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Immunodeficiency Caused by Viruses

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ABSTRACT

Immunodeficiency is caused by many factors. One of these factors is viral transmission. Viruses like HIV, Ebola, and Measles have plagued humanity for decades, but why are they so significant? These viruses have different proteins on their membranes or envelopes that guide them to a specific host cell so they can replicate efficiently. In this process, cells die due to viral-induced apoptosis and therefore affect the body system that the cells are a part of. In these viruses' case, they affect the immune system by directly replicating in immune cells or affecting cells which results in secondary infections and diseases. HIV (Human Immunodeficiency Virus) has proteins which guide it to CD4-T cells, a vital part of the immune system which triggers immune responses in the body. Other viruses such as Measles, Rabies, and Ebola are guided to epithelial cells, which are cells that line the organs and skin of the body. This makes the host vulnerable to secondary infections and diseases. Understanding these viruses is vital to improve current treatments for them and therefore improve society.

Introduction

Viruses have been around since the beginning of history. They were not described in the form we know today, but rather were thought to be sins or punishment for the wrongdoings of the people. Today, viruses play an important part in the ecosystem of the world. They are life in its simplest form, or in other words, a complex mix of organic molecules that replicate in a host cell. Viruses are also known as obligate intracellular pathogens (Goulding, n.d), or obligate parasites.

The immune system is one of the body systems that go into how humans live every day. It protects the body from harmful substances, such as viruses, that can make one ill. What makes a person sick is when the immune system is "weak or can't fight particularly aggressive germs" (InformedHealth.org, 2006). The immune system is key for fighting disease-causing pathogens in the body.

When viruses first enter the body, they go through different replication steps in order to create new virions to infect more cells. There are six steps for viral replication: attachment, penetration, uncoating, replication, assembly, and virion release (Ryding, 2003). The first step, attachment, is when the virion's proteins bind to the cell's surface, where they interact with specific receptors in order to find a compatible host cell. Next, viruses enter the cell by binding with the cell membrane. Then, the virus' capsid degrades due to enzymes, releasing its genetic material. This triggers the fourth step, which is replication of the viral components, and they are then assembled into individual virion units. Finally, the cell releases the viruses so they can further replicate (this usually involves the bursting of the host cell).

Many viruses make a human ill by attacking their immune system. Infamous viruses such as HIV (Human Immunodeficiency Virus, which causes AIDS, an immunodeficiency disease) and HCMV (Human cytomegalovirus) primarily attack the immune system and make someone immunocompromised, or more vulnerable to other diseases. Most of the viruses that cause immunodeficiency cause secondary infections or diseases, or in other words, they do not cause the immunodeficiency themselves (a good example of this is HIV).

In 1999, a 45-year-old male farmer was diagnosed with HIV and was treated using different treatments for HIV (da Silva et al., 2013). Due to his decreased immunity, he was also infected with visceral leishmaniasis, an infection caused by sand flies and is more common in tropical areas such as Southern America, which is

where this farmer is located. This case study is a testament to how vulnerable a host can be after being infected with HIV and how it can change one's immune system and damage it in such a way that infections can get into the body easier.

Though the number of viruses that attack a host through these tactics is very small, they are still very dangerous and can pose a huge risk for those who might be infected, animals and humans alike. Discovering what makes these viruses up and discussing the solutions to them is important and helpful for our society to enhance the way of living.

Methodology

The purpose of this paper is to explain the methods by which viruses can affect the immune system and immunodeficiency of a host. The method primarily used for this paper and its results is data collection. Using search engines such as Google Scholar and EBSCO Host, a variety of journal articles and excerpts from texts were found which were related to this topic. Keywords were used, such as "immunodeficiency", "*Mononegavirales*", and "immune system". These three keywords were vital to finding sources that were reliable and were able to be used for this topic. This research article depended on previous studies and research to draw conclusions. Most sources were found to be case studies of past cases of these specific viruses, while other sources were public medical institutions informing the general public on the different aspects of these viruses. Using a compilation of these sources, a correlation was made between viral infection and the host cell types. Analyzing different sources from various parts of the world helps to ensure differing perspectives and makes sure that each perspective is thoroughly explained.

Viruses

Locally, viruses that cause immunodeficiency are not discussed thoroughly, but throughout all the sources found, there is one virus that is currently going around in New Jersey, as of 2023 and 2024. It is called respiratory syncytial virus (RSV) and can lower immunity (Mayo Clinic Staff, 2023), but it does not cause immunodeficiency itself. It usually affects small aged children and older adults. RSV (not to be confused with Rous Sarcoma Virus) is a virus of the genus *Orthopneumovirus* (within the family *Pneumoviridae* and the order of *Mononegavirales*), as the World Health Organization (n.d.) writes. Nationally, the most well-known virus that causes immunodeficiency is human immunodeficiency virus (HIV). In 2021, the United States diagnosed 36,136 new patients with HIV (cdc.gov). HIV is a retrovirus which means that it replicates by RNA/DNA integration and it can stay dormant in a host cell until an exterior stimulus triggers the DNA to separate from the host DNA and start replicating each viral component. AIDS (an immunodeficiency disease acquired from HIV) became a problematic epidemic in the late 20th century, starting in 1981. Globally, The World Health Organization (2023) writes that HIV enters the picture as it still affects people in countries today, killing around 40 million people so far. HIV seems to be the most infamous virus to cause immunodeficiency in a human in the world, but there are many more affecting third-world countries on a smaller scale, but not small enough to go unnoticed. HIV was a problem in the late 20th century and people around the world did not know what to do, as there was almost no information about this virus.

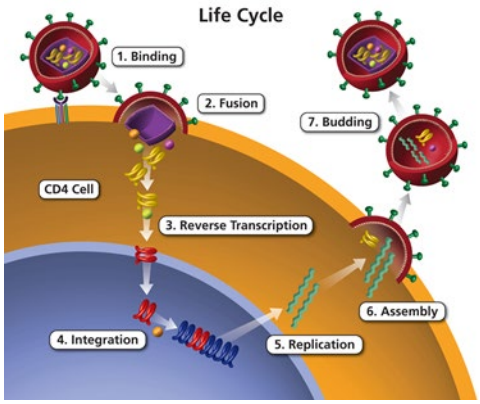

Figure 1.1. Human Immunodeficiency Virus (HIV) and its replication process (HIV.gov, n.d.). When it latches onto the CD4-T cell, the virus then binds into the membrane and integrates its genetic material into the genetic material of the cell and forces it to create viral materials, which are then formed into a HIV virion and bud out of the cell.

HIV (Human Immunodeficiency Virus)

Human immunodeficiency Virus, also known as HIV, is a virus which is transmitted through bodily fluids and sexual activity. Figure 1.1 above shows a visual representation of HIV's replication cycle. The viral attachment proteins on its envelope (called gp41 and gp160) lead it to CD4-T cells (LibreTexts, n.d). Once it gets to the cell, it binds with the cell membrane and injects its genetic material into the cell. Through viral replication, the cell goes through apoptosis, which is programmed cell death. This damages the CD4-T cell, weakening an important part of the immune system, which is triggering responses to pathogens. Weakening this part of the immune system makes a human more vulnerable to secondary diseases and infections. This weakens a human in order to establish the final and fatal stage of Human Immunodeficiency Virus, Acquired Immunodeficiency Syndrome.

AIDS (Acquired Immunodeficiency Syndrome)

AIDS, or Acquired Immunodeficiency Syndrome, is a disease which is known to be the one of the later stages of human immunodeficiency virus when the body's immune system is damaged beyond repair (HIV.gov). In the late 20th century, AIDS was common for people who were infected with HIV as it was still a new phenomenon. AIDS ultimately led to death due to its very fatal symptoms and its late effects (when someone's immune system is very weak). This disease, along with secondary infections and diseases, contributed to most of the deaths from HIV. This is a disease which is developed along the course of untreated HIV, not a disease that can be contracted.

Mononegavirales

The order of *Mononegavirales* includes many infamous viruses such as *Rabies lyssavirus* (Rabies), *Ebola virus* (Ebola), *Human Respiratory Syncytial Virus* (HRSV), and many more (Liang, 2020). These viruses are known to make people immunodeficient and make them more susceptible to diseases and other viruses. They contain certain attachment proteins that damage cells vital to the immune system's function or the protection of the exterior of the body.

This order comprises of viruses that contain single-stranded negative RNA as genetic material (Easton et al., 2008). It contains four families: *Bornaviridae*, *Rhabdoviridae*, *Filoviridae*, and *Paramyxoviridae*. *Bornaviridae* is a family of viruses in which the viruses are enveloped with a helical nucleocapsid (Payne, 2021). *Rhabdoviridae* is most infamous for *Rabies lyssavirus*, also known as the virion which causes human rabies. *Filoviridae* contains the well-known virus Ebola. Finally, *Paramyxoviridae* infects vertebrate hosts and contains viruses such as Pneumonia. This order is known for its virions that have large envelopes.

Many of these viruses are known to attack epithelial cells, which line the outer layer of the skin (epidermis) and several organs (Daly, 2023). This weakens the body's integrity to fend off infections and diseases.

Measles (Morbillivirus)

Measles, also known as Rubeola, is a virus of the family *Paramyxoviridae*. It is characterized by rashes, coughs, and many other symptoms (Boston Children's Hospital, n.d). Though it can be prevented with a vaccine, it is still prominent in countries where the vaccine is not widely available. It then spreads through people with measles who travel to different countries. This virus can be very fatal if not treated but thanks to immunization in the United States, it is not as big of a problem as it used to be. The relevance of this virus is that the viral attachment proteins of *Morbillivirus* lead it to epithelial cells (Vries et al., 2015), which, when damaged, can make the host very vulnerable to diseases.

Rabies (Rabies Lyssavirus)

Rabies is caused by the virus *Rabies lyssavirus*, which is a virus of the family *Rhabdovirus*. It can be transmitted through animal to human contact. If an animal bites a human, the saliva of the animal can contain rabies and infect the person (NCEZID, 2019). It can cause severe damage to the brain, which is very fatal. When someone is infected with rabies, they might be showing symptoms of influenza, such as weakness, discomfort, fever, or a headache (NCEZID, 2021). Then, the person starts showing signs of mental deterioration, such as anxiety, confusion, and agitation. Then, the disease progresses to the next stage, which includes hydrophobia (the fear of water). Once rabies is clinically diagnosed, it is fatal. Less than 20 cases of human survival from rabies have been documented (NCEZID, 2021). This just shows how dangerous rabies is. It also can cause secondary diseases and infections because of its viral attachment protein, RABV G. This protein also attacks epithelial cells and therefore destroys the lining of the skin and organs, so the host is more vulnerable to secondary infections and/or diseases.

Ebola (Ebola Virus)

The Ebola virus is a virus of the family *Filoviridae*. It is often fatal (WHO, n.d.). The virus can be transmitted through animal to human contact; a person can get very close to an animal who has Ebola and its bodily fluids. Ebola then spreads through the population through direct contact with other bodily fluids. It can also spread through contaminated water. Some early symptoms of this virus are fever, fatigue, and headache; this is a pattern seen mostly in viral families of the order *Mononegavirales*. Though it can be treated and prevented with vaccines that are available, it still has a significant impact on people living in countries where there is no treatment available or where the environment is poorly maintained. Ebola attacks epithelial cells, fibroblasts, monocytes, macrophages, and many more cells, which are all important parts of the immune system in the human body (CDC, 2023).

RSV (Respiratory Syncytial Virus)

Respiratory Syncytial Virus, also known as RSV, is a respiratory virus that causes influenza-like symptoms. Majority of the time, people recover within a week or two, but RSV is unpredictable; it can get fatal. Kids that are up to 6 months old and older adults are at a greater risk for developing severe RSV (CDC, n.d.). It is a virus of the family *Paramyxoviridae*, the same family as Measles. This virus attacks the epithelial cells of the airways, which can lower their defense against this virus, which is why this can get serious. This virus is transmitted through contact and breathing in viral droplets from sneezing or coughing by people who are infected by RSV, so it is very contagious.

Immunodeficiency

The immune system is one of the most important systems in the body, as it protects people from pathogens and foreign substances in the body but, when it is damaged, that is what is called immunodeficiency. Immunodeficiency can be caused by many different things, such as cell damage, gene mutations, unhealthy diets, and a number of other causes. Viruses specifically target cells that are part of the immune system so they can replicate more efficiently and make a human's immune system more vulnerable to other diseases and viruses. For example, HIV attacks CD4-T cells. These cells are responsible for triggering immune responses to foreign pathogens in the body, but when CD4-T cells are binded to these viruses and are forced to replicate the viruses, they go through programmed cell death (apoptosis). This can significantly weaken the immune system and leads to AIDS, which is the last stage of HIV. Understanding what makes a person immunodeficient is very important. Viruses, in this context, can definitely cause immunodeficiency in a human by damaging cells that are vital to the body's protection. Immunodeficiency can be diagnosed using different methods, such as blood tests.

Blood tests can be useful in determining whether a person has enough immunoglobulins in the blood and they measure the levels of different blood cells (Mayo Clinic, 2022). White blood cells are an integral part of the immune system, so it is important to make sure someone has enough to fight against a potential pathogen. If there are more white blood cells than normal, then it means that the immune system is fighting an infection or any other pathogen in the body. When under threat, the immune system fights these illnesses by sending more white blood cells to the source of the illness.

Immunodeficiency Caused by Viruses

The cells in the immune system all work together to facilitate a response against foreign pathogens in the body. Leukocytes go through the blood and tissues in order to detect a pathogen (Pfizer, n.d.). This triggers CD4-T cells to produce cytokines (Klimpel, 1996), which in turn regulate immune functions and antiviral responses. All these cells are also attacked by viruses so that viruses can replicate without having to worry about the immune system.

Though they are not part of the immune system, epithelial cells are vital in protecting the body from viruses and diseases entering the body. They line the organs and skin acting as a membrane. They can line the outer layer of the skin, intestines, respiratory tract, abdominal cavity, and sweat glands. They can be different shapes and can be arranged in different ways depending on their location and use (Cleveland Clinic, n.d.). Many viruses (especially in the family *Mononegavirales*) attack these epithelial cells, leaving a host vulnerable to diseases and infections other than the initial virus. This is called a secondary disease/infection.

Treatments

There are treatments for immunodeficiency. One can treat and prevent infections that have lowered the immune system's integrity and help the immune system regenerate itself, or one can perform immunoglobulin therapy. Immunoglobulin therapy consists of antibody proteins which are needed for the immune system to fight infections (Mayo Clinic, 2022). Some people might choose immunoglobulin therapy over immunosuppressants because one's immune system cannot make enough antibodies to treat infections (Shehata, 2023). This treatment can promote a healthier immune system and acts as a support to it. Once started, IVIg is repeated every few weeks.

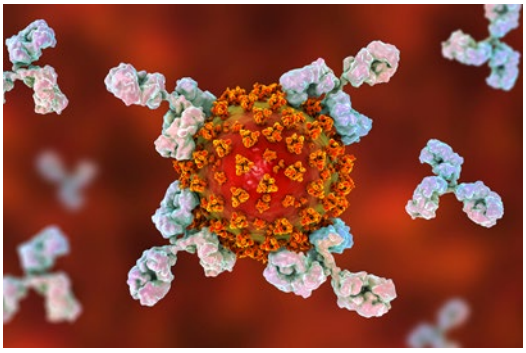

Figure 1.2. A group of antibodies are seen blocking the viral spikes from accessing a cell's membrane in the body (Ghose, 2022).

Monoclonal Antibodies

Antibodies are protein components made in the immune system that circulate in the blood and neutralize foreign substances (NIH, 2024). New antibodies can be made after the immune system is exposed to a foreign substance (known as an antigen), and can then protect against these substances in the future. Understanding antibodies is very important because they could be a game changer for virology in the future.

Monoclonal antibodies are synthesized antibodies that can act exactly like normal human antibodies. They can be made in four different ways (ACS, 2023):

- Murine: Made from mouse proteins (end in *-omab*)
- Chimeric: Made from part mouse and part human (end in *-ximab*)
- Humanized: Made from small parts of mouse proteins and attached to human proteins (end in *-zumab*)
- Human: Made from fully human protein (end in *-umab*)

Right now, the majority of the time, they are used to treat cancer. As seen in 1.2, antibodies work by blocking the spikes of a virus from penetrating the cell membrane, essentially protecting the cell from viral replication and therefore expelling viral particles through waste (called lowering the viral load). But, these antibodies can be found in patients who have completely survived the effects of a certain virus and have returned to their past way of living, and they can be mass produced to help people who are suffering with the effects of a virus now.

Results & Discussion

All viruses have certain proteins on their membranes which are known as viral attachment proteins. They help the virus find a certain host cell which will help them replicate. For example, in HIV, the envelope proteins only bind with CD4-T cells, which are a type of white blood cell. These cells trigger an immune response if it recognizes a virus, germ, or any other pathogen. So, when HIV enters these cells in order to replicate, it kills

the cell in the process and therefore slowly kills the immune system. The host then starts succumbing to secondary infections and diseases which enter the body.

Viral attachment proteins can be considered as a "lock and key"; in this case, a cell is the lock and the proteins are the key. Once the virus attaches to the cell, the virus' genetic material enters the cell and creates the parts needed for viral replication. Another instance of this viral attachment is with measles, rabies, HCMV, and many other viruses. Their viral attachment proteins all target epithelial cells, which are cells that layer organ and skin linings. Once these cells are damaged, infections and diseases have easier means of reaching the body and penetrating the skin, making a human ill.

Viral attachment proteins are a very important part of viral replication. If these proteins do not attach to the host cell, then viruses cannot replicate. As said previously, viral attachment proteins fit with the cells' capsids like a lock and a key. Here is where antibodies come in handy; they can block viral spikes from entering the cell's membrane and completely avoid the issue of viral attachment and viral replication. This then decreases the viral load of the body and therefore it travels through the abdomen and is expelled as waste. Antibodies are a key component of a solution in the future, so it is very important to recognize this now.

Limitations

There are many limitations to this research paper. The research that was conducted was based mostly on case studies and public health websites; there are not many experiments done on this area of virology. This means that there would need to be extensive research done in order to come to a complete conclusion. Also, this solution is completely theoretical; it is difficult to analyze the real-world effect of this as nature can be unpredictable. Mutations can happen anytime and so it is difficult to analyze antibodies of each type of virus there is. Viruses of these types are difficult to work with and finding antibodies for these viruses is rare because most of these cases have ended up in death. While writing this research paper, I did not have access to a lab so I could not perform experimentation of my own to yield sufficient results; this paper was written with the help of many public health institutions and books that were found during the data collection.

Conclusion

Viruses can cause immunodeficiency in humans. They find cells that are integral parts of the immune system and use them to replicate at a rapid pace. When cells are pushed to their limit, they perform programmed cell death, also known as apoptosis, which damages the system that they are integrated into. In this context, it is the immune system being greatly affected. Whether it is direct or indirect causes, the immune system gets damaged during its toil of fighting against a virus.

This research paper focuses on the viruses that affected people in the late 20th century and viruses still affecting mankind now. These viruses, especially viruses that belong to the family *Mononegavirales*, all target epithelial cells in their pursuit for replication. These cells act as a membrane to control what enters and exits certain organs and the skin. But, when these cells are damaged, they cannot control the entry of certain infections, which causes secondary infections in people.

Focusing on viral replication, it is caused by viral spikes penetrating a cell membrane. Antibodies directly prevent this by completely blocking off viral entry into the cell, which could be a solution to these viruses. Using antibodies, especially monoclonal antibodies, can definitely help with finding the right treatment to these unforgiving viruses. These viruses have been labeled as unpredictable and dangerous, but if patterns in viral attacks are identified, it could change how humanity views these viruses forever.

Some recommendations that could be made are that there needs to be more experimentation done on this topic to completely solidify the basis of patterns in viral attacks. There needs to be more analysis done on

these individual viruses to identify what the viral spikes are made up of and if there are any outstanding similarities between these viruses which enable them to attack the same type of cell. If these results could be accomplished, then there needs to be more extensive research done on antibodies and how they are formed in the body when approached with a foreign substance. If these recommendations are met, then there could be possible solutions to these viruses in the near future.

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