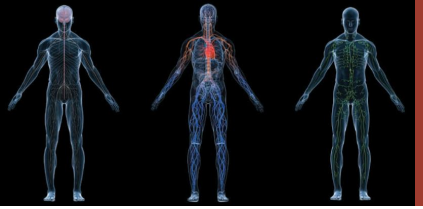


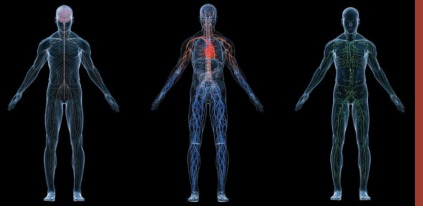




Work of breathing

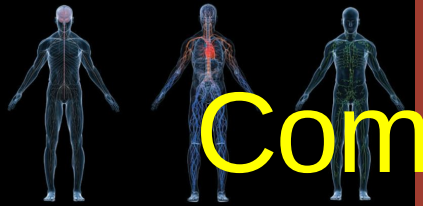
Work in the respiratory system is of 2 major types (discussed in the previous lecture):

1. *Work to overcome elastic forces (70%):* that required to expand the lungs against the lung and chest elastic forces. Two third is duo to surface tension and one third is duo to elastic fibers.
2. *Work to overcome non-elastic forces (30%):* that required to overcome:
    1. The viscosity of the lung and chest wall structures (20%).
    2. *Airway resistance work (80%):* that required to overcome airway resistance to movement of air into the lungs.



Minimal Volume

- The lungs, if alone, (outside the body) or during open-chest surgery, will collapse up to 150 ml air **= minimal volume MV (this is not anatomic dead space volume even though it is 150 ml)**. MV is used for medico legal purposes (WHY?). MV is also known as unstressed volume or resting volume of the lung.

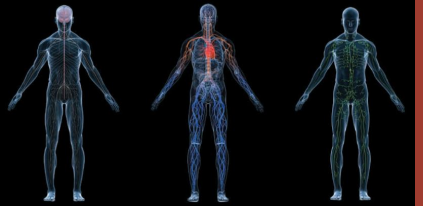


Compliance

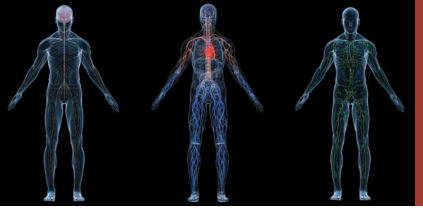
- Distensibility (stretchability):
  - How easy the lungs can expand. How much force we need to expand the lung? If the force is small, then the lung is stretchable.
- It is the change in lung volume per unit change in transpulmonary pressure.

$$\Delta V / \Delta P$$

- Lung is 100 times more distensible than a child balloon. **This means, 100 times more distending pressure is required to inflate a child toy balloon than to inflate the lung.**
  - Compliance is reduced when distension is difficult.



- AN ELASTIC STRUCTURE MUST BE AUTOMATICALLY COMPLIANT. A COMPLIANT STRUCTURE NEEDS NOT TO BE ELASTIC. For the lung to be efficient compliant, it must return back to resting volume following inspiration, otherwise it keeps inflating. GUM is compliant but not elastic and a RUBBLE BAND is compliant and elastic.
- ELASTANCE = 1/COMPLIANCE but this term is rarely used.



Compliance…cont.

COMPLIANCE is the ability of the lung to stretch

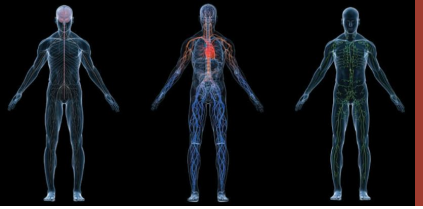
Specific compliance = C/FRC to correct for differences in lung volume between a child and an adult.

C_L = 200ml/cm H_2O. For the lung alone

C_W = 200ml/cm H_2O. For the thoracic wall alone

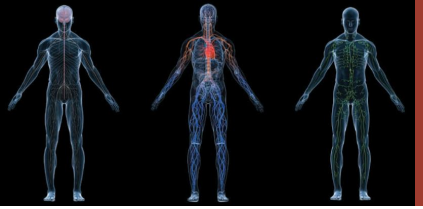
C_S = 100ml/cm H_2O. S stands for lung-thorax system (For both)

Inflating one balloon is easier than inflating two balloons, one inside the other. The two balloons are the lung and the thorax.

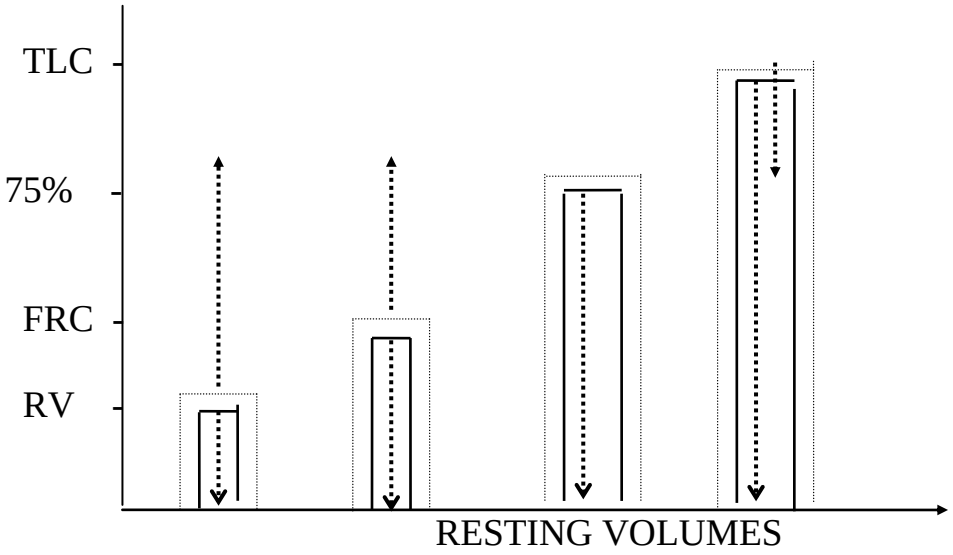


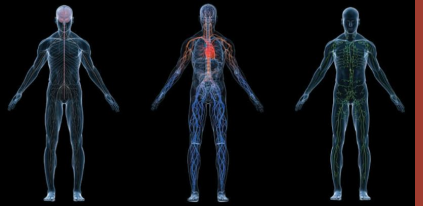
Elasticity

- Tendency to return to initial size after distension.
- High content of elastin proteins.
  - If the lung is very elastic and resist distension…this means high recoil tendency or high collapsing forces Too much recoil tendency is bad (high collapsing forces) and too little recoil tendency is also bad (high compliance).
- Elastic tension increases during inspiration.
- **Elastance E or Elasticity**: describes the resistance of an object to deformation by an external force and is equal to 1/C.
- It is a measure of the tendency of a hollow organ to recoil toward its original dimensions upon removal of a distending or compressing force. It is the reciprocal of compliance



RESTING VOLUMES

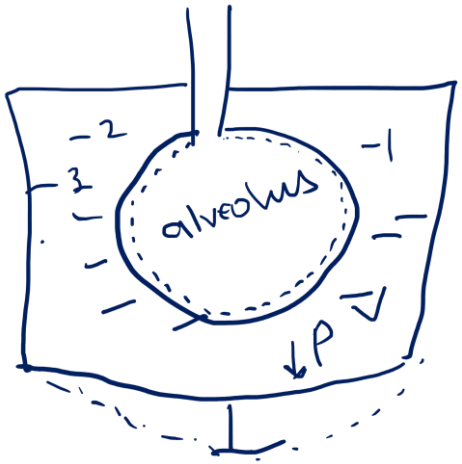


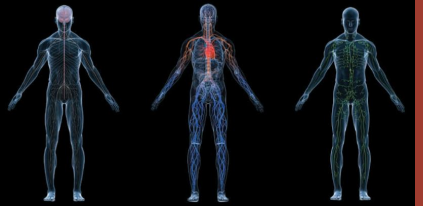


- If expanding and collapsing forces are equal, the net force would be zero and the system is neither tending to collapse nor to expand. This occurs at FRC. At all volumes smaller than FRC, collapsing forces of the lung are less than the expanding forces of the thorax and the net force would be expanding force. At this point if muscles are relaxed while air outlet is closed, alveolar volume would ↑ and Palv would↓. The magnitude of alveolar sub-atmospheric P reflects the strength by which the system is tending to expand.
- At large volumes when the tendency to collapse is more than that to expand, the lung-thorax system is tending to collapse, alveolar volume would ↓ and Palv ↑ reflecting the collapsing forces.

BINDING BETWEEN LUNGS & THORAX.

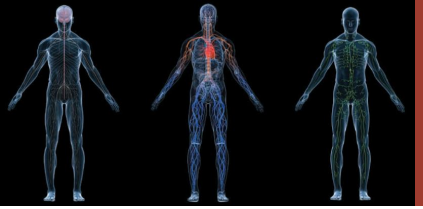
- Lungs are covered by a visceral pleura & the mediastinum & chest wall are lined by parietal pleura. Both pleural surfaces are covered with a thin film of fluid & the intermolecular forces of this film between the two surfaces holds the lungs against the thorax. It is like two glasses slide over each others but not easily separated.





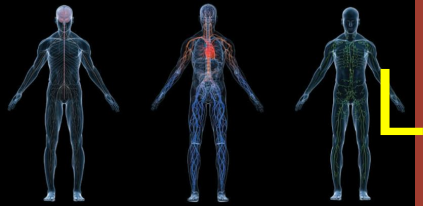
Intrapleural Pressure

- The magnitude of the intrapleural pressure equals the separate elastic forces of the lungs or chest wall rather than the sum of their combined forces. It reflects either the strength of the collapsing elastic lung tissue or the strength of the expanding chest wall force
- Since chest wall elasticity usually remains unchanged in respiratory pathology, "P_{pl}" reflects the elastic strength of the lungs. At all volume P_{pl} reflects how strongly the lungs are tending to collapse. P_{pl} can be measured using a tube inside the esophagus.



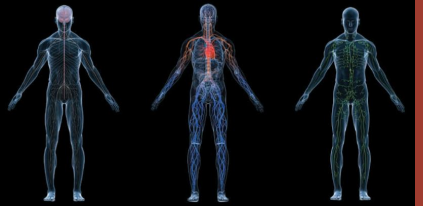
Relaxation Curve

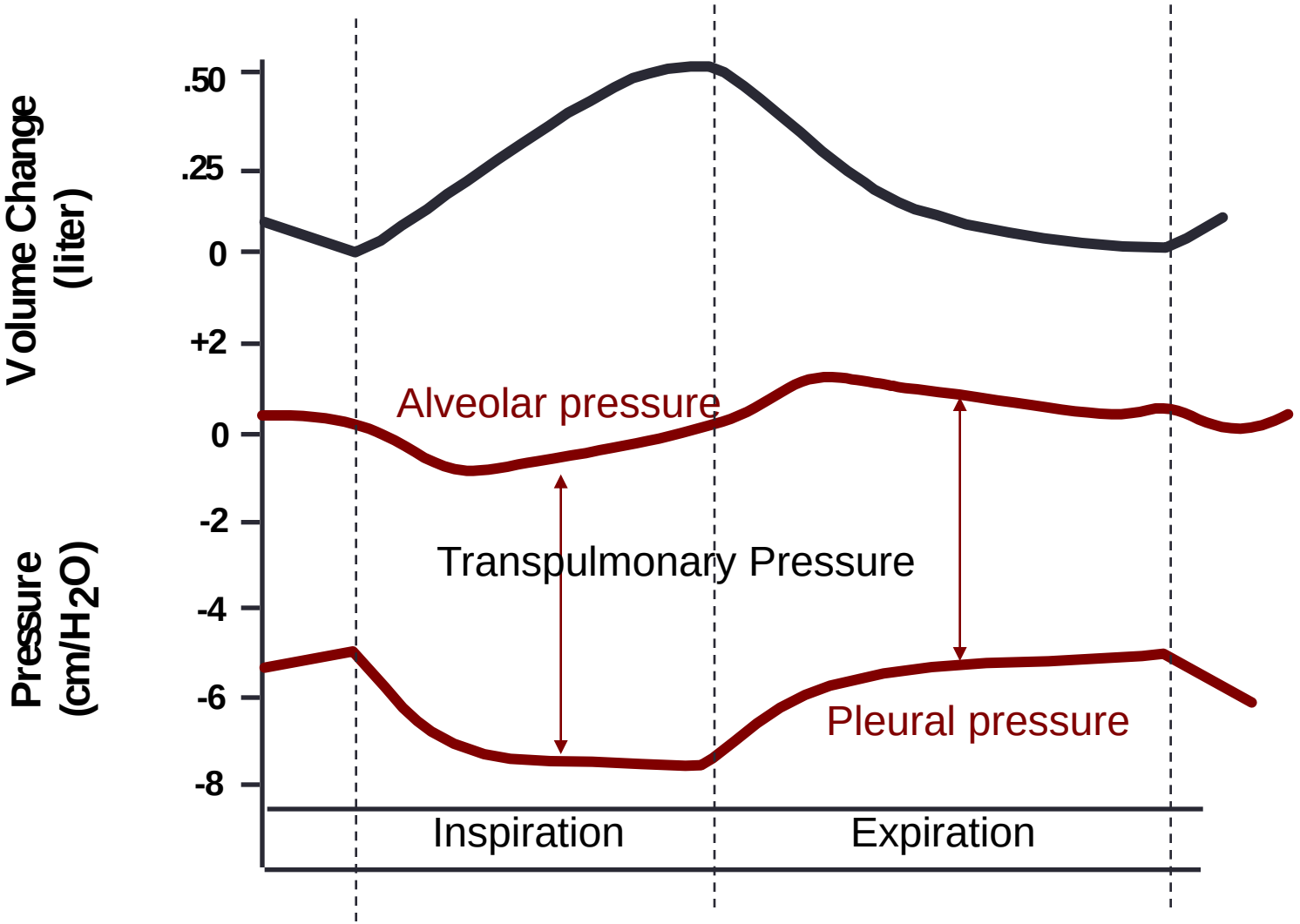
- When generating the **Relaxation Curve**, all respiratory muscles (inspiratory & expiratory) are relaxed and we plot volume versus intra-alveolar pressure.
- At each lung volume we can study whether the lung-chest wall system is tending to expand or to relax.
- Relaxation curve is generated under static conditions when no air flow occurs.
- Under these conditions, Ppl reflects the strength of the elastic forces of the chest wall

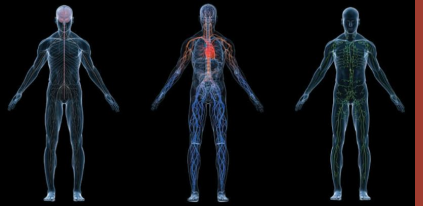


Lung-Thorax Resting Volume

- In vivo, we can't measure P_{alv} below residual volume.
- To move the system from FRC you need to apply force such as muscle contraction…but to bring it back to its resting volume (FRC) is passive. This is another way to look at inspiration is active and expiration being passive process.

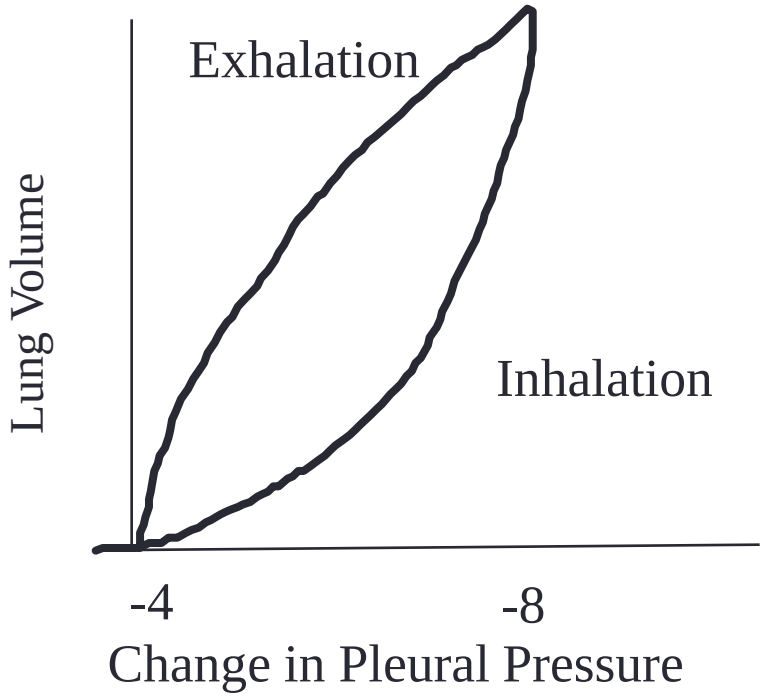


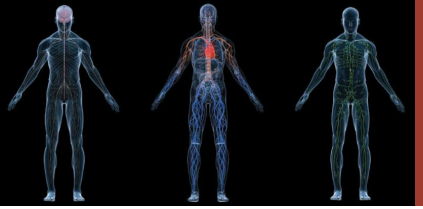




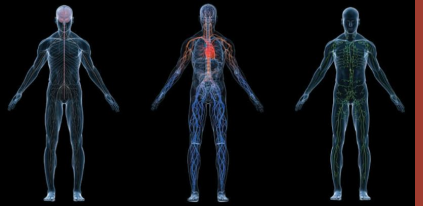
COMPLIANCE OF LUNGS

- Determined by elastic forces
- Elastic forces
  - lung tissue… one third
  - surface tension…two thirds

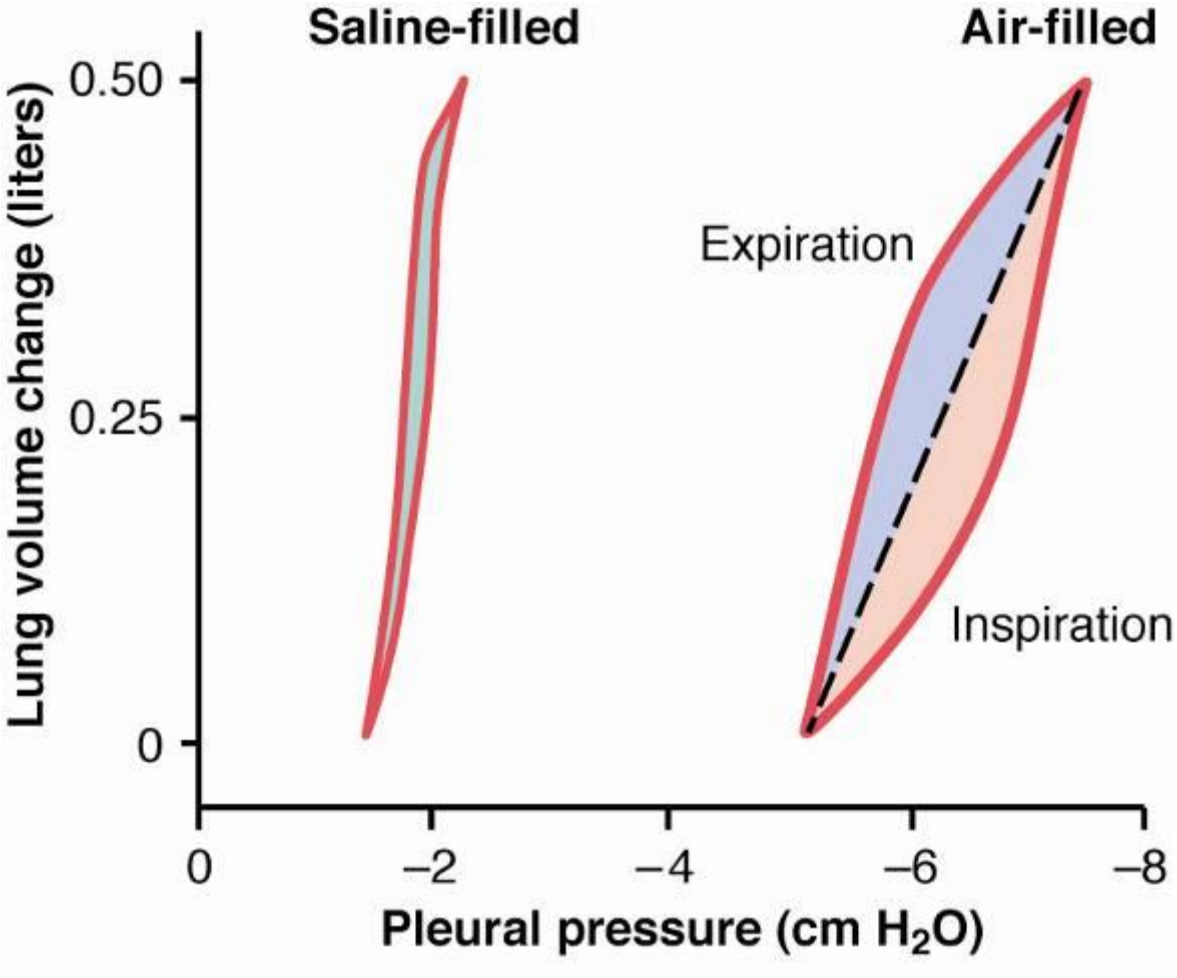


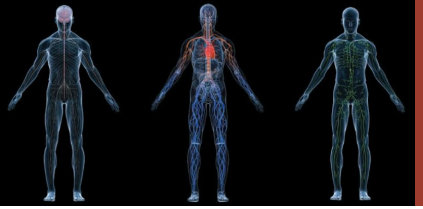


- If an alveolus at 100 µ (at FRC)
- is lined with water, it needs -21 mmHg for stabilization…inflation pressure…to prevent it form collapse
- - If lined with interstitial fluids, it needs -13 mmHg of pressure is enough for stabilization
- - If lined with surfactant, in this case we only need -4 mmHg for alveolar stabilization



Compliance of Lungs





Pressure-volume curve.

How much P you need to inflate the lung with air or with saline (Normal saline is isotonic solution made of 0.9% NaCl).

P in case of air is big, in case of saline is small.

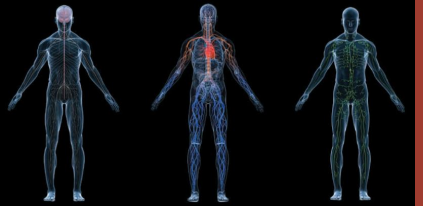
In saline-filled lung P is needed to oppose elastic forces because there is no **T**. However, in air-filled lung, The pressure is needed to oppose elastic forces plus surface tension **T**. Thus the difference between them at certain volume is T.

This curve is generated while lungs outside the body.

At phase (1) we need high ΔP before any small change in V, …this means that it is not wise to start inhaling from totally collapsed lung…you put too much effort to re-inflate the lung such as in IRDS.

2. Phase 2 : alveolar recruitment. This phase starts when we reach a critical opening pressure = pop-open pressure= …. Surfactant lowers the critical opening pressure.

phase (3) lung become stiff again (elastic limit reached)



Hysteresis: During Deflation, different relationships exist for lung filled with air.
This indicate that reverse process does not follow the same path as forward process, known as **hysteresis**.

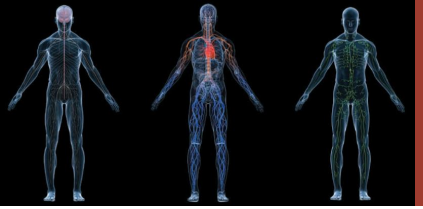
- Hysteresis is great between zero and TLC volume; negligible at V_T around FRC, and moderate at VC range
- Hysteresis means: Less pressure is needed to keep alveoli patent than to open them. Open alveoli support one another and are relatively stable. Greater pressure difference is required to open a previously closed airway than to keep an open airway from closing.

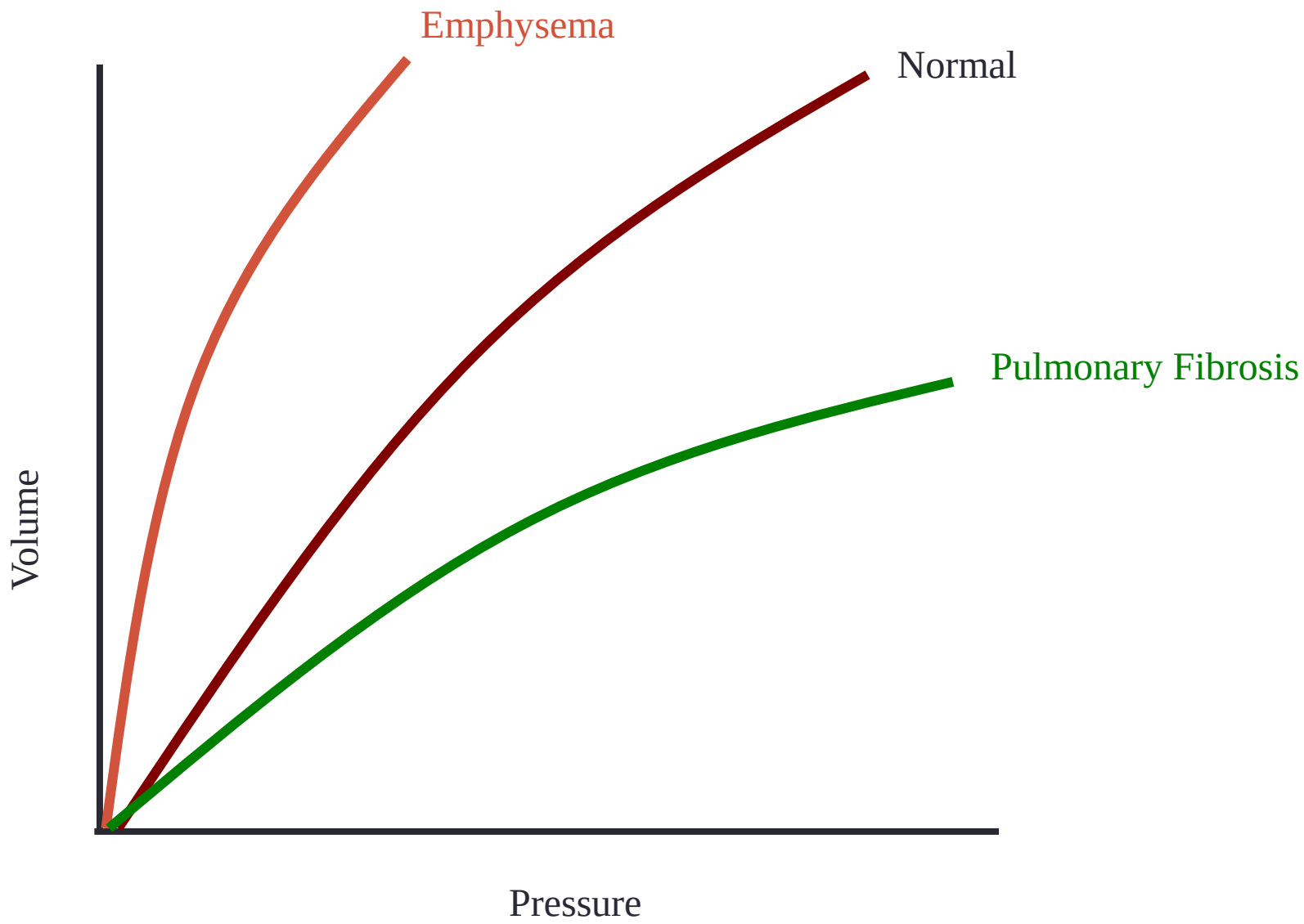
Once the critical opening P has reached the major respiratory effort is used in stretching the elastic fibers within the system.
During deflation, alveoli remain open at lower pressure, alveolar closing P is much less than alveolar opening pressure because of surfactant.

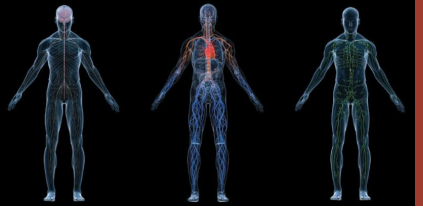
Only deflation curve is used to analyze lung compliance, because inflation curve is complicated by alveolar requirement and not solely dependent upon lung elasticity.
In RDS the deflation curve moves closer to the inflation curve…no surfactant in RDS (Displacement to the right). That means that higher P is necessary to hold the lungs inflated.
During inflation, surfactant molecules spread apart $\rightarrow\uparrow$ T, in deflation they are compacted and much better orientation$\rightarrow\downarrow$T….at same concentration. During deflation surfactant becomes more efficient.

With Surfactant:

1) low opening P.
2) low inflation P.







Too much compliance is bad and too little compliance is bad too. Too much of a good thing can kill you!!! الفضيلة تقع بين رذيلتين

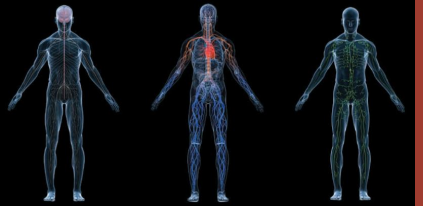
Lung compliance refers to how much effort is required to stretch lungs and chest wall

Lung compliance (CL) = change in lung volume per unit change in inflating pressure

"*The extent to which the lungs will expand for each unit increase in transpulmonary pressure*"

Each increases in transpulmonary pressure by 1 cm of water, increases the lung volume 0.2 liters

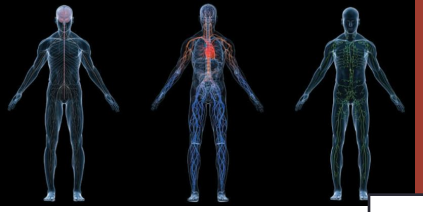
- A lower-than-normal compliance means the lungs and thorax are harder to expand
- Conditions that decrease compliance
  - Pulmonary fibrosis
  - Pulmonary edema
  - Respiratory distress syndrome



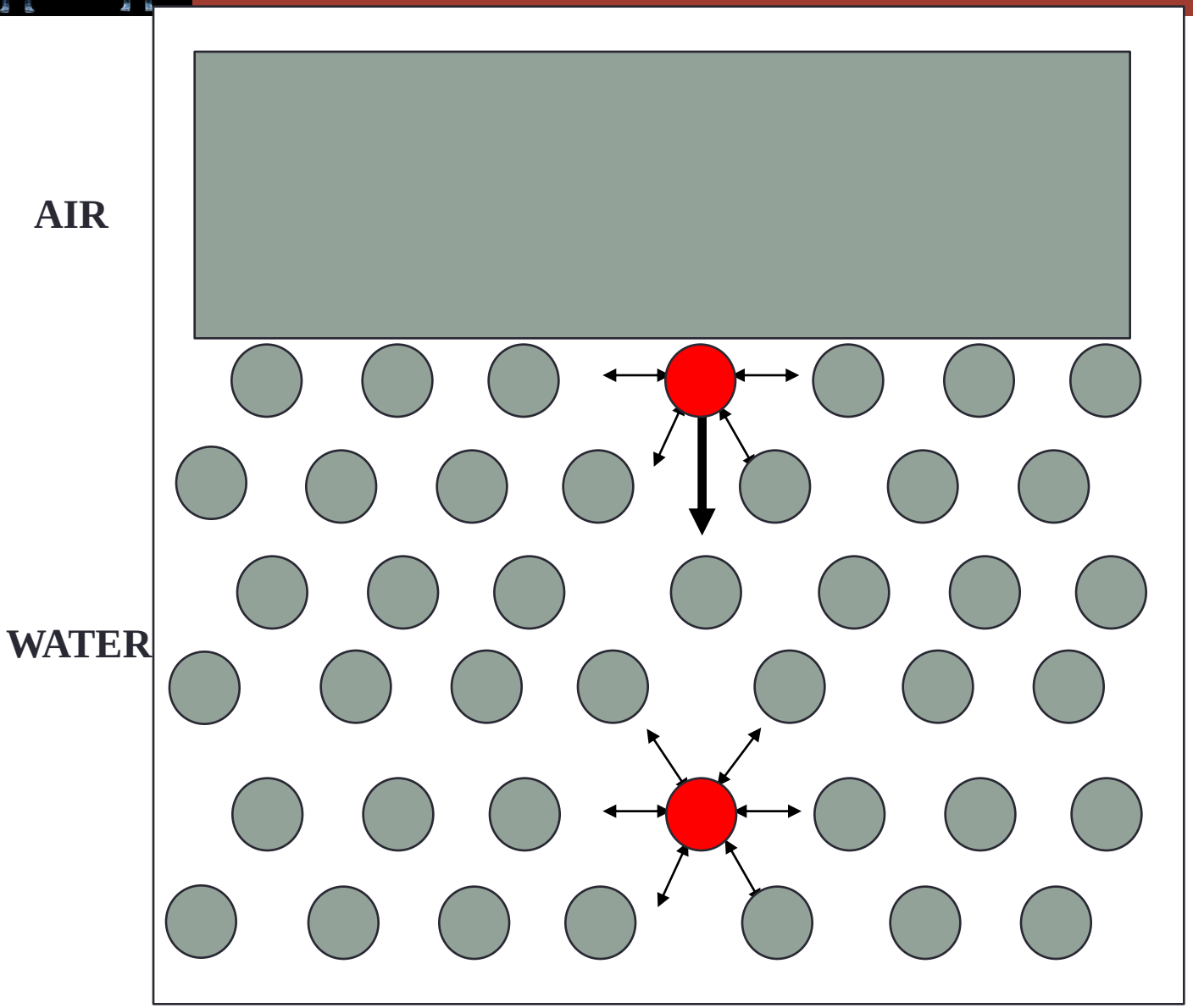
Compliance of Lungs

Surface tension T can be looked as a collapsing force which is going to collapse the alveoli…

- T is duo to attraction of water molecules at air-water interface… cohesion forces
- T is reduced by the presence of surfactant

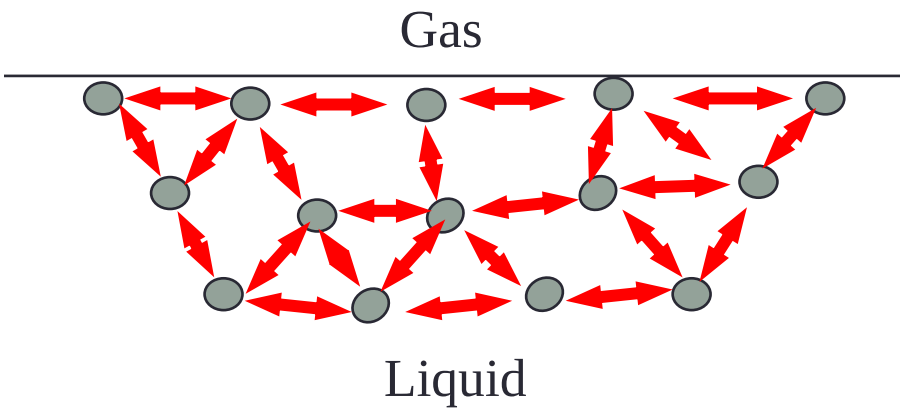


SURFACE TENSION- asymetrical forces acting at an air/water interface produce a net force acting to decrease surface area



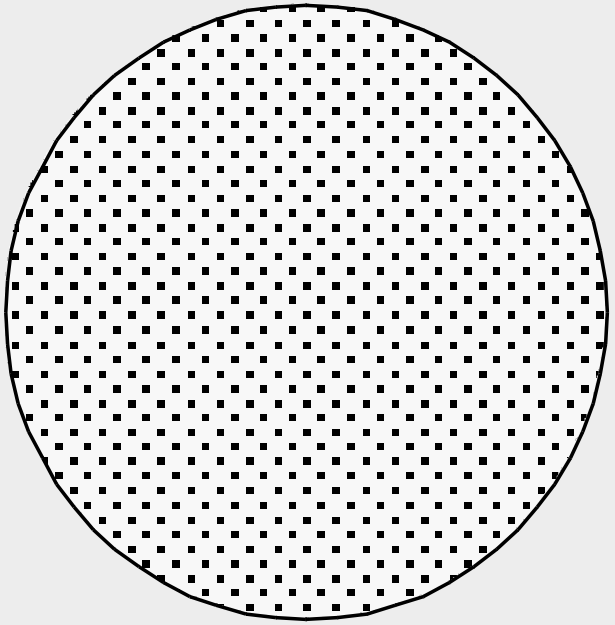
Surface Tension and recoil of the lung

Molecular interactions resulting from hydrogen bonds between water molecules in liquid but not between water and air.



When water forms a surface with air, the water molecules on the surface of the water have an especially strong attraction for one another. Therefore, the water surface is always attempting to contract.

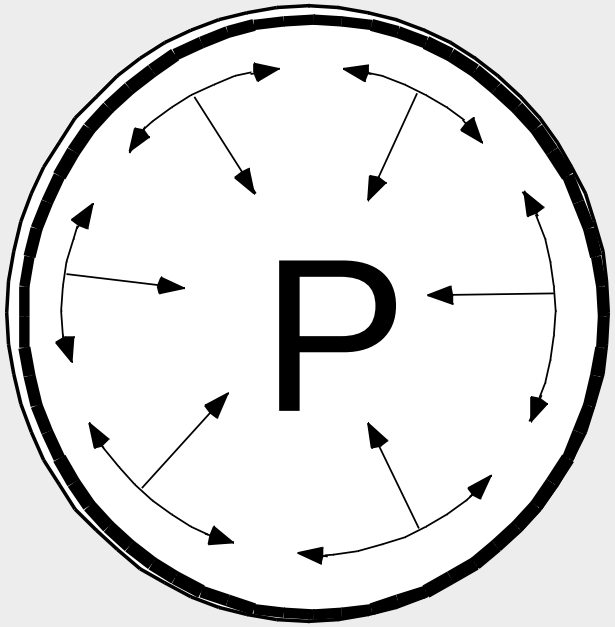
Liquid filled alveolus



No Surface Tension

Because there is no air/water interface

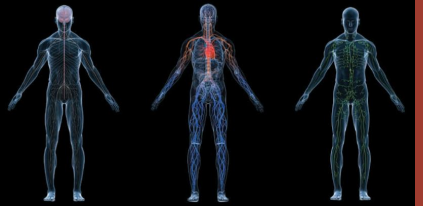
Gas filled alveolus with thin liquid layer



+ Surface Tension

↑ Recoil Pressure

↓ Compliance



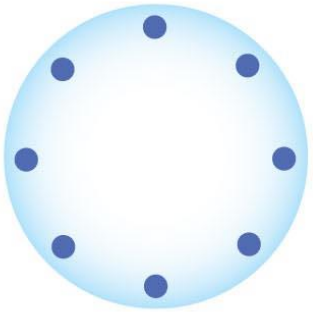
Surfactant

- ***Surfactant***: Means surface-active agent
- Surfactant is produced by Alveolar type II cells
  - It is Glyco(2%)-lipo(90%)-protein(8%) plus calcium ions.
  - Disrupts the surface tension & cohesion of water molecules
  - Maturation of surfactant needs T_4, prolactin, estrogen, and other steroids (GC)
    - prevents alveoli from sticking together during expiration

Law of LaPlace: P = 2T/r

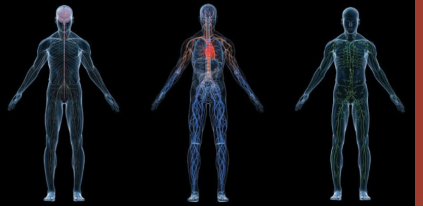
P = pressure
T = surface tension
r = radius

According to the law of LaPlace, if two bubbles have the same surface tension, the small bubble will have higher pressure.

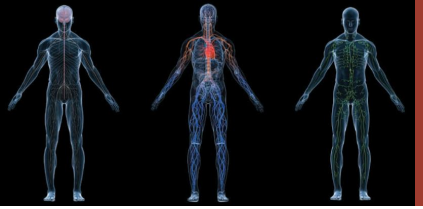


r = 2
T = 2
P = (2 × 2)/2

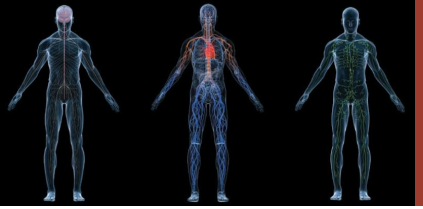
r = 1
T = 1
P = (2 × 1)/1



- Surfactant has one hydrophilic head (glycerol moiety) and two parallel hydrophobic fatty acids tails (phospholipid) facing alveolar air. Thus, the hydrophobic portion is oriented towards the air, and the hydrophilic portion facing the wall of the alveoli (hidden)
- It is a complex mixture of phospholipids, proteins, ions
- Produced by type II alveolar epithelial cells
- Surfactant reduces surface tension forces by forming a monomolecular layer between aqueous fluid lining alveoli and air, preventing a air/water interface



- **Functions of surfactant**
- 1) ↓ Surface tension forces which otherwise will pull inward and drive fluids into alveoli.
- 2) Makes surface tension volume dependent. Therefore surfactant prevents alveoli from being overstretched.
- 3) Promotes alveolar stability.
- 4) Prevent lung edema by decreasing T. Otherwise, high T will suck fluids from the wall of the capillaries.
- 5) Reduces work of breathing, reducing the muscular effort needed to expand the lungs.
- 6) Lower elastic recoil at lower lung volume, preventing collapsing of alveoli at expiration. In RDS they collapse.
- ***Alveolar stability: means small alveoli coexist with large alveoli because of:***
- ***1. Surfactant makes surface tension" volume dependent and thus at the same intra-alveolar pressure small alveoli and large one coexist. If we don't have surfactant, then the lungs contain hyperinflated alveoli and totally collapsed alveoli***
- ***2. alveolar traction (alveolar interdependence) alveolar walls are attached to each other.***



Laplace's Law

T = P x r/ 2 or P = 2T/r

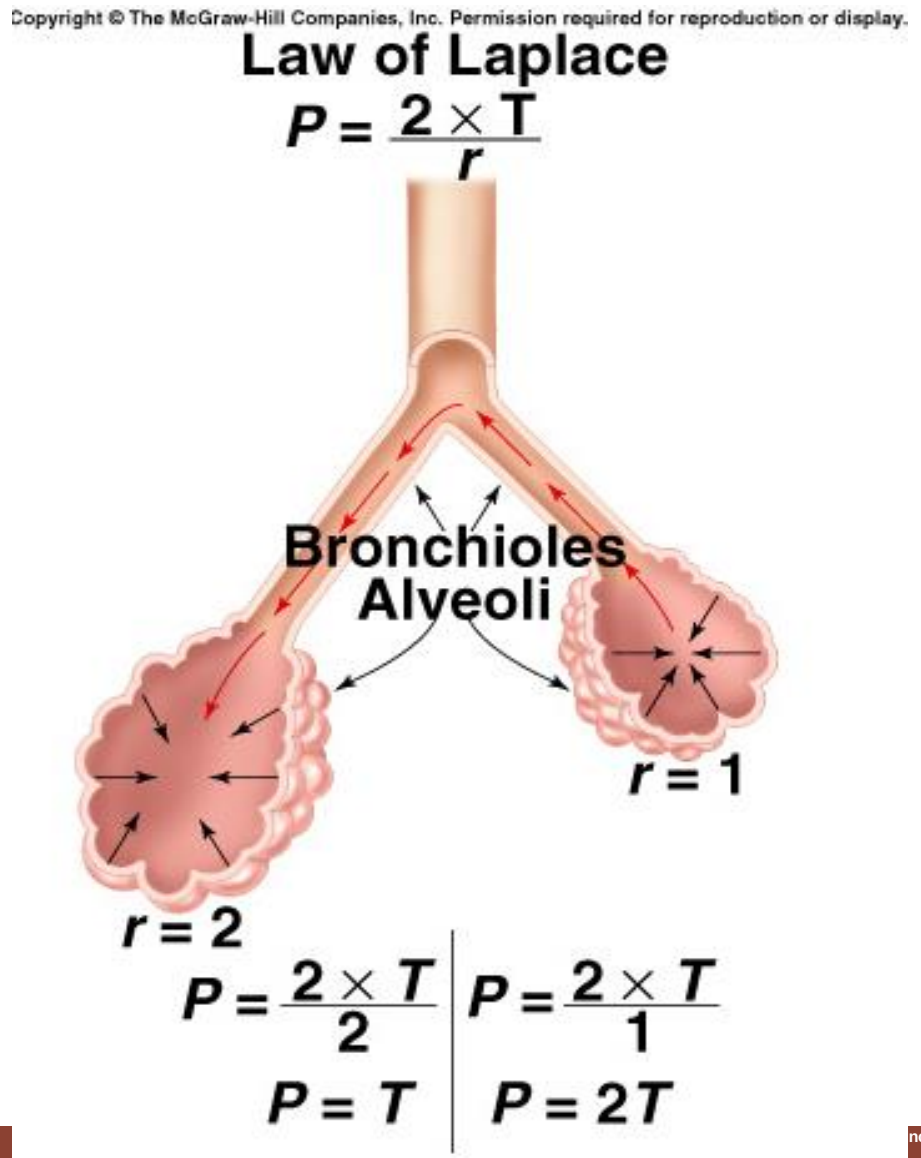
P = pressure required to prevent alveolar collapse <u>at rest</u>
T = surface tension
r = radius…

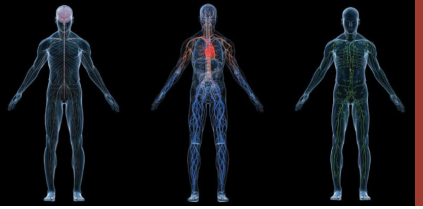
- **The smaller the radius , the larger the pressure required to prevent collapse…this point is important in IRDS where alveolar diameter is extremely small.**

  - **If T = 2; r = 2; P = 2**
  - **If T = 2; r = 4; P = 1**

Surface Tension… Law of Laplace (continued)

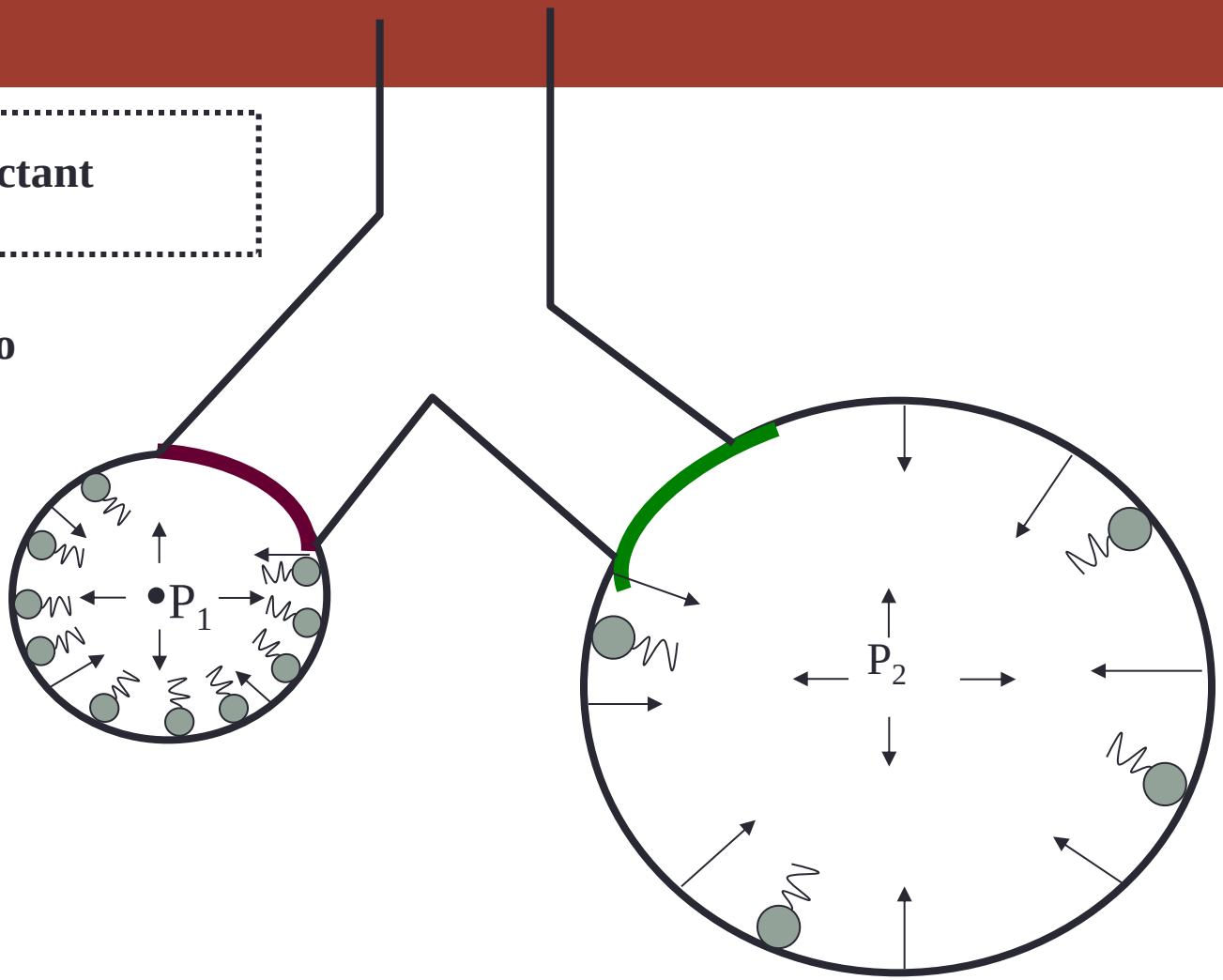
- Law of Laplace:
  - Pressure in pleural cavity is directly proportional to surface tension; and inversely proportional to radius of alveoli.
  - Pressure in smaller alveolus would be greater than in larger alveolus, if surface tension were the same in both.





Pulmonary surfactant

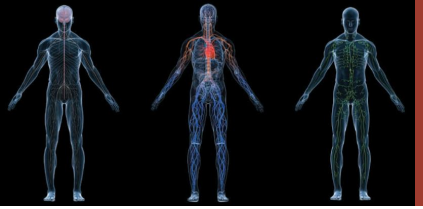
P_1 = Pressure required to prevent alveoli #1 from collapsing.



P_2 = Pressure required to prevent alveoli #2 from collapsing.

Deficiency of Surfactant causes collapse of the lungs

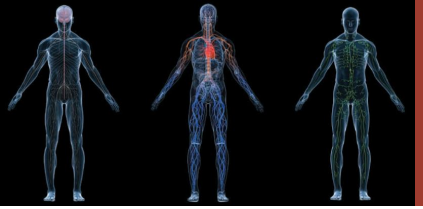
- IRDS: Respiratory distress syndrome (in premature babies)
- ARDS: Acute Respiratory distress syndrome in adults and children
- Since lung inflation requires large pleural pressure drops, deep breaths are difficult for patients with Restrictive Ventilatory Defects RVD; These patients exhibit shallow and rapid breathing patterns.



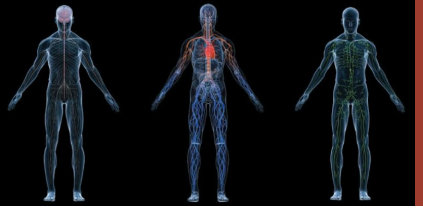
- IRDS (respiratory distress syndrome in infants or newborn):

Birth Weight (g)	**Incidence of IRDS**
501-750	86%
751-1,000	79%
1,001-1,250	48%
1,251-1,500	27%

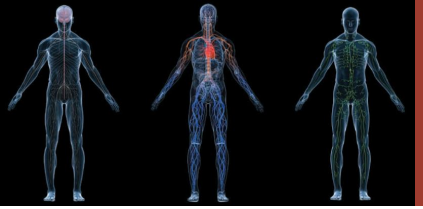
- The incidence decreases with advancing gestational age, from about 50% in babies born at 26-28 weeks, to about 25% at 30-31 weeks. The syndrome is more frequent in infants of diabetic mothers and in the second born of premature twins.
- RDS affects about 1% of newborn infants and is the leading cause of death in preterm infants
- 10-50% is the mortality in RDS.
- RDS is the most common cause of death in the first month.
- In Western countries, it is the commonest cause of death in non-malformed children under the age of 15 years.
- Clinically: RR > 60/min, expiratory grunting (صوت الخنزير), and persistent inspiratory rib retraction all starting within 4 h of birth.
- Collapse of the alveoli → hypoxemia → pulmonary vascular hypertension → shift of the blood from right atrium to left atrium through foramen ovale and/or **patent ductus arteriosus**→ right to left shunt→ Pulmonary edema → suffocation because of collapse (Atelectasis). Complications include metabolic disorders (acidosis, low blood sugar), patent ductus arteriosus, low blood pressure, chronic lung changes, and intracranial hemorrhage. The disease is frequently complicated by prematurity and its additional defects in other organ function.



- **Treatment**
- Oxygen is given with a small amount of continuous positive airway pressure ("**CPAP**"), and intravenous fluids are administered to stabilize the blood sugar, blood salts, and blood pressure. If the baby's condition worsens, an endotracheal tube (breathing tube **PEEP** positive end expiratory pressure) is inserted into the trachea and intermittent breaths are given by a mechanical device. An exogenous preparation of surfactant, either synthetic or extracted from animal lungs, is given through the breathing tube into the lungs. One of the most commonly used surfactants is **Survanta**, derived from cow lungs, which can decrease the risk of death in hospitalized very-low-birth-weight infants by 30%. Such small premature infants may remain ventilated for months.
- **Prediction of lung Maturation (lung maturation):**
- - All are taken from amniotic fluids.
- 1. Lecithin-to sphingomyelin ratio>2 indicate maturity
- 2. The presence of phosphatidylglycerol in amniotic fluids is even much better index.
- 3. surfactant/albumin (S/A) ratio (mg/g). A ratio <35 indicates immature lungs, between 35-55 is indeterminate, and >55 indicates mature surfactant production



- **ARDS… "A" stands for Acute and not for Adult**
- - Known under different names: shock lung, endotoxin lung, wet lung, septic lung, post-traumatic lung, machine lung. After exposure to hyperbaric O2, toxic gases...etc
- ARDS was defined as the ratio of arterial partial oxygen tension (PaO_2) as fraction of inspired oxygen (FiO_2) below 200 mmHg in the presence of bilateral alveolar infiltrates on the chest x-ray
- **Pulmonary artery wedge pressure** < 18 mmHg (obtained by pulmonary artery catheterization), if this information is available; if unavailable, then lack of clinical evidence of left ventricular failure suffices
- Acute Lung Injury
- - A PaO2/FiO2 ratio less than 300 mmHg with bilateral infiltrates indicates acute lung injury (ALI). Although formally considered different from ARDS, ALI is
- usually just a precursor to ARDS…..Note: the term acute lung injury was abandoned. Therefore, 3 categories of ARDS were proposed (mild, moderate, and severe) based on the



Additional slide…just take a look…you don't have to memorize any of the following numbers

They further subdivided the ARDS into ,,,, despite they have divided the ARDS into these 3 catego they stayed consistent with the definition

Berlin criteria for ARDS severity

PaO_2/FiO_2 ratio	Inference
200 - 300 mm Hg	Mild ARDS
100 - 200 mm Hg	Moderate ARDS
< 100 mm Hg	Severe ARDS

ARDS is characterized by an acute onset within 1 week, bilateral radiographic pulmonary infiltrates, respiratory failure not fully explained by heart failure or volume overload, and a PaO_2/FiO_2 ratio < 300 mm Hg

	ARDS		
	Mild	Moderate	Severe
Timing	Acute onset within 1 week of a known clinical insult or new/worsening respiratory symptoms		
Hypoxemia	PaO_2/FiO_2 201–300 with PEEP/CPAP ≥ 5	PaO_2/FiO_2 ≤ 200 with PEEP ≥ 5	PaO_2/FiO_2 ≤ 100 with PEEP ≥ 10
Origin of Edema	Respiratory failure associated to known risk factors and not fully explained by cardiac failure or fluid overload. Need objective assessment of cardiac failure or fluid overload if no risk factor are present		
Radiological Abnormalities	Bilateral opacities*	Bilateral opacities*	Opacities involving at least 3 quadrants*
Additional Physiological Derangement	N/A	N/A	$V_{E\,Corr}$ > 10 L/min or C_{RS}<40 ml/cmH_2O

*Not fully explained by effusions, nodules, masses, or lobar/lung collapse; use training set of CXRs; $V_{E\,Corr} = V_E \times PaCO_2/40$ (corrected for Body Surface Area)