CELL MEDIATED IMMUNITY

* Cell-mediated Immunity (CMI) is an adaptive immune response that is primarily mediated by thymus-derived small lymphocytes, called T-cells.

* Two types of T cells are considered. T_H - T Helper cells; T_C - Cytotoxic T cells.

* TH cells are important as they maximize the capabilities of the immune system. They do not destroy infected cells or pathogens, but they activate and direct other immune cells to do so. Hence their name is TH. The major roles of TH cells are to stimulate B cells to secrete antibodies, to activate phagocytes, to activate T_C cells and to enhance the activity of Natural Killer (NK) cells. Another name for TH cells is $CD4^+$ T cells ($CD4$ positive cells) because they express the surface protein $CD4$. TH cells are sub-divided based on the cytokines they secrete after encountering a pathogen.

* TH_1 cells secrete many different types of cytokines, the principal being **Interferon-γ** (IFN-γ), **Interleukin-2** (IL-2) and **Interleukin-12** (IL-12). IFN-γ has many side effects including activation of macro-phages to deal with intracellular bacteria and

parasites IL2 stimulates the maturation of killer T cells and enhances the cytotoxicity of NK cells IL-12 induces the secretion of INF-γ The principal cytokines secreted by TH2 cells are **Interleukin 4 (IL4)** and **Interleukin 5 (IL5)** for helping B-cells

* The major function of TC cells is cytotoxicity to recognize and destroy cells infected by viruses, but they also play a role in the defense against intracellular bacteria and certain type of cancers. Intracellular pathogens are usually not detected by macrophages and antibodies, and clearance of infection depends upon elimination of infected cells by cytotoxic lymphocytes. T killer cells are specific in sense that they recognize specific antigens. Alternative terms for T killer cells are **CD8+ T cells**, cytotoxic T cells and CTLs (cytotoxic T lymphocytes). CD8+ T cells secrete **INF-γ** and the inflammatory cytokine tumour necrosis factor (TNF).

Reference : 1. N. Arumugam, (2013). Immunology, Saras Publication, Nagercoil.

2. Henry Frich (2003). Immunology, Net source.

Hypersensitivity

★ Allergies result from an inappropriate and excessive immune response to common antigens. substances that causes allergies are called allergens. They include dust, moulds, pollen, certain foods and some medicines (like penicillin).

★ Allergy involves mainly IgE antibodies and histamine. Mast cells secrete the histamine.

★ A common manifestation of allergy is asthma.

★ Sometimes an allergen may cause a sudden, violent and fatal reaction in a sensitive individual. This is called anaphylaxis.

★ Deleterious inflammatory responses caused by the effector molecules of the immune system that lead to tissue damage and in some cases can cause the death of an individual is termed as hypersensitivity.

★ Although the word hypersensitivity implies an increased response, the response is not always heightened, but may, instead be an inappropriate immune response to an antigen.

★ Hypersensitive reactions may develop in the course of either humoral or cell-mediated responses. There are four types of Hypersensitive reactions.

Type I Hypersensitivity

This type of hypersensitivity is mediated by IgE and occurs when antigen exposure induces crosslinking of IgE bound to mast cells and basophils with release of vasoactive mediators. Typical manifestations include systemic anaphylaxis and localised anaphylaxis such as hay fever, asthma, hives, food allergies and eczema.

Type II Hypersensitivity

This is mediated by IgG1 - mediated cytotoxic hypersensitivity. In this type of reaction antibodies directed against cell surface antigens mediates the cell destruction via complement activation or ADCC.

Type - III Hypersensitivity

It is related through immune - complex activation. In this pathway, Ag - Ab complexes deposited in various tissues induce complement activation and an ensuing inflammatory response mediated by massive infiltration of neutrophils.

Type - IV Hypersensitivity

Type - IV Hypersensitivity mediated through cellular effectors. Here, sensitized TH1 cells release cytokines and thus activating macrophages or TC cells which mediate direct cellular damage.

Reference : 1. N. Arumugam, (2013). Immunology, Saras Publication, Nagercoil.

2. Bpdden mowell (2002). Immunology, Net source.

(a) Innate Immunity (Non-specific)

Innate immunity comprises all those natural defense mechanisms with which an organism is protected from infection. As a strategy, innate immunity consists of various types of barriers that prevent entry of foreign agents into the body. The pathogens that enter the body are quickly killed by some components of the immune system. This is the **first line of defense** in most animals. Innate immunity comprises of the following four types of barriers.

1. Anatomical barriers

These barriers block the entry of micro organisms into the body.

The **skin** and **mucous membrane** lining the respiratory and intestinal as well as the reproductive passages constitute the barriers.

Mucous material entraps foreign micro organisms.

The ciliary movements produced by the epithelial lining cells expel out micro organisms from the body.

2. **Physiological barriers**

Factors like body temperature, pH and various body secretions prevent the growth of pathogens.

For example fever response inhibits the growth of many pathogens.

Acidity of the stomach contents due to HCl secretion kills ingested microorganisms.

Lysozyme present in secretions like tears and saliva digest bacterial cell walls.

Certain cells like WBC when infected with a virus respond by releasing anti-viral proteins called **interferons**.

Interferons in turn make the cells in the vicinity resistant to viral infections, making resistant to viruses.

3. **Phagocytic barriers**

Phagocytosis performed by macrophages and neutrophils.

Macrophages are large irregularly shaped cells that engulf microbes, viruses and cellular debris.

Monocytes can be converted into macrophages in response to an infection.

These cells are provided with **bacterolytic enzymes** and **free radicals** which destroy the pathogens.

4. **Inflammatory barriers**

Usually an infection or tissue injury results in redness and swelling, along with pain and production of heat that may result in fever.

The above phenomenon is known as **Inflammatory response**, which is due to release of histamine, serotonin & prostaglandin, released by mast cells.

At the site of inflammation, there may be leak of vascular fluid which contains serum proteins with anti-bacterial activity.

Further there is an influx of phagocytic cells into the affected area. These responses inhibit and destroy micro organisms.

These responses inhibit or destroy the invading organisms.

Besides the phagocytes, there are Natural killer cells (NK cells) (T lymphocytes) kill virus-infected cells and some tumour cells of the body by creating perforin lined pores in the plasma membrane of the target cells. The pores allow the entry of water into target cells which then swells and burst

Acquired Immunity (Specific Immunity)

Acquired immunity also known as adaptive or specific immunity is capable of recognising and selectively eliminating specific micro organisms.

Acquired immunity is found only in vertebrates.

It supplements the protection provided by innate or natural immunity.

It is generated in response to an infection or encounter to micro organisms in question.

Specific defense mechanisms require several days to be activated, following the failure of non-specific defense mechanisms. The features of adaptive immunity are

(i) specificity

- It is the ability to distinguish differences among various foreign molecules

(ii) diversity

- It can recognise a vast variety of foreign molecules.

(iii) discrimination between self and non-self

- It is able to recognise and respond to molecules that are foreign (non-self) to the body. At the same time, it can avoid response to those molecules that are present with the body (self-antigens) of the animal.

(iv) memory

- when the immune system encounters specific foreign agent eg- microbe for the first time it generates an immune response that eliminates the invader. The immune system retains the memory of the encounter for a prolonged interval. As a result, a second encounter with the same microbe evokes a heightened immune response.

Specific immunity employs two major groups of cells -

(a) lymphocytes (b) Antigen presenting cells.

A healthy individual contains one trillion lymphocyte

The lymphocytes are of two types - T lymphocytes and B-lymphocytes.

Both the type of lymphocytes are produced in bone marrow.

The process is called hematopoiesis.

Some immature lymphocytes destined to become thymocytes migrate via blood to the thymus where they mature and differentiate as T cells.

The B-cells mature in bone marrow itself.

The B-cells and T-cells together generate two types of specific immunity viz., CMI and AMI or Humoral immunity.

(a) Cell-mediated Immunity / CMI

Cell-mediated immunity is the responsibility of a subgroup of T cells called cytotoxic T lymphocytes (CTLs)

An activated CTL is specific to a target cell which has been ingested and kill the target cell by a variety of mechanisms.

This prevents the completion of the lifecycle of the pathogen and its growth since it depends on an intact host cells to do that.

cell-mediated Immunity is also involved in killing of cancerous cells.

(b) Antibody mediated Immunity or Humoral Immunity

Antibody mediated Immunity or humoral Immunity involves the synthesis of specific antibody molecules called Immuno-globulins by B-lymphocytes.

Each antigen has many antigenic determinants, each of which matches a specific antibody and binds to it.

The B-cells direct the antibody mediated Immunity.

The antibody molecules (Igs) may be bound to a cell membrane in the form of receptors or they may remain free.

The free antibodies have three main functions -

(i) Agglutination of particulate matter

(ii) Opsonisation or coating over bacteria to facilitate recognition and phagocytosis by Phagocytes.

(iii) Neutralisation of toxins released by bacteria.

Adaptive Immunity may be active or passive.

Active Immunity elicited by pathogen or vaccine.

passive Immunity conferred by transfer of Immune products like antibodies from an individual to non-Immune individual.

Reference : 1. N. Arumugam, (2013). Immunology, Saras Publication, Nagercoil.

2. Fredrick sladen (2005). Immunology, Net source.

RHEUMATOID ARTHRITIS

Rheumatoid Arthritis (RA) is an autoimmune disorder that can cause joint pain and damage throughout your body.

The joint damage that RA causes usually happens on both the sides of the body.

It is a generalised disease affecting the connective tissues of the whole body.

It localises the involvement of musculo skeletal system.

It is an inflammation of the synovial membrane.

Rheumatoid arthritis is considered to be of autoimmune origin.

It is an immunological disorder against an unknown antigen.

RA is a chronic disease marked by symptoms of inflammation and pain in the joints.

The symptoms occur during periods of flares or exacerbations.

Other times are known as periods of remission — when symptoms disappear completely.

The symptoms include joint pain, joint swelling,

joint stiffness, loss of joint function and deformities

The levels of certain substances like acute phase reactants are elevated during inflammatory conditions

Treatments may include medications, alternative or home remedies, dietary changes and specific type of exercise

The medications that reduce pain and inflammation are non-steroidal anti-inflammatory drugs (NSAIDS), corticosteroids and acetominophen.

Anti-inflammatory diet contains lot of omega-3 fatty acids which include fatty fish like salmon, Tuna, Herring and mackerel.

Chia seeds, flax seeds and walnuts. Antioxidant rich food and vitamin A, C, E and selenium help reduce inflammation.

Types of RA include seropositive RA, seronegative RA and Juvenile idiopathic arthritis (JIA)

Reference 1. N. Arumugam (2013) Immunology, saras publication, Nagercoil.

2. Brenda. B. Spriggs, Net sourse.