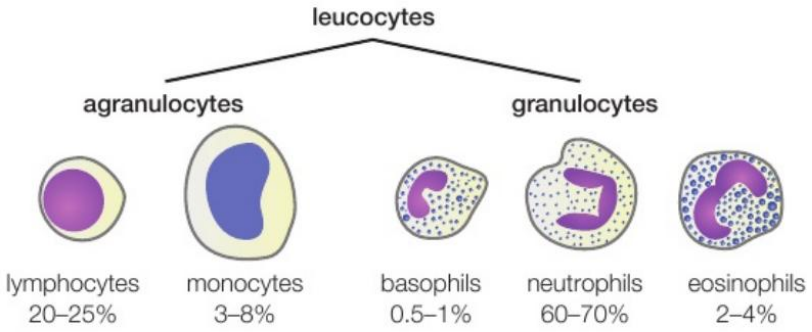
Immunity

11.1 The Immune System

It is the capability of multicellular organisms to resist harmful microorganisms.

The immune response takes place in 4 main stages:

1. Pathogens are engulfed by phagocytes (phagocytosis).
2. T-cells are activated by phagocytes.
3. B-cells are activated by T-cells which then divide into plasma cells.
4. More antibodies are made by plasma cells for a specific antigen.



▲ **fig A** The main types of leucocyte in human blood.

Granulocytes are Leucocytes with granules in the cytoplasm. The granules absorb stain & you can see them under the microscope. These cells have lobed nuclei (with round projections). They are involved in the non-specific responses to infection. Granulocytes include;

1. Basophils: are part of the non-specific immune system. They have a 2-lobed nucleus. They produce histamines involved in inflammation & allergic reactions.
2. Neutrophils: are part of the non-specific immune system. They engulf & digest pathogens by phagocytosis. They have multi-lobed nuclei. Upto 70% of all leucocytes are neutrophils.
3. Eosinophils: are part of the non-specific immune system. They are stained red by eosin stain. They are important in the non-specific immune response of the body against parasites, in allergic reactions & inflammation, and in developing immunity to disease.

Agranulocytes: are leucocytes that do not have granules in their cytoplasm. Their nuclei are round & do not have lobes. They are involved in the specific immune response to infections. Agranulocytes include;

1. Monocytes: are a part of the specific immune system. They are the largest of the leucocytes. They can pass from the blood into the tissues to form cells called macrophages. Macrophages also play an important part in the specific immune system. They engulf pathogens by phagocytosis.

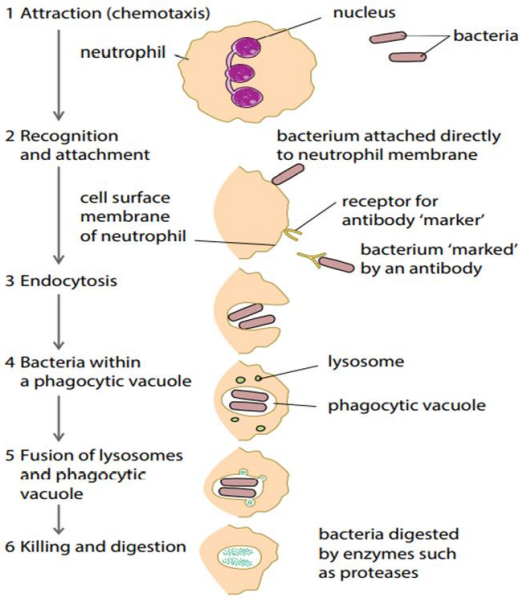
2. Lymphocytes: are small leucocytes with very large nuclei that are vitally important in the specific immune response of the body.

Cells of the Immune System: The cells of the immune system originate from the bone marrow. There are two groups of these cells involved in defence:

Phagocytes (neutrophils and macrophages): Phagocytes are produced throughout life in the bone marrow. They are stored there before being distributed around the body in the blood. They are scavengers, removing any dead cells as well as invasive microorganisms.

Neutrophils: They are a kind of phagocyte and form about 60% of the white cells in the blood. They travel throughout the body, often leaving the blood by squeezing through the walls of capillaries to 'patrol' the tissues. During an infection, neutrophils are released in large numbers from their stores, but they are short-lived cells.

- **Chemicals** released by pathogens, as well as chemicals released by the body cells under attack (e.g. 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).

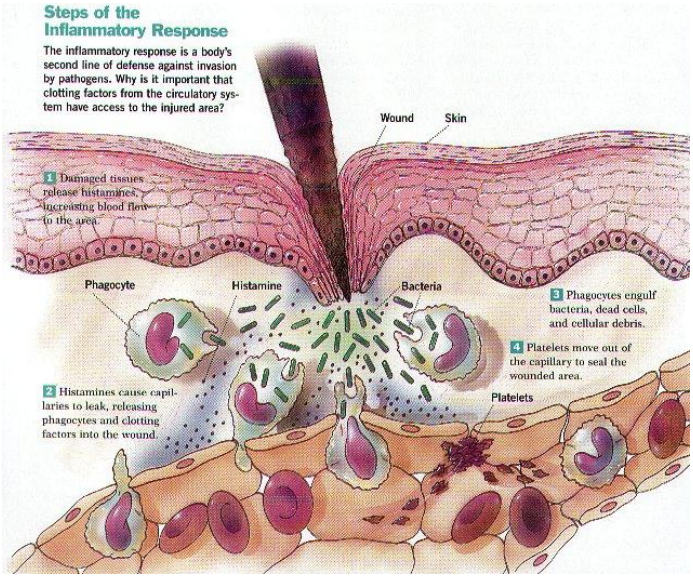


- Once attached to a pathogen, the **cell surface membrane** of a neutrophil extends out and around the pathogen, **engulfing it** and trapping the pathogen within a **phagocytic vacuole**.
- This part of the process is known as **endocytosis**.
- The neutrophil then secretes **digestive enzymes** into 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: They are also phagocytes but are larger than neutrophils and tend to be found in organs such as the lungs, liver, spleen, kidney and lymph nodes, rather than remaining in the blood. After they are made in the bone marrow, macrophages travel in the blood as monocytes, which develop into macrophages once they leave the blood and settle in the organs, removing any foreign matter found there.

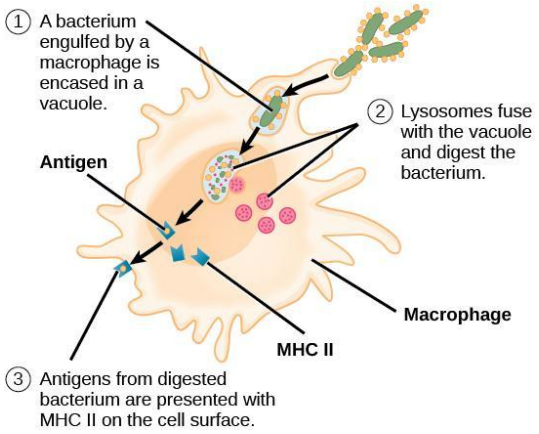
Produced & Stored In	Phagocytes are continuously produced & stored in the Bone Marrow before being distributed around the body in the blood.
Function	Removing dead cells & invasive microorganisms. They carry out non-specific immune responses. Both carry out phagocytosis, but the process is different for each type of phagocyte.

- 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 recognized by lymphocytes (another type of white blood cell).



Phagocytosis by Macrophages Overview:

1. The foreign antigens on a pathogen are recognized by a phagocyte.
2. The phagocyte's cytoplasm moves around the pathogen to engulf it.
3. The pathogen is now trapped in a phagocytic vacuole (a bubble) in the phagocyte's cytoplasm.
4. Fusion of lysosome occurs with the phagocytic vacuole. Pathogen is broken down by lysozymes, the enzymes found in lysosome.
5. Then the phagocyte presents the pathogen's antigens. In order to activate other cells of the immune system, it sticks the antigens on its surface.

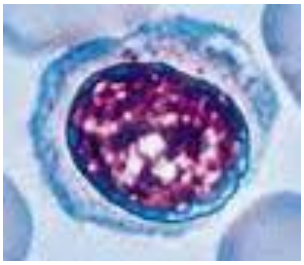


Antigen Presenting Cells: Antigen presentation is the process by which cells in the immune system display foreign molecules, such as those from pathogens or cancer cells, on their surface for recognition by other immune cells.
APCs are a group of immune cells that are capable of processing and presenting antigens for *recognition by T cells* to initiate the adaptive cellular immune responses.
Types of APC's:

- Macrophages
- B lymphocytes
- Cancerous Cells
- Virus Infected Cells
- Cells from a donated organ
- Dendritic Cells

Dendritic cells are present in tissues that are in contact with the body's external environment, such as the skin (where there is a specialized dendritic cell type called the Langerhans cell), and the inner lining of the nose, lungs, stomach and intestines.

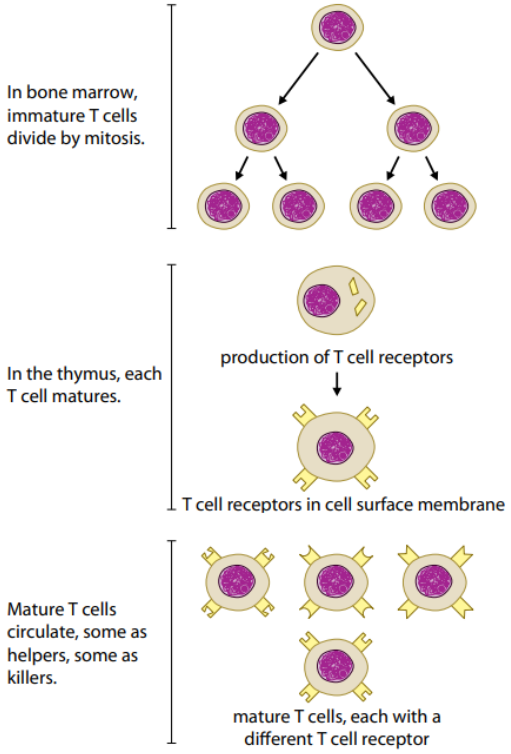
Lymphocytes: are another type of white blood cell. They play an important part in the specific immune response. They are smaller than phagocytes. They have a large nucleus that fills most of the cell. They are produced in the bone marrow before birth. There are 2 types of lymphocytes (with different modes of action). 2 types:



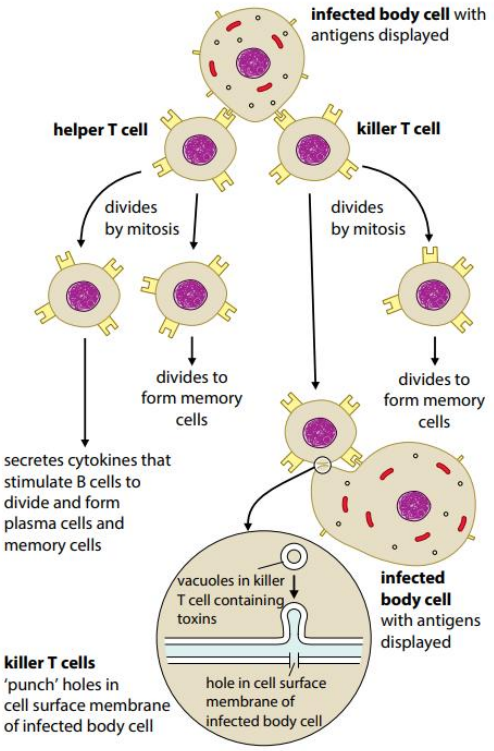
- B-lymphocytes (B Cells)
- T-lymphocytes (T Cells)

Activation of T-Cell Mediated Immunity:

- A T- lymphocyte (T-cell) is another type of white blood cell.
- 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 receptor proteins on its surface are capable of binding to complementary antigens supplied to it by the phagocytes.



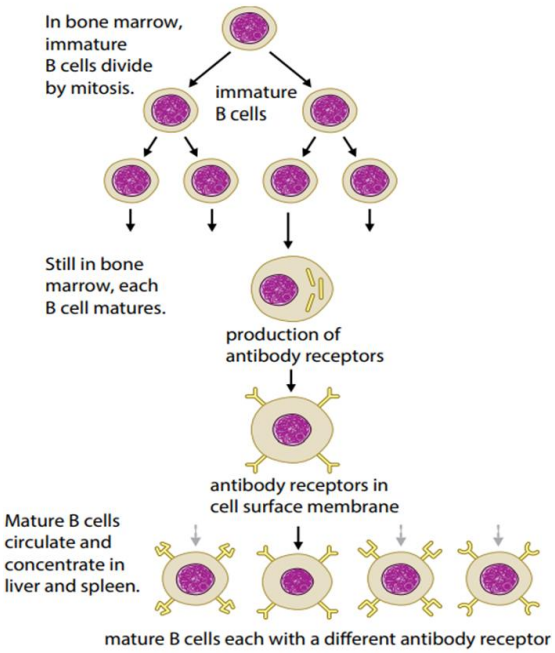
- This antigen-presenting host cell might be a macrophage or a body cell that has been invaded by a pathogen and is displaying the antigen on its cell surface membrane.
- As a result, T-cell is activated.
- These activated T-lymphocytes (those that have receptors specific to the antigen) divide by mitosis to increase in number (similar to the clonal selection and clonal expansion of B lymphocytes) and differentiate into two main types of T cell:
    - Helper T cells and Killer T cells



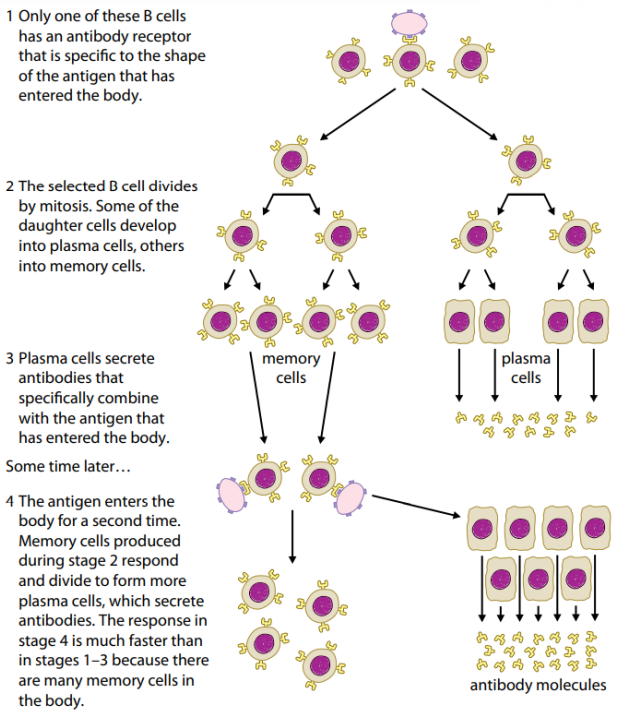
- Different kinds of T-cells respond in various ways. For e.g. Helper T-cells (T_H cells) aid in the release of chemical signals like cytokines and interleukins which stimulate and activate cytotoxic T-cells (T_C cells) and phagocytes that kill foreign and abnormal cells.
- Furthermore, TH cells also facilitate in activating B-cells.
- Both T helper and Cytotoxic killer cells can divide to form memory cells.

<u>Activation of B-Cells Humoral Immunity:</u>

- B-lymphocytes (B-cells) are also a kind of white blood cells.
- 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.

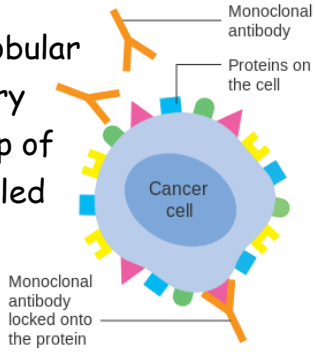


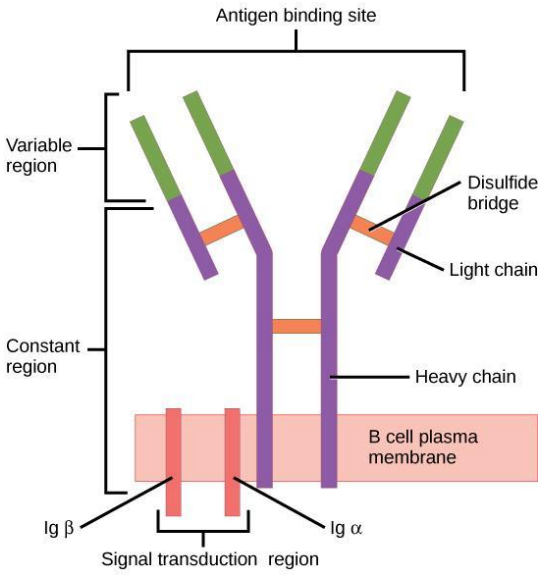
- Part of each antibody molecule forms a glycoprotein receptor that can combine specifically with one type of antigen.
- If that antigen enters the body, B-lymphocyte cells with the correct cell surface receptors will be able to recognise it and then divide by mitosis (clonal selection).
- During a primary immune response, B-lymphocytes divide repeatedly by mitosis (clonal expansion) and differentiate into two main types of cell:
  - Plasma cells, Memory cells. These two cell types each have a specific function.
- They're masked with antibodies - proteins capable of binding antigens to create an antigen-antibody complex. Since each B-cell has a different shaped antibody, different ones end up binding with different shaped antigens.
  - When a B-cell meets a complimentary shaped antigen which fits the antibody on its surface, it binds to it.
  - B-cell is activated by this and the substances released from helper T-Cells → Clonal selection.
  - Plasma cells are formed by the division of activated B-cell.



<u>Antibodies by Plasma Cells:</u> Plasma cells are clones of the B-cell. They secrete lots of antibodies called monoclonal antibodies which are specific to the antigen. These antibodies bind to the antigens present on the surface of the pathogen in order to form loads of antigen- antibody complexes.

- Antibodies are all globular glycoproteins with quaternary structure. They form the group of plasma proteins called immunoglobulins.

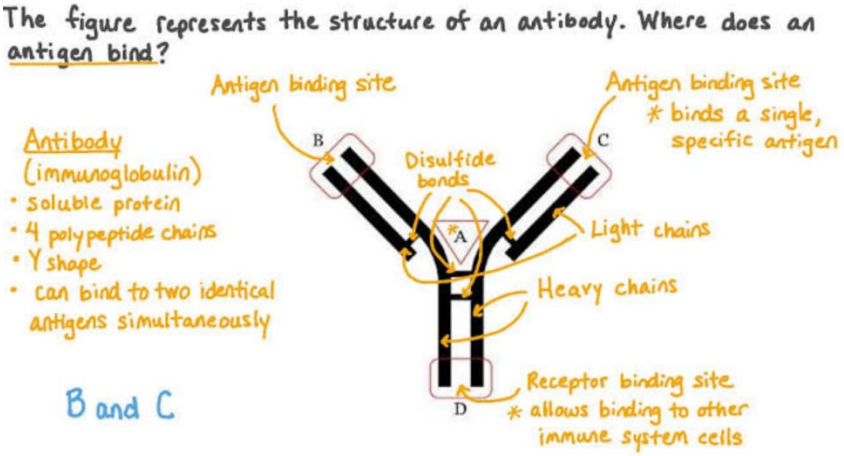




- The basic molecule common to all antibodies consists of 4 polypeptides chains: two 'long' or 'heavy' chains (which is represented as Y-shaped),and two 'short' or 'light' chains.
- Disulfide bonds hold both the chains together.
- Each polypeptide chain has a constant region and variable region.
- The 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.

Type of Antibody	Location	Functions / Traits
IgD	Always attached to B-Cells.	Activates B-Cells.
IgM	Can be attached to B-Cells or free in blood plasma.	Largest Antibody (actually huge compared to the rest)/ first Ig released in primary response.
IgG	75%-85% of all antibodies in the blood.	Most abundant in blood plasma, can cross placental barrier so IgG is passive immunity to fetus.
IgA	Secretions such as saliva, tears, intestinal juice & milk.	Secretory IgA b/c bathes body surfaces/important first defense.
IgE	Mucosal lining of respiratory & GI tracts/tonsils.	Troublemaker antibodies involved in allergies.

- 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

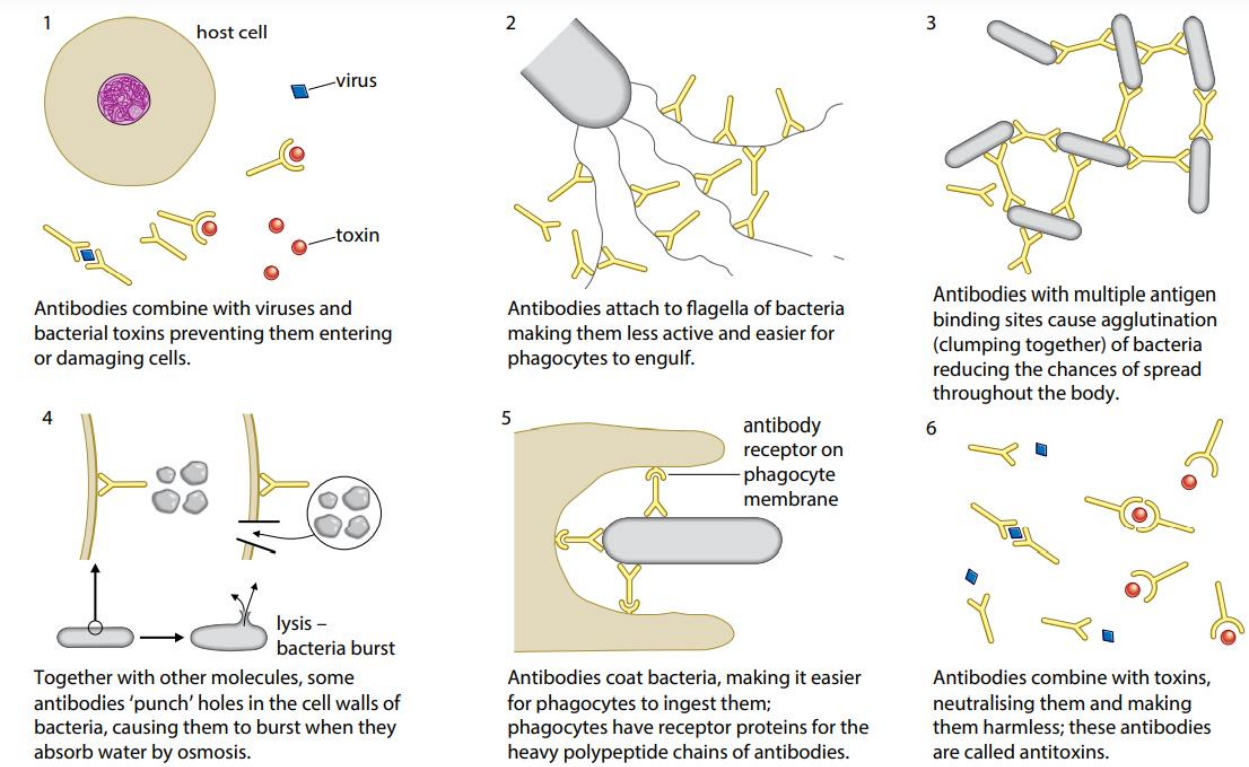
generally composed of 110 to 130 amino acids and includes both the ends of the light and heavy chains

- 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 and 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.

<u>Function of Antibodies:</u>

- Antibodies are produced by B-Lymphocytes.
- Antibodies bind to specific antigens that trigger the specific immune response. Every antigen has 1 antibody.
- Antigens include pathogens & their toxins, pollen, blood cell surface molecules & the surface proteins found on transplanted tissues.
- Antibodies are divided into 5 major classes (isotypes), each with a different role.
- The function of antibodies differ:
    - Antibodies can combine with viruses and toxins of pathogens example bacteria to block them from entering or damaging cells.
    - Antibodies can act as anti-toxins by binding to toxins produced by pathogens (example the bacteria that causes diphtheria and tetanus) which neutralizes 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 make 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.



WBC Count & Infectious Diseases:

Blood tests are regularly carried out by doctors to help them diagnose diseases and assess the success of treatments. The number of different types of white blood cells in the blood can provide information about what type of infection someone might have, the severity of the infection, or whether the treatment that has been prescribed is working. For example:

- Neutrophils in the blood increase in number during bacterial infections and when tissues become inflamed and die.
- Lymphocytes in the blood increase in number during viral infections and tuberculosis.
- The human immunodeficiency virus HIV invades and destroys Helper T-Cells, so blood tests of HIV+ patients are designed to record the number of specific types of T-Cells present. Monitoring declines in these T-Cells enables doctors to assess the harm, the infection is causing on the immune system of HIV+ patients.

HIV Replication inside the helper T-Cells of the host:

- The attachment protein joins with a receptor molecule found on the cell membrane of the host's helper T-cell.
- Release of capsid into the cell takes place where it uncoats and releases RNA (genetic material) into the cytoplasm of the cell.
- Within the cell, reverse transcriptase is used in making a complementary strand of DNA by the help of the viral RNA template.
- From this, double stranded DNA is created and added into the DNA of human.
- Enzymes from the host cell are used in making viral proteins from the viral DNA present within the DNA of human.
- Viral proteins assemble into new viruses and develop from the cell and continue to infect other cells.

Antigens: Every cell in the human body has markers on its surface that identify it. Microorganisms, such as bacteria and viruses, also have their own unique markers. These markers are called antigens and they allow cell-to-cell recognition. Antigens are found on cell surface membranes, bacterial cell walls, or the surface of viruses. Some glycolipids and glycoproteins on the outer surface of cell surface membranes act as antigens. Molecules (usually proteins) that are capable of generating an immune response when detected by the body are called antigens. Generally, they are found on cell surfaces and are used by the immune system to detect:

- Abnormal body cells (e.g. pathogen infected or cancerous cells)
- Pathogens (disease causing organisms)
- Cells from other organisms of the same species (e.g. organ transplants)
- Toxins

<u>Self & Non-Self Antigens:</u>

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

- Self Antigens: Antigens produced by an organism's own body cells. Self antigens do not stimulate an immune response.
- Non-Self Antigens: Antigens not produced by an organism's own body cells, e.g. the antigens found on pathogenic bacteria and viruses. Non-self antigens stimulate an immune response.

<u>There are 2 types of Immune Responses:</u>

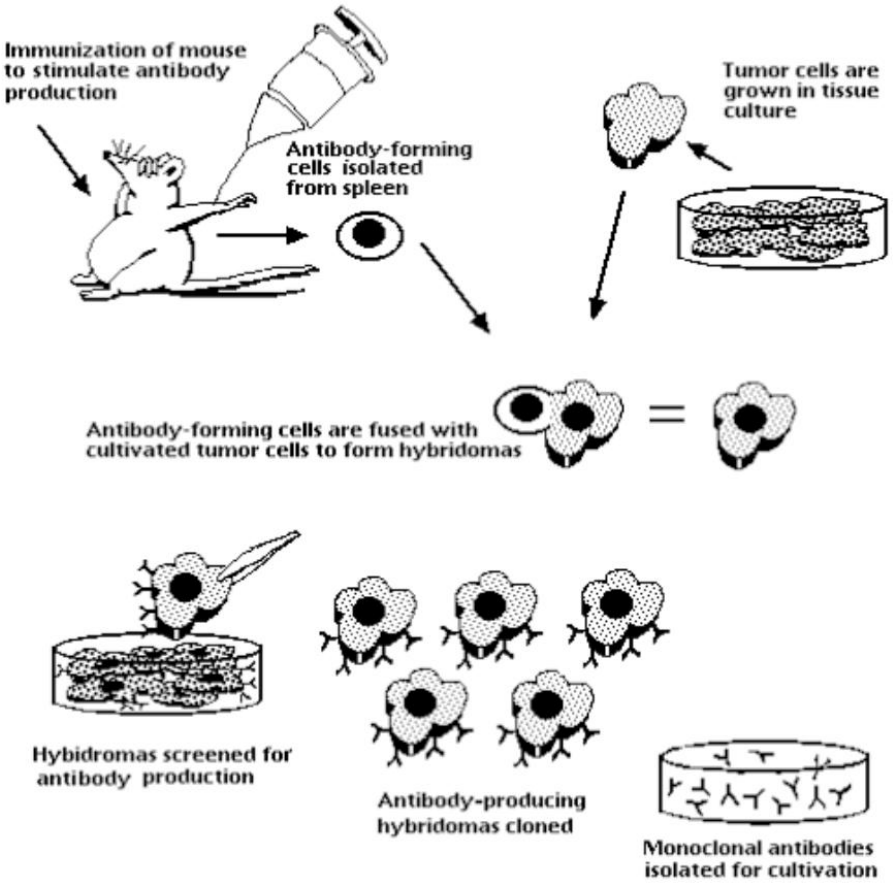
- Primary Immune Response: slow responding to a newly encountered antigen.
- Secondary Immune Response: responding to a previously encountered antigen.

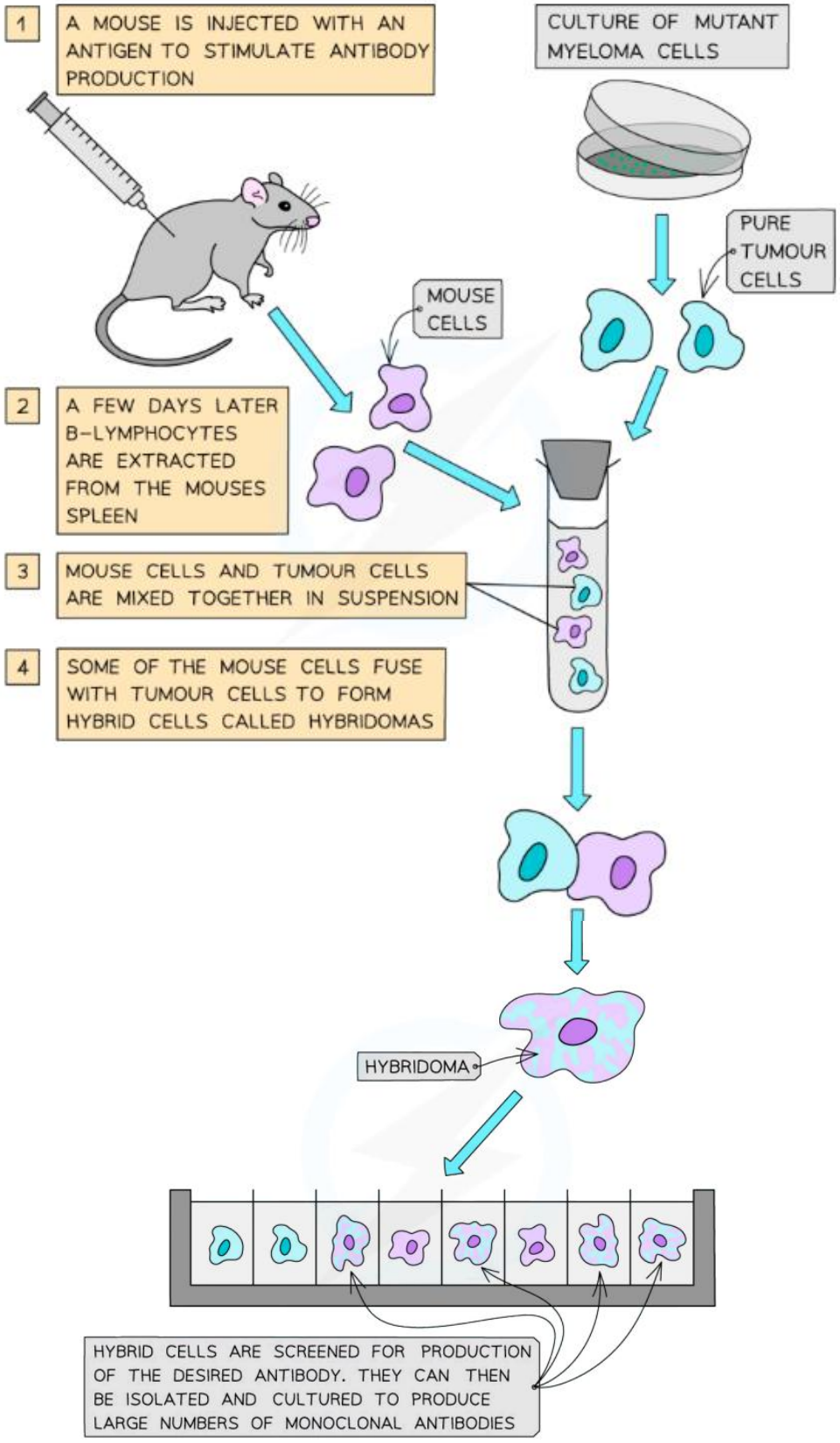
Primary Immune Response	Lymphocytes are another type of white blood cell. They play an important part in the specific immune response

	They are smaller than phagocytes and they have a large nucleus that fills most of the cell They are produced in the bone marrow. There are two types of lymphocytes with different roles in the immune response B-lymphocytes, or B cells & T-lymphocytes, or T cells The action of lymphocytes is triggered by exposure to non-self antigens: When a pathogen enters the body its antigens are displayed by antigen presenting cells. These antigens may be on the surface of macrophages after phagocytosis, on the surface of infected cells, or on the surface of the pathogens themselves B-lymphocytes remain in the bone marrow until they are mature and then spread through the body, concentrating in lymph nodes and the spleen.
Secondary Immune Response	Secondary response is the quick and strong immune response provided by the immune system if the same pathogen invades the body again. Clonal selection occurs faster. The secondary immune response usually gets rid of the pathogen before the individual exhibits any kind of symptoms (as they are immune to the pathogen). 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.

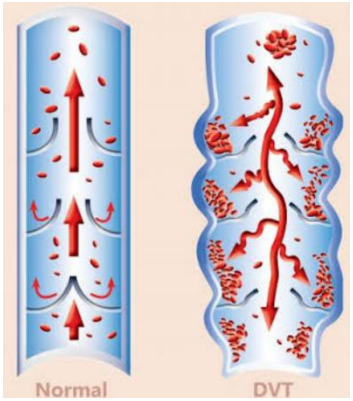
Monoclonal Antibodies: are a single type of antibodies that can be isolated & cloned. Antibodies are proteins which have binding sites complementary in shape to certain antigens.

Making Monoclonal Antibodies using the Hybdridoma Method	Monoclonal antibodies are artificially produced antibodies produced from a single B cell clone. The hybridoma method is a method used to make monoclonal antibodies (Mabs). The method enables large quantities of identical antibodies to be produced. The hybridoma method solved the problem of having B cells that could divide by mitosis but not produce antibodies and plasma cells that could produce antibodies but not divide, by the fusion of plasma cells with tumor cells. This method was established in the 1970s. Monoclonal antibodies bind antigens, in the same way naturally produced antibodies do. • They are produced by injecting mice with an antigen that stimulates the production of antibody-producing plasma cells.

	• Isolated plasma cells from the mice are fused with immortal tumor cells, which result in hybridoma cells. The fusion of plasma and tumor cells can be assisted with the use of fusogens such as polyethylene glycol or an electric current. • These hybrid cells are grown in a selective growth medium and screened for the production of the desired antibody. • They are then cultured in a selective growth medium & screened to produce large numbers of monoclonal antibodies. Monoclonal antibodies have multiple applications to include diagnostics, treating disease, food safety testing and pregnancy testing.
	


1
A MOUSE IS INJECTED WITH AN ANTIGEN TO STIMULATE ANTIBODY PRODUCTION
CULTURE OF MUTANT MYELOMA CELLS
PURE TUMOUR CELLS
MOUSE CELLS
2
A FEW DAYS LATER B-LYMPHOCYTES ARE EXTRACTED FROM THE MOUSES SPLEEN
3
MOUSE CELLS AND TUMOUR CELLS ARE MIXED TOGETHER IN SUSPENSION
4
SOME OF THE MOUSE CELLS FUSE WITH TUMOUR CELLS TO FORM HYBRID CELLS CALLED HYBRIDOMAS
HYBRIDOMA
HYBRID CELLS ARE SCREENED FOR PRODUCTION OF THE DESIRED ANTIBODY. THEY CAN THEN BE ISOLATED AND CULTURED TO PRODUCE LARGE NUMBERS OF MONOCLONAL ANTIBODIES

Uses	• Medical Treatments ➢ Blood Typing before transfusions ➢ Tissue typing before transplants ➢ Direct Monoclonal Antibody Therapy: Some cancer can be treated using monoclonal antibodies which are designed with a binding site complementary in shape to the antigens on the outside of the cancer cells. The antibodies are given to the cancer patient and attach to the cancer cells. While the antibodies are bound to the cancer antigens, this prevents chemical binding to the cancer cells which enables uncontrolled cell division. Therefore, the monoclonal antibodies preventing cancer cells growing, and as they are designed to only attach to cancer cells they do not cause harm to other normal cells. ➢ Indirect Monoclonal Antibody Therapy: Cancer can also be treated with the monoclonal antibodies complementary in shape with the antigens on the outside of cancer cells which have drugs attached to them. This cancer drugs are therefore delivered directly to the counter cells and kill them. This reduces the harmful side effects that traditional chemotherapy and radiotherapy can produce. This is often referred to as bullet drugs. ➢ Rabies virus can be treated by injecting purified antibodies. ➢ Prevention of transplanted organ rejection, achieved by intervening with the T-cells involved in the rejection process. ➢ Treatment for diseases caused by the overproduction or inappropriate production of B-cells (e.g. leukemia, multiple sclerosis and myasthenia gravis); the antibody (rituximab) binds to cell surface receptor proteins on B-cells (not plasma cells) and causes the death of the cells. ➢ Prevention of blood clotting following angioplasty procedures; here monoclonal antibodies bind to receptors on the platelet surface thereby inhibiting fibrinogen from binding and subsequent clotting from ensuing. ➢ Targeted treatment of breast cancer; Herceptin is a monoclonal antibody used to treat breast cancer, it recognises receptor proteins on the surface of cancer cells and binds to them allowing the immune system to identify and destroy them. ➢ Treatment of melanoma (a type of skin cancer); the antibody (ipilimumab) binds to a protein produced by T-cells (whose role is to reduce the immune response) which results in the immune system remaining active against the cancer cells. • Medical Diagnosis

	➢ HIV ➢ Streptococcus Bacteria ➢ Cancer ➢ Influenza ➢ Hepatitis ➢ Chlamydia ➢ Covid-19 ➢ Differentiating b/w Zoster Sine Herpete & Simplex Herpes ➢ Deep Vein Thrombosis: Injecting a mouse with human fibrin (the main protein found in blood clots). This activates the plasma cells to produce antibodies against fibrin. These cells are collected from the mouse spleen. The plasma cells are then fused with tumor cells forming hybridomas that produce anti-fibrin antibodies. To detect where the antibodies are binding to fibrin molecules, a radioactive chemical (producing gamma radiation) is attached to the antibodies making them radioactively labelled. A gamma-ray camera is used to detect where these radioactively labelled antibodies have attached to a fibrin molecule, hence indicating where blood clots can be found.  • Pregnancy Tests • Antibodies in breast milk
Problems	Monoclonal Antibodies were produced by mice, rabbits or other lab animals, triggering an immune response when introduced to humans. Ethical Issues: Animal Rights abused.
Solutions	Genetically modifying the antibody polypeptide chains so that the amino acid sequences are now human not mouse or rabbit sequences. Altering the type and position of the sugar groups (antibodies are glycoproteins) attached to the heavy polypeptide chains to reflect those found on human antibodies.

Memory Cells & Long Term Immunity:

There are 2 types of Immunity:

- Active Immunity: is acquired when an antigen enters the body triggering a specific immune response. Memory cells are produced giving long-term immunity. In a primary response, the antibody concentration takes 2 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.

- Passive Immunity: is acquired without an immune response. Antibodies & therefor memory cells are not produced

Active Immunity	Natural	Exposure to Microbes
	Artificial	Vaccines
Passive Immunity	Natural	Fetus receives antibodies across the placenta from their mothers. Babies receive the initial breast milk from mothers (the colostrum) which delivers a certain time of antibody (IgA).
	Artificial	Injection or transfusion of antibodies take from a person's plasma who had been exposed to the disease. E.g. tetanus where an anti-toxin is used. The antibodies were collected from people whose immune system had been triggered by a vaccination to produce tetanus antibodies.

Feature	**Active**	**Passive**
Production of antibodies	Produced by the body	Not produced by the body
Time before antibodies appear in the 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 during pregnancy)
Artificial	Vaccination	Antibodies are manufactured and injected / infused into the body (e.g. monoclonal antibodies given by blood transfusion)

Vaccines:

A vaccine is a preparation/suspension containing antigens which is used to stimulate an immune response artificially.

It may contain a whole live microorganism, a dead one, a harmless version (known as a live attenuated organism), a harmless form of an inactivated toxin (known as a toxoid) or a preparation of surface antigens.

Vaccines are either given by injection into a vein or muscle, or taken orally (by mouth).

Some are produced using techniques of genetic engineering. 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.

Vaccines give protection against specific diseases and boost the body's defence against infection from pathogens without the need to be exposed to dangerous diseases that can lead to death. The level of protection in a population depends on the proportion of people vaccinated. Vaccines are a dead, harmless or altered form of a disease causing pathogen which contain specific antigens, to be introduced into the body. In this weekend state, the pathogen cannot cause illness but can provoke an immune response. Lymphocytes produce complementary antibodies for the antigens. The antibodies target the antigen and attach themselves to it in order to create memory cells. The memory cells remain in the blood and will quickly respond to the antigen if it is encountered again in an infection by a life pathogen. As memory cells have been produced this immunity is long lasting.

- Harmless pathogen injected.
- Antigens trigger an immune response. It can take days for a lymphocyte making complementary antibodies to be activated.
- Lymphocyte able to produce complementary antibodies multiplies, antibodies are released.
- Memory cells lasting years are produced. If antigen is encountered again, antibodies are produced much faster. This is long term immunity.

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.

Vaccines at a childhood stage, keep the disease at a low level within populations due to herd immunity. This makes it difficult for a pathogen to spread within that population, as those immunized are protected & unlikely to contract it as the levels of disease are so low.

Problems with Vaccines:

- Poor response: Some people do not respond at all, or not very well to vaccinations.
- Live virus and herd immunity: People vaccinated with a live virus may pass it out in their feces during the primary response and may infect others. This is why it is better to vaccinate a large number of people 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 (e.g. malaria) have too many antigens on their cell surface membranes making it difficult to produce vaccines that would prompt the immune system quickly enough. Despite of years of research, there are no vaccines for the common cold.
- Antigenic concealment: Some pathogens evade attack by the immune system by living inside cells. 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 (e.g. HIV) or by remaining in parts of the body that are difficult for vaccines to reach (e.g. Vibrio cholerae – cholera, remains in the small intestine).
- Ethical Issues: Some people disagree with the idea of testing all vaccines on animals before humans. Sometimes the vaccine tests on humans may not guarantee 100% results. Some people avoid taking the vaccines due to the fear of side effects, but are being protected by herd immunity. This is claimed to be unfair by some. If an epidemic of a new disease appears, difficult decisions about who should be vaccinated first will arise.
    - Monoclonal Antibodies: Issues related to animal rights and the use of animals to produce cells to create monoclonal antibodies arise.

Live Attenuated Vaccines	Inactivated Vaccines
• Live attenuated vaccines contain whole pathogens (e.g. bacteria and viruses) that have been 'weakened.'	• Inactivated vaccines contain whole pathogens that have been killed ('whole killed') or small parts ('subunit') of the

• These weakened pathogens multiply slowly allowing for the body to recognize the antigens and trigger the primary immune response (plasma cells to produce antibodies). These vaccines tend to produce a stronger and longer-lasting immune response. • They can be unsuitable for people with weak immune systems as the pathogen may divide before sufficient antibodies can be produced. • An example of this type of vaccine is the MMR (Measles, Mumps and Rubella).	pathogens (e.g. proteins or sugars or harmless forms of the toxins – toxoids). • As inactivated vaccines do not contain living pathogens they cannot cause disease, even for those with weak immune systems. • However these vaccines do not trigger a strong or long-lasting immune response like the live attenuated vaccines. Repeated doses and / or booster doses are often required. • Some people may have allergic reactions or local reactions (e.g. sore arm) to inactivated vaccines as adjuvants (e.g. aluminum salts) may be conjugated (joined) to the subunit of the pathogen to strengthen and lengthen the immune response. • An example of a whole killed vaccine is polio vaccine. • An example of a toxoid subunit vaccine (where inactivated versions of the toxins produced by pathogens are used) is Diphtheria.