

Starling Forces.

Learning Objectives.

At the end of this module, you should be able to :

- 1. Give a brief description of bulk flow**
- 2. Define the principle of starling Forces**
- 3. Name all four Starling Forces**
- 4. Understand how changes in pressure can influence movement across the capillary wall.**

In the circulatory system the capillaries are referred to as exchange vessels. This is because their thin walls allow the movement of many materials to cross them with relative ease. There are three mechanisms whereby capillary exchange can occur :

- **Diffusion**, which depends on the presence of a concentration gradient across the capillary wall.
- **Bulk flow**, which depends on mechanical forces (pressures) across the capillary wall.
- **Vesicular transport**, which depends on the formation of specific transport systems in the capillary wall.

Most nutrients pass from the circulation to the cells, and many by-products of cellular metabolism pass in the opposite direction, by simple diffusion, according to their concentration gradient.

The exact route for diffusion of a substance depends upon a number of factors, the two most important being the degree of lipid solubility and molecular size. Lipid-soluble substances such as oxygen, CO₂, alcohol, fatty acids, steroid hormones and many anaesthetic agents, are able to pass directly across the endothelial wall. Small

lipid-insoluble molecules and ions such as glucose, amino acids, urea, Na^+ , K^+ and non-steroid hormones, can pass readily via intercellular clefts, or fenestrations when these are present.

Water can pass via either of the two routes mentioned above. Diffusional exchange across all capillary beds has been estimated to occur at the phenomenal rate of 55,000 ml/min. This exchange is bidirectional and completely balanced, so there is no net diffusion of water molecules in either direction.

Vesicular transport is reserved for the specific transport of large molecules, usually proteins, but not all capillaries are capable of this.

The rate of exchange of materials varies considerably between different capillary beds. The capillaries in the brain are the least permeable, whereas the sinusoids of the liver are among the 'leakiest'. The amount of protein in the lymphatics draining various tissues is often used as an indicator of the degree of exchange occurring across a capillary bed. Judged on this basis, the relative 'leakiness' of various capillary beds is: liver > other abdominal organs > thoracic organs > muscles and skin > eye and brain.

Bulk flow is dependent upon mechanical forces. The forces involved at the capillary bed are hydrostatic forces and osmotic forces, and these are often referred to as Starling's forces.

Hydrostatic forces

The blood within the capillary exerts a hydrostatic pressure against the capillary wall. It is therefore a force tending to 'push' fluid out of the capillary into the tissues. Because the capillary offers resistance to flow as blood passes through it, there is a drop in hydrostatic pressure from the arterial end (where blood enters from a meta-arteriole) to the venous end (where blood flows into a venule). Typical values are 35 mmHg and 17 mmHg respectively.

The tissues offer a slight back pressure, the extent of which depends on fluid pressures (tissue turgor) and the degree of tissue compression. However, because it is small, and highly variable, both from site to site and from moment to moment, tissue hydrostatic pressure is usually conveniently ignored and counted as zero.

Osmotic forces

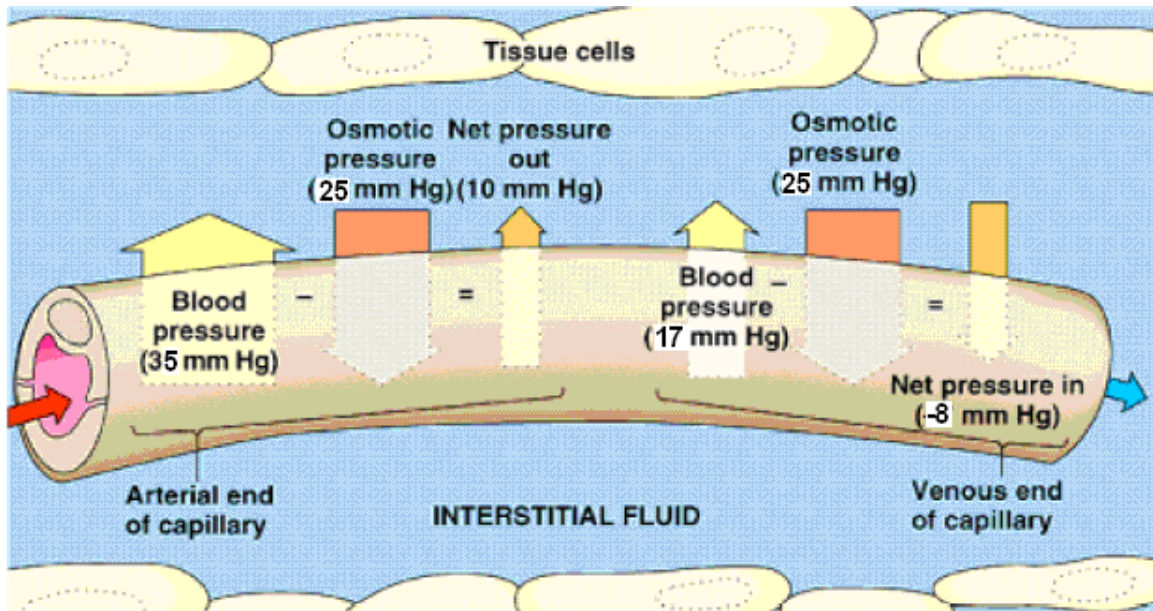
The combined concentration of the plasma proteins, which amounts to approximately 70 g/litre, exert an osmotic pressure of 26 mmHg. This is often referred to as the colloid osmotic pressure, or sometimes the plasma oncotic pressure. It can be imagined as a force tending to 'pull' fluid into the capillary from the tissues.

As tissue fluids do contain some protein, the tissues will also exert some osmotic pressure. The value for this will vary between 0.1 mmHg (in cerebral tissue) and less than 6 mmHg (in liver). In skin and muscle beds it is typically 1 mmHg. So the combined osmotic forces exert a net osmotic pressure of 25 (26 minus 1) mmHg.

Filtration, reabsorption & tissue drainage

At the arterial end of the capillary, the hydrostatic pressure exceeds the net osmotic pressure by 10 (35 minus 25) mmHg. This is termed the net filtration pressure. Thus, fluid tends to leave the capillary at its arterial end. This amounts to an estimated net filtration rate of 14 ml/min across all capillary beds in the body.

At the venous end of the capillary, net osmotic pressure exceeds hydrostatic pressure by 8 (25 minus 17) mmHg. This can be described either as a net filtration pressure of -8 mmHg, or as a net absorption pressure of +8 mmHg. Either way, there is a tendency for fluid to re-enter the capillary at its venous end. This amounts to a net reabsorption rate of 12 ml/min across all capillary beds.



It will be evident that net filtration at the arterial end and net reabsorption at the venous end of the capillary do not quite balance. Overall filtration forces exceed reabsorption forces, so, over time, fluid is gradually lost from the capillaries at the rate of around 2 ml/min. This fluid enters the lymphatic vessels, to be returned eventually to the circulation via the thoracic and right lymphatic ducts.

The situations relating to fluid exchange in the pulmonary circulation and renal circulation differ significantly from the general situation outlined above. This is partly due to differences in the hydrostatic forces involved, and in the case of the kidney, also due to important anatomical considerations.

The pressure of blood exiting the right ventricle varies between 25 mmHg (systolic pressure) and 10 mmHg (diastolic pressure). The mean pulmonary arterial blood pressure is therefore 15 mmHg. Even though the resistance offered by the pulmonary vessels is very low compared with systemic vessels, the mean hydrostatic pressure in the capillaries of the lung is only 8 mmHg. So net filtration pressure is 8 minus 26 = -17 mmHg. In other words, there is no net filtration in pulmonary capillaries, only net absorption. This is an important safety factor that keeps the tissues of the lung comparatively 'dry'.

The arterial arrangement at the kidney means that the hydrostatic pressure at the glomeruli is 55 mmHg. This ensures that there is an overwhelming tendency for filtration to take place. What is more, in the kidney the sites for filtration and reabsorption are anatomically separated. Whereas net filtration occurs in the glomeruli, net reabsorption occurs in the vasa recta.

Oedema

As has been discussed, most fluid that leaves the capillary beds and enters the tissues is taken up by the lymphatic vessels and returned to the circulation, so there is no accumulation of fluid in the tissues. Under some circumstances, however, fluid accumulation may occur, and is termed oedema.

Oedema occurs in situations where there is one or more of the following:

- An increase in capillary hydrostatic pressure.
- A decrease in plasma osmotic pressure.
- A decrease in lymphatic drainage.

Any situation that increases capillary hydrostatic pressure will increase the net filtration pressure, hence the tendency for fluid to enter the tissues. This condition can occur simultaneously in many capillary beds, as in cardiac failure ('backing up' in capillaries due to increased venous pressures associated with poor venous return), or in a single capillary bed due to a local inflammatory reaction.

Whenever protein concentrations in the plasma fall, the plasma osmotic pressure will be diminished, thus reducing the force leading to reabsorption of fluid back into the capillary. This is the underlying cause for oedema associated with protein starvation (kwashiorkor), liver disease (most plasma proteins are produced in the liver) or severe burns (where proteins are lost from the circulation).

If the lymphatic vessels are incapable of removing filtered tissue fluid as quickly as it accumulates, oedema can arise. This occurs where lymphatic vessels are surgically

removed (e.g in a radical mastectomy) or become blocked, for instance by parasitic worms (e.g elephantiasis).

An increase in capillary permeability on its own will not cause oedema unless changes in the balance of forces affecting bulk flow also occur. Some of the situations outlined above (e.g inflammation and burns) also increase capillary permeability, hence accentuating the effects of fluid imbalance.

Starling Forces and Factors.

Ernest Henry Starling was a physiologist working mainly at University College London, together with his brother-in-law, Sir William Maddock Bayliss. Starling is most famous for developing the Starling equation, describing fluid shifts in the body (1896) His other major contributions to physiology were:

- The "Frank-Starling law of the heart", presented in 1915 and modified in 1919.
- The discovery of peristalsis, with Bayliss
- The discovery of secretin, the first hormone, with Bayliss (1902) and the introduction of the concept of hormones (1905)
- The discovery that the distal convoluted tubule of the kidney reabsorbs water and various electrolytes

The Starling equation is an equation that illustrates the role of hydrostatic and oncotic forces (the so-called Starling forces) in the movement of fluid across capillary membranes.

The Starling equation reads as follows:

$$J_v = K_f([P_c - P_i] - \sigma[\pi_c - \pi_i])$$

where:

- $([P_c - P_i] - \sigma[\pi_c - \pi_i])$ is the net driving force,
- K_f is the proportionality constant, and
- J_v is the net fluid movement between compartments.

By convention, outward force is defined as positive, and inward force is defined as negative. The solution to the equation is known as the net filtration or net fluid movement (J_v). If positive, fluid will tend to **leave** the capillary (filtration). If negative, fluid will tend to **enter** the capillary (absorption). This equation has a

number of important physiologic implications, especially when pathologic processes grossly alter one or more of the variables.

According to Starling's equation, the movement of fluid depends on six variables:

1. Capillary hydrostatic pressure (P_c)
2. Interstitial hydrostatic pressure (P_i)
3. Capillary oncotic pressure (π_c)
4. Interstitial oncotic pressure (π_i)
5. Filtration coefficient (K_f)
6. Reflection coefficient (σ)

Pressures are measured in millimeters of mercury (mmHg), and the filtration coefficient in milliliters per minute per millimeter of mercury ($\text{ml}\cdot\text{min}^{-1}\cdot\text{mmHg}^{-1}$).

In essence the equation says that the net filtration (J_v) is proportional to the net driving force. The first four variables in the list above are the forces that contribute to the net driving force, and are the 'Starling Forces'.

Filtration coefficient

The filtration coefficient is the constant of proportionality. A high value indicates a highly water permeable capillary. A low value indicates a low capillary permeability. The filtration coefficient is the product of two components:

- capillary surface area
- capillary hydraulic conductance

Reflection coefficient

The reflection coefficient is often thought of as a correction factor. The idea is that the difference in oncotic pressures contributes to the net driving force because most capillaries in the body are fairly impermeable to the large molecular weight proteins.

Many body capillaries do have a small permeability to proteins such as albumins. This small protein leakage has two important effects:

- the interstitial fluid oncotic pressure is higher than it would otherwise be in that tissue
- not all of the protein present is effective in retaining water so the **effective** capillary oncotic pressure is lower than the **measured** capillary oncotic pressure.

Both these effects decrease the contribution of the oncotic pressure gradient to the net driving force. The reflection coefficient (σ) is used to correct the magnitude of the measured gradient to 'correct for' for the ineffectiveness of some of the oncotic pressure gradient. It can have a value from 0 up to 1.

- Glomerular capillaries have a reflection coefficient close to 1 as normally no protein crosses into the glomerular filtrate.
- In contrast, hepatic sinusoids have a low reflection coefficient as they are quite permeable to protein. This is advantageous because albumin is produced in hepatocytes and can relatively freely pass from these cells into the blood in the sinusoids. The predominant pathway for albumin and other proteins to enter the circulation is via the lymph.

KEY LEARNING POINTS.



- 1. Capillary exchange can occur by diffusion, bulk flow, and vesicular transport.**
- 2. Bulk flow depends on mechanical forces – hydrostatic force and osmotic force.**
- 3. Hydrostatic force is where the blood held within a capillary exerts a force which encourages fluid to leave the capillary.**
- 4. Osmotic force is created by the presence of proteins within the blood, and acts to encourage fluid to move into the capillary. This is also known as oncotic pressure.**
- 5. Where hydrostatic pressure exceeds osmotic pressure, fluid will move out of the capillary. This usually occurs at the arterial end of the capillary bed.**
- 6. Where osmotic pressure exceeds hydrostatic pressure fluid tends to move into the capillary. This usually occurs at the venous end of the capillary bed.**
- 7. Oedema is the build up of extra-cellular fluid and usually occurs with an increase in hydrostatic pressure, a decrease in osmotic pressure, or a decrease in lymphatic drainage.**
- 8. The four Starling forces are a. capillary hydrostatic pressure, b. interstitial hydrostatic pressure, c. capillary oncotic pressure, d. interstitial oncotic pressure.**