TOPIC: INNATE IMMUNITY

Key Knowledge:

- The innate immune response including the steps in an inflammatory response and the characteristics and roles of macrophages, neutrophils, dendritic cells, eosinophils, natural killer cells, mast cells, complement proteins and interferons
- The role of the lymphatic system in the immune response as a transport network and the role of lymph nodes as sites for antigen recognition by T and B lymphocytes

INNATE IMMUNE SYSTEM

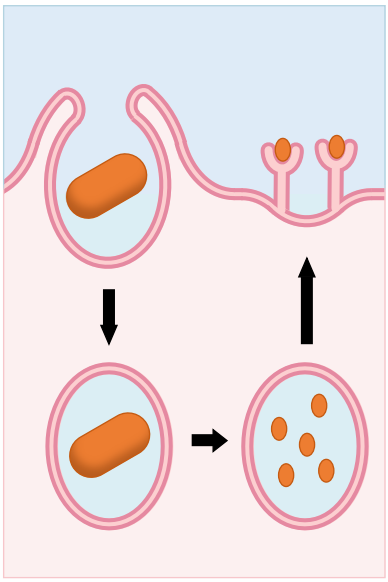
The second line of defence against infectious disease is the innate immune system, which is **non-specific**:

- It does not differentiate between different types of pathogens (it does not recognise antigens)
- It responds to an infection the same way every time (i.e. it has no immunological memory)

The principal components of the innate immune system include phagocytic leukocytes, the inflammatory response, complement proteins, cytokines and fever.

PHAGOCYTOSIS

Certain types of white blood cells (leukocytes) can engulf foreign bodies. These phagocytes are non-specific, but can detect generic characteristics called pathogen-associated molecular patterns (PAMPs). After infected tissues release chemotactic chemicals to recruit phagocytic leukocytes, the phagocyte will engulf the pathogen by surrounding it with cellular extensions (pseudopodia) and internalising it within a vesicle. The vesicle is then fused to the lysosome and the pathogen is digested. The antigenic fragments from the pathogen may then be presented on the surface of the phagocyte in order to stimulate the third line of defence (adaptive). **Neutrophils** are short-lived phagocytes that respond rapidly to infection, while **monocytes** (macrophages) are longer lived and capable of sustained action. Finally, a **dendritic cell** is a type of phagocyte that is particularly suited to the role of antigen presentation (more so than macrophages).



COMPLEMENT PROTEINS

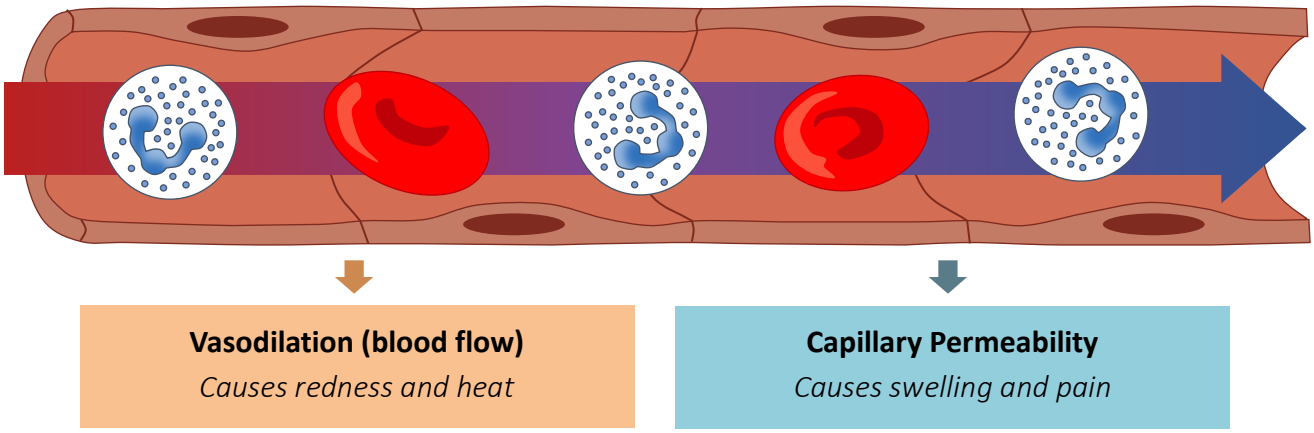
Complement proteins are a group of antimicrobial chemical agents that are produced in an inactive form that circulates within the bloodstream. In response to immune activation, a cascade of reactions will ensue that help to protect the body from infection. Complement proteins function in a variety of ways:

- **Chemotaxis:** They can function as chemical signals to attract the phagocytes to sites of infection
- **Opsonisation:** They will coat pathogens to enhance their identification by the phagocytic leukocytes
- **Membrane attack:** They will form a porous complex in a bacterial cell wall, causing the cell to rupture
- **Inflammation:** They can intensify the inflammatory response to improve phagocyte recruitment

While complement proteins are part of the innate immune system, they can also be activated by specific antibodies that are generated as part of the adaptive immune response.

INFLAMMATION

The inflammatory response is a non-specific mechanism by which the body improves leukocyte access to sites of infection. When tissue damage occurs, **mast cells** (localised) or basophils (circulating) release a chemical called **histamine**. Histamine causes local vasodilation and increased capillary permeability to improve the recruitment of white blood cells to the damaged region. While inflammation is necessary to allow phagocytes to access infected tissue, there are unavoidable side effects. Increased blood flow causes redness and heat, while increased permeability releases fluids that cause swelling and tenderness (pain).



CYTOKINES

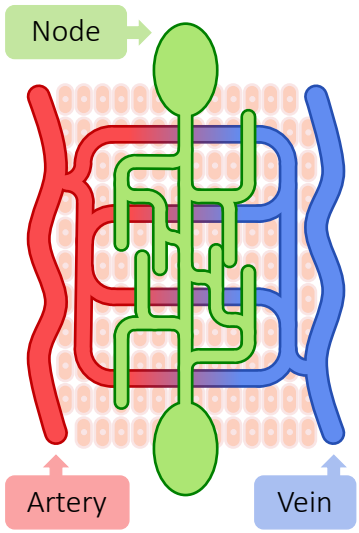
Cytokines are proteins that are released from white blood cells (leukocyte) and function to regulate immune activity. Cytokines are used to activate lymphocytes in response to pathogenic entry and also increase the resistance of surrounding body cells to infection. For example, interferon is released from virally-infected cells and functions to recruit natural killer cells and reduce susceptibility of neighbouring cells to infection by activating endogenous antiviral agents.

FEVER

A fever is an abnormally high temperature associated with infection. Fevers may help to combat infection by reducing the growth rate of microbes. It may also increase the metabolic activity of body cells and activate heat shock proteins to strengthen the immune response. Fevers are triggered by the release of prostaglandins, which stimulate the hypothalamus to raise the core body temperature. Up to a certain point a fever may be beneficial, but beyond a tolerable limit it can cause damage to the body's own cells.

LYMPHATIC SYSTEM

The lymphatic system is a secondary transport system that functions to drain fluid from all around the body. The fluid within this system is called **lymph** and is rich in white blood cells. The lymphatic system functions to filter the fluid in the body and remove pathogens to prevent infections. When a phagocytic leukocyte engulfs a pathogen and become an antigen presenting cell, it will be transported to the lymphatic system in order to present the antigenic fragment to **lymphocytes** (adaptive immune cells). These lymphocytes are produced by primary lymphoid organs (e.g. bone marrow) and reside in secondary lymphoid organs (i.e. lymph nodes). The lymphatic system therefore functions as an important link between the innate and adaptive immune responses.



TYPES OF IMMUNE CELLS

There are a variety of white blood cells (leukocytes) that are involved in coordinating an immune response:

NEUTROPHILS

Most abundant type of leukocyte and functions as the first responder to a microbial infection

Neutrophils destroy pathogens via phagocytosis but are **not** involved in antigen presentation

They are short-lived with a circulating life span of less than a day (forms pus when destroyed)

MONOCYTES

Monocytes are also involved in phagocytosis – they are slower to respond but are longer lasting

Unlike neutrophils, monocytes are involved in antigen presentation (link to the adaptive system)

Monocytes include macrophages and dendritic cells (specialised for antigen presentation)

EOSINOPHILS

Function as the primary responder to large multicellular parasites (e.g. helminths)

Do not phagocytose, but instead release chemical products that perforate cell membranes

BASOPHILS / MAST CELLS

Release the chemical histamine to initiate an inflammatory response (e.g. allergic reactions)

Mast cells and basophils are similar, but mast cells are localised while basophils will circulate

LYMPHOCYTES

Are responsible for the **adaptive** response (will *specifically* target the antigens on pathogens)

B cells produce antibodies, while T_C cells target intracellular pathogens (cancers and viruses)

Helper T cells (T_H) reside in the lymph nodes and release cytokines to activate the lymphocytes

NATURAL KILLER CELLS

Natural killer (NK) cells are a type of *non-specific* lymphocyte (do **not** target particular antigens)

NK cells respond to interferon release and will target and destroy virally-infected or cancer cells

They function in a manner that is analogous to cytotoxic T cells (but are non-specific in action)

IMMUNE CELLS ANALOGY

Neutrophils are like street cops *(first responders)*, while monocytes are longer lasting *(durable riot police)*. Eosinophils deal with larger pathogens by releasing chemicals *(like fumigators)*, while mast cells / basophils trigger inflammatory responses *(firemen)*. Natural killer cells are responsible for compromised tissues *(like a bomb disposal technician)*, while lymphocytes target specific pathogens *(as well-trained special forces)*.

INNATE (NON-SPECIFIC) IMMUNE RESPONSE

Neutrophil
Street cop

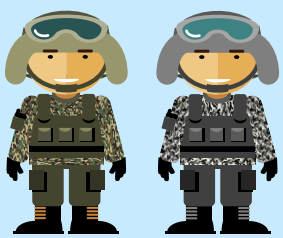
Eosinophil
Fumigator

Basophil
Fireman

Monocytes
Riot police

Natural Killer
Bomb disposal

ADAPTIVE RESPONSE



Lymphocytes (B + T)
Special forces soldiers