Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Commentary

COVID-19 Vaccine

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Rapid spread of severe acute respiratory syndrome coronavirus (SARS-CoV-2), the infection that causes coronavirus disease 2019 (COVID-19), has affected millions of lives since its emergence in December 2019 in Wuhan, China.[1] Public health and mitigation measures, such as social distancing, masks, and hand washing to prevent the spread of SARS-CoV-2, has been met with some resistance and resulted in mixed success based on implementation efforts.[2] As a result, there has been a global urgency for vaccine development. Within a month of the outbreak, scientists sequenced the SARS-CoV-2 genome and used similarities between SARS-CoV-1 and SARS-CoV-2 to accelerate the vaccine discovery process.[3] Currently, there are over 180 vaccines in various stages of development worldwide.[3] Recently, 2 vaccines have received Emergency Use Authorization (EUA) by the Food and Drug Administration (FDA) and 20 others are undergoing phase 3 clinical trials in the United States (US).

Currently available vaccines induce an immune response to the SARS-CoV-2 spike protein.[3] The spike protein on the SARS-CoV-2 engages cell-surface receptors to gain entry into host cells. The use of messenger RNA (mRNA) to encode the spike protein is a novel approach in vaccine development. To facilitate the uptake of mRNA into cells, it is attached to a lipid nanoparticle. Once the mRNA enters the cell, the virus spike proteins are made to induce an immune response.[4] COVID-19 vaccines are the first mRNA vaccines to be studied in large scale clinical trials and approved for clinical use. Unlike other types of vaccines, mRNA vaccines are not infectious and do not incorporate into the host genome. They are also easier to manufacture synthetically once the genome sequence is known.[3,4] However, vaccine distribution has been a challenge since approved mRNA vaccines require cold temperatures to maintain chemical integrity.

In the US, Operation Warp Speed (OWS) was formed to facilitate the development, manufacturing and distribution of vaccines.[5] In order to receive EUA, a vaccine must result in 50% fewer cases of symptomatic COVID-19 compared to placebo and report at least 2 months of safety data (ie, the anticipated timeframe for the development of vaccine-related complications).[6] The first vaccine to receive EUA from the FDA is the mRNA vaccine BNT162b2 by Pfizer and BioNTech. This 2 dose vaccine was found to be 95% effective in preventing severe COVID-19 infection.[7] The 43,538 trial participants included 8.4% with diabetes and 35.1% meeting the criteria for obesity (defined as a body mass index equal to or greater than 30.0 kg/m^2). Of note, vaccine efficacy against COVID-19 after the first dose was only 52%, with a median follow-up less than 21 days. The second vaccine was the mRNA-1273 from Moderna, with a vaccine efficacy of 94.1%. This trial enrolled approximately 30,000 participants, of whom 9.5% and 6.7% carried a diagnosis of diabetes and obesity, respectively.[8] Vaccine efficacy was 80% after the first dose, with a median follow-up of 28 days. Despite the efficacy for both vaccines after a single dose, 2 doses are recommended by the Centers for Disease Control and Prevention at this time given the lack of data for sustained protection after a single dose (Table).

Both vaccines report similar side effect profiles, which includes both local (pain, erythema, swelling, and lymphadenopathy) and systemic side effects (fevers, headaches, myalgia, nausea, or vomiting) with no safety concerns (Table). The first dose of the vaccine acts to prime the immune system, while the second dose strengthens the immune response.[7,8] As a result, side effects were more pronounced after the second dose. During phase 1-3 clinical trials for both vaccines, participants with a history of allergic reaction were excluded from randomization. Of the over 1.8 million doses of Pfizer-BioNTech mRNA vaccines administered, 21 cases of anaphylaxis have been reported. No deaths have occurred as a result of anaphylaxis. Furthermore, all patients recovered and most had resolution within 15 minutes of onset of symptoms. Of note, 81% (17 of 21) had a history of allergies.[9] Similarly, of the over 4 million doses of Moderna vaccine that have been administered to date, 10 cases of severe anaphylaxis have been reported. Nine of these occurred within 15 minutes of vaccine administration and 1

Abbreviations: COVID-19, coronavirus disease 2019; EUA, Emergency Use Authorization; FDA, Food and Drug Administration; mRNA, messenger RNA; OWS, Operation Warp Speed; SARS-CoV-2, severe acute respiratory syndrome coronavirus; US, United States.

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Table
Characteristics of 2 mRNA vaccines that are approved for Emergency Use Authorization Use in the United States by the FDA

	BNT162b2 (Pfizer/BioNTech)	mRNA-1273 (Moderna)
Type	mRNA in lipid nanoparticles	mRNA in lipid nanoparticles
Efficacy	95%	94.1%
Storage Requirements	-70°C +/- 10°C	-20°C
Doses	2 doses, 21 days apart	2 doses, 28 days apart
Shelf Life once thawed	5 days	30 days
Percent participants with diabetes	8.4%	9.5%
Percent participants with obesity	35.1%, with BMI $\geq$ 30.0	6.7% with BMI $\geq$ 40.0
Race/Ethnicity of study participants	82.9% White, 27.9% Hispanic or Latinx, 9.2% Black, 4.2% Asian, 0.5% Native American	79.2% White (of which 20.5% Hispanic/Latino), 10.2% Black, 4.6% Asian, 0.9% Native American/Pacific Islander
Male/Female	50.6% Male, 49.4% Female	52.7% Male, 47.3% Female
Age	$\geq$ 16 years	$\geq$ 18 years
Local Side Effects	Pain (78%)	Pain (90%)
After 2nd Vaccine	Redness (6%)	Redness (9%)
	Swelling (6%)	Swelling (13%)
Systemic Side Effects	Fever (16%)	Fever (17%)
After 2nd Vaccine	Chills (35%)	Chills (49%)
	Headache (52%)	Headache (62%)
	Fatigue (59%)	Fatigue (67%)
	Myalgia (37%)	Myalgia (62%)
	Arthralgia (22%)	Arthralgia (45%)

occurred within 30 minutes of vaccine administration with no anaphylaxis or death reported.[9,10]

Despite the progress to date, challenges with vaccine availability, manufacturing, and distribution remain.[5] As new vaccines become available, these pressures will be mitigated. Until then, creative solutions to address vaccine availability are being debated, including a phased rollout and the use of a single versus dual vaccine dose. In the US, a phased rollout is underway based on risk profiles with health care providers, individuals over the age of 65 years, and patients with underlying medical conditions such as diabetes and obesity allocated to receive the vaccine in Phase 1.[6] Phase 2 aims to vaccinate all individuals over the age of 16 years who have previously not been vaccinated. Other endocrine patients at risk of developing severe complications, such as those with adrenal insufficiency, at risk for thyroid storm, or undergoing treatment for certain endocrine cancers, might also benefit from early vaccinations despite limited data. Contraindications to the vaccine are severe or immediate allergic reaction (eg, anaphylaxis) to a previous dose of mRNA COVID-19 vaccine or to polysorbate or polyethylene glycol.[11] Current recommendations also encourage immunocompromised individuals, pregnant/lactating people, and individuals with history of other allergies to receive the vaccine after risk assessment and appropriate counseling, given limited data.[11] At this time, neither vaccine is approved for use in children.

Another challenge facing vaccine rollout and uptake has been vaccine hesitancy. In a recent survey conducted by the Pew Research Center, only 60% of respondents said that they would get the vaccine if one were available to them. Demographic and regional variations were noted, with only 54% of women (vs 67% men), 42% Blacks (vs 61% Whites, vs 83% Asians), 55% low-income families (vs 71% high-income), and 50% Republican-leaning individuals (vs 69% Democrat-leaning) reporting acceptance of COVID-19 vaccination.[12] These differences are not unique to the United States and exist worldwide.[2] Experts currently estimate that approximately 80% of the population will need to be vaccinated to gain adequate herd immunity.[2] Hesitant attitudes toward vaccines will only hinder the development of herd immunity. Further complicating the need for urgent vaccination is ongoing mutations. Scientists are now tracking 3 more infectious variants of SARS-CoV2, B.1.1.7 (British variant), 501Y.V2 (South African variant), and P.1 (Brazil variant). Although both Pfizer and Moderna report effectiveness against new variants, both companies recently announced that they are working on a booster since antibody response may be less with some variants.[13]

It is important to note that there are 3 other vaccine candidates that are currently in late-stage phase 3 trials. Two of these vaccines, Ad26.COV2.S by Johnson & Johnson and ChAdOx1 nCoV-19 by AstraZeneca, use genetic instructions for the SARS-CoV-2 spike protein encoded in double stranded DNA to induce an immune response.[14,15] The third vaccine, NVX-Cov2373 vaccine by Novavax, utilizes a stabilized form of the coronavirus spike protein to induce an immune response. All 3 vaccines remain stable without extreme refrigeration. Interim analysis from phase 3 trials report an overall efficacy of 70.4% in a 2 dose ChAdOX1 nCov-19 vaccine,[15] 66% with the 1 dose Ad26.COV2.S vaccine[16] and 89.3% with the 2 dose NVX-Cov2373 vaccine.[17] These vaccines also note a lower efficacy with newer strains and have not reported any serious safety concerns to date.

Historically, vaccines have revolutionized the care of many communicable diseases.[6] Campaigns to vaccinate at-risk individuals have been the key. This is especially true for those living with diabetes and the influenza vaccine. There is a significant difference in the uptake of influenza vaccination in individuals with diabetes compared to age-controlled individuals without diabetes.[18] With the introduction of mRNA vaccines, we are in a unique position as endocrinologists to help combat vaccine hesitancy in our patients who are at high risk for developing COVID-19. Several studies have noted that COVID-19 has a higher incidence in patients with diabetes and obesity as well as those over the age of 65 years. For instance, a case series in New York that included 5700 patients revealed that 33.8% had diabetes. Furthermore, an increased severity of illness from COVID-19 is noted in these individuals leading to more hospitalizations, intensive care unit admissions, longer length of hospital stay, and death.[19–21] During this crisis, what can we do as endocrinologists?

All patients who are evaluated in our practice should be assessed for their willingness to take one of the COVID-19 vaccines. For patients with negative views, we should be ready to address their concerns regarding side effects and to answer questions about the rapidity of vaccine development and the use of mRNA technology. As the number of cases of COVID-19 increases in the United States, patients will likely know someone who has developed

COVID-19 or will have contracted COVID-19 themselves. It is likely that these personal connections and stories are going to have a bigger impact on vaccination decisions than statistics.[22] Consumer behavior has long been driven by a sense of community and trust. We can use a similar approach when trying to increase vaccine uptake in our patient population.[22] During the first phase of vaccine rollout, many health care workers utilized social media to post personal images of vaccination. Social media and personal connections played a big role in increasing confidence in COVID-19 vaccines among health care workers. We need to carry this forward into our practice. A wearable token that identifies health care workers as "vaccinated against COVID-19" will help boost public trust in the vaccine. Surveys of the general population have shown that intent and trust in getting vaccinated increases as people see others getting vaccinated.[22]

Endocrinologists have been in the forefront of vaccination strategies, as we led efforts to vaccinate our patients living with diabetes against infections such as influenza and pneumococcal diseases. Now, we are called upon once again to educate our diabetic as well as our nondiabetic patients on the risk-benefit of COVID-19 vaccinations. With the pandemic intensifying, our role as endocrinologists is simple – to help develop herd immunity starting with our most vulnerable patient population.

Disclosure

The authors have no multiplicity of interest to disclose.

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