Extension Topic A: Infectious Diseases (Part 1)

1. Introduction

Immunology is the study of the body's defence against infection at cellular and molecular levels. The following are the questions we would address in this topic:

How does the body prevent pathogens from entering the body?

When infection occurs, how does the body eliminate the pathogen?

How does the body develop long-lasting immunity to many infectious diseases we encountered once before?

2. Learning Outcomes

a. Describe the specific (adaptive) and non-specific (innate) immune systems including active and passive, natural and acquired immunity.

b. Outline the roles of B lymphocytes, T lymphocytes, antigen-presenting cells and memory cells in specific primary and secondary immune responses.

c. Explain the relationship of the molecular structure of antibodies to their functions, using IgG as an example.

d. Explain how genetic recombination during development results in millions of different antibody molecules (including somatic recombination, hyper-mutation and class switching).

3. References

Judith Owen, Jenni Punt, Sharon Stranford. Kuby Immunology, 7th Edition.

Murphy KM, P Travers, M Walport (Eds.) Janeway's Immunobiology. 8th Edition.

Pommerville, Jeffrey C. Alcamo's Fundamentals of Microbiology: Body Systems.

Contents

4. Pathogens, Antigens and Epitopes

Notes to self

Infection is the process where a **pathogen** invades and multiplies in its host. There are 5 classes of pathogens that **invade the body to cause diseases**: viruses, bacteria, fungi, protozoa and worms.

A pathogen has many different components that can be recognised by cells of the immune system i.e. many different **antigens**. Antigens are substances that **induce an immune response** as they are **recognised by cells** of the immune system and **antibodies**. An antigen can be a foreign protein, carbohydrate, lipid or nucleic acid. e.g. a bacterium's antigens can be found on its cell wall and flagellum, a virus's antigens can be found on its viral glycoprotein.

Cells of the immune system and antibodies usually do not bind to the entire antigen molecule. **Epitopes** are the **parts on a single antigen** that contact the antigen-binding site of an antibody or T cell receptor. An epitope is also known as an **antigenic determinant**. (Fig. 1)

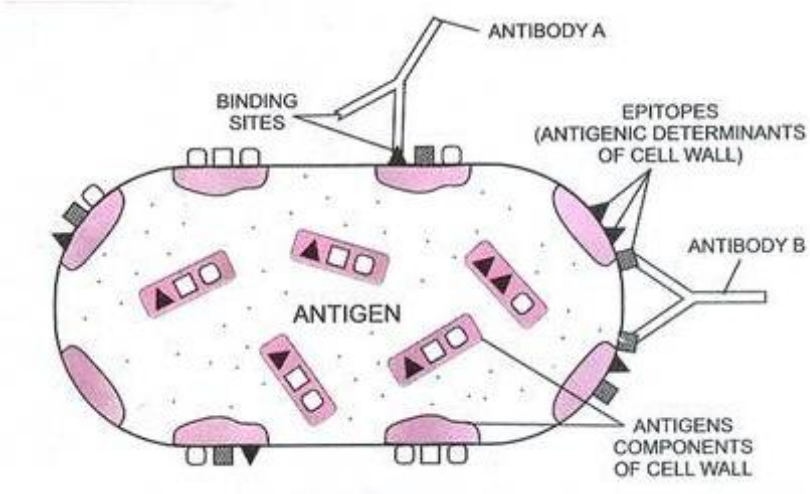
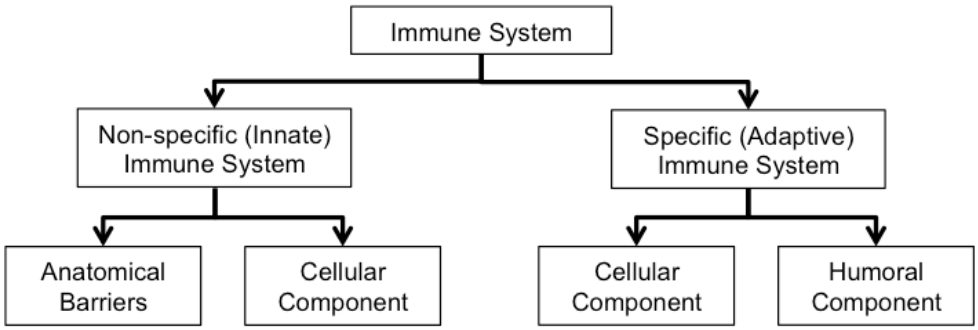


Fig. 1: Diagram showing an antigen with epitopes (antigenic determinants); an antigen has many epitopes. Two attached antibodies are also shown.

5. Overview of the Components of the Immune System

The immune system is typically divided into two categories, the non-specific **innate immune system** and the **adaptive immune system**:



Notes to self

The innate immune system has anatomical features that function as **barriers to infection**.

"Humoral" comes from the term, humour, which means body fluid. Thus, "humoral" refers to molecules found in extracellular fluid such as **secreted antibodies**.

Most cells of the immune system are derived from **hematopoietic stem cells** and develop through the process of **differentiation** into functionally mature blood cells of different lineages.

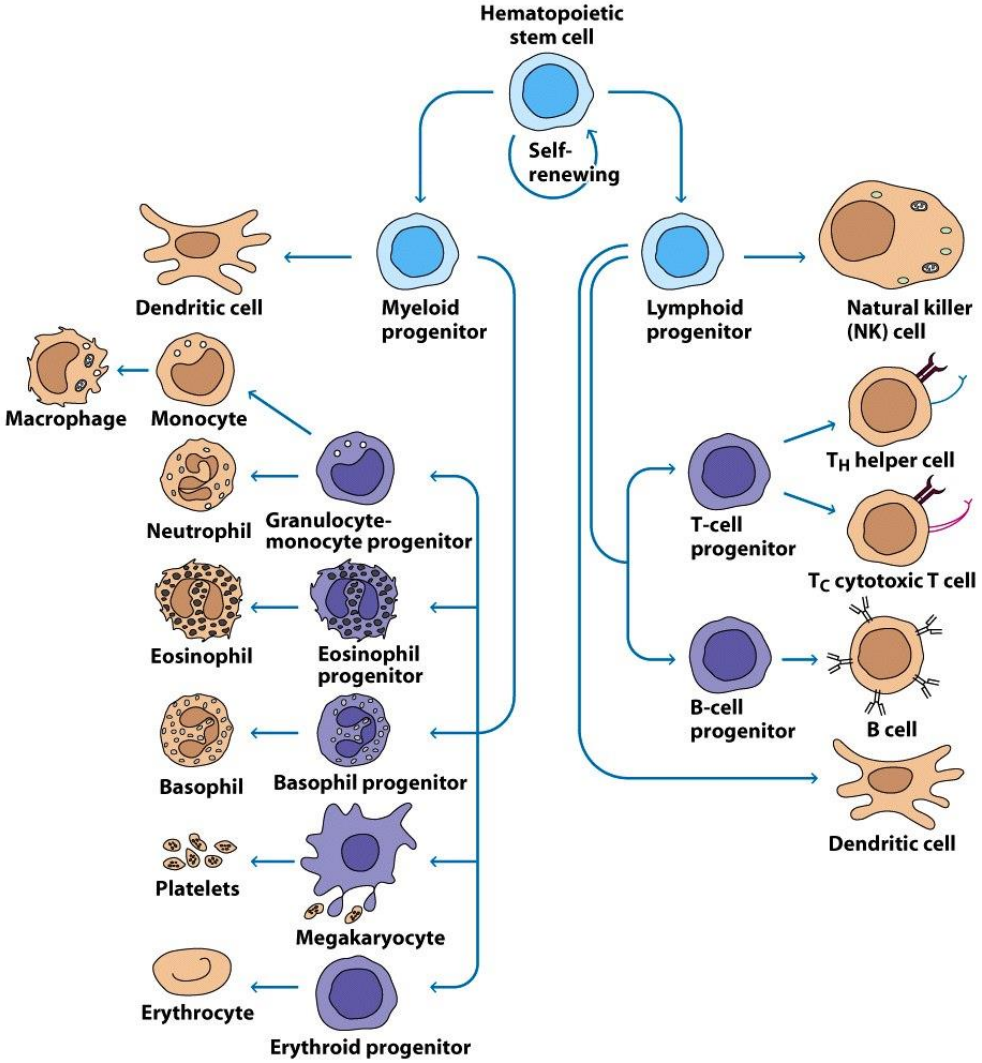


Fig. 2: Haematopoietic stem cell differentiates to either myeloid progenitor cell or lymphoid progenitor cell. Progenitor cells cannot self-renew and are committed to a particular cell lineage. (Source: Kuby Immunology 7th Edition)

Cellular components of innate immunity e.g. **phagocytes such as macrophages, dendritic cells and neutrophils**. Neutrophils are found in the bloodstream while macrophages and dendritic cells mostly reside in tissues of the body.

Cells involved in adaptive immunity e.g. lymphocytes such as **T lymphocytes (or T cells)** and **B lymphocytes (or B cells)**.

Notes to self

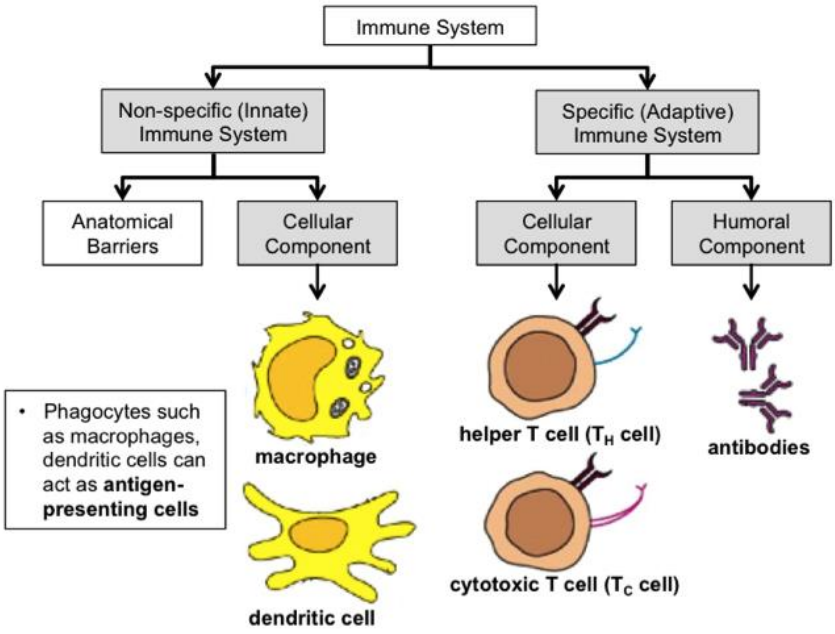


Fig. 3: Summary of components of the non-specific innate immune system and specific adaptive immune system.

Although the innate and adaptive immune systems have distinct characteristics, there is interplay between these two systems. Components of innate immune system influence the adaptive immune system and vice versa.

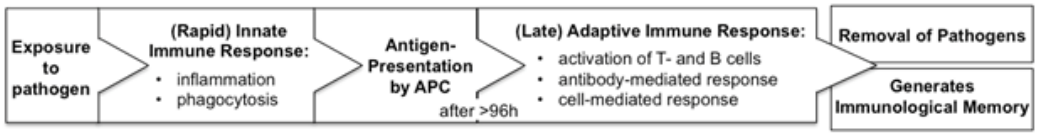
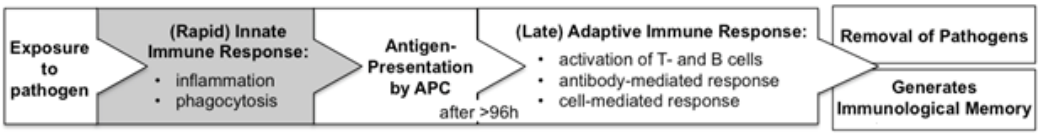


Fig. 4: Overview of Immune Response

6. Immune Response - Innate Immunity



The non-specific innate immune system is the first line of defence upon exposure to a pathogen. Any pathogen that breaches the **anatomical barrier** (e.g. **skin** is the first line of defence of innate immunity) will be greeted by **cells of innate immunity** (e.g. **macrophage** is the second line of defence of innate immunity). Macrophages are always present under the skin and other tissues to function as "guards" against any pathogen that has penetrated the anatomical barrier.

Innate immunity is **not specific** to any pathogen and has **no memory** (i.e. no improved response on repeated exposures to same pathogen).

Notes to self

This response to an encounter with a pathogen occurs **rapidly**. The first line of host defence is immediate as it consists of mechanisms that are **ready to kill** and resist an invader at any time.

First line of defence of innate immunity (anatomical barriers to infection):

- Epithelial cell layers such as **skin**, mucous membranes lining the respiratory tract and gastrointestinal tract are barriers that prevent penetration of microorganisms.
- Secretions such as **saliva** and **tears** wash away potential invading microorganisms to prevent their attachment.
- These secretions also contain antimicrobial substances to kill these microorganisms. e.g. **lysozyme** is an antibacterial protein that cleaves glycosidic bonds of peptidoglycans in cell walls of bacteria, leading to lysis.
- Other chemical barriers include acidic **pH**.

Some pathogens may have evolved strategies to penetrate the epithelial cell barrier, or wounds may have disrupted the epithelial layer to allow pathogens to enter the body. The second line of defence occurs to **kill the pathogen**.

Second line of defence of innate immunity (cellular components):

- Cellular components of innate immunity e.g. **phagocytes such as macrophages, dendritic cells and neutrophils**.
- Most tissues contain resident populations of macrophages that function as 'guards' for innate immune system. These macrophages can recognise these pathogens that have penetrated the epithelial barrier and carry out **phagocytosis**. (Fig. 5)

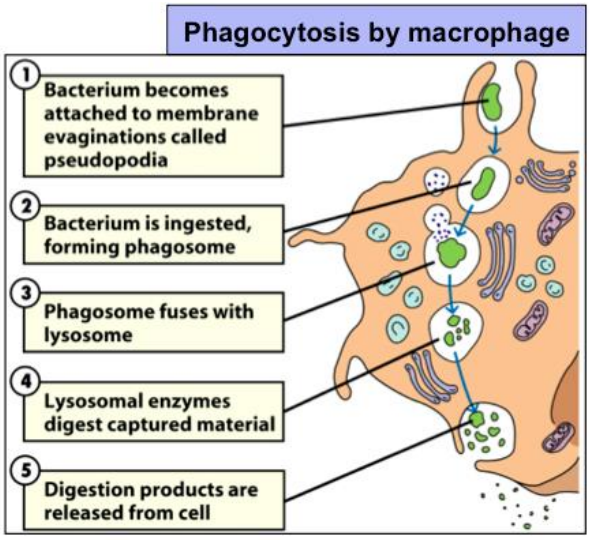


Fig. 5: Phagocytosis and degradation of pathogen

- Other roles of macrophages:
  - Clears dead cells and cell debris by phagocytosis when there is no exposure to pathogen.
  - Acts as **antigen-presenting cell** to activate adaptive immune response.
  - **Induce inflammation** by secreting signalling proteins e.g. cytokines and chemokines.

- Role of neutrophils:
  - Neutrophils circulate in the blood and respond to an infection by migrating to the site of infection and then leave the blood capillaries to the damaged tissue to carry out phagocytosis. They are short-lived as after engulfing the pathogens and destroying them, neutrophils die.

Notes to self

The innate immune system also initiates steps to bring the pathogen to the attention of lymphocytes to **activate the adaptive immune system** by **antigen presentation**. This is to resolve the infection successfully should the pathogen evades innate immune responses.

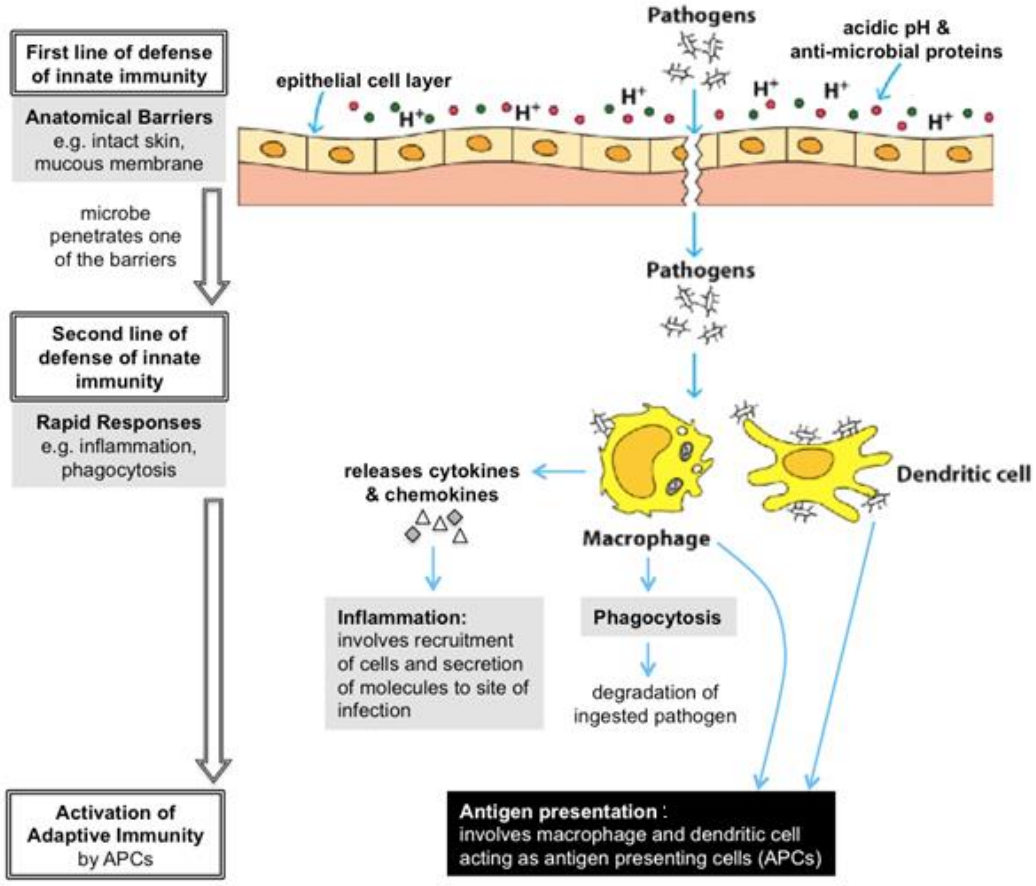


Fig. 6: Overview of the innate immune responses. (Modified: Kuby Immunology 7th Edition) Note: Cytokine is a small signalling protein made by a cell that affects the behaviour of other cells, e.g. to stimulate proliferation and differentiation of T cells during T cell activation. Chemokine is a small chemoattractant protein that stimulates the migration and activation of cells such as phagocytic cells and lymphocytes.

Notes to self

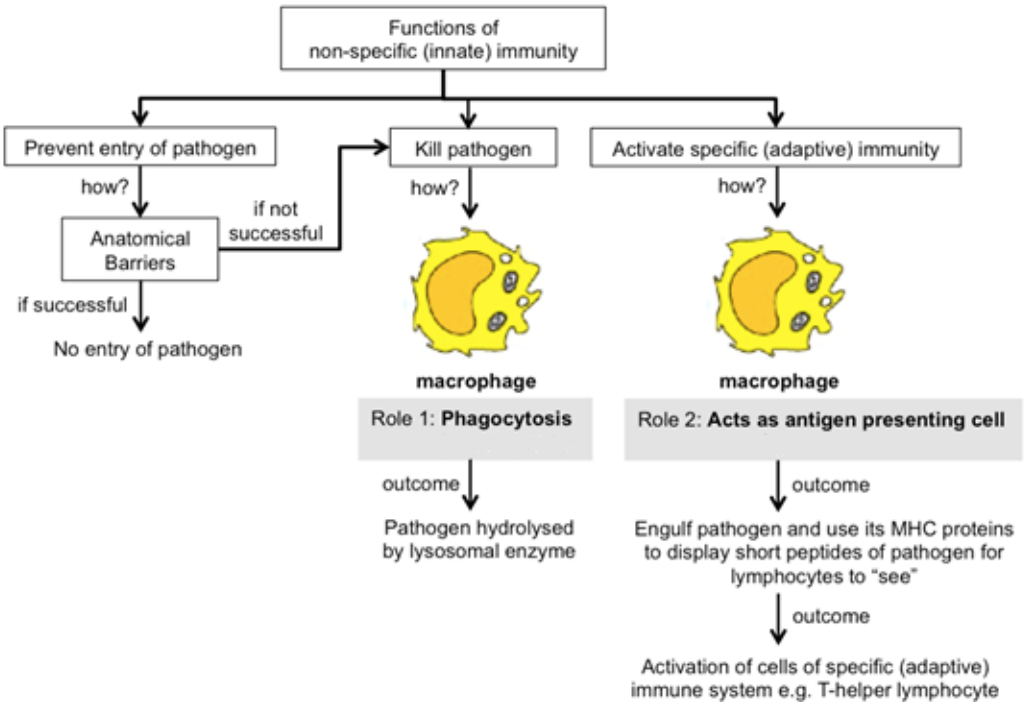
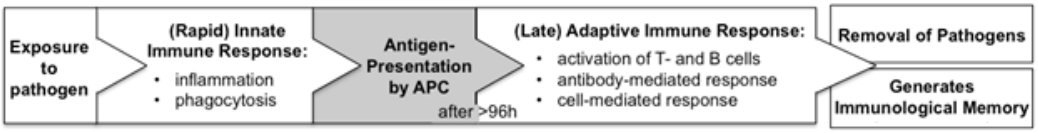


Fig. 7: Summary of the role of innate immunity in response to pathogen infection.

7. Antigen Presentation



Antigen presentation is the display of peptides bound to membrane proteins called MHC (major histocompatibility complex) proteins on the surface of an **antigen-presenting cell** (APC).

APCs such as macrophages and dendritic cells take up antigens via phagocytosis and process ('cut up') them into short peptides before presenting the peptides on their surface to naïve T cells.

Notes to self

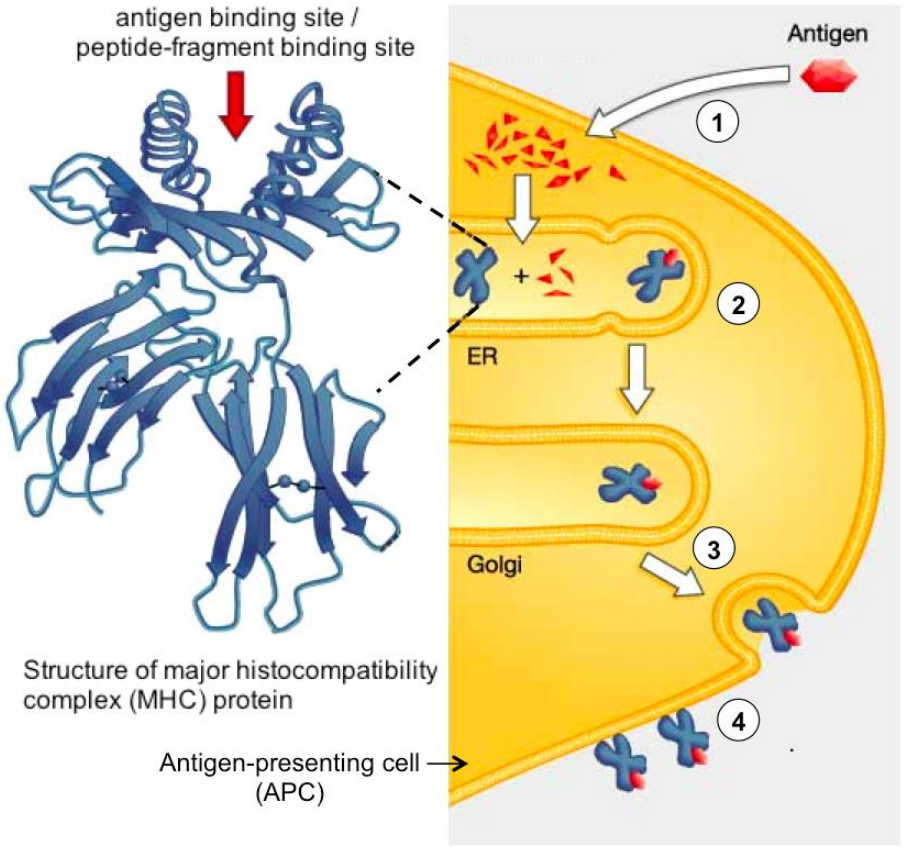


Fig. 8: The expression of antigen on MHC protein at the cell surface membrane of APC.

Antigens presented are recognised by specific T cell receptors on **naïve T cells** and this results in **activation** of these cells to **effector T cells**. APC is therefore a link between the innate and adaptive immune systems.

- Naïve cells have not encountered the specific antigen that they are programmed to respond to.
- Effector cells have been activated by APCs or antigens and ready to function in an immune response.

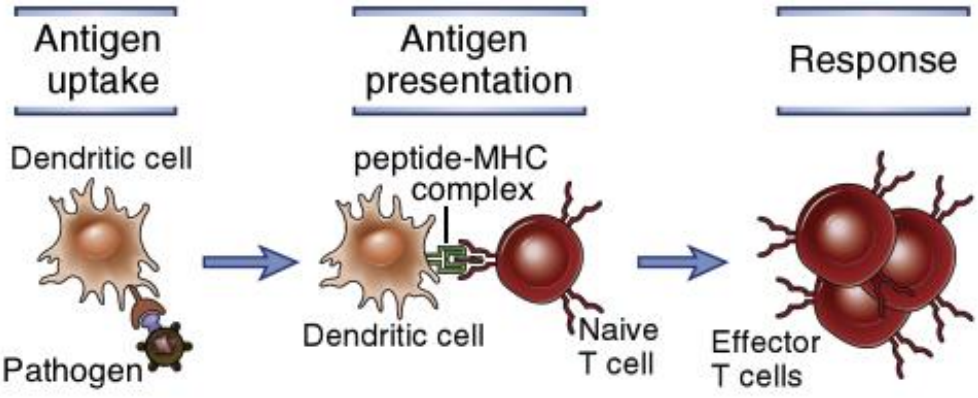
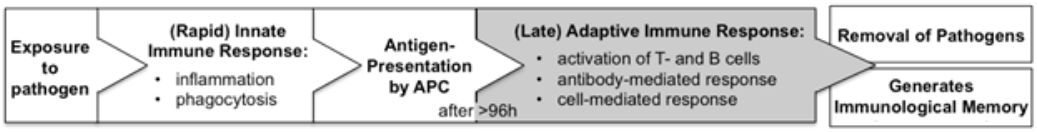


Fig. 9: Dendritic cell acts as APC to display antigen on MHC protein to naïve T cell. (Modified: Cellular and Molecular Immunology, Abul K. Abbas)

8. Immune Response - Adaptive Immunity

Notes to self



The innate and adaptive immune responses make up an integrated host defence system where APCs link the two immune systems. Innate immune response sets the scene for the induction of adaptive immune response which requires a few days to establish.

Adaptive immune response involves the **activation of T cells** and **activation of B cells** with the eventual production of specific **antibodies** to clear the infection.

a. Activation of T Cells & Role of T Cells in Adaptive Immunity

Recall:

Antigen-presenting cells (APCs) e.g. macrophages and dendritic cells are phagocytic cells that:

Phagocytose pathogens and process ('cut up') the **antigens** from the surface of the pathogen into short peptides

↓

peptides of **antigens are bound to MHC proteins** to form peptide:MHC complex

↓

peptide:MHC complex are presented at the cell surface membrane of APC

↓

APC **presenting** the short peptides from **antigen to naïve T cells**

Only the **specific** naïve T cell with **T cell receptor (TCR)** that is **complementary conformation** to the antigen displayed on MHC protein on APC can bind.

After antigen presentation, the specific naïve T cell becomes **activated** to undergo:

1) **clonal expansion** (i.e. a single cell stimulated to undergo proliferation to produce large numbers of genetically identical daughter cells), and
2) **differentiation** into **effector T cells** (e.g. either **T helper cells** or **cytotoxic T cells**) that are ready to function in the adaptive immune response.

After carrying out their respective functions, at least 90% of these effector cells die by apoptosis and the rest differentiate to **memory T cells** (refer to section on immunological memory).

Notes to self

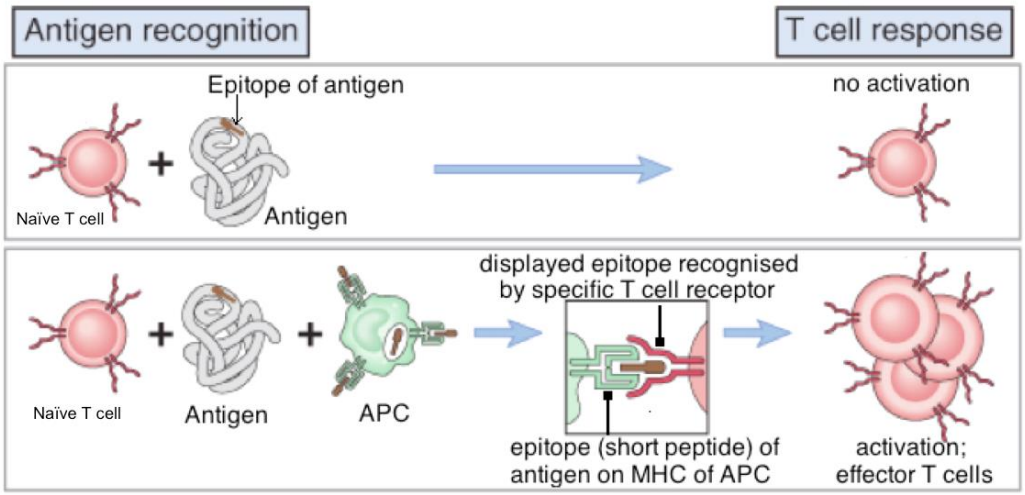


Fig. 10: APCs are required for activation of specific naïve T cells to form effector T cells (e.g. cytotoxic T cells or T helper cells). The antigen has to be processed into short peptides and the epitope displayed on MHC protein, before the complementary T cell receptor on the surface of T cells can recognise and bind. (Modified: Cellular and Molecular Immunology, Abul K. Abbas)

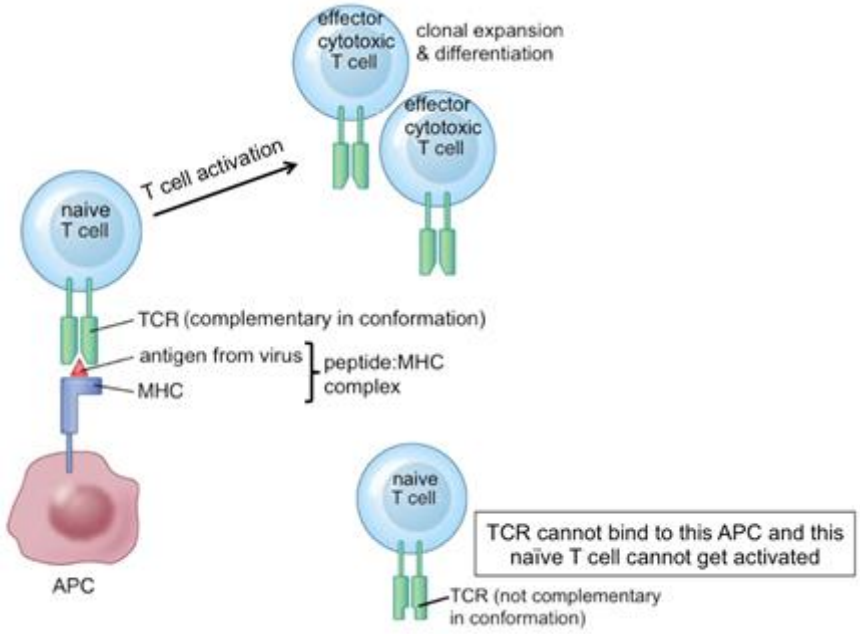


Fig. 11: Only specific naïve T cells will bind to a specific antigen displayed on surface of APC.

Role of cytotoxic T cells: to kill infected cells.

Notes to self

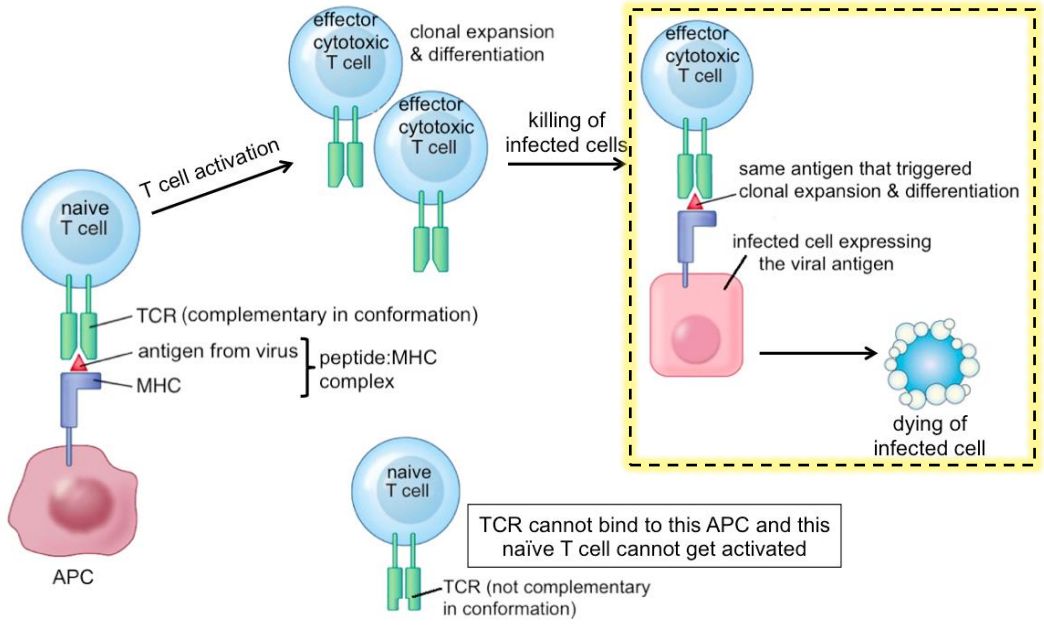


Fig. 12: Role of cytotoxic T cells is to kill infected cells.

How do cytotoxic T cells kill infected target cells?

Cytotoxic T cells release **pore-forming molecules** called **perforins** as well as **granzymes**. Perforin forms pores in the infected cell's membrane which can eventually lead to **cell lysis**. These pores also allow for granzymes to diffuse in and activate enzymes involved in **apoptosis of the infected cell**.

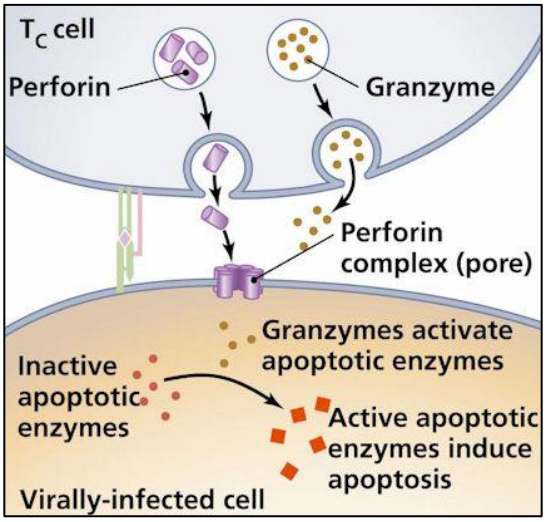


Fig. 13: Two killing methods by cytotoxic T cell (T_C cell) on infected target cell.

Role of T helper cells:
activate specific B cells to make antibodies for **antibody-mediated response**, via secretion of cytokines.

Unlike cytotoxic T cells, T helper cells do not directly participate in destruction of pathogens.

b. Activation of B Cells & Role of B cells in Adaptive Immunity

Notes to self

2 processes are required to activate B cells:

- Binding of antigen to the specific B cell receptor on B cells
- T helper cell with specific T cell receptor that binds to the peptide:MHC complex on cell surface membrane of B cells

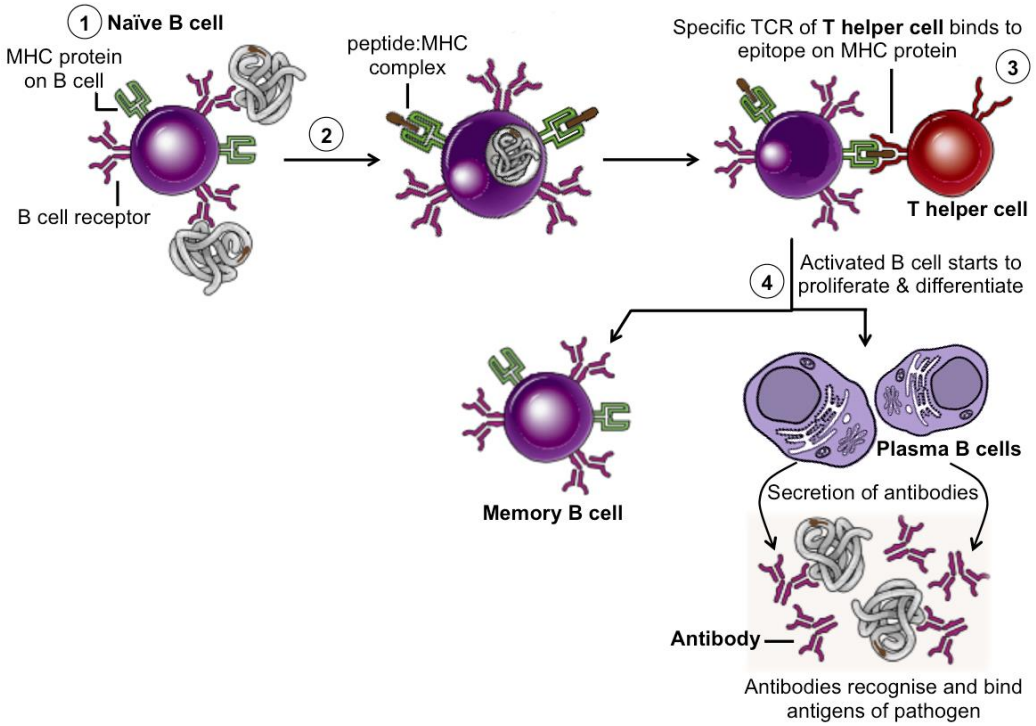


Fig. 14: T helper cells are required to stimulate activation of B cells to proliferate and differentiate into antibody-secreting plasma cells.

B cell activation:

(1) Each B cell has one **specific** type of **B cell receptor** (BCR) on its cell surface that can recognise an epitope and **bind** to the **specific antigen**. When a B cell encounters the antigen with epitope that is complementary to its BCR, antigen binding occurs.
(2) The BCR together with the bound antigen are endocytosed into the B cell. The antigen is processed into short peptides and attached to MHC proteins.
(3) The peptide:MHC complexes are transported to the cell surface membrane of B cell where the peptide is recognised and bound by **antigen-specific T helper cell**. (Recall that antigen-specific T helper cells are derived from activation of naïve T cells through antigen presentation)
(4) The interaction between T helper cell and B cell stimulate cytokine secretion from T helper cell. In turn, these cytokines activate the antigen-specific B cell to undergo clonal expansion. Some of these cells of the expanded B cell population **differentiate** into two types of cells:
    - **antibody-secreting plasma cells**
    - **memory B cells**

Notes to self

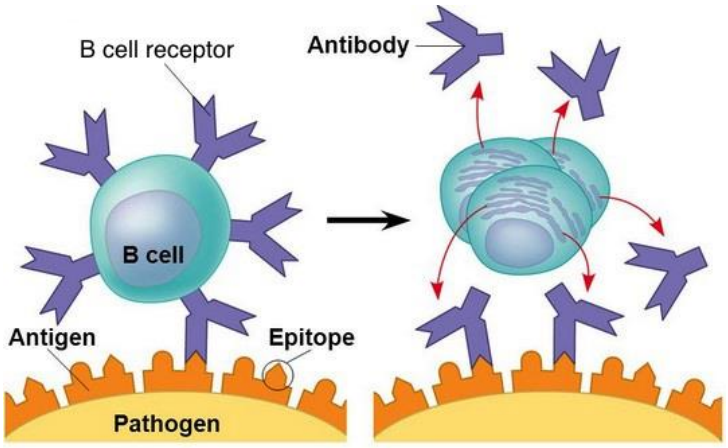


Fig. 15:
Upon B cell activation with the help from T helper cell, B cell differentiates into antibody-secreting plasma cell.

Role of Plasma cells:

In **antibody-mediated response**, the antibodies secreted by plasma cells protect the body against **extracellular pathogens** and **toxins** secreted by pathogens into extracellular space.

Antibodies mediate the clearance and destruction of pathogens in a variety of ways:

- **Neutralisation of pathogen or toxin**
  Antibodies recognise and bind to the antigens on the pathogen to prevent the pathogen from attaching to specific host cell receptor and gain entry into host cell. Neutralisation by antibodies is also important in preventing bacterial toxins from entering host cells.

- **Opsonisation to facilitate phagocytosis**
  Opsonisation is the process of binding of antibodies to the antigens on pathogen to mark the pathogen for uptake by phagocytes.

Notes to self

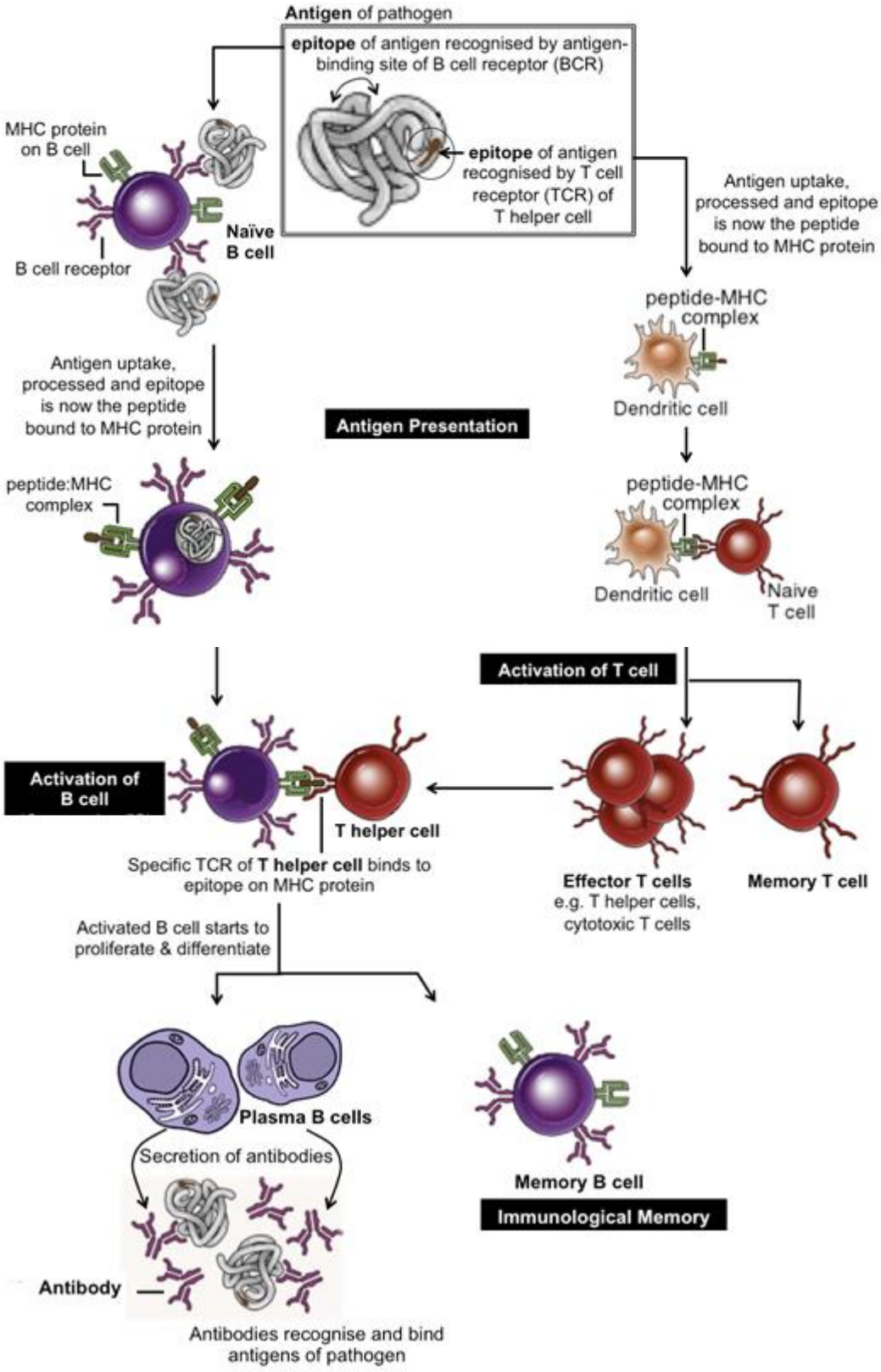


Fig. 16: Overview of how naïve T and B cells become activated to become effector cells.

Notes to self

In Summary:

The adaptive immunity consists of **cell-mediated immune response** and **antibody-mediated response**.

Lymphocytes such as **T and B cells** make up the cellular component of adaptive immunity:

- Each B cell and T cell is specific for a particular antigen.
- Each T cell has a **specific** type of **T cell receptor** on its cell surface that can recognise and bind to specific antigen.
- Each B cell has a **specific** type of **B cell receptor** on its cell surface that can recognise and bind to specific antigen. B cell receptor is structurally different from T cell receptor. B cell receptor also binds to a different epitope of an antigen from T cell receptor.

Cell-mediated immune response mediated/brought about by T cells will protect against intracellular pathogens by killing cells that contain these pathogens. This response will also protect against extracellular pathogens by helping to activate B cells to become antibody-secreting plasma B cells.

Antibody-mediated response is mediated/brought about by the antibodies that are secreted by plasma B cells. This response will protect against extracellular pathogens and toxins secreted by pathogens into extracellular space.

Key characteristics of adaptive immunity are:

- high level of **specificity** for a particular pathogen
- shows **memory** (i.e. remembers the particular pathogen that previously invaded the body and **responds more quickly** to the re-exposure to the **same pathogen**)

c. Antibodies (or Immunoglobulins)

Notes to self

Antibodies belong to a family of globular proteins called immunoglobulins (Ig). They are secreted by plasma B cells to mediate the clearance and destruction of pathogens in a variety of ways.

There are 5 different classes of antibodies, IgG, IgM, IgA, IgD and IgE. IgG is the predominant antibody in blood serum.

	IgG	IgM	IgA	IgD	IgE
Secreted forms of Ig					
Heavy chain	gamma chain	mu chain	alpha chain	delta chain	epsilon chain
Light chain	kappa chain or lambda chain				
No. of antigen binding sites	2	10	4	2	2

Fig. 17: Different classes of immunoglobulins.

<u>Structure of IgG</u>:

IgG is a globular protein with **quaternary structure**.

- Consists of **4 polypeptide chains** (2 identical **heavy chains** and 2 identical **light chains**).
- Each light chain pairs with a heavy chain, held together by disulfide bonds and non-covalent interactions e.g. hydrogen bonds, hydrophobic interactions, ionic bonds.
- The 2 heavy chains are linked by disulfide bonds and non-covalent interactions.

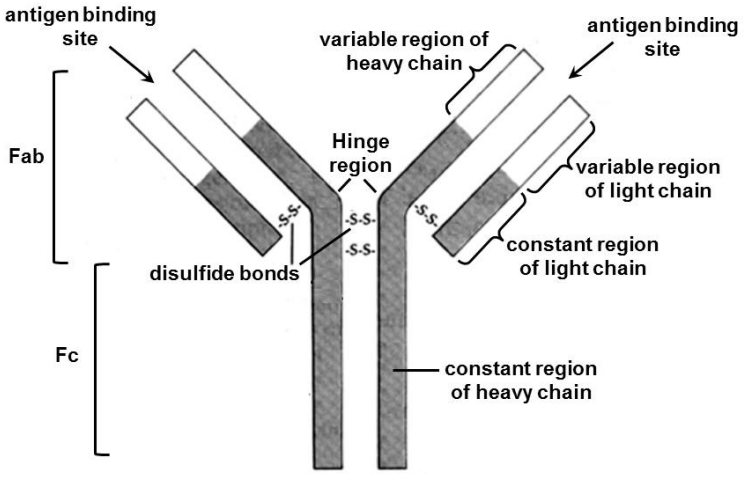


Fig. 18: Structure of IgG.

Each light chain is divided into 2 regions, the **variable (V_L) region** and **constant (C_L) region**.

Notes to self

Each heavy chain is divided into 2 regions, the **variable (V_H) region** and **constant (C_H) region**.

In the quaternary structure, **one V_H** and **one V_L** are brought together to form **one antigen-binding site**, which is specific to bind to an epitope of an antigen.

Each antibody has **2 identical antigen-binding sites**.

Each IgG has **2 Fab** (fragment of antigen-binding) portions and **1 F_C** (fragment crystallisable) portion.

- **Fab** portion of the antibody contains **antigen-binding site** to **bind** to **epitope of antigen**. This allows antibody to bind to and prevent the pathogen or toxin from attaching to host cell receptor. Antibodies therefore **neutralises the pathogen or toxin**.
- After antibodies bind to a pathogen, **Fc** portion of these antibodies **binds to the Fc receptor** on the phagocyte to **promote phagocytosis**. The F_c portion therefore is involved in **opsonisation**.

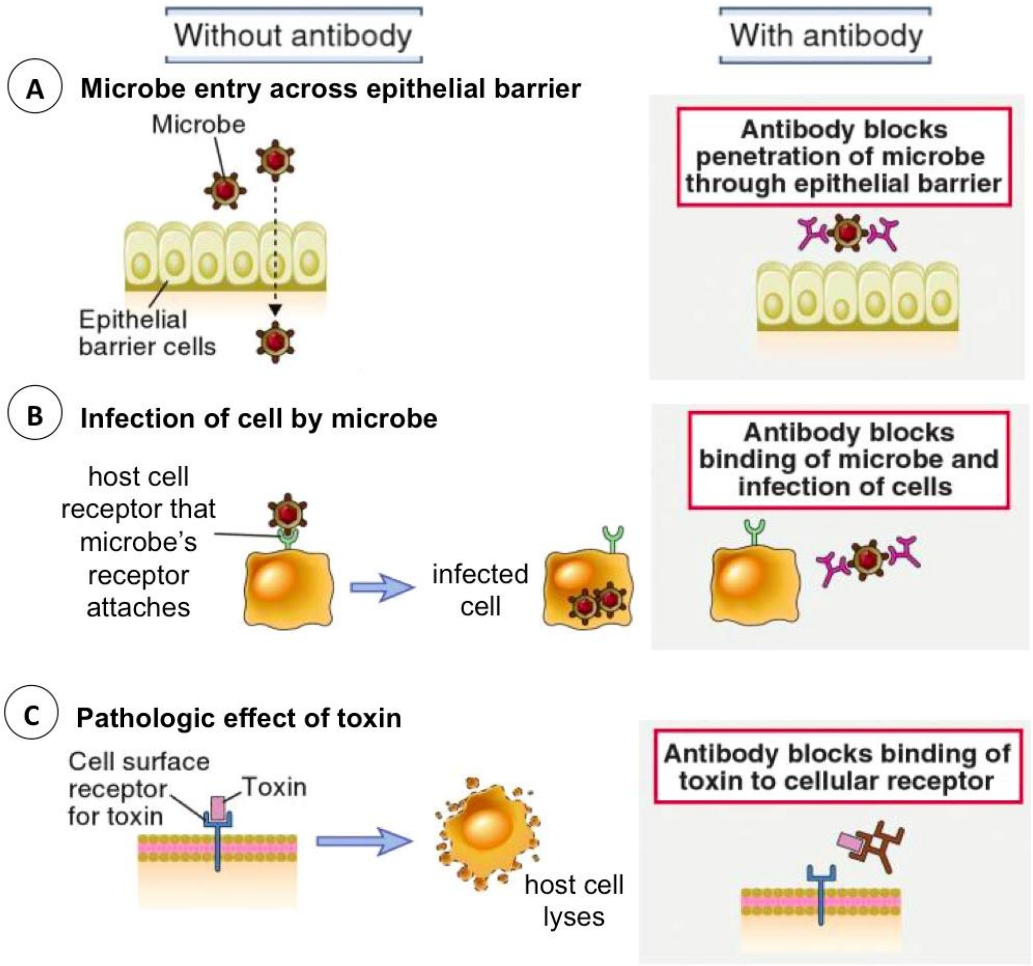


Fig 19: Neutralisation of pathogen or toxin by antibodies at their Fab portions.

Notes to self

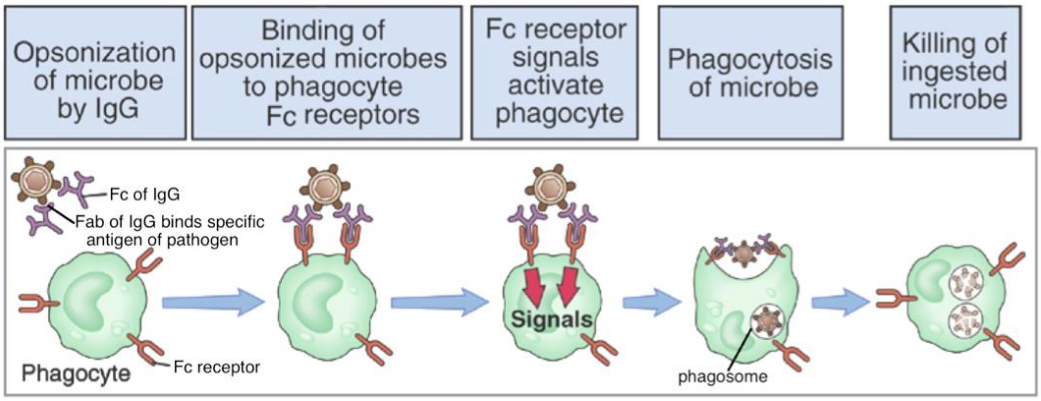


Fig. 20: Opsonisation by antibodies to promote phagocytosis to destroy the pathogen.

Fab and Fc portions are joined at the **hinge region**, which is a short sequence of amino acid residues (Fig. 16). This hinge region enables the antibody molecule to be **flexible**. Flexibility at the hinge region allows Fab portion to adopt a wide range of angle, thus allowing antibody to **bind to epitopes** that are spaced at variable distances apart.

9. Mechanisms to Generate Huge Variety of Antibodies

Notes to self

Chromosomal locations of immunoglobulin genes in human:

- Heavy chain gene locus is on chromosome 14;
- Kappa (κ) light chain gene locus is on chromosome 2;
- Lambda (λ) light chain gene locus is on chromosome 22.

A **heavy chain gene** contains **V** (variable) **gene segments, D** (diversity) **gene segments, J** (joining) **gene segments** and **C** (constant) **segments**.

A **light chain gene** contains **V** (variable) **gene segments, J** (joining) **gene segments** and **C** (constant) **segments**.

The **multiple gene segments** contribute to the vast number of heavy chain gene and light chain gene diversities.

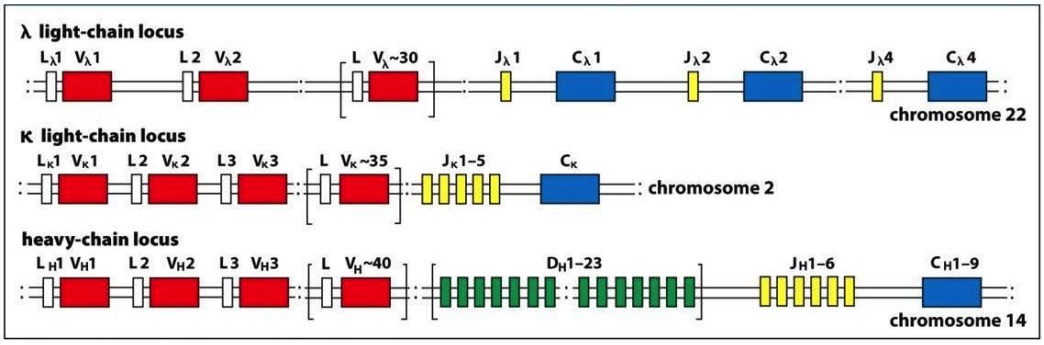


Fig. 21: Immunoglobulin (Ig) heavy and light chain gene loci.

The number of heavy and light chains that can be produced by human is more than the number of genes in the entire human genome. What mechanism(s) could lead to this? The mechanisms for generating antibody diversity are:

- somatic recombination (or VDJ recombination)
- somatic hypermutation
- combinatorial pairing of heavy and light chains
- class switching

a. Somatic Recombination / V(D)J Recombination

Somatic recombination or **V(D)J recombination** is a type of **DNA rearrangement** where gene segments that are initially separated from one another are brought together by enzymatic removal of intervening sequences followed by joining of the gene segments. Somatic recombination occurs **during B cell development in the bone marrow**.

VDJ Recombination & Heavy Chain Production:

The process of **VDJ recombination** at the **heavy chain gene locus** involves selection of one V segment, one D segment and one J segment to form a rearranged VDJ segment. The rearranged VDJ segment **codes for the variable region of heavy chain (V_H)**.

Steps involved in the production of heavy chain in an immature B cell:

Notes to self

(1) **Rearrangement of a D gene segment with a J_H gene segment** forms DJ rearrangement.
(2) **Rearrangement of a V gene segment with the DJ rearrangement** forms VDJ rearrangement.

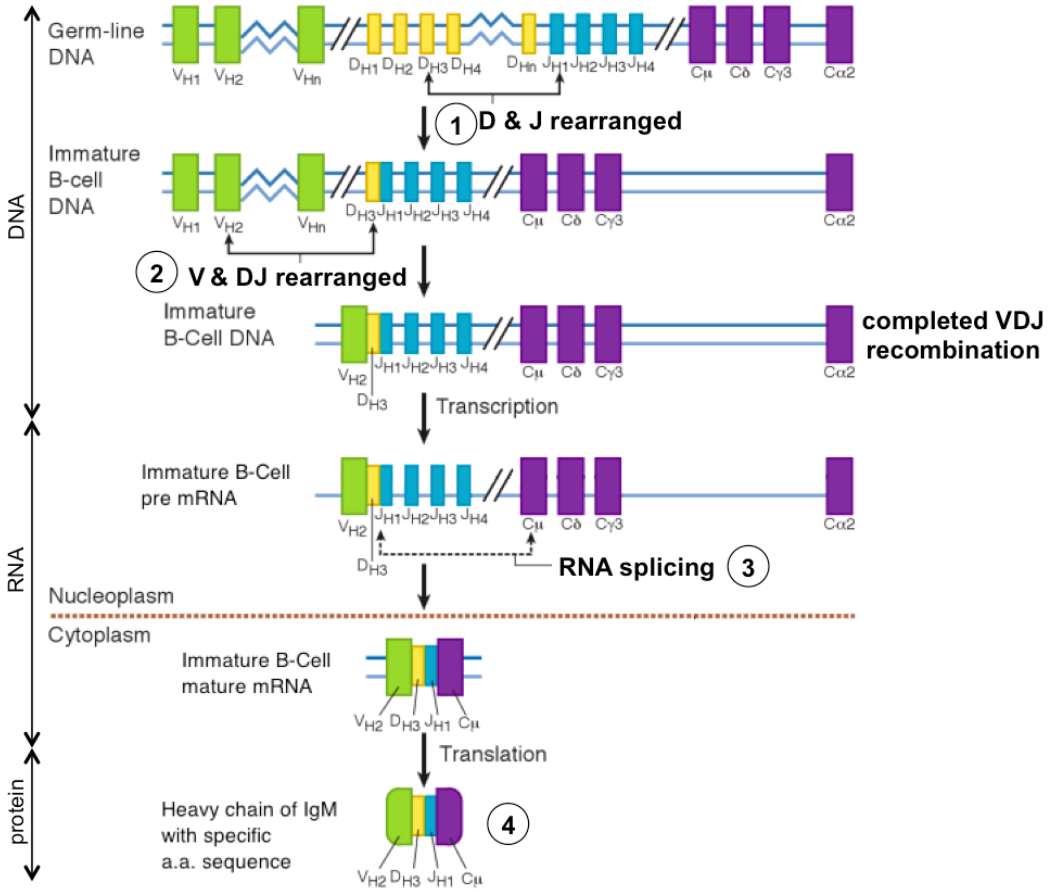


Fig. 22: Production of heavy chain in an immature B cell.

After VDJ recombination, transcription occurs:

(3) The pre-mRNA contains the VDJ exon and the constant segments. The pre-mRNA undergoes **RNA splicing** so that VDJ exon and Cμ are joined.
(4) The mature mRNA codes for a μ heavy chain that has a specific V_H.

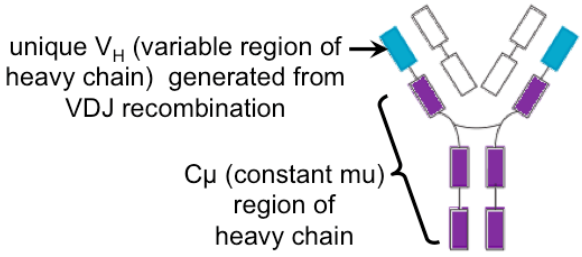


Fig. 23: Shaded parts show heavy chain of IgM.

VJ Recombination & Light Chain Production:

Notes to self

The process of **VJ recombination** at the **light chain gene locus** involves selection of one V gene and one J segment to form a rearranged VJ segment that will **code for the variable region of light chain (V_L)**.

Unlike the heavy chain gene locus, light chain gene locus does not have D gene segments.

Steps involved in the production of light chain in an immature B cell:

(1) **Rearrangement of a V gene segment to a J gene segment** forms VJ rearrangement.

After VJ recombination, transcription occurs:

(2) The pre-mRNA undergoes **RNA splicing** so that the VJ exon and the Cκ light chain constant segment are joined.
(3) The mature mRNA codes for a κ light chain that has a specific V_L.

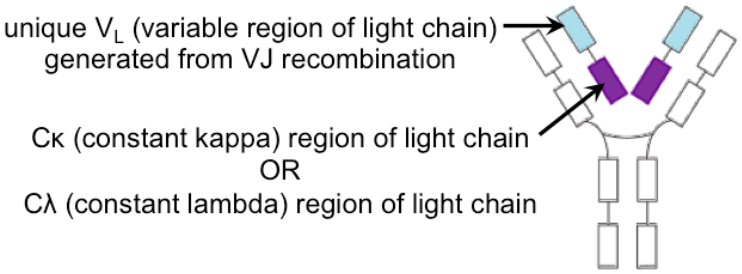


Fig. 24: Shaded parts show light chain of an immunoglobulin.

Notes to self

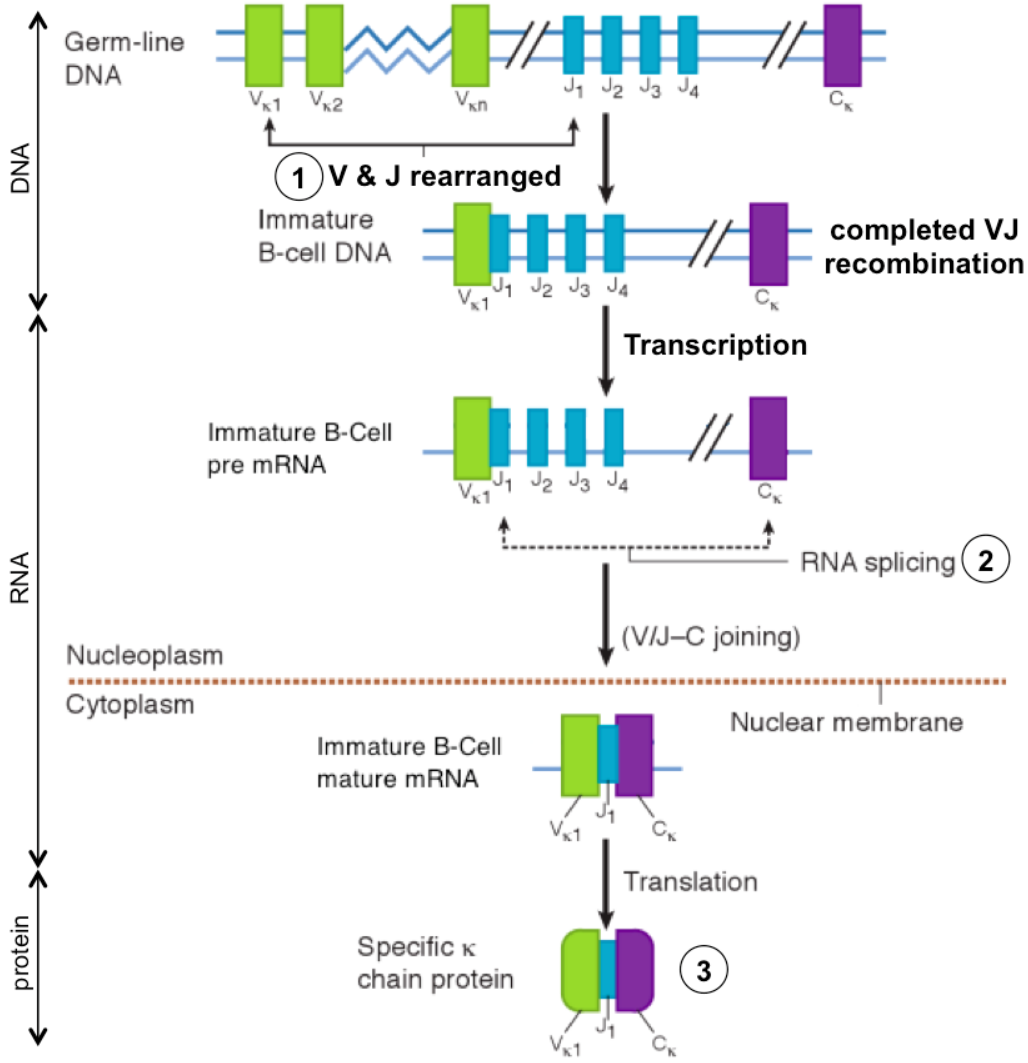


Fig. 25: Production of κ (kappa) light chain in an immature B cell.

The multiple V, D and J gene segments allow for the generation of many possible distinct antibody molecules, each with unique antibody binding sites. The table below illustrates the estimated number of possibilities:

	Estimated no. of heavy chain segments	Estimated no. of kappa (κ) light chain segments	Estimated no. lambda (λ) light chain segments
V	40	40	30
D	24	-	-
J	6	5	4
No. of possible combinations	5760 (40 x 24 x 6)	200 (40 x 5)	120 (30 x 4)

As a result, the estimated number of possible heavy-light chains that can be generated is (5760 x 200) + (5760 x 120) = 1.84×10^6

b. Somatic Hypermutation

Notes to self

Somatic hypermutation is a random **point mutation** in the **rearranged VDJ region** of heavy chain gene locus and the **rearranged VJ region** light chain gene locus. It is called "hypermutation" because it occurs at a much higher rate compared to the normal rate of mutation.

Thus, somatic hypermutation further diversifies the variable regions (V_H and V_L) of the antibody for antigen binding.

Somatic hypermutation occurs only in **activated B cells** (i.e. after mature B cells have been activated by the specific antigen that their B cell receptors (BCRs) can recognise and bind). The process therefore takes place outside the bone marrow.

Activated B cells divide rapidly by mitosis during **clonal expansion**, and some of these B cells can undergo somatic hypermutation. As a result, each of these B cells with a mutation will acquire slight amino acid difference in the **variable regions** of the BCR on the cell surface membrane (i.e. changes in antigen-binding sites of BCR on the cell surface membrane).

Some point mutations result in the B cells expressing **low affinity** BCRs on their cell surface membrane.

Some point mutations result in the B cells expressing **higher affinity** BCRs on their cell surface membrane.

By using **somatic hypermutation** to make changes in the antigen-binding sites of the BCR, BCR can be "fine-tuned" to have **higher affinity for its specific antigen**. These B cells that express higher affinity BCRs on their cell surface membrane are selected for **clonal expansion** and **differentiation**. This is known as **affinity maturation**:

- These B cells differentiate into **antibody-secreting plasma cells**. The antibodies secreted by these plasma cells will have high binding affinities for the specific antigen.
- The antigen-binding sites of the BCR and the antigen-binding sites of the antibody secreted from plasma cell are the same.
- The difference between BCR and the secreted antibody lies in their constant region of heavy chains due to an event, class switching.
- Some of these B cells can also differentiate into **memory B cells**.

c. Class Switching

Notes to self

There are 5 different classes of antibodies, IgG, IgM, IgA, IgD and IgE, with IgG being the predominant antibody in blood serum.

Different class of antibody contains **different constant-region** of the **heavy chain**.

Like somatic hypermutation, class switching occurs only in **activated B cells**. Unlike somatic recombination (or V(D)J recombination), class switching occurs in the presence of antigen.

Class switching is the process of an individual B cell switching to synthesise different class of antibody e.g. from IgM to IgG. The process is induced by small molecules released from T helper cells during B cell activation.

Class switching occurs only at the **immunoglobulin heavy chain gene locus**.

- The **variable region** of the **heavy chain (V_H)** that was previously generated during VDJ recombination in B cell development **remains unchanged**.
- Only the **constant region** of the **heavy chain (C_H)** of antibody **changes**.
- During class switching, a B cell with V_H DNA linked to C_μ (mu chain of constant region of heavy chain) DNA undergoes rearrangement. The V_H DNA becomes linked to another gene segment of constant region of the heavy chain (C_H) gene locus.
  e.g. when V_H DNA becomes linked to C_Y (gamma chain of constant region of heavy chain) DNA, the B cell will switch to synthesise IgG antibodies.

Therefore, class switching allows for expression of antibodies that have the same antigen specificity (as V_H remains unchanged) but have different function (due to different type of C_H).

10. Immunological Memory

Notes to self

Apart from activating the lymphocytes to rid the host of pathogens, the establishment of a population of **memory cells** to protect against re-infection is also a consequence of **adaptive immunity**.

Immunological memory is established to ensure a rapid re-induction of antigen-specific antibody on subsequent encounters with the same pathogen, thus providing long-lasting protection against it.

Memory cells are **generated following primary response to antigen**. They are long-lived lymphocytes that **mediate a secondary response to subsequent encounters with the antigen**.

Primary immune response of the body to an antigen occurs on the first occasion it is encountered.

- Presence of **lag period** (~3 to 6 days) between encountering antigen and production of antibody. Lag period reflects the time required for cell division (or clonal expansion) and differentiation of T cells to effector T cells and B cells to plasma cells.
- Response is also **weaker** than secondary immune response, as shown by **antibody concentration rising gradually**.

Secondary immune response of the body to the **re-exposure** to **same antigen** and recognised by adaptive immune cells.

- Response mediated by memory cells is **faster** (within hours). This is possible as it is not necessary to go through the process of activating naïve B and T cells in order to trigger cell-mediated and antibody-mediated responses. Memory B and T cells can be reactivated easily, thus respond quickly to a subsequent attack by the same pathogen.
- Response is also **stronger** than primary immune response, as shown by antibody concentration peaking at much higher level and quicker as compared to during primary response.

Notes to self

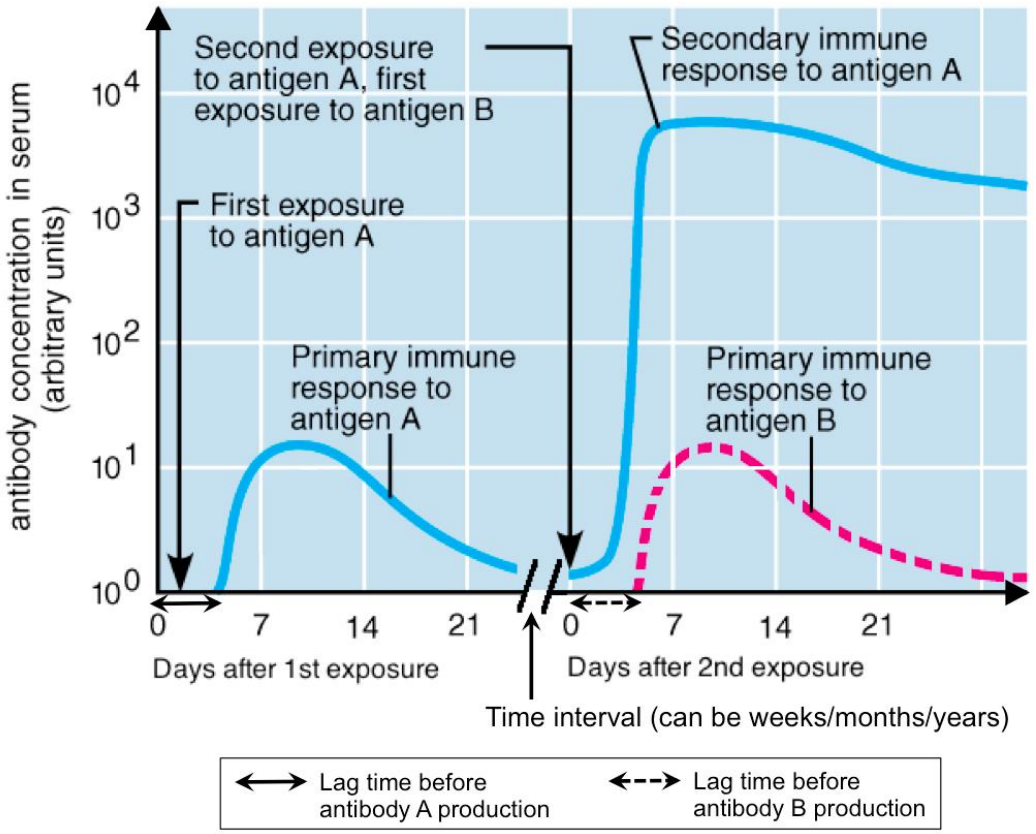


Fig. 26: Concentration of serum antibody following primary and secondary exposure to antigens. (Modified: Human Anatomy and Physiology, Elaine Marieb)