



Tissue Fluid

After studying this Factsheet the student should know and understand:

- the nature of tissue fluid and lymph
- the functions of tissue fluid
- the formation and drainage of tissue fluid
- the cause of oedema

As cells become more differentiated and specialised, the less capable they are of surviving independently. They are less able to protect themselves from toxic chemicals, pH changes or extreme temperatures and, if fixed in position within a tissue, cannot seek food, ingest solid bits of food or move away from their own toxic products. The substance that bathes cells and performs these vital functions for them is called **tissue fluid** (or **interstitial fluid** or **intercellular fluid**).

Remember - do not confuse intercellular fluid and extracellular fluid. **Extracellular fluids** are all fluids outside the cells including blood plasma, tissue fluid, lymph, cerebro-spinal fluid, synovial (joint) fluid and the aqueous humour of the eye. The term **intercellular fluid** refers to tissue fluid only. Do not confuse either of these terms with intracellular fluid - the fluid inside cells.

The tissue fluid is 'serviced' by the blood and lymph in the following ways:

- the blood transports oxygen, nutrients and hormones to the tissues where they move out of the capillaries (at the arterial end) into the tissue fluid. The mechanisms of movement involved include osmosis, diffusion and filtration. These substances are passed into the cells and the cells pass wastes into the tissue fluid.
- a large proportion of the waste materials pass from the tissue fluid back into the blood in the capillaries (at the venous end).
- the remaining waste products pass into the lymph in the lymph vessels. The lymph is returned to the blood stream (where the main lymph vessels join the subclavian veins).

The difference in protein content between the blood plasma and the tissue fluid is because protein molecules are too large to pass through the capillary membranes and so are retained in the blood. This is important since these proteins help to maintain the osmotic pressure of blood.

The lymph nodes, which are situated in lymph vessels, store and manufacture lymphocytes which are released to the lymph. Lymphocytes are 'immunity' cells which secrete antibodies and other 'cytotoxic' substances. Other white blood cells, such as the phagocytic neutrophils, escape through the capillary walls to the tissue fluid by the process called diapedesis (the cells push between the capillary wall cells using their pseudopodia).

Bacteria in the tissues, tissue fluid and lymph can be destroyed in the following ways:

- by phagocytosis by neutrophils present in the tissue fluid and lymph.
- by phagocytosis by macrophages in the lymph nodes through which the lymph is filtered.
- by antibodies and cytotoxins secreted by the lymphocytes.

Remember – capillary walls are lined by a very thin pavement epithelium and its basement membrane of fine connective tissue fibres. In places, called fenestrations, the cells are missing and only the basement membrane is present. It is mainly the basement membrane that acts as a 'molecular sieve' preventing protein loss from blood.

Production and drainage of tissue fluid

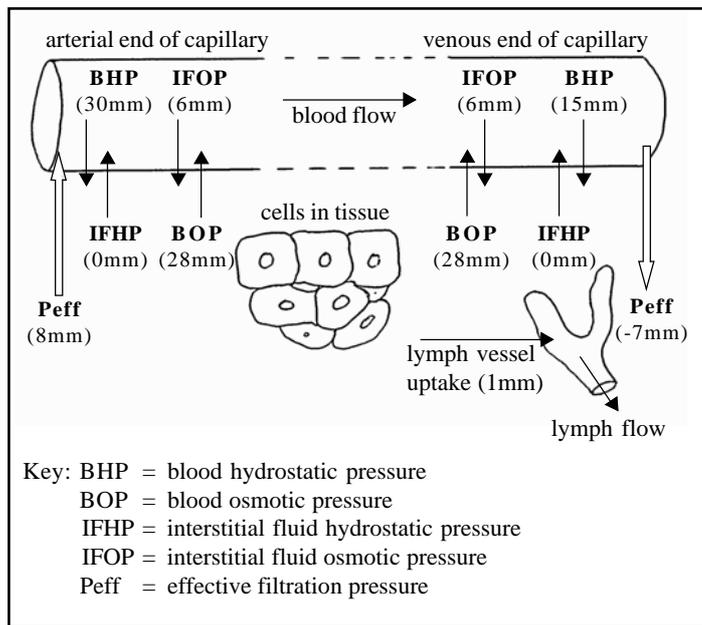
The movement of water and dissolved substances (except proteins) through capillary walls occurs by diffusion and filtration but is dependent on various opposing hydrostatic forces or pressures. Some pressures force fluid out of capillaries into the surrounding tissue spaces and this results in filtration of the fluid. So that fluid does not remain in the tissue spaces and accumulate, opposing pressures force fluid from the tissues spaces back into the blood capillaries and this results in reabsorption of fluid. Any fluid not reabsorbed into the capillaries is returned to the blood as lymph, via the lymphatic vessels.

Table 1. The main differences between blood plasma, tissue fluid & lymph

	blood plasma	tissue fluid	lymph
position	in arteries, capillaries and veins.	between cells in tissues.	in lymph vessels, which have the same structure as veins.
protein content	high	very low	very low
oxygen and nutrient content	high	high (arterial end) low (venous end)	low
waste content	low (since constantly removed via kidneys)	low (arterial end) high (venous end)	high
cell content	carries many red blood cells and white blood cells in approximate ratio red:white of 1000:1	contains many white cells which escape from blood, (e.g. neutrophils)	contains same white cells as tissue fluid plus lymphocytes made in the lymph nodes.

The production and drainage of tissue fluid is illustrated in Fig 1 and explained in the text below the diagram.

Fig 1. The production and drainage of tissue fluid



Four basic pressures are involved in tissue fluid formation and drainage. These are:

- **blood hydrostatic pressure (BHP)** This blood pressure tends to force fluids out of capillaries into the tissue fluid. BHP averages about 30 mm of mercury at the arterial end of the capillary bed and about 15 mm of mercury at the venous end. This fluid carries out oxygen, sugars, amino acids, salts, vitamins and some hormones from the blood plasma to the tissue fluid. However, proteins which have a large molecular size cannot escape through the differentially permeable capillary membranes and so remain in the blood. This filtration means that tissue fluid contains only a small quantity of protein.
- **interstitial fluid hydrostatic pressure (IFHP)** This tissue fluid pressure tends to move fluid from the tissues back into the blood. Its value is generally very small and can vary from positive to negative values. (In the calculations below we shall use a value of 0 mm of mercury at both ends of the capillary bed).
- **blood osmotic pressure (BOP)** This pressure generally has a value of about 28 mm of mercury at both arterial and venous ends of the capillary bed. The pressure arises mainly from the high concentration of non-diffusible plasma proteins in the blood. The BOP tends to move fluid from the tissue fluid back into the capillaries.
- **interstitial fluid osmotic pressure (IFOP)** This pressure generally has a value of about 6 mm of mercury at both ends of the capillary bed. It arises due to the presence of small quantities of protein within the tissue fluid. Only minute quantities of protein leak from capillaries into the tissue fluid, but proteins such as enzymes and some hormones may actually be secreted into the tissue fluid by cells. This pressure tends to move fluid from capillaries into the tissue fluid.

Whether fluid moves in or out of capillaries depends on how the pressures interact together. If the forces moving fluid out of capillaries are greater than the forces moving fluid into capillaries then the production of tissue fluid (filtration) will occur. This happens at the arterial end of capillaries. If the forces moving fluid into capillaries are greater than the forces moving fluid out of capillaries then tissue fluid will tend to be drained back to the blood (reabsorption). This happens at the venous end of capillaries.

The term **effective filtration pressure (Peff)** is used to show the direction of fluid movement. It can be calculated by the equation:

$$\text{Peff} = \begin{array}{l} \text{forces moving fluid} \\ \text{out of capillaries} \end{array} - \begin{array}{l} \text{forces moving fluid} \\ \text{into capillaries} \end{array}$$

$$\text{Thus Peff} = (\text{BHP} + \text{IFOP}) - (\text{IFHP} + \text{BOP})$$

Thus at the arterial ends of the capillary bed
 $\text{Peff} = (30 + 6) - (0 + 28) = 8 \text{ mms of mercury.}$
 This net outward force moves fluid out of the capillaries to form tissue fluid.

At the venous end of the capillary bed
 $\text{Peff} = (15 + 6) - (0 + 28) = -7 \text{ mms of mercury.}$
 This net inward force tends to draw fluid back into the capillaries.

The net inward force is less than the net outward force (by 1 mm of mercury) and so not all the tissue fluid formed can drain back to the capillaries. The remainder is forced into the lymph vessels to be returned as lymph to the blood, via the lymph drainage system.

***Exam hint** – examiners will not expect you to remember the actual values for the different pressures but you need to know whether they are large or small so that you can show how they relate together in tissue fluid circulation. Questions may be asked as data interpretation exercises.*

Oedema and its causes

Oedema is the accumulation of fluid within the tissues and is due to an imbalance of filtration and reabsorption between tissue fluid and plasma. It usually appears first at the ankles which become swollen with fluid. The following are some of the possible causes:

- raised blood hydrostatic pressure (BHP) in capillaries due to an increase in venous pressure. This could be due to obstruction of venous return due to cardiac inefficiency or to blood clots blocking the veins.
- decreased plasma proteins that lower blood osmotic pressure (BOP). Blood protein may be lost due to liver disease, kidney disease, malnutrition or from burns.
- increased capillary membrane permeability will raise interstitial fluid osmotic pressure (IFOP) by letting considerable quantities of plasma proteins leak from the blood into the tissue fluid. Increases in capillary permeability can result from bacterial or viral infection or be caused by chemical, thermal or mechanical agents (eg. bruising).
- increased extracellular fluid volume as a result of fluid retention. In kidney inefficiency the person may not be capable of voiding large volumes of water but still drinks a normal volume. This extra water tends to raise the blood plasma volume and thus raises the blood hydrostatic pressure (BHP).

***Exam hint** – questions relating to oedema are more likely to occur in examinations testing units about Health and Disease.*

Practice Questions

Remember – recommended units for measuring pressure are now the **pascal (Pa)** or **kilopascal (kPa)**. In physiology and medical practice the units ‘mms of mercury’ are still commonly used, simply because nearly all the instruments used for measuring pressures are calibrated in ‘mms of mercury’ and it would cost vast sums of money to replace them. Also, having two types of unit in use could result in serious medical errors occurring.
 1mm of mercury = 133.3 Pa.
 BHP = 3999 Pa. IFOP = 799.8 Pa. BOP = 3732.4 Pa.
 Data interpretation questions may use mms of mercury or pascals.

1. (a) State **two** features of capillaries that enable tissue fluid to be formed. 2
 - (b) About 85% of the tissue fluid is reabsorbed at the venous end of the capillary. Describe what happens to the tissue fluid that is not reabsorbed. 3
 - (c) List **three** differences in the composition of tissue fluid at the arterial end of the capillaries to the tissue fluid at the venous end of the capillaries. 3
 - (d) When tissue fluid is inadequately reabsorbed, it accumulates in the tissues causing swelling (oedema). Suggest **two** possible causes for oedema. 2
- Total 10**
2. (a) Distinguish between:
 - (i) tissue fluid and lymph, 1
 - (ii) tissue fluid and plasma, 2
 - (iii) extracellular fluid and intercellular fluid. 2
 - (b) The equation below for effective filtration pressure relates the different pressures involved in forming tissue fluid. The table gives some actual values for some of these pressures and also some normal values bracketed in italics.

$$P_{eff} = \frac{\text{forces moving fluid out of capillaries}}{\text{out of capillaries}} - \frac{\text{forces moving fluid into capillaries}}{\text{into capillaries}}$$

$$\text{Thus } P_{eff} = (BHP + IFOP) - (IFHP + BOP)$$

pressures in mm of mercury	arterial end of capillary bed	venous end of capillary bed
blood hydrostatic pressure (BHP)	?	16 (<i>15</i>)
interstitial fluid osmotic pressure (IFOP)	6	6
interstitial fluid hydrostatic pressure (IFHP)	0	-1 (<i>0</i>)
blood osmotic pressure (BOP)	28	28
effective filtration pressure (P_{eff})	10 (<i>8</i>)	? (<i>-7</i>)

- (i) Use the equation to calculate the missing values on the table. Show your working. Only use the actual values. 4
- (ii) Comment on the values shown in the table. 3

Total 12

Answers

1. (a) ref to very thin pavement epithelium (of wall);
 ref to fenestrations/cell gaps in wall;
 ref to differentially permeable capillary walls (so that proteins cannot cross it); max 2
 - (b) taken up into lymph vessels (as lymph);
 aided by a positive tissue fluid hydrostatic pressure/pressure of 1 mm of mercury;
 returned to blood system (at subclavian veins)
 bacteria filtered out of lymph by phagocytes in lymph nodes;
 lymph nodes release lymphocytes into the lymph; max 3
 - (c) arterial end contains higher concentration of oxygen than venous end;
 arterial end contains a higher concentration of glucose/amino acids/any correct named nutrient than venous end;
 arterial end contains a lower concentration of waste products/correct named product than venous end; (only allow urea if liver is specified) 3
 - (d) raised blood hydrostatic pressure/possible causes of this;
 decreased plasma protein concentration/possible causes of this;
 raised capillary wall permeability/possible causes of this;
 fluid retention/possible causes of this; max 2
- Total 10**
2. (a) (i) tissue fluid is present between cells/in tissues but lymph is within the lymph vessels;
 lymph tends to contain more lymphocytes than tissue fluid; max 1
 - (ii) tissue fluid contains very little protein but plasma contains a lot;
 tissue fluid is between the cells/in tissues but plasma is within the blood vessels;
 tissue fluid does not contain red cells but plasma does; max 2
 - (iii) extracellular refers to all body fluids outside cells;
 intercellular fluid refers only to tissue fluid between the cells;
 blood plasma/lymph/tissue fluid/cerebrospinal fluid/synovial fluid/aqueous humour are all examples of extracellular fluid;
 (look for two examples for one mark) max 2
- (b) (i) $P_{eff} = (BHP + IFOP) - (IFHP + BOP)$
 $10 = (BHP + 6) - (0 + 28)$;
 BHP = 32 mm ;
 $P_{eff} = (16 + 6) - (-1 + 28)$;
 $P_{eff} = -5$ mm; 4
 - (ii) the effective filtration pressure forming tissue fluid is higher than the norm;
 the effective filtration pressure reabsorbing tissue fluid is less than the norm;
 thus oedema may occur/tissue fluid may accumulate between cells; 3
- Total 12**

Acknowledgements;

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