

Pathology

Fluid and Haemodynamic Derangements

- 1. Describe how the movement of water and low molecular weight solutes, such as salts, between intravascular and interstitial spaces, is normally controlled.**

The movement of water and LMW solutes between the intravascular and interstitial spaces is controlled primarily by the opposing effects of vascular hydrostatic pressure and plasma colloid osmotic pressure. Normally, the outflow of fluid from the arteriolar end of the microcirculation to the interstitium is nearly balanced out by the inflow at the venular end. A small residual amount of fluid may be left in the interstitium and is drained by the lymphatic vessels, ultimately returning to the blood via the thoracic duct.

- 2. What are the two main contributors to increase in interstitial fluid?**

Either, increased capillary pressure or diminished colloid osmotic pressure can result in increased interstitial fluid. If the movement of water into tissues exceeds lymphatic drainage, fluid accumulates. An abnormal increase in interstitial fluid is called oedema.

- 3. What is Anasarca?**

Anasarca is a severe, generalised oedema with widespread subcutaneous tissue swelling.

- 4. What is the definition of a transudate? List four causes of transudates.**

Oedema caused by increased hydrostatic pressure or reduced plasma protein and is typically protein-poor. Four causes are heart failure, liver failure, renal failure and malnutrition.

- 5. What is the definition of an exudate? What are two broad categories of the causes of exudates?**

Exudates can be inflammatory or non-inflammatory. It is a protein-rich exudate that is the result of increased vascular permeability.

6. Outline the general sequence of events leading to haemostasis at a site of vascular injury:

Arteriolar vasoconstriction occurs immediately and markedly reduces blood flow to the affected area. This is mediated by neurogenic mechanisms and augmented by the local secretion of potent local factors, such as endothelin.

Primary Haemostasis: the formation of the platelet plug. Disruption of the endothelium exposes subendothelial vWF and collagen, which promote activation and aggregation of platelets. Activation of platelets causes a dramatic shape change as well as the release of secretory granules. Within minutes the secreted products recruit additional platelets, which undergo aggregation and form the primary haemostatic plug.

Secondary Haemostasis – deposition of fibrin. Tissue factor is also exposed at the site of injury. Tissue factor is a membrane bound procoagulant that is normally expressed by subendothelial cells in the vessel wall. Tissue factor binds and activates factor VII, setting in motion a cascade of reactions that culminates in thrombin generation. Thrombin cleaves fibrinogen to fibrin as well as recruiting additional platelets. This sequence is referred to as secondary haemostasis.

Clot stabilisation and reabsorption. Polymerized fibrin and platelet aggregates undergo contraction to form a solid, permanent plug that prevents further haemorrhage. At this stage, counterregulatory mechanisms are set into motion that limit clotting to the site of injury, e.g. t-PA.

7. What are the primary abnormalities that lead to thrombosis?

- a. Virchow triad:
 - i. Endothelial injury
 - ii. Stasis/turbulent blood flow
 - iii. Hypercoagulability

8. What are lines of Zahn? What do they signify?

Lines of Zahn are grossly and microscopically apparent laminations that form in thrombi. They are pale deposits of platelets and fibrin that alternate with darker red cell rich layers. Such deposits signify that the thrombus is formed in flowing blood. Their presence can therefore distinguish clots that occur post-mortem.

9. List, in decreasing order of frequency, the most common sites of arterial thrombi:

- i. Coronary
- ii. Cerebral
- iii. Femoral

10. If a patient survives the initial thrombus formation, list the four events that occur in the following days/weeks

- i. Propagation – thrombi accumulate additional platelets and fibrin
- ii. Embolization – Thrombi dislodge and travel to other sites in the vasculature
- iii. Dissolution – the result of fibrinolysis., which can lead to the rapid shrinkage and total disappearance of recent thrombi. In contrast, extensive thrombi deposition and cross-linking in older thrombi renders them more resistant to lysis.
- iv. Organisation and recanalization – Older thrombi become organised by the ingrowth of endothelial cells, smooth muscle cells and fibroblasts. Capillary channels form and re-establish the continuity of the lumen. Eventually only a fibrous lump may remain to mark the original thrombus.

11. Define 'embolus'

An embolus is a detached intravascular solid, liquid or gaseous mass that is carried by the blood from its origin to a distant site, where it often causes tissue dysfunction or infarction. The vast majority are dislodged thrombi, hence the term 'thromboembolism'.

12. What are the characteristic features of fat embolism syndrome?

Pulmonary insufficiency, neurological symptoms, anaemia and thrombocytopenia. It is fatal in 5-15% of patients

13. Describe the morphological classification of infarctions

- i. Red infarcts – occur in tissues with loose tissue, e.g. lung; in venous occlusions, e.g. testicular torsion; in tissues with dual circulations, e.g. small intestine; in tissues previously congested by sluggish venous outflow; and when flow is re-established to an area of previous arterial occlusion and necrosis.
- ii. White infarcts – occur with arterial occlusions in solid organs with end-arterial circulation and where tissue density limits the seepage of blood from adjoining capillary beds into the necrotic area.

14. Define 'shock'

Shock is a state in which diminished cardiac output or reduced effective circulating blood volume impairs tissue perfusion and leads to cellular hypoxia.

15. Complete the table below

Type of shock	Clinical Example	Principal Mechanisms
Cardiogenic	MI Ventricular rupture Arrhythmia Tamponade PE	Failure of myocardial pump resulting from intrinsic myocardial damage, extrinsic compression or obstruction to outflow
Hypovolaemic	Fluid loss, e.g. haemorrhage, vomiting, diarrhea, burns or trauma	Inadequate blood volume or plasma volume
Shock with systemic inflammation	Overwhelming microbial infection, superantigens, trauma, burns and pancreatitis	Activation of cytokine cascades, peripheral vasodilatation and pooling of blood; endothelial activation/injury; leucocyte induced damage, DIC.

16. Outline the three general phases of shock:

- i. An initial non-progressive phase during which reflex compensatory mechanisms are activated and perfusion of vital organs is maintained
- ii. A progressive stage characterized by tissue hypoperfusion and onset of worsening circulatory and metabolic imbalances, including lactic acidosis
- iii. An irreversible stage that sets in after the body has incurred cellular and tissue injury so severe that even if the haemodynamic defects are corrected, survival is not possible.