Processes involved in inflammation (p. 131 - 134)

The inflammatory process includes:

1. Vascular response
   - Initially the lumen size decreases (vasoconstriction)
   - There is then vasodilation, which increases blood flow through capillary bed (accounts for redness) —> hyperanaemia —> then reaches a stage where there's an increase in permeability of endothelium, allowing proteins and fluid to move out.
2. Cellular responses
   - Cells in blood flow towards the periphery (marginalised).
   - Endothelium will express adhesion molecules, which makes WBCs stick to it (pavementing).
   - WBCs migrate between endothelial cell gap into extravascular space. This is an active process (emigration), but if it's forced out (RBCs) then it's not an active process (diapedesis). Once they arrive they will they'll undertake phagocytosis.
3. Chemical mediators
   - Histamine —> released by mast cells, basophils (WBC) and platelets. Increases permeability, vasodilation and endothelial activation.
   - Kallikrein-kinin System (Bradykinin) —> same as histamine but just slower.
   - Complement —> cascade of activation of proteins, in which the end job is cell lysis or phagocytosis.

Types of inflammation — characteristics (p. 137)

Acute Inflammation	Chronic Inflammation
- Starts rapidly & ends quickly too - Neutrophils predominate (they're faster but short lived) - After 24hrs Monocytes become abundant (slower but longer lived in vascular space) • Neutrophils —> Monocytes	- Takes longer to commence & ends longer too - Lymphocytes predominate

Blood components involved in fibrinolytic activity (p. 151)

Plasminogen, which is then converted to its active form plasmin (responsible for fibrin (clot) breakdown).

- plasminogen binds to the clot and is converted to plasmin.

Which vitamins are necessary for production of which clotting factors?

Vitamin K is needed for the production of factors: 2, 7, 9, 10

Role of chemical mediators of inflammation — histamine, prostaglandin, bradykinin

Histamine —> made from mast cells (connective tissue) and basophils (WBC). They are released in response to injury —> so fluid can leak out of the vessels. Histamine is a vasodilator and chemotactic (brings WBCs to the area).

Prostaglandin —> promotes vasodilation

Bradykinin —> similar to histamine but longer lasting (vasodilator). It's produced by plasma proteins.

Roles / outcomes of the complement cascade, what activates it?

It's a cascade of activation of proteins, which there are 3 cascades: (p. 135, 164)

1. Classical
2. MB-Lectin
3. Alternative

It's outcome is cell death, and it's done either by opsonisation (phagocytosis), inflammation or forming a membrane attack complex (MAC), which is a hole in the membrane of the bacteria.

It's triggered by antigens and antibodies complexing together.

Liver cirrhosis — pathological characteristics (p.83)

A chronic disease of the liver marked by degeneration of cells, inflammation and fibrous thickening of tissue (a typical result of alcoholism or hepatitis).

There's going to be proliferation (rapid increase number in) of both hepatocytes as nodules & fibroblasts (cells of connective tissue) as scar tissue. The fibroblasts there start to proliferate to a point where it's considered hyperplasia, which is essentially scar tissue (hence surface of liver is no longer smooth).

The disturbance of the normal hepatic architecture is irreversible.

Phenylketonuria — what type of disorder?

PKU is a recessive genetic disease, which is characterised by the inability to convert phenylalanine to tyrosine, as the enzyme for it, phenylalanine hydroxylase (PAH) is mutated.

Patients must be on a long-life strict diet, and incorporate supplementation of the amino acids necessary in small amounts.

Characteristics of benign vs malignant tumours (p. 38)

Benign —> meaning it does no harm (not able to create another tumour), however people can die from it

Malignant —> a tumour capable of creating another tumours in a different site (even after removal). If it does it'd be called a secondary tumour.

Classification / nomenclature of tumours

The 2 clinical classifications are: benign and malignant.

1. Tumours composed of one parenchymal cell type, e.g. epithelial tumours.
2. Tumours with different types of cells from the same germ layer (mixed tumours), e.g. salivary glands, breast.
3. Tumours with different types of cells derived from more than one germ layer (teratogenous), e.g. totipotential cells in gonads or in embryonic rests.

Most common cancers in Australia, and common metastatic sites (p. 191)

The most common cancers in Australia (excluding non-melanoma skin cancer) are prostate, colorectal (bowel), breast, melanoma and lung cancer. These five cancers account for over 60% of all cancers diagnosed in Australia.

Common metastatic sites include: lymph nodes, but can also spread to the liver, pleura, adrenal glands, bone and brain.

Normal types of tissue growth and cell death (p. 45, 51, 67)

During tissue growth, it could utilities a combination of any of the following ways, which are considered normal tissue growth:

1. Multiplicative (hyperplasia)
2. Auxetic (hypertrophy)
3. Accretionary (hyperplasia & hypertrophy combined

Atrophy —> when there's a decrease in the size of tissue (could be the whole organ). It can be both due to a physiological and pathological reason.

e.g. Physiological: could be a part of morphogenesis (hands start out as paddles and cells are lost via apoptosis, to form fingers).

Apoptosis is a process of cell death that is considered normal. It's an energy dependent process, in which is a biochemical mode of cell death, which implies certain biological features, not just any cell death. Can be triggered by a range of pathological stimuli.

Pathological responses in tissues — hypertrophy, hyperplasia, metaplasia, atrophy (p. 53)

Hypertrophy —> increase in cell size.

Hyperplasia —> increase in cell number.

Metaplasia —> the abnormal change in the nature of tissue (mature cells).

Atrophy —> waste away, especially as a result of the degeneration of cells.

Characteristics / mechanisms: necrosis and apoptosis (p. 67, 71)

Apoptosis	Necrosis

- Energy dependent — programmed cell death.
- Normal functional role in morphogenesis.
- Cell shrinks but retains its cell membrane, which eventually gets phagocytes or fragmented.
  • retaining the cell membrane is very important as it doesn't trigger an inflammatory reaction.
- Intrinsic pathway:
  • decreased Bcl-2 —> increases apoptosis
  • decreased Bax —> decreases apoptosis
  • it's about the balance between those two
  • p53 protein interacts with Bcl-2 to induce stoppage of cell cycle to initiate DNA repair, but if it's beyond repaid, it will induce apoptosis
- Extrinsic pathway:
  • involved TNFα and Fas receptor
  • if lymphocytes are producing antibodies for antigens that already normally in our body, then through the extrinsic pathway, they're set for apoptosis
	- Not energy dependent.
	- Not normal, is a result of bioenergetic failure.
	- Always stimulated by a pathological stimulus.
	- When cells die via necrosis, they don't retain their membrane integrity and their contents are spilled out in the extracellular environment and there's an inflammatory response.
	
	- Different types include: (study from p. 71)
	  • Coagulative (most common)
	  • Liquefactive (colliquative)
	  • Caseous
	  • Fat
	  • Gangrene

Difference between and examples of labile, stable and permanent cell types (p. 46)

Labile —> very high cell turnover, e.g. epithelium.

Stable cells —> don't normally have a high turnover, however if there's an injury to the organ, the stems cells that resign in that organ can readily move into mitotic state and start to divide to replace the cells that are lost, e.g. hepatocytes.

Permanent cells —> don't go under any regenerations, they have very few stem cells, e.g. neurons, skeletal.

Immunoglobulin types, locations (p. 162)

Immunoglobulins are antibodies and are produced by plasma cells.

There are various different types:

- IgM —> secreted form is mostly found in blood (largest).
- IgG —> (smallest)
- IgA —> stimulated by plasma cells of the intestinal and respiratory mucosa. Also secreted in breast milk (protection for baby).
- IgD —> synthesised by B lymphocytes (B cell) and located in its membrane.
- IgE —> found in membranes of mast cells and basophils.

Hypersensitivity responses: types and which immunoglobulins involved (p. 165)

- Type I —> IgE, releasing histamine and other mediators.
- Type II —> IgE and IgM
- Type III —> IgG, but can be IgM or IgA
- Type IV —> mediated by T cells rather than by antibodies

Processes involved in normal healing (p. 79)

There are 2 ways tissue is repaired:

1. Complete restitution —> loss in the population of labile cells (high turnover), that has now been completely restored, e.g. epidermis. Wouldn't be able to tell if there was any damage.
2. Organisation —> When the damage is too deep, which forms a scar.

Haemostasis (stopping blood flow) —> inflammation —> proliferation —> maturation.

Mechanisms / processes involved in hypoxic and ischaemic injury (p. 64)

Refers to lack of O_2 to tissues —> oxidative phosphorylation unable to continue —> increased rate of glycolysis —> pyruvate unable to enter CAC —> pyruvate reduced to lactate —> pH lowered

ATP supply decreases —> pumps in membrane relying on ATP will start to fail:

1. Na^+/K^+ ATPase pump —> altered membrane potential —> water enters cell to balance osmotic pressure —> swelling —> ER ribosomes detach —> affects protein synthesis.
2. Calcium ATPase pumps —> calcium comes in and builds up in cytosol —> causes activation of: proteases, phospholipase and endonucleases, which breakdown cytoskeleton, membrane and DNA, respectively.