

LECTURE 5

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IMMUNITY

Read Chapter 16 in your text before proceeding.

THE IMMUNE RESPONSE

Immunity vs. Innate Resistance

The human body resists foreign (nonself) materials, such as toxins and microorganisms by two major mechanisms, **Immunity** and **Innate Resistance**. Innate resistance is termed “innate” because it is present at birth and cannot be acquired. Specifically, any physiological or anatomical feature of your body that renders you resistant to infection by a microorganism falls in the category of innate resistance. For example, skin may be too tough for penetration by an infectious agent or the GI tract may be too acidic or too alkaline for survival of a microbe. In either case, an infection fails to establish because of an inborn anatomical or physiological feature, not because of immunity. In order for a defense mechanism to be categorized as true immunity, antigens (foreign materials) and antibodies (protective proteins produced by the immune system) must be involved. If those two materials are not involved, a true immunity does not exist.

An unfortunate variation of the immunity theme occurs when, for any of a variety of possible reasons, the body fails to recognize a component part as “self” and directs its immune defenses against its own tissues. Such a condition is referred to as an **autoimmune** response/reaction. Such a reaction can be problematic and is thought to be the underlying cause of disorders such as lupus erythematosus, multiple sclerosis, rheumatoid arthritis, toxic thyroid, etc.

Elements of the Immune Response (Humoral vs. Cellular Immunity)

Normally, as the immune system becomes “competent” around the time of birth, “self” tissues are recognized by the MHC (major histocompatibility complex) proteins expressed on cell surfaces. Once recognized as “self”, a normal immune system will not attack such components. Thus, by definition, anything not recognized as “self” becomes antigenic (foreign) and subject to attack by the immune system. This attack by the immune system involves two phases: (1) **humoral** (blood borne) **immunity** by means of soluble antibodies (immune globulins-Ig’s) dissolved in blood plasma; and (2) **cellular immunity** involving antibody that remains attached to the cell surfaces of “killer” cells as well as phagocytic macrophages. This two-phased attack requires specialized WBC’s, known as **lymphocytes**, of which there are two types, **B-Cells** and **T-Cells**. Both of these

lymphocyte types can produce antibodies, but their use of antibody is dramatically different. When stimulated by an antigen, a B-Cell can differentiate into a **plasmacyte** (plasma cell), and plasma cells can produce the soluble antibodies called **immune globulins (Ig's)**. There are many types of immune globulins. (IgM, IgA, IgE, etc).

At this point, we are interested in one particular type, the IgG, which used to be known as gamma globulin. IgG's are "Y" shaped molecules with the two ends of the Y's being custom tailored to fit the antigen that stimulated their production. As a result, they are highly specific. They are relatively low in molecular weight which means that they are small and **are filterable**, meaning they will pass through capillary pores to end up in any fluid compartment of the body. They are transplacental, so a newborn actually has the entire IgG complement of its mother through simple exchange across the placenta. Basically, these are the **soluble** antibodies associated with B-cell or humoral immunity.

Although "Killer" T-Cells also produce antibody, the immune response they direct is somewhat different. In these cells, the antibody molecules are not released. Instead, they remain attached to the cell surface so that the entire cell becomes immunologically active. "Killer" T-cells, also known as CD8's or cytotoxic T lymphocytes (Tctl's), are members of a major class of T-cells called "effector" T's because they are effective in antigen attack. These are the immunologically active elements of the cellular response. "Regulator" T-cells are the second major T-cell type. There are two types of regulator T's, "Helper" or CD4's and "Suppressor", a CD8 type also. These are regulator T's because they are instrumental in controlling the total immune response. For example, CD4's help or boost both phases of the immune response by secreting "lymphokines" that activate other lymphocyte types of the immune response.

All blood cells originate as stem cells in bone marrow. Lymphocytes are no exception. If in early life you expose these newly produced blood cells to the liver and the spleen, they are said to have had a BURSAL influence and will differentiate into a particular type of immune cell, the B-Cell. Once they differentiate into mature B-Cells, they colonize lymph nodes and forever produce the B-Cells that occur in peripheral circulation and are responsible for humoral immunity.

Looking at the other line of specialization, some of these stem cell products (immature lymphocytes) actually pass through the thymus gland which exerts its influence very early by influencing these immature lymphocytes to become Thymic lymphocytes or T-Cells. They also colonize lymph nodes and remain there throughout life producing the three T-cell types.

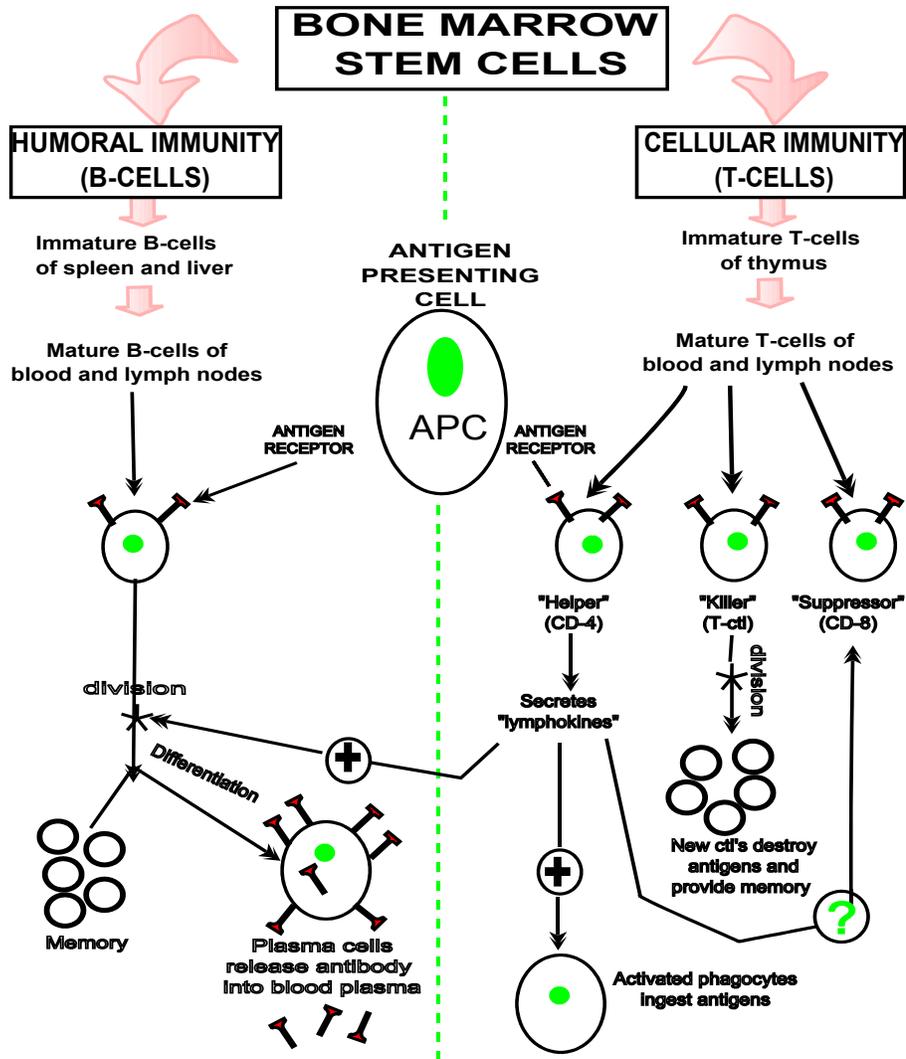
Notice that antigens have to be processed by phagocytic antigen presenting cells (APC) before they can be passed to mature B- and T-cells to activate them. Upon activation, mature B-cells become plasmacytes and produce and release antibody specific for the antigen.

Mature, activated T-cells perform a variety of functions depending upon their type. CD4's secrete lymphokines to activate other cellular elements as well as to

stimulate the humoral response. “Killer” T’s divide and attack antigen. “Suppressors” are proposed to help keep the response in check.

Notice that division of cells on both the humoral and cellular sides provides populations of immunologically active cells that persist over time as “immunological memory.”

Details of the two phases of immunity, humoral and cellular, are summarized in the chart below:



Review Questions:

1. If HIV attacks CD4 lymphocytes, what immunological problems would you expect in infected people?
2. Why is CD4 count a major criterion in evaluating the stage of HIV progression?

3. What is specifically meant by HIV-positive (seroconversion)?
4. Why do you suppose lymph nodes are concentrated in the neck, groin, and intestinal mesenteries?

DISCUSSION QUESTIONS: (Post answers to the “Patho Discussion Group”)

1. How is it possible for an infant born to an HIV-positive mother to be uninfected?
2. Would such an infant test HIV-positive at birth? Why?
3. Assuming no subsequent exposure, after 5 years would the child test HIV-positive? Why?