

Objectives

- List the principal cells and tissues of the immune system
- Summarize the main differences between innate and adaptive immunity
- Appreciate innate, humoral and cell mediated immune responses
- Describe how lymphocytes respond to foreign antigens
- Describe how humoral and cell-mediated immune responses are induced by microbes and other foreign substances
- Appreciate inflammatory response

INTRODUCTION

- IMMUNITY

- Refers to protection against infections.
- The Immune system consist of a collection of cell, tissues and molecules that defend the body against infectious microbes

- IMMUNE RESPONSE

- This refers to the coordinated reaction of the immune system against infections and other foreign substances

INNATE AND ADAPTIVE IMMUNITY

The body's defence against microbes consist of two main reactions;

INNATE IMMUNITY:

- This is mediated by various cells and proteins which have been made ready in the body to fight microbes. They respond immediately to an infection.

Consist of four (4) major components;

- epithelial barriers
- phagocytic leukocytes (neutrophils and macrophages)
- natural Killer (NK) cells
- plasma proteins

INNATE AND ADAPTIVE IMMUNITY

ADAPTIVE IMMUNITY

- More powerful than innate immunity
- Normally silent and responds to the presence infections by becoming active
- Consists of Lymphocytes and their products
- Cells of innate and adaptive immunity are recruited to infected sites by the process of inflammation to be activated and rid the body of infectious agents and dead tissues

CELLS AND TISSUES OF THE IMMUNE SYSTEM

- All cells of the immune system develop from precursors in the bone marrow
- They then circulate in the blood and are stored in the lymphoid organs (lymph nodes, spleen, tonsils)
- They quickly migrate to any site of infection where needed

CELLS AND TISSUES OF THE IMMUNE SYSTEM

- **White blood cells (Leucocytes)**

- Major phagocytes being neutrophils and monocytes
- Monocytes mature into macrophages when they enter tissues

These cells ingest and destroy microbes

Macrophages also help to repair damaged tissues

CELLS AND TISSUES OF THE IMMUNE SYSTEM

- **Lymphocytes**

- The most important cells of the adaptive immunity

- Classified into two;

- B lymphocytes: mature in the *bone marrow* and secrete antibodies

- T lymphocytes: mature in *thymus* and function to combat microbes that live within cells and are beyond the reach of antibodies

CELLS AND TISSUES OF THE IMMUNE SYSTEM

- There are two main types of T-lymphocytes
 - Helper - T cells or lymphocytes
 - Cytotoxic T lymphocytes (CTLs)

Helper -T cells: They function to help B lymphocytes produce the most effective antibodies and also macrophages to kill ingested microbes

Cytotoxic T lymphocytes: kills infected host cells

Regulatory T cells: control immune responses and prevent inappropriate reactions

CELLS AND TISSUES OF THE IMMUNE SYSTEM

- Lymphocytes are distinguished by the expression of surface proteins. The proteins are named according to the nomenclature "CD"
- Helper T cells are named CD4+
- Cytotoxic T Lymphocytes are named CD8+

Antigen-presenting cells (APCs): These are special kind of cells which capture the foreign substance and display them to lymphocytes in order to initiate immune response. One major type are **dendritic cells**

Major cell types involved in immune and inflammatory responses

Cell type	Principal function
T lymphocyte	Help for B cells and macrophages (CD4+ helper cells), killing of infected and tumour cells (CD8+ cytotoxic T lymphocytes)
B lymphocyte	Antibody production (B cells develop into plasma cells, which make antibodies)
Dendritic cells	Capture and display of foreign (e.g. microbial) antigens
Macrophages	Phagocytosis and killing of microbes; antigen capture and display; tissue repair
Neutrophils	Phagocytosis and killing of microbes

Let us test ourselves now

Give an overview of innate and adaptive immunity

INNATE IMMUNE DEFENCE

- Once the epidermal and mucosal barriers have been compromised the innate immune defence starts to function
- It functions against microorganisms found in the interstitial tissues and vascular compartments
- The defence mechanism is mostly by **phagocytosis** and the activation of the **alternative complement pathway** (Complement system)
- The function of the innate immune system is critical for the activation of cells for the adaptive immune response

INNATE IMMUNE DEFENCE

- The main cells responsible for this immune response are the mononuclear leucocytes (agranulocytes) and granulocytes
 - Mononuclear leucocytes involved include; Monocytes, Macrophages
 - Granulocytes include: Neutrophils, Basophils, Mast cells and Eosinophils

INNATE IMMUNE DEFENCE

- Mononuclear secrete numerous molecules in order to facilitate the destruction of microbes. Some of these include;
 - Lysozymes to break down bacteria cell membrane , ROS etc
 - Cytokines
 - Various bioactive lipids
 - Other molecules most of which also serve as inflammatory mediators

INNATE IMMUNE DEFENCE

- Monocytes also possess numerous receptors that interact with the environment. These include receptors for
 - Chemotaxis
 - Complement proteins (as leucocyte activators or opsonisation)
 - Promoting adherence
 - Cytokines (include macrophage activation factor (MAF) and macrophage inhibitory factor (MIF))

INNATE IMMUNE DEFENCE

Granulocytes

- Neutrophils are the most important in terms of phagocytosis
 - The receptors sensitive to macrophages are similar to neutrophils
 - Eosinophils are poor phagocytic cells but play important roles in extracellular killing of parasites such as helminths
 - Basophils are non phagocytic
-
- Macrophages and Neutrophils therefore demonstrate a high phagocytic activity

PHAGOCYTOSIS

- The major function of the innate immune system is to dispose of microbes and dead body cells through a process of phagocytosis
- The process is carried out by monocytes which mature in tissues into macrophages
- Phagocytosis is a multistep process and the major mechanism by which microbes are removed from the body

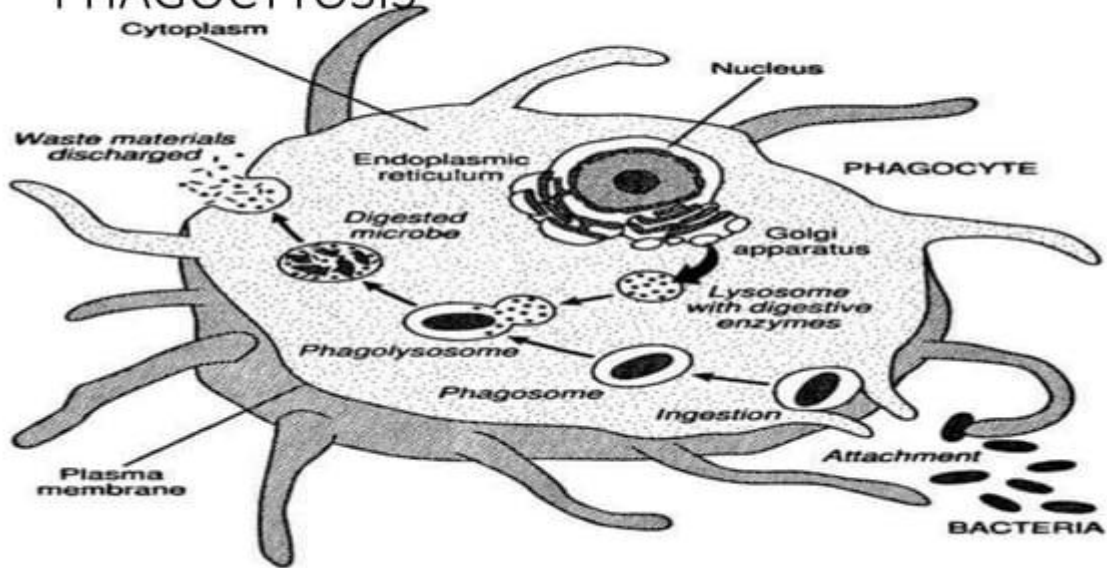
PHAGOCYTOSIS

Stages in phagocytosis

- Movement of phagocyte towards microbe (chemotaxis)
- Attachment/adherence of microbe to phagocyte surface
- Endocytosis of microbe leading to formation of phagosome
- Fusion of phagosome with lysozyme
- Killing of microbes
- Opsonisation is the process of making the microbe easier to phagocytose

- This is achieved by the aid of molecules called opsonins

PHAGOCYTOSIS



PHAGOCYTOSIS

The complement system

- Two general pathways for complement activity exist
- **The classical pathway:** The classical pathway operates with the highly specific immune system and is initiated when certain antibodies unite with antigens and stimulate the complement system into action.
- **Alternative pathway:** The alternative pathway is nonspecific and is initiated by tumours, cell wall components of bacteria, and various microorganisms

PHAGOCYTOSIS

Alternative complement pathway

- Plays a crucial role in innate immune defence
- Comprises of at least 20 different serum proteins
- Mostly denoted by the letter C and a number eg C3 etc

Three major functions include;

- Opsonisation of microbial membranes; This promotes adherence of the microbe to the cell membrane of the phagocytic cell
- Activation of leucocytes: Enhances the effect of leucocytes to immune function
- Lysis of target cell membrane: Involve the formation of membrane attack complex (MAC) which leads to formation of membrane pores and microbial cell lysis

Test yourself

Give an overview of the innate immune system

ADAPTIVE IMMUNE RESPONSE

Overview

- The adaptive immune system is composed of two main parts
 - Humoral immune response and
 - Cell mediated immune response

Overview

- Humoral immunity is the form of immunity that is mediated by antibodies.

- Cell mediated or cellular immunity is mediated by T cells and is effective against intracellular microbes

OVERVIEW

RECOGNITION OF ANTIGENS BY LYMPHOCYTES

- The immune system should in normal sense have the ability to recognise any microbe or foreign substance that might enter the body
- It should then elicit an appropriate immune response *specific* for that microbe or foreign substance

OVRVIEW

RECOGNITION OF ANTIGENS BY LYMPHOCYTES

- Antigen receptors of B cells are membrane bound antibodies
- They recognise whole microbes or molecules (chemical, toxins)

- Antigen receptors of T cells are structurally similar to antibodies
- T cell receptors recognise only small peptides displayed on peptide display molecules call MHC
- Human MHC are called HLA (Human Leucocyte Antigen): these pick up peptides from intracellular microbes and display these peptides for recognition by T cells

OVERVIEW

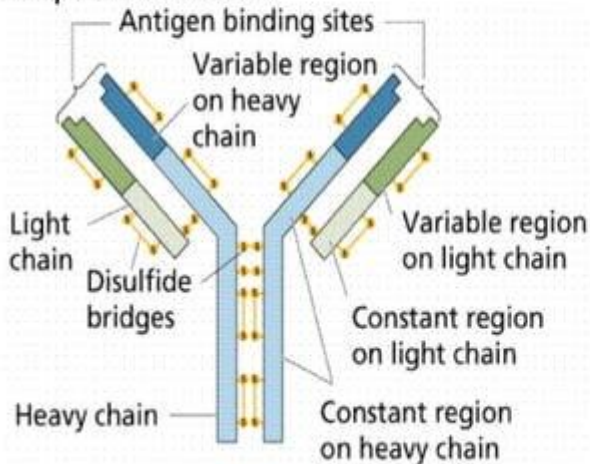
RECOGNITION OF ANTIGENS BY LYMPHOCYTES

- **ANTIGENS:** These are the substances recognised by the lymphocytes
 - If the recognised substance elicits an immune response, it is termed immunogen
- The immune system recognises and directs responses to enormous number of antigens by generating a large number of lymphocytes each with a specific antigen receptor

OVERVIEW

RECOGNITION OF ANTIGENS BY LYMPHOCYTES

IMMUNOGLOBULINS (Ig) or ANTIBODIES: These are the antigen receptors of B cells



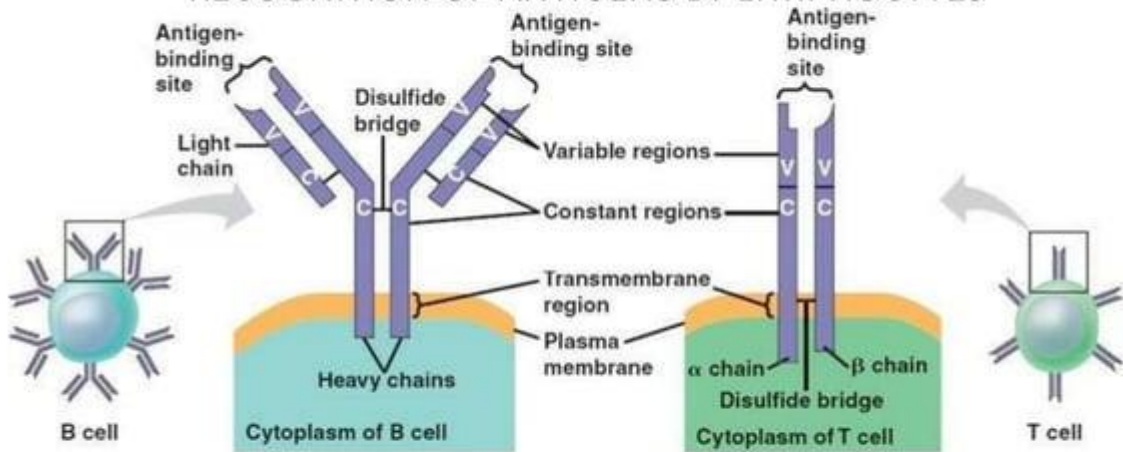
OVERVIEW

RECOGNITION OF ANTIGENS BY LYMPHOCYTES

- Antigen Receptors of T cells (TCRs) are structurally similar to antibodies
- They recognise only small peptides called MHC (Major Histocompatibility Complex) molecules
- In humans they are called HLA (Human Leukocyte Antigen)
- These pick up peptides from intracellular microbes and display these peptides for recognition by T cells

OVERVIEW

RECOGNITION OF ANTIGENS BY LYMPHOCYTES

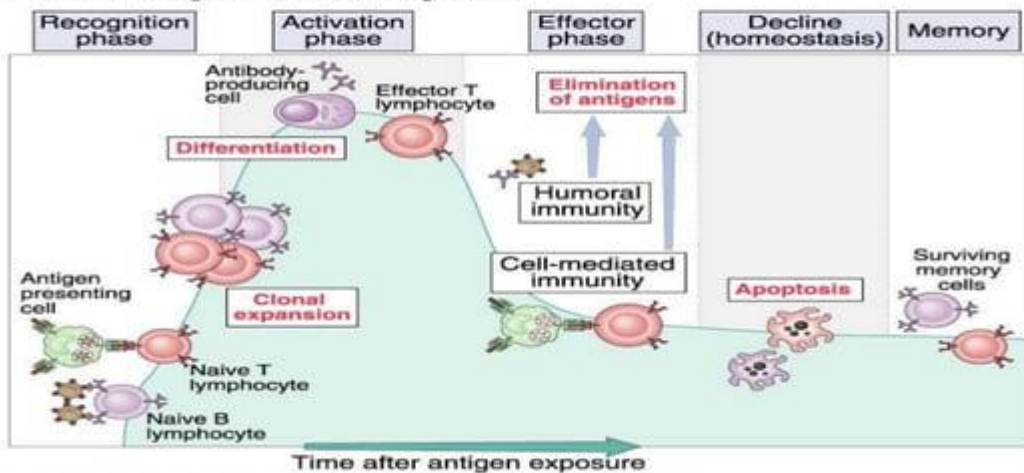


(a) A B cell receptor consists of two identical heavy chains and two identical light chains linked by several disulfide bridges.

(b) A T cell receptor consists of one α chain and one β chain linked by a disulfide bridge.

Stages in adaptive immune response

Phases of adaptive immune responses.



Humoral Immune Response

- This is the type of immune response that is mediated by antibodies. (Antibodies are produced from B lymphocytes)
- In this type of immune response, antibodies are secreted into mucosal lumen, blood and interstitial fluids
- The humoral immune response is effective only against extracellular microbes to which antibodies can easily access.

Humoral Immune Response

Recognition of antigens by B lymphocytes

- Antigens present in blood or enter through the epithelia are first concentrated in the lymph nodes and other lymphoid tissues
- Antigens are recognised by small number of B cells and undergo two important changes
 - Firstly, B cells divide: this leads to an increase in antigen specific cells
 - Secondly, B cells start producing and secreting more antibody

Antibody secreting cells are termed plasma cells and these are the effector cells of the B cells

Humoral Immune Response

Recognition of antigens by B lymphocytes

- If the antigen is a protein, there is the activation of helper T cells
- Helper T cells will then interact with specific antibody secreting cells and enhance antibody secretion
- Helper T cells also stimulate B cells to secrete different classes of antibodies

Humoral Immune Response

Antibody isotypes

Antibody Isotope	Isotype-specific effector functions
IgG	<p>Opsonization of antigens for phagocytosis by macrophages and neutrophils</p> <p>Activation of the classical pathway of complement</p> <p>Antibody-dependent cell mediated cytotoxicity mediated by natural killer cells and macrophages</p> <p>Neonatal immunity: transfer of maternal antibody across the placenta and gut</p> <p>Feedback inhibition of B cell activation</p>
IgM	<p>Activation of the classical pathway of complement</p> <p>Antigen receptor of naive B lymphocytes*</p>
IgA	<p>Mucosal immunity: secretion of IgA into the lumens of the gastrointestinal and respiratory tracts</p>
IgE	<p>Antibody-dependent cell-mediated cytotoxicity involving eosinophils</p> <p>Mast cell degranulation (immediate hypersensitivity reactions)</p>
IgD	<p>Antigen receptor of naive B lymphocytes*</p>

Cell mediated Immune Response

Recognition of antigens by T lymphocytes

- T lymphocytes recognise antigens displayed by MHC molecules on the surfaces of antigen presenting cells
- The T cells are designed to recognise antigens present in different cellular compartments ie. Phagocytic vessels for CD4+ cells and cytoplasm for CD8+ cells.

The process of antigen recognition and by T lymphocytes

- This will be extensively discussed during class lecture period

Immunological memory

- Antigen-specific cells that have the capacity to live for long are generated after an encounter with a specific antigen
- These are termed memory cells
- The number of memory cells increase with age
- They respond more quickly and powerful than naïve lymphocytes
- This is the goal of vaccination, thus to stimulate strong and effective memory immune response

Let us test ourselves now