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## SARS-CoV-2 vaccine candidates: A beginning of the end of COVID-19 pandemic- Editorial

With the emergence of the novel coronavirus, severe acute respiratory syndrome 2 (Sars-CoV-2) came the harsh realization of how unprepared various government entities and societies were for a pandemic. The following year reigned in an economic and public health catastrophe, from which we are still slowly recovering today. In response, the brightest minds in the world collaborated and put scientific discovery into hyper drive, resulting in numerous vaccines' production – the quickest in history. To grasp the basic science behind vaccination, one must understand that every virus is different in the 'SWs and how' it infects its host. As variable as the virus is, so is its host immune response depending on viral load, infection location, host gender, age, and immune status.

### COVID-19 characteristics

Upon examination, the Sars-CoV-2 structure is of the coronaviridae family: pleomorphic, positive sense, ssRNA, enveloped viruses with surface projections composed of spike (S) protein [1]. The S protein is the essential component of the virus for attachment, fusion, and entry into the host cell [1]. Sars-CoV-2 binds and enters the host cell via the human angiotensin-converting enzyme 2 (hACE2) receptor binding the viral S protein [1]. This receptor is expressed all over the human body, but mostly in the pulmonary, neurological, and gastrointestinal systems, explaining the general clinical picture. The Sars-CoV-2 virus is a highly contagious virus spread via respiratory droplets, direct contact, or fomites. Symptom presentation between hosts differs significantly and can include fever, dry cough, fatigue, shortness of breath, chills, muscle aches, headache, GI disturbances, and weight loss [2,3]. Presentation in patients with comorbidities, such as diabetes or hypertension, is more severe and accounts for most deaths around the world. Thus, the vaccine must dually provide rapid and sustainable eradication of the virus. To achieve this, scientists must determine the immunological response – humoral or cell-mediated response and antibody isotype – that the vaccine must elicit [4]. Globally, the virus has spread like wildfire, leading to staggering numbers of infections and death. Therefore, society can grasp the dire nature of vaccine production and distribution.

### Vaccine variations

In the past, vaccines have taken many forms including the following: polysaccharide, conjugate, live-attenuated, inactivated, sub-unit, and many others. Polysaccharide vaccines and their conjugate counterparts are amongst the oldest created. These vaccines, composed of capsular polysaccharides, were born in the 1970s and produced sufficient immune responses in adults, but provided no protection in infants and adolescents [5]. Shortly after, a few scientists linked these capsular polysaccharide vaccines to carrier proteins and elicited strong immunogenicity in children, as well [5]. The live-attenuated vaccines (LAVs), like the Varicella vaccine, has an inherent ability to recruit both the innate and adaptive immune systems via toll-like receptors [1]. It can also be derived via several methods, such as reverse genetics [1]. However, to establish safety and efficacy, LAVs require lengthy clinical trials and nucleotide substitution may occur forming recombinants after vaccination is completed [1]. Inactivated or "killed" viruses, are evidently safer than live-attenuated viruses. Its infrastructure is premade, allowing for quick production, but it does require a booster vaccination to sustain a strong immune response and these vaccines are difficult to maintain and handle [1].

DNA vaccines are stable within a wide range of temperatures and can be developed rather quickly in comparison [1]. The downside is though they elicit an innate and adaptive immune response, it is not robust [1]. Additionally, DNA may insert into the host genome causing cellular abnormalities and resultant self-antibody production [1]. A subunit vaccine does not contain live portions of a virus and thus is safer [1]. It is disadvantaged by the fact that it induces a suboptimal immune response, and the recruitment of plasma cells (memory B cells) in a future infection is unlikely [1]. Subunit vaccines also require an adjuvant to boost immunogenicity [1]. Adjuvants can either increase the half-life of the vaccine in serum or diminish the immune response [1].

As of July 2020, a vaccine that produces antibodies to neutralize the S protein has been the primary goal of all contenders [1]. At this time, two mRNA vaccines and one viral vector vaccine have begun distribution across the world: Moderna mRNA-1273, BioNTech/Pfizer BNT162b2, and Oxford AstraZeneca ChAdOx1 nCoV-19, respectively [6]. mRNA vaccines are a reasonably new technology. They are non-infectious mediums with almost no integrative abilities and thus close to zero potential risks of mutagenesis [1]. With various alterations, the mRNA vaccine can have minimal immunogenicity with increased stability [1]. As a result of minimal immunogenic reactions, the vaccine can be rapidly developed and repeatedly administered [7]. mRNA vaccines, unfortunately, are unstable [1]. On the other hand, viral vector vaccines are highly accurate mediums as well – they can deliver genes to specific target cells with high efficiency [1]. Gene transduction and immune response induction are also highly efficient, leading to a sustained expression of antigens [8]. These vaccines recruit cytotoxic T lymphocytes, ensuring the prompt destruction of virally infected cells [9]. The drawback with these vaccines is that the host may have a predisposed immune response to the vector, decreasing its efficacy [1]. The viral vector may also insert itself into the host genome, as with the DNA vaccine, and lead to cancer [1].

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### Moderna mRNA-1273

The Moderna mRNA-1273 vaccine is an mRNA vaccine composed of synthetic genetic material within a Lipid Nanoparticle (LNP) [1]. The mRNA strand within the Moderna vaccine encodes a full-length stabilized S protein, which is the viral form before completing fusion with the host cell [1]. Administration potentially elicits a specific S protein antiviral response while being relatively safe because it does not contain any components of the inactivated virus or live pathogen [10]. To assess the safety and efficacy profile of the vaccine, phase 3 of the Coronavirus Efficacy (COVE) trials began in July 2020 [10]. The vaccine was administered 28 days apart in the deltoid muscle of the same arm [10]. Evidence from the COVE trials indicates that the mRNA-1273 vaccine has short-term efficacy in preventing symptomatic COVID-19 infection among a diverse adult population [10]. All severe COVID-19 infections occurred in the group receiving placebo injections, which means that mRNA-1273 has a severe illness preventative effect, too. After primary analysis, this vaccine showed an efficacy of 94.1% for preventing symptomatic COVID-19 infection compared with the placebo injection in participants that were seronegative at baseline [10]. The trials show that the vaccine is safe, with minimal local reactions but moderate to severe systemic reactions after the second dose, including transient fatigue, myalgia, arthralgia, and headache in about 50% of participants. These side effects were resolved by day two post-vaccination and had no resulting sequelae [10].

### BioNTech/pfizer BNT162b2 mRNA

The BioNTech/Pfizer vaccine is also an optimized mRNA vaccine [1]. The genetic sequence encodes for the Sars-CoV-2 receptor binding domain (RBD), which is this vaccine's neutralizing antibody target [1]. The RBD is component of the S protein – specifically the S1 subunit – and due to the addition of a T4 domain, the BNT162b2 vaccine elicits a large immunogenic response [1]. The mRNA sequence is contained within a cationic LNP, which makes delivery into target cells efficient [1]. The vaccine is unique to other mRNA vaccines, as it stimulates a robust IgG response that is far stronger than the Sars-CoV-2 infection itself [1]. Trials for the BNT162b2 vaccine also began in July 2020 and was administered 21 days apart with the same methods. Overall, participants that received the BioNTech/Pfizer vaccine had more complaints of local injection site reactions than the placebo group; systemic side effect profiles included fatigue, headache, fever, or a combination of the three, which subsided 1–2 days after administration of the second dose [11]. Primary analysis of efficacy showed a value of 95.0% in those with no history of previous Sars-CoV-2 infection and 94.6% in participants with a known history of the disease [11]. Interestingly, analysis among several demographic groups determined an efficacy value of 94.6% in a group with hypertension [11]. This trial went one step further than the Moderna trial by testing the efficacy of one dose versus two, resulting in a value of 52%, which indicates early protection [11].

### ChAdOx1 nCoV-19 viral vector

On the other hand, the ChAdOx1 nCoV-19 vaccine formulated by AstraZeneca, also known as AZD1222, is a recombinant adenovirus viral vector vaccine. It was also optimized for mRNA codon and, interestingly, synthesized with tissue plasminogen activator (tPA) [1]. These modifications, along with placement within a shuttle plasmid, allow for escalated immunity in intra-muscularly vaccinated participants [1]. Previous studies conducted by Ou et al. indicate that one dose should elicit a sufficient immunologic response [6]. Administration of doses occurred at varying intervals with a range of 32–86 days due to vaccine manufacturing issues [12]. Primary analysis resulted in a true efficacy of 70.4% in participants who received both vaccine doses and 64.1% in those who received one dose [12]. Across all studies, the ChAdOx1 nCoV-19 vaccine had a decent safety profile with an acceptable balance of serious adverse events [12]. Cases of hemolytic anemia (1) and transverse myelitis (3) were possibly associated with vaccination, though very rare [12]. All patients with serious side effects are in stable or improving condition [12].

### Vaccine handling

The current issues at hand is mass production rate, accessibility, and affordability for the general public. COVAX, a joint initiative between Gavi, the Vaccine Alliance, the World Health Organization, and the Coalition for Epidemic Preparedness Innovations, will ensure the equal and fair distribution of COVID-19 vaccines [13]. The ChAdOx1 nCoV-19 vaccine by AstraZeneca is part of this coalition, making each dose available for \$4 and able to be stored at 2–8 °C [13]. BNT162b2 created by BioNTech/Pfizer is not part of COVAX, making a dose available for \$20. Maintenance is also tricky since it must be at –70 °C [13]. Once thawed; however, the vaccine can be kept in a conventional refrigerator for up to five days [13]. The mRNA-1273 vaccine via Moderna is also not a member of COVAX; patrons must store it at –20 °C with an unclear price per dose at this time [13].

Vaccination has proven to protect society from the horrifying consequences of infection for centuries. Though the initial concern with Sars-CoV-2 vaccine production was its streamlined nature, none of the vaccine production groups skipped proper protocol steps as defined by the Food and Drug Administration (FDA). All clinical trial data and procedures are available for transparency and tested with accuracy among willing volunteers. No matter how the dose may be stored or sold, all eligible members of society must take all necessary steps to try and receive the vaccine to prevent the further spread and mutation of the virus, as infection rates will continue to rise without adequate preventative measures and mass vaccination.

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#### Guarantor

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#### Declaration of competing interest

Authors declare no competing interests.

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