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Recent Advances in Clinical Trials

COVID-19 Vaccines, Immunity, and Effect on Children

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Vaccine technologies

The Oxford/AstraZeneca and Johnson & Johnson vaccines use adenoviral vectores technology which is different than the mRNA technology used by Pfizer and Moderna.

The edenovital vectores technology, use a genetically engineered (modified) version of the common cold virus that usually spreads only among chimpanzees. This altered virus carries a gene from the novel coronavirus 'spike protein'. After injection it will trigger an immune response against SARS-CoV-2 virus.

With mRNA technology, once the synthetic mRNA that contains information about 'spike protein' is injected, it will enter human cells and instructs them to produce the 'spike' protein which is found on the surface of SARS-CoV-2. The body then recognizes the spike protein as an invader, and produces antibodies against it. Afterwards the mRNA strand will be disposed by the cell.

Although the efficacy of the Oxford/AstraZeneca's vaccine is less than of the pfizer's & Moderna's vaccines, it was 70% effective at preventing symptomatic coronavirus infections, according to their study

The previous (traditional) vaccines uses either a live/weakened virus such as measles, mumps, rubella & varicella vaccines or uses inactivated virus such as polio, Hepatitis A and influenza vaccines, while others use parts or toxins of the virus/bacteria such as HPV, Hepatitis B, Diphtheria and Tetanus.

So, what are 'spike' proteins?

In brief, the viral envelope of coronaviruses is made up of 3 proteins, the membrane protein (M), the envelope protein (E), and the spike protein (S). The S protein is a highly glycosylated and large type-I transmembrane fusion protein that plays a crucial role in penetrating host cells and initiating infection (Figure 1).

Spike proteins of coronaviruses can be divided into two important functional subunits, S1 subunit, which forms the globular head of the S protein, and S2 that forms the stalk of the protein and is directly embedded into the viral envelope. Upon interaction with a potential host cell, the S1 subunit will recognize and bind to receptors on the host cell, whereas the S2 subunit, which is the most conserved component of the S protein, will be responsible for fusing the envelope of the virus with the host cell membrane [1].

Without the S protein, SARS-CoV-2 would not be able to interact with the cells of potential hosts to cause infection. Thus, the S protein is a perfect target for vaccine and antiviral research studies. Furthermore, S protein is a major inducer of neutralizing antibodies which are protective antibodies that are naturally produced by our immune system.

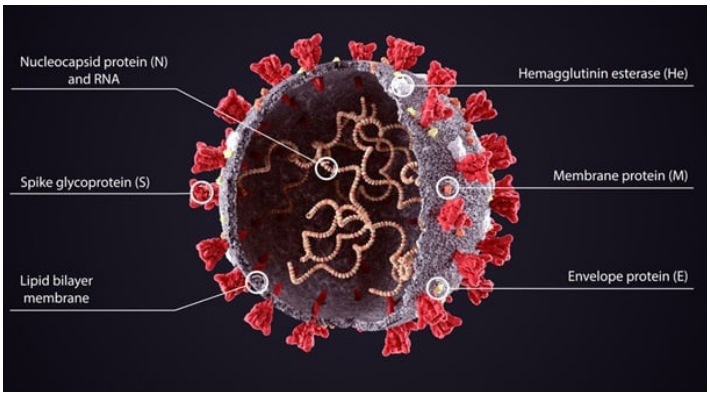

Figure 1: Image Credit: Orpheus FX/Shutterstock.com.

What type of immunity do COVID-19 vaccines provide?

There are two main types of immunity that can be achieved with vaccines. One is the "effective immunity", which can prevent a pathogen from causing serious disease, but can't stop it from entering the body or replicating. The other is "sterilising immunity",

which can prevent infections entirely, by producing "neutralising antibodies" that defend the body from pathogens by sticking to their outer surface and preventing them from interacting their host targets, such as cells lining the nose, throat or lungs. The latter is the desirable outcome of all vaccines, but not easily achieved. However, that is not a problem.

So, what type of immunity do COVID-19 vaccines provide?

The available COVID-19 vaccines have not been studied primarily on their ability to prevent transmission; instead, their efficacy was assessed by whether they could prevent symptoms from developing and reduce the disease, although there are some early signs that it might [2].

With COVID-19, the neutralising antibodies that recognise the virus, binds to the spike protein on its surface that it uses to enter cells (Figure 2). Even if the antibody response isn't optimal, other aspects of immune memory can kick in when the virus invades, such as cytotoxic T cells and non-neutralising antibodies, which will slow the viral replication and consequently reduce the disease. Moreover, vaccinated people are less likely to transmit enough viruses to cause severe disease. This in turn means that the people getting infected in this situation are going to transmit fewer viruses to the next susceptible person [3-5].

Further research and clinical trials are underway which will shed more light on this vaccine and the type of immunity it provides. Meanwhile it is important to continue wearing masks and practice social distancing even after vaccination until we reach herd immunity.

How long mRNA and spike proteins last in the body?

mRNA is very fragile, its broken down and removed from the body by enzymes that degrade and destroy it within few days. The spikes proteins lasts few weeks only, the immune system will attack and destroy them too because they are not part of our natural body (Pfizer).

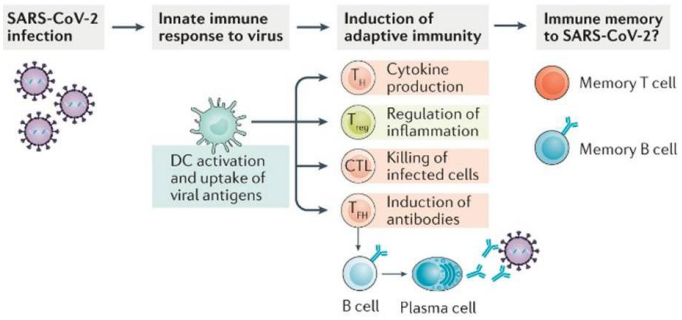

Figure 2: Immune response to SARS-Cov2.

COVID 19 and Children

Why children are not severely affected by Covd -19?

Here are some of the hypotheses

- Angiotensin converting enzyme-2 (ACE2) is the main receptor for the entry of SARS-CoV-2 into human cells. This receptor is present on many cells including epithelial cells of the nasopharynx, lungs, heart, kidney, liver and others. The expression of ACE2 increase with age, hence children express less of ACE2 in their nasal and lung epithelium. It has also been suggested that children have ACE2 receptors with a lower affinity for SARS-CoV-2 and a different distribution across body sites, making the entry of SARS-CoV-2 into cells more difficult. In addition to the ACE2 receptor, SARS-CoV-2 entry into cells involves transmembrane serine protease-2 (TMPRSS2), which cleaves the viral spike protein. TMPRSS2 has been reported to increase with age as well [6] (Figure 3).

- There are other coronaviruses that spread in the community and cause diseases such as the common cold. Since children often get colds, their immune systems might be primed to provide them with some protection against COVID-19. Furthermore, infection with commonly circulating coronaviruses leads to long-lasting T cell immunity to spike protein.

- SARS-CoV-2 can infect endothelial cells and cause vasculitis. This could also explain why patients with conditions that affect the endothelium, such as diabetes and hypertension, are at greater risk for severe COVID-19. The endothelium in children is less pre-damaged compared with adults and the coagulation system also differs, which makes children less prone to abnormal clotting.

- Children have a lower prevalence of the comorbidities that have been associated with severe COVID-19 in adults, such as hypertension, diabetes, and chronic kidney, lung and heart disease.

- Vitamin D has anti-inflammatory and anti-oxidative properties, and vit D deficiency has been associated with an increased risk for the development of respiratory tract infections. In many countries, vitamin D is routinely supplemented in infants younger than 1 year of age and in some countries even up to the age of 3 years.

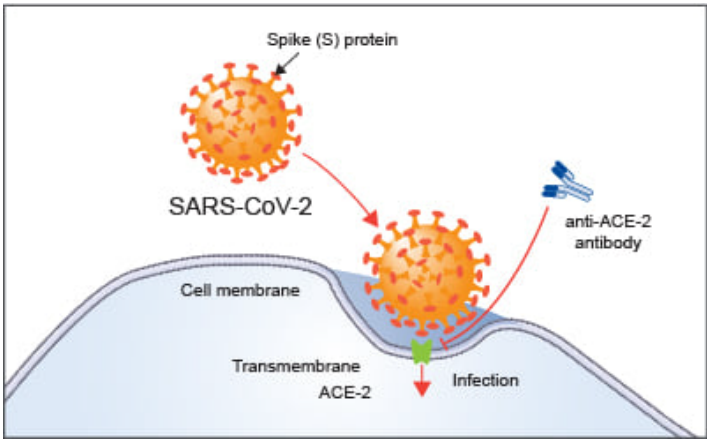

Figure 3: ACE-2 is the host cell receptor responsible for mediating infection by SARS-CoV-2 (figure from mdsystems.com).

Delta variant

The Delta variant known as B.1.617.2, is the most contagious variant of this virus so far, initially found in India, and became

the dominant strain in the UK, and now in the US. The good news is that, 2 doses of the Pfizer vaccine is 88% effective against the Delta variant, compare to the single dose 33%, according to the latest research data. Therefore, it is important to get the 2nd dose and not ignore it.

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