DP IB Biology: HL

Your notes

11.1 Antibody Production & Vaccination

Contents

11.1.1 Antigens


Your notes

Antigens

- Every organism has cells with **unique molecules** on the cell surface membrane which act as **markers** to **identify it**
- These unique markers are **macromolecules** and they allow **cell-to-cell recognition**
- The **immune system** has the ability to distinguish between 'self' and 'non-self' based on these molecules
  - **Microorganisms** (both pathogenic and non-pathogenic), such as **bacteria** and **viruses,** trigger an **immune response** as the immune system recognises their markers as being **non-self**
  - Molecules that trigger an immune response in this way are named **antigens**
  - **Antigens** are found on cell surface membranes of cancer cells, bacterial cell walls, the envelopes of viruses and even pollen grains
  - Some **glycolipids** and **glycoproteins** on the outer surface of cell surface membranes act as antigens
- **Allergies** are the result of an immune response triggered by antigens on the surface of an **allergen**, such as pollen

Examiner Tip

The different **types of pathogen** include viruses, bacteria, fungi and protozoans.

Blood Transfusions & Antigens


Your notes

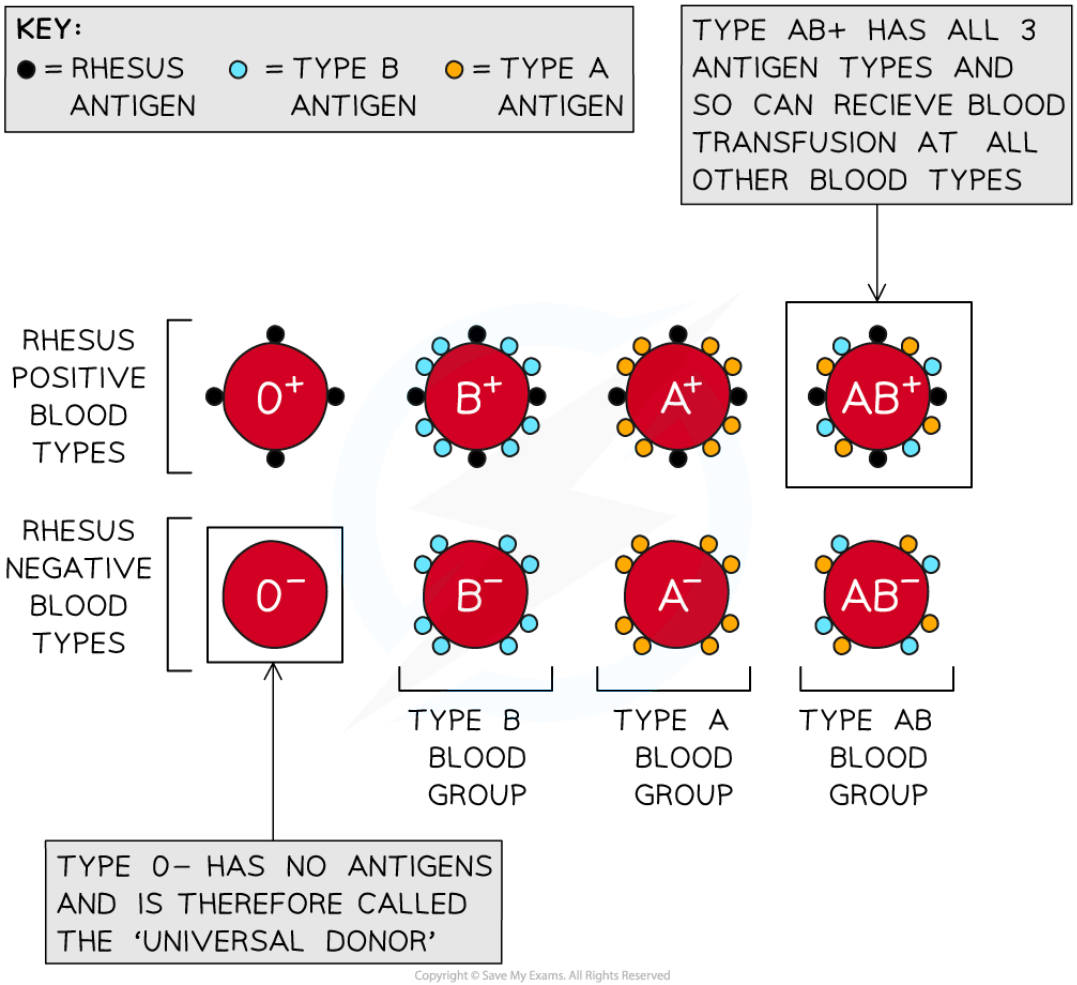
Antigens on red blood cells

- Red blood cells have **specific markers** on their surface known as **antigens** which **determine the blood group** of an individual
- If a **transfusion** is given to an individual with mismatched blood group, the antigens on the red blood cell surface will trigger an immune response
- There are two **antigen markers** that must be considered:
  - The **ABO marker** - this determines whether the individual is **blood group A, B, AB or O**
  - The **Rhesus (Rh) marker** - this determines whether the individual is rhesus **positive** or rhesus **negative**

Determining ABO blood types

- **Blood type A** has a **type A antigen** consisting of an initial 'H' marker which is modified with another molecule called N-acetylgalactosamine
- **Blood type B** has a **type B antigen** consisting of an initial 'H' marker which is modified with another molecule called galactose
- **Blood type AB** has **type A and B antigens** consisting of two 'H' markers one of which is modified with N-acetylgalactosamine and the other with galactose'
- In **blood type O,** the 'H' marker is not modified and so there are no A or B antigens

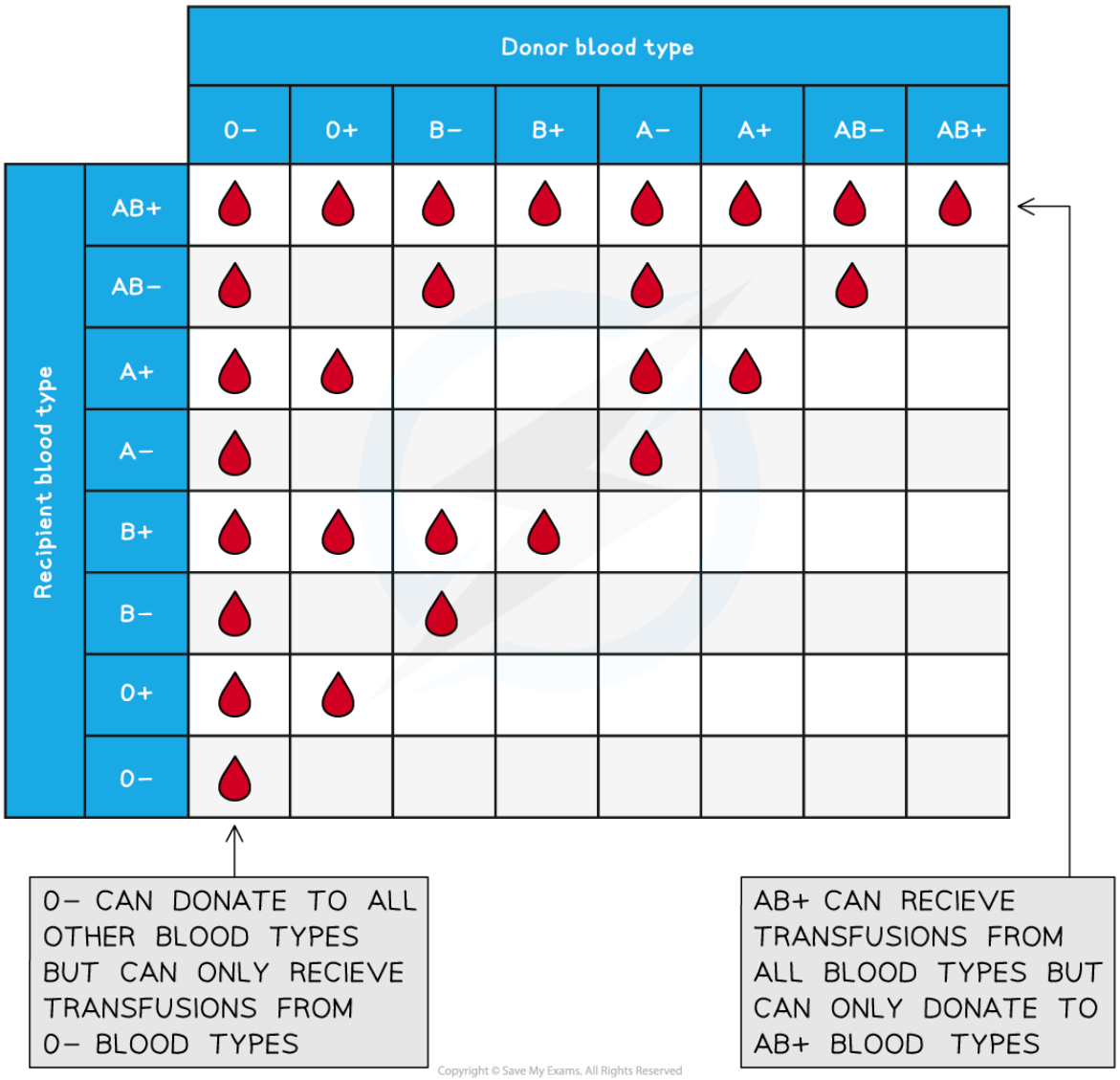
Your notes



Blood type is determined by the presence or absence of specific antigen markers on the surface of the red blood cells

- If a transfusion is given to someone of an **incompatible blood type,** an immune response will occur due to the presence of antibodies in the recipient's blood that bind to blood cells with non-self antigens
- An immune response may result in **agglutination** of the blood in the blood vessels and **could be fatal**
  - Agglutination is when red blood cells clump together due to the binding of antigens and antibodies
- **Compatible** blood types means **not** using blood that has a **different type of antigen** to the patients blood

Your notes



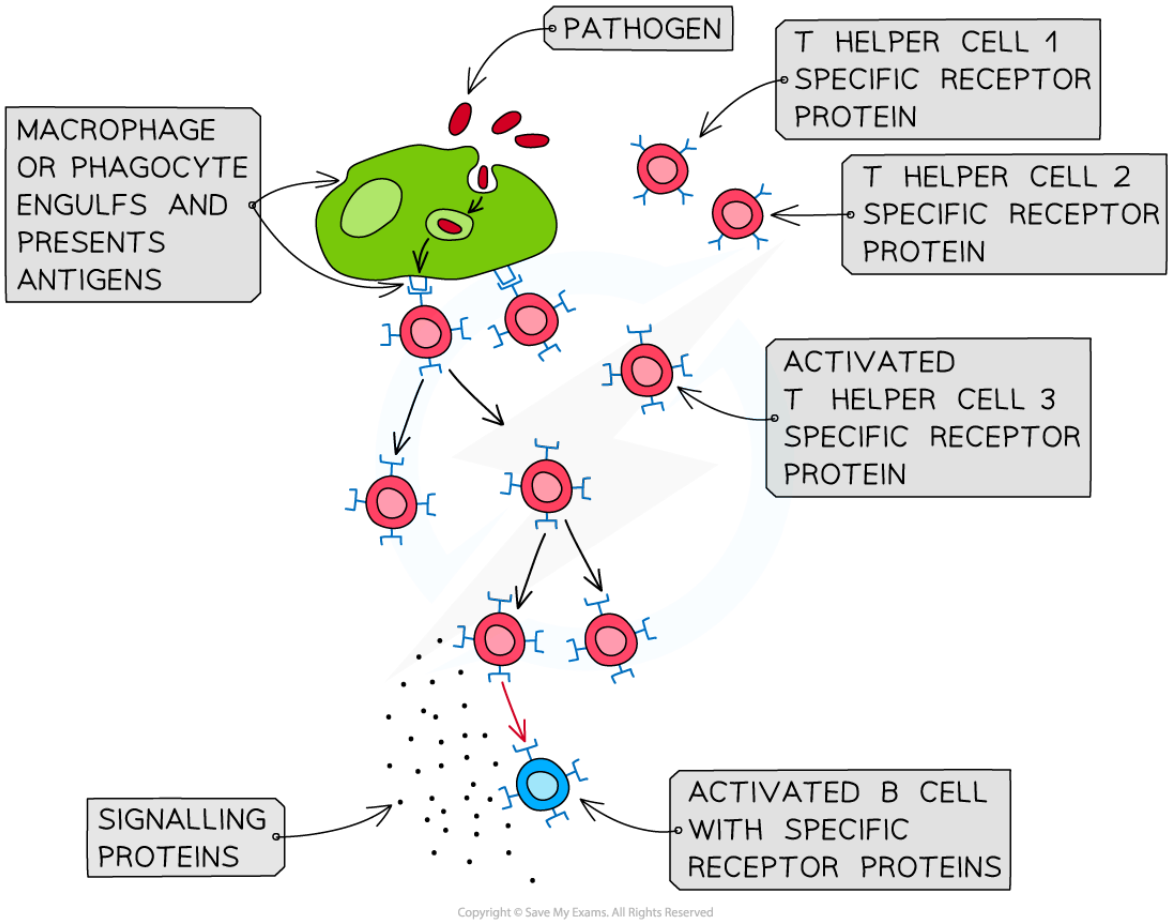
Blood type must be compatible when carrying out a transfusion to prevent coagulation of blood in blood vessels

11.1.2 Specific Immune Response

Your notes

Specific Immune Response

- T-Helper cells (a type of lymphocyte that responds to specific antigens) and mature B cells (another type of lymphocyte) have specific receptors located on their cell surface membranes
  - These receptors have a **similar structure to antibodies** and are each **specific to one antigen**
  - Note that lymphocytes are a type of white blood cell involved in the specific immune response; there are several different types of lymphocyte
- When phagocytes engulf pathogens, they **present the pathogen antigens** on their own cell surface membrane
  - A cell with non-self antigens on its surface membrane is known as an antigen presenting cell
- The T-helper cell with the **complementary receptor proteins to the antigen** will bind to the antigen and become **activated** by the phagocyte
- **Activated T-helper cells** then bind with **complementary receptors** on the surface membrane of specific **B-lymphocytes**
- On binding, the **T-helper cells** releases **signalling proteins** and **activate these B-cells**



Antigens activate complementary T-helper cells which go on to activate complementary B-cells


Your notes

Plasma Cells

- During an immune response, B-lymphocytes **mature** to form **two types of cell**: **plasma cells** and **memory cells**
- **Plasma cells** produce large volumes of **antibodies** specific to the single type of antigen that triggered the immune response
- The cells are specialised with large amounts of rough endoplasmic reticulum which promotes **protein synthesis** to make the required antibodies
- As B-cells only produce one type of antibody, only a **small proportion of the genes are expressed** in the nucleus

Clonal Selection & Expansion

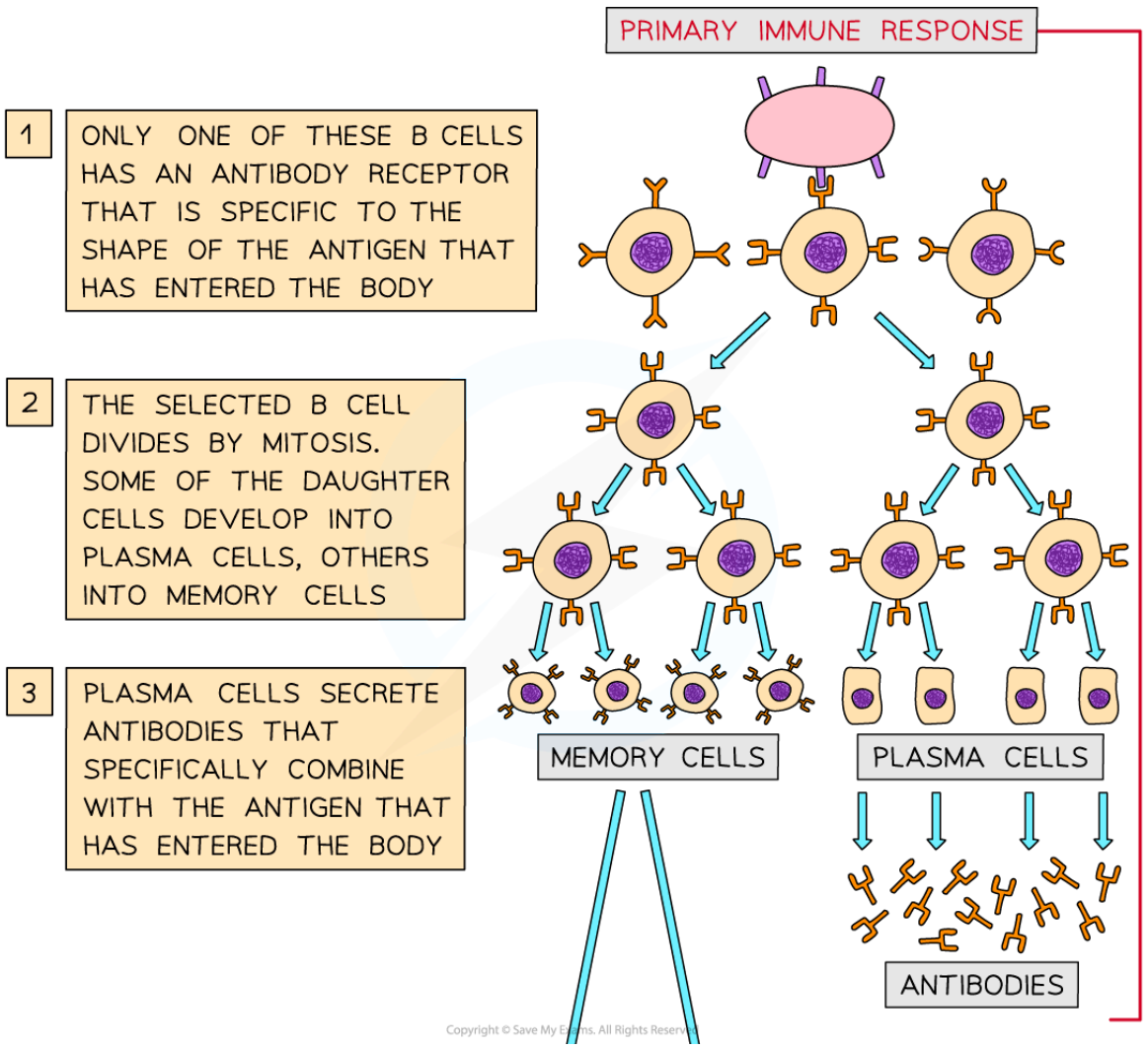

Your notes

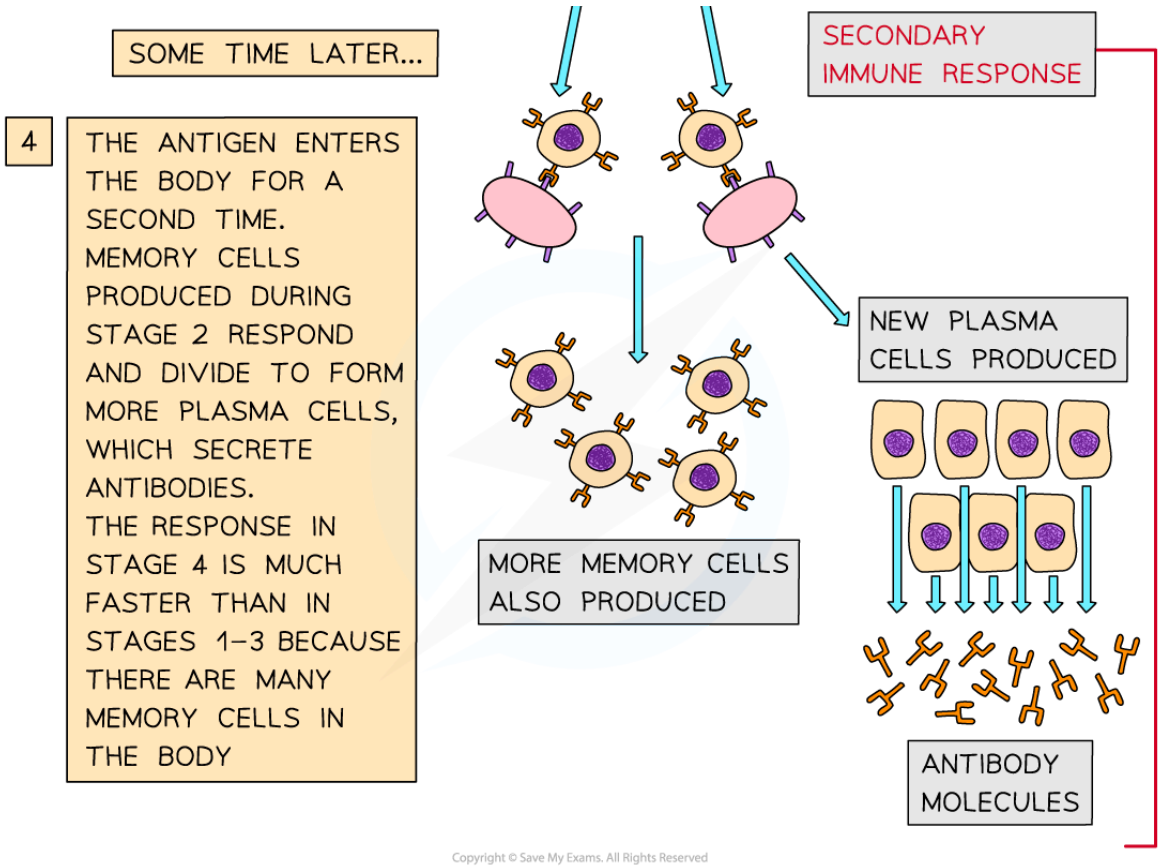
- **Clonal selection** involves **identifying and activating a B-cell** with the **complementary receptor** to the target antigen
- **Clonal expansion** can then occur
  - The **activated B-cell divides by** mitosis to create many clones of itself
    - Each **clone** will produce **the exact same antibody**, complementary to the target antigen
- Some of these mature B-lymphocytes differentiate into plasma cells
- The other B-lymphocytes become **memory cells** that remain and circulate in the blood
  - Whilst the antibodies produced by the plasma cells are only present for a matter of weeks or months, memory cells form the basis of **immunological memory** – the cells can last for **many years** and often a lifetime

The primary and secondary immune response

- A **primary immune response** occurs in response to a **newly encountered antigen**
  - This is a relatively **slow response** as the immune system takes time identifying the complementary antibody for each new antigen it encounters
  - The infection may result in **symptoms being presented** whilst the immune system identifies and manufactures the correct antibodies
- **Secondary immune response** in response to a **previously encountered antigen**
  - The memory cells with the correct antibody, are already circulating in the blood so the response is **more rapid,** producing more antibodies than the primary response, in a much shorter time frame
  - **Symptoms do not develop** as the pathogen can be destroyed before significant cell damage occurs

Your notes





During a secondary immune response, memory cells that remained in the blood divide very quickly into plasma cells (to produce antibodies) and more memory cells. Whereas a primary response occurs much more slowly.

Your notes

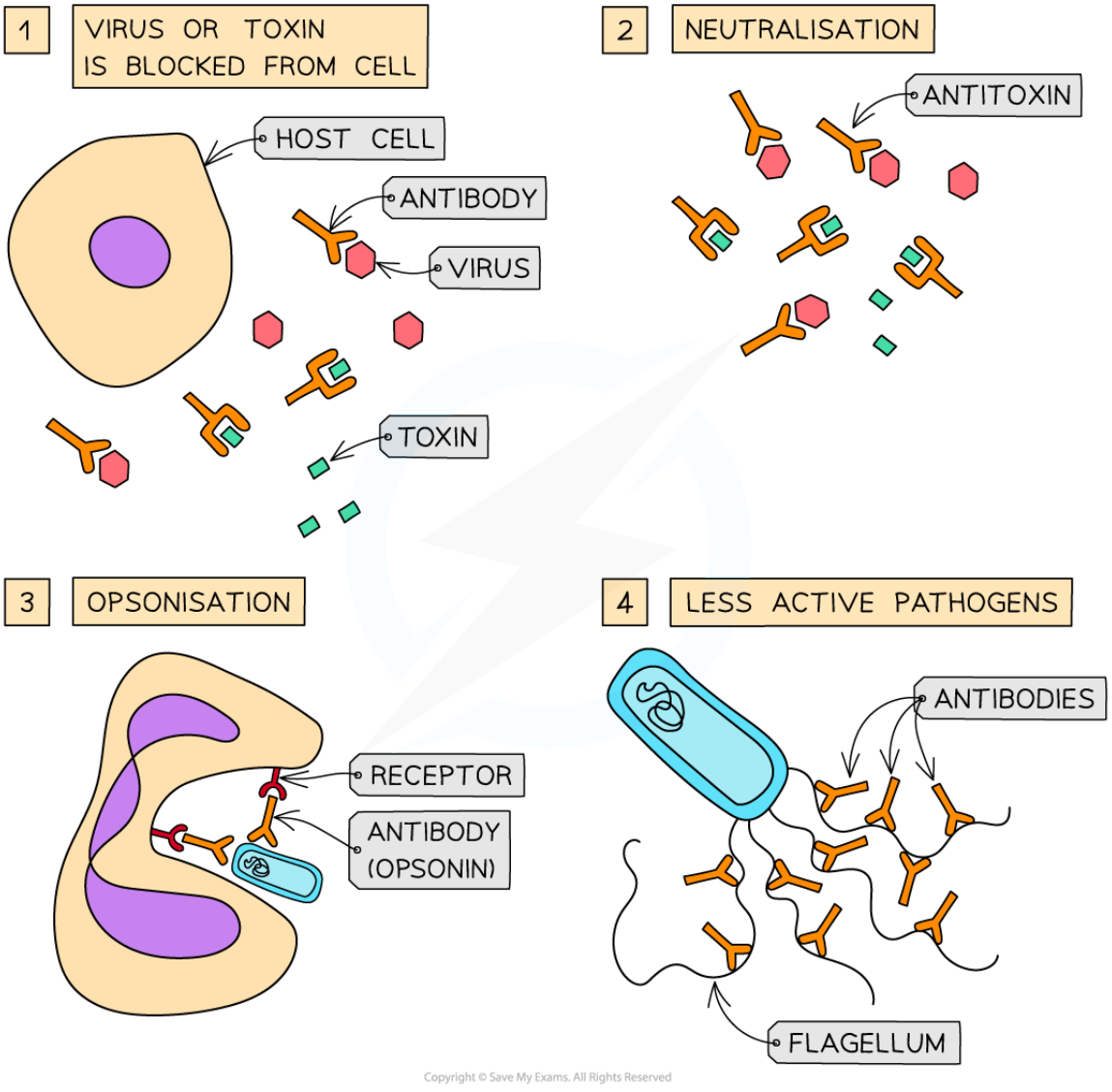
11.1.3 Antibodies, Vaccines & Immunity

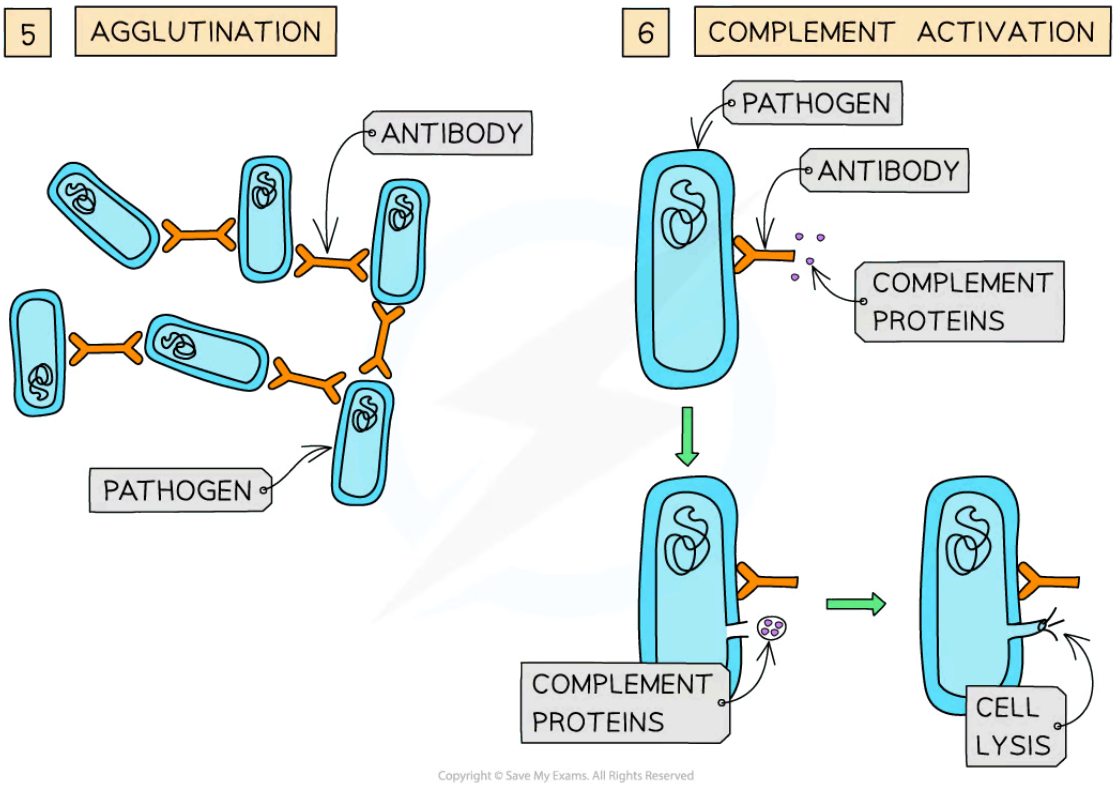
Your notes

Antibodies: Function

- The function of **antibodies** produced by B-cells is to **destroy pathogens** within the body
- This can be done either **directly**, or by **recruiting other immune cells**
- Antibodies aid the destruction of pathogens in several ways:
  - **Agglutination**
    - 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 or taken into cells, instead the **clumps are removed by the lymphatic system** and digested by **phagocytes**
  - **Opsonisation**
    - Antibodies 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
  - **Neutralisation** of viruses and bacteria
    - Antibodies can **combine with viruses and toxins of pathogens** (e.g. bacteria) to **block them** from entering or damaging cells
  - **Activity reduction**
    - Antibodies can **attach to the flagella of bacteria** making them **less active**, which makes it easier for phagocytes to do phagocytosis
  - **Neutralisation of toxins**
    - 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
  - **Complement activation**
    - Antibodies can **trigger proteins**, called complement proteins, which **create holes in the cell walls of pathogens** causing them to **burst** (cell lysis) when ions are absorbed and water moves in by osmosis

Your notes





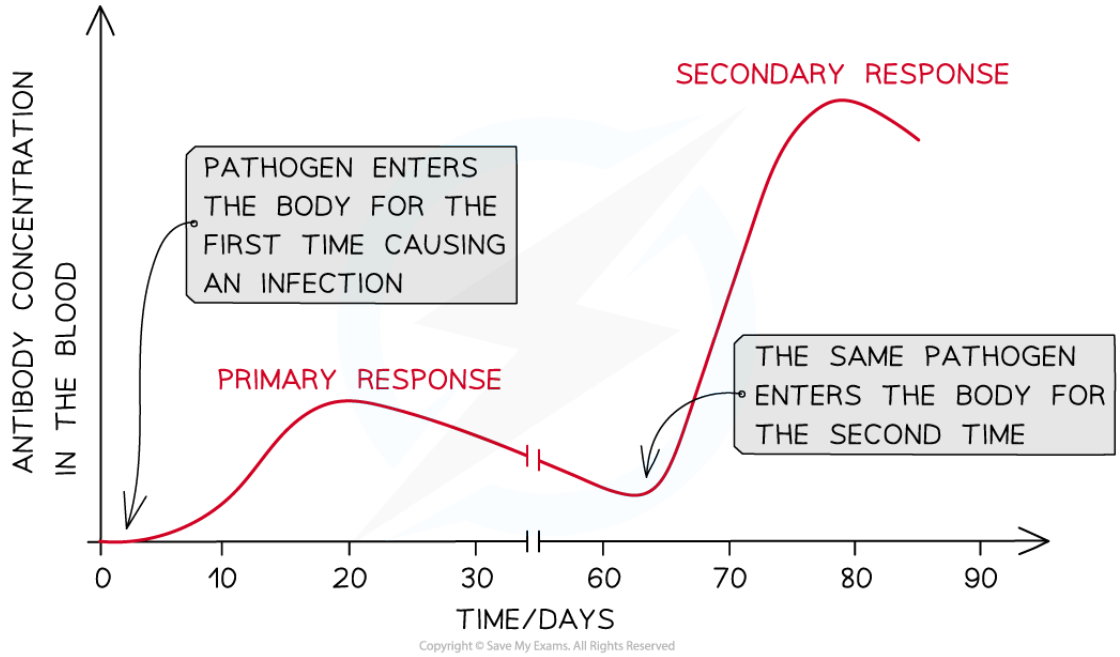
The functions of antibodies vary according to which type of antigen they act on

Your notes

Immunity

Your notes

- Immunity is initiated when **exposure to a specific antigen** results in the production of **complementary antibodies** and **memory cells**
- This first exposure to an antigen **triggers the primary immune response**
- The **primary immune response** leads to the **development of immunity** if memory cells and antibodies which persist in the bloodstream after the pathogen has been eliminated
- The **secondary immune response** occurs when the **same antigen is found in the body a second time**
  - The **memory cells recognise the antigen, divide very quickly** and differentiate into antibody-producing plasma cells and more memory cells
  - The response to a previously encountered pathogen is, relative to the primary immune response, **extremely fast**
  - This means that the **infection can be destroyed and removed before the pathogen population increases** too much and symptoms of the disease develop



The secondary response is much larger and more rapid than the primary response

Examiner Tip

Immunological memory (made possible by memory cells) is the reason why catching certain diseases twice is so unlikely. For example, there is only one strain of the virus that causes measles, and each time someone is re-infected with this virus, there is a very fast secondary immune response so they **do not get ill**.

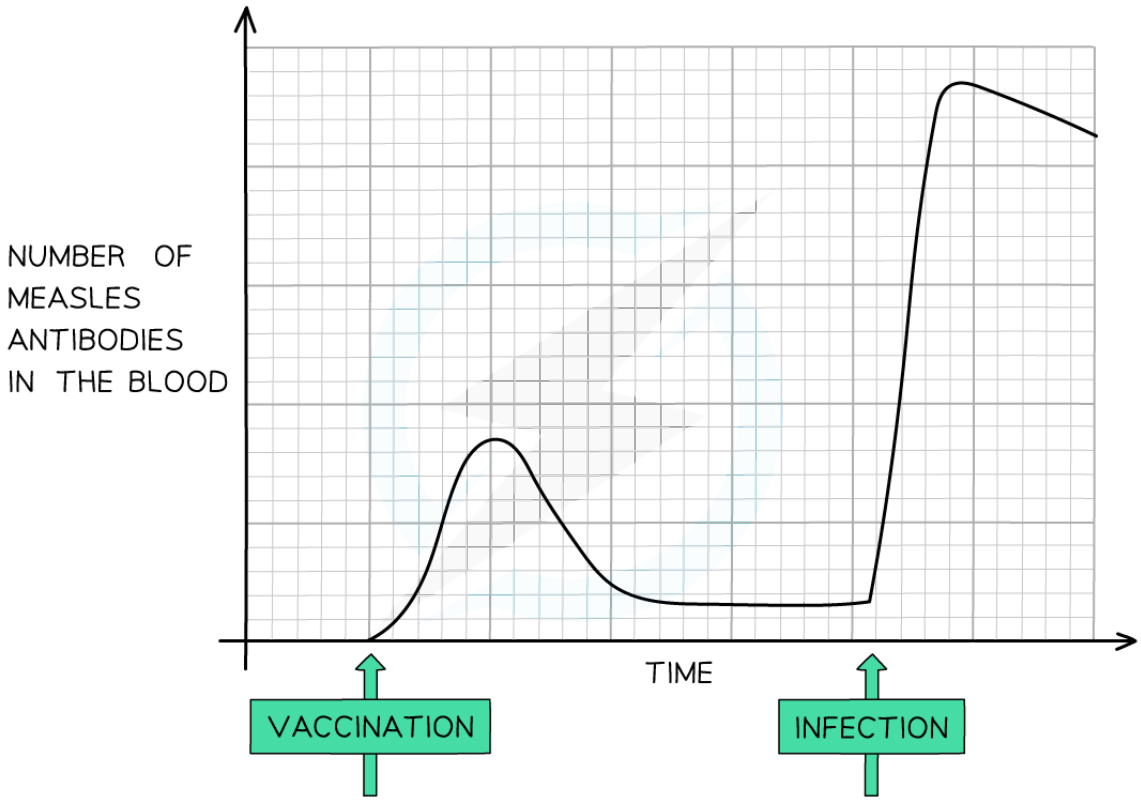
However, some infections such as the common cold and influenza are caused by viruses that are constantly developing into **new strains**. As each strain has different antigens, the primary immune response (during which we often become ill) must be carried out each time before immunity can be achieved.


Your notes

Vaccines & Immunity

Your notes

- A vaccine is a source of **antigens** that are intentionally put into the body to **induce immunity**
- Vaccines cause a **specific immune response** where antibodies are released by plasma cells
- There are different types of vaccine, including
  - **Live attenuated** - these are **weakened versions of the pathogen**
  - **Inactivated** - these are **killed, non-living components of pathogens** or even just the **antigens** alone
- Vaccines are administered either by **injection** or **orally** (by mouth)
  - 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 memory cells recognise the antigen when re-encountered and produces antibodies, in what is a **faster, stronger, secondary response**



Examiner Tip

Remember vaccines trigger the primary immune response (T helper cells trigger B plasma cells to secrete specific antibodies) which leads to the production of memory cells which will give a faster and larger (higher concentration of antibodies) secondary response.

Your notes

11.1.4 Smallpox Vaccine & Eradication

Your notes

Jenner's Ethics

Introduction

- The principles underpinning vaccinations were discovered by **Edward Jenner** in the 1700s when he developed the **first smallpox vaccine**
- Smallpox was a highly infectious disease caused by the **variola virus** which first emerged thousands of years ago
  - Notable **symptoms** of smallpox included **fever** and an extensive **rash** with **pus filled pustules**
  - Long term effects included scarring and blindness
  - There was a **30% death rate** in those who contracted the disease
- **Variolation** was a method used to try and protect people from the most serious symptoms
  - Variolation involved scratching material from smallpox pustules into the arms of patients
  - **Symptoms** resulting tended to be **less serious** than those of naturally infected patients
    - The pustules tended to contain pus, a substance that contains dead white blood cells and destroyed pathogens
    - Sometimes the pus contained functional pathogens so variolation could still cause disease and death.
- Edward Jenner observed that milkmaids who had been exposed to **cowpox** were showing a level of immunity to smallpox
- He **hypothesised** that they were protected due to their **exposure to the cowpox virus** which was similar but less serious
- Jenner combined his observations and the method of variolation to develop a **cowpox inoculation** which he tested on a 9 year old boy
  - He took pus from the skin lesions caused by cowpox and scratched it into the skin of a patient
- The inoculation proved **successful;** when Jenner later attempted to infect the boy with the variola virus **no illness developed**

NOS: Consider ethical implications of research; Jenner tested his vaccine for smallpox on a child

- There are many topics of interest in scientific fields which have significant **ethical implications**
- In the modern-day there are procedures in place that set the criteria to ensure that **ethical decisions are made** and **ethical procedures are followed** whilst working within **controversial** and **sensitive scientific topic areas**
- This consideration of ethics in science has been developed over time and with the establishment of working groups such as the **World Health Organisation**
- Edward Jenner carried out primitive investigations into vaccinations in 1790 when there was no existence of a **Research Ethics Committee** as there is now
  - He did his first tests **without** any initial **laboratory research or animal testing**
  - His first patient was a **small boy who he exposed to the deadly smallpox virus** in the hope that his vaccination would work

- Under current legislation, Jenner's methods would **not be approved** or even considered by an ethical review committee


Your notes

Eradication of Smallpox

- **Herd immunity** is one approach to protecting populations from diseases
  - Herd immunity arises when a **sufficiently large proportion of the population has been vaccinated** (and are therefore immune) which makes it difficult for a pathogen to spread within that population
  - Those who are **not immunised are protected** and unlikely to contract it as the **levels of the disease are so low**
- Smallpox emerged thousands of years ago but outbreaks occurred periodically for many years afterwards and was still widespread as late as 1966 in South Africa, Africa and Asia.
- The WHO began an **eradication programme against Smallpox** in 1967, stating their intention to eradicate the virus within ten years
- The WHO did not declare smallpox eradicated until 1980
- The programme focused on:
  - **Vaccination**
    - The aim was to vaccinate more than 80% of populations at risk
    - If a case of smallpox was reported, **ring vaccination** would occur
    - This is where everyone in the household with the reported case, the surrounding 30 households, relatives and anyone else who had contact would get vaccinated
  - **Surveillance**
- The **success** of the program was attributed to the following factors:
  - The **virus was stable** – it did not mutate therefore its surface antigens did not change, therefore the same vaccine could be used worldwide which made it cheap to produce the vaccine
  - The **vaccine was a 'live attenuated'** version, being produced from a harmless strain of a similar virus
  - The **vaccine could be transported** without becoming unviable, as it could be freeze-dried and kept at high temperatures for up to 6 months, thus it was suitable for the tropics
  - The **smallpox variola virus only infects humans** so was easily **traced** and **monitored** (compared to other diseases which re-emerged after being masked within animal populations)
  - **Symptoms were obvious** and developed quickly so vaccination of close contacts was effective in preventing human to human transmission
  - Vaccination gave **long lasting immunity** so reinfection was unlikely

11.1.5 Zoonosis

Your notes

Zoonosis

- Some diseases are **species specific** whilst others can **cross species barriers** to infect multiple different species
- Species-specific disease may be **unable to cross the species barrier** for many reasons:
  - If a species does not possess the **necessary receptors** to be at risk of infection
  - If the **body temperature** of the organism doesn't reach temperatures required for the development of the disease
- **Zoonotic diseases are those which can cross the species barrier** from animal to human
- This is a growing **global concern** due to the close relationships between humans and animals meaning the disease may be difficult to control and eradicate
- This may potentially lead to **pandemics** such as that caused by COVID-19
- Animal products may also be affected by zoonotic disease which poses a further issue
- Some zoonotic **diseases** can initially **emerge from animal populations** before developing into human only strains e.g. HIV

Table to show some examples of human only and zoonotic diseases

Disease	Species First Infected	Status
Bird flu	Geese	Zoonotic
Tuberculosis	(Believed to be) Humans	Zoonotic
HIV	Chimpanzee (as simian immunodeficiency virus)	Zoonotic
Bubonic Plague	Fleas and rats	Zoonotic
COVID-19	Unconfirmed	Zoonotic
Measles	Humans	Human only
Diptheria	Humans	Human only
Polio	Humans	Human only

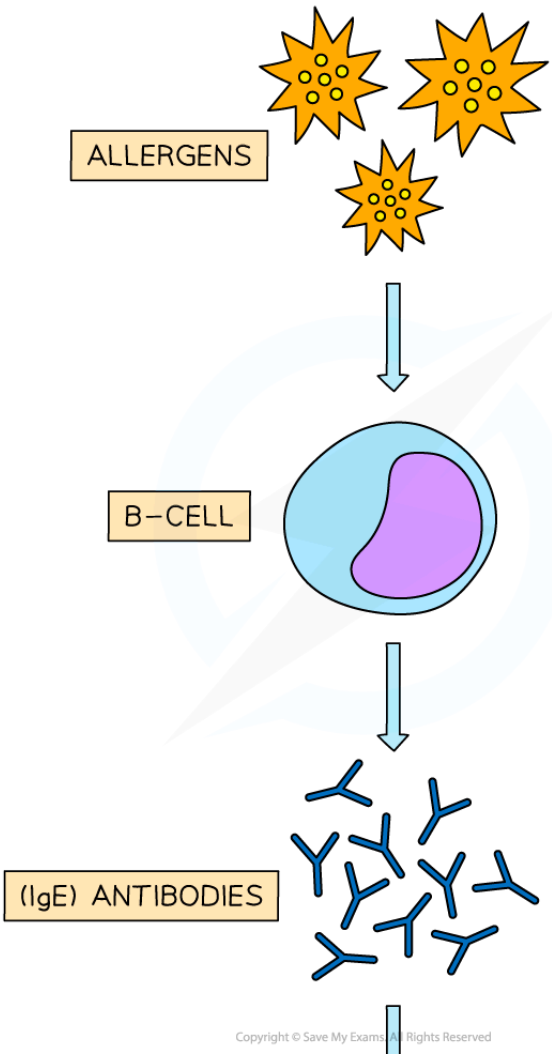
11.1.6 Histamines


Your notes

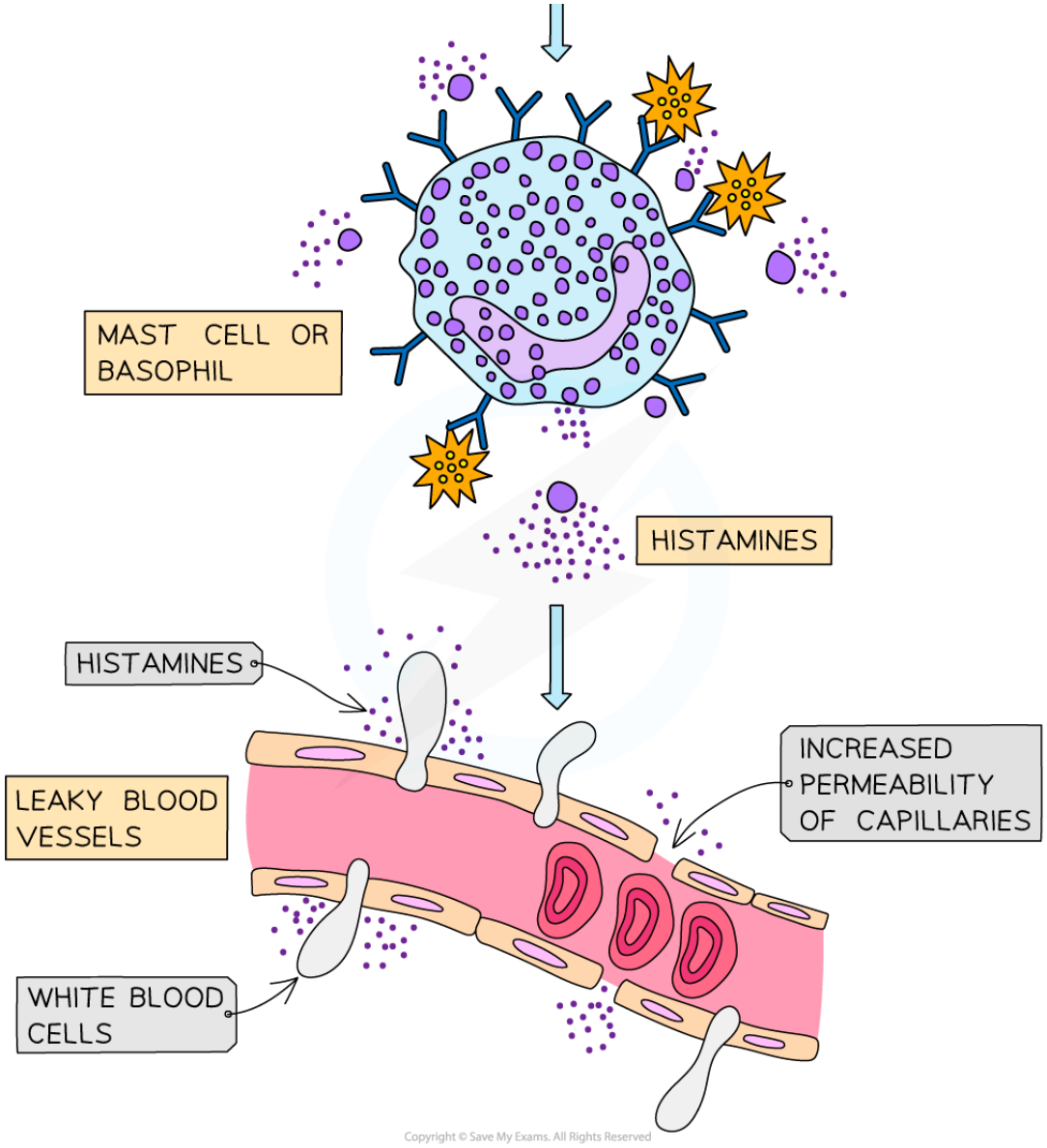
Production of Histamines

- Histamines are **chemicals** created by the body in **response to allergens** such as pollen, pet dander, food substances or dust
- **Allergens are antigens** and so they are encountered by **B-cells** (a type of white blood cell) which respond by **producing antibodies** (called IgE antibodies)
- The IgE antibodies **stimulate histamine production** by immune cells:
  - One type are **mast cells**, which are found in the connective tissue
  - Another type are **basophils** which are a type of white blood cell that circulate in the blood
- Release of histamines into the bloodstream leads to **dilation of blood vessels** increasing blood flow to the affected areas
- Increased permeability of blood vessels increases the amount of fluid leaving the vessels leading to **inflammation** and triggering both **specific** and **non-specific responses** by other immune components found in the blood

Your notes



Your notes



Allergens trigger antibody release from B-cells which stimulate mast cells or basophils to release histamines, causing blood vessels to dilate and leak therefore leading to inflammation

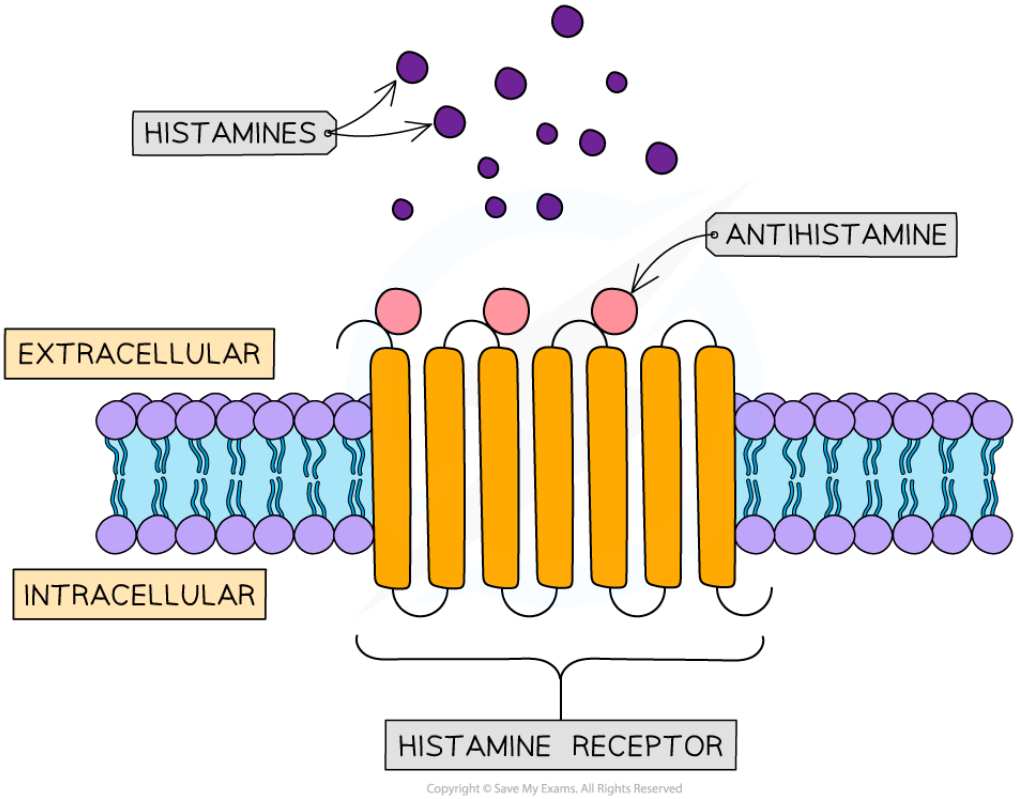
Examiner Tip

Whilst you do not need to know the specific detail of IgE antibody production, you should be able to link antibody production to the activation of B-cells in response to antigens encountered.

Effects of Histamines

Your notes

- Histamines also bind to **receptors** elsewhere in the body causing other symptoms associated with allergic reactions
  - **Minor symptoms** may include a runny nose, itchy skin and eyes or sneezing
  - More **serious symptoms** may include extensive body rashes, hives or swelling which can result in anaphylaxis
- A serious allergic reaction could be life-threatening
- In order to relieve the symptoms and reduce the effect of an allergic reaction, **antihistamines** can be taken which **bind to histamine receptors** on body cells and act as an **inhibitor** to prevent histamine binding



Antihistamines bind to the histamine receptors in the cell membrane blocking the histamine from binding

11.1.7 Monoclonal Antibodies


Your notes

Creating Hybridoma Cells

Introduction

- Monoclonal antibodies (Mabs) are **artificially produced antibodies** produced from a single B cell clone
- The **hybridoma method** is used to **make monoclonal antibodies**
- 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
- This method was established in the 1970s
- Monoclonal antibodies **bind antigens,** in the same way naturally produced antibodies

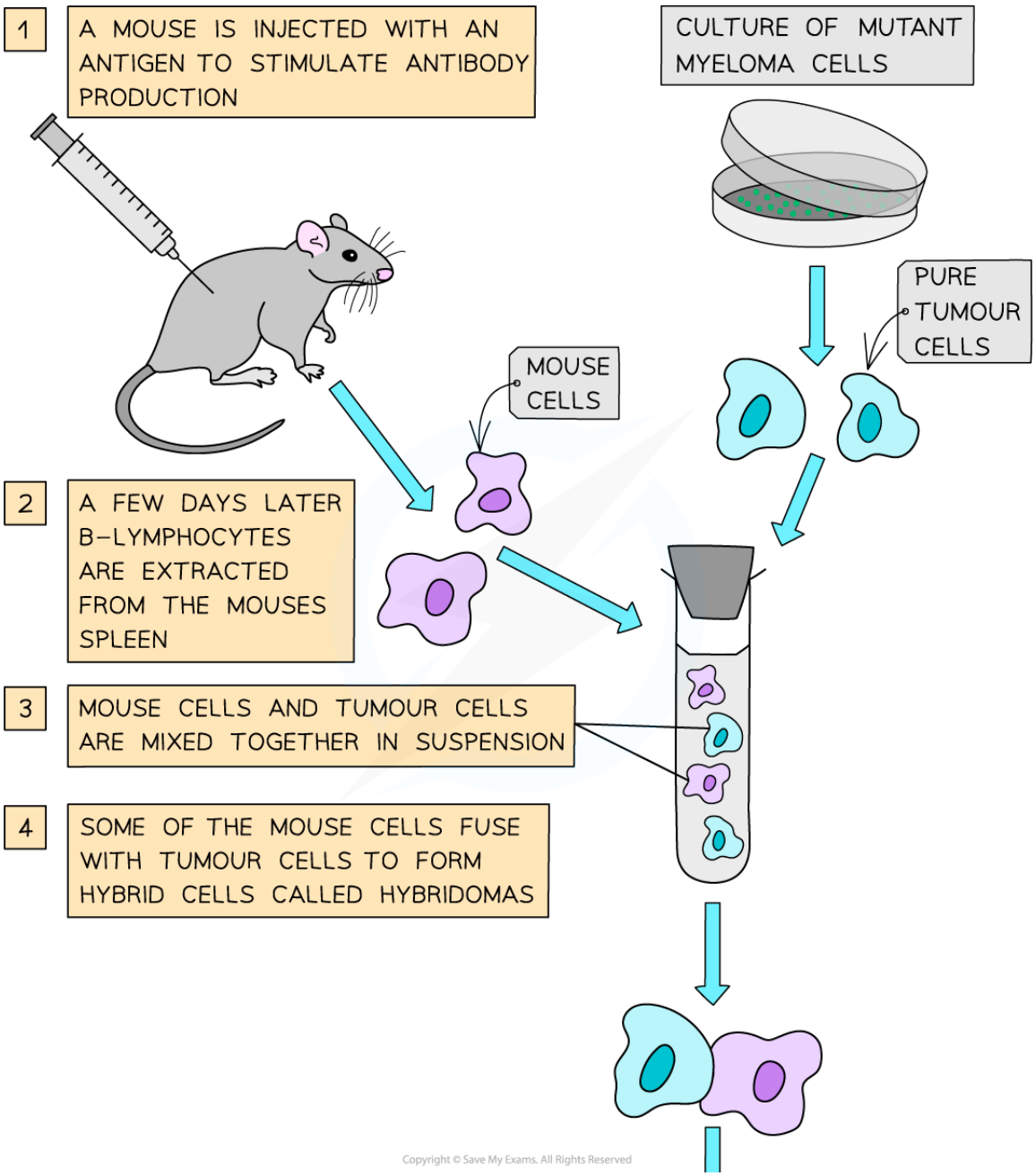
Creating Hybridoma cells

- Hybridoma cells are created by **combining specific antibody producing B cells with myeloma (tumour) cells**
- Plasma cells producing the required antibodies are **created by injecting mice with the target antigen** to trigger an immune response
- This results in plasma cells **producing the required antibodies** to complement the target antigen
- These plasma cells are removed from the spleen of the mouse before being **fused with immortal myeloma cells** cultured in the lab to make hybridoma cells
- Hybridoma cells producing the required monoclonal antibody can then be isolated and used in **large scale monoclonal antibody production**

Producing Monoclonal Antibodies

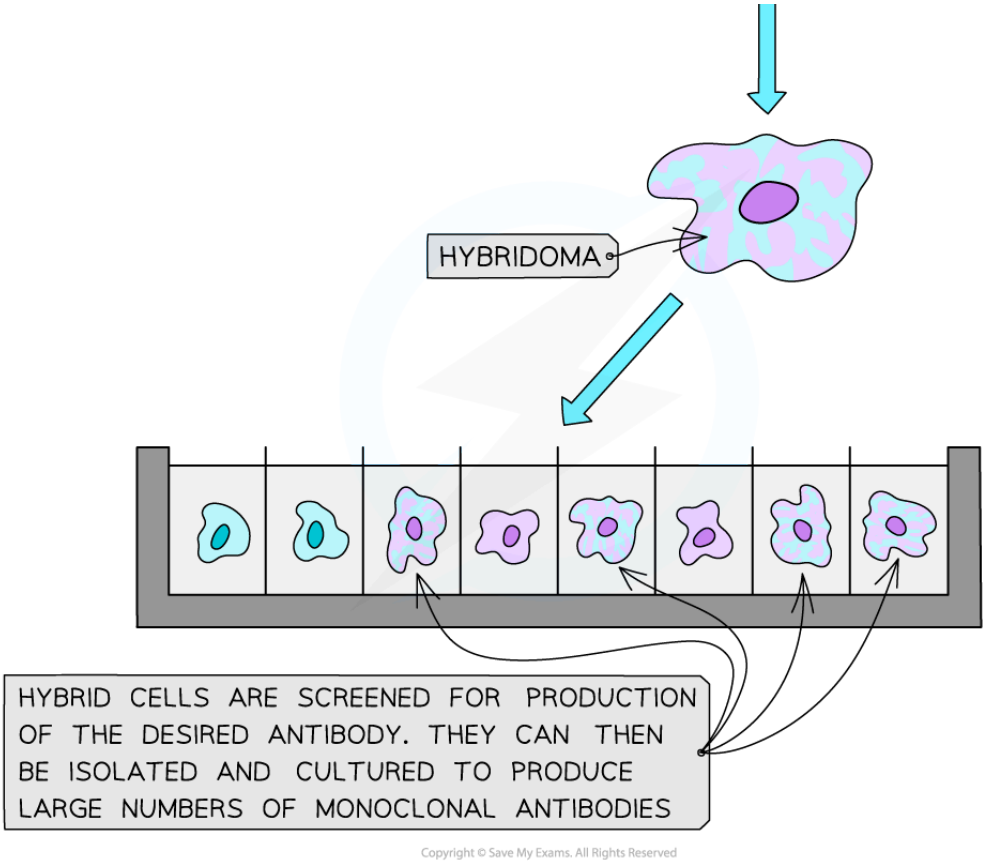

Your notes

- The hybrid cells produced using the hybridoma method above, are **grown in a selective growth medium**
- A mix of hybridoma cells producing several different types of antibody can then be **screened to identify and isolate the hybridoma producing the desired antibody**
- A **culture** of these hybridoma cells can then be encouraged to divide by mitosis in optimum conditions in a **fermenter** to **produce identical clones** all producing identical antibodies - monoclonal antibodies
- Monoclonal antibodies are **complementary to the original antigen** injected into the mouse initially
- Monoclonal antibodies have multiple applications to include the **diagnosis of many different diseases** such as HIV, malaria, COVID-19, or even the treatment of diseases such as rabies
- Additionally, they may be used in food safety testing and pregnancy testing



Your notes

Your notes

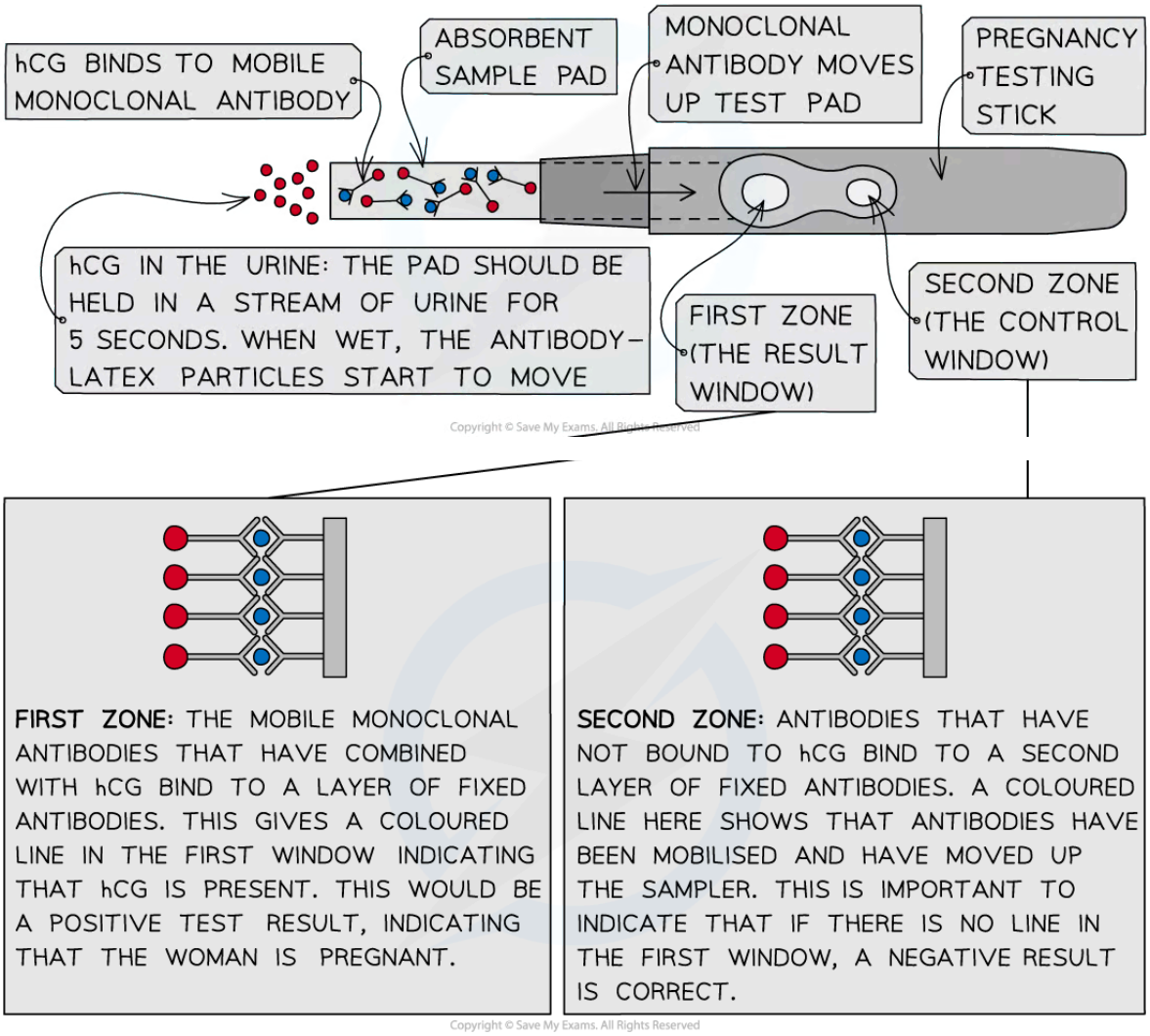


The hybridoma method is used to produce monoclonal antibodies

Pregnancy Test Kits

Your notes

- Urine samples can be used in **pregnancy testing**
- Pregnancy testing sticks **contain monoclonal antibody molecules** that are **specific to a hormone produced during pregnancy** (that therefore becomes present in the mother's urine)
  - This hormone is **human chorionic gonadotropin** (**hCG**), which is secreted by the early embryo after it has implanted in the uterus
  - The **antibodies** in the testing sticks all originate from a **single clone of B lymphocyte cells** that all produce the same antibody specific to hCG
  - This minimises the chances of false test results



Monoclonal antibodies are used to detect the presence of the hormone hCG in the urine of pregnant women.

Examiner Tip

Remember monoclonal antibodies are produced from a **hybridoma cell** - a cell formed by the **fusion of plasma cells and tumour (cancer) cells,** which divide continuously therefore producing large quantities of a wanted **antibody**.

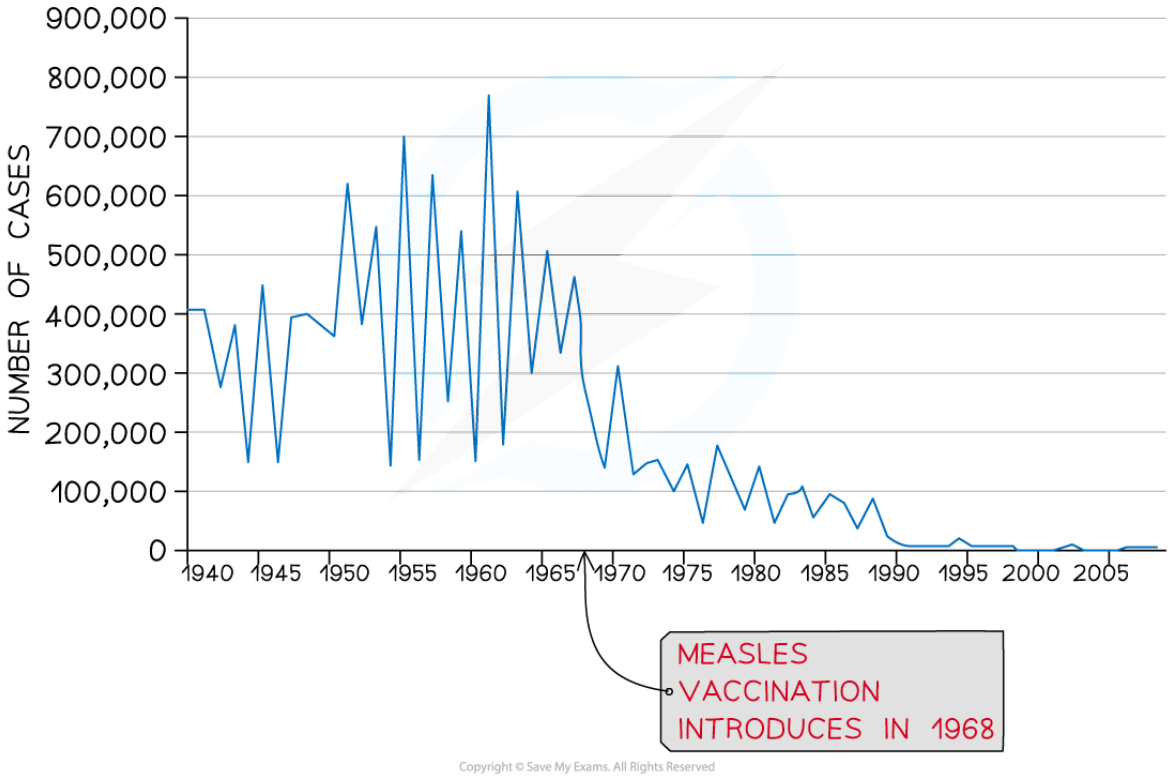
Your notes

11.1.8 Skills: Analysing Epidemiological Data

Your notes

Analysing Epidemiological Data

- **Epidemiology** is the study of the **distribution and incidence of diseases** in the population and the associated or contributory risk factors
- It has contributed to our **understanding of many diseases** including lung cancer and coronary heart disease
- Monitoring diseases in populations is important in understanding the seriousness of the disease and the mechanisms behind the spreading of the disease in order to develop contingencies to minimise the damage done
- Data collected can be used to **devise vaccination programs**, such as that used to eradicate polio in the 1980's
- It also allows more **specific targeting** of the spread of disease in smaller geographical regions and populations where outbreaks are documented
- Analysis of epidemiological data highlights trends in the **success of vaccination programs** and also highlights the failures e.g. When outbreaks occur due to lack of vaccination uptake



Epidemiological studies show the impact of a vaccination program on the incidence of measles

Important factors affecting epidemiological analysis


Your notes

- There are some factors that contribute to the analysis of disease that need to be considered:
  - **Populations generally increase** year on year which can contribute to an increase in outbreaks of disease
  - Improvements in **health care, sanitation**, and **medical advances** can influence data on disease
  - **Climate, disease presence and survival**, mean diseases exist at different levels of exposure in different regions