Basic Medical Immunology & Microbiology
GMS 6141
University of South Florida
Burt Anderson, PhD

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Slide 1:

Hello and welcome. This is course 6XXX, Basic Medical Immunology & Microbiology. Please familiarize yourself with the specific details needed to take and pass this course. It is expected that students taking this course have had a course in biochemistry and are familiar with basic human organ and tissue function. The course will follow Elsivier's Integrated Immunology & Microbiology as text. The glossary in the syllabus and Immunology for Medical Students will be helpful, and the other recommended texts provide for more in depth explanations. Please remember this is a basic course and the knowledge regarding these subjects, especially immunology, is expanding at an enormous rate. We will not go into great detail on these subjects, but our goal is to provide the student with a solid background of information leading to the understanding of the basics of these subjects. Web sites that might be helpful include www.wickipedia.com, www.webmd.com, www.cdc.org and www.asm.org.

The first part of the course is Section 1, Chapters 1 through 10 and is devoted to Immunology, while Section 2, Chapters 11 through 16, covers Medical Microbiology.

Definitions

- Immunity: the ability to respond to foreign substances including molecules and microbes
- Immune System: The specific molecules, cells, tissues and organs that function to provide protection from foreign substances
- Immune Response: the bodies response to a foreign substance involving cells and molecules of the immune system reacting with the substance to render it harmless

Slide 2:

Immune in its simplest form means free from. In this context, we use the term to mean free from disease. Hence immunity has come to mean the body's ability to be free from or resist disease. Scientifically and medically, immunity means the ability to respond to foreign substances including molecules and microbes. We speak of the "immune system" as the specific molecules, cells, tissues and organs whose job is to provide protection from foreign substances. The entire, sometimes complicated, response to foreign substances to render them harmless is the immune response.

Chapter 1
Introduction to Immunity and Immune Systems

- Many organs and tissues of the body serve as a defense system to protect against pathogenic invaders.
- The immune system functions to eliminate infectious agents, toxins and malignancies.
- In order to eliminate foreign substances, the immune system must distinguish between self and non-self, this is a chief function.

Slide 3:

Chapter 1. Introduction to Immunity and Immune Systems. The body is protected from invaders and malignancies by many organs and tissues. The immune system is designed to protect us and constantly surveys for invaders including microorganisms, toxins and malignancies. To do this, the immune system must be able to distinguish between self and non-self before it can protect us from invaders. Therefore, first and foremost, the immune system must be able to distinguish between that which belongs or self and that which is foreign and must be protected against or non-self. If the immune system does not recognize a pathogen or toxin as foreign, it will not react with it leaving us open to invasion. If it recognizes self as foreign, it actually causes disease by reacting with self.

Innate Immune System

- The two components of the immune system are the innate and adaptive immune systems
- The innate system
  - is the first line of defense
  - Is present from birth
  - Consists of non-specific components available before any insult
  - Halts or slows invaders while the adaptive system is generated or up regulated
  - Utilizes preformed effector molecules to recognize broad structural motifs highly conserved within microbial species

Slide 4:

The immune system consists of two compartments that overlap, the innate and adaptive immune systems. The innate system is present at birth, is mostly non-specific in nature, and is referred to as the first line of defense against invasion of our bodies. It is first to prevent and inhibit pathogens from invading our bodies. Its components are in place and available before the onset of insult, and certain of these components are responsible for triggering signal pathways to promote inflammation and lead into the adaptive immune system.

Innate Immunity Components

Table 1-1. Innate Defensive Components

Component	Effectors	Function
Anatomic and physiologic barriers	Skin and mucous membranes Temperature, acidic pH, lactic acid Chemical mediators	Physical barriers to limit entry, spread, and replication of pathogens
Inflammatory mediators	Complement	Direct lysis of pathogen or infected cells
	Cytokines and interferons	Activation of other immune components
	Lysozymes	Bacterial cell wall destruction
	Acute-phase proteins and lactoferrin	Mediation of response
	Leukotrienes and prostaglandins	Vasodilation and increased vascular permeability
Cellular components	Polymorphonuclear cells • Neutrophils, eosinophils • Basophils, mast cells	Phagocytosis and intracellular destruction of microorganisms
	Phagocytic-endocytic cells • Monocytes and macrophages • Dendritic cells	Presentation of foreign antigen to lymphocytes

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Table 1-1 lists three different components of the innate system, their specific effectors and their function. Anatomic barriers include the intact skin and mucous membranes. These prevent pathogens from entering the body. A cut or burn compromises the barrier and allows entry of pathogens. Our body temperature, the pH of our body fluids and the various chemicals on our skin and in our mucous membranes limit the entry and spread of pathogens and are physiologic barriers. We also have inflammatory mediators that we will more fully define later in the course such as complement, cytokines and other mediators that lyse pathogens or activate other arms of the immune system. Last, but not least, are the cellular components of the innate system. These cells, primarily the polymorphonuclear cells (PMNs) and phagocytic-endocytic cells play important rolls in defense against pathogens. The PMNs ingest, digest and destroy pathogens while the phagocytic monocytes, macrophages and dendritic cells also act to present antigens to lymphocytes. We will see later how and why this presentation works.

Adaptive Immune System

- The adaptive immune system is also called the acquired immune system
- It is specific in nature, meaning that it recognizes foreign substances, called antigens, via receptors for them on lymphocytes
- There are two kinds of lymphocytes, B lymphocytes or B cells and T lymphocytes or T cells

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The adaptive immune system, also called the acquired immune system follows the innate system in that the adaptive system takes time to develop (it adapts). It takes time because, unlike the innate system which is non-specific, the adaptive system is specific. That is, it recognizes a specific foreign substance, called antigen, by its chemical make-up via complimentary receptors on lymphocytes (a specific type of white blood cell) . A given lymphocyte receptor is specific for a given antigen. The adaptive system is comprised of two types of lymphocytes, B lymphocytes or B cells and T lymphocytes or T cells.

B Lymphocytes

- B lymphocytes or B cells have surface immunoglobulins that act as antigen receptors
- When antigen reacts with the B cell immunoglobulin, the B cell differentiates into a plasma cell
- The plasma cell secretes the immunoglobulin molecules or antibodies into the cells environment
- B cells, plasma cells and antibodies make up the humoral immune response

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The humoral immune response is comprised of B cells, plasma cells and immunoglobulin molecules called antibodies. The surface receptors on B cells that are specific for an antigen are immunoglobulins. A given B cell has many immunoglobulin molecules on its surface and all of them are specific for only one antigenic component or epitope. The specific portion of an antigen that reacts with a receptor is called an epitope or sometimes a determinant group. So we need many different B cells to respond to the thousands of antigenic epitopes that are part of the molecules on and secreted by pathogens. When an antigen reacts with a B cell, signal transductions take place, some of which are responsible for the B cell differentiating into a plasma cell. The plasma cell acts as a factory and produces thousands of antibodies specific for the antigen and secretes them outside the cell. These antibodies travel throughout the body via the blood and lymph and react with the pathogens and their products such as toxins.

T Lymphocytes

- T lymphocytes or T cells have a surface receptor similar to the immunoglobulin on B cells
- The T cell receptor (TCR) is NOT secreted
- T cell activation requires antigen presenting cells (APCs)
- APCs have surface molecules called human leukocyte antigens (HLAs) that are coded for by a gene region known as the Major Histocompatibility Complex (MHC)
- These cells and their molecules form a pathway for presentation and recognition of antigens and form the cellular immune response

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T lymphocytes or T cells have surface receptors for antigens that are different but similar to those on B cells. We will look at the similarities and differences later. The T cell receptors are not secreted, therefore the T cells have to come in contact with the antigen giving rise to the terminology, cellular immunity. T cells require a complex system of antigen recognition. They require a second set of cells in order to be activated. This second set of cells, termed antigen presenting cells (APCs) have surface molecules called human leukocyte antigens (HLAs) that are coded for by a gene region called the Major Histocompatibility Complex (MHC). Throughout the text, HLAs are often referred to as MHC molecules. Think of the MHC as a cluster of genes coding for surface molecules (HLAs) that present antigens to T cells. We will learn how these cells interact later, but for now we should understand that the T cells, APCs and their molecules form a pathway for presentation and recognition of antigens called the cellular immune response. There are four main types of APCs, monocytes, macrophages, dendritic cells and B cells. Of these, B cells are lymphocytes and the other 3 are phagocytes.

Comparison of Innate and Adaptive Immune Systems

Table 1-2. Key Elements of the Innate and Adaptive Immune Systems

Innate	Adaptive (Acquired)
Rapid response (minutes to hours)	Slow response (days to weeks)
PMNs and phagocytes	B cells and T cells
Preformed effectors with limited variability Pattern recognition molecules recognizing structural motifs	B-cell and T-cell receptors with a diverse array of highly selective specificities
Soluble activators	Antibodies (humoral response)
Proinflammatory mediators	Cytokines (cellular response)
Nonspecific	Specific
No memory, no increase in response upon secondary exposure	Memory, maturation of secondary response

PMNs, polymorphonuclear neutrophils.

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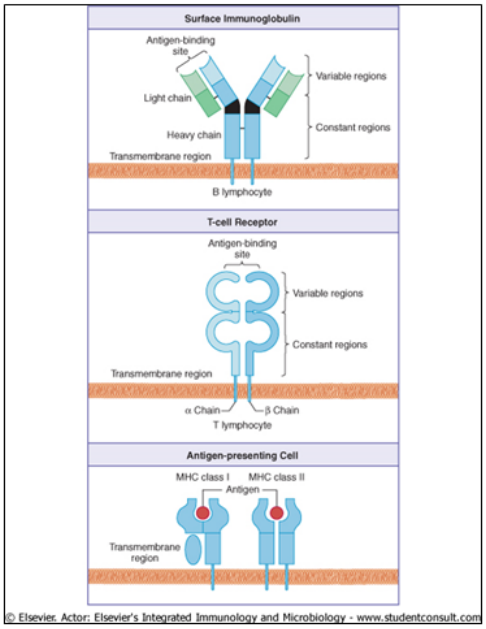
Table 1 – 2 This Table compares the innate and adaptive immune systems. Important things to remember from this table are that the innate system is rapid to respond to invasion while the adaptive system takes days or weeks. The innate system cells are the PMNs and other phagocytic cells while the adaptive system is comprised of T and B lymphocytes. The innate system is non-specific. For example, a PMN will phagocytose any pathogen while a B or T cell will react only with one specific antigen. The innate system has no memory. That is, whether the system sees a pathogen for the first time or the tenth time, the response is the same. The adaptive response has memory such that when it sees the same antigen a second time, it remembers it and responds faster and to a greater degree. We will study the adaptive system in detail to see how it recognizes antigens, distinguishes them from self and then remembers them.

B Cell, T Cell Receptors and MHC Molecules



Slide 10:

Fig 1-1 . This slide compares the surface receptors on B and T cells. The top 2 sections of this slide show that the immunoglobulin molecule on the surface of a B cell and the T cell receptor on the surface of the T cell are similar but different. We will go into greater detail about these molecules later. The bottom section shows a simplified version of MHC molecules on the surface of an APC. As you can see, the MHC molecules are termed class I or II. They are responsible for presenting the antigen to the T cell.

Specificity of Adaptive Response by Lymphocyte Receptors

- The generation of antigen binding specificity of T and B cells occurs before antigen exposure through DNA rearrangement
- Receptors of high diversity and binding potential are created to react with virtually all antigens
- Before our lymphocytes see specific antigens, they have the ability to react with them because of their ability to rearrange their DNA.

Slide 11:

The specificity of the receptors on T and B cells occurs before these cells ever come into contact with the antigen through a process called DNA rearrangement which we will study later on. There are thousands of receptors for the thousands of different antigens. In this way, we have the ability to react with virtually every antigen that enters our body. It is somewhat difficult to comprehend that we have a specific adaptive immune response for every antigen that we might see. It does not seem efficient, but that's the way it is. It took many years of experimenting to determine that fact and many more to determine how it's done.

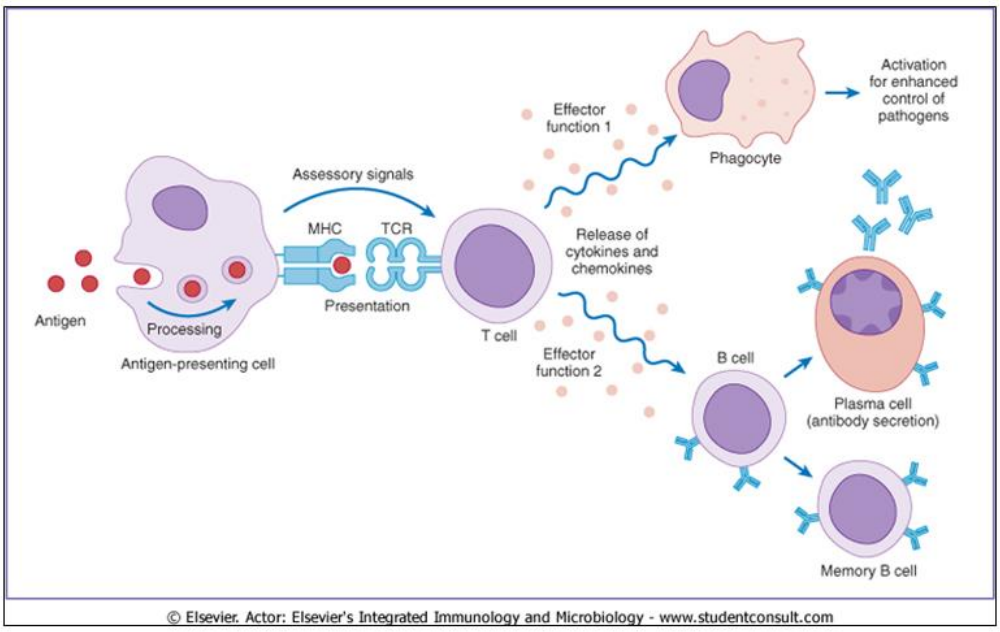
Clonal Selection

- There are small numbers of B cells or T cells that express the same antigen receptor.
- When reacted with its specific antigen, B or T cells undergo activation, proliferation and differentiation
- This process is called clonal selection since a small number of cells programmed to react with a specific antigen, react with the antigen and then multiply producing large clones of cells that also react with that antigen.

Slide 12:

In the organs and tissues of the immune system along with the blood and lymph are small numbers of B or T cells that have receptors on their surface that are specific for one antigen. When these cells come in contact with that antigen, signal transductions occur that cause the cells to undergo activation, proliferation and differentiation. This entire process is called clonal selection in that the progeny of these activated cells are clones of the originals and will react with the antigen. In this manner many cells are produced to combat the invader, and also certain of these cells will remain in the body providing immunologic memory to start the process again if that particular antigen comes into the body again. In other words, a lymphocyte that reacts with antigen A is stimulated to, not only react against that antigen, but to undergo rapid reproduction of itself so that there are many more cells that will react with antigen A.

Overview Of Adaptive Immune Interactions



Slide 13:

Fig 1-2 illustrates certain events that occur when a specific antigen enters the system. On the left side, the antigen is ingested and processed by an APC. The APC then presents the antigen to a T cell via MHC to TCR transfer. Upon receiving the antigen, the T cells signal transduction systems are employed. The T cell releases various molecules that enhance other phagocytic cells and, depending on the type of antigen, activate B cells and or other T cells (not shown).

Primary and Secondary Antibody Responses

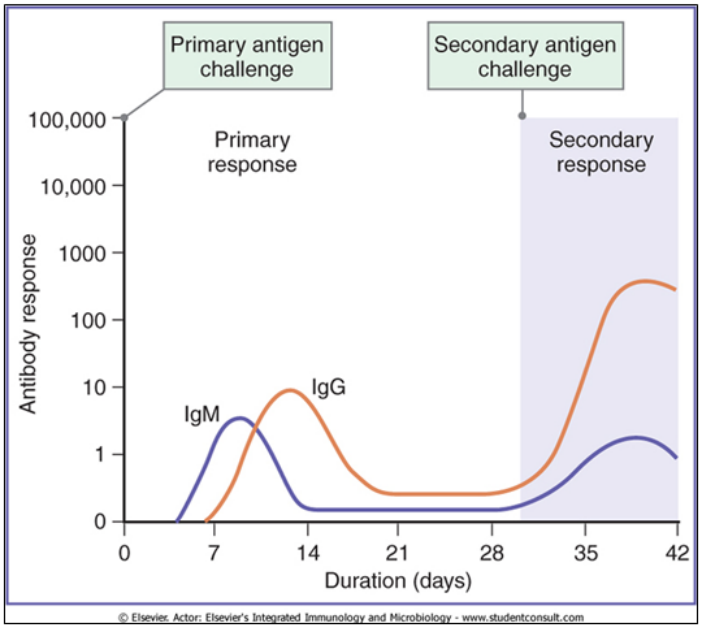


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Fig 1-3 illustrates what happens when the humoral adaptive immune system is confronted with the same antigen for a second time. IgM and IgG represent the immunoglobulins secreted from the plasma cells into the blood where they can be quantitated. Primary antigen challenge on day 0 takes days to weeks to develop and reaches about 8 to10 on the scale. (The antibody response on the Y axis has no real meaning but serves to show the magnitude of the response.) Secondary response occurs when the system sees the same antigen a second time (shaded portion). The response is faster to develop and is produced in higher quantities. This slide illustrates that the humoral adaptive immune response has memory. If it didn't have memory, the secondary or anamnestic response would be the same as the primary, but it is a bigger response and occurs more quickly. The secondary response may be days later or years later. It is why vaccines work or why, when we've had measles, we don't get that disease again. The adaptive immune response has seen it once, remembers it and is ready to defend against it faster and to a greater extent if it ever invades again.

Immunologic Diseases

- Deficiency or dysfunction
- Immunodeficiency: absence of one or more elements of the immune system, congenital or acquired during life
- Dysfunction: an immune response detrimental to the host

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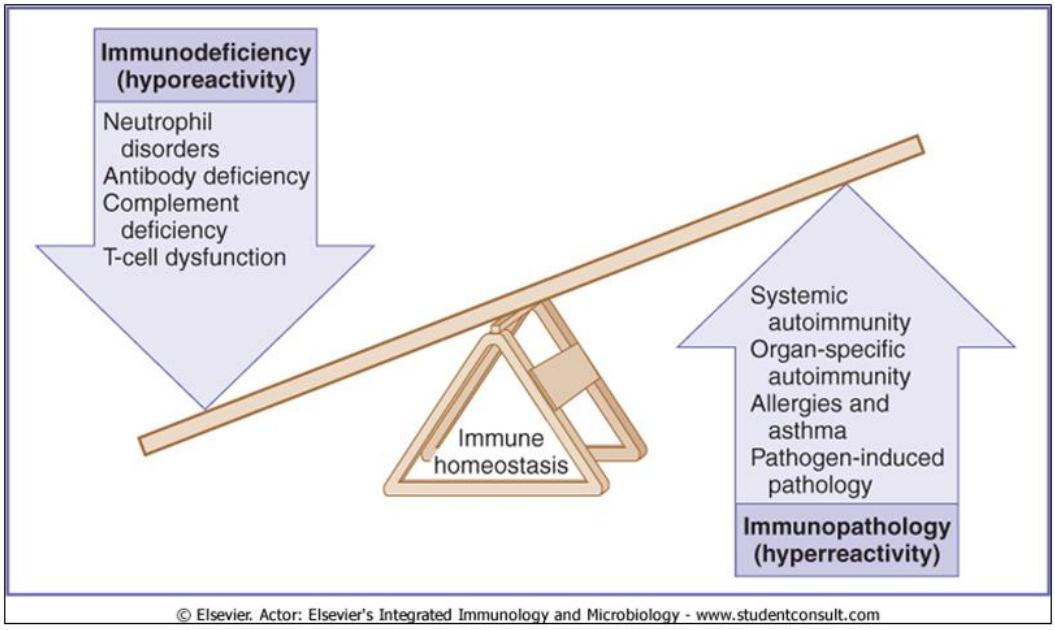
As we have seen and will see, the immune system has many parts and performs many duties. When the immune system is not working properly, it is called an immunologic disease. These diseases fall into two main categories, deficiency and dysfunction. Deficiencies can be congenital or acquired after birth. If acquired after birth, they can be transient or somewhat permanent. If they are gene related (congenital), they are permanent. Dysfunctions may be due to inappropriate or overresponses and are often detrimental to the host. There are many immunologic diseases. Hayfever is a very common dysfunction disease. Sometimes the adaptive immune system reacts against self. This is called autoimmunity or an autoimmune disease. Immunodeficiency diseases are much rarer than autoimmune diseases.

Immune Balanced Response



Slide 16:

Fig 1-4 illustrates the need for a normal homeostatic immune response. Too little or too much or inappropriate response results in an imbalance that is detrimental to the host and can result in serious disease. For now, don't worry about remembering the specifics on either side of the slide, but understand the picture that shows hypo or hyper immunity most often result in a disease state.

Key points of Chapter 1

- Chief function of the immune system
- Two components of the immune system and their characteristics
- Adaptive immunity and specificity
- B and T cells
- Clonal selection
- Adaptive humoral immunity memory
- Two types of immune disease
- Balance needed in immune system

Slide 17:

This slide lists important points covered in Chapter 1. Test yourself by trying to explain each item. When you hesitate, go back to the slides or the books for help. Look up words and phrases that you are unsure about.