The Relationship between Antibodies and the Immune System

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I. Abstract

The human body defends itself from outside pathogens through the immune system. There are two types of immunity, innate immunity and adaptive immunity. In innate immunity, the body utilizes a general responses to initially combat pathogens. In the adaptive immune response, T and B lymphocytes fight the pathogens. Antibodies are proteins made by B lymphocytes that help combat bacteria and toxins in the body. They come in five different classes; IgM, IgD, IgG, IgE, and IgA. Each class is determined by its structure, which in turn facilitates its function. However, often functionality may twist into dysfunctionality, which in the human body can cause damage, termed immunopathology. There are three types of antibody related immunopathologies; type I, type II, and type III. These antibody related diseases range from simple allergy to rheumatoid arthritis. The following is an overview of their function and dysfunction.
II. Overview of Immunology.

A) The Immune Response

The human body is composed of many different organ systems. While the nervous system, cardiovascular system, endocrine system, and others are all incredibly fascinating in their own right, they would be vulnerable to attack without the immune system protecting them. Like any good fortification, the immune system has many walls that “outsiders” must break through before reaching the precious vital organs. It starts with the outmost layer, the skin and mucous barriers. Rich in antibiotics and coated in helpful bacteria, they provide a harsh landing to any pathogen that finds its way to the human body. These “good” bacteria help keep the skin clean of pathogens trying to break through.

The next line of defense is the innate immune system. Its job is to detect intruders that have ventured too deep into the body’s structures, and then arrange for their inactivation, destruction, and removal. It does this through the use of pattern-recognition receptors (PRR) that can detect harmful damage to a cell (called damage-associated molecular patterns, or DAMP) or detect foreign molecular structures not native to the human body (pathogen-associated molecular patterns, or PAMP). PAMPs are often motifs found on harmful pathogens and are absent on “good” pathogens. Some PRRs found in the human body are known as toll like receptors (TLR), which are found all over the body on almost every cell. For example, TLR-3 recognizes double stranded RNA, commonly found in viruses.

Once enough PRRs bind a cell showing signs of DAMPs or pathogens showing PAMPs, inflammation, caused by the release of immune cytokines and chemokines, attract dendritic cells,
which then phagocytose (Figure 1) the damaged cell or pathogen, becoming mature dendritic cells. These mature cells then leave the local area and travel in the lymphatics to the nearest lymph node, where they present the antigen (using MHC class I or class II molecules) they have consumed to lymphocytes.

Lymphocytes are a type of mononuclear white blood cells. There are two types, T cells and B cells. Both contribute to the adaptive immune system, the third wall of defense against pathogens. T cells focus on surveying the surfaces of cells, looking for those that are infected or damaged. Once a mature dendritic cell reaches T cells in a lymph node, a T cell will bind the dendritic cell at MHC class II if the dendritic cell presents a pathogen the T cell can recognize. Once bound, that T cell will mature into a T lymphoblast and proliferate into active T cells and memory cells. Some T cells will migrate to the site of inflammation to help the pathogen. B cells on the other hand, protect the extracellular spaces of the body (i.e. fluids, blood, secretions) by releasing antibody into these fluids. When the Thf cell (a type of T helper cell) interacts with the correct mature B cell, the B cell gathers its IgD and IgM receptors at one spot on the surface. B cells see free antigen. The antigen is processed and when the threshold for recognition is met, the B cell activates. From there some proliferate and differentiate into memory cells and into B lymphoblasts which mature into plasma cells (which churn out antibodies).

Once the pathogens have been taken care of by the T and B cells, the active cells will begin to die off. However, memory cells can last for decades, leading to a faster and more effective secondary response should the body encounter this pathogen again. This is known as immunity.
B) Anatomy and Physiology of the Innate Immune System

The innate immune system starts and is comprised by components in the blood. White blood cells help to destroy foreign pathogens. Damage to the body triggers three separate cascades; the plasma kinin cascade, the complement cascade, and the coagulation cascade. The plasma kinin generates an inflammatory mediator called bradykinin, which causes vasodilation at the site of damage through the binding of B2 on vessel cells (a GPCR). The complement cascade to form membrane attack complexes, which lyse foreign bacteria. Lastly, platelets clot the damage to keep inflammation local through the coagulation cascade (Figure 2). These cascades are triggered by cytokines and are important in the healing process.

When it comes to white blood cells, there are four different types involved in the innate immune response; monocytes/macrophages, neutrophils, eosinophils, and basophils. Monocytes are mononuclear white blood cells found in the blood and account for 2-8% of the total white blood cell count. This is because once they leave the blood stream and move into the tissues, they activate and become macrophages (Figure 3). Macrophages are extremely large mononuclear white blood cells, whose primary job is to engulf and digest...
cellular debris, foreign substances, and anything else that does not belong in the human body. Similar to dendritic cells, macrophages may also present antigens to the cells of the adaptive immune system.

Neutrophils (Figure 4) are polymorphonuclear white blood cells that release granules (which is why they are often called granulocytes) and comprise 40-60\% of the total white blood cell count. They get their name from staining a neutral color from the hematoxylin+eosin stain. In the case of neutrophils, the granules that are released in an immune response contain reactive oxygen species (ROS) which begin to break down any pathogen recognized by TLRs. The first to arrive to the site of trauma or infection, neutrophils can often resolve the issue on their own. They are also phagocytic cells. Neutrophils can be considered the Swiss army knife of the innate immune system.

Eosinophils are polymorphonuclear white blood cells that help in combating parasites and comprise 1-4\% of the total white blood cell count. They get their name from the granules within them stains with the acidic eosin stain. They work by releasing histamines and proteins such as ribonuclease, deoxyribonuclease, and lipase (among others). When responding to a parasitic attack, eosinophil chemotactic factor of anaphylaxis (ECF-A) is released by mast cells and draws in eosinophils to attack the parasite by producing Major Basic Proteins, which kill the parasite.

Lastly, not much is known about Basophils which comprise 0.5-1\% of the total white blood cell count. Also polymorphonuclear white blood cells, they are stained blue by the basic hemotoxylin stain. That being said, their granules are similar to those of mast cells. It has been
hypothesized that basophils migrate from the blood stream to the periphery and become mast cells in the tissues.
C) Anatomy and Physiology of the Adaptive Immune System

The cells of the adaptive immune system are lymphocytes, which are mononuclear white blood cells. These are further subdivided into T and B cells. T lymphocytes (T cells) begin development in the bone marrow and then move to the thymus. At this point, the T cells have markers for both CTL (CD8) and Th (CD4). The T cells begin to downregulate one of the markers, becoming either CTLs or Ths (CD8 is downregulated in Th and CD4 is downregulated in CTL). If they do not, they are killed via apoptosis (programmed cell death), or they remain in the Thymus. T helper cells then move to a secondary lymphoid organ and mature into Th0, which can become Th1, Th2, Th17 cells, T follicular helper cells (Tfh), or regulatory T cells (figure 5). Th1 help recruit macrophages to the inflammation site. Th2 help begin the healing process. Th17 release potent cytokines to help fight pathogens. Tfh cells help B cells make different antibodies. Regulatory T cells down regulate the other helper T cells once the immune response is complete. Cytotoxic T cells directly kill pathogens. After maturation in the Thymus, Th cells migrate to secondary lymphoid tissues.

B cells begin their maturation in the bone marrow and end in secondary lymphoid organs. First a Pro-B cell makes mu chain in the cytoplasm (the heavy chain of the antibody IgM) and then a Pre-B cell makes full IgM in the cytoplasm. An immature B cell then begins to express IgM on the surface of the cell, followed by IgD, which identifies the B cell as fully mature. If a B cell responds to the “self-antigen” while still in the bone marrow, it will undergo apoptosis. This
process is known as clonal deletion. Once a B cell matures (having the ability to make antibodies), it migrates to the secondary lymphoid tissues.

Secondary lymphoid tissues include the spleen, the gut associated lymphoid tissue (GALT), and the lymph nodes. The spleen mainly stores T and B cells and disposes of old red blood cells. The GALT has specialized mucosal cells, which are gatekeepers, ingesting proteins and particles as big as viruses and transporting them to the abluminal side, to be ingested by dendritic cells. Lastly, the lymph node (shown in figure 6) is the primary site of antigen presentation for the bloodstream. Lymph flows through, and any antigen presenting cell may present antigens to the T and B cells which reside. The Cortex is where B cells reside, the para cortex is where the T cells reside, and dendritic cells lie in between the germinal centers (where B clones grow during an immune response) and the para cortex. All secondary lymphoid organs have a similar structure. For example, Peyer’s patches in the GALT have germinal centers where B lymphocytes proliferate.
D) Antibody Structure and Function

An antigen is a foreign substance that produces an immune response. Antibodies are proteins that bind to epitopes of antigens (specific regions of the antigen) and trigger another process to occur. Antibodies consist of at least two heavy chains and two light chains. The classes of heavy chains are gamma, epsilon, delta, alpha, and mu while the types of light chains are lambda and kappa. Each chain also includes a variable region and constant region(s). The variable region is what binds the epitopes of antigens. What leads to antibody diversity is the complementarity-determining regions (CDR), which are variations in amino acids in the variable region. All of this is summarized in Figure 7.

The five classes of antibodies are determined by which heavy chain was coded from the DNA. The classes are IgM, IgD, IgG, IgE, and IgA. These correspond to their heavy chains, which are; mu, delta, gamma, epsilon, and alpha respectively. Each has a unique structure which in turn effects their function.

If mu was used during transcription, then an IgM antibody would be the result. This antibody consists of a pentamer held together by a j chain. This antibody activates complement similar to IgG, but with five hundred times the potency. However, due to its size, it could thicken the blood in high quantities, and cannot leave the blood vessels. It also cannot pass through the placenta from mother to fetus, meaning the fetus must make its own IgM. This makes it the first antibody made.
Next, when delta is used in transcription, the results is an IgD antibody. This antibody will become the B cell receptor, and so not much is found in the blood stream. That being said, IgD expression is a critical step in B cell maturation.

If gamma was transcribed, then the outcome is an IgG antibody. This is the most abundant antibody in the blood stream and is used to activate the complement system. In addition neutrophils have an IgG receptor, which when bound, helps to phagocytose bound antigen. IgG is the only class of antibody to pass the human placenta from mother to fetus, providing early protection for the unborn and newborn child. IgG is critical in opsonizing (making something easier to engulf) bacteria, playing a vital role in clearance of said bacteria.

If epsilon was selected during transcription, then the cell would create IgE antibodies. Once this antibody is generated, it seeks out and binds mast cells. From there, it becomes cross linked by antigenic antibody (such as antigen made by a parasitic worm). Once cross linked, IgE activates mast cells, which release histamine (over the course of a few minutes) and produce eosinophil chemotactic factor of anaphylaxis (over the course of 4-10 hours after being cross linked). These help mediate the immune response.

If alpha was transcribed, then the outcome would be an IgA antibody. Two IgAs are assembled into a dimer using a j chain.
They are secreted into interstitial space. Epithelial cells with IgA receptors bind IgA and move it across the epithelial cell into the luminal side. IgA is exocytosed and the receptor becomes secretory component. From there, IgA can sterically hinder pathogens from binding epithelial cells and help activate complement\(^5\). The classes of antibody and their locations are summarized in Figure 8.
II. Antibody Related Diseases

A) Type I Immunopathology

Allergy (also known as Type I Immunopathology) is a defect in IgE. In a correct response, a worm enters the body and produces a particular antigen. This antigen then crosslinks IgE, causing the mast cells to release histamine and ECF-A. When someone has an allergy, an antigen known as an allergen crosslinks IgE bound to mast cells. What results is an unneeded immune response, which can range from mild to fatal.

The immune response of an allergic attack differs, based on how the allergen came into contact with the host. If inhaled, the symptoms will be in the oral, nasal, or the conjunctival mucosa. This leads to increases mucus production and difficulty breathing as well as itchy and watery eyes. If inhaled deeply, symptoms may arise in the lungs, which will lead to labored breathing. If ingested, a host may exhibit symptoms in the gut or skin. And while skin contact is an uncommon cause in allergy, eczema is an example of an allergy with a reaction on the surface of the body (such as the skin or epithelial cells of the digestive tract). Eczema is chronic dry skin which tends to be self-worsening. Micro damage to skin cells caused by irritating the dry skin lead to the release of cytokines, which worsens the condition, and can eventually lead to secondary bacterial infections.

With an allergic reaction there are two phases. The first phase happens within seconds of exposure and involves histamine, a cytokine released by mast cells after IgE is crosslinked, which increases vasodilation and capillary permeability. This allows an increase in the amount of white blood cells in the area of interest and allow them to diffuse between the capillary walls.

Figure 9: An infant with eczema
They react to the allergen, leading to an unnecessary reaction. The second phase begins four to ten hours after exposure. It involves prostaglandins (increase vasodilation, platelet aggregation, and inflammation), and leukotrienes (increase inflammation), which are collectively known as eosinophil chemotactic factor of anaphylaxis (ECF-A).

Allergic reactions are triggered by a variety of allergens in the environment. The examples in Figure 10 relay what percentage of 3,500 Europeans have reactions to the allergens. This data is similar to what is seen in North America, and can be classified as specific or non-specific. Specific allergens are those that cross-link IgE and cause an immune response. Non-specific allergens, such as dust, irritate the host system, but are not IgE mediated.

One of the most well-known forms of allergy is asthma. Asthma causes the airways to become constricted and fill with mucus. This causes difficulty breathing during an asthma attack. The damage from the immune responses can cause fibrosis later in life, furthering the difficulty to breath. The chief way to diagnose asthma is with a spirometer. It measures how much air a patient breaths out in one second and compares that to a standard. A second chief tool for diagnosing allergy is skin testing. Allergen is injected intradermally (different allergens and different concentrations) and if there is an allergy, an inflamed red mark will be seen on the skin. Another tool for diagnosing is the CAP-FEIA (capsule-fluorescent enzyme immunoassay). It consists of three parts; the allergen in question, patient IgE, and animal antibody against human
IgE with a fluorescent tag. If the fluorescent indicator is an IgE level of 0.4kU/I, then the patient is allergic. Otherwise, family history is a strong indication of a patient having an allergy. If a parent has an allergy, there is a 33% chance of passing on an allergy to their offspring\textsuperscript{10}.

There are many treatments for allergies. It starts by simple avoidance, for example if you do not come into contact with bees, you will not need to worry about a bee venom allergy. This becomes harder when the allergen is everywhere, such as dust mites. Next would be antihistamines, which can stop the immediate symptoms. It is most effective if the allergic response is acute. If someone does have severe allergic reactions, they may carry an epi pen as well. This syringe is full of epinephrine, a potent vasoconstrictor and smooth muscle relaxer, which helps to relieve bronchoconstriction and maintain blood pressure. Another treatment option are glucocorticoids, which block both prostaglandin and leukotriene production. However they have multiple side effects (such as hyperglycemia and muscle weakness) and they induce apoptosis to eosinophils (leading to a weaker immune system). Next are LABAs (long-acting beta-2 agonists) which rapidly reduce bronchoconstriction and are often given in combination with an inhaled steroid. However, these treatments are expensive, which means lower income patients may not have access to them.

One experimental treatment is immunotherapy, where a patient receives “allergy shots” of dilute allergen extracts. There are administered once or twice a week with increases in concentration until the patient is tolerant. An example can be seen in Dr. Nurmatov’s oral immunotherapy (OIT) for peanut allergies. He and his team took 28 children aged 1 to 16 years old with peanut allergies. They divided them randomly into an experimental group and a control group. The experimental group received small amounts of OIT over a 48 week period (the control group got placebo). After the trial, the experimental group was able to ingest an amount of
allergen without having an allergic reaction than the control group\textsuperscript{36}. Nurmatov’s strategies and immunotherapy in general are based upon the Hygiene Hypothesis, which states exposure to environmental dirt and infections help our immune systems mature naturally. Immunotherapy attempts to force the immune system to adapt and desensitize to a harmless stimulus. However, there is the possibility of a fatal allergic attack too high of a price for treatment. In Dr. Nurmatov’s experiments, half of the children had an allergic response requiring antihistamines, and two more had serious reactions requiring epinephrine.
B) Type II Immunopathology

A type II immunopathology is caused by the actions of antibodies against a specific tissue in the host, and is therefore a form of autoimmunity. Damage to the tissue is done through two general mechanisms. The first is complement-mediated damage. Autoantibodies bind the target tissue and activate complement, leading to lysis (by lysosomes or reactive oxygen species) and phagocytosis. The second mechanism is stimulatory hypersensitivity. Autoantibodies bind a cell-surface receptor and behave as an agonist (activating the receptor).

Autoantibodies are produced in a variety of different ways. One way is Foreign+Self-hybrid. A self-reactive B cell binds an antigen that has both foreign and self-epitopes. The antigen is digested and broken down, and the B cell presents the foreign epitope on MHC class II, which is then recognized by follicular T helper cells. The follicular T helper cell engages the co-receptors and activates the B cell. This causes the B cell to make antibodies against the antigen, but since the B cell recognized the self-antigen, all the antibodies are against self. Similarly, a cross-reaction is when a foreign antigen is similar in structure to a self-antigen, and the antibodies target both. Another way is for the B cell itself to be dysfunctional, known as a forbidden clone. It is a B cell which has escaped the clonal deletion process. This forbidden clone goes on to mature when it encounters self-antigen. It then makes antibodies against self.

Figure 11

\[\text{Foreign + Self Hybrid antigen}\]
Antibodies can also cause damage passively when given from one person to another. The foreign antibodies attach and opsonize host cells, leading to complement damage. Likewise, innocent bystander is when a drug attaches to host cells, and the immune system responds to the drug. In an attempt to bind the drug, it also damages the cells as well. When antigen is sequestered from the blood brain barrier, the immune system may respond and attack the host’s brain because the immune system recognizes antigens from the blood brain barrier as foreign. Lastly, failure in the regulatory mechanism of antibodies can cause exaggerated responses, eventually leading to a self/non-self-discriminatory breakdown.

To determine if an immune response is what causes the symptoms or is a byproduct, Dr. Ernst Witebsky formulated the Witebsky’s Postulates in 1957. It states a series of experiments to identify the cause of an immune response that appears to be autoimmune in nature. First, the autoantibody must be regularly found in patients with the disease in question. Next is to identify the antigen and cause the disease in animals by immunizing them with that antigen. Then transfer the disease to normal animals with antibody from the immunized animals. If the animal begins to show symptoms, then it is an autoimmune diseases. In this category of immunopathology, diseases include Goodpasture’s syndrome, systemic lupus erythematosus, and rheumatoid arthritis.

Goodpasture’s syndrome occurs when patients develop antibodies against type IV collagen, which is integral to the basement membranes of both the kidney and lungs. This leads inflammation of the kidneys (glomerulonephritis) and lungs
(pneumonitis). Goodpasture’s syndrome may be triggered by a viral respiratory infection or upon inhalation of hydrocarbon solvents. Symptoms include bloody urine, pale skin, shortness of breath and coughing up blood. If diagnosed before any damage is done, treatment is typically plasmapheresis, where they replace whole blood from the patient with whole blood from a donor without the autoantibodies. After the kidney has begun to fail, dialysis and kidney transplants become needed.

While the cause of systemic lupus erythematosus (lupus for short) is unknown, it is a devastating condition. It is considered a type II pathology because there are autoantibodies to double stranded DNA. This not only causes kidney and lung damage, but also a “butterfly” rash over the cheeks and bridge of the nose. Further symptoms include headaches, abdominal pain, arrhythmias, and swelling in the legs. Although no cure exists, treatments are available to alleviate the symptoms, such as anti-inflammatories and analgesics.

Lastly, rheumatoid arthritis is caused by the autoantibody “rheumatoid factor”, an IgM anti IgG. This causes complement complexes that deposit at the joints, causing painful swelling that can eventually result in bone erosion and joint deformity. Another way for rheumatoid arthritis to occur is by having autoantibodies against synovium (the lining of the membranes that surround the
joints). This results in thickening of the synovium, which can eventually destroy the cartilage and bone within the joint. Common symptoms include swollen joints and weight loss\textsuperscript{22}. Treatments include steroids and disease-modifying antirheumatic drugs (such as methotrexate)\textsuperscript{28}, which can slow the progression of the disease.

The hallmark test for diagnosing type II immunopathologies is the Enzyme-Linked Immunosorbent assay, better known as the ELISA. First off, the antigen in question must be at least divalent. For example, the physician is looking for rheumatoid factor. They would start by coating a plate or wells with human IgG (what rheumatoid factor binds). Then they add the patient’s serum, and wash anything that is not bound. Lastly, they add an antibody against rheumatoid factor that is also coupled to an enzyme. This enzyme converts a colorless substrate to a colored product. So, they add substrate, wash the plates or wells, and measure the intensity of the product color in a plate spectrophotometer\textsuperscript{8}. 
C) Type III Immunopathology

As stated previously, the purpose of the immune system is to recognize, inactivate, destroy, and remove anything harmful to the host. Type III immunopathology arises when antibody-antigen complexes are not destroyed or removed. Normally, antibodies (IgM, IgG, and IgA) form complexes with antigen, which then grow to a size of about a million Daltons. These complexes are then removed by the reticuloendothelial system (RES), which consists of phagocytes and reticular connective tissue (a network of type III collagen fibers found in lymphatic tissue). However, complexes that activate complement but are too small to be rapidly removed by the RES and get stuck to the basement membranes of filtering organs and cause a multitude of issues.

An example of this mechanism is IgA nephropathy. It is a common form of primary glomerulonephritis and the leading reason for kidney transplant. After an immune response takes place (i.e. after a bacterial infection\(^3\)), the body has a higher amount of antibodies in its system. One kind of antibody is a subclass of IgA known as IgA\(^1\). IgA\(^1\) has an unusually large hinge region, which in IgA nephropathy has no terminal sugars in the hinge, generating a new epitope (N-acetyl-galactosamine). Cross reactive antibodies to this epitope are common in human plasma. Therefore IgA and IgG bind IgA\(^1\) and the complexes become trapped in the renal glomerulus\(^3\).

As with other immunopathologies, there are many ways of achieving a diagnosis, such as blood testing, cryoglobulins, and renal biopsy. Blood testing looks at the total hemolytic level
(CH$_{50}$), which shows if the patient has normal complement levels. This is measured by adding dilutions of the patient’s serum to antibody-coated animal red blood cells and observing the maximum serum dilution that will cause fifty percent of the cells to lyse and compare those dilutions to a normal standard. A low CH$_{50}$ is often associated with type III immunopathology. Another useful diagnosing tool is the use of cyroglobulins. Since type III complexes do not precipitate out of the solution at normal temperatures, you simply refrigerate them for 24 hours (because immune complexes become less soluble at lower temperatures). After incubation, if complexes appear as a fluffy white precipitate, it indicates a type III immunopathology. Lastly, a renal biopsy can easily diagnose a type III immunopathology if there are complexes. Sections of the kidney, containing at least one glomerulus, are placed on a slide and overlaid with fluorescein-labeled animal antibodies to human immunoglobulin. After incubation the slide is rinsed and examined under an ultraviolet microscope. The basement membrane is visualized as the site of tiny clumps of antigen-antibody complex, known simply as a “lumpy-bumpy” pattern. This pattern strongly indicates type III immunopathology$^{33}$.

Treatment options for type III immunopathology are few. Anti-inflammatory, antihistamines, and even immunosuppression are known to be useful. Although, those are only taking care of the symptoms and not the cause. Even state of the art treatments for IgA nephropathy are not much better, with current methods including controlling hypertension,
decrease of urinary protein excretions, and the inhibition of progression to end-stage kidney
disease. These are accomplished through the use of renin-angiotensin-aldosterone system
inhibitors and steroids. New areas in immunotherapy are exciting, with monoclonal antibodies
against B cells and inflammatory cytokines.
D) Antibody Deficiency

Relatively simple to define, antibody deficiency is where a patient has low levels of one or more classes of antibodies. The most common antibodies to be affected are IgM, IgG, and IgA. It can be caused by a variety of factors, mostly relating to the patient’s genetic makeup. One mechanism for deficiency is the inability to class switch B cells to make other antibodies besides IgM. This is known as X-linked hyperIgM syndrome. Another mechanism is that B cells have difficulties maturing into plasma cells (seen in IgA deficiency), which causes common variable hypogammaglobulinemia, where all antibodies are lower than normal. Lastly, drugs such as phenytoin (used to treat seizures) and sulfasalazine (used to treat rheumatoid arthritis) are known to cause genetic mutation is B cells, causing them to not be able to make specific antibodies or to make ineffective antibodies.

Selective IgA deficiency can arise from multiple causes. One way is when there is a deficiency in the “polymeric Ig receptor,” which normally secretes IgA into the mucous membrane. The malfunction cause the receptor to not work, and therefore no IgA is secreted, leading to unmeasurably low levels in the blood and secretions. Another mechanism is that B cells that class switch to IgA cannot mature to plasma cells. The number of B cells class switched to IgA is the same as normal, but the B cells produce significantly less IgA. This inability to mature could also be due to a lack of cytokines such as IL-4, IL-6, IL-7, and IL-10\(^7\).
Diagnosing is typically done through serum electrophoresis. Serum is applied to a gel which has a current run through it so it has one positive side and one negative side. The proteins in the gel begin to separate into groups; albumin, alpha one, alpha two, beta and gamma. If gamma is lower than normal, then the patient has some form of antibody deficiency. From there, classes and subclasses are identified through single radial diffusion. A sample of the antibody in question is taken from the patient’s serum and put into a gel that has antigen for that antibody. Complements will form in a ring from the starting point. The further the ring, the more concentrated the antibody. The patient’s test is then compared to standard to estimate their antibody concentration.

When it comes to treatment, there are not many options and there is no cure. Intravenous antibodies can be donated to a patient with antibody deficiency if they need them to help fight off an infection. Also, simple antibiotics can help the patient fight the increased amounts of infections. Also, most patients with an antibody deficiency are given a bracelet or tag identifying them, as to prevent unneeded contact with infectious persons. If an infection or illness becomes too much for antibiotics to handle, a patient can be given intravenous antibodies, typically IgG.
III. Conclusion

In summary, the immune system is critical to the defense of the human body, from cells to organ systems. Both types of immunity, innate immunity (what you are born with) and adaptive immunity have their own strengths and weaknesses. While a good first response, the innate immune system does not have the ability to handle new pathogens. The adaptive response is slower, but learns from past encounters to bolster its capability to handle the same infection again.

In the adaptive immune response, T and B lymphocytes are the cells fighting the pathogens. T cells come in two main varieties, cytotoxic T cells and helper T cells. While CTL attack and destroy pathogens directly, helper T cells use cytokines to call in other cells and help them, such as phagocytes and B cells. B cells help fight off pathogens by creating antibodies. Antibodies are proteins that help combat bacteria and toxins in the body by forming immune complexes with the pathogens. This makes them easier to spot by the rest of the immune system, destroying and clearing them out quicker. They come in five different classes; IgM, IgD, IgG, IgE, and IgA. Each class is determined by its structure which in turn facilitates its function.

However, the human body is prone to defects, which can lead to damage. Antibody dysfunction occurs in a variety of ways; overreacting to a harmless stimuli, attacking the host, not forming complements correctly, or simply not having enough. Comprehending each of the classes’ mechanisms and how they can go wrong can help patients inflicted with antibody related diseases. These diseases include rheumatoid arthritis, goodpasture’s disease, and IgA nephropathy. While not as devastating as other global diseases, they deserve attention and understanding none the less.
IV. References


V. Appendix A

At SARSEF’s Future Innovator Night, I had a table with pipe cleaners and pompoms. I also had two poster boards, one with a title and basic picture on how IgG is made and the other with pictures of bacteria. I explained to kids how IgG is made, how it works, and what it targets. They will then make an IgG antibody like they are a B cell, with pipe cleaners and pick a pompom antigen for their antibody. They will then write their name on a sticky note and stick it to the bacteria (like an antibody would).

Photos:

*Poster 1*
Poster 2 before Future Innovator Night:

Poster 3 before Future Innovator Night:
During Future Innovator Night 1:

During Future Innovator Night 2:
VI. Appendix B

Poster from Physiology Poster Session 2017

Nobody is Immune!
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Abstract
The immune system responds to infection and injury by producing antibodies to the invading antigens. Antibodies bind to the antigens and mark them for destruction by phagocytes. The innate immune system, on the other hand, is made up of nonspecific defenses that are activated by the presence of certain patterns on the surface of pathogens. These defenses include physical barriers such as the skin and mucous membranes, as well as the complement system and interferons.

The Immune System

Type II Immunopathology
Type II occurs when antibodies against cell are made. Diagnosis is done through an in vitro assay. Treatment range from anti-inflammatories to anti-inflammatory pharmaceuticals.

Type I Immunopathology
Allergy is caused by a defect in T cells, which become sensitized and activated by an allergen. This causes an unnecessary immune response and complications.

Antibody Deficiency
Some mechanism causes B cells to not make enough of one or more classes of antibodies. Diagnosis is done by serum electrophoresis or radial diffusion. Treatment is commonly done through increasing antibodies.

Type III Immunopathology
Caused by complement deposits in basement membrane that cannot be removed by RBCs. Diagnosed by blood test, erythrocytes, and biopsy. Treatment includes anti-inflammatory drugs and immunosuppression.

Conclusion
It is important to recognize that while the immune system is critical for survival, an overactive immune system can also be detrimental. For example, chronic inflammation can lead to autoimmune diseases, while an overactive immune system can lead to allergies. Understanding the mechanisms that regulate the immune system is crucial for developing effective treatments for these conditions.

References

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