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Understanding COVID-19 Vaccines and Immunity

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ABSTRACT

COVID-19 Vaccines are currently the talk of the world. The internet is full of memes on COVOD-19 vaccines - myths more than truths. In this commentary we further review some of the issues related to the success and failure of COVID-19 vaccines, and the theoretical and practical elements on vaccinations and immunity that the dental health care providers have to be knowledgeable, so as to offer advice and guidance to their team, the patients, as well as the public.

1 INTRODUCTION

As discussed in our previous article,[(1)] there are a number of coronavirus disease 2019 (COVID-19) vaccines belonging both to the traditional, and the next generation vaccine platforms, currently reaching the arms of millions in many regions of the world, from the UK to Brazil. Additionally, at the time of writing, there were at least 10 vaccines approved for early or limited use, and a further 20 vaccines in large scale, Phase III, final trials.[(2)] The vast majority of these should see the light of day in 2021.

A popular assumption is that COVID-19 vaccines will provide herd or population immunity that can reduce transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in the community, leading to a resumption of pre-COVID-19 'normalcy' in the near future. In general, to reach herd immunity, and to suppress community transmission of the virus, about 50–70% of the population would have to be immune to a specific virus, either through naturally acquired immunity (via asymptomatic or symptomatic infection) or artificially acquired immunity through a successful vaccination process. For example, herd immunity against measles requires approximately 95% of a population to be vaccinated while the threshold for polio is lower, at approximately 80%.[(3)]

The proportion of the population that must be vaccinated against SARS-CoV-2 to induce herd immunity is unknown, as yet, although experts opine that a 60–70% immune population will stop the community spread of the disease. Considering the scientific, societal and political obstacles that need to be overcome to achieve this figure, it is dawning on the scientific community that COVID-19 vaccines may not be the panacea for this dreaded disease, in the shorter term. As a community, we may have to continue to resort to other protective measures, such as mask-wearing and hand hygiene, for the foreseeable future. To reap optimal benefits from vaccinations, and to reach the magic target levels required for herd immunity, a fuller understanding of how vaccinations prevent disease is important for healthcare workers, in particular, to offer advice and guidance to their team, the patients, as well as the public, as discussed below.

2 VACCINE VAGARIES

Vaccines and vaccination procedures have had their fair share of proponents and opponents since their introduction some two centuries ago by Edward Jenner, in the UK, to prevent smallpox. This said, vaccines continue to prevent scores of bacterial and viral infections, while a few others such as polio and smallpox have been virtually or totally eliminated.

Clearly, vaccines are not the panacea for infectious disease for a variety of issues. Whenever a new vaccine, such as for COVID-19, is introduced, these issues resurface, leading to intense scrutiny among health professionals as well as the public. Some of these, appertaining to vaccines in general would also be applicable to COVID-19, and include:

- Vaccine-induced immunity;
  - neutralizing versus binding antibodies;
  - effective versus sterilizing immunity;
- Vaccines and side effects;
- Vaccine non-responders;
- Pre- and post-vaccination serology;
- Booster vaccinations;
- Vaccine hesitancy.

3 BASICS OF HOW COVID-19 VACCINES WORK

An outline of how a vaccine inhibits natural infection is given below to understand the nuances of the COVID-19 vaccine functionality (Figure 1).

The aim of a vaccine is to stimulate the body's own protective immune response, mainly antibody-producing B cells and the enabling T cells, so that, if an individual encounters a specific viral pathogen, then the immune system can quickly recognize and destroy the invading virus and terminate the disease process. For the vaccines against SARS-CoV-2, the goal is to produce antibodies against the spike (S) protein or the proteins on the receptor binding domain (RBD) on the viral surface (Figure 1). The numerous spikes on the viral surface initiate its attachment to susceptible human cells (via the receptor binding proteins), allowing it to enter the cell, and hijack the DNA of the cell to produce a viral progeny that will re-infect other cells and cause the infection. Neutralizing the critical functionality of the protruding spikes that facilitate viral entry, with the vaccine-induced, preformed antibodies, and backed by the enabling T cells, prevents the infection.[1]

4 VACCINE-INDUCED IMMUNITY

Antibodies produced by the B cells of the immune system (Figure 1) can vary both in quantity as well as in quality. In general, antibodies can be divided into two basic types: neutralizing (NAb), and non-neutralizing antibodies (nNAb). The antibodies that block entry of the pathogen into the host cells, and stop the infection, are called neutralizing antibodies, and should be distinguished from binding antibodies or non-neutralizing antibodies (nNAb). As the name implies, the latter bind to the pathogen, but do not interfere with viral entry into the host cells, possibly because they do not bind to the correct region of the virus. However, binding antibodies play a contributory role in attacking the invading virus by signalling the immune cells, after which the virus is processed and destroyed by the recruited immune cells.[4]

Neutralizing antibodies, on the other hand, can neutralize the virus even without the support of other immune cells. For instance, in the case of COVID-19, the neutralizing antibodies bind to the spike (S) antigens on the viral surface and render the 'spikes' ineffective in attaching to the host cells, thereby stopping the virus in its tracks (Figure 1). The holy grail of the vaccine manufacturers, therefore, is to produce neutralizing antibodies, rather than binding antibodies. The currently approved COVID-19 vaccines are all extremely effective in producing these neutralizing antibodies.

The neutralizing antibody response of an individual can also be sub-categorized into two different types: an effective antibody response and a sterilizing antibody response.[5] There is a nuanced, but important clinical difference between these, as effective immunity prevents the vaccinee from contracting the illness and the development of antibody-mediated immunity. However, the vaccinee may have an asymptomatic infection and become a silent carrier of the disease over a period of time. Consequently, the vaccinee may unknowingly become a 'silent spreader' of SARS-CoV-2 for an indeterminate period.

In the case of sterilizing immunity, the very high level of seroconversion completely prevents virus multiplication in a vaccinee's cells, and prevents the further transmission of the virus to another. Sterilizing immunity is a key goal of vaccine manufacturers and it will not be clear which of the available COVID-19 vaccines provides what type of immunity, and to what proportion of vaccinees, until all the clinical trials are completed and mass vaccination results are evaluated. Nevertheless, there is hope, as there are a number of vaccine precedents for epidemic-prone diseases, such as measles, polio and hepatitis B, where the vaccination process does not produce sterilizing immunity.

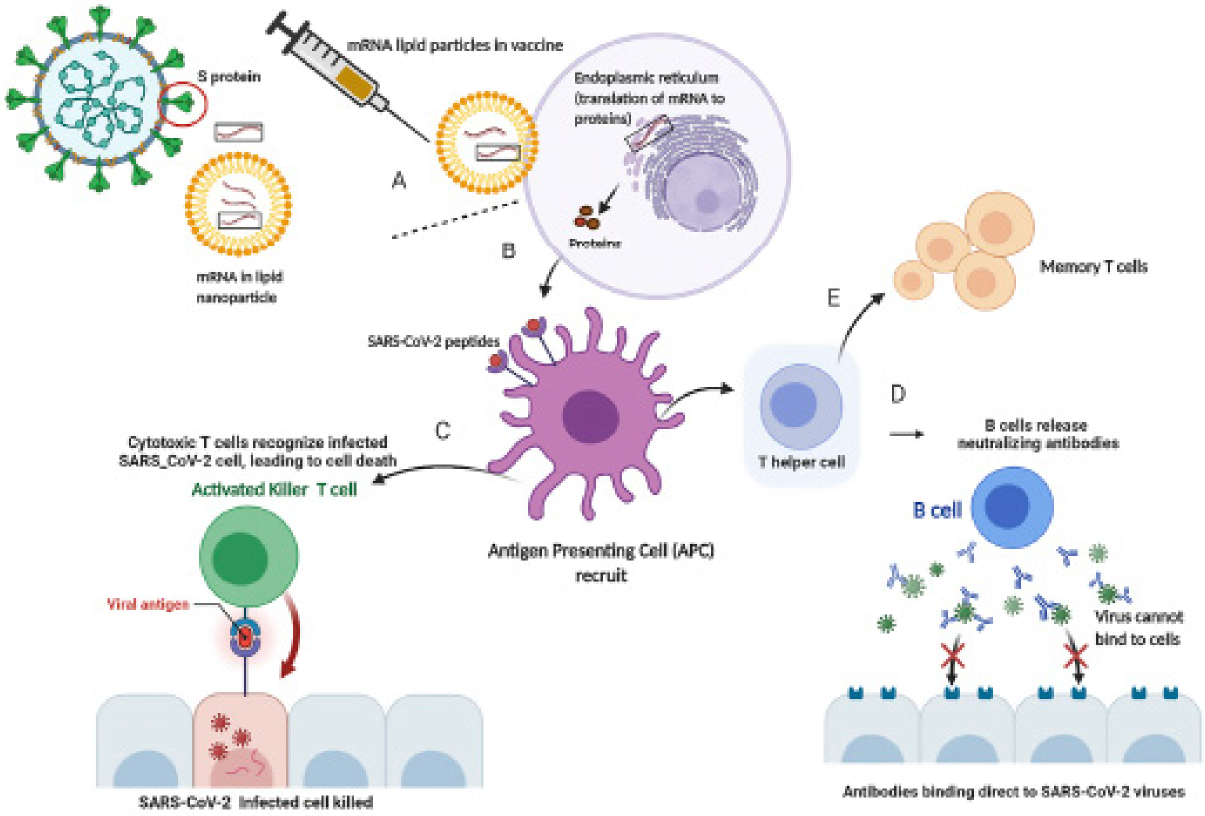

Fig. 1: A highly simplified representation of how a vaccine works (as exemplified by the lipid nanoparticle mRNA vaccine for COVID-19). A. The vaccine containing mRNA of SARS-CoV-2 with the code for either the Spike (S) protein or the receptor-binding domain (RBD) proteins, within lipid particles are administered to the vaccinee. B. Once injected, the lipid particles are 'ingested' by vaccinees' cells. The protein-making machinery in these cells is instructed to produce viral proteins (i.e. S or RBD antigens), that are displayed on the cell surface of antigen-presenting cells (APC) (purple). C. APC then recruit T cells (green) that are activated to kill SARS-CoV-2-infected cells (lower left panel). D. APC also recruit B cells (blue) that are primed to produce neutralizing antibodies to the viral S and RBD proteins, preventing viral attachment to host cells and stopping the infection (lower right panel). E. Long-lived memory B and T cells (light brown) are also produced simultaneously that can patrol the body for any incoming viruses for months/years and rekindle an identical B and T cell response. (Image courtesy Dr Kausar Fakhruddin; software Biorender.com)

5 VACCINES AND SIDE EFFECTS

Despite the availability of numerous effective and efficacious vaccines over the last half a century or so, there is a significant proportion of the population who are hesitant to take any vaccine (see below) due to the side-effects of the vaccines. However, the vast majority of the side effects of current COVID-19 vaccines appear to be minor with injection site pain, rash and soreness, to headache, muscle aches and malaise lasting 3 or 4 days.

In this context, when a vaccine is offered to a dental team member, the team leader may have the responsibility of providing information on the currently offered vaccine type, side effects and other relevant details to the prospective vaccinee in consultation with the local medical care provider, depending on the requirements of the local jurisdictions. This will be a dynamic scenario that needs to be astutely monitored, as the database on the new vaccines, including their side effects, is still rudimentary. COVID-19 vaccine side effects, and reports of these are now available in real time (https://medshadow.org/covid19-vaccine-side-effects/)

6 NON-RESPONDERS

Some of the current next generation mRNA vaccines have an efficiency approaching 95%, while this figure may be lower for other vaccines. Hence, depending on the vaccine strain, a very small number of vaccinees will not seroconvert and/or develop neutralizing antibodies. It is, as yet, unclear how such non-responders, who do not develop optimal levels of antibody, should be employed in a clinical environment. Practitioners should, therefore, be aware of this pitfall and await guidance on these immune correlates that are yet to be developed, and deal with such situations as per the stated policies of local jurisdictions.

7 PRE- AND POST-VACCINATION SEROLOGY

Once an individual consents to be vaccinated, establishing the vaccinees immune status is important both before, and after the single- or two-dose vaccination procedure – at least in theory, in accordance with previous immunization regulatory practices. This said, having individuals checked before vaccination, in the current circumstances where vaccines are reaching millions of arms worldwide, is a daunting prospect and appears to have been disregarded for practical reasons. There are also some who argue that if a person has contracted COVID-19, there is no necessity for vaccination, pointing to the fact that there are only a handful of documented re-infection reports, even after 100 million cases of confirmed disease worldwide.[(6)] And even among the rare cases of re-infection, their disease courses were reported to be milder, and without hospitalization. Pre-immunization serology testing for those who recently contracted COVID-19 appears to be a contentious issue that needs to be resolved in earnest.

On the other hand, it is highly likely that post-vaccination serology testing would be required for dental care professionals because they appear to be at significant risk for COVID-19 by virtue of their work environment, where many aerosol generating procedures are undertaken on a daily basis.[(7)] Post-vaccination serology is usually performed by measuring the antibody titre 4–8 weeks after the second dose (e.g. hepatitis B vaccinations). It would also be reassuring to know the post-vaccination antibody status of a vaccinee to ensure that they do not belong to the small minority of non-responders (e.g. 5–10% for mRNA vaccines).

8 BOOSTER VACCINATIONS

It is also unclear, as yet, whether booster doses are necessary for the COVID-19 vaccines after the initial two-dose vaccine, and if so, how often these should be administered. A good example is the influenza vaccine, which requires annual boosting to maintain seropositivity for the prevalent sub-type of the virus. It may be that the regularity and frequency of the antigenic shifts we are witnessing in SARS-CoV-2, with the arrival of various 'viral variants', will necessitate an annual vaccine boost either for the old strain of the virus or a newly circulating variant.

9 VACCINE HESITANCY

Although not strictly falling under the remit of the clinical responsibility of the dental professionals, the issue of vaccine hesitancy by the public is a contentious issue that requires informed discussion and debate among the profession and the public.

Vaccine hesitancy is defined as a delay in acceptance, or refusal, of vaccination by the community despite the availability of vaccination services.[(8)] It is a complex societal problem, fuelled by numerous myths, rumours and fears about the disadvantages of vaccines, not least because of the associated media hyperbole and hype. Maintaining public confidence in COVID-19 vaccines, and increasing vaccine uptake and minimizing vaccine hesitancy will be crucial to eradicate the disease. Dental practitioners can play a key contributory role here by educating their patients and the public on the myths and the truths of COVID-19 vaccines. Certainly, this task will be much easier when there is firm data on vaccine side-effects in the fullness of time.

10 CONCLUSIONS

The foregoing commentary exposes the complex, multi-dimensionality of COVID-19 vaccines which, clearly, will be the latest addition to the infection control armamentarium of dental professionals. The notion that the vaccines and vaccine-induced herd immunity will be a panacea ushering a new dawn of pre-COVID-19 dental practice needs to be tempered by the realization of a yet unfolding and volatile viral ecosystem where the only predictability is the unpredictability of the disease itself.

11 COMPLIANCE WITH ETHICAL STANDARDS

12 CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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