CPAT3201 Practice Exam Questions by Lecture order

Module 1: Inflammation

Lecture 1 - Acute Inflammation - mediators

- Give a general outline of the host defences involved against microorganisms.
- bacterial/ fungi/ parasite/ viral breached of barriers → innate immunity (non-specific responses) → activation of macrophages → adaptive immunity (specific responses)

- What is the relationship between inflammation and immunity?
- = Inflammation is defined as the reaction of vascularised living tissue to local injury/ infection, characterised by movement of fluid (water + proteins) and leukocytes from blood into tissue.
    - **Stereotypic** (always the same response)
- It is the essential and fundamental step in triggering immunity, propriate activation of early defense enables correct activation of innate and adaptive immune response; consequently leads to appropriate removal of dead tissue and healing
    - Coordinated processes for localisation and elimination of stimuli

- Define inflammation.
- = the reaction of vascularised living tissue to local injury/ infection, characterised by movement of fluid (water + proteins) and leukocytes from blood into tissue.

- Describe the different types of inflammation and key features of each.
- Acute inflammation:
    - Rapid onset (mins-hours), stereotypic response, movement of fluid + neutrophils
    - Doesn't necessary develop into chronic inflammation (rarely happens)
- Chronic inflammation:
    - Prolonged response (days-years), specific response, macrophages + T/B cells, fibrosis → scar tissue, neo-angiogenesis

- Explain the physiology underlying the four cardinal signs of inflammation.
- Redness - ↑blood flow (hyperaemia/ erythema)
- Heat - ↑blood flow (hyperaemia/ erythema)
- Swelling - fluid movement from blood to tissue (exudation)
- Pain - ↑sensitivity of pain receptor within tissue (hyperalgesia)

- T/F: Inflammation only occurs in the presence of pathogens.
- F - inflammation is a stereotypic response disregarding the type of stimuli.

- Describe the difference between transudate and exudate.
- **Transudate**: fluid (water)
- **Exudate**: protein rich + fluid

    - Consequence of hyperaemia (↑blood flow), fluid move from blood into affected tissue via PCA and PCV.
        - Vasodilation @ Pre-capillary arterioles
        - ↑permeability of inter-endothelial gap @ Post-capillary venules
        - Order of movement: Water → proteins → cells (neutrophils)
    - intensity/ duration of exudation varies and depends on the nature of stimulating agent.

- In more severe inflammation, immediate/prolonged exudation is caused by what?
- Caused by damage to endothelial cells in vasculature, may consequently leads to haemorrhage.

- Define hydrostatic and colloid osmotic pressure. What should they both be under normal physiology?
- **Colloid osmotic pressure** - inwards pressure (from tissue to blood), as concentration of solutes is larger in the blood vessels, so fluid follows into the blood vessels.
- **Hydrostatic pressure** - outwards pressure (from blood to tissue), as blood is flowing from arteriole to highly resistant capillaries, so fluid flows into tissue.
- Under normal:
    - exact balance between osmotic pressure and hydrostatic pressure.
    - Intact tight junctions between endothelial cells.

- Describe what the different components in exudate aim to achieve.
- Fluid:
    - Dilution of toxin
    - ↑lymphatic drainage
- Plasma proteins:
    - Antibody, complement system, fibrin → immobilise, limit the pathogen
    - **Opsonins**: molecules/ particles that facilitate macrophages phagocytic activities.
        - E.g. complement complexes (C3b)
- Neutrophil:
    - Destruction of pathogens
- What is the difference between vasoactive and chemotactic mediators of inflammation?
- Vasoactive mediators - act of the vasculature (blood vessels), e.g. causing vasodilation of precapillary arterioles or increasing endothelial permeability of post-capillary venules.
    - Amines (histamine)
    - Lipid-derived (prostanoids, leukotrienes)
    - Plasma-derived (complement fragments)
- Chemotactic mediators: produce and release signals to recruit and stimulate immune cells (e.g. for neutrophils)
- Identify one vasoactive mediator and explain its source and its mechanism of action.
- Histamine - both vasodilation (@PCA) and ↑permeability (@PCV).
    - Source: Preformed mast cells/ platelets.
- What are anti-inflammatory drugs commonly used for? Identify one category of drug and describe its mechanism of action.

- Anti-inflammatory drugs are commonly used for disorders involving excessive inflammation such as arthritis, meningitis, atherosclerosis, etc.
- Corticosteroids ⊣ phosopholipase A2 (∴⊣ arachidonic acid)
- NSAIDs ⊣ cyclo-oxygenases (∴⊣ prostanoids)
- Zileuton ⊣ lipoxygenases (∴⊣ leukotrienes)
    - Normally: leukotrienes → ↑permeability

- Which key mediators cause sensitisation of pain receptors during inflammation?
- PGE2 and PGI2 → ↑AP to CNS ∴ ↑ pain under same level of physical stimulus

Lecture 2 - Neutrophils and Macrophages

- Explain the roles of neutrophils in inflammation.
- To kill pathogens (particularly bacteria) (innate immune response)
- Release chemotactins (chemoattractants) → attract other neutrophils/ macrophages

- Compare the **kinetics, structure, biochemistry** and **function** of neutrophils and monocytes/macrophages.
- Neutrophils:
    - Kinetics:
        - Produced in bone marrow at 1.5 million cells per second (extremely high number)
        - Terminally differentiated → can't proliferate & short-lived
    - Structures:
        - Poly-morpho nucleus (PMN)
        - No ER/ golgi → no protein synthesis
        - Polarised (lamellipodium - head, uropod - tail)
        - Few mitochondria
    - biochemistry:
        - No protein synthesis
        - **Anaerobic glycolysis** (glycogen)
    - Function:
        - Stereotypic innate immune response + production of chemoattractants → 1st line of defence for elimination of pathogens
            - Surface NADPH oxidase Phagocytosis → releases active enzymes + ROS
        - Neutrophil extracellular traps (NETs)
        - **myeloperoxidase**-dependent anti-microbial mechanisms -predominantly makeup neutrophil granules (NOT macrophages)
- Monocytes:
    - Kinetics:
        - Produced in bone marrow at 100,000 cells per second, much lower number than neutrophils
        - Can differentiate into macrophages→ proliferate & long-lived

        - Live in tissue for weeks/months
    - Structure:
        - Single-lobed nucleus
        - Prominent ER/ golgi → +++protein synthesis
        - +++mitochondria
        - Irregular border (macrophages)
    - Biochemistry:
        - +++protein synthesis
        - **Aerobic respiration/ anaerobic glycolysis**
    - Function:
        - Elimination of pathogen (specific response) (phagocytosis + degradation of debris)
        - Production of cytokines (chemoattractant)
            - Macrophage is the major source for IL-1 and TNF

- Explain the mechanisms of neutrophil emigration.
- **Step 1: Endothelial activation**
    - Neutrophil cell surface interacts with **selectin** ligands located on surface of endothelial cell wall.
- **Step 2: Rolling**
    - Neutrophil continues to move along and interacts with more selectins, sequentially slows down.
    - **Integrins** are inactive in rolling phase.
- **Step 3: Adhesion**
    - **Integrins** are now active.
    - Integrin located on neutrophil interact with integrin ligands located on endothelial cell wall.
- **Step 4: emigration (= diapedesis)**
    - After successfully stopped and adhered onto endothelial wall, neutrophil self-reacts near the interendothelial gap (homotypic interaction). This interaction allows emigration of neutrophils from blood into subendothelial tissue.
    - Emigrated neutrophil follows the [chemotactic] gradient to travel towards the site of infection.
- Newly expressed selectins.
- Constitutively expressed integrins.

- How is neutrophil movement in tissues influenced?
- Vasoactive mediators and cytokines (chemoattractant gradients)
    - Neutrophils migrate towards locations with highest [chemoattractants] from locations with low [ ].

- What is the mechanism of action of killing by neutrophils?
- recognition
    - Pathogen recognition via pathogen-associated-molecular-patterns (PAMPs)

- Formation of phagosome (phagocytosis)
    - Directed by NADPH oxidase expressed on neutrophil cell surface → ROS production
    - Neutrophil membrane surround pathogen → engulf into vacuole
- Formation of phagolysosome
    - phagolysosome
        - Fusion of phagosome with lysosome → amplification of enzymatic activities
    - Oxidative burst (formation of ROS)
        - Triggered by NADPH oxidase
- Elimination of pathogen + death of neutrophil → release of NETs

- What are NETs?
- **Neutrophil extracellular traps** (NETs), released upon death of neutrophils
- Neutrophil DNA coated with antimicrobial proteins (granules) → death of neutrophils → release coated DNA fragments → traps & eliminate pathogens + further attracts neutrophils/ macrophages

- Explain the roles of macrophages in inflammation.
- Elimination of pathogen (specific response) (phagocytosis + degradation of debris)
- Production of cytokines (chemoattractant)

- Name two examples of important cytokines in inflammation and explain their systemic effects.
- Interleukin-1 (IL-1) & Tumour necrosis factor (TNF)
    - Produced predominantly by macrophages/ different types of cells
    - Synergistic/ amplification effects on each other
        - ↑vascular adhesion molecules production (∴ ↑ migration of neutrophils)
        - Potent immunomodulatory → ↑T cell proliferation
        - inflammation-induced fever
        - ↑leukocytes production from hematopoietic stem cells in bone marrow

- Explain the importance of PRRs. What do they recognise? Name an important subfamily of PRRs.
- Pattern Recognition Receptors (PRRs) expressed on host's immune cells, act as the triggering system for innate immunity. They enable host recognition of pathogens as non-self via PAMPs, consequently leads to activation of adaptive immunity and downstream elimination of pathogens.
- In the case of sterile inflammation (inflammation occurred without pathogens), PRRs recognise DAMPs released from damaged cells/ tissue, thus activates downstream healing proc
- An important subfamily of PRRs is Toll like receptors (TLRs) - e.g. TLR4 recognises **lipopolysaccharide of G-ve** microbes.

Lecture 3 - Chronic Inflammation

- Explain the difference between granuloma and granulation tissue.
- Granuloma
    - **Centre → periphery**

    - Predominantly macrophages (various phenotypes)/ lymphocytes/ fibroblasts
    - Response to **persistent irritant**
    - Aim: Attempts to prevent the pathogen disseminating into surrounding tissue
- Granulation tissue
    - **Periphery → centre**
    - **Newly formed + blood vessels + fibroblasts**
    - Attempts to heal damaged tissue via fibrosis
        - Part of healing process: Deposition of collagen → scar formation
    - Aim: repair process

- What are the possible outcomes of acute inflammation? For each outcome, provide one example of a pathology where this outcome commonly occurs.
- Resolution: acute restoration of original structure
    - E.g. blister
- Organisation: formation of granulation tissue → acute healing by fibrosis (collagen formed by fibroblast)
    - E.g. acute pericarditis
- Suppuration: pus formation
    - E.g. ulcer or abscess
- Chronic inflammation: suppurative/ granulomatous/ mixed
- Longer term healing: fibrosis/ cellular regeneration

- What is fibrinogen?
- A glycoprotein, converted into fibrin by thrombin during coagulation/ clotting.
- Part of exudate → fibrin mesh

- *Describe the important characteristics of the three types of chronic inflammation and provide an example for each?
- **Chronic suppurative** → more commonly known as acute inflammation constantly reactivated
    - Neutrophils (**poly**morphonuclear cells) → this is not typical of chronic inflammation
    - Pus formation
    - Diffused fibrosis
    - E.g. chronic abscesses/ ulcers
- **Chronic granulomatous** - most commonly referred to as “chronic inflammation”
    - **#1 Foreign body**
        - **Mono**nuclear cells predominant (giant cells + epithelioid cells)
        - Diffused fibrosis
        - E.g. Indigestible surgical suture (cotton wool)
    - **#2 Unknown origin**
        - **Mono**nuclear cells predominant (langhans giant cells + epithelioid cells)
            - Monocytes → epithelioid cells → langhans giant cells
        - Peripheral fibrosis
        - E.g. sarcoidosis