11.1: The Innate Immune System: An Overview

Skills to Develop

1. Compare adaptive (acquired) immunity with innate immunity.
2. Compare immediate innate immunity with early induced innate immunity.
3. Define the following:
   a. pathogen-associated molecular patterns (PAMPs)
   b. pattern-recognition receptors (PRRs)
   c. antigen
   d. immunogen
   e. epitope.

In Units 1-4 we looked at microorganisms: how they replicate, why some are potentially more pathogenic than others, and how we can control them with antimicrobial agents. Units 4 and 5 are devoted to the ways in which the body defends itself against microbes and other potentially harmful cells and molecules. The body has two immune systems: the innate immune system and the adaptive immune system. Unit 5 deals with innate immunity while Unit 6 will cover adaptive immunity. Let's first briefly compare acquired and innate immunity.

Innate immunity

Innate immunity is an antigen-nonspecific defense mechanisms that a host uses immediately or within several hours after exposure to almost any microbe. This is the immunity one is born with and is the initial response by the body to eliminate microbes and prevent infection. Innate immunity can be divided into immediate innate immunity and early induced innate immunity.
Immediate innate immunity begins 0 - 4 hours after exposure to an infectious agent and involves the action of soluble preformed antimicrobial molecules that circulate in the blood, our found in extracellular tissue fluids, and are secreted by epithelial cells. These include:

- antimicrobial enzymes and peptides;
- complement system proteins; and
- anatomical barriers to infection, mechanical removal of microbes, and bacterial antagonism by normal body microbiota

These preformed innate defense molecules will be discussed in greater detail later in this unit.

Early induced innate immunity begins 4 - 96 hours after exposure to an infectious agent and involves the recruitment of defense cells as a result of pathogen-associated molecular patterns or PAMPS binding to pattern-recognition receptors or PRRs. These recruited defense cells include:

- phagocytic cells: leukocytes such as neutrophils, eosinophils, and monocytes; tissue phagocytic cells in the tissue such as macrophages;
- cells that release inflammatory mediators: inflammatory cells in the tissue such as macrophages and mast cells; leukocytes such as basophils and eosinophils; and
- natural killer cells (NK cells).

Unlike adaptive immunity, innate immunity does not recognize every possible antigen. Instead, it is designed to recognize molecules shared by groups of related microbes that are essential for the survival of those organisms and are not found associated with mammalian cells. These unique microbial molecules are called pathogen-associated molecular patterns or PAMPS and include LPS from the gram-negative cell wall, peptidoglycan and lipoteichoic acids from the gram-positive cell wall, the sugar mannose (a terminal sugar common in microbial glycolipids and glycoproteins but rare in those of humans), bacterial and viral unmethylated CpG DNA, bacterial flagellin, the amino acid N-formylmethionine found in bacterial proteins, double-stranded and single-stranded RNA from viruses, and glucans from fungal cell walls. In addition, unique molecules displayed on stressed, injured, infected, or transformed human cells also act as PAMPS. (Because all microbes, not just pathogenic microbes, possess PAMPs, pathogen-associated molecular patterns are sometimes referred to as microbe-associated molecular patterns or MAMPs.)

Most body defense cells have pattern-recognition receptors or PRRs for these common PAMPS (see Figure 1) and so there is an immediate response against the invading microorganism. Pathogen-associated molecular patterns can also be recognized by a series of soluble pattern-recognition receptors in the blood that function as opsonins and initiate the complement pathways. In all, the innate immune system is thought to recognize approximately $10^3$ of these microbial molecular patterns.

Flash animation illustrating signaling toll-like receptors on defense cells: LPS and TLR-4.

html5 version of animation for iPad illustrating signaling toll-like receptors on defense cells: LPS and TLR-4.
Examples of innate immunity include anatomical barriers, mechanical removal, bacterial antagonism, antigen-nonspecific defense chemicals, the complement pathways, phagocytosis, inflammation, fever, and the acute-phase response. In this current unit we will look at each of these in greater detail.

**Adaptive (acquired) immunity**

Adaptive (acquired) immunity refers to antigen-specific defense mechanisms that take several days to become protective and are designed to react with and remove a specific antigen. This is the immunity one develops throughout life. During adaptive immunity, antigens are transported to lymphoid organs where they are recognized by naive B-lymphocytes and T-lymphocytes. These activated B- and T-lymphocytes subsequently proliferate and differentiate into effector cells.

An antigen is defined as a substance that reacts with antibody molecules and antigen receptors on lymphocytes. An immunogen is an antigen that is recognized by the body as nonself and stimulates an adaptive immune response. For simplicity we will use the term antigen when referring to both antigens and immunogens. The actual portions or fragments of an antigen that react with antibodies and lymphocyte receptors are called epitopes.

As we will see later in Unit 5, the body recognizes an antigen as foreign when epitopes of that antigen bind to B-lymphocytes and T-lymphocytes by means of epitope-specific receptor molecules having a shape complementary to that of the epitope. The epitope receptor on the surface of a B-lymphocyte is called a B-cell receptor and is actually an antibody molecule. The receptor on a T-lymphocyte is called a T-cell receptor (TCR).

It is estimated that the human body has the ability to recognize $10^7$ or more different epitopes and make up to $10^9$ different antibodies, each with a unique specificity. In order to recognize this immense number of different epitopes, the body produces $10^7$ or more distinct clones of both B-lymphocytes and T-lymphocytes, each with a unique B-cell receptor or T-cell receptor. Among this large variety of B-cell receptors and T-cell receptors there is bound to be at least one that has an epitope-binding site able to fit, at least to some degree, any antigen the immune system eventually encounters. With the adaptive immune responses, the body is able to recognize any conceivable antigen it may eventually
The downside to the specificity of adaptive immunity is that only a few B-cells and T-cells in the body recognize any one epitope. These few cells then must rapidly proliferate in order to produce enough cells to mount an effective immune response against that particular epitope, and that typically takes several days. During this time the pathogen could be causing considerable harm, and that is why innate immunity is also essential.

Adaptive immunity usually improves upon repeated exposure to a given infection and involves the following:

- antigen-presenting cells (APCs) such as macrophages and dendritic cells;
- the activation and proliferation of antigen-specific B-lymphocytes;
- the activation and proliferation of antigen-specific T-lymphocytes; and
- the production of antibody molecules, cytotoxic T-lymphocytes (CTLs), activated macrophages, and cytokines.

Acquired immunity includes both humoral immunity and cell-mediated immunity and will be the topic of Unit 6.

Exercise: Think-Pair-Share Questions

Compare and contrast how innate immunity and adaptive immunity are typically initiated in response to microbes.
We will now take a closer look at innate immunity.

Summary

1. The body has two immune systems: the innate immune system and the adaptive immune system.
2. Innate immunity is an antigen-nonspecific defense mechanisms that a host uses immediately or within several hours after exposure to almost any microbe.
3. Innate immunity is the immunity one is born with and is the initial response by the body to eliminate microbes and prevent infection.
4. Immediate innate immunity begins 0 - 4 hours after exposure to an infectious agent and involves the action of soluble preformed antimicrobial molecules that circulate in the blood and in extracellular tissue fluids.
5. Early induced innate immunity begins 4 - 96 hours after exposure to an infectious agent and involves the recruitment of defense cells as a result of pathogen-associated molecular patterns or PAMPS binding to pattern-recognition receptors or PRRs.
6. Adaptive (acquired) immunity refers to antigen-specific defense mechanisms that take several days to become protective and are designed to react with and remove a specific antigen.
7. Adaptive immunity is the immunity one develops throughout life.
8. An antigen is defined as a substance that reacts with antibody molecules and antigen receptors on lymphocytes.
9. The actual portions or fragments of an antigen that react with antibodies and lymphocyte receptors are called epitopes.

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