Section 1 Physiology

Chapter 1.1

# Respiratory Physiology

## 1.1.1 Lung Volumes and Control of Breathing – Emily Johnson and Ben Cornwell

### Can you draw and explain the volumes and capacities of the lung?

*You should be able to draw, label and add values to the spirometer trace. You should practise doing this until you are confident with it and can talk it through as you draw it.*

Most lung volumes can be measured using a spirometer. The tidal volume is the volume of a normal breath and in an adult is around 500 ml (Figure 1.1.1.1). The functional residual capacity (FRC) is the volume of air left in the lungs at the end of normal expiration with the subject in the standing position and is around 3,000 ml in a normal adult. It can be considered as the volume of air in the lungs when the elastic recoil of the lungs is equal to the outward force of the chest wall and diaphragm tone. This is an important volume as it acts as an oxygen reserve, maintaining oxygenation of blood passing through pulmonary capillaries during expiration or breath-holding. FRC increases with subject height and in males. It is important to realise that it decreases approximately 1,000 ml in the supine position due to the upward force of the abdominal contents.

Inspiratory reserve volume is the volume that can be inspired over and above the normal tidal volume and equals approximately 2,500 ml. Inspiratory capacity is the total volume that can be inspired above FRC and equals around 3,000 ml.

Vital capacity is the maximal volume that can be expired after a maximal inspiration and is around 4,500 ml.

Expiratory reserve volume is the additional volume that can be expired at the end of expiration and is approximately 1,500 ml. Residual volume is the volume of air remaining in the lungs at the end of maximal expiration and is approximately 1,000–1,500 ml.

### Which volumes cannot be measured using simple spirometry?

The residual volume cannot be measured by spirometry and therefore any lung capacity which includes this volume can also not be measured. These are the total lung capacity and the functional residual capacity.

### What is the difference between a volume and a capacity?

A capacity is the sum of two or more volumes. Therefore, a volume is directly measured, whereas a capacity is deduced from the measured volumes. For example, the vital capacity is the sum of expiratory reserve volume, tidal volume and inspiratory reserve volume.

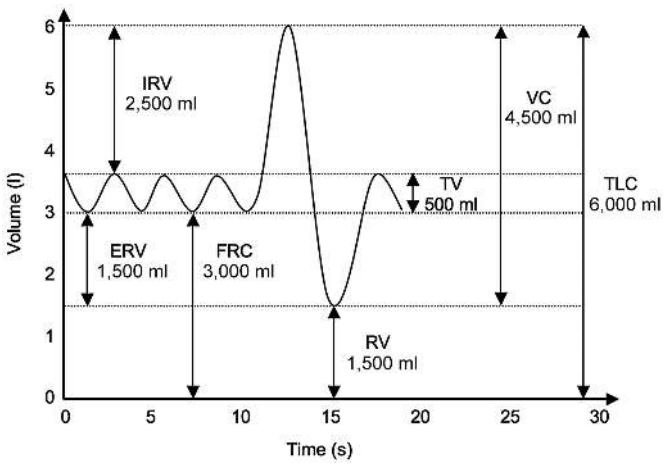


**Figure 1.1.1.1** Lung volumes.
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## What is closing capacity?

Closing capacity is the lung volume at which airways close. It is equal to the residual volume plus the closing volume. In healthy young subjects the closing capacity is less than the FRC, so airway closure does not occur in normal breathing. Closing capacity increases with age, increased intrathoracic pressure and smoking. In neonates, infants, the supine person aged 40 and the standing person aged 65, the closing capacity is equal to FRC. Once closing capacity exceeds FRC, there is airway closure and gas trapping in normal breathing.

## What is the work of breathing?

The work of breathing is the work required to move the lung and chest wall. In normal breathing the muscles of inspiration do all the work and expiration is passive. The forces that have to be overcome to expand the lung are divided into elastic forces and non-elastic forces. The non-elastic forces are also called frictional forces and encompass airway and tissue resistance. Half of the work of the inspiratory muscles is in overcoming the non-elastic forces. The other half is in overcoming the elastic forces, which is then stored as potential energy in the lung tissue. This potential energy is released on expiration as the elastic tissue returns to its resting state, and it is used to overcome frictional forces. In increased airway resistance or increased respiratory rate, the work of expiration may exceed the potential energy stored so expiratory muscles are recruited and expiration becomes active. When the lung is inflated to larger volumes or compliance is low, there will be more work required to overcome the elastic forces and so more energy stored at the end of inspiration. The work done to overcome the non-elastic forces is lost as heat. This is increased in rapid respiratory rates or high airway resistance.

The work of breathing can be demonstrated using pressure–volume curves of the lung on inspiration and expiration (Figure 1.1.1.2).

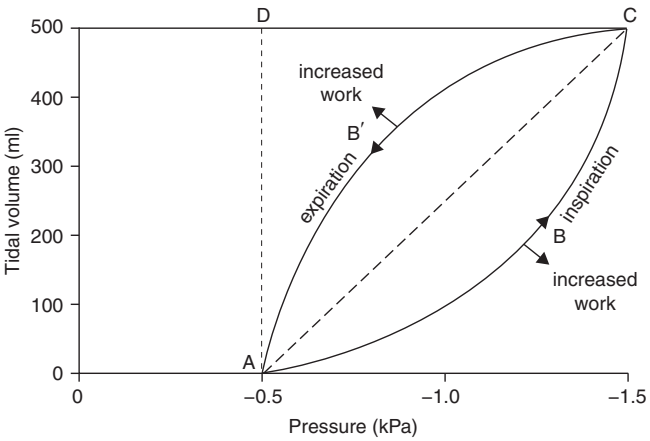


**Figure 1.1.1.2 Work of breathing**.
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#### Inspiratory work

- ACDA area = work to overcome elastic tissues
- ABCA area = work to overcome viscous resistance and friction.

#### Expiratory work

- CB′AC area = work to overcome airway resistance (within area ACDA therefore supplied from stored energy UNLESS increased work causes curve to bow to the left)
- Difference between CB′AC and CDAC areas = lost as heat energy.

*You should learn these pressure–volume curves and the areas relevant to the work of breathing. Practise drawing and explaining them.*

## How is alveolar ventilation controlled?

Alveolar ventilation is controlled by feedback loops. The system of control has three main components:

- A control centre, which is the medullary respiratory centre
- Effectors, which are the respiratory muscles
- Sensors feeding information to the central control, which are chemoreceptors and other types of receptors.

The respiratory centre lies across the pons and medulla, consisting of three groups of neurones. The medullary centre is in the reticular formation below the floor of the fourth ventricle. It has a dorsal respiratory group responsible for the control of inspiration and a ventral group responsible for the control of active expiration. Within the lower pons, the apneustic centre is thought to stimulate prolonged inspiration, and in the upper pons the pneumotaxic centre is thought to shorten the inspiratory breath.

The respiratory centre coordinates synchronised activity to the muscles of respiration, which are the diaphragm, intercostal muscles, abdominal muscles and accessory muscles such as sternocleidomastoid. The stimulation of these muscle groups increases their work and ventilation as a result.

## Tell me more about the chemoreceptors and other sources of input to the respiratory centre.

The afferent input into the respiratory centre comes from three sources: central, peripheral and others.

Central chemoreceptors are situated near the ventral surface of the medulla and respond to hydrogen ion ($H^+$) concentration in brain extra-cellular fluid. This is proportional to arterial partial pressure of $CO_2$. If ventilation is decreased, $PaCO_2$ will rise and an increased amount of $CO_2$ diffuses across the blood–brain barrier. This liberates more $H^+$ ions which diffuse into the extra-cellular fluid and stimulate chemoreceptors. It is important to note that $H^+$ and $HCO_3^-$ ions are unable to cross the blood–brain barrier directly, so it is the $CO_2$ diffusion which drives this process. This is an especially sensitive control mechanism because the pH of CSF is usually 7.32, with less protein buffering than in plasma, so smaller pH changes are detected as a result. In a chronically raised $PaCO_2$ such as in chronic obstructive pulmonary disease (COPD), compensatory changes occur and $HCO_3^-$ ions are actively transported across the blood–brain barrier.

Peripheral chemoreceptors are situated in both the carotid bodies and the aortic arch. These receptors respond primarily to low $PaO_2$, though the carotid bodies' chemoreceptors are also capable of responding to a raised $PaCO_2$, albeit to a lesser degree than the central chemoreceptors. Both receptors project to the nucleus tractus solitarius within the medulla. The carotid body afferent is the glossopharyngeal nerve (CN IX), and the aortic body afferent is transmitted by the vagus nerve (CN X).

Other afferents include stretch receptors within bronchial smooth muscles, which project via the vagus to cause an increased expiratory time and reduced respiratory rate upon distension (the Hering–Breuer reflex). Irritant receptors lie between airway epithelial cells and cause bronchoconstriction and hyperventilation in response to noxious gases. Juxtacapillary receptors, or J-receptors, are non-myelinated C fibres in the alveolar walls that respond to circulatory changes and can cause shallow fast breathing and apnoea. Joint and muscle receptors are also thought to influence ventilation by stimulation of the respiratory centre when limbs move, such as in exercise. Arterial baroreceptors decrease ventilation when they increase blood pressure, and pain and temperature receptors can also influence ventilation.

Lastly, voluntary control can modulate the ventilation from higher centres with cortical input having the ability to override brainstem control (breath-holding). The limbic system and hypothalamus can also modulate ventilation in response to emotional states.

# 1.1.2 Respiratory Compliance and Surface Tension – Rebecca Leslie and James Douglas

## What is the normal intrapleural pressure?

The intrapleural pressure is normally negative due to the lungs natural tendency to collapse inwards and the chest wall's tendency to spring outwards. When standing, intrapleural pressure at the end of a normal, passive breath (the functional residual capacity) is usually $-5$ $cmH_2O$. There is also a vertical pressure gradient due to gravitational forces, meaning that in the upright patient, intrapleural pressure is more negative

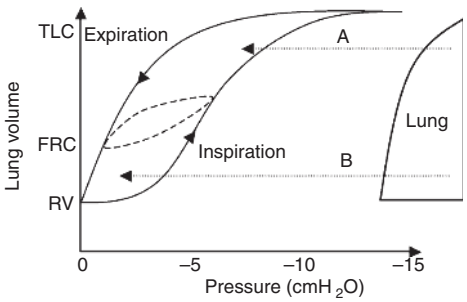


**Figure 1.1.2 Whole-lung pressure–volume loop.**
Modified with permission from Cross, M. and Plunkett, E. 2008. *Physics, Pharmacology and Physiology for Anaesthetists: Key Concepts for the FRCA*. Cambridge: Cambridge University Press. © M. Cross and E. Plunkett 2008.

at the apices (usually quoted to be −8 $cmH_2O$) and less negative at the bases (in the region of −3 $cmH_2O$).

The intrapleural pressure becomes more negative during normal ventilation. It normally changes by 3–4 $cmH_2O$ unless the inspiration is particularly forceful or the airway resistance increases. During expiration the intrapleural pressure returns back to normal. During forced expiration the intrapleural pressure may even exceed zero and can exceed airway pressure.

## What is compliance?

*To answer this question you should draw a pressure–volume curve. You should practise drawing this curve so you can draw it quickly and easily when answering any question on respiratory compliance.*

Compliance is the change in volume per unit pressure change (Figure 1.1.2). Therefore, total respiratory compliance refers to how easily the lungs expand, and it is represented by the gradient of the pressure–volume curve.

The normal expanding pressures of the lung are between –5 and –10 $cmH_2O$. At these pressures, the slope of the pressure–volume curve is steep, so for a small change in pressure there is a large change in volume. Therefore, it can be said at these pressures that the lung is remarkably compliant. The compliance of the normal lung at FRC is approximately 200 $ml/cmH_2O^{-1}$.

At higher expanding pressures, the lung is stiffer and much less compliant, as demonstrated by the flatter part of the curve.

## What are the components that influence respiratory compliance?

The two main components to respiratory compliance are lung compliance and chest wall compliance.

The lung compliance is determined by the elastic recoil properties of the pulmonary connective tissue and the surface tension at the fluid/air interface within the alveoli. The lungs expand in response to the pressure gradient across their surface. This is called the transpulmonary pressure and is produced by the respiratory muscles. Transpulmonary pressure is the difference between alveolar pressure and intrapleural pressure. Alveolar pressures during quiet ventilation can be approximated to atmospheric pressure, so transpulmonary pressure effectively equates to intrapleural pressure.

The lung compliance at FRC is 200 $ml/cmH_2O$. At high transpulmonary pressures the lung compliance drops. This is because the elastic fibres are fully stretched close to

their elastic limit. In emphysematous lungs, destruction of these elastic fibres leads to increased lung compliance and the resetting of the FRC to a higher volume.

In contrast, chest wall compliance is reduced by diseases such as ankylosing spondylitis, where the chest wall becomes virtually rigid and FRC is much reduced.

In the respiratory system, the lungs and thoracic cage work together during inspiration and expiration. Total respiratory compliance is therefore the combination of the lung and chest wall compliances. The relationship between these factors can be expressed by the formula:

$$1/\text{Total respiratory compliance} = 1/\text{Lung compliance} + 1/\text{Chest wall compliance}$$

## Describe the difference between static and dynamic compliance.

Static and dynamic compliance represent two different methods of determining compliance. Static compliance is the change in volume per unit change in distending pressure when there is no airflow within the lungs. The distending pressure is the transpulmonary pressure which, during quiet breathing, is equal to the intrapleural pressure because alveolar pressure is the same as atmospheric pressure. Therefore, to determine the compliance we need to know the intrapleural pressure, which can be approximated by measuring the oesophageal pressure. This is done by asking the subject to swallow a small balloon on the end of a catheter. The subject takes a maximal inspiration and then breathes out into a spirometer in steps of 500 ml. The lungs are given a few seconds to stabilise after each exhalation and then the oesophageal pressure is recorded. This process is repeated until the patient has breathed out their total lung capacity. These measurements can then be used to produce a static pressure–volume curve. The lung compliance at specific lung volumes can be calculated by the slope of the curve.

In dynamic compliance the pressure–volume curve is plotted continuously throughout the respiratory cycle during spontaneous breathing or mechanical ventilation and is also affected by airway resistance. For this reason, the pressures recorded in dynamic compliance for a given volume are always higher than those recorded in static compliance, and as a consequence the lung compliance is found to be lower.

## What factors influence compliance?

*Remember always to first classify your answer.*

Compliance is influenced by physiological and pathological factors.

**Physiological factors include:**

- Posture: the lungs are more compliant when the patient is upright, and compliance declines when the patient becomes supine
- Age: compliance increases with age due to the gradual loss of lung elastic tissue
- Pregnancy: the FRC is reduced and the lungs become less compliant.

**Pathological factors include:**

- Pulmonary Fibrosis: compliance is reduced due to an increase in fibrous lung tissue
- Acute Respiratory Distress Syndrome (ARDS): decreases compliance during the fibrotic phase

- Pulmonary Oedema: reduces lung compliance via an unknown mechanism
- Atelectasis: decreases lung compliance as greater pressure is required to overcome surface tension and recruit alveoli that have collapsed
- Increased Pulmonary Venous Pressure: decreases lung compliance because the lungs become engorged with blood
- Emphysema: compliance is increased by the destruction of elastic tissue in the lung.

## What is hysteresis?

Hysteresis is where an output variable differs according to whether the input variable is increasing or decreasing. For example in the pressure–volume curve the inspiration and expiration curves are not identical but form a loop where the expiration curve differs from the inspiration curve, see Figure 1.1.2. This loop is known as hysteresis.

Hysteresis normally results from the absorption of energy, often as friction. The area of the loop represents the amount of energy expended or wasted as heat (through elastic tissues and airway). In the pressure–volume curve the lung loses energy when the elastic tissues stretch and then recoil and in order to overcome airway resistance. A factor that reduces this wasted energy and thus improves the efficiency of the breathing cycle is the reduction of alveolar surface tension by surfactant.

## What causes surface tension in the alveoli?

*First demonstrate your understanding of what surface tension is by defining it and then move on to what causes it in the alveoli.*

Surface tension (represented as T) refers to the attraction of particles in the surface layer of a fluid which acts to minimise its surface area. It is the force acting across an imaginary line 1 cm long in the surface of a liquid, giving it the units of force per unit length ($N.m^{-1}$ or $dyne.cm^{-1}$).

The alveoli are lined by a thin layer of fluid. This fluid contributes to the surface tension acting on the alveoli because the attractive forces between these water molecules are greater than the attractive forces at the air–fluid interface. This results in the liquid surface area becoming as small as possible, and tending to collapse the alveolus.

This behaviour can be seen when blowing a soap bubble on the end of a tube. The liquid molecules in the surface of the bubble have much stronger attractive forces than the forces between the liquid and the air at the liquid–air interface. This means that the surface of the bubble contracts as much as possible which creates a sphere that has the smallest surface area for a given volume of air and generates a pressure within the bubble.

## How can you predict the pressure inside a bubble or alveolus?

*With this question they are testing your knowledge and understanding of Laplace's law. First state Laplace's law and then explain how this equates to the lung.*

Laplace's law states that the pressure in a bubble or alveoli is proportional to two times the surface tension divided by the radius of the bubble, therefore $P = 2T/r$. This means that internal pressure is inversely proportional to the radius.

From this law it can be demonstrated that an alveolus with a small radius will have a greater pressure inside it than a larger alveolus. In the lung, alveoli of various sizes are

interconnected; because smaller alveoli have a higher pressure inside them, Laplace's law dictates that there will be a tendency of the smaller alveoli to collapse into the larger alveoli. In addition, the inward force created by this surface tension will also tend to suck fluid into the alveoli; this is called transudation.

## How are these problems minimised in the lung?

In the lung the problems of surface tension are overcome by the production of surfactant by type 2 pneumocytes. Surfactant is a mixture of phospholipids, of which dipalmitoyl phosphatidylcholine (DPPC) is the most important constituent. The molecules of DPPC are hydrophobic at one end and hydrophilic at the other end. As a result, they align themselves over the surface of the liquid which lines the alveoli. Their intermolecular repulsive forces oppose the normal attractive forces between the liquid molecules so reduce the surface tension.

If the alveoli shrink, the molecules of surfactant become closer together and consequently repel each other more. This further reduces the surface tension and helps prevent the alveoli from collapsing. It also equalises the pressure within small and large alveoli.

## What are the advantages of surfactant?

Surfactant lowers the surface tension in the alveoli and as a result increases the compliance of the lung and reduces the work required to expand the alveoli.

In addition, surfactant prevents the transudation of fluid into the alveoli from the surrounding capillaries. Surface tension forces in the alveoli not only tend to collapse the alveoli, but also tend to suck fluid into the alveolar spaces from the capillaries. Surfactant reduces these surface tension forces and therefore helps to keep the alveoli dry.

Surfactant also increases the stability of the alveoli. We know that the pressure generated by the surface forces of the alveolus is inversely proportional to the radius, so if the surface tensions are the same then the pressure in the small alveolus is greater than the pressure in the large alveolus. However, if surfactant is present the surface tension in a small alveolus is much smaller than the surface tension in a large alveolus. This reduces the tendency for the small alveoli to empty into the large alveoli, and overall the alveoli are more stable.

## What happens if there is no surfactant?

*Base your answer to this question on the three functions of surfactant that you have already mentioned. It is also worth mentioning infant respiratory distress syndrome in your answer.*

Without surfactant, lungs would be non-compliant, with areas of atelectasis and a tendency to pulmonary oedema because the alveoli would become filled with transudate. These are the pathophysiological features of infant respiratory distress syndrome.

Infant respiratory distress syndrome is a syndrome which occurs when babies are born prematurely before adequate levels of surfactant are produced. Ideally this condition is prevented by administering maternal steroids (such as betamethasone) prior to delivery which induces the production of fetal surfactant; however, this is not always achievable and it is now possible to treat these infants by instilling synthesised surfactant into their lungs.

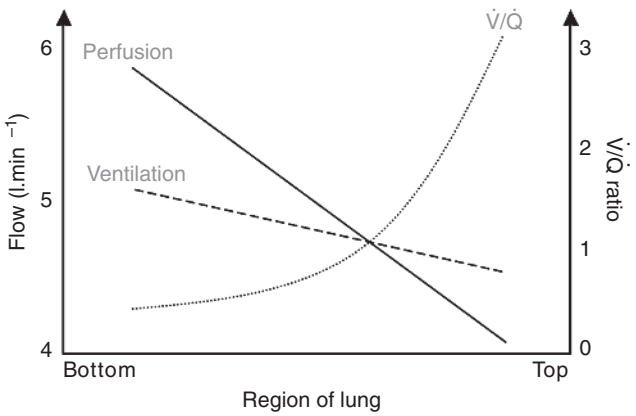


**Figure 1.1.3.1 Ventilation/perfusion.** Reproduced with permission from Cross, M. and Plunkett, E. 2008. Physics, Pharmacology and Physiology for Anaesthetists: Key Concepts for the FRCA. Cambridge: Cambridge University Press. © M. Cross and E. Plunkett 2008.

## 1.1.3 Ventilation, Perfusion and Dead-Space – Rebecca Leslie and James Douglas

### How is the blood flow distributed within the lungs?

*When answering this question it is a good idea to draw a graph with the region of the lung on the x axis and blood flow in litres per minute on the y axis. Remember to always label your axes and add on an appropriate scale. See Figure 1.1.3.1.*

In the upright lung the blood flow increases linearly from the bottom to the top. At the apex of the lung the blood flow is very low. This effect is mainly determined by gravity and the hydrostatic pressures within the blood vessels. The pressure difference between the bottom and the top of the lung could be as high as 30 $cmH_2O$. This is a large pressure difference for the low-pressure pulmonary circulation.

### What will happen to the blood flow if the patient lies down?

The pulmonary blood flow is very dependent on posture. If the patient lies down, the blood flow to the posterior regions of the lungs will become greater than to the anterior regions of the lungs. The difference between the apex and base of the lung will diminish in a supine patient.

### How can you measure the distribution of blood flow in the lungs?

Radioactive xenon can be used to determine the distribution of blood flow in the lungs. The radioactive xenon is dissolved in normal saline and then injected into a peripheral vein. Xenon has a very low blood–gas partition coefficient (poorly soluble in blood), so when it reaches the pulmonary capillaries it will quickly move from the blood into the alveolar gas. If the patient breath-holds, the distribution of the radioactive xenon can be measured by counters over the chest wall.

An MRI scan, with intravenous gadolinium, can also be used to measure pulmonary perfusion.

## Tell me about the distribution of ventilation within the lungs.

It has been found that there are significant differences in the ventilation of different regions of the lungs, although this is to a lesser extent than variations in perfusion. Due to gravitational forces intrapleural pressure at the apex is significantly more negative than at the base. This results in the apical alveoli being more distended and so ventilate on the flatter part of the pressure–volume curve, where compliance is low, thus resulting in relatively less ventilation, see Figure 1.1.2.

## How can you demonstrate this difference in ventilation?

*Remember to keep it simple. This is the sort of question where they are expecting some lateral thinking; they do not necessarily expect you to have learnt this. Just think logically about how this could be done, and mention principles without worrying about the specifics.*

The regional variations in ventilation can be demonstrated by asking the patient to inhale radioactive xenon gas. A radiation camera can then determine the volume of radioactive xenon throughout the chest cavity.

## What causes this variation in ventilation?

*To explain this concept it will be beneficial to draw a graph with intrapleural pressure (with values becoming more negative to the right) on the x axis, and lung volume on the y axis, see Figure 1.1.2 in the previous chapter.*

*This curve is an upward sloping sigmoid curve and helps to explain why more ventilation occurs at the bases of the lungs compared to the top. Remember to always label your axes and draw diagrams big enough for the examiners to see easily.*

The intrapleural pressure is less negative, and therefore greater, at the bases of the lung when compared to the apex. The reason for this difference in intrapleural pressure has to do with the weight of the lung. In order to balance out the downward acting force due to the weight of the lung, the pressure below the lung must be greater than the pressure above it. As a result the pressure near the bases is approximately $-2.5$ $cmH_2O$ compared to the pressure at the apex which is roughly $-10$ $cmH_2O$.

If lung volume is plotted on a graph against intrapleural pressure, with values becoming more negative towards the right, an upward-sloping sigmoid curve is formed. From this curve it is evident that at resting state pressures of $-2.5$ $cmH_2O$, like those at the bases of the lung, there is only a small volume of gas. However, for a small decrease in intrapleural pressure, for example when a patient takes a breath, there is a large increase in lung volume (indicated by the steep part of the sigmoid curve). This steep section of the curve represents the highly compliant lung bases.

At the apex of the lung, where intrapleural pressure at resting state is approximately $-10$ $cmH_2O$, from the graph you can see that there is already a large volume of gas in the alveoli. When the patient takes a breath and the pressure becomes more negative there is very little change in volume of gas in this area of the lung because the alveoli are already fully expanded. This is why the curve flattens out at this point, representing lower compliance.

So in summary, the bases of the lung have a small resting volume, but a large changing volume, so ventilation is good. In contrast at the apex the resting volume is large and a change in pressure results in only a small change in volume with inspiration.