***LEC.1: CMED 136***

**INTRODUCTION TO IMMUNOLOGY**

As soon as the microorganisms were shown to cause disease, scientists worked to explain how the body defends itself against their invasion.

*Elie Metchnikoff* (Russian born scientist) hypothesized that specialized cells in the body destroy invading organisms.

Metchnikoff reasoned that certain cells in animals are able to ingest and destroy foreign material and he called these cells phagocytes (***cells that eat*)**and proposed they were primarily responsible for the body’s ability to destroy invading microbes.

From microorganism’s standpoint, the tissues and fluids of the human body are much like a culture flask filled with a warm nutrient rich solution and it is surprising that the body is generally sterile.

If this were not the case, microbes could simply degrade our tissues, just as they readily break down the bodies of dead animals.

Like other multicellular organisms, humans have several mechanisms of defense that provide protection against disease and disease causing organisms.

\**The study of immunology therefore deals with* ***host defense reactions to foreign******(non self)*** *entities known as antigens,* ***antigen recognition molecules*** *and* ***cell mediated host defense*** *functions as they relate to immunity to* ***disease, hypersensitivity (allergy), autoimmunity, immunodeficiency and transplantation.***

**Fundamentals of Innate and Adaptive Immunity**

**Innate (non˗adaptive) Immunity**

The first line of defense against microorganisms is the intact skin and mucus membranes. If a microorganism breach this line and enter the body, then the innate arm of the immune system (second line of defense) is available to destroy the invaders.

Innate immunity had been called a *non˗specific defense.* It is resistance that is preexisting and is not acquired through contact with a nonself entity called an **antigen.**

**\*An antigen can be defined as the substance that causes an immune response.**

It includes barriers to infectious agents e.g.

* *Skin and mucous membranes*
* *Phagocytic cells*
* *Inflammatory mediators*
* *Complement components*

Because the components of the innate arm are preformed and fully active, they can function immediately upon entry of the microorganisms.

Recent discoveries show that most of the components of innate immunity detect molecules associated with invading microbes or tissue damage a feature called **pattern recognition**. Some of the molecules recognized include parts of bacterial cell walls and other compounds unique to microbes as well as substances associated with damaged host cells.

**Acquired (Adaptive) Immunity**

In addition to innate response, vertebrates have evolved a more specialized and highly specific defense system, providing protection called adaptive immunity (Third line of defense).

It is crucial to note that this arm of the immune system takes several days for this arm to become fully functional. It occurs after exposure to an antigen and is mediated by either antibody or lymphoid cells. Each time the body is exposed to a microbe or foreign material, the adaptive defense system first ***learns*** and then ***remembers*** the most effective response to that specific material so that it reacts accordingly when that material is encountered again.

An important action of the adaptive immune response is the production of **Y**, shaped protein called antibody. These bind specifically to antigens, thereby targeting them for destruction or removal by other host defenses.

Adaptive immunity can either be passive or active:

**Passive Immunity** Is transmitted by antibodies or lymphocytes reformed in another host. The advantage of passive immunization is the prompt availability of large amounts of antibodies but the disadvantage are the short life span of these antibodies and possible hypersensitivity reactions if antibodies are from another species.

**Active Immunity** Is induced after contact with foreign antigens e.g. in clinical or subclinical infection, immunization with live or killed infectious agents or their antigens, transplantation of foreign cells or exposure to microbial products. The host here actively produces antibodies and lymphoid cells and acquires the ability to respond to the antigens. The advantages of active immunity include long term resistance based on memory of prior contact with antigens, capacity to respond faster and to a greater extent on subsequent contact with the same antigen.

**Overview of the innate defenses**

First line defenses are the barriers that separate and shield the interior of the body from the surrounding environment. They constitute the initial obstacles microbes must overcome to invade the tissues.

These **anatomical barriers** which include the skin and the mucous membranes not only provide physical separation but are often bathed in secretions that have antimicrobial properties.

Sensors within the body recognize when the first line barrier have been breached and relay that information to other components of the host defenses.

Certain cells have **pattern recognition receptors (PRR)** on their surface which recognize groups from compounds unique to microbes sending signals to alert other components of the host defense triggering a protective response.

Another type of sensor is a series of proteins always present in blood and tissue fluids, these proteins are collectively called **Complement system** because they complement the adaptive immune defenses.

When invading microorganisms or tissue damage is detected, an inflammation response occurs involving many components of the innate defenses. During this response, cells that line local blood vessels undergo changes that allow complement system components and other proteins to leak out into tissues. Phagocytes (Cells that specialize in engulfing and digesting microbes and cell debris) also leave the bloodstream and accumulate in the tissues.

Some phagocytes play a dual role, destroying invaders while communicating with cells of the adaptive immune system.

The innate arm of our host defenses perform two major functions:

* Killing invading microbes
* Activating acquired (adaptive) immune process

***First line defense***

The body’s boarders serve as the first line of defense against invading microbes and although some boarders are thought of as being inside the body, they directly contact the external environment e.g. Digestive tract (Mouth to anus), Respiratory tract.

**Physical Barriers**

1. *The Skin*

The skin is the most difficult for microbes to penetrate. Dermis with tightly woven fibrous connective tissue and epidermis with multilayers of epithelial cells.

The outermost sheet is made of dead cells filled with water repellant keratin protein making it a dry environment.

The skin cells continually slough off taking with them any microbe that might be adhering.

1. *Mucous membranes*

Mucous membrane line the digestive tract, respiratory tract and genitourinary tract. They are continually bathed with mucus or other secretions that help wash microbes from the surface.

Most mucous membranes have mechanisms that move microbes towards areas where they can be eliminated e.g. peristaltic movement of the intestinal tract, constantly beating cilia lining the respiratory tract moving materials away from the lungs to the throat.

**Antimicrobial substances**

Skin and mucous membranes are protected by a variety of antimicrobial substances that inhibit or kill microorganisms. For example, the salty residue that accumulates on skin as perspiration evaporates inhibits all but salt tolerant microbes.

**Lysozyme**, the enzyme that degrades **peptidoglycan**, is in **tears, saliva** and **mucus**. It is also found within the body in phagocytic cells, blood and the fluid that bathes tissues.

**Peroxidase enzymes,** which breaks down hydrogen peroxide to produce reactive oxygen species are in saliva and milk; They are also found within body tissues and inside phagocytes.

**Lactoferrin** is an iron binding protein in saliva, mucus and milk, it is also found in some types of phagocytes. A similar compound, transferrin, is in blood and tissue fluid. Iron is one of the major elements, so withholding it prevents microbial growth.

**Defensins,** are short antimicrobial peptides **produced by neutrophils** and **epithelial cells.** They insert into bacterial membranes, forming ores that damage cells.

**Normal Microbiota (Flora)**

The normal microbiota (Flora) is the population of microorganisms that routinely grow on the body surface of healthy humans. Although these organisms are not technically part of the immune system, they provide considerable protection. e.g.

* By **competitive exclusion** of pathogens by covering binding sites against pathogens.
* The normal microbiota population also **consumes nutrients** that could otherwise support the growth of less desirable organisms.
* Some normal microbiota produce compounds toxic to other bacteria.

*Examples;*

***Propionibacterium species*** in the hair follicles of the skin degrades *lipids*, releasing *fatty acids* that inhibit the growth of many pathogens.

***Escherichia coli*** in the gastrointestinal tract synthesizes *colicin*, a group of proteins toxic to certain bacteria.

***Lactobacillus species*** growing in the vagina produces lactic acid as a fermentation end product resulting in an acidic pH that inhibits the growth of some pathogens.

It is important to note that some normal biota is also essential to the development of the immune system as certain microbes are encountered, the system learns to distinguish harmless ones from pathogens

**Cells of the immune system**

The process of formation and development of blood cells is called **hematopoiesis.**

All blood cells including those important in the body’s defense, originate from the same cell type, the **hematopoietic stem cell** found in the bone marrow.

As with other types of stem cells, hematopoietic cells are capable of long term self-renewal, hence they can divide repeatedly.

Hematopoietic stem cells are induced to develop into the various types of blood cells by a group of proteins called **Colony Stimulating Factors (CSFs)**.

The general categories of blood cells and their derivatives including;

* *Red blood cells (Erythrocytes)* ˗ Carry oxygen in the blood
* *Platelets* ˗ Important for blood clotting
* *White blood cells (Leukocytes)* ˗ Important in host defense

Leukocytes can be divided into four broad groups;

* **Granulocytes**
* **Mononuclear phagocytes**
* **Dendritic cells**
* **Lymphocytes**