A CHANGE IN POSTURE

Below is a set of graphs showing some cardiovascular parameters during a change in posture from supine to standing, and then to supine again.

1. What happens to the stroke volume when standing up after a period of lying supine? Explain why this change occurs.

   Standing up increases the venous pooling of blood in the most dependent parts of the body. (Veins are, after

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all, capacitance vessels.) This redistribution of blood causes a reduction in the intrathoracic blood volume returning to the heart. Through the Frank-Starling mechanism, this causes a reduction in the stroke volume (by 30–40%). This rises again when going back to the supine position, in response to increased venous return.

2. What happens to the arterial pressure during this period?
Despite changes in the physiologic environment and stroke volume, reflex responses ensure that there is little change in the arterial pressure.

3. What is the physiologic relationship between the cardiac output (CO) and the arterial pressure normally?
The arterial pressure is defined as the product of the CO and the systemic vascular resistance (SVR) and may be considered as the afterload. An increase of this places a negative feedback on any further rise in the CO.

4. What physiologic mechanisms ensure that the arterial pressure is maintained after standing?
The changes that occur may be understood by considering the relationship of the arterial pressure to the heart rate and SVR.

\[
\text{Arterial pressure} = \text{CO} \times \text{SVR}
\]

where \( \text{CO} \) = heart rate \( \times \) stroke volume

\[
\therefore \text{Arterial pressure} = \text{heart rate} \times \text{stroke volume} \times \text{SVR}
\]

There is a fall in the stroke volume, so in order to maintain the blood pressure (BP), the heart rate and the SVR must increase

- Carotid baroreceptor stimulation is reduced following a fall in the pulse pressure on standing.
This causes a reduction of vagal cardiac stimulation, and an increase in sympathetic nervous system (SNS) stimulation of the heart and peripheral vasculature.

- There is, therefore, an increase in the heart rate by 15–20 beats per minute.
- Increased peripheral SNS activity stimulates arteriolar vasoconstriction – increasing the SVR.
- There is also some venoconstriction, limiting the amount of peripheral blood pooling.
- There is a sympathetically-mediated inotropic effect on the myocardium, limiting the fall in the stroke volume and CO.
- As a result of increases in the heart rate and SVR, the arterial pressure may actually rise slightly on standing.

5. Give some common causes for postural hypotension.
   - Failure to increase the CO during standing:
     - Simple vaso-vagal syncope
     - Fixed heart rate or bradycardia: β-blockers, heart block, sick sinus syndrome
     - Myocardial diseases: cardiomyopathy, other cardiac failure
   - Reduced stroke volume:
     - Fixed afterload: aortic stenosis, pulmonary embolism
     - Dehydration, diuretics
   - Reduced SVR:
     - Vasodilator drugs, e.g. α-blockers, nitrates, antidepressants
     - Pregnancy
     - Sepsis
     - Autonomic failure, e.g. chronic diabetes mellitus
1. Define the pH.
The pH is $-\log_{10} [H^+]$.

2. What is the pH of the blood?
7.36–7.44.

3. Where does the $H^+$ in the body come from?
Most of the $H^+$ in the body comes from CO$_2$ generated by metabolism. This enters solution, forming carbonic acid through a reaction mediated by the enzyme carbonic anhydrase.

$$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$$

Acid is also generated by
- Metabolism of the sulphur-containing amino acids cysteine and methionine
- Anaerobic metabolism, generating lactic acid
- Generation of the ketone bodies: acetone, acetoacetate and $\beta$-hydroxybutyrate

4. What are the main buffer systems in the intravascular, interstitial and intracellular compartments?
In the plasma the main systems are:
- The bicarbonate system
- The phosphate system ($HPO_4^{2-} + H^+ \rightleftharpoons H_2PO_4^-$)
- Plasma proteins
- Globin component of haemoglobin

*Interstitial*: the bicarbonate system
*Intracellular*: cytoplasmic proteins.

5. What does the Henderson–Hasselbalch equation describe, and how is it derived?
This equation, which may be applied to any buffer system, defines the relationship between dissociated and
undissociated acids and bases. It is used mainly to describe the equilibrium of the bicarbonate system.

\[ \text{CO}_2 + \text{H}_2\text{O} \rightleftharpoons \text{H}_2\text{CO}_3 \rightleftharpoons \text{H}^+ + \text{HCO}_3^- \]

The dissociation constant,

\[ K = \frac{[\text{H}^+][\text{HCO}_3^-]}{[\text{H}_2\text{CO}_3]} \]

Therefore

\[ [\text{H}^+] = K \frac{[\text{H}_2\text{CO}_3]}{[\text{HCO}_3^-]} \]

Taking the \( \log_{10} \)

\[ \log_{10}[\text{H}^+] = \log_{10} K + \log_{10} \frac{[\text{H}_2\text{CO}_3]}{[\text{HCO}_3^-]} \]

Taking the negative log, which expresses the pH, and where \(-\log_{10} K\) is the pK

\[ \text{pH} = \text{pK} - \log_{10} \frac{[\text{H}_2\text{CO}_3]}{[\text{HCO}_3^-]} \]

Invert the term to remove the minus sign:

\[ \text{pH} = \text{pK} + \log_{10} \frac{[\text{HCO}_3^-]}{[\text{H}_2\text{CO}_3]} \]

The \([\text{H}_2\text{CO}_3]\) may be expressed as \(\text{pCO}_2 \times 0.23\), where 0.23 is the solubility coefficient of \(\text{CO}_2\) (when the \(\text{pCO}_2\) is in kPa).

The pK is equal to 6.1.
Thus,

\[
pH = 6.1 + \log_{10} \frac{[\text{HCO}_3^-]}{\text{pCO}_2 \times 0.25}.
\]

6. Which organ systems are involved in regulating acid-base balance?

The main organ systems are:

- **Respiratory system**: this controls the \( \text{pCO}_2 \) through alterations in the alveolar ventilation. Carbon dioxide indirectly stimulates central chemoreceptors (found in the ventro-lateral surface of the medulla oblongata) through \( \text{H}^+ \) released when it crosses the blood-brain barrier (BBB) and dissolves in the cerebrospinal fluid (CSF).

- **Kidney**: this controls the \([\text{HCO}_3^-]\), and is important for long-term control and compensation of acid-base disturbances.

- **Blood**: through buffering by plasma proteins and haemoglobin.

- **Bone**: \( \text{H}^+ \) may exchange with cations from bone mineral. There is also carbonate in bone that can be used to support plasma \( \text{HCO}_3^- \) levels.

- **Liver**: this may generate \( \text{HCO}_3^- \) and \( \text{NH}_4^+ \) (ammonia) by glutamine metabolism. In the kidney tubules, ammonia excretion generates more bicarbonate.

7. How does the kidney absorb bicarbonate?

There are three main methods by which the kidneys increase the plasma bicarbonate:

- Replacement of filtered bicarbonate with bicarbonate that is generated in the tubular cells.

- Replacement of filtered phosphate with bicarbonate that is generated in the tubular cells.

- By generation of ‘new’ bicarbonate from glutamine molecules that are absorbed by the tubular cell.
8. Define the base deficit.

The base deficit is the amount of acid or alkali required to restore 1 l of blood to a normal pH at a pCO₂ of 5.3 kPa and at 37°C. It is an indicator of the metabolic component to an acid-base disturbance. The normal range is −2 to +2 mmol/l.
1. What is meant by the ‘equilibrium potential’ for an ion?

The equilibrium potential of an ion is the potential difference at which that ion ceases to flow down its electrochemical gradient across the cell membrane. It is calculated by the Nernst equation.

2. What is meant by the ‘resting membrane potential’ for a cell?

This is the potential difference across the cell membrane. This occurs due to the ionic fluxes of Na\(^+\), K\(^+\), and Cl\(^-\) across the membrane, the sizes of which are determined by their electrochemical gradients. It is calculated by the Goldman equation, which takes into account the contribution of the equilibrium potentials of each species of ion that crosses the membrane.

3. What is the typical value of the resting membrane potential for a neurone?

A typical value is \(-70\) mV. The value is negative because the interior of the cell is negatively charged with respect to the exterior.

4. What is the importance of the Na\(^+\)/K\(^+\) pump for the equilibrium potential?

This pump, which is ATPase-driven, transports 3 Na\(^+\) out of the cell for 2 K\(^+\) pumped in. It helps to maintain the internal and external ionic environment that progressively alters as ions naturally flow down their electrochemical gradients. In doing so, it maintains and sustains the potential difference across the cell (Resting membrane potential).
5. What is an action potential? Draw and label the axes of a typical action potential for a neurone.

This is defined as the rapid change in the membrane potential (depolarisation) that occurs following stimulation of an excitable cell. It is followed by a rapid return to the resting membrane potential (repolarisation).

![Diagram of an action potential](image)


- Note that depolarisation is an ‘all-or-none’ response, in that the action potential is generated only when the threshold potential is reached by the stimulus. Sub-threshold stimuli do not generate the action potential.
- For any individual excitable cell, each action potential is of the same amplitude, and propagated at the same speed.

6. Briefly describe the ionic basis for the action potential.

The changes in the fluxes of ions that account for depolarisation may be summarised in the following
Once the threshold potential is reached by the stimulus, the voltage-sensitive Na\(^+\)-channels open, causing a rapid influx of Na\(^+\) into the cell. This causes depolarisation, and the membrane potential becomes positive. Once open, the Na\(^+\)-channel closes again within milliseconds.

During the initial opening of the Na\(^+\)-channels, a positive feedback loop is initiated; so more channels open up, leading to rapid depolarisation.

The cell would remain depolarised if it were not for the rapid closure (inactivation) of the Na\(^+\)-channels.

At the same time there is a constant background movement of K\(^+\) out of the cell. This has the effect of placing a limit on the change of membrane potential during the depolarisation phase of the action potential.

During repolarisation, there is the opening of the voltage-sensitive K\(^+\)-channels, leading to loss of K\(^+\) from the cell, causing the membrane potential to return to its initial value.