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Basic Immunology: Vaccination and Herd Immunity

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Abstract

The current coronavirus disease (COVID-19) infection cases range from mild to deadly. The virus has brought the world down to its feet. Knowledge application to battle COVID-19 indicates that humans can fight any deadly malady if they have proper immunology education and know humans' immunity pattern. This paper introduces the basic knowledge of immunology, the components, and the actions of immunity. The idea of vaccination and the controversy regarding this topic is mentioned. The study found the importance of vaccination and herd immunity, with the example of the current case of the COVID-19 pandemic. Thus, the importance of vaccination and herd immunity is correlated with the recognition of immunology.

Keywords: *Immune cells, innate immunity, adaptive immunity, vaccination, herd immunity*

Abstrak

Kes jangkitan semasa penyakit coronavirus (COVID-19) meliputi daripada kes ringan sehingga kes yang menyebabkan kematian. Virus ini telah membawa dunia berada di paras bawah. Aplikasi pengetahuan untuk memerangi COVID-19 menunjukkan bahawa manusia dapat melawan penyakit yang membawa kematian jika mereka mempunyai pengetahuan imunologi yang bersesuaian dan mengetahui corak imuniti manusia. Jurnal ini memperkenalkan pengetahuan asas terhadap imunologi, komponen, dan tindakan imuniti. Idea vaksinasi dan kontroversi mengenai topik ini juga dinyatakan. Kajian itu mendapati pentingnya vaksinasi dan imuniti kelompok, dengan contoh kes semasa pandemik COVID-19. Oleh itu, pentingnya vaksinasi dan imuniti kelompok dikaitkan dengan pengiktirafan imunologi.

Katakunci: *Sel Imun, mmune cells, imuniti semula jadi, imuniti adaptif, vaksinasi, imuniti berkelompok*

Introduction

Immunology is the subject where it is learned how the human body fights against pathogens and foreign unwanted particles that can affect or destroy the body cells and organs. The foreign substances can be bacteria, protozoa, virus, or parasitic organisms, etc. They are also called Agents. A part of the foreign substance is called an epitope. Sometimes, the body also has to fight its own cells, such as cancer cells, in order to save itself from deteriorating. This subject involves studying the immune system, an intricate system and involves the collection of cells dedicated to defending the body. The immune system is so important for the survival of the human body that, if it is absent, even the slightest infection may end up being fatal. However, the human body does not acquire strong immunity the moment it is born. It builds up within time as the body grows. It learns about the pathogens and keeps getting stronger by producing fighting cells to fight them. The immune

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system function is to recognise and determine foreign substances and defend against them in several ways. To put it simply, it undergoes the process of immunosurveillance (Coico, 2021).

The way the immune cells work in a collective and coordinated manner when a foreign substance enters the body is known as the immune response. There are various ways in which the immune response works to combat antigens. There are the first line and second line of the barrier, which will be discoursed later in this paper. It is important to note that immunity does not win over pathogens all the time, and it may become self-harming, too. For example, a common variable immunodeficiency (CVID) and severe combined immunodeficiency (SCID) are instances of inborn immunodeficiencies. In these cases, both the immune and adaptive responses can be disabled, resulting in infections. Another case is where autoimmunity happens. Here, the immune system falsely attacks its tissues, resulting in a chronic inflammatory condition and tissue impairment. Type 1 diabetes and multiple sclerosis are some examples of autoimmunity. This phenomenon of self-destruction of body tissues is called immune dysfunction (Parham, 2015).

Despite having self-immune cells, the body sometimes needs to rely on external defence mechanisms, such as vaccination. Vaccination is a great means of making an individual capable enough to fight the invading pathogen in their bodies. Vaccinating everyone in a community will culminate into herd immunity. Acquiring herd immunity through vaccination can be a great way of reducing the risks of spreading infection among individuals (Dowdy and D'Souza, 2020). This paper will discuss immunity, what it does and how it works. Moreover, the first and second lines of the barrier will be discussed. It will also highlight the fundamentals of vaccination and misconceptions that are present in the use of vaccines. The current phenomenon of COVID-19 will be mentioned to share the knowledge of how an infectious disease can become deadly and how vaccination can be an effective solution for this. Herd immunity and its functions will broadly converse.

The synopsis of the types of immunity and how it works.

Immunity comprises of two types, namely, innate immunity and Adaptive Immunity. The innate immunity does not have specificity or memory, while adaptive immunity is specific and has memory (Gleichmann, 2020). It is important to recognise the cells that work together to understand how these two processes take such an action against the pathogens.

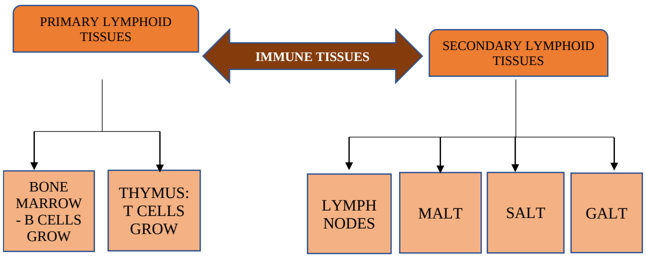

Figure 1: An introduction to the basic immune cells presents in the human body. Adapted from Warrington et al., (2011).

The Figure 1 above displays the basic immune cells involved in starting an immune response. Here, the basic immune cells have been divided into two main parts: 1) Primary Lymphoid tissues (thymus and bone marrow), where the lymphocytes (B and T cells) grow and mature. B-lymphocytes grow and develop in bone marrow, whereas thymus is where the T-lymphocytes develop; 2) Secondary lymphoid tissue: organs that assemble the antigens to activate the lymphocytes that can be found in the primary lymphoid tissues (Warrington et al., 2011). Other immune cells are phagocytes (neutrophils and macrophages), MAST cells, Natural killer cells (NK cells), basophils, and eosinophils. They are all derived from the hematopoietic stem cell (HSC). Phagocytic cells' role is to eat up the pathogens and eliminate them from the body altogether (Chaplin, 2010). The sources of all the immune cells are summated below in (Figure 2), illustrating the physical microenvironment of hematopoietic stem cells and their emerging roles in articulating applications.

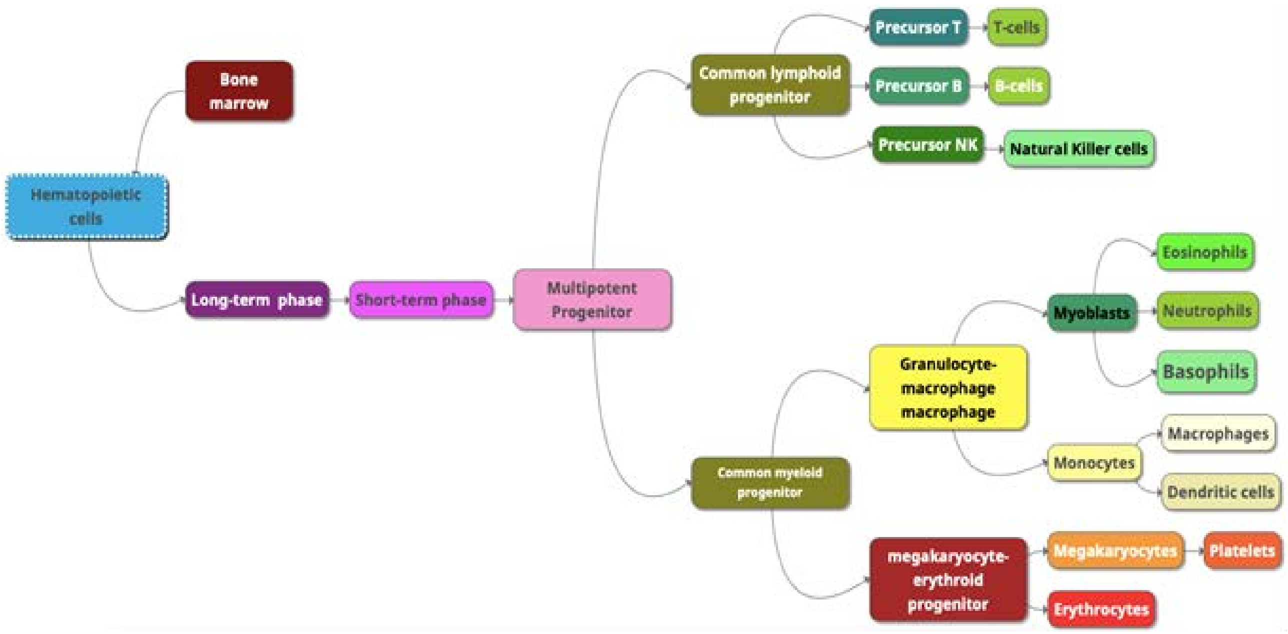

Figure 2: Summary of the sources of immune cells. Modified from Zhang et al., (2019)

However, innate and adaptive immunity should not be mistaken as being mutually exclusive. The former and the latter are rather correlative to each other. Both are connected via dendritic cells, which carry pathogen invasion from the innate immunity response to the adaptive immune system cells. They share this information in the form of antigens (Science ABC, 2018). Both systems are not perfect and tend to have errors, which results in "host vulnerability". Each of the systems also has a humoral and cell-mediated immune response, which act in slightly different ways than each other (Warrington et al., 2011). Besides the differences, Innate and adaptive immunity are closely connected, where the molecules of PAMPs (pathogen-associated molecular pattern) play a key role (Figure 3). The PAMPs are found on the exterior of pathogens, which induce the uptake of antigen and processing. The processing is done by special subgroups of APCs (antigen-presenting cells), DCs (Dendritic cells), ensuing in the upregulation maturation markers of DC. The matured DCs display the antigens from pathogens to the naïve T-helper cells and T-cytotoxic cells. This step is done with the help of MHC class-II and MHC class-I molecules, respectively. As a result, cytokines are released by DCs, triggering differentiation into the effector cells of B and T lymphocytes. Finally, antibodies are released from B and T effector cells, which play essential roles in conducting an immune response. After carrying out the immune response, these cells can be stored as memory cells so that the same response is enhanced when encountered more than once, also known as the secondary immune response (Bárcena & Blanco, 2013).

Innate immunity

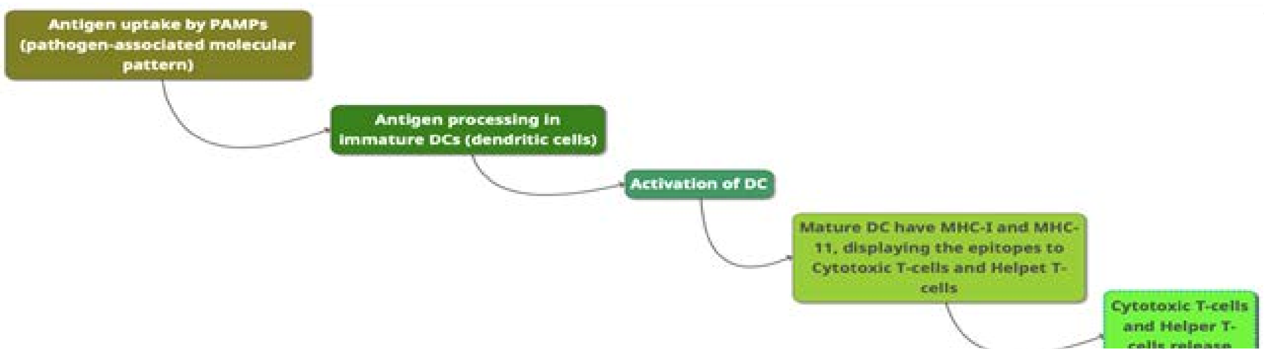

Figure 3: Antigen display by APCs (Dendritic cells) in the humoral and adaptive immune response. Adopted and adapted from (Bárcena & Blanco, 2013).

The innate immune system forms the first line of defence, such as in the skin, mucous membranes, etc. Therefore, whenever a pathogen enters a body, the innate immunity works first. This natural barrier sets up a suitable environment for adaptive immunity to later occur using Antigen Presenting Cells (APCs). It also reduces the workload for adaptive immunity. Innate immunity is non-specific and does not acquire immune memory, as the cells cannot memorise the pathogens they encounter. Their activity does not depend on the prior exposure of the antigens. It has four types of non-specific safeguarding barriers: external (skin), phagocytic, physiologic (temperature), and inflammatory (MAST cells). Their main function is to gather all the immune cells by discharging cytokines at the sites of inflammation. Cytokines are "immune mediators" that promotes phagocytosis. The phagocytic cells (e.g., macrophages) engulf and clear the dead cells from the body. Cytokines also have a subset of cells called chemokines that direct the immune cells to infection sites.

There are two categories of innate immunity responses: humoral (antibody-mediated) and cellular (cell-mediated). In the humoral response, leukocytes (e.g., phagocytes, NK cells, dendritic cells) attack the antigens directly or indirectly via different activation pathways. Secreted antibodies and proteins mediate this response in the extracellular fluids. For instance, in an inflammatory response, when the MAST cells find any pathogen, histamine molecules are discharged in the form of a signal. This step alerts the body, and blood is rushed to the site of infection. Moreover, leukocytes are recruited there, stopping the non-self-particle from entering the body (Science ABC, 2018).

The cell-mediated response occurs in a complement system. The characteristic Pathogen-Associated Molecular Patterns recognise the microbes (PAMPs) found on the microbes' exterior, and the Pattern-Recognition Receptors (PRRs), carry out the same job. NK cells detect intracellular infection and target viruses. Eosinophils can also target larger infective microbes, such as parasitic worms. Neutrophils and macrophages are involved in phagocytosis that takes place in cellular response. However, thanks to science and technology advancement, scientists can now make the immune system gain memory. According to (Rusek et al., 2018), epigenetic reprogramming and complex regulations can, indeed, be used to train the innate immune system to have memories.

Adaptive immunity

Adaptive immunity is specific and has immune memory. It only comes into play when the innate immunity is not enough to fight the pathogens. It depends on the antigen, making it slower to react between the disclosure to antigen and the utmost response. Adaptive immunity is developed along with the growth of the human body. This immune system adapts to the surrounding microbes' presence. The adaptive immune cells specifically recognise and remove the foreign antigens from the body. It has enhanced response to a further similar attack (the secondary immune response) because of its immune memory. The immunologic memory can be obtained via antigen recognition, lymphocyte activation and antigen elimination (Merlo & Mandik-Nayak, 2013).

In the humoral adaptive immune response, the B-cells play a major role. When a pathogen invades the B-cells, it is activated as the receptors of the B-cells recognise the pathogen and bind to the antigen, with specificity. Then, the B-cells take help from T-helper cells from cellular immunity. T-helper cells secrete cytokines, which changes B-cells to plasma cells. Antibodies are produced from plasma cells for the exact pathogen. The antibodies neutralise extracellular pathogens and eliminate phagocytosis (Science ABC, 2018).

On the other hand, in the cellular adaptive immune response, the T-cells perform a major function. These cells take signals from the APCs (dendritic cells/macrophages), which have the MHC class I and MHC class II receptors to activate the T-lymphocytes. Then, they are differentiated into the effector T-cells or memory T-cells. Furthermore, the cytotoxic T-cells kill wipe out the affected or dying cells. The B-cells also generate antibodies specific to the pathogens' antigens, and tag them, signalling the macrophages to come and kill them anywhere in the body. Simultaneously, B and T memory cells record all the formerly confronted infections for enhanced reactions, if the body contracts the same infection in the future (Merlo & Mandik-Nayak, 2013).

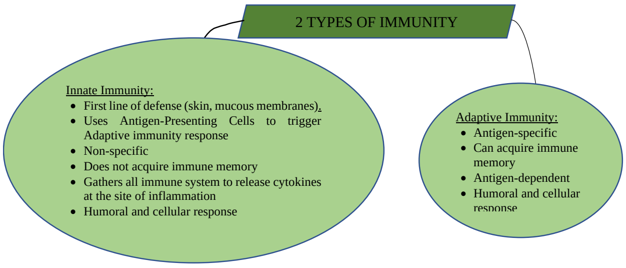

Figure 4: Differences between innate and adaptive immunity. Adopted and adapted from (Science ABC, 2018)

The fundamentals of vaccination

When talking about vaccination, it is crucial to understand the concept of immunity. Vaccination encompasses the antigens' self-versus-non-self-recognition roles. The vaccination provides proper protection from bacterial, viral or fungal diseases when the antigen-specific effector cells are being produced, indicating that the vaccine is working. Numerous aspects influence decisions when accomplishing vaccines, such as activating a specific section of the immune system or the enlargement of immunological memory. Once the vaccine is made, it can be administered in the form of inactivated virus or a live-attenuated virus ("The different types of COVID-19 vaccines," 2021).

The inactivated form of a vaccine involves the killing and fragmenting of the target bacterial cell or pathogen. The fragments could be surface proteins or cell wall fragments. These fractions are used in the vaccine serum. When these fragments are injected, human cells take them in, process them, and present them on the surface. These cells are often called APCs (antigen-presenting cells). Then, macrophages or neutrophils can recognise them, induce phagocytosis, or humoral, or cell-mediated immune responses. This vaccine does not need to wait to start working its effects until it reaches the cells. It can be directly recognised in blood serum by the lymphocytes roaming around in the tissue fluid before entering the APCs. As the name goes, an inactivated form of vaccine consists of either the whole virus or bacteria or fractions of the target pathogen, which can be cultured to breed and exterminated using physical and chemical methods ("The different types of COVID-19 vaccines," 2021).

The pathogen particles are unable to multiply as they are disintegrated and elicit an adaptive immune response. If fractional vaccines are targeted to be made, further treatment of the organism can be done to absolve only the specific parts to be constituted in the vaccine, e.g., the polysaccharide capsule of pneumococcus. As the vaccines are inactivated, they cannot duplicate and proliferate, so multiple doses are consistently needed. Usually, the first dose does not stimulate immune response but does after the second and third doses. The immune response is very similar to humoral immunity, with little or no cellular immunity. This is why more than one dose is needed to increase the efficacy of such vaccines. However, the advantage is that these vaccines do not lead to infectious disease, even in patients with immunodeficiency. They are more intact and reliable than live vaccines. These can be conveniently reserved and transferred over long distances without needing freezing. Usually, the toxin is concealed or restrained by heat or chemical treatment, such as Diphtheria and Tetanus vaccines. It is crucial to use adjuvants for inactivated vaccines, e.g., aluminium salts, which may save from inflammation (Zoppi, 2021).

On the other hand, the live-attenuated vaccines comprise the whole pathogen being weakened, in some way, to disable their functions of infecting and causing harmful responses in the recipients' body. Killing the target pathogens may result in losing the surface proteins, which are needed to induce proper reaction when injected into the recipient's body. Thus, the pathogens are not directly killed. Instead, they are only weakened and encapsulated in lipid or any other carrier vesicles and administered. These are established by compressing the pathogen's virulence while making sure it is feasible. Live vaccines come from the pathogenic bacteria or virus, which are manipulated in a science laboratory. These wild pathogens are frequently cultured in cells, weakening their reproducibility. Thus, they cannot duplicate it efficiently. As they are introduced to new environments, they become less able to unfold to acclimate to the new setting, becoming feeble to their natural host, humans. It is important to note that this process takes almost years to make a proper vaccine. These mRNA containing pathogens travel to the nucleated cells, processed and expressed by the APCs and trigger the immune system to produce antibodies against them. However, this type of vaccine's drawback is that when they are expressed, the immune cells, such as macrophage or T-lymphocytes, cannot recognise and distinguish the epitopes as non-self. Thus, immune responses are not produced, sometimes (Kollaritsch & Rendi-Wagner, 2013).

Additionally, the attenuated microbes have a high chance of reverting to their original virulent form and cause the disease. Unfortunately, this type of vaccine is not suggested for patients who have undergone chemotherapy, as they are already immunocompromised. Live attenuated vaccines need refrigeration, which may be expensive. The presence of other contaminants can also result in unforeseen post-vaccine complications. However, this vaccine can replicate and produce immunity. It does not cause diseases like measles and mumps vaccines. Live-attenuated vaccines can be considered to be as close as to a natural infection. So, the immune response to such vaccines is practically the same as that produced by a natural contagion. Stronger immune responses can be made in the recipient's body with only one or two doses and have a long-lasting immunity (Plotkin & Mortimer, 1988; Plotkin et al., 2013; "Different Types of Vaccines | History of Vaccines," n.d.).

Even after all these, there will still be a small percentage of the population that will not have a good response to the vaccines. It may happen because of the presence of the genetic determinants. Luckily, herd immunity can be acquired, where most of the population becomes immune, so the chances of susceptible individuals contacting infected individuals are low.

Misconceptions regarding vaccines and vaccination

Despite having such intricate coordination of fighting pathogens, the immune system itself is not enough, sometimes. There are microorganisms with such complicated structures and genes that the immune cells get confused on how to eliminate them. This is where the need for vaccines come. Vaccines are made of the dead form of the same microbes that have caused the disease. This way, the weaker form of the pathogen aid in inducing an immune response in the infected person's body, producing and storing the memory cells to fight the similar pathogen, should they encounter them again. Vaccines are known to prevent the same disease from happening again, rather than curing it ("Basics of Vaccines | CDC," 2012). However, vaccines cannot be made overnight. The structure and the function of the virus that causes the disease need to be concluded first. Only then a proper vaccine can be made. The common misunderstanding is that the revival of the immune system results in protective immunity.

The way a vaccine is made, and its functions, have been questioned by humans all the time. For instance, when the Zika vaccine was developed, there has been concerns about its approval process and the success rate. Since it took quite a long time to make the vaccine, the public had already posed many false scientific claims about the vaccine in the meantime. Furthermore, a community of people who are always cynic about vaccines already made things worse. Moreover, it is hard to change people's opinion on something they already believe. They assume that vaccines have deadly after-effects, and the pharmaceutical companies are selling them only to boost profits (Dredze et al., 2016).

Another study was conducted by (Bert et al., 2019) on an Italian pregnant women group. Some did not rely on the idea that vaccines can avert possibly harmful diseases and disagreed with the notion that children should be immunised to protect other children. They did not accept that vaccination could alleviate the risks and that a healthy lifestyle is enough to survive an epidemic. Some also thought vaccines are not regulated properly before being released, and their side effects could be fatal. Interestingly, some also admitted that they assume that autism might be connected to vaccination (Bert et al., 2019).

The fact that individuals have a different level of immunity should not be disregarded. Some might have weaker immunity than others and could fight even mild diseases such as chickenpox. Some may be more prone to infection than others. One can never guarantee whose infection might end up being deadly. Thus, vaccines are made for everyone to acquire adaptive immunity. Vaccines do cause side effects, but most of them are almost always mild, except for some unfortunate cases. Vaccines enormously reduce the risk of infection by functioning along with the body's natural defences, resulting in a safe and developed immunity ("Understanding How COVID-19 Vaccines Work," 2021).

Herd immunity and its function

The concept of herd immunity is to make enough number of individuals immune to a specific disease so that the rest of the individuals in the community is safe, even without getting vaccinated. The target is to make the most of the population immune to the disease, which will provide herd protection to those who are not immune to the disease, thus, called herd immunity. Many past breakouts have been brought under control by applying herd immunity, such as chickenpox, mumps, and measles. Herd immunity requires as many people as possible to be vaccinated, even though they have not contracted the disease yet. This way, they will be ready to fight the disease, shall they ever get it. This idea had seemed to work great in the past cases of viral diseases. Before the vaccine for those diseases were made, innate and adaptive immunity responses were not enough for the ones with the weaker immune system (Dowdy and D'Souza, 2020). It is substantial to consider the rate at which the infection is spreading, the modes of transmission, and how an individual is acquiring immunity from that particular wide-spreading disease in the population to understand herd immunity (Smith, 2019).

Herd immunity occurs when a virus is there but cannot spread as it confronts people who are already immune to it. According to (Betsch et al., 2017), herd immunity can work as a social benefit, depending on individual and social decisions. The recognition of herd immunity by many individuals will result in strong protection and provide a well-vaccinated society, despite not giving vaccines to each and everyone in the community. Herd immunity lessens the possibility of an infected individual to make active contact with a responsive individual. Vaccinating the groups in a community well enough to gain herd immunity will minimise the extent of transmission of the pathogen after entering the population (Smith, 2019).

If enough number of people are immune, the probability of a new outbreak decreases. It can be achieved via broad-scale vaccination programs, where campaigns are carried out to inform people about the importance of vaccination (Aschwanden, 2020). In a study conducted by Betsch et al., (2017), it was observed that when people were taught the concept of herd immunity, there were enhanced willingness from the individuals to get vaccinated. Thus, it is important to disseminate the knowledge to reduce these "immunity gaps" to increase the social acceptance of vaccination.

A little insight on COVID-19 herd immunity

In the current case of COVID-19, this novel viral disease became pandemic because the population was naïve to this newly discovered viral strain. Furthermore, the late discovery of the case, that this disease could spread via human transmission, also contributed to such dynamic spread of the disease worldwide. A simple simulation can be pictured to demonstrate the case of COVID-19 becoming a pandemic. Firstly, three main characters are introduced as uninfected, infected and carrier, in a community. A carrier is having the pathogen in their bodies but not expressing it. These carriers also have equal contribution in spreading the disease as the infected individuals (Rao, 2006). When these three characters are not maintaining any social distance, they increase the risk of transmitting the coronavirus to each other by close contact. However, if, at least, one of them gets vaccinated, they alleviate the possibility of being infected themselves by the deadly virus. Furthermore, if most of the people in that community decide to get vaccinated and keep maintaining strict social distances, wear masks and sanitize hands, they collectively contribute to containing the COVID-19 spread in their vicinity. The main idea is that besides maintaining the precautionary guidelines for COVID-19, vaccination gives the immunity to fight the virus and eliminate them from the body. If the vaccination is continued to be given to almost everyone in that community, it will provide herd immunity, which will help bring this infectious disease under control. Moreover, despite having vaccine refusers in the society, the immune ones can prevent the disease from spreading drastically.

Nevertheless, the arguments above are only theoretical. In reality, many factors play a role in containing an infectious disease, such as divergence in population density, the age structure of the population, and cultural attitude. Moreover, the way the COVID-19 virus is transmitted from one individual to another may vary, which also seems to affect the transmission dynamics within communities (Randolph & Barreiro, 2020). It also takes about 12-18 months for a new vaccine to be made for a novel pathogenic strain. A lot of trials and errors must be conducted before confirming a successful vaccine for all. A successful vaccine can boost immunity in most of the individuals in a population. Fortunately, modern science and scientists' immense effort has recently helped develop a few vaccines, such as the Pfizer-BioNTech COVID-19 vaccine and many more. Thus, it is highly hoped that the world will soon fight and overcome this deadly infectious disease.

Conclusion

The immune system is so important for the survival of the human body that, if it is absent, even the slightest infection may end up being fatal. Vaccines can reduce the threat of infection and give a developed immunity, despite some of the misconceptions. Herd immunity greatly helps in containing any infectious disease. During an epidemic or a pandemic, infected patients shall undergo self-quarantine to avoid spreading the disease to others and, in turn, containing the disease in the community. Lastly, the current pandemic, COVID-19, gives us much knowledge of how deadly an infectious disease can be and the importance of vaccines in fighting them. To educate people about the severity of a disease, and how it can be controlled by working collectively, various vaccination campaigns can be initiated, and the social media platforms can be utilized to disseminate alertness by making different simulations and awareness videos.

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