**Invertebrate Innate Immunity** – Invertebrates rely solely on innate immunity. Circulating insect immune cells are capable of phagocytosis, engulfing and destroying foreign substances by forming a vacuole that fuses with a lysosome.

**Vertebrate Innate Immunity** - In mammals, innate defenses include skin and mucous membranes that protect organ systems open to the external environment such as the digestive, respiratory, reproductive, and urinary system. Nostril hairs filter incoming air, and mucus in the respiratory tract traps most microbes and dirt that get past the nasal filter. Cilia on cells lining the respiratory tract then sweep the mucus and any trapped microbes upward and out.

Microbes that breach a mammal’s external barriers, such as those that enter through a cut in the skin, are confronted by innate defensive cells. These are all classified as white blood cells, although they are found in interstitial fluid as well as blood vessels. Most, such as abundant neutrophils, are phagocytes. Macrophages are large phagocytic cells that wander through the interstitial fluid, “eating” any bacteria and virus infected cells they encounter. Natural killer (NK) cells, another types of white blood cell, are not phagocytes.
The inflammatory response is a major component of our innate immunity. Any damage to tissue, whether caused by microorganisms or by physical injury – even just a scratch or insect bite – triggers this response. You can see the signs of the inflammatory response if you fail to properly treat a cut. The area becomes red, warm, and swollen.

Diagram 1:

1. The damaged cells soon release chemical alarm signals such as histamine
2. The chemicals spark the mobilization of various defenses. Histamine, for instance, induces neighboring blood vessels to dilate and become leakier. Blood flow to the damaged area increases, and blood plasma passes out of the leaky vessels into the interstitial fluid of the affected tissues. Other chemicals attract phagocytes
3. The white blood cells mustered into the area engulf bacteria and the remains of any body cells killed by them or by the physical injury. Many of the white cells die in the process, and their remains are also engulfed and digested. The pus that often accumulates at the site of an infection consists mainly of dead white cells and fluid that has leaked from the capillaries during the inflammatory response.
The lymphatic system, which is involved in both innate and acquired immunity, consists of a branching network of vessels, numerous lymph nodes, the tonsils and adenoids, the appendix, and the spleen. It also includes the bone marrow and the thymus which are the sites where white blood cells develop. The lymphatic vessels carry a fluid called lymph, which is similar to interstitial fluid but contains less oxygen and fewer nutrients. The lymphatic system has two main function: to return tissue fluid to the circulatory system and to fight infection.
When the innate immune response fails to ward off a pathogen, the acquired immune response provides a second line of defense. Acquired immunity, found only in vertebrates, is a set of defenses that are activated only after exposure to pathogens.

Any foreign molecule that elicits an acquired immune response is called an antigen. Antigens may be molecules that protrude from pathogens or other particles, such as viruses, bacteria, mold spores, pollen, house dust, or the cells surfaces of transplanted organs. When the immune system detects an antigen, it responds with an increase in the number of cells that either attack the invader directly or produce immune proteins called antibodies. An antibody is a protein found in blood plasma that attaches to one particular kind of antigen and helps counter its effects.

Acquired immunity has a remarkable “memory.” It can “remember” antigens it has encountered before and react against them more promptly and vigorously on subsequent exposures. Acquired immunity is usually obtained by natural exposure to antigens, but it can also be achieved by vaccination. In this procedure, the immune system is confronted with a vaccine composed of a harmless variant or party of a disease-causing microbe, such as an inactivated bacterial toxin, a dead or weakened microbe, or a piece of a microbe. The vaccine stimulates the immune system to mount defenses against this harmless antigen, defenses that will also be effective against the actual pathogen because it has similar antigens.
Lymphocytes, white blood cells that spend most of their time in the tissues and organs of the lymphatic system, are responsible for the acquired immune response. Like all blood cells, lymphocytes originate from stem cells in the bone marrow. As shown in Figure 3, some immature lymphocytes continue developing in the bone marrow; these become specialized as B lymphocytes, or B cells. Other immature lymphocytes are carried by the blood from the bone marrow to the thymus, a gland in the upper chest. There the lymphocytes become specialized as T lymphocytes, or T cells. Both B cells and T cells eventually make their way via the blood to the lymph nodes, spleen, and other lymphatic organs.

Figure 3: The development of B cells and T cells
As molecules that elicit the acquired immune response, antigens usually do not belong to the host animal. Most antigens are proteins or large polysaccharides on the surfaces of viruses or foreign cells.

As shown in Figure 4, an antibody usually recognizes and binds to a small surface-exposed region of an antigen, call an antigenic determinant (also know as an epitope). An antigen-binding site, a specific region on the antibody molecule, recognizes an antigenic determinant have complementary shapes, like an enzyme and substrate or a lock and key.
**Clonal Selection** – the production of a lineage of genetically identical cells that recognize and attack that specific antigen that stimulated their proliferation. Clonal selection is the mechanism that underlies the immune system's specificity and memory of antigens.

Diagram 2:

1. The row of three cells at the top of the figure represents a vast repertoire of B cells in a lymph node, each with its own specific type of antigen receptor embedded in its surface. The cells’ receptors are in place before they ever encounter an antigen.
2. The first time an antigen enters the body and is swept into a lymph node, antigenic determinants on its surface bind to the few B cells that happen to have complementary receptors. Other lymphocytes, without the appropriate binding site, are not affected.
3. Primed by the interaction with the antigen, the selected cell is activated: It grows, divides, and differentiates into two genetically identical yet physically distinct types of cells. Both newly produced types of cells are specialized for defending against the antigen that triggered the response.
4. The first group of newly cloned cells are effector cells (or plasma cells), which combat the antigen.
5. The second group of cells produced by the activated B cells are a smaller number of memory cells, which differ from effector cells in both appearance and function. Memory cells may last for decades and remain in the lymph nodes, poised to be activated by a second exposure to the antigen.
Diagram 3: When memory cells produced during the primary response are activated by a second exposure to the same antigen, they initiate the secondary immune response. This response is stronger and faster than the first. The selected memory cells multiply quickly, producing a large second clone of lymphocytes that mount the secondary response. Like the first clone, the second clone includes effector cells that produce antibodies and memory cells capable of responding to future exposures to the antigen.
Figure 5 is a simplified diagram explaining antibody structure. Each Antibody molecule is made up of four polypeptide chains, two identical “heavy” chains and two identical “light” chains. The parts colored in shades of pink represent the fairly long, heavy chains of amino acids that give the molecule its Y shape.
Diagram 4: Effector mechanisms

1. Neutralization – Antibodies bind to certain surface proteins on a virus or bacteria coat, thereby blocking its ability to infect a host cell
2. Agglutination – Clumping together of viruses, bacteria, or foreign eukaryotic cells making it easier for phagocytosis
3. Precipitation – The antibody molecules link dissolved antigen molecules together. This makes the antigen molecules precipitate out of solution as solids. Precipitation out of solution as solids thus enhancing engulfment by phagocytes
4. Activation of complement system – Activated complement system proteins can attach to a foreign cell and poke holes in its plasma membrane, causing cell lysis
Monoclonal antibodies (mAb) – an antibody secreted by a clone of cells and, consequently, specific for the one antigen that triggered the development of the clone.

One common use of monoclonal antibodies (mAb’s) is in home pregnancy tests. The most popular type of test uses mAb’s to detect a hormone called human chorionic gonadotrophin present in the urine of pregnant women. When urine is applied to the testing strip, it moves through a series of bands that contain different mAb’s.
Diagram 6: The activation of a helper T cell and its roles in immunity

### Diagram 6:

1. The macrophage ingests a microbe and breaks it into fragments – foreign antigens (orange).
2. Then molecules of a special protein (green) belonging to the macrophage, which we will call a self protein (because it belongs to the body) bind the foreign antigens.
3. Then the self protein displays the nonself molecules.
4. Helper T cells recognize and bind to the combination of a self protein and a foreign antigen – called a self-nonself complex – displayed on an antigen-presenting cell (the macrophage).
5. Interleukin-2 (protein) makes the helper T cell itself grow divide, producing both memory cells and additional active helper T cells.
6. Second, interleukin-2 helps activate B cells, thus stimulating the humoral immune response.
7. Third, it stimulates the activity of cytotoxic T cells.
The self-nonself complex on an infected body cell is like a red flag to cytotoxic T cells that have matching receptors.

Diagram 7:
1. The cytotoxic T cell binds to the infected cell. The binding activates the T cell, which then synthesizes several new proteins that act on the bound cell, including one called perforin.
2. Perforin is discharged and attaches to the infected cell’s membrane, making holes in it. T cell enzymes then enter the infected cell and promote its death by apoptosis.
3. The infected cell dies and is destroyed.
AIDS (Acquired immunodeficiency syndrome) results from infection by HIV, the human immunodeficiency virus. Although HIV can infect a variety of cells, it most attacks helper T cells. As HIV depletes the body of helper T cells, both the cell mediated and humoral immune responses are severely impaired. This drastically compromises the body’s ability to fight infections.

Once HIV is in the bloodstream, proteins on the surface of the virus can bind to proteins on the surface of a helper T cell. Attached to the T cell, the RNA genome of HIV is reverse transcribed, and the newly produce DNA is integrated into the T cell’s genome.