CHAPTER 1
INTRODUCTION

Resistance to infectious diseases relies on both INNATE and ADAPTIVE modes of immunity. While both are effective and significant, a major focus of this course is ADAPTIVE IMMUNITY, that mode of immunity which exhibits SPECIFICITY and MEMORY.

Two systems of adaptive immunity protect all vertebrates, namely CELLULAR and HUMORAL immunity. The consequences of both of these classes of immune responses may be harmful as well as beneficial, and are mediated by cells of the highly distributed LYMPHOID SYSTEM.

INNATE versus ADAPTIVE IMMUNITY

INNATE IMMUNITY

The body's first line of defense against pathogenic organisms (including bacteria, fungi and viruses) is the physical barrier provided by the skin, by the epithelium and mucus secretions of the alimentary tract and lungs, etc. This level of protection, however, is relatively non-specific; it distinguishes little, for example, between the bacterial organisms Staphylococcus and Streptococcus, or between the viral agents causing polio and smallpox. A next level of defense is manifested by a variety of cells and serum molecules which may promote ingestion and killing of potentially infectious organisms, cells including macrophages, neutrophils and dendritic cells, and molecules including complement and defensins. These modes of protection are present in all healthy individuals, and are essentially unchanged following repeated challenges by the offending pathogens - that is to say they do not display memory, and are collectively referred to as INNATE IMMUNITY. Mediators of innate immunity contribute to the complex process of development of INFLAMMATION. However, as we will discuss later, the mechanisms of non-specific inflammation overlap and interact extensively with those mediating adaptive immune responses, which will be clearly illustrated in the modes of action of dendritic cells, macrophages and complement.

Although relatively non-specific, innate immunity is highly effective and centrally important to our well-being, as evidenced by the consequences of damage to this system by trauma (e.g. wounds which damage epithelium and may get infected, ionizing radiation which can inhibit the inflammatory response) or by disease (e.g. emphysema, which causes greatly increased sensitivity to bacterial infection in diseased lungs). In fact, as we will see, loss of effective innate immunity can have as deadly consequences as any loss of adaptive immune function.

ADAPTIVE IMMUNITY

What is classically meant when referring to the "immune system", however, is not the non-specific manifestations of innate immunity, but the complex system of immune reactions known as ADAPTIVE IMMUNITY (including both humoral and cellular immunity, defined
The discipline of immunology can be approached from two distinct perspectives:

1) **Historical/Medical outlook: Resistance to Infectious Disease.** The adaptive immune system can confer **specific** resistance to many infectious diseases, *e.g.*, smallpox. This example illustrates two key features of immune reactions, namely **specificity** and **memory**. Having recovered from smallpox (or having been vaccinated) makes one resistant ("immune") to being infected with smallpox later - the immune system exhibits **memory**. Resistance to smallpox, however, does *not* make a person resistant to **measles, mumps, diphtheria** or other diseases caused by unrelated organisms - the immune system thus shows **specificity**.

2) **Biological approach: Recognition of "Self" Versus "Non-self".** Quite apart from its importance in resistance to infectious disease, the immune system has been of tremendous interest to biologists interested in the nature and mechanisms of immunological **specificity**, one aspect of which can be regarded as an organism's ability to distinguish **self** from **non-self**. The single-celled amoeba, for instance, ingests food by phagocytosis; how does it distinguish a particle of food from one of its own pseudopods? (Note that the same question may be asked of a macrophage.)

![Figure 1-1](image_url)

**Figure 1-1**

For multicellular organisms the problem becomes even more complex -- they must be capable of recognizing their own diversity of normal cell types as **self** while at the same time retaining the ability to recognize **foreign** particles and cells and reacting against them.

The biological concept of **specificity**, particularly in the context of cell surface recognition, extends into many other areas, *e. g.* that of control of cell proliferation and differentiation. As a result, the problem of immunological specificity has attracted study by many scientists whose basic interests lay in the areas of differentiation and tumor biology.
Let’s define the following two terms in the context of adaptive immunity:

**IMMUNITY - Acquired resistance to infectious disease displaying specificity at the molecular level.** We’ve already noted that many factors other than the adaptive immune system contribute to resistance to disease, for instance the barrier to microorganisms provided by our skin and other membranes and phagocytic cells ("innate immunity"). These are not acquired, however, nor do they exhibit the specificity required by this definition, and therefore they are not by themselves considered an expression of the "adaptive immune system".

**IMMUNE RESPONSE - Reactivity against a target displaying specificity at the molecular level.** The targets of such reactivity may be disease-producing organisms, or may be completely harmless substances such as foreign red blood cells or foreign serum proteins. One major criterion for effective reactivity under normal circumstances is that the target be "foreign" to the responding organism, although we shall see that immune responses may be directed against "self" components as well. We shall also learn of many factors that may affect the magnitude of immune responses to various targets.

**ROLES OF THE IMMUNE SYSTEM**

**Resistance to infectious disease.** From a medical or evolutionary standpoint, this is highly beneficial, and obviously a central role of the immune system. Deficiency in the ability to mount effective immune responses leads to increased susceptibility to infection by bacteria, fungi and viruses. (The largely discredited idea that the immune system also effectively seeks out and destroys cells which are undergoing neoplastic transformation, i.e. "immune surveillance", is discussed in Chapter 23.)

However, the immune system does not always act in a manner beneficial to the organism; some immune responses result in considerable harmful effects and may be fatal, as illustrated by the following examples:

**Allergy.** Immune responses to food and to plant and animal products in our environment may result in the various manifestations of allergies. Hay fever and allergies to foods and animal products are very common, and while they often are not very serious, they may sometimes be life-threatening, such as in the case of severe asthmatic reactions or anaphylactic shock.

**Autoimmunity.** The normal ability of the immune system to distinguish self and non-self can be disrupted by a variety of influences, resulting in damaging and potentially lethal reactivity to normal "self" components. Rheumatoid Arthritis (RA) and Systemic Lupus Erythematosus (SLE) are two examples of many such autoimmune reactions.

**Graft rejection;** the rejection of foreign tissues and organ transplants is a “normal” consequence of immunological specificity; however, the ultimate result of immune rejection of a heart or liver transplant, for instance, may be fatal. Much research is stilled aimed at discovering more effective methods to prevent immune rejection of grafts, while at the same time maintaining the recipient's ability to resist infectious organisms.
THE LYMPHOID SYSTEM: ORGAN OF IMMUNITY

We will discuss later the many different cell types which are directly or indirectly involved in immune responses. One cell type, however, the LYMPHOCYTE, is centrally involved in all adaptive immune responses.

No single, localized organ is responsible for immune reactivity, but rather it involves a wide variety of organs which include lymph nodes, spleen, Peyer's patches, tonsils, thymus and bone marrow. These are collectively known as the LYMPHOID SYSTEM, by virtue of the fact that they all contain large numbers of the white blood cells known as lymphocytes. Each has a unique structure and role in immune responses, which we will examine in some detail later (Chapter 16).

TWO SYSTEMS OF IMMUNITY PROTECT VERTEBRATES:

   HUMORAL AND CELL-MEDIATED (“CELLULAR”) IMMUNITY

Immune responses can generally be categorized as either humoral or cellular.

HUMORAL IMMUNE RESPONSES are those mediated by antibodies in various body fluids (“humors”), including blood, saliva and the mucous secretions of the lungs and intestinal tract (the nature and structure of antibodies will be discussed in Chapters 3 and 4, and the cellular basis for humoral immunity in Chapter 15). In general, the humoral response offers protection from infections caused by organisms which are extracellular, a category which includes most bacteria as well as many of their toxic products (e.g., diphtheria and tetanus toxins). Hay fever and food allergies are examples of humoral responses which are harmful to the host.

CELL-MEDIATED IMMUNE RESPONSES are not mediated simply by antibodies, but require the direct participation of immunologically reactive cells (to be discussed in Chapters 11 and 12). Cell-mediated immunity is responsible, in general, for resistance to infectious organisms which are primarily intracellular. This includes resistance to viral infections as well as to certain bacteria (e.g., the Mycobacterium responsible for tuberculosis). Immunity to fungal infections and graft rejection are also largely the responsibility of the cellular immune system.

The ability of immune serum to transfer humoral immunity promoted early studies which identified the relevant effector molecules, the ANTIBODIES. In the next few chapters we will examine the structure and function of antibodies, which are the mediators of humoral immune responses, and proceed in later chapters to examine the features of cell-mediated immune responses.
CHAPTER 1, STUDY QUESTIONS:

1. What are the defining differences between INNATE and ADAPTIVE immunity?
2. What are the differences between HUMORAL and CELL-MEDIATED immunity?
3. What are some of the biological and medical consequences of immune reactions?