**Mechanics of Breathing:**  
There is negative pressure breathing, and positive pressure breathing.   
Inspiration is active, because it needs contraction of diaphragm, expiration is passive, and it takes only relaxation of diaphragm.   
When diaphragm relaxes, it ascends up, and makes the intra-pleural pressure less negative (for example -6). When the diaphragm contracts it makes the intra-pleural pressure -4. So this is a compressing pressure, where it causes the intrapulmonary, and the intra-alveolar pressure to ascend from negative to +1.   
The lung should become small for the air to get out.  
In order to get the air in, we need driving force. The driving force needs to overcome the airway resistance.   
R∝ 1/r4 (R: resistance , r: radius)  
  
**Airways :**  
We have 23 generations.  
1-16 is called the **conducting zone**(anatomic dead space)  
17-19 is called the transitional zone   
20-23 is called the respiratory zone  
We can also assume that generations 17 through 23 are the **respiratory zone**  
Generation zero (which is the trachea), is surrounded by cartilage ( C-shaped cartilage) so it’s non-collapsible. There is some sort of support.   
But in small bronchioles there is no cartilage at all, the bronchioles with 1 mm diameter do not have cartilage, they are on their own (they should protect themselves).   
The end result which we should achieve is to reach the alveoli. Sometimes however, the airways are obstructed.   
The large airways, have **large diameter**, so small particles will not obstruct them.   
For example, mucous and blood will not obstruct the trachea and the large airways. The presence of cartilage on the large airways and the fact that they have cartilage protects these airways from being obstructed.

**Small airways:**

**The four major problems of small airways:**   
1) their diameter is small; easily obstructed.   
2) They have no cartilage; no support.   
3) They are surrounded by smooth muscle cells. If these smooth muscle cells were irritated by any reason (extrinsic or intrinsic), they will contract and cause broncho-constriction (narrowing).  
4) They are lined from the inside with respiratory epithelium. In case of inflammation, edema will form (swelling), which leads to narrowing of the airways. The respiratory epithelium has goblet cells which secrete mucus (mucus; protein plus water), if the goblet cells are stimulated, too much mucus is produced (obstructing the airways). The water will be reabsorbed by the cells, leaving the protein in the blood, and we will end up with solid blood which will constrict the airways.  
  
**We have 4 take-home messages:**  
1) In order to force air to enter the alveoli, you need pressure difference. The pressure difference you need is equal to 1 mmHg (in or out). Which means the **airway resistance is small and negligible**. Therefore, I need little force because I’m facing little resistance. If I face more resistance, I will need more force.

2) The airway resistance is small. Assuming it equals 1 unit, if we fractionate this 1 unit for it to reach the alveoli, it will be as follows:

Note: Where does most of the airway resistance reside? In the arterioles.   
40% before you reach the larynx   
40% in the first 4 generations.   
20% up to generation number 15.

From 15 and beyond almost there is no resistance.  
**Most of the airway resistance resides in the large airways.**  
(As we learned before, most of the total peripheral resistance resides in the arterioles not in the capillaries. It depends on cross sectional area).  
🡺 Most if the airway resistance resides in the large airways not in the small airways, in the upper airways.

3) If we have a disease condition or a pathophysiological problem, there will be an increase in the airway resistance. This increase, come from small airways; because of the 4 reasons we mentioned earlier.   
**So, in a pathophysiological disease condition, we expect this increase in airway resistance to take place in the small airways.**

4) If we have an increase in airway resistance, do you think we are going to face more resistance during inspiration or expiration? Which one is more difficult when there is an increase in airway resistance?   
If there is airway resistance in the small airways (which are usually surrounded by pleural cavity), the pleural pressure will (usually) be minus 4. Due to narrowing, inspiration will be affected (minus 4 will become minus 6). Minus 6 is an opening pressure, which means that it will open the closed airways. Hence, the air will get in.  
On the other hand, during expiration; (minus 4 won’t help) we need more pressure. In order to achieve high pressure, we need to press the lung. Due to this the pleural pressure will become positive. This is the closing pressure, it will undergo compression.   
Normally we have small airway resistance, and we need +1 mmHg to get air out. In this case, the pressure should be positive. If air doesn’t go out it means that the pressure is zero.   
Pleura is made up of two layers, one covers the lung (visceral pleura), and the other lines the thorax from the inside (parietal pleura). Between these two layers is a potential space called pleural space. (true space- if it becomes full with water we will have **pleural effusion** or if it becomes full with air we will have **pneumothorax**).The pressure in the intrapleural space is negative.

Let’s assume that airway resistance increased 10 times. So we have to increase the pressure also 10 times to get the air out – the same amount of air that has entered. How? We are going to compress against the lung. This is to decrease the volume, and in turn increase the pressure. The problem with this is that when we compress the lung, we compress the small airways too (because both the airways and the lung (alveoli) are surrounded by pleura).   
At this point, any increase in the pressure won’t be useful and will even cause obstruction in the airways.

Main cause for the increase in the airway resistance is smoking. The damage made is irreversible.  
When air gets out, the patient will wheeze during expiration.   
The patient learns to close his lips (in order to increase the pressure). This technique prevents the patient from sleeping because this maneuver is voluntary and he should always close his lips during expiration. Other patients might use the continuous positive airway pressure (CPAP); the mask will create a positive pressure to keep the airways opened.

There is however, no problem during inspiration  
  
**To conclude, airway resistance is manifested during expiration, not during inspiration. If wheezing occurs during inspiration too, the patient is in a critical condition.**   
  
  
**Airway resistance diseases:**  
1) Emphysema (enlargement of the lung)  
2) Chronic bronchitis   
There is an overlap between Emphysema and chronic bronchitis. If a patient has emphysema, he must have some sort of chronic bronchitis, and vice versa. There is no pure chronic bronchitis or pure emphysema.   
Both are **irreversible diseases.**  
In both diseases there is an increase in the airway resistance.

**Emphysema:**   
The alveoli are made of cells, and cells are from protein and lipids. Lysosomes are free to act as proteases to start digesting the cell. Hence, there must be anti-proteases. Those prevent the enzymes from functioning. Smoking inhibit anti-protease, anti-proteases now do not work, so proteases are now free to digest the wall of alveoli. We end up with big sacks in the lung (that’s why we call it emphysema) – too much air in the lung, the air is not going out. (air can get in but we cannot get it out).  
When the wall is destructed, the surface area available for diffusion decreases.   
Alveolus is surrounded by capillaries; sometimes one alveolus is surrounded by 1000 capillaries. There are 300–600 million alveoli.

Collagen and elastin are also present. Elastin is a protein which opens the airways. If elastin is digested, the airways will be closed.  
The area available for diffusion is 50 – 100 m2.  
  
**Chronic bronchitis:**  
Due to inflammation, edema and mucous 🡺 airways will close.  
  
Smoking 🡺 no antitrypsin 🡺 trypsin now is free to work, digesting the walls of the alveoli. When it digests the wall of the alveoli, it digests the capillaries too. The problem here is that we do not only have a decrease in the surface area and increase in the airway resistance, but also a decrease in capillary area (capillary bed).   
When you decrease capillary area, the surface area will decrease too, and the capillary’s resistance will increase. Because: R∝ 1/A4 (R: resistance , A: surface area)  
  
Right ventricle pumps 5L = Q (cardiac output) = ΔP / R(pulmonary)  
if Pulmonary resistance is increased, the pressure should increase too. ( 8 – diastolic , 24 – systolic , the mean is almost 14) but 14 is not enough, it should become 25 (becomes the afterload on right ventricle). Dilatation will happen in the right ventricle, and eventually failure 🡺 Corpulmonale.  
Corpulmonale = Right ventricle dilatation ± Right ventricle failure (due to lung diseases)  
  
  
