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11.1 Antibody Production & Vaccination

IB Biology - Revision Notes

11.1.1 Antigens

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

Exam Tip

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

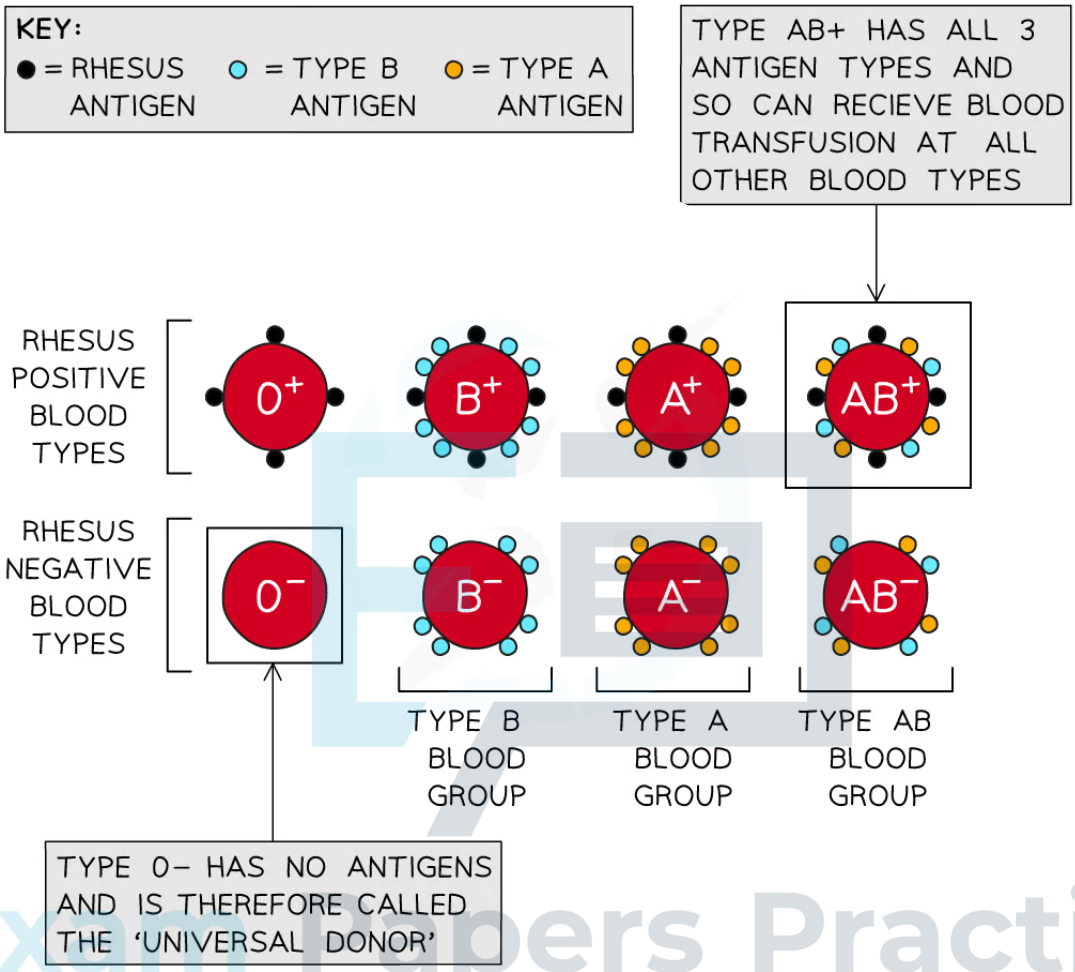
Blood Transfusions & Antigens

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



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

11.1.2 Specific Immune Response

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**

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

- **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

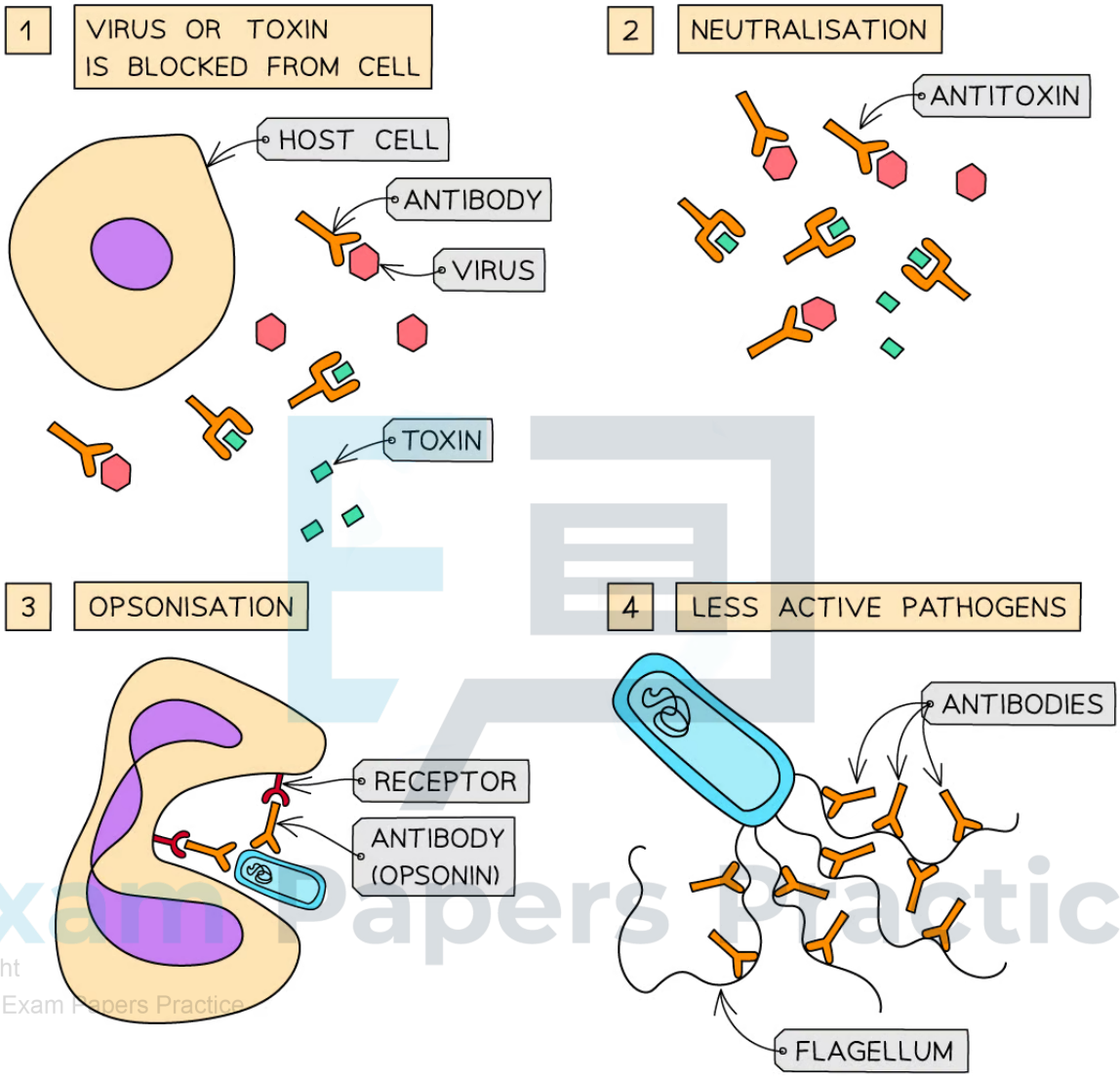
The primary and secondary immune response

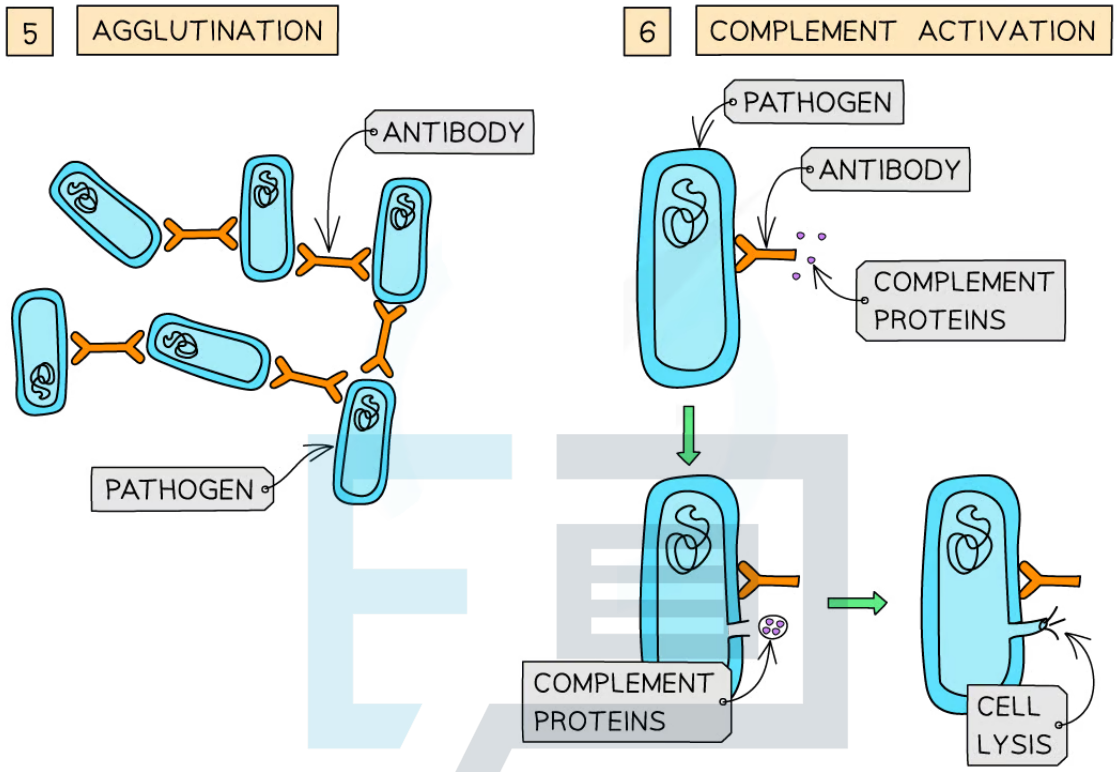
- A **primary immune response** occurs in response to a **newly encountered antigen**
  - This is a relatively **slow response** as the immune system takes time identifying the complementary antibody for each new antigen it encounters
  - The infection may result in **symptoms being presented** whilst 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

11.1.3 Antibodies, Vaccines & Immunity

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

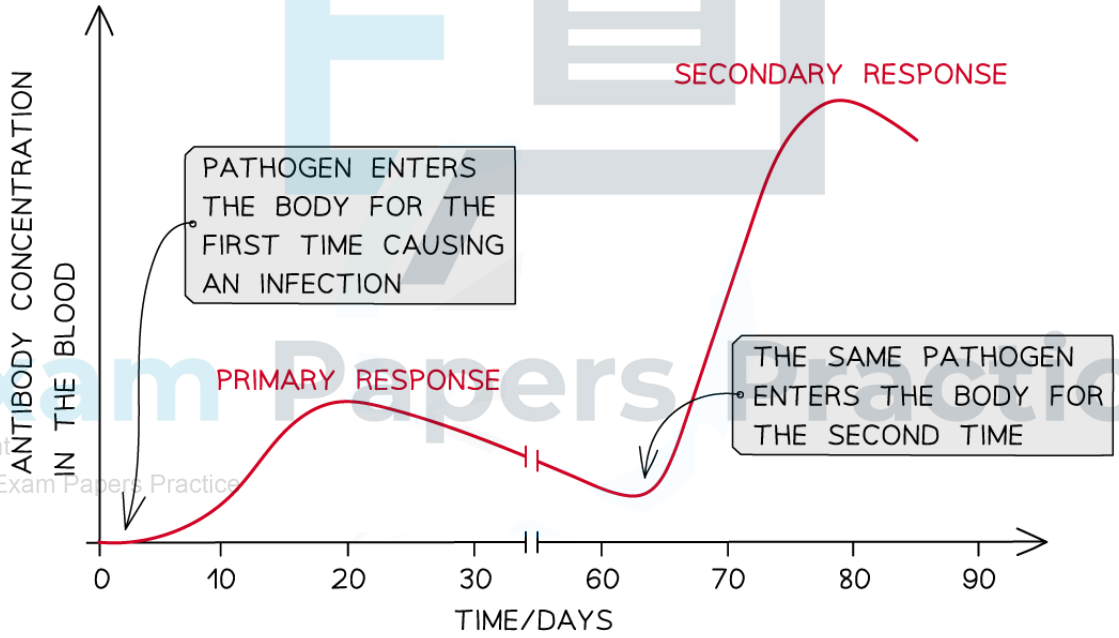




The functions of antibodies vary according to which type of antigen they act on

Immunity

- 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

Vaccines & Immunity

- 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**

11.1.4 Smallpox Vaccine & Eradication

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

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

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

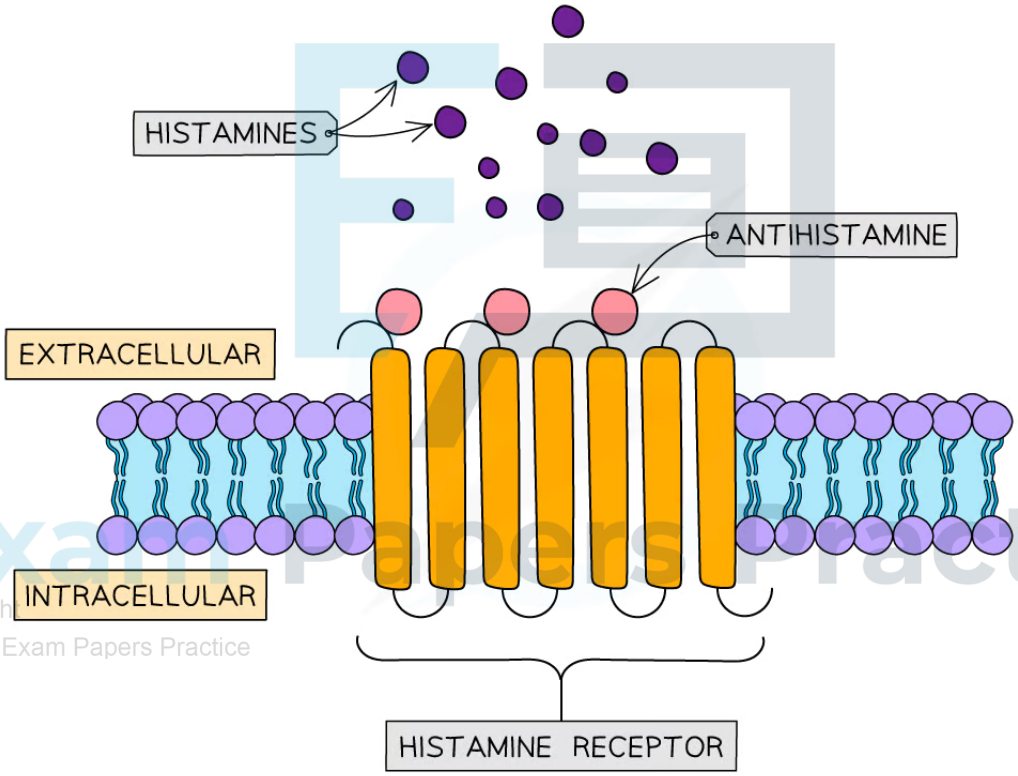
11.1.6 Histamines

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

Effects of Histamines

- 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

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

- 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

Pregnancy Test Kits

- 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