❖ IRDS, Infantile Respiratory Distress Syndrome

- RDS is the leading cause of death in the newborns, and the most common cause of death first 15 years of life (excluding the malformed babies).
- RDS is the lack of lung surfactant, can be infantile (IRDS) or Acute (ARDS).
- Production of surfactant in the lungs of fetus takes time, so early delivery results in RDS.

Examples of Labor Induction (Induced early delivery):

1- Oxytocin-Induced early labor

2- Caesarean section, Due to toxemia (Pre-Eclampsia) of pregnancy.

However, before inducing a labor, prediction of the degree of lung maturity must take place due to the high mortality rate (10%-50%) of IRDS that depends on the received medical care and gestational age, in earlier gestational period the mortality rate is higher. This can be done by looking for "**Lung Maturity Markers**" in the amniotic fluid taken by **Amniocentesis**.

PS: Amniocentesis is done through inserting a needle through the abdomen and uterine wall into the amniotic sac to obtain a sample of the amniotic fluid, this procedure should be carried out by a specialist, in order to make sure to avoid any possible injury to the fetus.

Lung Maturity Markers:

1- Lecithin-Sphingomyelin Ratio:

Should be more than 2, lower than 2 indicates immaturity of the lungs.

2- phosphatidylglycerol:

Should be present, its absence indicates immaturity of the lungs.

3- Surfactant-Albumin ratio (mg/g):

Should be more than 55, if less than 35 the lungs are definitely immature.

(35-55 is the border line, above indicates maturity and below, below 35, indicates immaturity)

Treatment of IRDS:

- Before labor (To the mother):

1- Delay the delivery as much as possible, since one day can make a difference.

2- Dexamothasone (Synthetic GC, C22), A very potent drug that accelerates the production of surfactants, almost 30 times more potent than the GCs synthesized naturally on our body which are usually C18 (Estrogen), C19 (Testosterone), C21 (GC like cortisol, and MC like aldosterone)

GC: Glucocorticoids, MC: Mineralocortcoids, C22: 22 carbons.

Most symptoms appear by the 1st 4 hours, mainly a severe stress with a very high respiratory rate of 60 breaths per minute. (*Tachypnea*)

- After Labor (To the baby):

1- CPAP (Continuous Positive Airway Pressure).

2- PEEP (Positive End-Expiratory Pressure)

At first we give CPAP in order to keep the airways opened, if it does not work we go for PEEP. Here we "incubate" the baby with a tube a machinery ventilator to allow respiration. It might take a week to remove

the tube and check for normal respiration, if the RDS is not solved you'll need get the tube back for another week so on.
PS: Sometimes it takes you a month to correct the breathing of the baby, and we use PEEP if CPAP failed. Also, treatment involves correcting the blood glucose, acid/base imbalance, electrolytes imbalance (mainly potassium and sodium) and other metabolic problems due to the lack of oxygen.

ARDS, Acute Respiratory Distress Syndrome.

Shock Lung, Toxic Lung, Septic Lung, Wet Lung.. All are names of a very serious condition of lack of surfactant, as part of a big picture of multi organ failure (It is not a disease by itself).

Diagnosis:

Diagnosis is made by looking at a whole picture of multi organ failure along will certain clinical manifestations of the ARDS and certain lab results, now we will be discussing the diagnostic laboratory results and tests of ARDS.

1- Inflammatory process at the chest x-ray.

2- PaO_2 /FiO_2 (Arterial oxygen pressure over the fraction of oxygen in inspired air)
Normally, the PaO2 is 100mmHg and the FiO_2 is 21%, so the PaO_2/FiO_2 is around 500. Up to a PaO_2 of 70 is normal, unless you give Oxygen double that of the atmospheric (FiO_2=42%) and the PaO2 did not change (Remained 70mmHg) so that the ratio now is:
PaO2/FiO2 = 70/.42 = 175, this is abnormal
PaO2/FiO2 > 300 ➔ Normal
PaO2/FiO2 <300 and >200 ➔ Acute Lung Injury
PaO2/FiO2 < 200 ➔ ARDS
PS: We never (only in very limited cases) give pure Oxygen (100% O_2) to a patient, because it is very toxic; it can injure the lung and decreases the surfactant causing RDS.

3- PCWP (Pulmonary Capillary Wedge Pressure)
Normally below 18, if it becomes higher than 18 this indicates ARDS and we need to check for a highly possible *left heart failure*. However, this test is not available in all hospitals, so we look for other markers along with the whole clinical picture of an ARDS patient.

The mortality rate of ARDS is very high, and it is not mainly due to the respiratory problem but due to the associated multi organ failure (ICU Patient).

Causes of ARDS (causes of lack of surfactant):

1- Giving pure oxygen (100% O2)
2- Smoking
3- Lack of hormones needed for surfactant, i.e. prolactin, estrogen, T4, and GCs.

For your health:
A deep inhalation every once and a while can provide you with a better spreading of the surfactant stored within the folds of alveoli even though the amount still the same.

Airway Resistance

The lungs work against two major forces to inflate the alveoli and carry out respiration:

1- Elastic Forces (Consumes 70% of the breathing work)

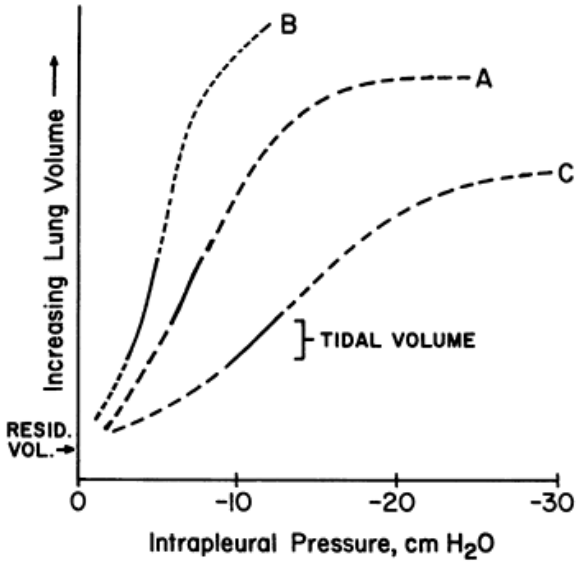
2- Non-Elastic Dynamic Forces (Consumes 30% of the breathing work):

- Airway Resistance => 80% of these 30%
- Tissue Viscosity => 20% of these 30%

Work of Breathing = ΔP * ΔV

Lungs' Compliance:

The amount of change of pressure required to cause a certain change in volume.



Increased Compliance:

Imagine we removed the elastic fibers, and the inflation (stretching) of alveoli has become much easier.. Is this good? To easily be capable of such inflation is it good?

- No elastic fibers means a very high compliance, which means shift to the left (B curve)

- This means that inspiration in now easier. However, **the expiration will no longer be passive**, which means that now it will be costing us more ATP and more oxygen.

Decreased Compliance:

As in RDS and Pulmonary Fibrosis, **the inflation will be harder which means the compliance will decrease and a shift to the right would occur (curve C)**.

Site of Airway Resistance:

We have 23 generations of airways, with cartilage distributed as the following:

Generation 0 (Trachea) => Surrounded by C-shaped cartilage, making it impossible to collapse even with high –ve pressure.

Generation 10-12 => Cartilage there also prevents collapsing.

Generation 13-23 => No cartilage, so there's no protection from collapsing. Actually, there we have smooth muscles which once irritated will drive bronchoconstriction and closure of airways.

Role of Elastic Fibers in protection of small airways from collapsing:

Elastic forces in lungs counter the inflation, which means that their presence demand more –ve interpleural pressure in lungs to drive the air in (Inhalation), this –ve pressure will **indirectly** cause the bronchioles (small airways) to remain open thus preventing their collapse.

No elastic fibers means that less –ve interplerual pressure is needed, which means that less –ve pressure is present to prevent the collapsing (the recoil tendency of the lung is decreased), this will lead to **"Obstructive disease, with normal bronchioles**" so that the obstruction is **external**. However, in cases like chronic bronchitis or bronchial asthma the closure is **internal** (from inside).

- Another theory says that the alveolar traction of elastic fibers is what drives this effect on bronchioles rather than the –ve pressure as mentioned in the previous theory.

Now, what is "Resistance"?

Resistance is the difficulty of something to occur, it is the reciprocal of "Permeability" and the higher the resistance, the less the permeability and vice versa.(here it can't be measured directly)

- Poiseuille's Law:

$$\text{Resistance} = \frac{8\eta L}{\pi R^4}$$

- Ohm's Law:

Flow = ΔP/ΔR

In Poiseulle's law, the only variant in the case of airways is their radius, so that the *resistance is inversely proportional to the 4th power of radius*, in another words; any slight change in radius of bronchioles will be reflected as a huge change in resistance. If we have a small change in the radius (narrowing), reflected with huge change in resistance this (according to Ohm's law) would need a huge change in pressure to overcome this change in resistance to maintain a constant flow, or "Respiratory Minute Ventilation"

RMV = TV * RR

RMV= .5 * 12 = 6L/minute (4.2 alveolar ventilation and 1.8 ADS ventilation) if the resistance is high you need to increase ΔP to maintain the same flow, increasing ΔP will immediately increase the work of breathing and it will account for more than 5% of the total oxygen consumption .

4 Take-Home facts regarding airway resistance:

1- Normally, we face no significant airway resistance (it is small and negligible), which will cause the very small driving force (ΔP=1mmHg) to be enough to drive the air in. Unlike the case of cardiac output, the resistance is really high which will cause us to need much more driving force carried by the heart.

2- Airway resistance is inversely proportional to the cross sectional area of the airway as a collection. So most of the airways resistance resides in the large airways, and it is distributed as the following along the respiratory tract:

- **Above the larynx (mouth, nose and larynx)** => 40% of resistance
- **1st 7 generations of airways** => 40% of resistance
- The left 20% of resistance is by **generations 8-15 of airways**.
- **Generations 15-23** => No resistance (*The highest cross sectional area, so the lowest resistance*)

3- In pulmonary diseases, the airway resistance is increased in small airways around 10 times more than large airways making them a preferable site of pathology, this is probably due to:

- **Their lack of cartilage**, which normally prevents large **airways** collapse.
- **The lining of the small airways is endothelial with goblet** cells secreting mucous secretion when stimulated, this mucous can easily block the small airways.
- **Small airways contain smooth muscles**, which causes bronchoconstriction when irritated.
- **Small airways are so small** that any mucous secretion can cause their closure.

4- Any increase in airway resistance will be manifested in expiration (exhalation) rather that in inspiration (inhalation):

In inspiration, the –ve pressure produced is an *opening pressure*, causing the obstructed airways to open.
In Expiration, the high +ve pressure (+6mmHg) produced to overcome the resistance (Ohm's law) caused by the obstruction would become a *closing pressure* that would cause further obstruction in airways and thus exacerbating the problem by increasing the resistance. In this case the expiration is prolonged.
Now, we reach a point that the airways become totally closed with resistance becoming infinity so that no matter how you increase the pressure you can never overcome the resistance. This will cause the wheezing heard in such a patient with obstructed airways during expiration at a distance or by using a stethoscope.
-In the obstructive lung diseases the problem is in the expiration while in the restrictive lung diseases it is in the inspiration.

" الإنسان الحزين: هو الذي يترك ما يستطيع فعله ويذهب لفعل ما لا يفهمه."
-جوته