The Immune System

Phagocytes: Origin & Mode of Action

Phagocytes are white blood cells that are produced continuously in the bone marrow

They are stored in the bone marrow before being distributed around the body in the blood

They are responsible for removing dead cells and invasive microorganisms

They carry out what is known as a non-specific immune response

There are two main types of phagocyte, each with a specific mode of action. The two types are:

- Neutrophils
- Macrophages

Primary Immune Response (Advanced)

Lymphocytes are another type of white blood cell

They play an important part in the specific immune response

They are smaller than phagocytes

They have a large nucleus that fills most of the cell

They are produced in the bone marrow before birth

There are two types of lymphocytes (with different modes of action).

The two types of lymphocytes are:

- B-lymphocytes (B cells)
- T-lymphocytes (T cells)

Antigens, Self & Non-Self

Every cell in the human body has markers that identify it

Microorganisms (both pathogenic and non-pathogenic), such as bacteria and viruses, also have their own unique markers

These markers are called antigens (which are macromolecules) and they allow cell-to-cell recognition

Antigens are found on cell surface membranes, bacterial cell walls, or the surfaces of viruses

Some glycolipids and glycoproteins on the outer surface of cell surface membranes act as antigens

Antigens can be either self antigens or non-self antigens:

Antigens produced by the organism's own body cells (those that the immune system does not recognise as foreign antigens) are known as self antigens

Self antigens do not stimulate an immune response

Antigens not produced by the organism's own body cells (those that the immune system recognises as being foreign eg. the antigens found on pathogenic bacteria and viruses or if a person receives a different blood type during a transfusion) are known as non-self antigens

Non-self antigens stimulate an immune response

Neutrophils

Chemicals released by pathogens, as well as chemicals released by the body cells under attack (eg. histamine), attract neutrophils to the site where the pathogens are located (this response to chemical stimuli is known as chemotaxis)

Neutrophils move towards pathogens (which may be covered in antibodies)

The antibodies are another trigger to stimulate neutrophils to attack the pathogens (neutrophils have receptor proteins on their surfaces that recognise antibody molecules and attach to them)

Once attached to a pathogen, the cell surface membrane of a neutrophil extends out and around the pathogen, engulfing it and trapping the pathogen within a phagocytic vacuole

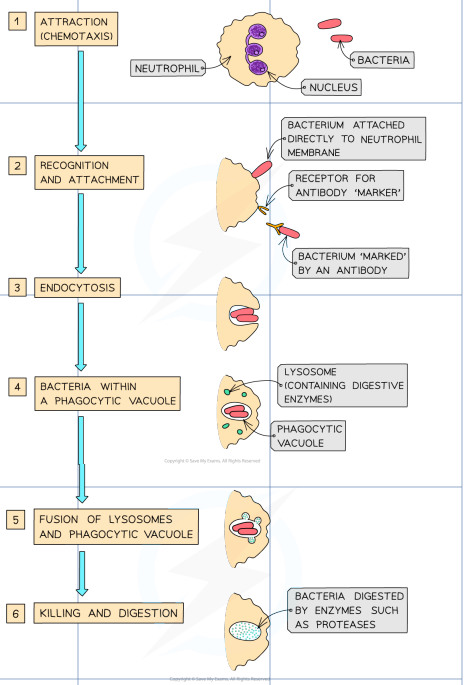
This part of the process is known as endocytosis

The neutrophil then secretes digestive enzymes into the vacuole (the enzymes are released from lysosomes which fuse with the phagocytic vacuole)

These digestive enzymes destroy the pathogen

After killing and digesting the pathogens, the neutrophils die

Pus is a sign of dead neutrophils



Macrophages

Macrophages are larger than neutrophils and are long-lived cells

Rather than remaining in the blood, they move into organs including the lungs, liver, spleen, kidney and lymph nodes

After being produced in the bone marrow, macrophages travel in the blood as monocytes, which then develop into macrophages once they leave the blood to settle in the various organs listed above

Mode of action:

Macrophages play a very important role in initiating an immune response

Although they still carry out phagocytosis in a similar way to neutrophils, they do not destroy pathogens completely

They cut the pathogens up so that they can display the antigens of the pathogens on their surface (through a structure called the major histocompatibility complex)

These displayed antigens (the cell is now called an antigen-presenting cell) can then be recognised by lymphocytes (another type of white blood cell)

The immune system

T-lymphocytes are activated when they encounter (and bind to) their specific antigen that is being presented by one of the host's cells (host cells being the human's own cells)

This antigen-presenting host cell might be a macrophage or a body cell that has been invaded by a pathogen and is displaying the antigen on its cell surface membrane

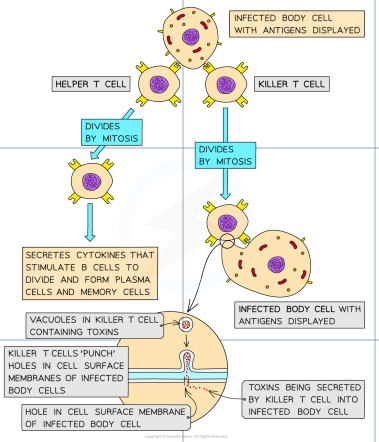
These activated T-lymphocytes (those that have receptors specific to the antigen) divide by mitosis to increase in number (similar to the clonal selection and clonal expansion of B-lymphocytes)

These T-lymphocytes differentiate into two main types of T cell:

- helper T cells
- killer T cells

Helper T cells release cytokines (hormone-like signals) that stimulate B-lymphocytes to divide and develop into antibody-secreting plasma cells. Some helper T cells secrete cytokines that stimulate macrophages to increase their rates of phagocytosis

Killer T cells attach to the antigens on the cell surface membranes of infected cells and secrete toxic substances that kill the body cells, along with the pathogen inside



B-lymphocytes

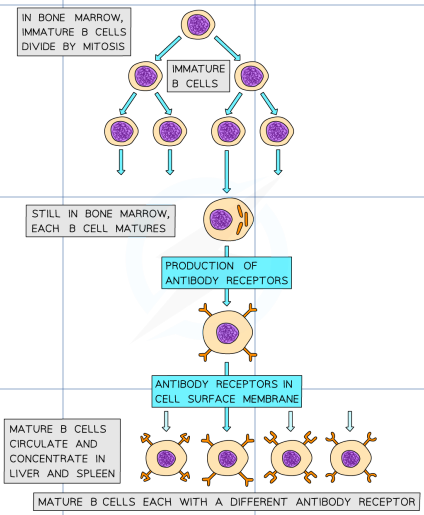
B-lymphocytes (B cells) remain in the bone marrow until they are mature and then spread through the body, concentrating in lymph nodes and the spleen

Millions of types of B-lymphocyte cells are produced within us because as they mature the genes coding for antibodies are changed to code for different antibodies

Once mature, each type of B-lymphocyte cell can make one type of antibody molecule

At this stage, the antibody molecules do not leave the B-lymphocyte cell but remain in the cell surface membrane

Part of each antibody molecule forms a glycoprotein receptor that can combine specifically with one type of antigen

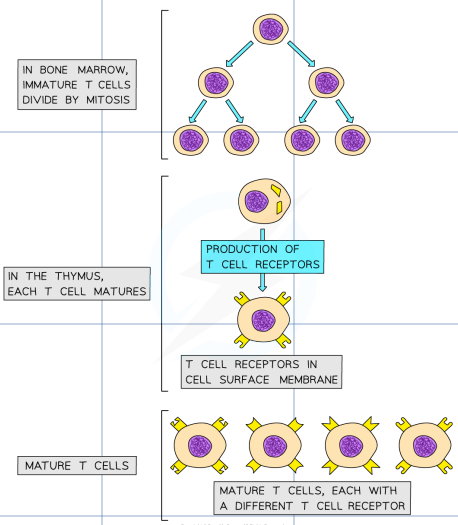


T-lymphocytes

Immature T-lymphocytes leave the bone marrow to mature in the thymus

Mature T-lymphocytes have specific cell surface receptors called T cell receptors

These receptors have a similar structure to antibodies and are each specific to one antigen



When an antigen enters the body for the first time, the small numbers of B-lymphocytes with receptors complementary to that antigen are stimulated to divide by mitosis

This is known as clonal selection

As these clones divide repeatedly by mitosis (the clonal expansion stage) the result is large numbers of identical B-lymphocytes being produced over a few weeks

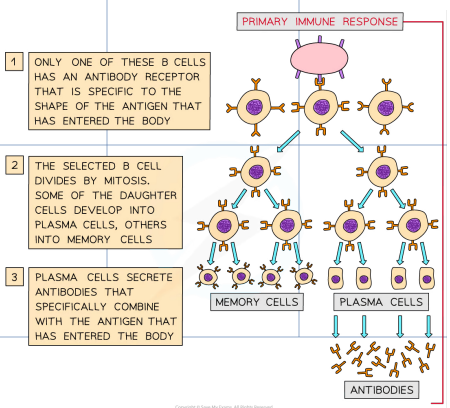
During an immune response, these B-lymphocytes then form two types of cell:

Some of these B-lymphocytes become plasma cells that secrete lots of antibody molecules (specific to the antigen) into the blood, lymph or linings of the lungs and the gut

These plasma cells are short-lived (their numbers drop off after several weeks) but the antibodies they have secreted stay in the blood for a longer time

The other B-lymphocytes become memory cells that remain circulating in the blood for a long time

This response to a newly encountered antigen is relatively slow and is known as a primary immune response



The immune system

Structure

Antibodies are globular glycoproteins called immunoglobulins

Antibodies have a quaternary structure (which is represented as Y-shaped), with two 'heavy' (long) polypeptide chains bonded by disulfide bonds to two 'light' (short) polypeptide chains

Each polypeptide chain has a constant region and variable region

The constant regions do not vary within a class (isotype) of antibodies but do vary between the classes. The constant region determines the mechanism used to destroy the antigens

There are 5 classes of mammalian antibodies each with different roles

The amino acid sequence in the variable regions of the antibodies (the tips of the "Y") are different for each antibody. The variable region is where the antibody attaches to the antigen to form an antigen-antibody complex

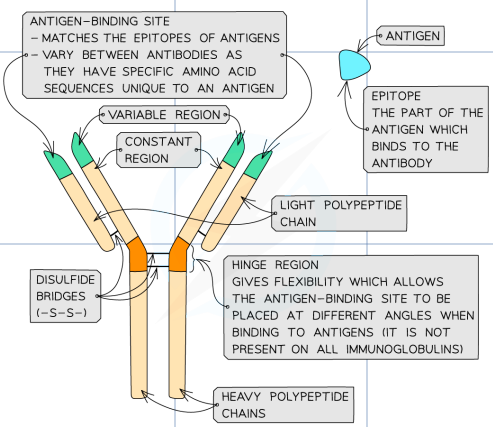
At the end of the variable region is a site called the antigen-binding site. Each antigen-binding site is generally composed of 110 to 130 amino acids and includes both the ends of the light and heavy chains

The antigen-binding sites vary greatly giving the antibody its specificity for binding to antigens. The sites are specific to the epitope (the part of the antigen that binds to the antibody)

A pathogen or virus may therefore present multiple antigens different antibodies need to be produced

The 'hinge' region (where the disulfide bonds join the heavy chains) gives flexibility to the antibody molecule which allows the antigen-binding site to be placed at different angles when binding to antigens

This region is not present in all classes of antibodies



Memory Cells & Long-Term Immunity

During an immune response, B-lymphocytes form two types of cell: plasma cells and memory cells

Memory cells form the basis of immunological memory – the cells can last for many years and often a lifetime

There are two types of immune response:

Primary immune response (responding to a newly encountered antigen)

Secondary immune response (responding to a previously encountered antigen)

Primary immune response

When an antigen enters the body for the first time, the small numbers of B-lymphocytes with receptors complementary to that antigen are stimulated to divide by mitosis

This is known as clonal selection

As these clones divide repeatedly by mitosis (the clonal expansion stage) the result is large numbers of identical B-lymphocytes being produced over a few weeks

Some of these B-lymphocytes become plasma cells that secrete lots of antibody molecules (specific to the antigen) into the blood, lymph or linings of the lungs and the gut

These plasma cells are short-lived (their numbers drop off after several weeks) but the antibodies they have secreted stay in the blood for a longer time

The other B-lymphocytes become memory cells that remain circulating in the blood for a long time

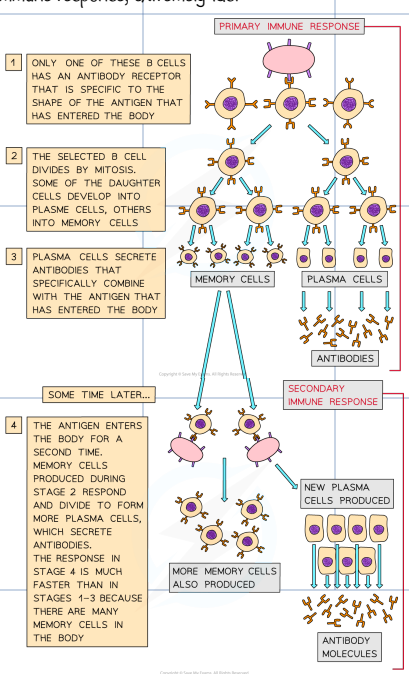
This response to a newly encountered pathogen is relatively slow

Secondary immune response

If the same antigen is found in the body a second time, the memory cells recognise the antigen, divide very quickly and differentiate into plasma cells (to produce antibodies) and more memory cells

This response is very quick, meaning that the infection can be destroyed and removed before the pathogen population increases too much and symptoms of the disease develop

This response to a previously encountered pathogen is, relative to the primary immune response, extremely fast



T-lymphocytes also play a part in the secondary immune response

They differentiate into memory cells, producing two main types:

- Memory helper T cells
- Memory killer T cells

Just like the memory cells formed from B-lymphocytes, these memory T cells remain in the body for a long time

If the same antigen is found in the body a second time, these memory T cells become active very quickly

The immune system

Feature	Active	Passive
Production of antibodies	Are produced by the body	Not produced by the body
Time before antibodies appear in blood	1–2 weeks	immediate
Presence of memory cells	yes	no
Induced by:		
Natural	Exposure to pathogen	Antibodies received from another organism (e.g. via the placenta or colostrum / breast milk)
Artificial	Vaccination	Antibodies manufactured and injected or transfused into organism (e.g. monoclonal antibodies delivered by blood transfusion)

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Function

Antibodies are produced by B-lymphocytes

Antibodies bind to specific antigens that trigger the specific immune response. Every antigen has one antibody

Antigens include pathogens and their toxins, pollen, blood cell surface molecules and the surface proteins found on transplanted tissues

Antibodies are divided into five major classes (isotypes), each with a different role

The function of antibodies differ:

Antibodies can combine with viruses and toxins of pathogens (e.g. bacteria) to block them from entering or damaging cells

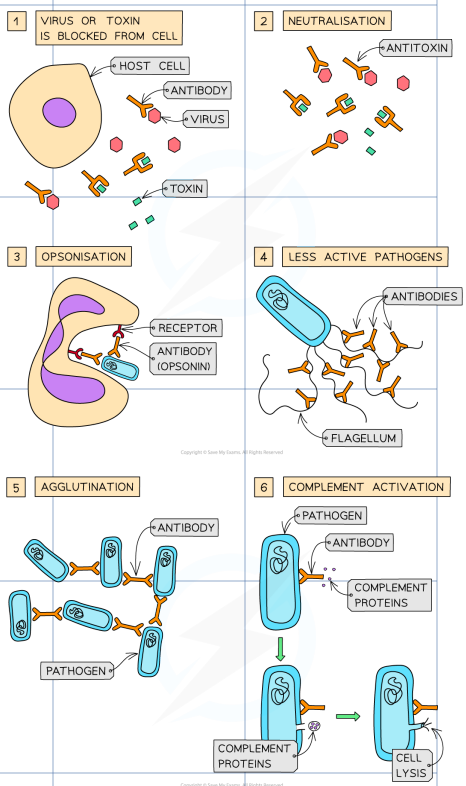
Antibodies can act as anti-toxins by binding to toxins produced by pathogens (e.g. the bacteria that cause diphtheria and tetanus) which neutralises them making them harmless

Antibodies can attach to bacteria making them readily identifiable to phagocytes, this is called opsonisation. Once identified, the phagocyte has receptor proteins for the heavy polypeptide chains of the antibodies, which enables phagocytosis to occur

Antibodies can attach to the flagella of bacteria making them less active, which makes it easier for phagocytes to do phagocytosis

Antibodies act as agglutinins causing pathogens carrying antigen-antibody complexes to clump together (agglutination). This reduces the chance that the pathogens will spread through the body and makes it possible for phagocytes to engulf a number of pathogens at one time

Antibodies (together with other molecules) can create holes in the cell walls of pathogens causing them to burst (lysis) when water is absorbed by osmosis



Passive immunity

Passive immunity is acquired without an immune response. Antibodies are not produced by the infected person

As the person's immune system has not been activated then there are no memory cells that can produce antibodies in a secondary response. If a person is reinfected they would need another infusion of antibodies

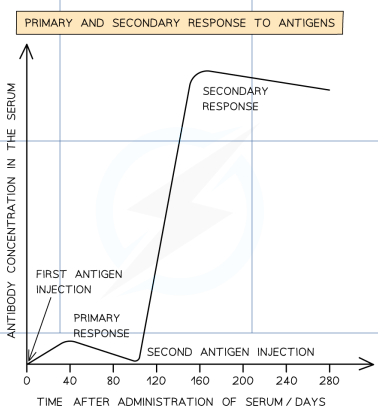
Depending on the disease a person is infected with (eg. tetanus) they may not have time to actively acquire the immunity, that is, there is no time for active immunity. So passive immunity occurs either artificially or naturally

Artificial passive immunity occurs when people are given an injection / transfusion of the antibodies. In the case of tetanus this is an antitoxin. The antibodies were collected from people whose immune system had been triggered by a vaccination to produce tetanus antibodies

Natural passive immunity occurs when:

Foetuses receive antibodies across the placenta from their mothers

Babies receive the initial breast milk from mothers (the colostrum) which delivers a certain isotype of antibody (IgA)



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Active immunity

Active immunity is acquired when an antigen enters the body triggering a specific immune response (antibodies are produced)

Active immunity is naturally acquired through exposure to microbes or artificially acquired through vaccinations

The body produces memory cells, along with plasma cells, in both types of active immunity giving the person long-term immunity

In active immunity, during the primary response to a pathogen (natural) or to a vaccination (artificial), the antibody concentration in the blood takes one to two weeks to increase.

If the body is invaded by the same pathogen again or by the pathogen that the person was vaccinated against then, during the secondary response, the antibody concentration in the blood takes a much shorter period of time to increase and is higher than after the vaccination or first infection

The immune system

A vaccine is a suspension of antigens that are intentionally put into the body to induce artificial active immunity. A specific immune response where antibodies are released by plasma cells

There are two main types of vaccines:

- Live attenuated
- Inactivated

Vaccines are administered either by injection or orally (by mouth). When a person is given a vaccine they have been given a vaccination

The vaccinations given by injection can be into a vein or muscle

Vaccinations produce long-term immunity as they cause memory cells to be created. The immune system remembers the antigen when reencountered and produces antibodies to it, in what is a faster, stronger secondary response

T-lymphocytes are activated when they encounter (and bind to) their specific antigen that is being presented by one of the host's cells (host cells being the human's own cells)

This antigen-presenting host cell might be a macrophage or a body cell that has been invaded by a pathogen and is displaying the antigen on its cell surface membrane

These activated T-lymphocytes (those that have receptors specific to the antigen) divide by mitosis to increase in number (similar to the clonal selection and clonal expansion of B-lymphocytes)

These T-lymphocytes differentiate into two main types of T cell:

helper T cells

cytotoxic T cells(also known as killer T cells)

Vaccines can be:

Highly effective with one vaccination giving a lifetime's protection (although less effective ones will require booster / subsequent injections)

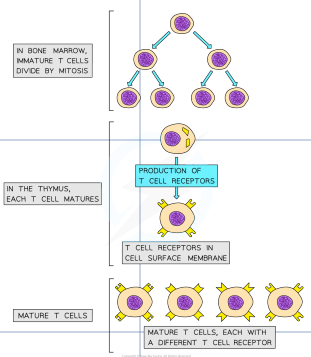
Generally harmless as they do not cause the disease they protect against because the pathogen is killed by the primary immune response

T-lymphocytes and the cellular immune response

Immature T-lymphocytes leave the bone marrow to mature in the thymus

Mature T-lymphocytes have specific cell surface receptors called T cell receptors

These receptors have a similar structure to antibodies and are each specific to one antigen



The T Lymphocyte Response

Lymphocytes are another type of white blood cell

They play an important part in the specific immune response

They are smaller than phagocytes

They have a large nucleus that fills most of the cell

They are produced in the bone marrow before birth

There are two types of lymphocytes (with different modes of action). The two types of lymphocytes are:

- T-lymphocytes (T cells)
- B-lymphocytes (B cells)

Unfortunately there can be problems with vaccines:

People can have a poor response (eg. they are malnourished and cannot produce the antibodies – proteins or their immune system may be defective)

A live pathogen may be transmitted (e.g. through faeces) to others in the population (ideally enough number of people are vaccinated at the same time to give herd immunity)

Antigenic variation – the variation (due to major changes) in the antigens of pathogens causes the vaccines to not trigger an immune response or diseases caused by eukaryotes (eg. malaria) have too many antigens on their cell surface membranes making it difficult to produce vaccines that would prompt the immune system quickly enough

Antigenic concealment – this occurs when the pathogen 'hides' from the immune system by living inside cells or when the pathogen coats their bodies in host proteins or by parasitising immune cells such as macrophages and T cells (eg. HIV) or by remaining in parts of the body that are difficult for vaccines to reach