IMMUNE SYSTEM

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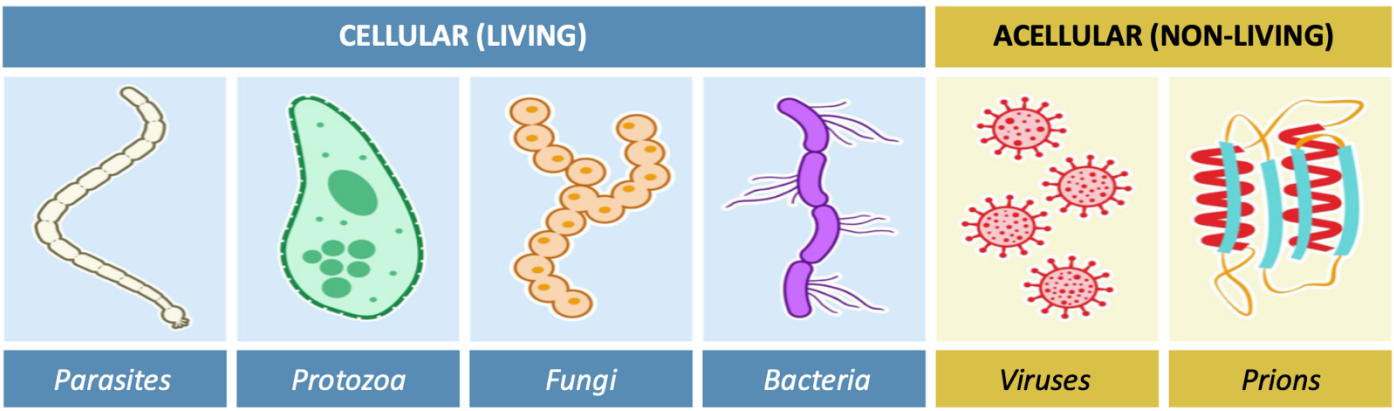
PATHOGENS

A pathogen is a **disease-causing agent** that disrupts the normal physiology of an infected organism. They can be either cellular (includes bacteria, fungi and parasites) or non-cellular (includes viruses and prions). A *virus* is an infective entity that inserts its genetic material into a host cell in order to multiply. A *prion* is an infectious protein that has folded abnormally into a disease-causing structure. *Bacteria* are prokaryotic cells that reproduce quickly and compete with host cells for space or nutrition. Disease-causing *fungi* typically colonise body surfaces, while parasites are organisms that feed on a host to the detriment of host survival. They can include either single-celled microparasites *(protozoa)* or multicellular macroparasites *(helminths)*.



IMMUNE SYSTEM

The immune system can be divided into three basic lines of defence against pathogenic infections:

- The first line of defence are the surface barriers that prevent the entry of pathogens into the host body
- The second line of defence are the non-specific defence mechanisms activated after infection occurs
- The third line of defence are the specific responses that target antigens produced by the pathogens

NON-SPECIFIC DEFENCES		SPECIFIC DEFENCES
First line of defence	**Second line of defence**	**Third line of defence**
• Physical barriers • Chemical barriers • Microbiological barriers	• Phagocytic leukocytes • Inflammatory response • Complement proteins	• Lymphocytes (B and T_H cells) • Antibodies (via plasma cells) • Memory cells

SURFACE BARRIERS

Most animals possess three distinctive types of barriers to prevent pathogens from accessing body tissue. Physical barriers function as obstructions that impede access to internal tissues, while chemical barriers consist of the chemical compounds released onto surfaces (or into cavities) to hinder pathogenic survival.

Physical Barriers:

- Intact skin consists predominantly of dead cells that line the body surfaces to prevent pathogen entry
- Mucous membranes consist of living cells that line internal cavities and secrete trapping fluids (mucus)
- Internal surfaces may be ciliated to aid in the removal of pathogens (via physical actions like coughing)

Chemical Barriers:

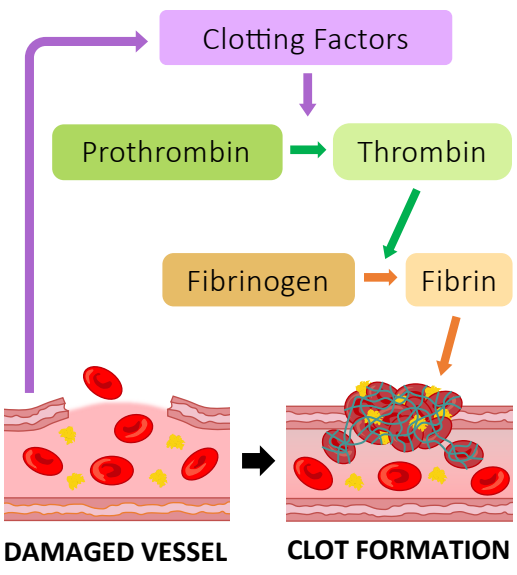
- Gastric secretions contain strong stomach acids (pH < 2) that function to destroy ingested pathogens
- Sweat and tears contain biochemical agents (e.g. lysozymes, lactic acid) that inhibit microbial growth
- Mucus secreted into the digestive and genitourinary tracts also contain biochemical defence agents

Microbiological Barriers:

- Natural flora (commensals) lines the gut, taking up space and preventing colonisation by pathogens

CLOTTING

If surface barriers are penetrated and pathogens gain access to body tissues, then a clotting cascade is activated to restore an intact external layer. Clotting is initiated by the release of **clotting factors** from damaged cells or platelets. These factors cause platelets to become sticky and form a solid plug, while also triggering coagulation by converting an inactive enzyme precursor (prothrombin) into an activated enzyme (**thrombin**). This will in turn convert soluble fibrinogen strands in the blood into insoluble **fibrin fibres**. The fibrin then associates with the platelet plug to form a fibrous clot at the region where the skin has been broken. When the damage site has been completely repaired, enzymes will dissolve the clot, leaving behind a layer of skin to act as an impermeable barrier to further infection.



INNATE IMMUNE SYSTEM

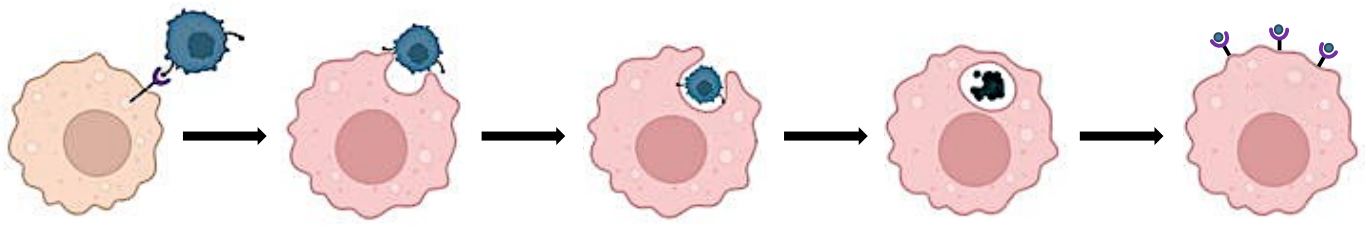
The second line of defence against infectious disease is the innate immune system, which is **non-specific**:

- 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 primary component of the innate immune system are the phagocytic leukocytes, which internalise and digest broad types of pathogens based on generic characteristics (pathogen-associated molecular patterns).

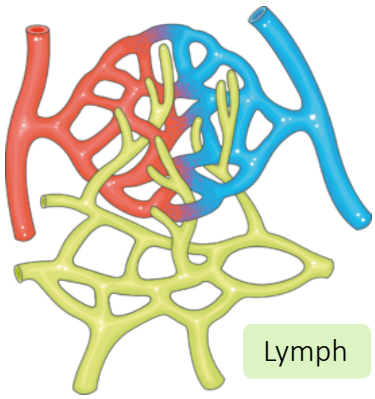
PHAGOCYTOSIS

Phagocytes are white blood cells (leukocytes) that can engulf foreign bodies. Phagocytes are non-specific and can only respond to broad categories of pathogens. Phagocytes are recruited to infected tissues when damaged cells release chemotactic chemicals. The phagocyte uses cellular extensions called **pseudopodia** to travel from the bloodstream via **amoeboid movement**. A pathogen is then surrounded by pseudopodia internalised within a vesicle (via endocytosis). The vesicle is then fused to **lysosomes** and the pathogen is digested. The antigenic fragments from the pathogen may then be presented on the cell membrane of the phagocyte (becoming an **antigen presenting cell**) in order to stimulate the third line of defence (adaptive).



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 will filter the fluid at sites called **lymph nodes** and remove pathogens to avoid infection. When a phagocytic leukocyte engulfs a pathogen and becomes an antigen presenting cell, it will be transported to the lymphatic system in order to present the antigenic fragment to lymphocytes (adaptive immune cells). Lymphatic systems therefore function as an important link between the innate and adaptive systems as it connects phagocytes and lymphocytes.



ADAPTIVE IMMUNE SYSTEM

The third line of defence against infectious disease is the adaptive immune system, which is **specific**:

- It recognises specific antigens in order to differentiate between different types of pathogens
- It produces a heightened response upon re-exposure to a pathogen (i.e. has immunological memory)

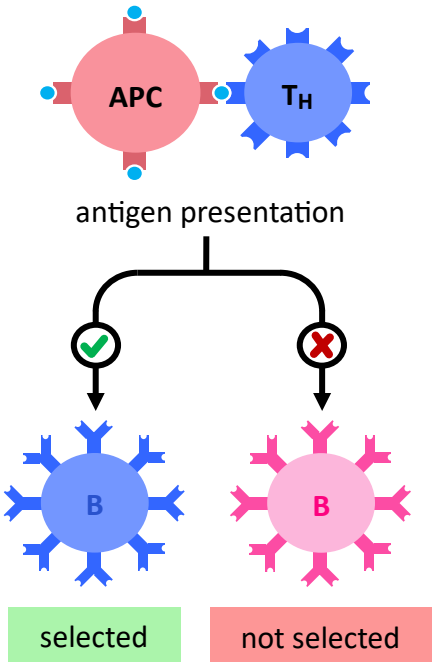
The principal components of the adaptive immune system are the lymphocytes residing in lymph nodes.

ANTIGENS

Antigens are molecular markers (typically glycoproteins) that are usually located on the outer surfaces of pathogens. These antigenic fragments are unique to the pathogen and can be used to target the pathogen specifically. Antigens will be targeted by specific proteins called **antibodies** (antigen = antibody generator).

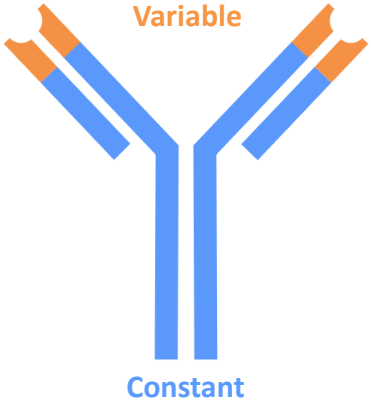
LYMPHOCYTES

The body contains millions of different B and T lymphocytes that each recognise a single, specific antigen. Only the appropriate lymphocyte can be activated by a particular antigenic fragment to divide and form identical clones (clonal selection / expansion). As each pathogen may contain many distinct antigenic fragments on their surface, a particular pathogen may stimulate several different B and T lymphocytes to form clones (this is called polyclonal activation). The proliferation of specific B cells first require activation by a specific **helper T cell** (helper T cells coordinate the entire adaptive immune response). Helper T cells are introduced to antigenic fragments by antigen presenting cells in the lymph nodes. The helper T cells will then release **cytokines** to activate naïve B lymphocytes that have also encounter the antigen. The B cells divide and differentiate to form a large quantity of short-lived plasma cells and a lesser quantity of memory cells. **Plasma cells** will produce antibodies that target the antigen and facilitate pathogen elimination.



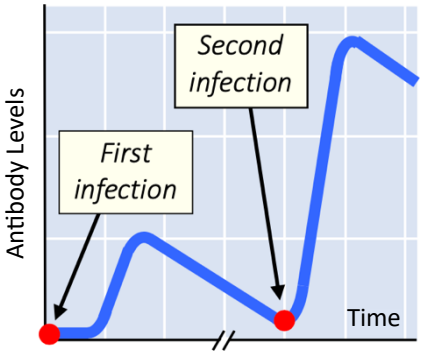
ANTIBODIES

Antibodies are proteins produced by B lymphocytes (and plasma cells) that are specific to a particular antigen. They are composed of four polypeptide chains that are connected by disulphide bonds to form Y-shaped molecules. Each antibody is composed of two heavy and two light chains, but differ in their **variable region** which is specific for a given antigen. The remainder of the antibody is constant and serves as a recognition site for immune cells. Antibodies facilitate pathogen destruction in a number of different ways, including via precipitation, agglutination and complement activation, but the primary way antibodies act to eliminate pathogens is via **opsonisation**.



MEMORY CELLS

When B and T lymphocytes divide and differentiate, a small proportion of clones will differentiate into memory cells. Memory cells remain in the body for years (or even a lifetime). If a second infection with the same antigen occurs, memory cells will produce a **secondary immune response** that is *faster* and *more potent*, such that the symptoms of infection do not normally appear. Because the individual no longer presents with the symptoms of infection upon exposure, the person is said to have developed immunological memory and is now immune.

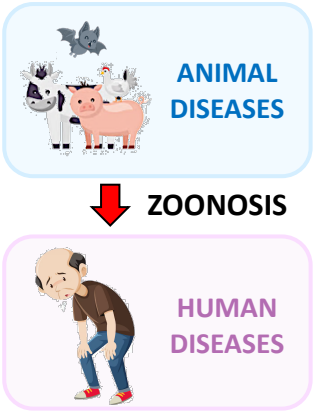


IMMUNODEFICIENCY

Immunodeficiency is a condition in which the immune system is either compromised or absent. As a result, the body cannot fight off pathogens and becomes increasingly susceptible to opportunistic infections. The human immunodeficiency virus (**HIV**) can cause acquired immunodeficiency syndrome (AIDS) by specifically infecting the helper T lymphocytes. With a reduction in the number of T_H cells, antibodies are unable to be produced and immunity is lowered. HIV is transmitted through the exchange of bodily fluids – including via unprotected sex, blood contact (e.g. unsafe needle injections) or maternal transmission during pregnancy.

ZOONOSES

A zoonosis is an infectious disease that can be transmitted from other species to humans. The pathogen can be transferred directly from a non-human host or may be transmitted by an unaffected intermediate species (referred to as a **vector**). The infected animals can act as a reservoir for the pathogen, allowing it to survive even if it is eradicated in humans – facilitating the re-emergence of diseases in populations where they had been eliminated. Zoonotic diseases are occurring with greater frequency due to increased urbanisation of regions heightening the exposure of humans to infected animals. Examples of zoonotic diseases include bovine tuberculosis, rabies and Japanese encephalitis.



Disease	Pathogen	Animal Source	Mode of Transmission
Tuberculosis	Bacterium *(M. bovis)*	Cattle	Unprocessed milk
Rabies	Virus *(R. lyssavirus)*	Wild animals / pets	Direct contact (bite / scratch)
Japanese encephalitis	Virus *(JEV)*	Pigs	Biological vector (mosquitoes)

ANTIBIOTICS

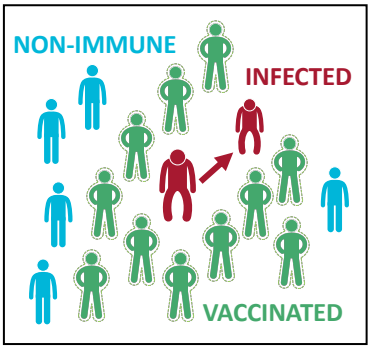
Bacterial pathogens can be treating with compounds that specifically target prokaryotic features (e.g. 70S ribosomes). These compounds are called **antibiotics**. Some bacteria have developed antibiotic resistance genes (via mutations), that enable them to survive antibiotic treatment. The bacteria can even pass these genes to susceptible colonies by bacterial conjugation (plasmid exchange), making antibiotics ineffective.

VACCINATION

Vaccination involves the injection of a biological preparation (vaccine) to provide active acquired immunity to a specific infectious disease. Vaccines consist of **attenuated pathogens** – either the antigenic fragments or the nucleic acid sequences that code for the antigens. The body will respond to a vaccine by initiating a primary response that results in the production of **memory cells**. When an individual is then exposed to the actual pathogen, the memory cells will trigger a more potent secondary immune response that prevents disease symptoms from developing (the individual is now considered to be immunised against the disease).

HERD IMMUNITY

Vaccinations confer immunity to vaccinated individuals but also indirectly protects the non-vaccinated people via herd immunity. When a sufficiently large percentage of a population is immune to infection, there is a reduced risk of infection for individuals who lack immunity. Herd immunity limits the spread of a pathogen to individuals who are particularly elderly, extremely young or may be immune compromised. The proportion of a population that needs to be vaccinated to confer herd immunity will be influenced by a range of factors – such as population density, mode of transmission and infectivity.



OUTBREAKS

An **epidemic** is an outbreak that occurs over a given time period within a particular community or region, while a **pandemic** occurs across a wider geographical area (e.g. global). Emerging trends can be measured via *percentage changes* (e.g. vaccine efficiencies) or *percentage differences* (e.g. age group comparisons).