The Immune System

Section 1.1 Immunity

Human beings are constantly covered in commensal bacteria, or good bacteria that live in an on our bodies without causing us harm. The total cell count of these good bacteria outnumbers that of our own body cells. These commensal bacteria have evolved alongside humans to become both dependent on us and nonpathogenic, but what about the countless bacteria and viruses in the world that haven’t evolved alongside humans, but rather at a quicker rate? These pathogenic bacteria rely on inefficient immune systems.

The immune system is made up of numerous cells that work together to protect the body from foreign pathogens, essentially keeping the host body healthy and unharmed. Immunity is divided into to categories that act on these pathogens in different ways in order to eradicate them from the body and help keep the sickness from happening again.

**Innate Immunity**

 Innate immunity includes primary defenses and first responders to any pathogen that may get into the body. It’s called “innate” immunity because the defenses included in this step are made up of cells that exist in the body from birth. Our body will go through this reaction whether this is the first pathogen it has seen or the hundredth.

There are three main innate immunity categories. The first is mechanical, which includes the epithelial layer of skin that covers most of our body. Tight- uniform cell sheets make it hard for pathogenic cells to squeeze their way into the body. Our respiratory and GI tracts also fall into the mechanical barrier category because of their antimicrobial mucus layer. Any time you find yourself with a runny nose your body is utilizing this mucus layer to expel intruders. The next level of immune defense is the chemical barrier. This barrier is made up of antimicrobial peptides, low pH in the gut, and fluids such as tears and saliva. If it were not for the low pH in your stomach any type of bacteria that was found in food would have the opportunity to harm the body. The third category of innate immunity is made up of normal body microbiota. The countless cells that cohabitate with us, as well as the numerous leukocytes that make up the immune system, create the microbiological barrier of innate immunity.

 If the physical barrier doesn’t provide enough defense, like when cuts exists in the skin, and the commensal bacteria is able to enter the body the innate immunity cells take over. Phagocytic leukocytes are the first responders when infections occur. Neutrophils and macrophages are sent in to the site of infection. Their job is to engulf the foreign microbes and secrete cytokines. Cytokines are small cells that specialize in signaling other cells. They make sure that only the necessary cells are recruited to fight the pathogen. This limits the amount of healthy tissue damage sustained by the host.

 Oftentimes an infection becomes too much for the innate immune response to eradicate on its own. In this case the macrophages and neutrophils keep the infection from spreading while a new type of cell, dendrites, is sent in to take a sample of the pathogen. This sample is transported to immunity centers such as lymph nodes and used to activate adaptive immunity.

**Adaptive Immunity**

 After the body has successfully identified the pathogen, adaptive immunity comes in and decides the best course of action based on the antigen. Adaptive immunity relies on the work of two types of leukocytes: B-cells and T-cells. These two cells types are antigen specific, meaning they target a specific antigen and, by default, are not as effective when it comes to general immunity. The specific antigen targeting is done in one of two ways.

 If the toxin is extracellular, such as an infection, then adaptive immunity will most likely progress with B-cells through humoral immunity. B-cells are created in the bone marrow. Here they are coded for random antigens. After the B-cell has been matched to a random antigen specific chain, it leaves the bone marrow and heads for a secondary lymph organ such as a lymph node. Once there, the B-cell undergoes negative selection to verify that the chain present on the B-cell isn’t specific to the human host. This reduces the chance of an autoimmune attack, which will be further discussed towards the end of this chapter.

After all self-reactive B-cells are eliminated the remaining cells undergo maturation. Some of the mature B-cells will begin differentiating into plasma cells. Plasma cells are specialized antibody secreting cells. The antibodies target the specific antigen they are designed for, paying close attention to the specific receptors it can bind with. Each antibody will have its own way of either neutralizing or eliminating the antigen, depending on what kind of immunoglobulin is present. For example, IgE is best for combatting a parasite in the body. This process ends by phagocytes engulfing the antigen that has been tagged by antibodies. The process of tagging an antigen for phagocytosis is called opsonization. This process simply involves antibodies binding to their specific antigen, surrounding it and creating a target for the phagocytes to attack. Simply put, opsonization displays the antigen in a way that ensures healthy cells are not unintentionally phagocytized.

 As all of the cells are finishing their job in eliminating the threat, the remaining mature B-cells come in. At this point they have further matured in the lymph node and become memory cells. These cells are the reason adaptive immunity is so specific.

 The second possible adaptive immune process is cell-mediated. While this process is similar in nature to humoral, it acts mostly on intracellular threats and uses T-cells. There are two different types of T-cells, helper T-cells (also known as CD4+) which are brought in to help manage the other cells in the immune response. Specifically helper T-cells do things such as activate macrophages to engulf pathogens, and enhance antibody production to increase opsonization. The second type of T-cell is cytotoxic T-cells (CD8+). Cytotoxic T-cells, unlike helper T-cells, can actively kill the pathogen on their own. They become activated against the specific antigen, much like B-cells have a specific receptor for specific pathogens, and kill the cell directly. Rather than targeting the antigen itself, T-cells rely on signals from other cells within the body to let them know where the antigen is. These signals are the result of MHC molecules that display peptides fragments that correspond to a pathogen. There are two types of recognizable MHC molecules: I and II, each of these molecules signals a different type of T-cell.

 MHC I exists in healthy cells throughout the body. When a pathogen comes in contact with these cells, such as when a virus attacks cells within the liver, then the MHC molecules found throughout the intestinal cells would display the virus peptide. In this case the CD8+, cytotoxic T-cell would recognize the signal and directly kill the cell that the peptides belong to.

 MHC II molecules work through a different process. Firstly, they are only found on antigen presenting cells of the immune system (like macrophages or dendritic cells). MHC II signals after the antigen-presenting cell has already engulfed the bacteria. CD4+ cells recognize this signal more effectively than CD8+. Helper T-cells then simply do their job. They delegate the other cells until the antigen is eliminated. Lastly, memory cells come in to “document” the process just like in humoral immunity.

 This is one of the most important steps because the documentation of the elimination process leads to memory cells. These mature B-cells remember how to combat the specific antigen for years after exposure. This memory ensures that when the body is confronted with a familiar pathogen it does not have to spend the same lengthy amount of time trying to figure out the best way to eliminate the threat. It speeds up the process the second time around.

Section 1.2 Immunity and Age

 When a new disease is discovered, physicians often note that children and the elderly are most likely to become ill. Young children are susceptible to illness simply because their immune systems have not been exposed to many diseases yet. As mentioned in the section above, memory cells are very important to the mature immune system because they shorten the amount of time a pathogen is alive and well in the body. Children have not yet had the opportunity to create these memory cells and therefore must fight toxins from scratch every time they are exposed.

The elderly are at risk because like most processes in the body, the effectiveness of our immune system declines, as we get older. This is simply because our cells become old along with us and don’t move as quickly as they used to. One apparent change is that our macrophages, which engulf pathogens and other unwanted cells, start to slow down. This is one reason why cancer is most common in the elderly. Macrophages are in charge of stopping the excessive cell production that causes a tumor. When they age they simply cannot keep up with the rapid growth of cancer cells.

 Another reason for the decline in the elderly’s immune function is antibody dysfunction. Humoral immunity relies on many antibodies to quickly bind to their designated antigen. In the elderly, less antibodies are made in response to antigens; this alone means that the timeline necessary to eradicate the pathogen is lengthened. The lengthened timeline coupled with the fact that antigens are harder to bind to with an aged immune system explains why the elderly seem to stay sick for longer periods of time. The decline in antibody function can also lead to less effective vaccinations and a higher likelihood of death from a simple seasonal influenza.

 Another very important aspect of aging immune function is the fact that it becomes more increasingly difficult for the body to distinguish between its own healthy cells and those of a foreign pathogen. This leads to the body attacking itself over the confusion, which is known as an autoimmune disorder.

Section 1.3 Common Immune Disorders

When the factors that make up the immune system are either non-existent or overactive in a person’s body they are diagnosed with an immune disorder. This type of disorder prevents the body from affectively battling against microorganisms and pathogens that could potentially infect the body. Immune disorders also make is easier to contract a virus in the first place.

Immune disorders are typically put into two categories: primary (or congenital) and secondary (or acquired). Physicians classify any immune disorder that a person is born with as a primary disorder; effectively, secondary disorders are acquired later in life. There are several commonly known immune disorders, which will be discussed in the remainder of this chapter.

**Common Variable Immune Deficiency (CVID)**

Common variable immune deficiency (CVID) is the most common primary immune disorder. CVID is usually diagnosed when a person shows a decrease in immunoglobulin (Ig) production. The disorder is considered variable because in its most mild form patients only show a decrease in IgA or IgG while in the most extreme cases all three of the immunoglobulin types show a decrease, coupled with a T-cell defect. Patients who are diagnosed with CVID will present with increased vulnerability to infections.

 Due to the increased likelihood of infections during early childhood, CVID is usually diagnosed later in life. Symptoms of the disorder include increased prevalence of ear infections, sinus infections, and pneumonia. Thankfully, treatment is usually pretty effective. Patients undergo repeated immunoglobulin replacement therapy, which takes active IgG antibodies from plasma and infuses them into the patient’s body. While this is reported to be a very effectively treatment it is not a permanent fix. Patients are still unable to produce their own Ig and eventually their metabolism burns through the infused sample.

**AIDS**

Acquired immunodeficiency syndrome (AIDS) is probably one of the most well known immune disorders. AIDS initially starts as an HIV- infection. After initial infection with the virus a patient can remain asymptomatic for up to 20 years. When a person’s T-cell count has dropped below 500 cells per cubic millimeter, the infection is believed to have progressed into AIDS. It’s not until after the onset of full-blown AIDS that patients can really begin to notice their infection.

 Helper T-cells are most greatly influenced by this infection. Their numbers start to drop, greatly increasing the amount of pathogens present in the blood (an occurrence known as viremia). With the increased presence of infections and no helper T-cells to combat the infections, patients experience symptoms such as enlarged lymph nodes, weight loss, and fever. While treatment is available, if the infections is not identified soon enough patients can die from something as simple as a common cold.

**Autoimmune Diseases**

Autoimmune diseases occur when the body no longer recognizes its own healthy immune cells. Since healthy cells are thought to be foreign, the body defends against the perceived threat by attacking its own cells. The symptoms and severity of those symptoms usually fluctuate depending on the specific type of autoimmune disease. With almost 80 types of specific autoimmune diseases, some are more severe than others. For example, one of the more common autoimmune diseases is rheumatoid arthritis. While this disease isn’t life threatening it does lead to extremely painful joint and tissue swelling.

 Another well-known type of autoimmune disease is lupus. This disease is believed to be caused by both a genetic predisposition and environmental factors such as medications and infections. Although lupus usually occurs in simple flare-ups that are easily controlled, there can be complications that can lead to death. Since the body is ultimately attacking itself complications are related to how serious the organ damage caused by the lupus is. For example, kidney damage is the most common cause of lupus-related deaths.

Summary

 This chapter discussed the basic way the immune system functions. The immune system is broken down into two distinct parts, innate and adaptive. Innate immunity is naturally present in our bodies. It consists of a physical barrier made up of our skins and mucosal glands, as well as enzymes throughout the body and microbiota within. Macrophages and neutrophils are part of the microbiota that responds first when a pathogen is able to breach the physical barrier. When natural innate immunity cannot handle an infection, our learned adaptive immunity steps in. Powered by memory cells, adaptive immunity drafts B-cells and T-cells that will effectively eliminate the pathogen based on how it has been eliminated before. When adaptive immunity has seen a pathogen before, the process moves along quicker because the body already knows what will be most effective. If the antigen is new to the body, memory cells stay behind after eradication adding a new pathogen to the arsenal of adaptive immune response.

 When we’re young this process can sometimes take as little as a few days to eradicate the pathogen however, as we age so does the immune system. This is why the elderly are more susceptible to disease. Oftentimes, elderly immune systems cannot distinguish between self and foreign, leading to autoimmune disorders like arthritis and lupus. Immune disorders occur when the body either overreacts to an antigen or is incapable of reacting properly at all. Common immune disorders include CVID which occurs when immunoglobulin are ineffective on antibodies. AIDS is a well-known immune disorder that occurs when helper T-cells are virtually wiped out, making cell-mediated immunity impossible.

 Our immune system, like all body systems, is specially designed to perform exactly as we need it to. Over centuries of evolution it has evolved just so, allowing us to cohabitate with necessary microbiota and effectively fight off foreign pathogens.

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