

Section 1

Physiology

Chapter

1.1

Respiratory physiology

1.1.1. Lung volumes and control of breathing – Emily K Johnson

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 practice doing this until you are confident with it and can talk it through as you draw it.

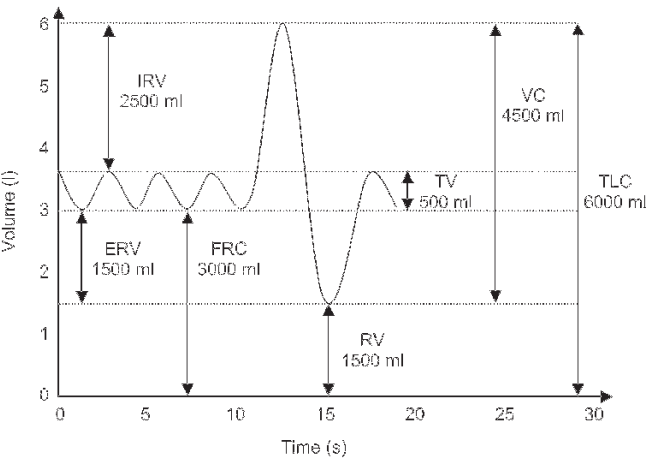


Figure 1.1.1a. Lung volumes. Reproduced with permission from Cross, M. and Plunkett, E. 2008. *Physics, Pharmacology and Physiology for Anaesthetists: Key Concepts for the FRCA*. Cambridge: Cambridge University Press. © M. Cross and E. Plunkett 2008.

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 1.1.1a). The functional residual capacity (FRC) is the volume of air in the lungs at the end of normal expiration with the subject in the standing position and is around 3000 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 1000 ml in the supine position due to the upward force of the abdominal contents.

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Inspiratory reserve volume is the volume that can be inspired over and above the normal tidal volume and equals approximately 2500 ml. Inspiratory capacity is the total volume that can be inspired above FRC and equals around 3000 ml.

Vital capacity is the maximal volume that can be expired after a maximal inspiration and is around 4500 ml.

Expiratory reserve volume is the additional volume that can be expired at the end of expiration and is approximately 1500 ml. Residual volume is the volume of air remaining in the lungs at the end of maximal expiration and is approximately 1000 to 1500 ml.

Which volumes cannot be measured using simple spirometry?

The residual volume cannot be measured 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 the expiratory reserve volume, the tidal volume and the inspiratory reserve volume.

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 intra-thoracic 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 airways 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 end inspiration. The work done to overcome the non-elastic forces is lost as heat. This is increased in rapid respiratory rates or high airways resistance.

The work of breathing can be demonstrated using pressure–volume curves of the lung on inspiration and expiration (Figure 1.1.1b).

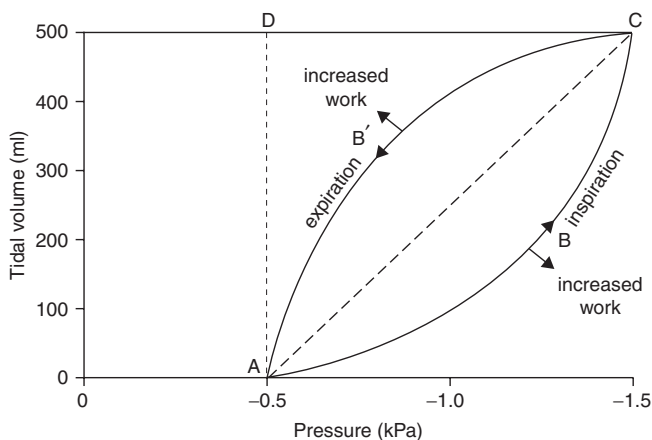


Figure 1.1.1b. Work of breathing. Modified with permission from Cross, M. and Plunkett, E. 2008. *Physics, Pharmacology and Physiology for Anaesthetists: Key Concepts for the FRCA*. Cambridge: Cambridge University Press. © M. Cross and E. Plunkett 2008.

- 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 airways 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. Practice 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 in the pons and medulla and consists 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, thought to be responsible for inspiration, and a largely dormant ventral group, thought to be responsible for expiration. The other two groups of neurones make up the apneustic centre in the lower pons and the pneumotaxic centre in the upper pons. Their exact involvement in respiration is not clear.

When the respiratory centre is appropriately stimulated it coordinates synchronised activity from the muscles of respiration, which are the diaphragm, the intercostal muscles, the abdominal muscles, and the accessory muscles, such as sternocleidomastoid. These muscle groups increase their work, and ventilation is increased appropriately.

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

The afferent input into the respiratory centre comes from a number of sources. Central chemoreceptors play an important role. They respond mostly to hydrogen ion (H^+) concentration in brain extra-cellular fluid. This is influenced by arterial partial pressure of CO_2 . These chemoreceptors are situated near the ventral surface of the medulla. 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 the chemoreceptors. This process is enhanced by the vasodilatation that accompanies increased arterial pressures of CO_2 . H^+ and HCO_3^- ions are unable to cross the blood-brain barrier, so it is increased $PaCO_2$ that affects central chemoreceptors. This is a very sensitive mechanism for increasing ventilation in response to raised CO_2 because the pH of CSF is usually 7.32 and there is less protein buffering than in plasma, so smaller pH changes are detected. 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 the carotid bodies and the aortic arch. The carotid bodies contain two types of glomus cells. Type 1 cells are rich in dopamine and are close to the end of the carotid sinus nerve. The glomus cells are affected by raised $PaCO_2$ and decreased pH, although pH has no effect on the aortic arch chemoreceptors. Peripheral chemoreceptors also mount a response to low PaO_2 and are the only receptors responsible for this response. Overall the peripheral chemoreceptors are only responsible for 20% of the body's response to a raised $PaCO_2$, with the rest being due to the central chemoreceptors; however, it is the peripheral chemoreceptors that act fastest.

Other receptors that feed information to the respiratory centre include lung stretch receptors in bronchial smooth muscle, which transmit signals in the vagus with large amounts of distension causing an increased expiratory time and reduced respiratory rate. This is the Hering-Breuer reflex. Irritant receptors lie between airway epithelial cells and cause bronchoconstriction and hyperventilation in response to noxious gases. J, or juxtacapillary, receptors are non-myelinated C fibres in the alveolar walls that respond to circulatory changes and can cause shallow fast breathing and apnoea. There are other receptors in the nose and upper airways that respond to mechanical and chemical stimuli. 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. To a certain degree ventilation is under voluntary control from higher centres and cortical input can override brainstem control centres. The limbic system and hypothalamus also have input in extreme emotional states.

1.1.2. Respiratory compliance and surface tension – Rebecca A Leslie

What is the normal intra-pleural pressure?

The intra-pleural pressure is normally negative due to the lungs natural tendency to collapse inwards and the chest walls tendency to spring outwards. When standing and at normal

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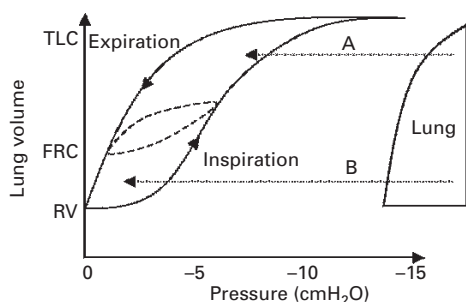
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Figure 1.1.2. Whole lung pressure–volume loop. Modified with permission from Cross, M. and Plunkett, E. 2008. *Physics, Pharmacology and Physiology for Anaesthetists: Key Concepts for the FRCA*. Cambridge: Cambridge University Press. © M. Cross and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

resting volume the intra-pleural pressure at the apex is -10 cmH₂O and at the base it is -2.5 cmH₂O.

The intra-pleural pressure becomes more negative during normal ventilation. It normally changes by 3–4 cmH₂O unless the inspiration is particularly forceful or the airway resistance increases. During expiration the intra-pleural pressure returns back to normal unless expiration is forced or resistance increased. During forced expiration the intra-pleural pressure may even exceed zero, and hence airway pressure.

What is compliance?

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

Compliance is the change in volume for a pressure change across the lung (Figure 1.1.2). Therefore compliance is how easily the lungs expand, and it represents the slope of the pressure–volume curve.

The normal expanding pressures of the lung are between -5 and -10 cmH₂O. 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 is approximately 200 ml/cmH₂O.

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 thoracic 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 it is produced by the respiratory muscles. Transpulmonary pressure is the difference between alveolar pressure and intra-pleural pressure. Alveolar pressures during quiet ventilation can be approximated to atmospheric pressure, so transpulmonary pressure equates to intra-pleural pressure. The lung compliance at FRC is 200 ml/cmH₂O. At high transmural pressures the lung compliance drops. This is because the elastic fibres are fully stretched close to their elastic limit.

The compliance of the chest wall at FRC is also found to be 200 ml/cmH₂O. The chest wall compliance is reduced by diseases such as ankylosing spondylitis where the chest wall becomes virtually rigid.

In the respiratory system the lungs and thoracic cage work together during inspiration and expiration. The respiratory compliance is therefore the combination of the lung and chest wall compliances.

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

Describe the difference between static and dynamic compliance

Static and dynamic compliance represent two different methods of determining compliance.

Static compliance is the volume change per unit change in distending pressure when there is no airflow. The distending pressure is the transpulmonary pressure, which during quiet breathing is equal to the intra-pleural pressure because alveolar pressure is the same as atmospheric pressure. Therefore to determine the compliance we need to know the intra-pleural pressure. We can estimate intra-pleural pressure by measuring 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.

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:

- Posture – the lungs are more compliant when the patient is upright, and compliance declines when the patient becomes supine
- Age – compliance is reduced at the extremes of age
- Pregnancy – the FRC is reduced and the lungs become less compliant.

Pathological factors can both increase and decrease lung compliance.

Diseases that decrease the compliance of the lung include:

- Pulmonary fibrosis – due to an increase in lung fibrous tissue
- Acute respiratory distress syndrome and pulmonary oedema – by preventing the inflation of alveoli

- Atelectasis – decreases lung compliance as greater pressure is required to recruit alveoli
- Increased pulmonary venous pressure – decreases lung compliance because the lungs become engorged with blood.

A disease that increases lung compliance is pulmonary emphysema where there is an alteration in the elastic tissue in the lung.

What is hysteresis?

Hysteresis is where a measurement differs according to whether the value 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. 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.

The definition of surface tension is the force acting across an imaginary line 1 cm long in the surface of a liquid. Surface tension is measured in dynes.

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 alveoli?

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 four times the surface tension divided by the radius of the bubble. Therefore $P = 4T/r$. This means that internal pressure is proportional to $1/\text{radius}$.

From this law it can be seen that an alveolus with a small radius will have a greater pressure inside it than a larger alveolus. Now imagine these alveoli are connected together. Because the smaller alveolus has a higher pressure inside it, it will tend to collapse into the larger alveolus. 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.

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. We previously mentioned how the 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 your 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 giving maternal steroids prior to delivery which induces the production of foetal surfactant, however this is not always achievable and it is now possible to treat these infants by instilling synthesised surfactant into their lungs.

1.1.3. Ventilation, perfusion and dead-space – Rebecca A Leslie

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 always label your axes and add on an appropriate scale. See Figure 1.1.3a.

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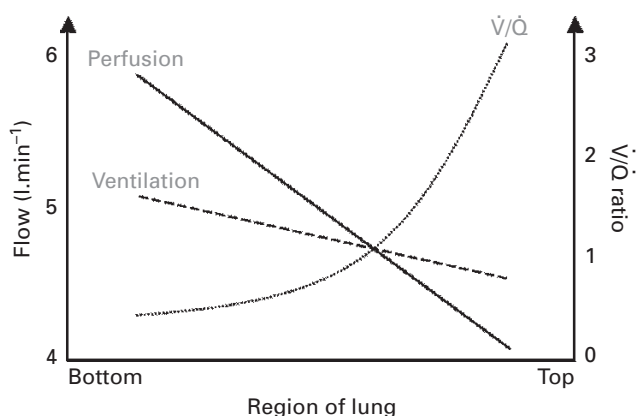
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Figure 1.1.3a. Ventilation/perfusion. Reproduced with permission from Cross, M. and Plunkett, E. 2008. *Physics, Pharmacology and Physiology for Anaesthetists: Key Concepts for the FRCA*. Cambridge: Cambridge University Press. © M. Cross and E. Plunkett 2008.

In the upright lung the blood flow decreases 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 cmH₂O which 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 solubility, 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.

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. The bases of the lung ventilate better than the upper zones.

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 intra-pleural 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, page 5. 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 always label your axes and draw diagrams big enough for the examiners to see easily.

The intra-pleural pressure is less negative, and therefore greater at the bases of the lung when compared to the apex. The reason for this difference in intra-pleural 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 $-2.5 \text{ cmH}_2\text{O}$ compared to the pressure at the apex which is $-10 \text{ cmH}_2\text{O}$.

If lung volume is plotted on a graph against intra-pleural 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 $-2.5 \text{ cmH}_2\text{O}$, like those at the bases of the lung, there is only a small volume of gas. However for a small decrease in intra-pleural 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).

At the apex of the lung, where pressure at resting state is approximately $-10 \text{ cmH}_2\text{O}$, 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.

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.

Therefore, like the blood flow, ventilation decreases from bottom to top of the lung. However it is worth mentioning that the regional differences in blood flow from the bottom to the top of the lungs vary more than the regional changes in ventilation.

This can be shown on another graph, with the rib number on the x axis, starting with the bottom and moving to the top of the lung (remembering that the bottom of the lungs is indicated by rib number 12, so the numbers decrease as you move to the right) and the blood flow in L/min and the percentage of lung volume on the y axis. A straight downward sloping line can be drawn for blood flow indicating a better blood flow at the bottom compared to the top of the lungs. Another straight downward sloping line can be drawn for the ventilation, however this line has a smaller gradient than for blood flow showing that although there are regional differences in ventilation, these are less noticeable than for blood flow, see Figure 1.1.3a.

What happens to the distribution of ventilation at very low lung volumes?

The main principle behind this question is that at low lung volumes the intra-pleural pressure increases, i.e. becomes more positive. If you remember this by using the graph that you drew for the last question showing intra-pleural pressure on the x axis and lung volume on the y axis you will be able to work out the answer.

At low lung volumes, for example at the reserve volume after a maximal expiration, the intra-pleural pressures become more positive because the lung is not so well expanded and the elastic recoil forces are smaller.