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Chapter

The COVID-19 Vaccines: The Current Standpoint

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Abstract

Coronavirus disease 2019 (COVID-19) is a global pandemic that has affected millions of people worldwide. Vaccination seems to be the potent solution to achieve herd immunity and limit viral spread. Various platforms have been utilized to manufacture COVID-19 vaccines such as adenovirus-based vaccines, inactivated virus, DNA-based vaccines, recombinant protein, or mRNA-based vaccines. This chapter covers different viewpoints and the present status of in-use vaccine including the advantages and disadvantages.

Keywords: SARS-CoV-2, vaccine, variant of concerns (VOCs)

1. Introduction

Coronavirus disease 2019 (COVID-19), first reported in Wuhan, China, was declared a pandemic by the World Health Organization (WHO) in March 2020. The WHO confirmed 364,191,494 cases of COVID-19, including 5,631,457 deaths as of January 2022.

Severe acute respiratory syndrome coronavirus 2 (SARS CoV 2), a single-stranded RNA virus, is the causative agent of COVID-19. This virus belongs to the coronavirus family, a group of enveloped viruses that primarily cause respiratory illness. The SARS CoV 2 genome is composed of a 30 kb RNA, five main open reading frames, four primary structural proteins—spikes (S), envelopes (E), membranes (M), and nucleocapsids (N), all of which trigger immunological responses (Figure 1). The entry of virus into host is via angiotensin-converting enzyme 2 (ACE2) receptor-mediated attachment of the S protein to the host cell. The internalization of viral S protein and subsequent integration into the host cell are mediated by the serine protease of the host cell, transmembrane serine protease 2 [1].

With the increasing global prevalence of COVID-19 cases, the development of an effective vaccine is imperative to contain the pandemic. Vaccinations have the capability to generate herd immunity in societies, which can reduce disease occurrence, transmission, and the social and economic detrimental impact of the disease. No specific antiviral treatment is currently available for public use. However, since the SARS CoV 2 genomic sequence was identified, >100 vaccine studies have been performed, ~50 of which have reached human experimentation, and several vaccines
are currently being administered to certain sections of the population (ourworldindata.org/covid-vaccinations). At present, only few numbers of vaccines have received FDA approval for public use.

2. COVID-19 vaccines: Platform

Vaccinations are the only safest and most cost-effective strategy for preventing COVID-19 disease transmission in public. The intent behind vaccine development is to induce a primary immune response by delivering altered or weakened antigens that normally cause disease, allowing the host to form immunological memory without getting infected naturally.

The most critical step in the development of vaccines is selecting the protective and immunogenic epitope. The primary targets to induce humoral immune response are S and N proteins of coronavirus. The receptor binding domain (RBD) of the S protein, followed by the N protein, is the primary antigenic target of SARS-CoV-2 for neutralizing human IgM, IgG, and IgA [2]. Long-term protection depends on the persistence of vaccine-induced antibodies above protective thresholds and/or the maintenance of immunological memory cells capable of quick and effective reactivation following subsequent exposure [3].

To combat this pandemic, there are chances that the world will certainly require more than a single vaccine type or single antigen/epitope to induce an immunological response that should cater to the need for broad target population coverage, high production volume, and storage and transportation requirements in addition to vaccine safety and effectiveness.

For the development of the COVID-19 vaccine, several vaccination platforms have been investigated, each with its own set of benefits and drawbacks (Table 1 shows the comparative chart of advantages and disadvantages of vaccines based on different platforms). The ongoing vaccine development trial involves classical molecular strategies that are based upon inactivated, modified live or attenuated virus, single peptides, or viral vectors (Figure 2) [4].
2.1 Whole virus vaccines

The whole virus vaccine consists of a weakened form of SARS-CoV-2, which has been attenuated or inactivated so that without causing any harmful effect it can induce a protective immune response. Inactivated vaccines can only induce humoral immune responses to SARS-CoV-2, whereas live-activated vaccines can stimulate both cellular and humoral immune responses [5].

2.2 Nucleic-acid-based vaccine

The nucleic-acid-based vaccine uses the genetic material of the pathogen as an active component of the vaccine. Based on the type of genetic material, it could be DNA or mRNA-based vaccines where RNA vaccine could be further subdivided
into mRNA vaccine. Both vaccination platforms can elicit primarily B- and T-cell responses, but with different risk profiles. In the current scenario of the COVID-19 pandemic, genetic material of SARS-CoV-2 is used to induce immune response [4].

2.3 Viral vector vaccines

Viral vector vaccines that are designed against SARS-Cov-2 use modified viral vectors that carry gene encoding of spike proteins. As a vector, these vaccines use modified versions of several viruses. Several different types of viruses have been utilized as vectors, the most frequently used are adenoviruses [5].

2.4 Protein subunit vaccines

Protein subunit vaccines are made of one or more purified antigens from the viruses or bacteria of interest that are capable of eliciting the immune response and imparting a protective response. In terms of SARS Cov-2, these are spike proteins (S), which have been produced in vitro. Two common forms of protein subunit vaccines are polysaccharide and conjugate vaccines against SARS-CoV-2. Polysaccharide vaccines comprise SARS-CoV-2 cell wall polysaccharides, whereas conjugate candidates are coupled to a polysaccharide chain with a carrier protein to generate a boost in the immune system response [4].

2.5 Virus-like particles (VLPs)

Virus-like particles (VLPs) are a type of protein vaccines that are made up of nanoparticles that look like viruses. VLPs are composed of some or all the proteins that make up the viral capsid, rather than a single protein. They resemble live attenuated or inactivated vaccines in that they can elicit strong cellular and humoral
immune responses while posing no risk of reversion since they lack the virus's genetic material [6].

2.6 Exosome-based vaccines

Exosomes are lipid bilayer coated extracellular vesicles secreted by a variety of cells. Their key role is to function in intercellular communication, and they have been reported to load RNA, DNA, and proteins in between cells. The key features of EV-based vaccines, including their ability to induce poor immunogenicity, mean EVs can be safely and efficiently used in vaccine development. The ability of EVs to preserve naïve antigen conformation and access to all organs via bodily fluids gives an added advantage compared with other delivery agents, such as lipid-based nanoparticles (LNPs) or viral vectors. Unlike other platforms, these vaccines are in the very preliminary phase of vaccine development. Although many companies including Capricor Therapeutics have shown positive preclinical results, none of them has still managed to enter phase 1 clinical trials [7].

3. COVID-19 vaccines: Current status

The US Food and Drug Administration (FDA) has approved three COVID-19 vaccines for emergency use: two messenger RNA-based vaccines (Pfizer and Moderna) and one adenoviral vector vaccine (Janssen). In case of a public health emergency, unlicensed drugs and vaccines are given emergency use authorization (EUA). Currently, as per the WHO data, there are 10 vaccines that have been granted for Emergency Use Listing (EUL) as of April 25, 2022 [8] (Table 2). Two vaccines (Moderna and Janssen) have completed phase 4 clinical trials successfully. At present, 153 COVID-19 candidates are in clinical trials and 196 candidates are in preclinical research worldwide [9]. Below is a brief description of three FDA-approved vaccines for COVID-19.

3.1 Pfizer–BioNTech (BNT162b2)

BNT162b2 is a lipid nanoparticle (LNP)-formulated, nucleoside-modified RNA vaccine that encodes the full-length SARS-CoV-2 spike (S) protein, modified by two proline mutations to ensure an antigenically optimal pre-fusion conformation that mimics the intact virus to trigger virus-neutralizing antibodies. This vaccine showed good safety and efficacy, and after about 12 days of vaccination, this vaccine has reportedly shown a reduction in the risk of SARS-CoV-2 infection. By April 2022, among all available vaccines, the Pfizer vaccine has shown to exhibit the highest efficacy of 95% and is WHO-approved in 103 countries. The minor side effects that were reported for this vaccine are pain at the injection site, fatigue, headache, muscle and joint pain, chills, fever, and diarrhea. While rare side effects include pericarditis, arrhythmia, deep-vein thrombosis, pulmonary embolism, myocardial infarction, intracranial hemorrhage, and thrombocytopenia [10].

3.2 mRNA-1273 Moderna

Moderna’s mRNA vaccine is a lipid nanoparticle-encapsulated nucleoside-modified messenger RNA (mRNA)-based vaccine. It encodes the SARS-CoV-2
full-length spike protein that has been prefusion stabilized. This spike glycoprotein regulates the adhesion to host cells. As a result, it is required for viral entry and hence serves as the primary target for the vaccine. The vaccine causes a strong binding and neutralizing response. Like the Pfizer vaccine, this is among those first vaccines that received EUA in December 2020. This vaccine has shown efficacy of 94% and is WHO-approved in 76 countries. The most common side effects are headache, injection site pain, fatigue, muscle pain, and chills. Rare side effects include nausea, vomiting, myocarditis, pericarditis, angioedema, and anaphylaxis [11].

### 3.3 Janssen vaccine/Ad26.COV2.S

Janssen’s Ad26.COV2 S vaccine is a recombinant human adenovirus type 26 that carries the full-length SARS-CoV-2 S protein and generates an antibody response against the SARS-CoV-2 infection. The Janssen vaccine is based on the deletion of the E1 gene and the replacement of it with the spike gene in inactivated adenoviruses. The adjuvant properties, scalability, and broad tissue tropism of adenoviral vectors are advantages. This vaccine shows an efficacy of 66.9%, and WHO has approved it in 75 countries. Like other vaccines, common localized side effects reported are pain at the inoculation site and systemic signs such as fever, headache, myalgia, or nausea [12]. Table 3 depicts the most used COVID-19 vaccine worldwide with the efficacy, storage temperature, and route of administration.

As per the World database (ourworldindata.org/covid-vaccinations), COVID-19 vaccination has been administered to 65.4% of the world’s population (April, 2022).

### Table 3

<table>
<thead>
<tr>
<th>Vaccine Name</th>
<th>Vaccine Type</th>
<th>Approval Status/Authorization</th>
<th>Clinical Trials</th>
</tr>
</thead>
<tbody>
<tr>
<td>Novavax Nuvaxovid</td>
<td>Protein Subunit</td>
<td>Approved in 37 countries</td>
<td>15 trials in 12 countries</td>
</tr>
<tr>
<td>Serum Institute of India</td>
<td>Protein Subunit</td>
<td>Approved in 4 countries</td>
<td>2 trials in 1 country</td>
</tr>
<tr>
<td>COVOVAX (Novavax formulation)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderna Spikevax</td>
<td>RNA</td>
<td>Approved in 85 countries</td>
<td>60 trials in 22 countries</td>
</tr>
<tr>
<td>Pfizer/BioNTech</td>
<td>RNA</td>
<td>Approved in 144 countries</td>
<td>73 trials in 26 countries</td>
</tr>
<tr>
<td>Comirnaty</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Janssen (Johnson &amp; Johnson)</td>
<td>Non-Replicating</td>
<td>Approved in 111 countries</td>
<td>20 trials in 22 countries</td>
</tr>
<tr>
<td>Ad26.COV2.S</td>
<td>Viral Vector</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oxford/AstraZeneca Vaxzevria</td>
<td>Non-Replicating</td>
<td>Approved in 138 countries</td>
<td>62 trials in 30 countries</td>
</tr>
<tr>
<td>Covishield (Oxford/ AstraZeneca)</td>
<td>Viral Vector</td>
<td>Approved in 47 countries</td>
<td>2 trials in 1 country</td>
</tr>
<tr>
<td>Bharat Biotech Covaxin</td>
<td>Inactivated</td>
<td>Approved in 14 countries</td>
<td>10 trials in 2 countries</td>
</tr>
<tr>
<td>Sinopharm (Beijing) Covilo</td>
<td>Inactivated</td>
<td>Approved in 91 countries</td>
<td>26 trials in 12 countries</td>
</tr>
<tr>
<td>Sinovac CoronaVac</td>
<td>Inactivated</td>
<td>Approved in 55 countries</td>
<td>37 trials in 9 countries</td>
</tr>
</tbody>
</table>

Table 3, WHO list of vaccines approved for emergency use listing (EUL).
Globally, 11.6 billion doses have been rolled out, with 9.82 million doses being given out every day. In low-income countries, just 15.7% of people have had at least one dose. Figure 3 shows a graphical representation of people in several nations who have been vaccinated against COVID-19.

4. Limitations of vaccines

Regardless of multiple attempts of developing vaccines for SARS-CoV-2, the chances of complete eradication of diseases still face various challenges, which may arise due to varied levels of efficacy or preexisting immunity or limited accessibility. Thus, an effective vaccine needs to overcome multiple obstacles as stated below:

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Vaccine/Manufacturer</th>
<th>Efficacy</th>
<th>Storage temperature</th>
<th>Route</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Pfizer BioNTech</td>
<td>95.3%</td>
<td>−80 degrees C to −60 degrees C</td>
<td>Intra-muscular</td>
</tr>
<tr>
<td>2.</td>
<td>AstraZeneca</td>
<td>63.09%</td>
<td>+2 degrees C to +8 degrees C</td>
<td>Intra-muscular</td>
</tr>
<tr>
<td>3.</td>
<td>Sputnik-V</td>
<td>91.6%</td>
<td>+2 degrees C to +8 degrees C (Dry form) −18.5 degree C (Liquid form)</td>
<td>Intra-muscular</td>
</tr>
<tr>
<td>4.</td>
<td>Moderna</td>
<td>94.1%</td>
<td>+2 degrees C to +8 degrees C (for 30 days)−50 degrees C to −15 degrees C</td>
<td>Intra-muscular</td>
</tr>
<tr>
<td>5.</td>
<td>Janssen/Johnson</td>
<td>66.3%</td>
<td>+2 degrees C to +8 degrees C</td>
<td>Intra-muscular</td>
</tr>
<tr>
<td>6.</td>
<td>Covaxin</td>
<td>78%</td>
<td>+2 degrees C to +8 degrees C</td>
<td>Intra-muscular</td>
</tr>
</tbody>
</table>

Table 3.
List of key features of commonly used COVID-19 vaccines with efficacy.

Figure 3.
Graphical representation of people vaccinated against COVID-19 for some countries as of Apr 27, 2022. Taken from https://ourworldindata.org/covid-vaccinations.
4.1 Long-term outcome

Since efficacy was determined based on short-term evidence, especially when other vaccines have shown efficacy declining with time. The antibody induction by of Moderna vaccine remained high among all age groups and lasted for 6 months after the second dose. After 6 months, there has been no further information [13]. Furthermore, current trials have revealed no long-term problems.

4.2 Preexisting immunity

Currently available SARS CoV 2 vaccines (AstraZeneca/Janssen) are based on the classical approach of viral vectors, particularly adenoviruses. Although adenovirus-based vaccines are well characterized, they are limited by preexisting immunity of the virus vector employed in the vaccine design, which may restrict the immune response against COVID-19 antigens, thereby decreasing their efficacy [14].

4.3 Antibody-dependent enhancement (ADE)

Another point of concern is the risk of reinfection with emerging viruses in the community due to a lack of long-lasting immunity. Multiple immunizations with such viral vectors, if not effective, could lead to a more complicated form of the disease, such as antibody-dependent enhancement (ADE), increasing the disease burden in a vaccinated person [15].

4.4 Variant protection

New variants of SARS-CoV-2 have the potential to complicate the effectiveness of current vaccines. In the United Kingdom, ChAdOx1 demonstrated 75% protection against one variant named B.1.1.7 (including asymptomatic infection). However, the AstraZeneca vaccine showed only 10% protection against the B.1.351 variant in a young population with a median age of 30 in South Africa, hence their AstraZeneca roll-out was ceased [16]. Thus, an effective approach for vaccine development is required, which can also overcome the issue of variant of concerns (VOCs).

4.5 Age groups

Age is also one of the crucial factors to check the effectiveness of vaccination. In all age groups and persons with comorbidities, further evaluation of the efficacy of all vaccines is necessary. Individuals above the age of 16 took part in Pfizer’s vaccine trials. Individuals 18 years and older were included in the Moderna, Oxford/AstraZeneca, and Janssen trials. At this time, Oxford/AstraZeneca appears to be more tolerated in older adults than in younger adults, and it has similar immunogenicity in all age groups following a booster dosage [17].

5. Future perspectives of vaccine development

Active immunization represents the most effective technique for combating the current COVID-19 pandemic and saving millions of lives around the world. The currently approved vaccines have been shown to reduce both mortality and the incidence
of severe COVID-19 infection, and they are now a critical weapon in the fight against SARS-CoV-2. The rising cases of variant of concerns (VOCs), on the other hand, continue to pose a threat to vaccine-induced immune protection, emphasizing the need for multi-coronavirus vaccine platforms capable of inducing a long-lasting protective immune response.

The key strategy for combating the COVID-19 pandemic is to develop vaccines that can induce long-lasting immunity and protect against circulating SARS-CoV-2 variants. Ongoing trials for SARS-CoV-2 vaccine construction are based on the principle of eliciting neutralizing antibodies (Nabs) against the S protein, thereby interfering with viral receptor binding. To date, research associated with COVID-19 vaccine development has focused primarily on antibody titers and the ability of antibodies to neutralize viral particles [18].

But, with the accumulating evidence of potential roles of more conserved non-spike viral antigens, such as nucleocapsid (N) proteins, which could bring a major victory in the battle against COVID-19 VOCs and can also overcome the existing issue of providing long-lasting immunity. Immunologically, a vaccine that targets the mutation-prone S protein, as well as the more stable and conserved N, is required to surmount the immune escape characteristics exhibited by SARS-CoV-2 variants [19].

The rapid development of the COVID-19 vaccine within such a short life span represents a remarkable landmark in the history of antiviral vaccine development. This progress has also given hope to the development of the long-time pending dream of developing an HIV vaccine. Many pharmaceuticals such as Moderna and Pfizer are trying to develop the HIV vaccine for past decades but have been unsuccessful in its clinical translation. Thanks to SARS-CoV-2, such rapid progression and successful results of the COVID-19 vaccine made decade long dream of HIV vaccine development possible now and such vaccine candidates are currently under clinical trials.

6. Conclusion

With the purpose of making world COVID free, available vaccines possess many drawbacks that need to be addressed. Besides following the proper implementation of preventive measures, we need to focus on all the major vaccination strategies to achieve a successful outcome. It is imperative to consider multiple antigens/multi-epitope vaccine to achieve long-term immunity and protection against a variant of concerns (VOCs). However, even though there are still numerous hurdles and unanswered concerns, the tremendous advances in COVID-19 vaccine research have given the world hope that this disease can be eradicated.
References


[14] Ghaebi M, Osali A, Valizadeh H, Roshangar L, Ahmadi M. Vaccine development and therapeutic design for...


