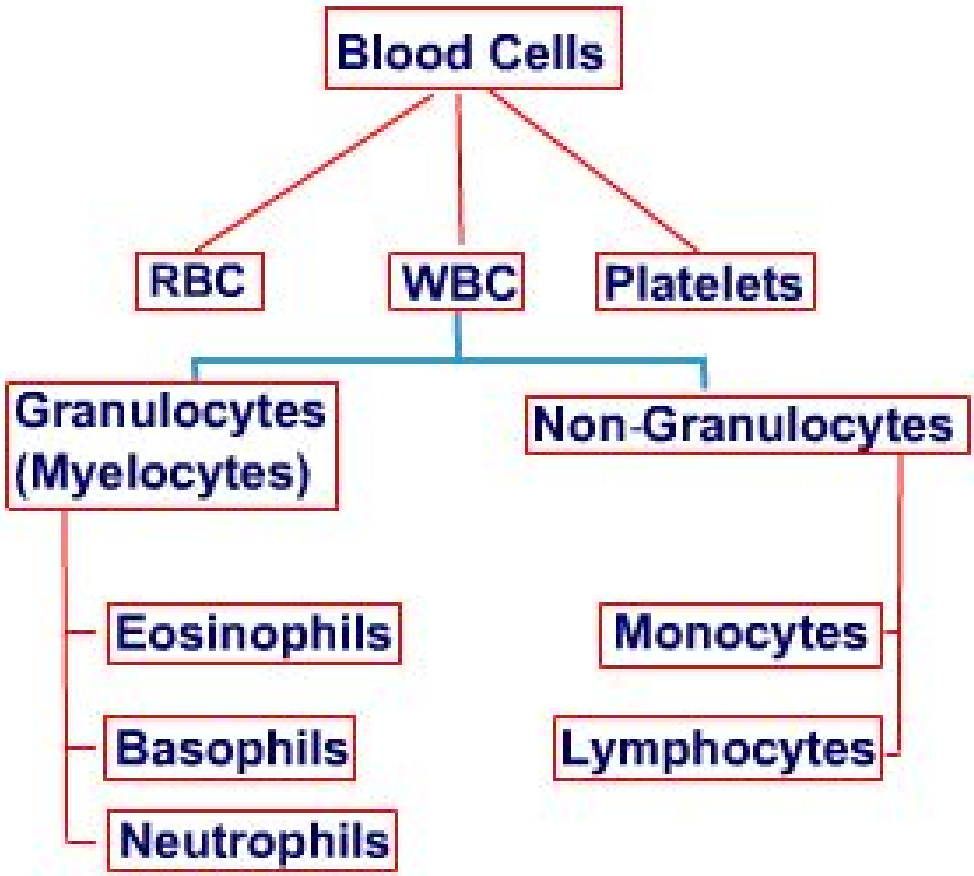
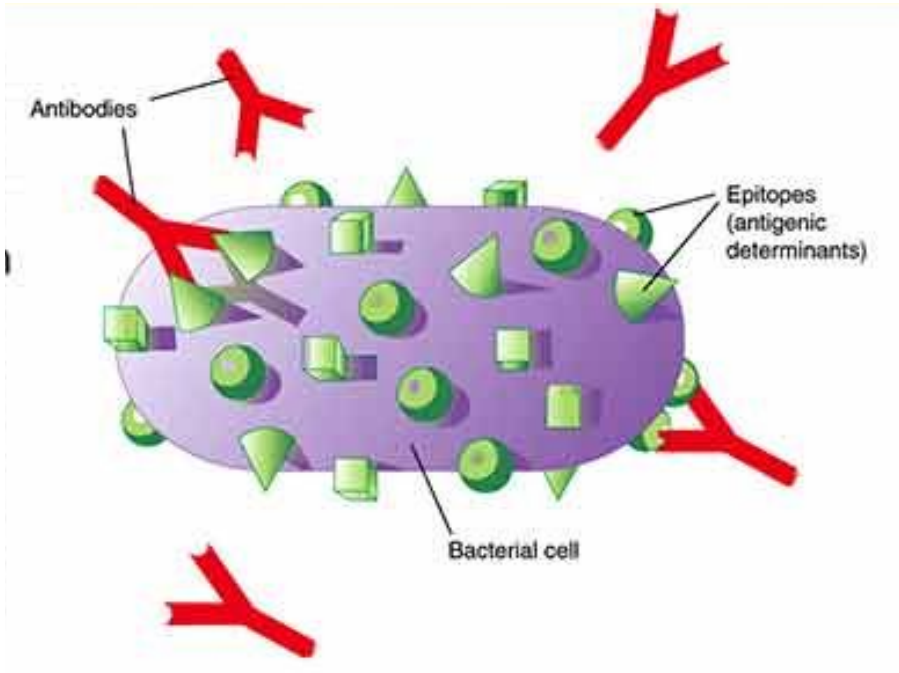
# Immune System

The immune system protects the body from invasion by pathogens (an entity that can cause harm to the body)

What cells are found in blood?



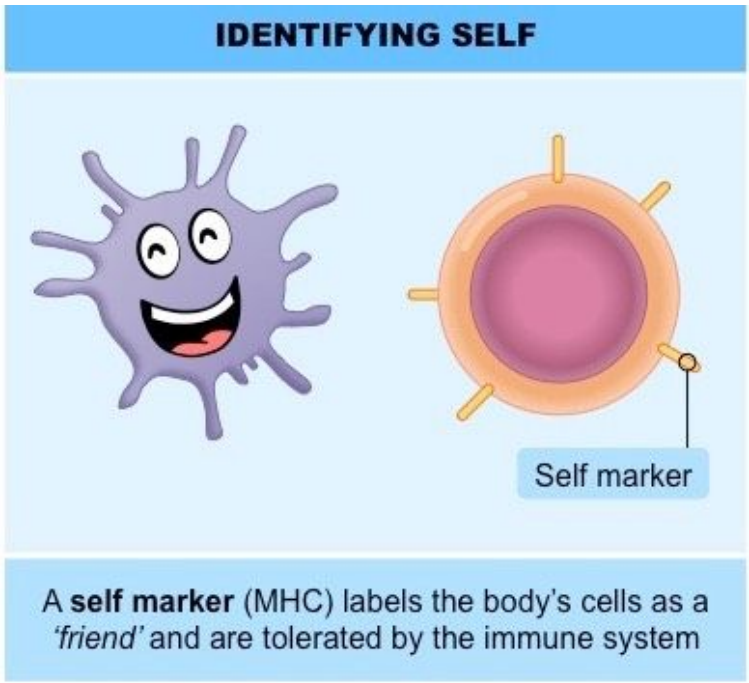
# Antigens vs Antibodies

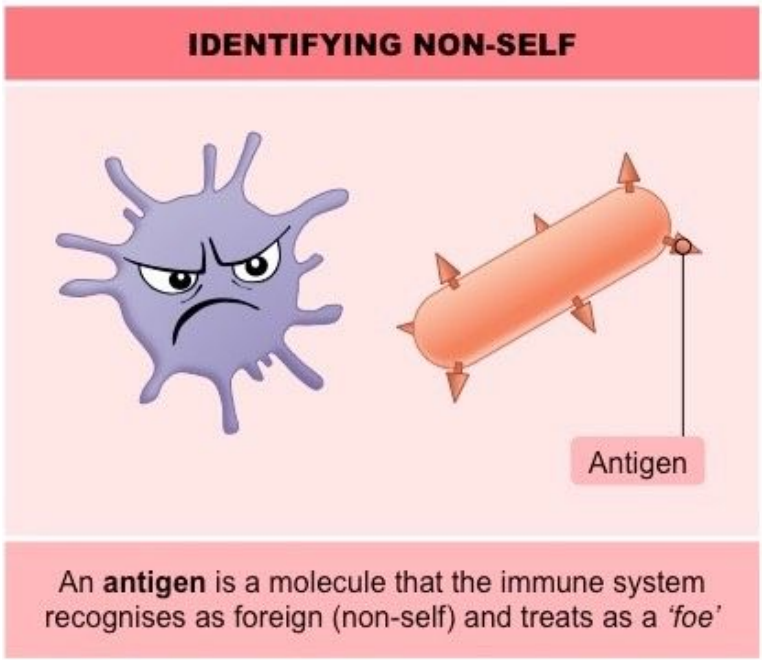



Antigen = A molecule found on the surface of cells e.g. glycoproteins, carbohydrates, etc. Each antigen has different tertiary structure.

Antibody = a Y-shaped protein, produced by the immune system, that can bind to complementary antigens. Each antibody can only bind to one type of antigen.

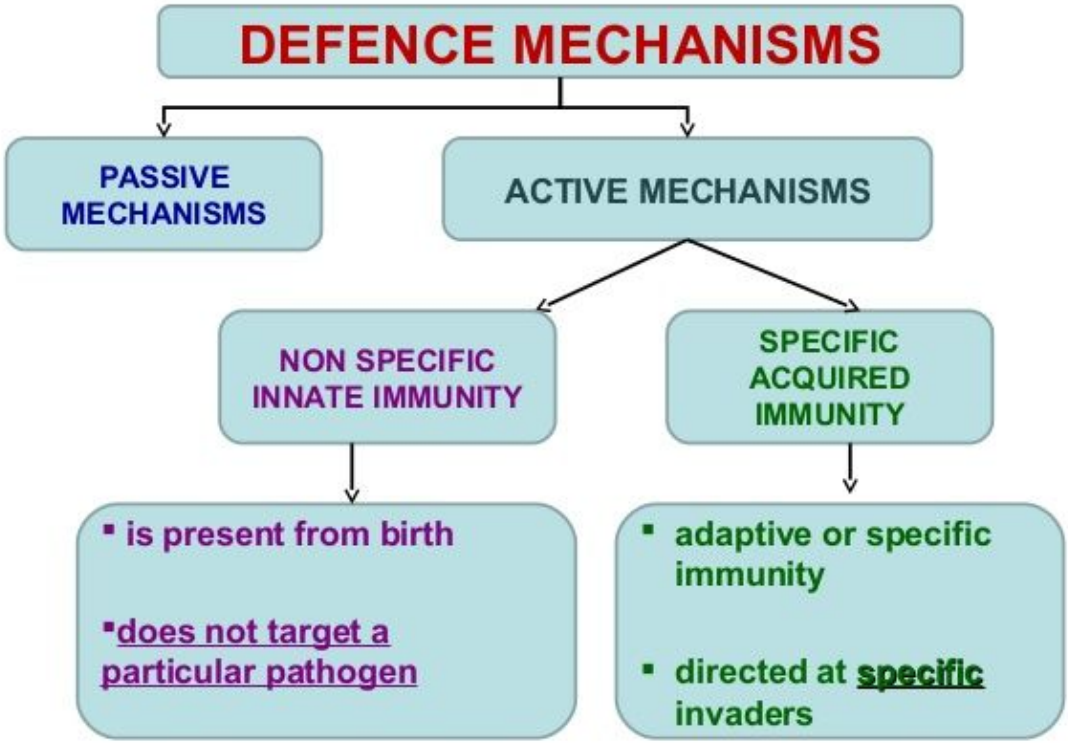
# Self -Antigens vs Non-self Antigens



## How the body eliminates immune cells that recognise self-antigens

- Early on in foetal development, the immune system contains immune cells (macrophages and lymphocytes) that recognise both self and non-self antigens
- The immune cells that recognise self-antigens are continuously inactivated (commit suicide)
- By the time the child is born, the immune system only contains immune cells that recognise non-self antigens
- The immune system also learns to tolerate bacteria that colonise the digestive system immediately after birth
- A breakdown of self-tolerance leads to autoimmune disorder (covered in more detail in the 1.15 lesson)


DEFENCE MECHANISMS
PASSIVE MECHANISMS
ACTIVE MECHANISMS
NON SPECIFIC INNATE IMMUNITY
SPECIFIC ACQUIRED IMMUNITY
▪ is present from birth
▪ does not target a particular pathogen
▪ adaptive or specific immunity
▪ directed at specific invaders

## Non-Specific Immune Response

First Line of Defence - Barriers to entry of pathogens

### SKIN

- Physical barrier to entry - no gaps between cells
- Waxy sebum on surface - waterproof, elastic
- Colonised by ‘normal’ flora - healthy bacteria that prevent colonisers from gaining a foothold
- Slightly acidic pH - not tolerated by most bacteria
- Sweat contains the enzyme lysozyme, which can destroy bacterial cell walls

(Discuss effects of antibacterial soaps/wipes - Triclosan favours antibiotic resistant bacteria)

## UPPER RESPIRATORY TRACT

- Trachea (airway) lined with goblet cells and ciliated epithelial cells
- Goblet cells produce mucous
- Mucous traps bacteria, debris, pollen
- Cilia waft the mucous upwards, towards the oesophagus (food pipe)

(See video: https://www.youtube.com/watch?v=miEEluVlemQ)

## DIGESTIVE SYSTEM

- Stomach contains Hydrochloric acid
- Low pH, 1-2
- denatures proteins and enzymes in pathogens
- Small and large intestine contain normal flora, which prevent colonisation by pathogens

## TEAR DUCTS

- in eyes
- tears clear dust and debris
- tears contain the enzyme lysozyme, which can kill bacteria

## Non-Specific Immune Response

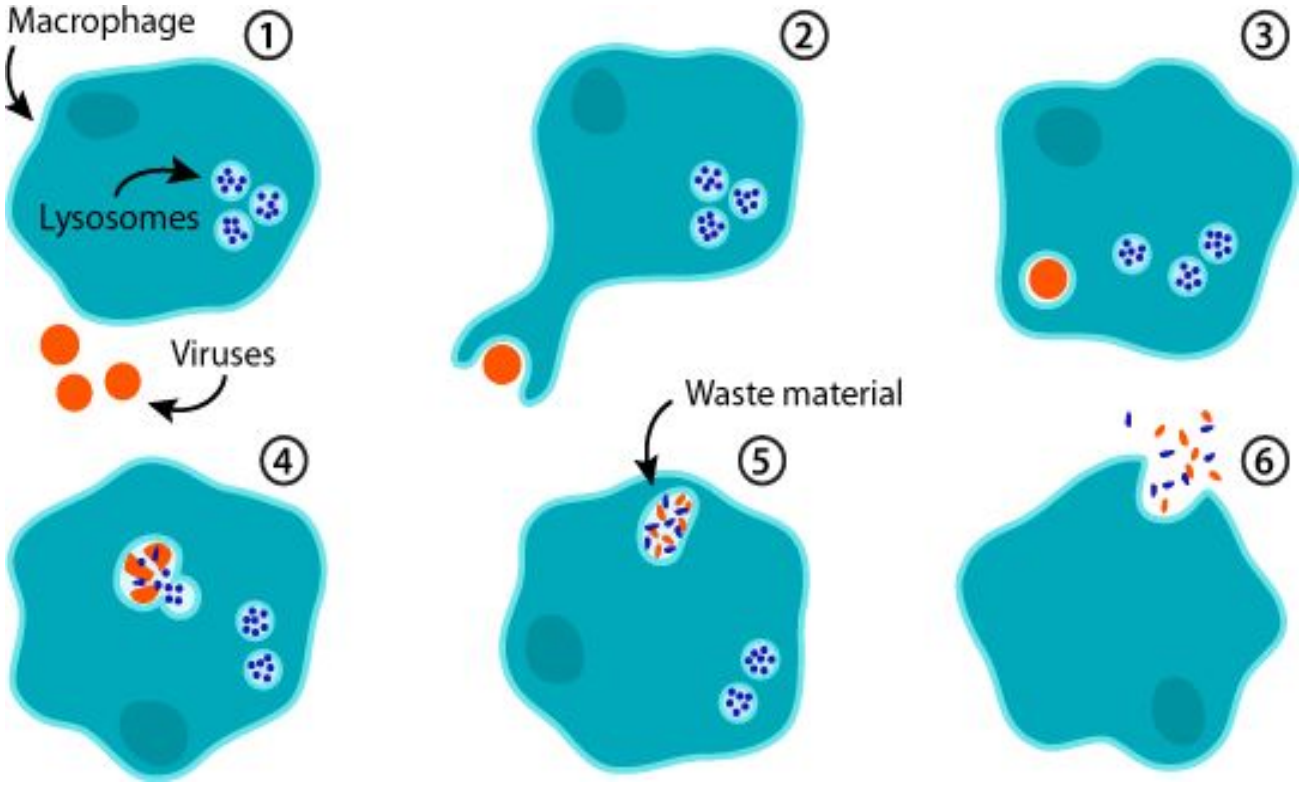
Second Line of Defence - Phagocytes, interferon and inflammatory response

### PHAGOCYTOSIS

The process in which pathogens are ingested and digested by phagocytes.

Phagocytes are found circulating in the blood, and can migrate to tissue in case of an infection.

They contain large number of **lysosomes** - which contain hydrolytic enzymes like protease, lipase, amylase




What happens to the digested pathogen?

- Some monomers absorbed
- Some monomers released
- Some monomers displayed on the surface - Antigen Presenting Cell **(APC)** -> activates the specific immune response

## Steps in Phagocytosis

- Phagocytes have many different receptors on their surface
- When a phagocyte encounters a pathogen, it binds to the antigen on the surface of the pathogen using its complementary receptors
- The cell membrane folds inwards and encloses the pathogen in a vesicle called a phagosome
- Phagosome fuses with lysosome
- Lysosome releases hydrolytic enzymes
- Which breaks down the pathogens (sugars, proteins, lipids) releasing the monomers

## INFLAMMATION

- Chemicals released by damaged cells attract white blood cells to the site of infection.
- Mast cells release histamine, which widens the gaps in the capillary walls, allowing white blood cells to migrate from blood to tissue (swelling)
- Phagocytes secrete chemicals called cytokines, which help with recruiting other blood cells and with tissue repair
- Temperature elevated (redness) to halt bacterial growth

## INTERFERON

- Proteins produced by virus-infected cells
- Binds to the surface of non-infected cells
- Triggers production of anti-viral proteins
- Prevents viral infection from spreading

## Specific Immune Response

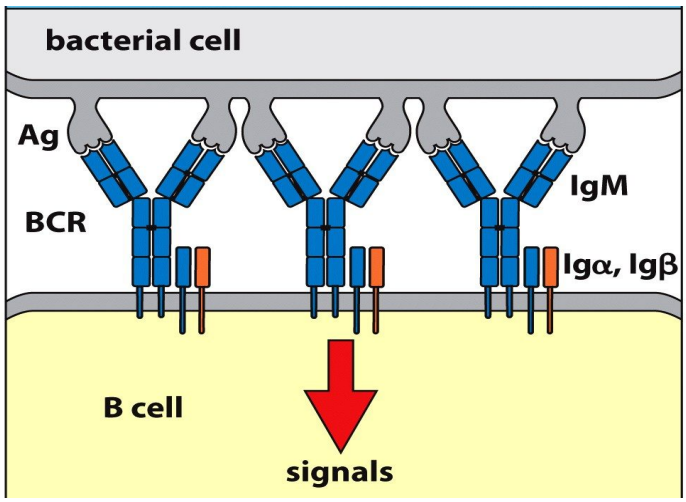
Third Line of Defence - B and T cells

### B-cell response

Step 1: Recognition of Antigen and activation

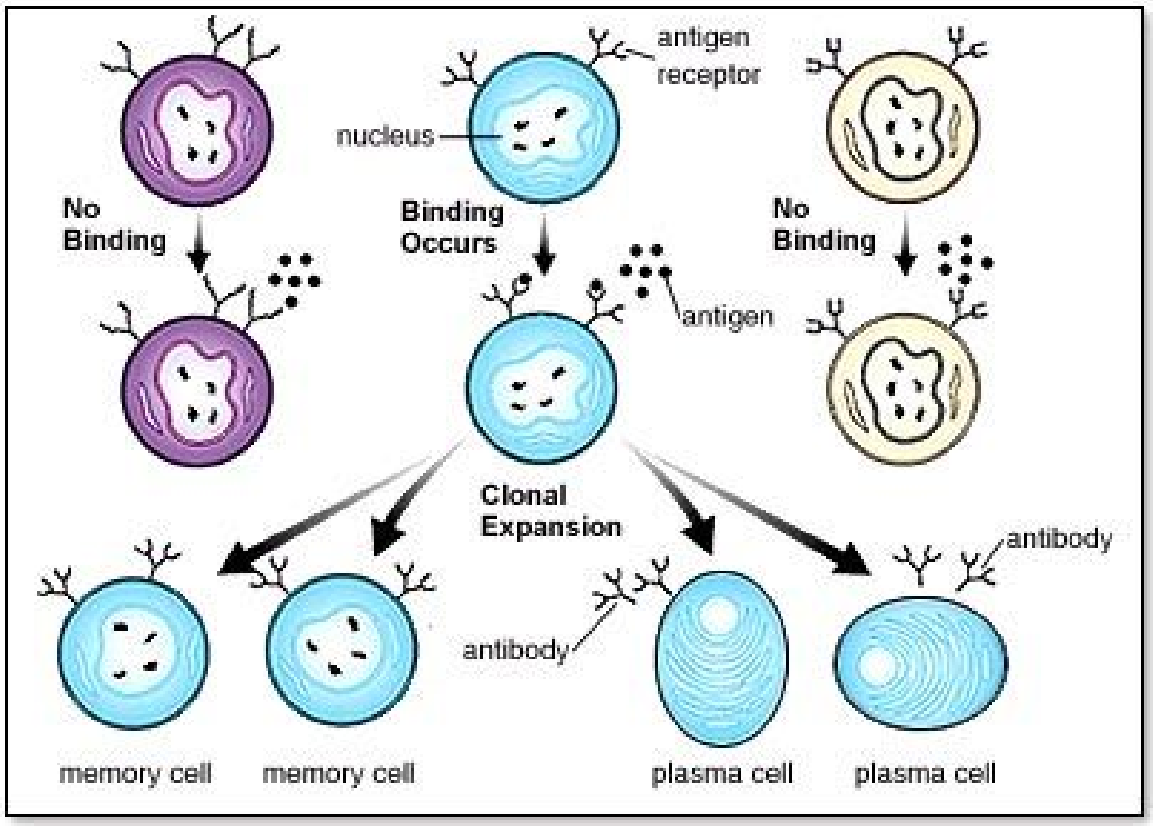
B-cells use the B-cell receptor to recognise antigens on the pathogen, or antigens on the surface of APCs like phagocytes

Each B-cell only displays one type of BCR

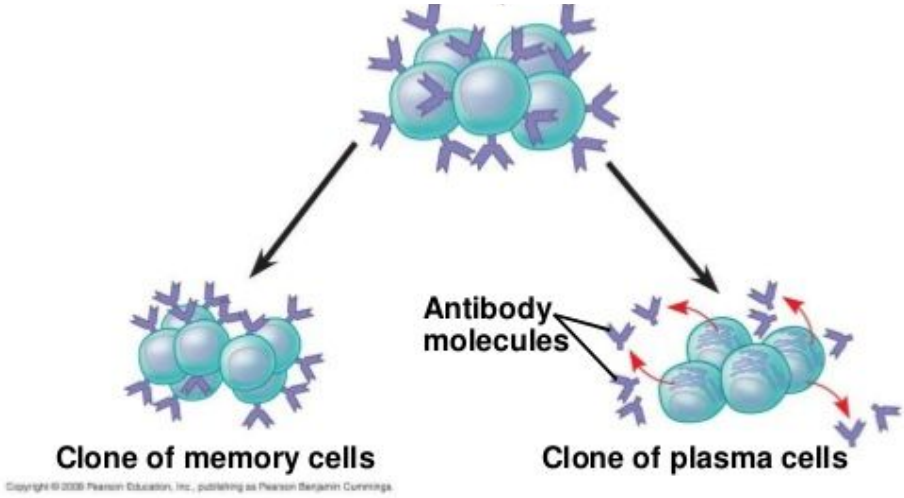



Cross-linking of receptors activates B-cells

Step 2:  B-cells undergo clonal expansion by mitosis
Step 3: B-cells differentiate into plasma and memory cells



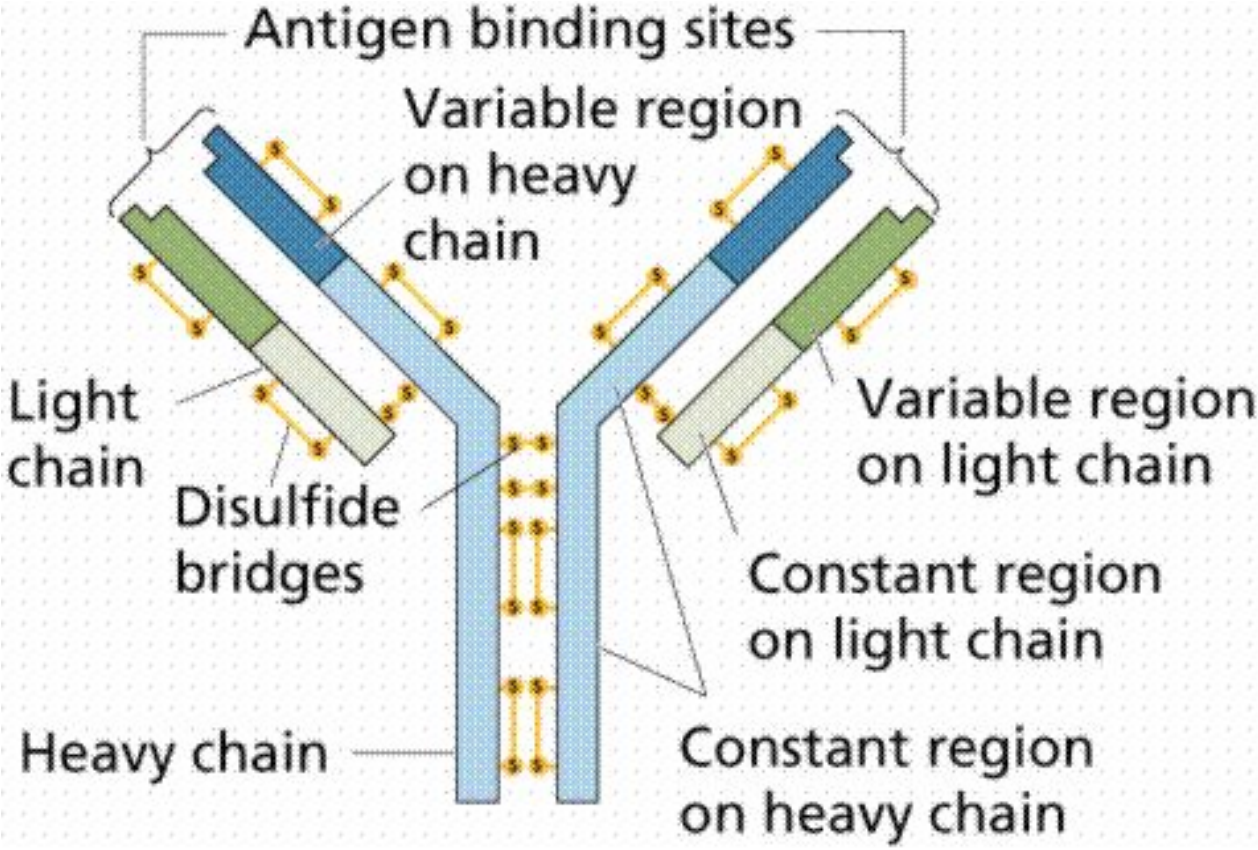
## Step 4: Plasma cells produce antibodies




Antibodies are a soluble form of the BCR.

Memory cells are used for secondary infections.

## Structure of the Antibody

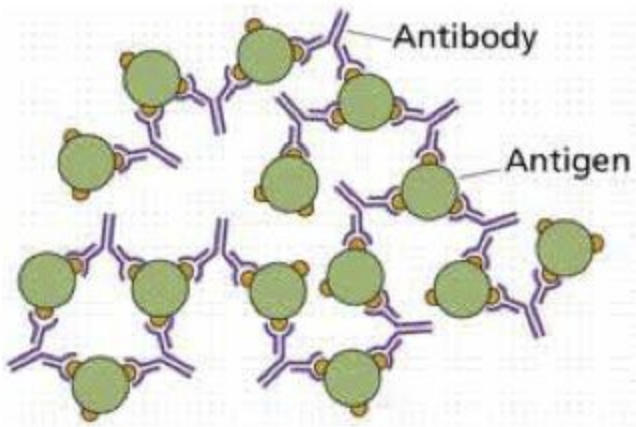


- Antibodies are proteins - quaternary structure
- Made of four polypeptide chains, each folded into its tertiary structure
- Two light chains (short) and two heavy chains (long)
- Two halves
    - Constant Region = sequence remains the same in all antibodies
    - Variable regions = sequence is unique for each type of antibody
- Each arm contains one antigen-binding pocket, formed by the variable region
- The two arms are joined together at the hinge region
- The hinge region, which is rich in disulphide bonds, allows the two arms to rotate independent of each other, so that each antibody can bind to two antigens

***One antibody can bind to (is complementary to) only one antigen***

**How to antibodies work?**

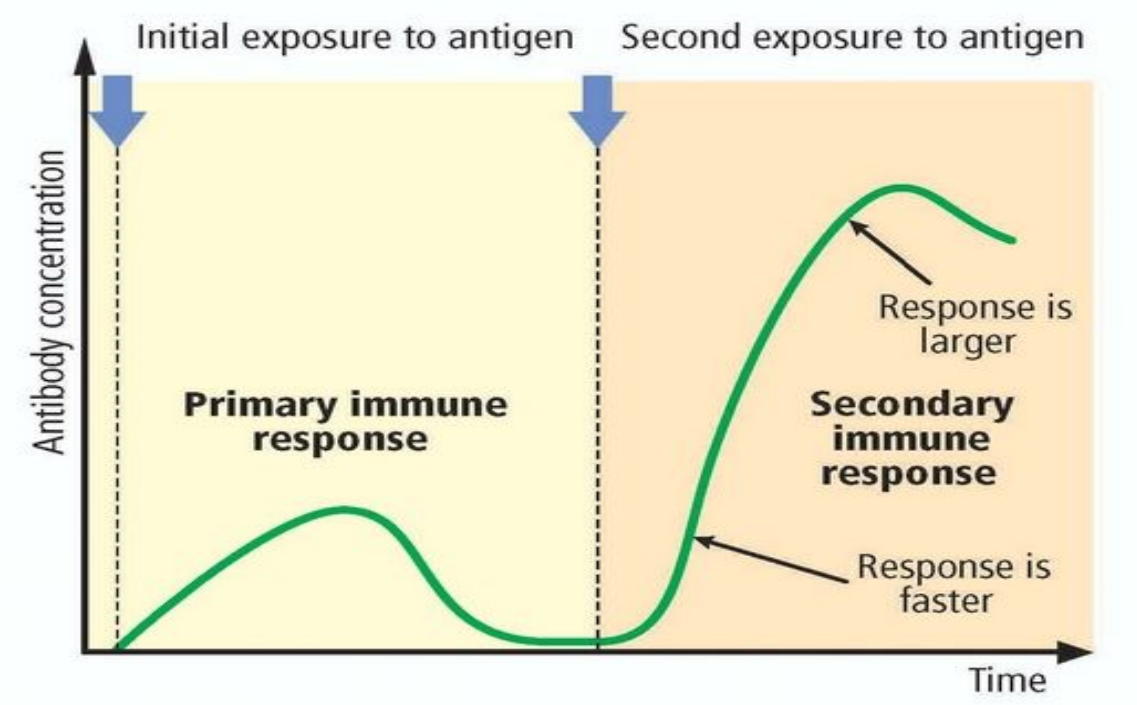
- One antibody is able to bind to two antigens
- This causes clumping of the pathogen = **agglutination**




- Agglutination prevents pathogens from attaching to surfaces
- Phagocytes also find it easier to digest ‘clumps’ of pathogens
- Rapid clearance of pathogen from the body

## Why does the immune system produce memory cells?

Memory cells are used during a secondary immune response - ie re-infection by the same pathogen




Memory exist in a state of readiness and have the ability to rapidly expand and fight off recurrence of the same disease

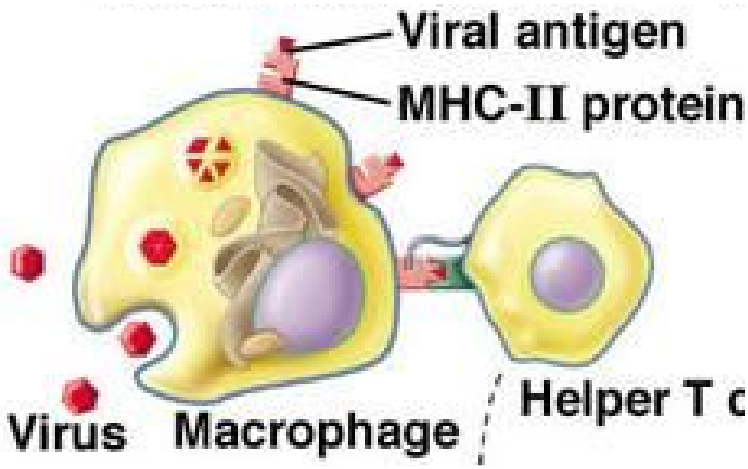
More plasma cells produced - larger antibody response

Faster response - more rapid clearance of the pathogen from the body

## T-cell response

Step 1: Activation of T-cells

T-cells have T-cell receptors (TCR) on their surface - they can be activated by antigens presented on the surface of an APC - like a B-cell or a phagocyte



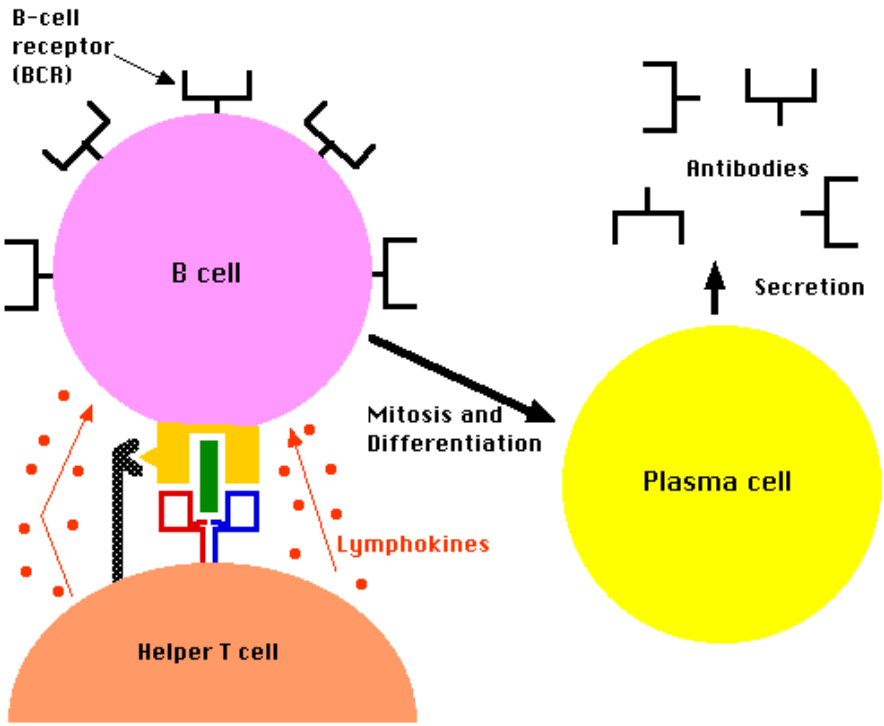

Step 2: T-cells undergo clonal expansion by mitosis

Step 3: T-cells differentiate into 3 distinct cell lineages

Bacterial infection: T-helper and T-memory
Viral infection: T-killer and T-memory (with some T-helper)

## Role of T-helper cells

- Central to the immune system, have CD4 receptors
- Produce chemicals called cytokines, which activate B-cells, and help them to differentiate into plasma cells



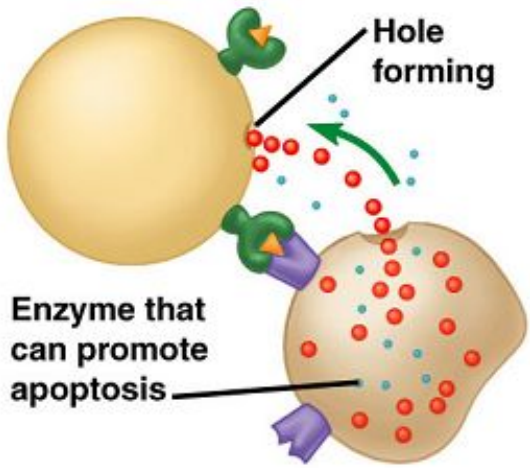

- Without T-helper cells antibody response is poor
- HIV virus attacks T-helper cells, compromising the immune system

## T-memory cells

- Used for a secondary antibody response

## T-cytotoxic or T-killer cells

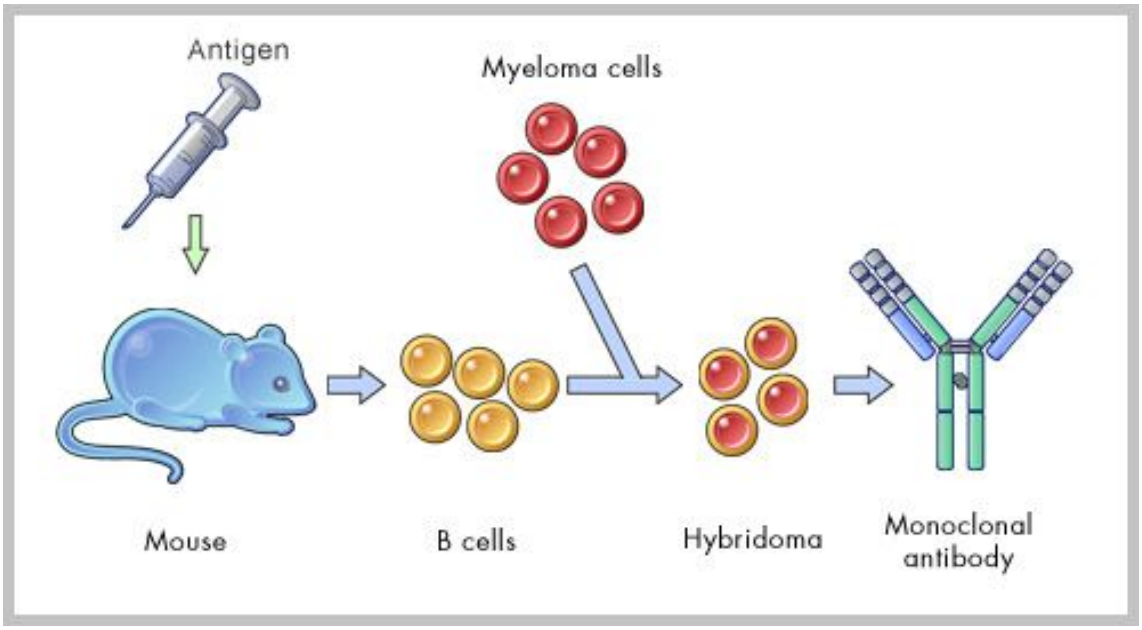
- Primary defense against viral infections
- Have CD8 receptors
- Able to recognise virus-infected cells
- Secretes chemicals called perforins, which punches holes in the surface of virus-infected cells, destroying it



## Monoclonal antibodies

- An antibody that binds to one complementary antigen
- Produced by fusing Plasma Cells with malignant B-cell
- Useful in research and diagnostics

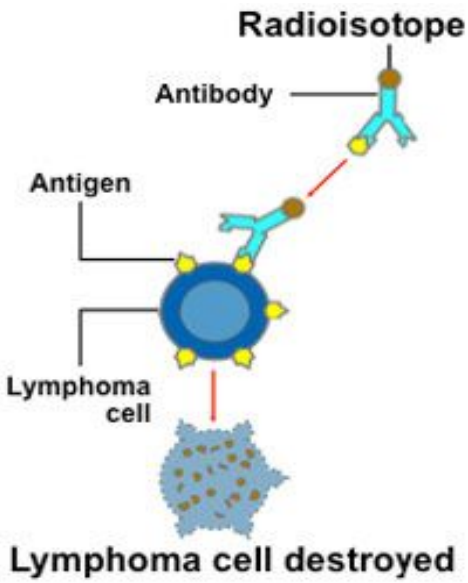
(Blood contains a mixture of antibodies = polyclonal)

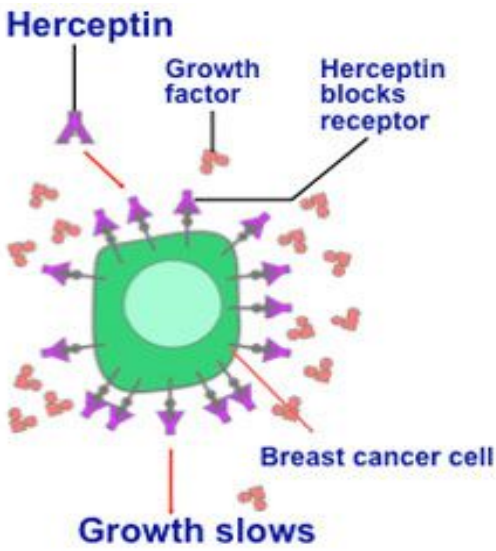


## Uses of Monoclonal Antibodies

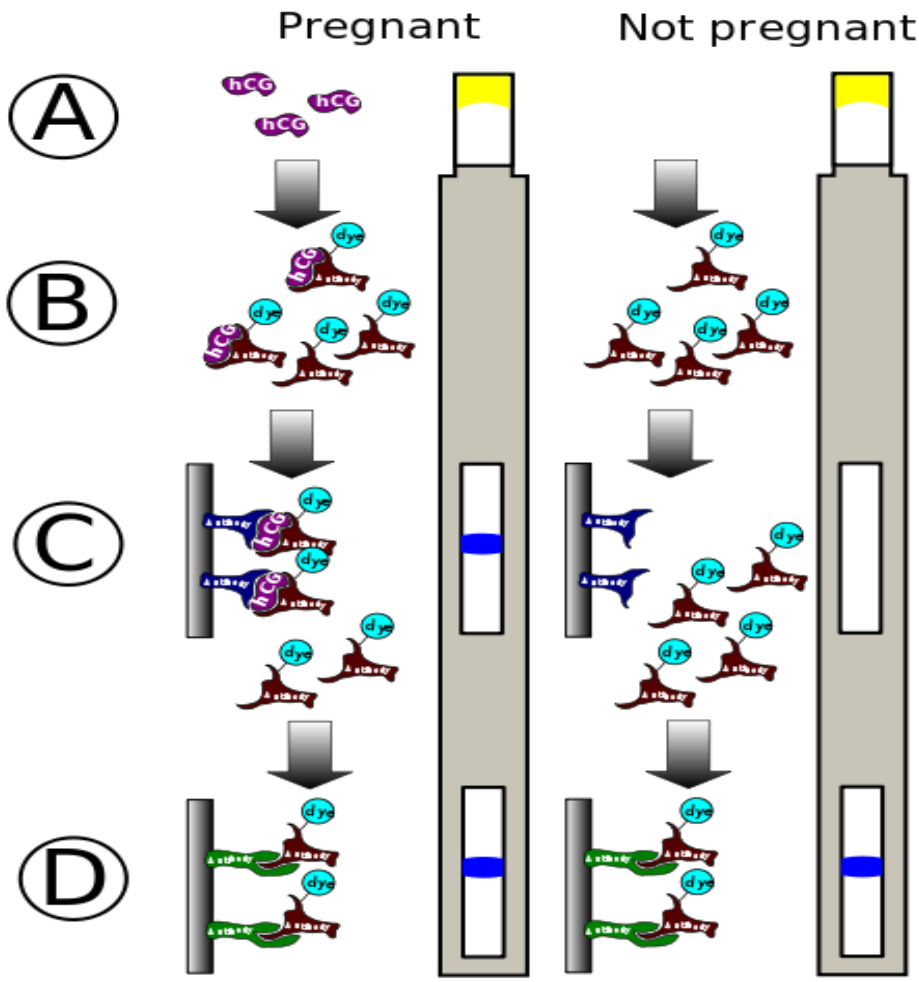
### 1. Cancer treatment

- drug targeting
- Using radioisotopes (targeted radiotherapy)
- Blocking growth factors



## 2. Pregnancy testing kits

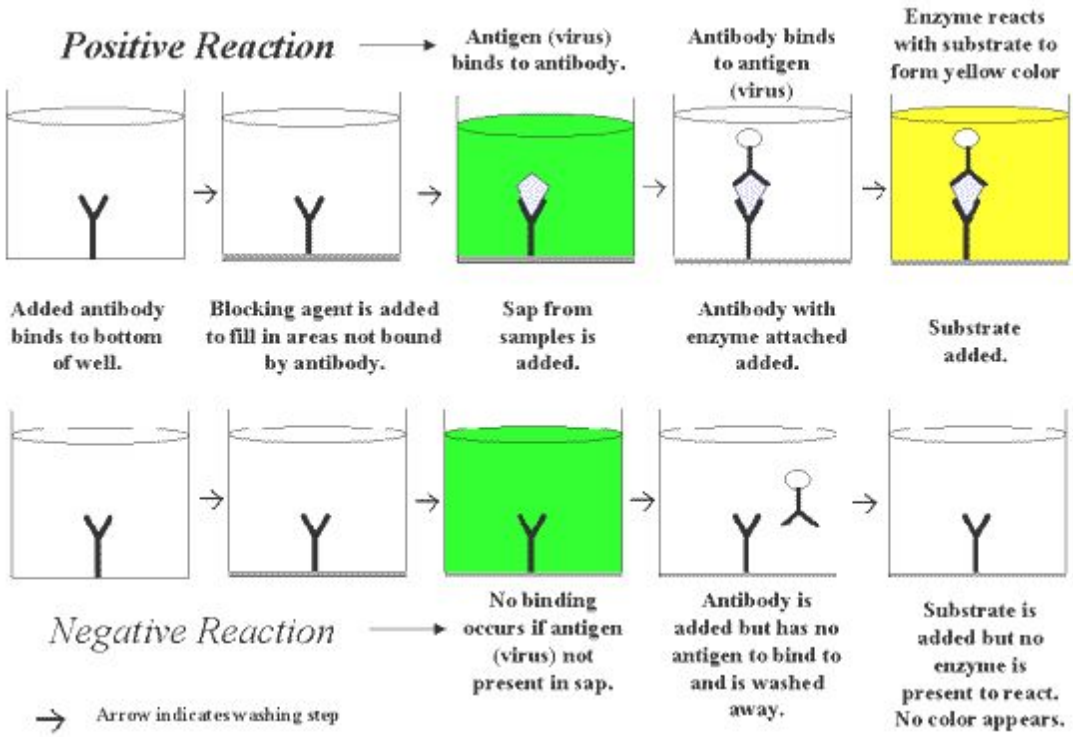



Test protein = HCG, produced by cells of the placenta
Control = albumin, a protein found in blood and urine

(Video:
https://www.youtube.com/watch?v=aOfWTscU8YM;
https://www.youtube.com/watch?v=dsX7tGDbBO4)

## 3. Diagnosis using ELISA - enzyme-linked assay

e.g. detecting HIV antibodies in blood

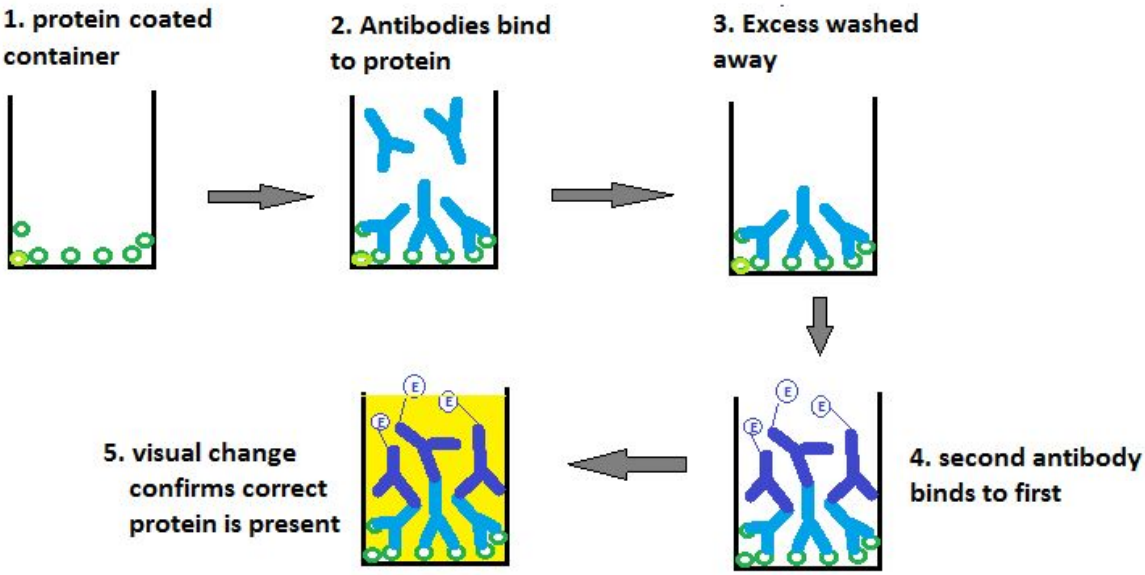



$1^{O}$ Antibody = immobilised, and complementary to antigen

$2^{O}$ Antibody = complementary to antigen, attached an enzyme that can convert a colourless substrate into a coloured compound

## E.g. detecting chlamydial antigens in blood

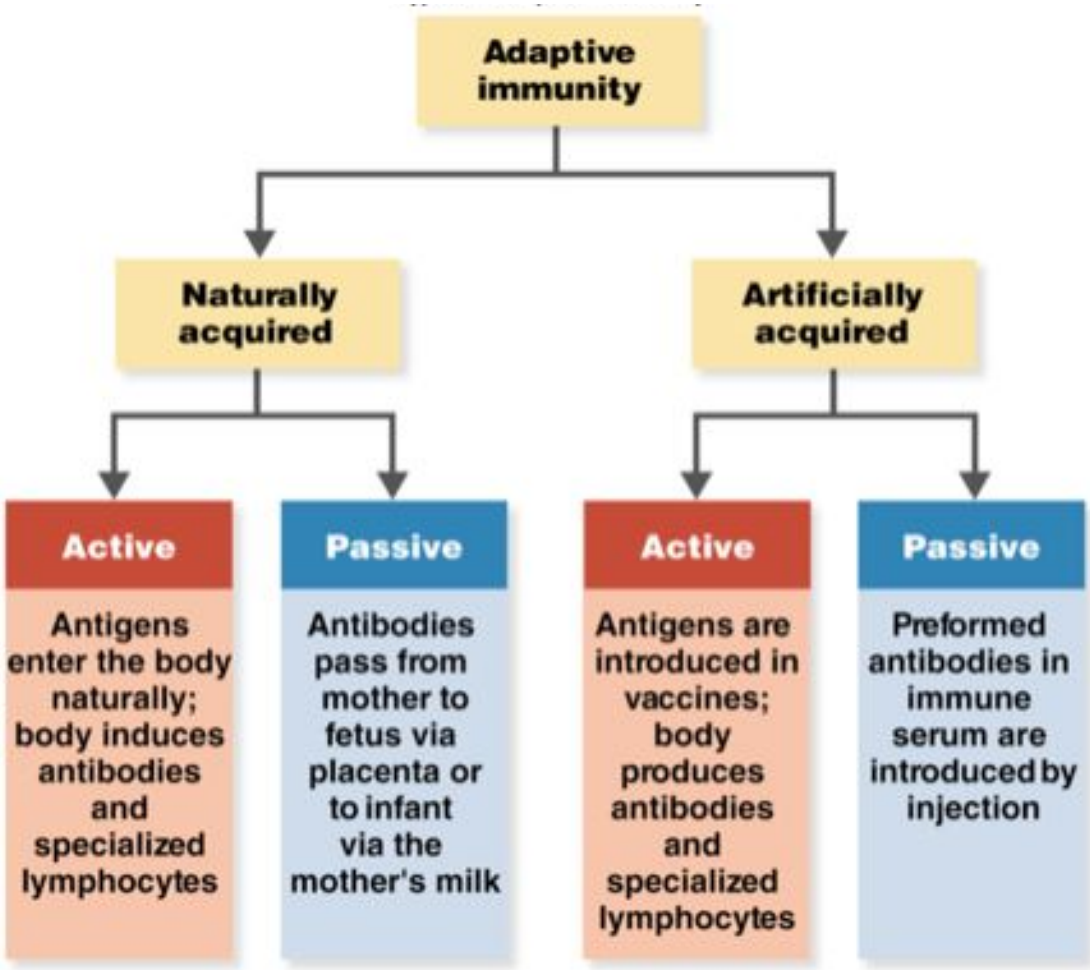
**Indirect ELISA**




$1^{O}$ Antibody = complementary to antigen

$2^{O}$ Antibody = complementary to $1^{o}$ antibody, and attached an enzyme that can convert a colourless substrate into a coloured compound

# TYPES OF IMMUNE RESPONSE



## Natural, Active

- Pathogen enters the body naturally
- Specific immune system triggered
- Memory cells produced

- Long-lasting immunity
- High levels of antibody over time

## Natural, Passive

- Body does not encounter antigen
- Instead, antibodies pass from one person to another i.e. mother to child (via placenta or breast milk)

- No memory cells
- Antibodies are proteins, so will eventually be destroyed
- Short-term immunity

## Artificial, Active (Vaccines)

- Antigen artificially introduced into the body
- Triggers the specific immune system
- Memory cells produced

## Artificial, Passive

- Monoclonal antibodies injected into body
- Offers immediate protection against pathogen
- No memory cells
- Short term immunity

E.g. Tetanus anti-toxin
Snake anti-venom
Rabies vaccines

Adv: Immediate effect

Disadv: Short-term, expensive

Two main types of Vaccines

## LIVE vaccines

- Live, but weakened strain of the pathogen
- Injected into body
- Triggers specific immune response
- Pathogen can multiply slowly, but does not cause infection
- Memory cells produced, and levels keep building up
- Protects against actual infection by pathogen

Adv:

- Long-lasting immunity due to memory cells
- Strong antibody response

Disadv:

- Risk of infection or side-effects in immunocompromised individuals - old, young, autoimmune disease like coeliac disease

Eg. BCG, MMR, children's flu vaccine

## INACTIVATED vaccines

- Heat-killed pathogen injected into body
- Heated to temperatures that do not alter the tertiary structure of the antigens on the surface
- Antigens recognised by immune system as non-self, triggers specific immune response
- Memory cells produced
- Protects against infection by actual pathogen

Adv: Low risk, minimal chance of infection

Disadv: Pathogens do not multiply in the body, so levels of memory cells lower than those produced by live vaccines

E.g. polio, whooping cough, adult flu vaccine

## Why vaccines don’t always work:

1. Person has already been exposed to the antigen before being given the vaccine = incubation period, where symptoms are not apparent

2. Immune system is compromised, leading to disease or side-effects

3. Antigenic variability: some bacteria and viruses have the ability to constantly vary the antigens on their surface - memory cells produced in primary infection cannot recognise these new antigens on reinfection

4. Everyone responds differently to vaccines - levels of antibody vary

Herd immunity: Not possibly to immunise 100% of the population - some people have ethical objections or are too ill to take vaccines

Goal is to immunise 95% of the population

Minimises risk of coming into contact with an infected individual - reduces chance of disease spreading

## Flu vaccines

Influenza virus shows antigenic variability - many different strains exist in the same year

Epidemiologists keeps track of the strains most likely to cause infection each winter

Flu vaccine is made by combining the top 5 strains likely to cause infection

However, if infected with a strain that is not in the vaccine then it is still possible to get ill with flu

Therefore, vaccine is given to very young or old, or pregnant women, but not normally available for free to people within the age range of 18-65 (in the UK) - as their immune system can cope with flu without any serious side-effects (cost:benefit ratio)