**Covid-19 and immunity**

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March 08, 2021

After a severe pandemic hit the globe, vaccination drives are in full bloom to achieve herd immunity and control the Covid-19 infection. More than 250 million vaccination doses have been administered in what we can safely say is the largest vaccination drive in the history of our world. Israel leads in doses administered per 100 people worldwide, followed by UAE, US, Chile, and Brazil. With most of the restrictions relaxed in Pakistan, experts are fearful of a third wave in the upcoming months. The re-opening of schools and other daily life processes is the need of the hour but at the same time, we have to understand that Covid-19 will not come under control unless herd immunity is achieved through vaccine administration.

The processes through which SARS CoV-2 hijacks the body systems are still under investigation. Since last year, scientists are trying to understand the methods this virus utilises to defeat our natural immune system. Needless to say, our immune system is highly specialised and developed to tackle any form of pathogen. However, it is made to learn as well. SARS CoV-2 is a new virus and our immune system is learning how to handle it.

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Immunity is the defense mechanism and the ability of human body to fight any thing which is not a part of the body. It is of two types; Innate (inherent) and Adaptive (acquired). In both of these types, different kinds of cells are involved which circulate in our blood and lymph system. They go from organ to organ and keep a check on any intruders that may be present.

Innate immunity is the first defense which tries to finish an intruder. In this action, certain chemicals like interleukins and interferon are released from specialised cells and they signal other type of cells to eat up the pathogen. Interferon is also given as an anti-viral drugs in the treatment against the Hepatitis-C virus. Innate immunity is a non-specific immunity; every cell of our innate immunity attacks every particle that is not a part of body. Shortly after it, the adaptive immunity kicks in. It involves two types of cells, B-cells and T-cells. B-cells make specific antibodies against specific pathogens while the T-cells directly attack the infected cells of body.

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T-cells have two further types of cells, Helper T-cells and Killer T-cells. It may not be difficult to understand their role as Helper cells help other cells and Killer cells kill the infected cells. Both B and T have memory cells which means they remember what kinds of antibody to make if they encounter the virus again any time. We can achieve adaptive immunity naturally or artificially. Natural immunity is either attained by child through the mother or through an infection. Artificial immunity involves vaccinations or convalescent plasma therapy. In active immunity, the body produces antibodies while in passive immunity the body takes antibodies from another source. The vaccines, thus, provide Active Artificial Adaptive Immunity.

One of the pressing issue scientists are facing is the availability of those antibodies which actually bind to SARS CoV-2 virus and inhibit its functions. These antibodies, known as Neutralising Antibodies, attach to the binding site on the virus and stop its working. The non-neutralising antibodies may bind to the virus but they do not reduce its functionality. Neutralising antibodies is an essential part of the host adaptive immune response that is induced against viral infections following natural infections or the administration of vaccine.

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A requirement for a successful SARSCoV-2 infection is the interaction between the Spike (S) protein and its functional receptor, the angiotensin converting enzyme 2 (ACE2), found on human cells. The receptor-binding domain (RBD) of SARS-CoV-2 Spike protein is important for this entry process and has been identified as a dominant target of many of the currently identified SARS CoV-2 neutralising antibodies in labs. It has been reported that a significant proportion of Covid-19 patients have a low level of neutralising antibodies because their immune system could not produce full adaptive immunity. This might have put the SARS CoV-2 virus under immune stress causing it to develop changes in its structure. Constant exposure of SARS-CoV-2 to these low levels of antibodies in infected individuals can promote the growth of antibody resistant SARS-CoV-2 in Covid-19 patients posing a great threat to public health. Hence, it is of extreme importance to follow the vaccine schedule and take its full dose as prescribed by the scientists.

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Multiple studies from Australia, UK, and the USA have reported 3-8 months of immunity after a Covid-19 infection. These studies have reported declining numbers of protective antibodies after natural SARS CoV-2 infections. Studies on SARS CoV-1 and MERS virus have showed that antibodies decline in numbers after three months and completely diminish after six years. Least to say, Covid-19 is new and perhaps these kinds of researches need more time into an infection to come up with a conclusive result.

Naturally, antibodies decrease in number after an infection, but it does not necessarily mean that immunity decreases after some time. This waning of antibodies, in the context of Covid-19, is under investigation by several research groups. One of the compelling evidence in favor of shorter Covid-19 immunity is reinfection. However, up until now, there are fewer reports of reinfections which, at this point, do not support the idea of shorter immunity against Covid-19. Nevertheless, together with an increasing evidence of multiple variants of SARS CoV-2, scientists are cautiously examining the need to administer booster shots of Covid-19 vaccines.

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Another important concept to understand is correlates of immunity. These are measurable compounds of the immune system which confirm the protection of the humans from an infection. In the UK, for example, antibodies against Rubella are measured in pregnant women to make sure that they are immune against the Rubella infection. However, in case of HIV, merely the presence of antibodies does not confirm immunity against this virus. What are those other elements of the immune system that must be present together with antibodies to completely protect against HIV is still not clear. For this reason, together with the mutating nature of HIV, we do not yet have any vaccine against it.

Initial studies have reported a decreased percentage of different types of white blood cells in severe Covid-19 infections. As stated earlier in the article, interferon is an antiviral and hence, it is assumed that an increased production of interferon producing cells should control the infection. However, there are conflicting reports on the production of interferon producing T-cells in severe cases and no study has been able to correlate the production of interferon-T-Cells with the disease severity of Covid-19 yet.

There are other compounds produced by T-cells, perforin and granzyme, which together kill the infected cells of the body to stop the spread of infection. Increased cytokine production in severe Covid-19 infections has also been correlated to increased viral load, loss of lung function, lung injury, and fatal outcomes. There, increased production in severe Cvoid-19 infections may indicate the role of our immune system in worsening the disease.

Another important component of our immune system is the different kinds of cytokines are associated with severe cases of Covid-19infections. Just like other coronaviruses, SARS CoV-2 antibodies levels are higher with severe symptoms whereas those with mild cases have lower levels of neutralising antibodies. This is a pattern seen with common cold coronaviruses where typically, milder symptoms and lower antibody levels are present. All these areas of research on Covid-19 are still developing and in their early stages. We have yet to know how these immune changes differ in the severity of infection. Previous studies on SARS CoV-1 and MERS provide indications that cellular immunity plays an important role in clearing the infection. As SARS CoV-2 is related to the said viruses, scientists are focusing on cellular immunity together with humoral immunity to define the immune correlates of Covid-19 control in infected patients.

The ACE2 sites on human cells are the binding sites for SARS CoV-2. There might be evidence that these ACE2 appear more in older populations with hypertension, heart and lung diseases. SARS CoV-2 infections become worse with underlying issues in health. This can be one of the reasons why the older population is under more attack than the younger one. One of the many reasons Pakistan has a lower infection rate in comparison to western countries is a younger population and increased immunity.

More sun exposure and open air house formats in rural areas could have also contributed to the lesser Covid-19 infection. Despite this, lower diagnostic testing and reporting are a major factor for lower numbers reported. Vaccination drives are going on around the world. The vaccines of Sinopharm and Covavax are being administered in Pakistan. There is lack of trust in these vaccines amongst our population which is why the registration remains low. It is important for the government to bridge the trust deficit otherwise many Pakistanis will not get their vaccine shots. Until we get a better understanding of how our immune system is working against this virus and until we achieve greater than 70 percent of herd immunity, we have to keep following standard operating procedures of hand washing, wearing masks, avoiding public and crowded places.