Immunity

Key Terms

Pathogen; A disease causing microorganism (eg bacteria, virus). Pathogens cause disease by killing body cells (often by replicating inside them) and producing toxic proteins.

Antigen; A protein* on the surface of a pathogen that is recognised as foreign by the body. It stimulates the immune response and causes the production of antibodies.

**At A-level it is acceptable to refer to antigens as proteins (and they often are due to their complicated, 3-D shapes. However other molecules such as glycolipids can also act as antigens. I will refer to antigens as proteins throughout these notes for the sake of simplicity.*

It is important to realise that pathogens do not produce surface proteins to deliberately act as antigens. They are important for the pathogens reproductive cycle and often bind to specific receptors on the host cell which allows the pathogen to infect them. They are not shapes normally found in the body which is why the immune system can recognise as foreign.

Antibody; Antibodies are proteins produced by B (plasma) cells, they are able to recognise and bind to one specific antigen.

Monoclonal Antibodies; A pure source of identical antibodies against one specific antigen. Used in research and medicine.

Memory cells; A type of B-cell produced following exposure to pathogen or vaccination. They remain in the body for many years and protect against infection by triggering a secondary immune response.

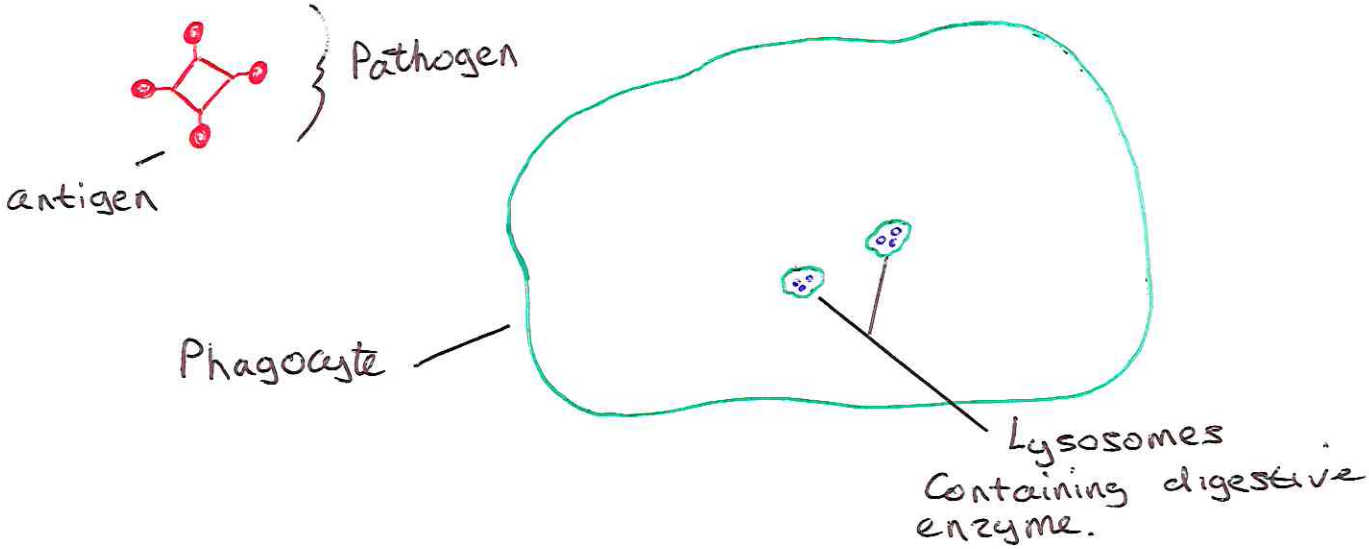
Non-specific immune response; Defense mechanisms that are always present but do not become more effective after exposure to a particular pathogen. Eg physical barriers such as the skin and the enzyme lysozyme in tears that breaks down bacterial cell walls.

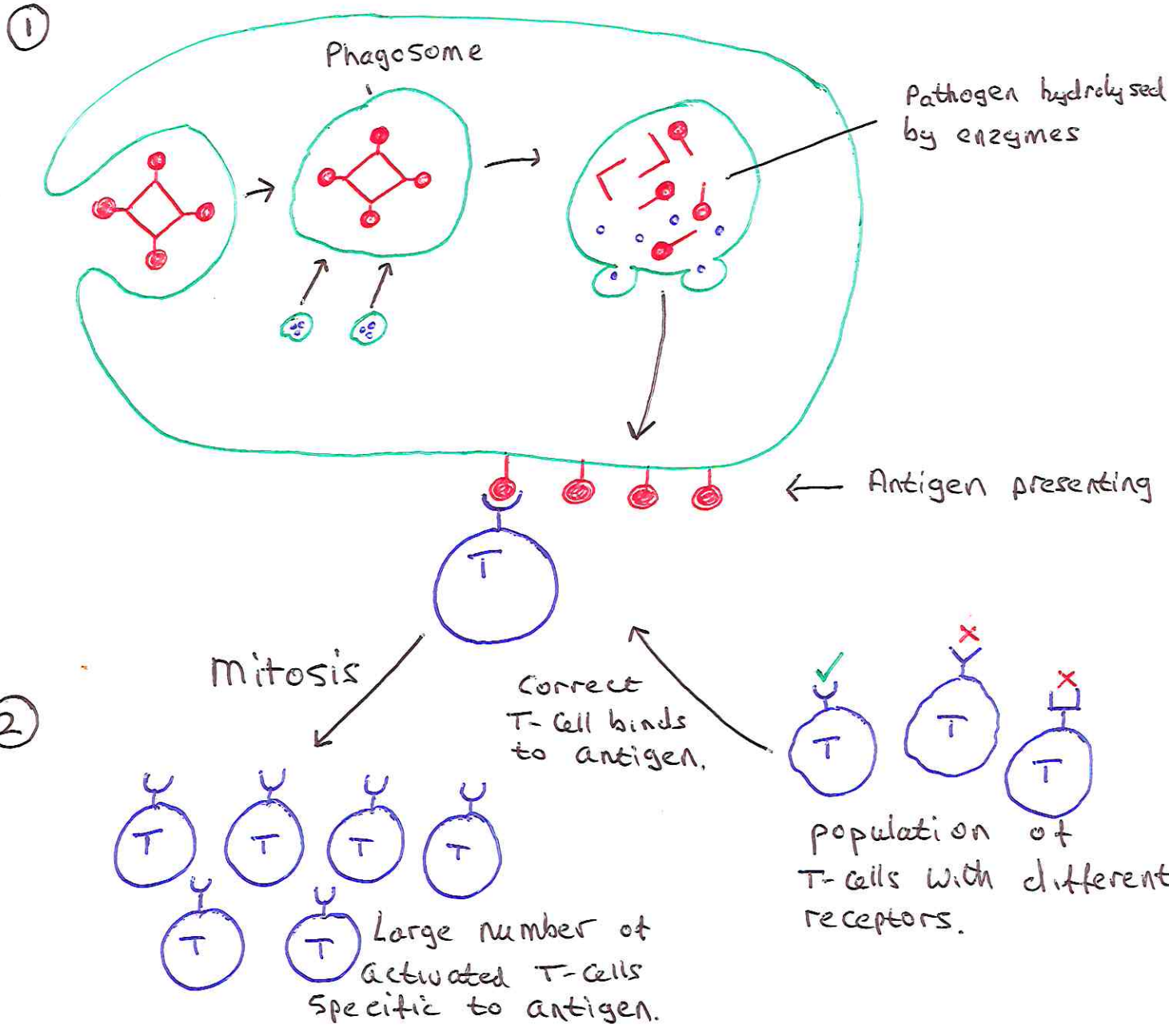
Specific immune response; A response that is specific to the antigen(s) of a particular pathogen. It involves T-cells (cell mediated) and B-cells (humoral). It leads to the production of memory cells to prevent re-infection.

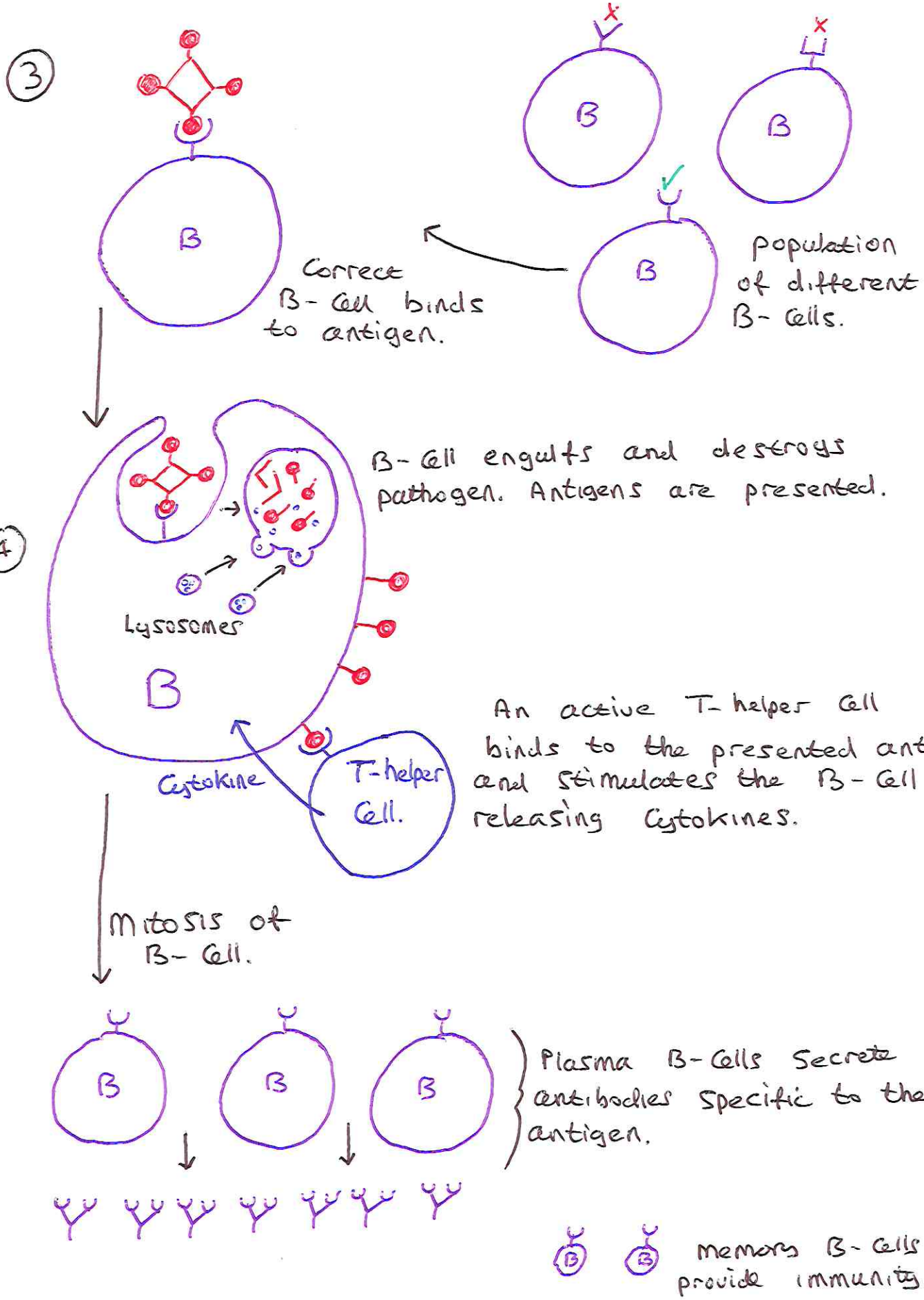
Active immunity; Permanent immunity due to the ability to produce antibodies from memory cells. This can be natural (after being infected once) or artificial (after being vaccinated).

Passive immunity; Temporary immunity due to the presence of antibodies in the blood (which will eventually be broken down) but no memory cells. This can be natural (the antibodies passed to a baby from mothers milk) or artificial (when doctor inject antibodies into a patient as treatment against infection or toxins).

Activation of the specific immune system






3
B
Correct B-Cell binds to antigen.
B
B
B
population of different B-Cells.
4
B-Cell engulfs and destroys pathogen. Antigens are presented.
Lysosomes
B
Cytokine
T-helper Cell.
An active T-helper Cell binds to the presented antigen and stimulates the B-Cell by releasing Cytokines.
Mitosis of B-Cell.
B
B
B
Plasma B-Cells Secrete antibodies specific to the antigen.
B
B
memory B-Cells provide immunity.

1) Phagocytosis; a white blood cell called a phagocyte engulfs the pathogen into a vesicle called a **phagosome**. The phagocyte also has smaller vesicles called **lysosomes** that contain digestive enzymes. The lysosomes fuse with the phagosome, exposing the pathogen to the digestive enzymes. The pathogen is **hydrolysed** into small pieces. The antigens from the destroyed pathogen are inserted into the surface membrane of the phagocyte. This allows other cells of the immune system to encounter the antigen and is known as **Antigen Presenting**.

2) T-cell activation; The blood contains a population of T-cells with different, randomly generated receptors that are able to recognise different specific antigens. When a T-cell with the correct receptor binds to the antigen presented by the phagocyte it becomes active and copies itself by mitosis; giving rise to a huge number of T-cells all with receptors able to recognise the antigen present on the invading pathogen. Different classes of T-cell are produced: **T-Helper** cells activate the correct, specific B-cell, **T-Killer** (**cytotoxic**) cells look for infected body cells displaying the antigen and kill them, destroying any pathogen inside in the process.

3) B-cell selection; There is also a population of B-cells with different specific receptors. If a B-cell has a receptor that is able to recognise and bind to the antigen then the cell can engulf the pathogen and act like a phagocyte. The pathogen is destroyed and the antigens are **presented** on the surface of the B-cell. **This is not yet enough to activate the B-cell**.

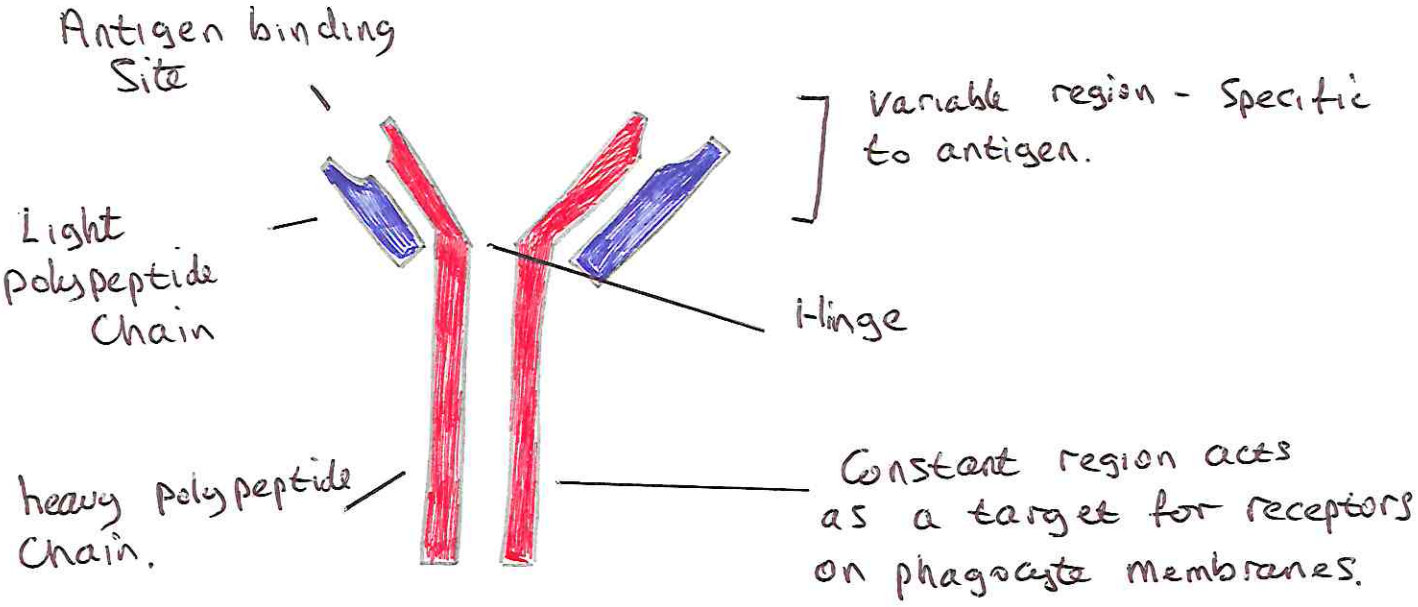
4) Activation of B-cell; Once the B-cell is displaying the antigen, a specific T-Helper cell has to bind in order to activate the B-cell. The T-Helper cells produce **Cytokines** which diffuse to the B-cell and activate it, causing the B-cell to divide by mitosis to produce huge numbers of identical cells able to recognise the antigen. The B-cell differentiates into 2 cell types; **Plasma cells** are large and their job is to secrete large amounts of antigen-specific **antibody**. **Memory cells** are smaller, they remain in the body for years and on contact with the antigen they immediately start to produce huge amounts of antibody. This is known as the **secondary immune response**, so much antibody is produced that the pathogen is destroyed before it can produce any symptoms – The person is now immune to the pathogen.

Antibodies

Antibodies are **quaternary** proteins produced by activated B (plasma) cells.

Antibody Features

- 2 heavy (larger) and 2 light (smaller) polypeptide chains.
- A constant region (common to all antibodies) that can act as a receptor for phagocytes.
- A variable region with 2 binding sites that can recognise and bind to 1 specific antigen, forming an **antigen-antibody complex**.
- A hinge, allowing the antibody to flex and bind to 2 separate pathogens.

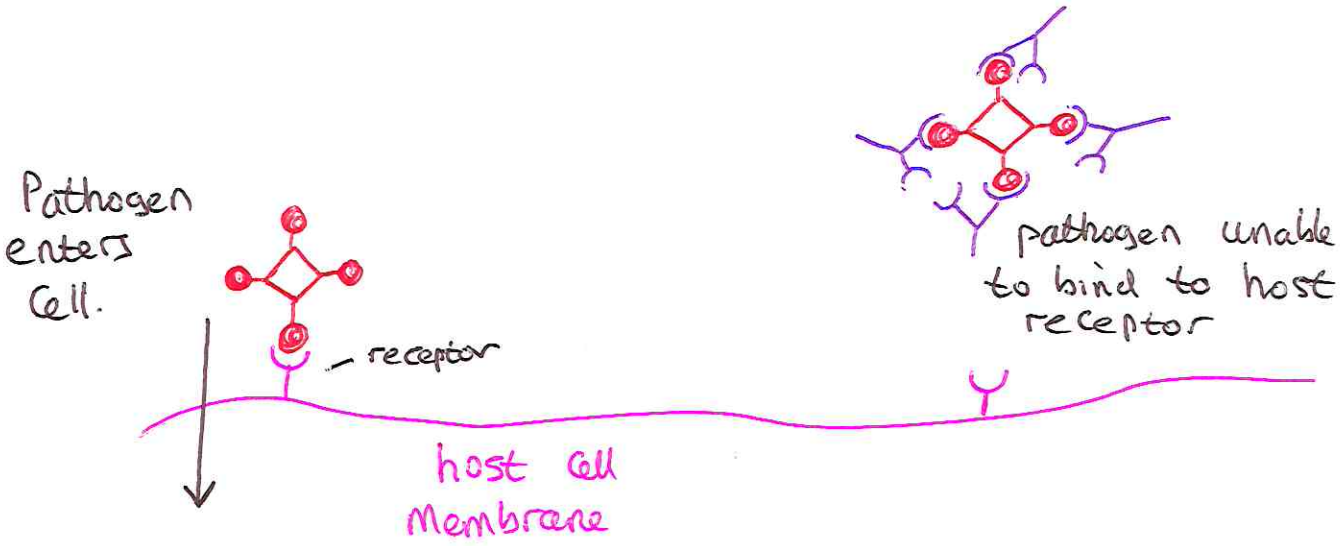


Antibody Function

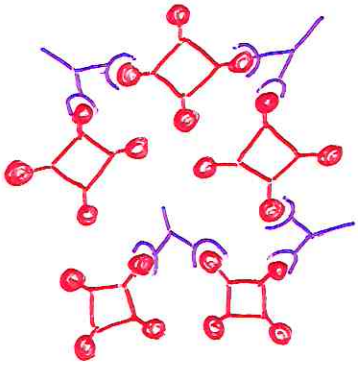
Antibodies do not kill pathogens, they help fight off infection in the following ways;

- **They increase the efficiency of phagocytosis;**
  Phagocytes are part of the non-specific immune system, however the surface membranes of phagocytes have receptor proteins that recognise the constant region of antibodies. Any pathogen that has been coated with antibody is much more likely to be engulfed and destroyed by phagocytes.

- **Masking important pathogen proteins;**
  Often the proteins that act as antigens play an important role in allowing the pathogen to infect host cells. For example, they may bind to specific receptors on the host cells' membrane. When they are covered up, the pathogen may no longer be able to enter the host;



- **Agglutination;**
  Antibodies have 2 independent antigen binding sites. This can cause pathogens to clump together in a process called agglutination. **Agglutinated** pathogen cannot enter host cells and is destroyed by phagocytes.



Agglutination of pathogen caused by antibodies.

Monoclonal Antibodies

There is often a lot of confusion about monoclonal antibodies, here is what you need to know;

- They are not a special type of antibody. They are produced by humans, under laboratory conditions for use in research and medicine.

- *What's special about monoclonal antibodies?* Monoclonal means 'from 1 clone', they are antibodies made by identical copies of 1 original B-cell. The antibodies are therefore identical and will all recognise the same specific antigen. Their specificity make them incredibly powerful tools as they will only bind in the presence of a specific antigen – they can be used to test the blood of a patient for specific pathogens, making diagnosis of disease much easier (See ELISA).

Making Monoclonal Antibodies

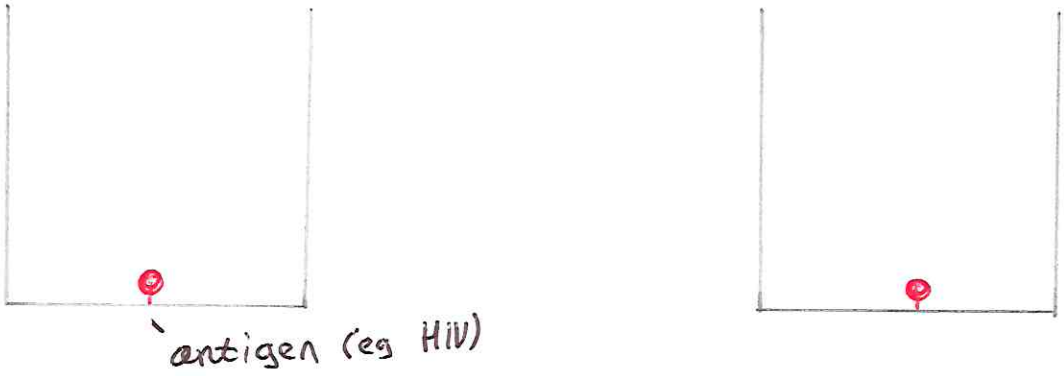
1. *Inject a test animal (eg rabbit) with the antigen you wish to make antibodies against*. The animal will undergo a specific immune response in a similar manner to that described on pages 2-3, resulting in a B-cell that recognises the specific antigen being activated.

2. *Identify the correct B-cell.* The B-cells are collected from the animal (often from the spleen) and individually tested until one is found that is able to recognise 'your' antigen.

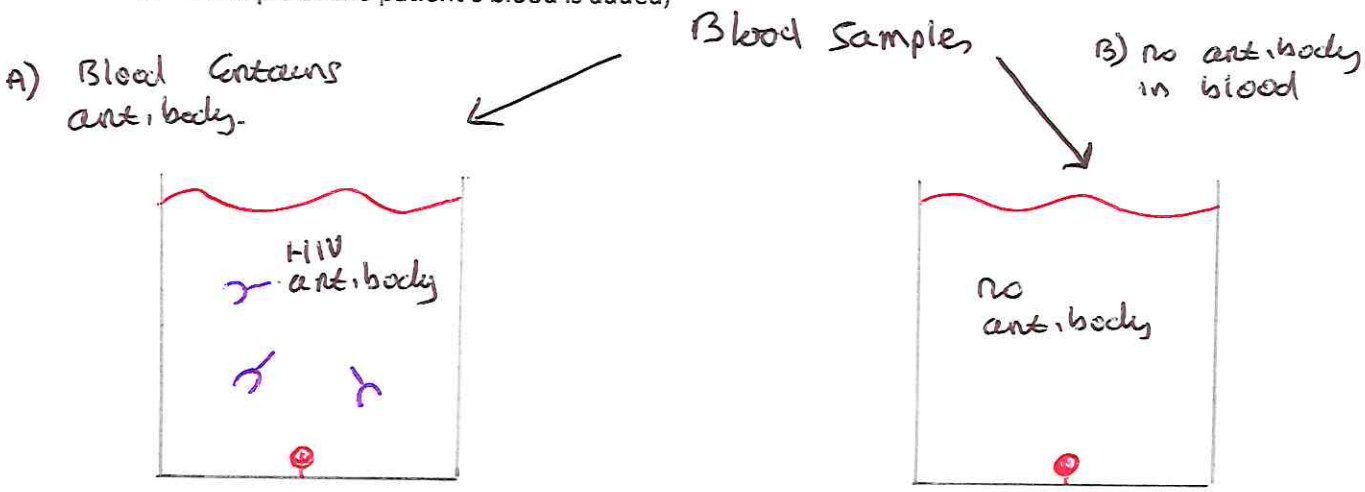
3. *Fuse the correct b-cell with a tumour cell.* This step is a bit technical and often causes confusion. The important part is finding a B-cell that will recognise (and therefore produce antibodies against) 'your' antigen. However, you are going to need lots of copies of the cell

The Elisa Test;

1. Small plastic containers are produced with the antigens from a particular pathogen (eg HIV) bound to them;



2. A sample of the patient's blood is added;

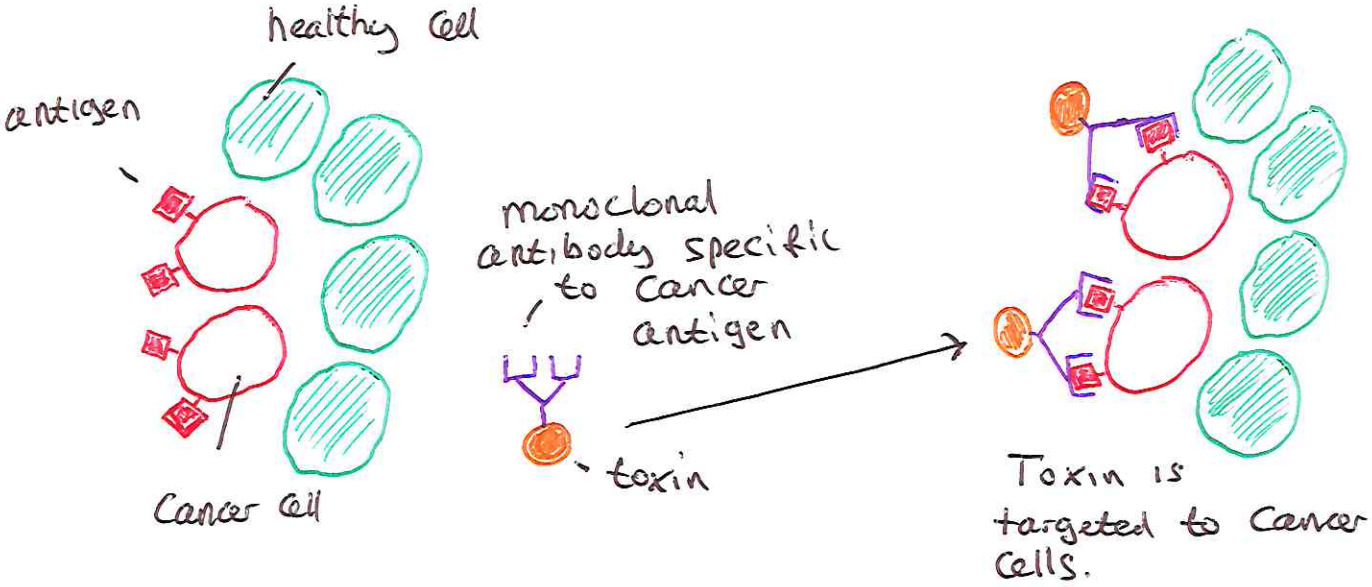


3. If the patient is infected with the pathogen then their blood will contain antibodies against the antigen. The antibodies will bind to the antigen on the container;

in order to produce large amounts of antibody. Unfortunately, B-cells are not that great at copying themselves. We can get around this by fusing the B-cell with a tumour (cancer) cell. Tumour cells will go on copying themselves (by mitosis) indefinitely and so can be used to make a cell that is a fusion between tumour and B-cell called a **Hybridoma**. Detergent is used to partially dissolve the plasma membranes of the cells, making them more likely to fuse together. the end result is a cell that will keep on copying itself in the laboratory whilst making large amounts of identical antibody against 1 specific antigen.

Uses of Monclonal Antibodies

1. *As a drug delivery system to treat cancer;* Often, when cells become cancerous they begin to display proteins on their surface that are not found in normal healthy cells. Monoclonal antibodies can be produced that specifically recognise these cancer antigens. The antibodies are attached to a powerful toxin and injected into the patient; because the antibodies will only bind to the proteins found on the cancer cells the toxin only accumulates around the tumour. The cancer cells are killed off with fewer side effects as the toxin is specifically targeted to the tumour.



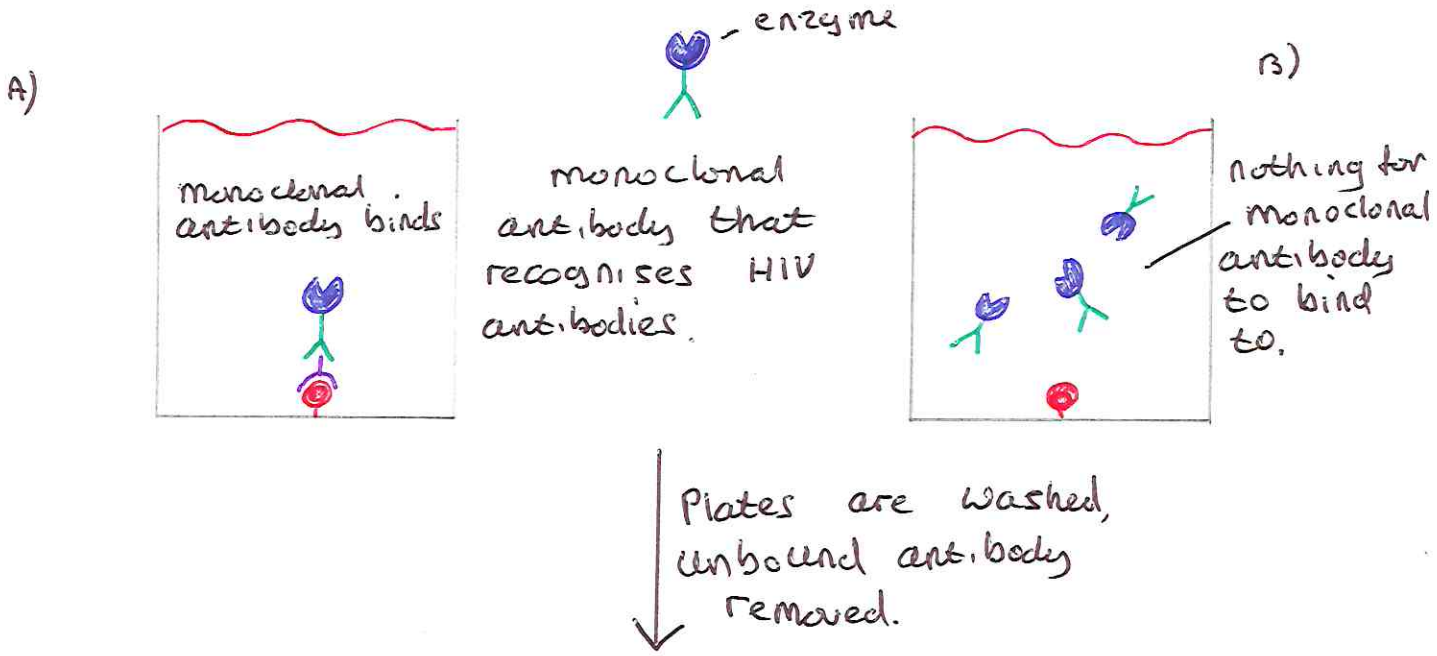
2. *The ELISA test;* Elisa is short for Enzyme Linked Immunosorbent Assay. It is a way of testing patients for the presence of specific antigens, or it can be used to test the blood of a patient for the presence of antibodies against a specific antigen – if their blood contains antibodies against HIV for example, then the patient must have been exposed to the antigen and is therefore infected with the pathogen. Monoclonal antibodies are essential for this test in order to ensure it is specific to a particular antigen.

The following page is a summary of 1 way in which the test can work.

4. A monoclonal antibody is added – this antibody specifically recognises the human antibody*. ***<u>It does not bind to the antigen!</u>*** The Monoclonal antibodies are attached to an enzyme – this will be important later on.

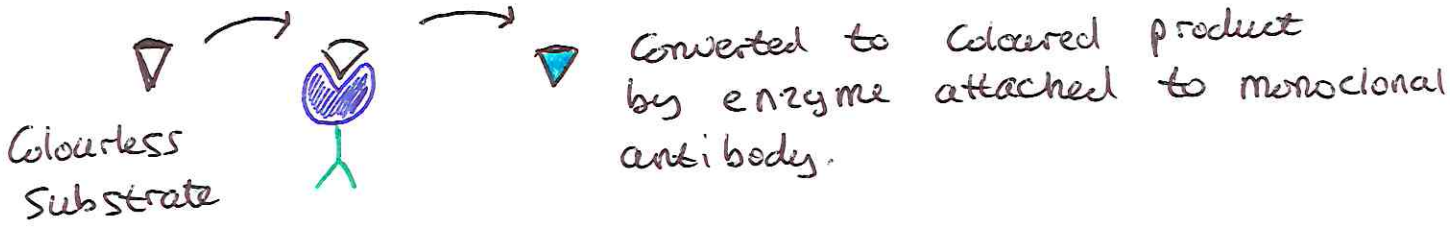
   **Remember that antigens are just proteins that the body recognises as foreign. Human antibodies can act as antigens if they are injected into another animal such as a rabbit. By injecting human antibodies against HIV into the rabbit we can produce monoclonal antibodies that will specifically recognise the human anti-HIV antibody.*

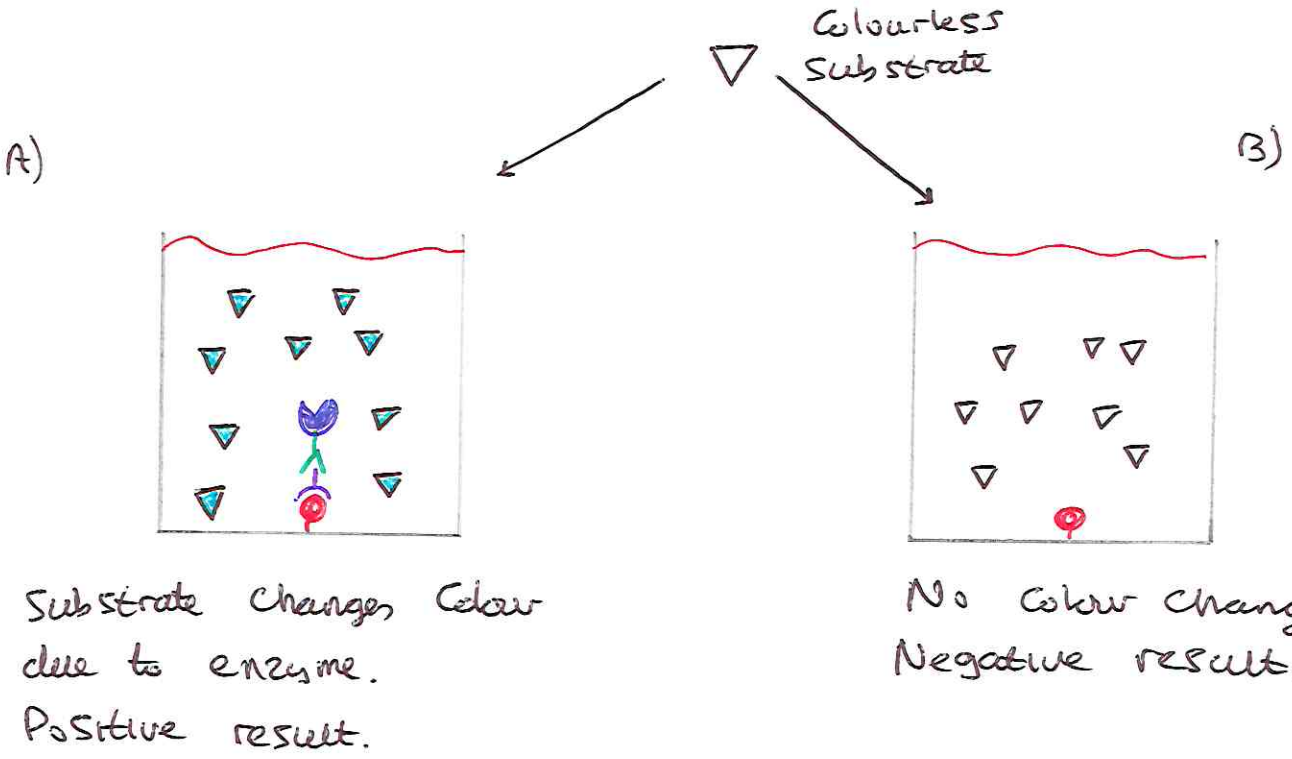
5. The plates are washed. This is a vital step because it removes any of the monoclonal antibody that is not complexed to the human anti-HIV antibody. Without this step the Monoclonal antibody (and therefore the enzyme) would always be present in the container and every sample would test positive for the pathogen!



6. A colourless substrate is added to the containers. If the patient's blood contained antibodies against the pathogen then the monoclonal antibodies (with the enzyme) will still be bound. **The enzyme converts the substrate into a coloured compound and the test is positive** – in order for the blood to contain the antibodies the pathogen must be in the patient's system.

   If the blood sample does not contain antibodies against the pathogen then the monoclonal antibodies (along with the enzyme) are removed at the washing step and there is no colour change when the substrate is added – **the test is negative.**





Vaccination

For some diseases (eg chickenpox), the best way to develop immunity is to actually become infected with the pathogen. The body will undergo a **Primary Immune Response** to the antigens on the pathogen (see pages 2-3) – the correct specific T and B cells will be activated and at the end of the process the body will contain memory cells that recognise the antigen.

If the body encounters the same pathogen a second time, the specific memory cells can react much more quickly than before to produce the **Secondary Immune Response** and much larger amounts of antibody are produced. The pathogen is destroyed before it can cause any symptoms – this is **Natural Active Immunity**.

Some pathogens cause symptoms that are too severe to risk being infected at all (eg Polio, TB). We can 'trick' the body into generating memory cells by using a vaccine. The vaccine is not an intact pathogen but it does contain the antigens. It is not able to cause disease but the antigens stimulate the immune system in the same way and cause the production of memory cells (even though the body has never been infected). If the pathogen is ever encountered the memory cells will cause a secondary immune response – this is **Artificial Active Immunity**.

Vaccines may not always work – for example if the person has a weakened immune system they may not be able to generate memory cells. We can still protect these people to some extent with **Herd Immunity.** This is where large numbers of people are vaccinated together (eg an entire school). Even if some people do not acquire immunity, the majority of the population are immune so there are very few hosts for the pathogen to replicate in. There is therefore a greatly reduced chance of encountering the pathogen.

Antigenic Variability

(The ideas behind this topic link to protein synthesis and DNA/RNA).

Antigens are proteins. They are therefore coded by the sequence of bases on the DNA/RNA. Some pathogens (the influenza virus for example) change, or mutate, the order of their bases very rapidly. This has the effect of altering the primary and tertiary structure of the antigens – leading to a change in shape. Memory cells that recognise flu antigens this year might not be able to recognise the different shape of the antigens next year. This is why vulnerable people need to take a flu vaccine every year – the antigen shape changes so quickly that memory cells from earlier vaccines will not be able to recognise them.