REPORT TO THE BOARDS OF HEALTH

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Vaccination Updates: COVID-19 and Influenza

COVID-19 VACCINE

At the time of this writing, there were 25 candidate vaccines for SARS-CoV-2, the virus that causes COVID-19, in clinical evaluation. Of those in clinical evaluation, five vaccines were in Phase 3, one in Phase 2/3, three in Phase 2, nine in Phase 1/2, and seven in Phase 1. There are an additional 138 candidate vaccines in preclinical evaluation.

Phases are the different steps a new drug or vaccine must go through to be approved and go to market for widespread human use. Prior to Phase 1 is the preclinical evaluation when a vaccine is given to animals such as mice or monkeys to see if it causes them to have an immune response. In Phase 1 safety trials, the vaccine is given to a small number of people to see if it is safe and that it stimulates their immune system. In Phase 2 trials, the vaccine is given to hundreds or thousands of people of different ages, ethnicities, and gender to determine the best dose, schedule, and age group for the vaccine to be most effective. These trials may be done in areas where there is a high rate of the infectious disease targeted by the vaccine. Phase 1/2 trials look at both safety and effectiveness at the same time on hundreds of people. Phase 3 trials are typically designed to evaluate how effective and safe the vaccine is on a very large scale, enrolling thousands to hundreds of thousands of subjects from the target population. They are conducted in conditions as similar to the those that the vaccine will be used in future routine use. Typically, these Phases take years to complete. However, with a new pathogen like SARS-CoV-2 causing an emergency situation, allowances are made to speed up the process.

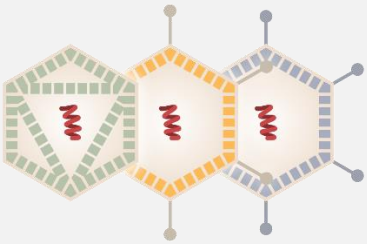
The top five most promising candidate vaccine platforms at this time include:

1. Oxford University's Jenner Institute ChAdOx1 nCoV-19 vaccine candidate, currently in Phase 3 trials in the US, UK, Brazil, and South Africa
2. Moderna, an RNA vaccine, now in Phase 3 trials
3. China's CanSino adenovirus vaccine, in Phase 2
4. China's Sinovac inactivated virus vaccine, in Phase 3
5. Novavax (recently awarded $1.6 billion from Operation Warp Speed), a protein subunit vaccine, in Phase 1/2

HOW DIFFERENT TYPES OF VACCINES WORK

Viral Vector Vaccines*

Vaccines that use a virus (adenovirus) to deliver coronavirus genes into cells and provoke an immune response.



Current day example: Ebola Vaccine (experimental/limited use)

Adenoviruses are common viruses that cause things like the common cold or stomach flu. Strains of adenoviruses that do not cause illness can be used as vectors, or carriers, of parts of other germs to create vaccines. No adenovirus vector vaccines exist yet for widespread use for other illnesses. A vaccine for Ebola has been developed using this technology for limited, small-scale use, and vaccines for HIV, Ebola, and malaria are being studied.

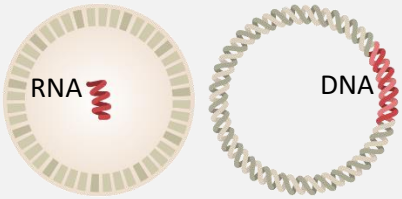
These are considered “live virus” vaccines. Some use weakened human adenoviruses; others use adenoviruses that infect animals. The risk for causing infection to humans is low but could be a concern to immunocompromised people.

Examples being studied include: Oxford University’s Jenner Institute ChAdOx1 nCoV-19 vaccine candidate (partnering with AstraZeneca), Phase 3; Johnson & Johnson, via subsidiary Janssen, Phase 1/2; CanSino Biologics/Beijing Institute of Biotechnology/ Canada's National Research Council, Phase 2.

Russia has claimed to have a fully developed and approved SARS-CoV-2 vaccine based on an adenovirus vector. However, it appears it has not gone through Phase 3 trials yet.

Genetic Vaccines

Vaccines that use one or more of the coronavirus’s own genes to provoke an immune response.



RNA Vaccine

Current day example: NONE

This is another type of vaccine that has never been made before. Particles of mRNA (messenger RNA) from SARS-CoV-2 is injected as a vaccine. This mRNA is taken up by our cells and goes to the part of the cell that makes proteins (called ribosomes). Our cells then make the target COVID-19 protein, which our body recognizes as foreign and produces an immune response. This is a quicker and easier way of creating a vaccine. Rather than mass creating the protein in a lab and injecting it as a vaccine, the instructions to create the protein is injected instead.

Examples being studied are: Moderna, now in Phase 3 trials; Imperial College, London, Phase 1/2; BioNTech/ Fosun Pharma/ Pfizer, Phase 2/3; German-based CureVac, Phase 2; California-based company Arcturus Therapeutics and Duke-NUS Medical School in Singapore, Phase 1/2.

DNA Vaccine

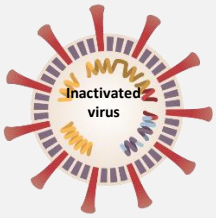
Current day example: NONE

This is a similar process to the mRNA vaccines and have also never been made before. A fragment of SARS-CoV-2 DNA that codes for the virus proteins is injected and the recipient’s cells create the protein so the immune system can mount a response.

Examples being studied are: Genexine Consortium, Phase 1/2; Indian vaccine-maker Zydus Cadila, Phase 2; Osaka University. Phase 1/2; Novio Pharmaceuticals/Beijing Advaccine Biotechnology, Phase 1/2; Zydus Cadila Healthcare Limited, Phase 1/2.

Whole-Virus Vaccines

Vaccines that use a weakened or inactivated version of the coronavirus to provoke an immune response.



Current day example: MMR

This is how many modern-day vaccines are made and have been made for decades. It is a slow process to create these vaccines as large volumes of virus need to be grown, typically in chicken eggs. They are then weakened so they do not cause illness.

Examples being studied are: Sinovac/ Instituto Butantan/ Bio Farma, in Phase 3 trial; Beijing Institute of Biological Products/ Sinopharm, Phase 3; Wuhan Institute of Biological Products/ Sinopharm, Phase 3; Institute of Medical Biology, Chinese Academy of Medical Sciences, Phase 2; Bharat Biotech/ Indian Council of Medical Research/ National Institute of Virology, Phase 1/2.

Protein-Based Vaccines

Vaccines that use a coronavirus protein or a protein fragment to provoke an immune response.

Current day example: Influenza, HPV

Many vaccines are made this way, using genes from the target viral protein (in this case SARS-CoV-2), splicing them into different viruses or organisms, then letting them mass produce the protein. The protein is then isolated out of the mix and injected as a vaccine to cause an immune response. This can also be a slow process due to the amount of time needed to grow the large amounts of viral protein that is needed. It is usually quicker than developing inactivated viral vaccine.

Examples being studied are: Novavax, Phase 1/2; Anhui Zhifei Longcom Biopharmaceutical/ Institute of Microbiology, Chinese Academy of Sciences, Phase 2; Novavax/ Emergent BioSolutions/ Praha Vaccines/Serum Institute of India, Phase 1/2.

The first FDA-approved vaccine for COVID-19 could be available late this year or early next year. Some candidate vaccines require two doses. If two doses are needed, we would need 650 million doses for the U.S., and 14 billion globally. We don't know how well the vaccine will work or how long it will last. In order to have herd immunity, we need 40% to 70% of the population to be immune. At this time, it is estimated that less than 15% of the population has been infected.

INFLUENZA VACCINE 2020-2021

It is more important than ever this year to get an influenza vaccine. Both influenza and COVID-9 can cause serious illness and have similar symptoms. Though less likely, it is possible to get ill with both viruses at the same time, which could cause more severe illness. Reducing illness and hospitalization due to influenza will help free up healthcare services needed to address the COVID-19 pandemic.

Announced August 19, annual influenza vaccine before December 31 is now required to attend all pre-schools, K-12, and post-secondary institutions in Massachusetts, though religious and medical waivers are allowed. This is the first state to make this requirement.

The composition of U.S. flu vaccines is reviewed every year and updated as needed to be the best match for the circulating viruses. For 2020-2021, trivalent (three-component) egg-based vaccines will contain:

- A/Guangdong-Maonan/SWL1536/2019 (H1N1) pdm09-like virus **(updated)**
- A/Hong Kong/2671/2019 (H3N2)-like virus **(updated)**
- B/Washington/02/2019 (B/Victoria lineage)-like virus **(updated)**

Quadrivalent (four-component) egg-based vaccines, which protect against a second lineage of B viruses, will also contain:the three recommended viruses above, plus B/Phuket/3073/2013-like (Yamagata lineage) virus.

There are two new vaccines licensed for use during the 2020-2021 flu season.

- The first is a **quadrivalent high-dose vaccine** licensed for use in adults 65 years and older. This vaccine **will replace the previously licensed trivalent high-dose vaccine**.
- The second new vaccine that will be available is a **quadrivalent adjuvanted vaccine licensed for use in adults 65 years and older.**
    - This vaccine is similar to the previously licensed trivalent vaccine containing MF59 adjuvant, but it has one additional influenza B component.

Ideally you should get you flu vaccine by the end of October, but vaccinations should continue to be offered as long as influenza cases continue to occur, and the vaccine is available. Vaccination too early in the season (e.g., July or August) may lead to dropping immunity later in the season, particularly among older adults.

How and where people get a flu vaccine may need to change some due to the COVID-19 pandemic. The goal is to encourage the flu vaccine to everyone 6 months old and above, while avoiding risks for COVID-19 transmission, such as crowded lines. Work has been ongoing to plan vaccination clinics at non-traditional sites and drive-thru models. These plans will be helpful when a vaccine for SARS-CoV-2 becomes available.

Resources

- For more information on where you can get a flu vaccine, visit www.VaccineFinder.org
- If interested in volunteering for a COVID-19 vaccination trial, go to COVID-19 Prevention Network https://www.coronaviruspreventionnetwork.org/
- To keep up to date on the status of all COVID-19 vaccine candidates, go to https://airtable.com/shrSAi6t5WFwqo3GM/tblEzPQS5fnc0FHYR/viwDBH7b6FjmIBX5x?blocks=hide *(Source: Kaur, S. P., & Gupta, V. (2020). COVID-19 Vaccine: A comprehensive status report. Virus Research, 198114.)*

Healthy Living Recommendations

1. Get an influenza vaccination as soon as they become available.
2. Get a SARS-CoV-2 vaccination as soon as a safe and effective vaccine has been approved and dosing has been recommended. Until that time, continue to rely on non-pharmaceutical interventions to prevent COVID-19. These include:
    a. Wash your hands often
    b. Avoid close contact
    c. Cover your mouth and nose with a mask when around others
    d. Cover coughs and sneezes
    e. Clean and disinfect
    f. Monitor Your Health Daily

Sources

Images from: Corum, J., Grady, D., Wee, S., Zimmer, C., 2020. Coronavirus Vaccine Tracker. The New York Times. https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.htmlSingh K, Mehta S. The clinical development process for a novel preventive vaccine: An overview. J Postgrad Med. 2016;62(1):4-11. doi:10.4103/0022-3859.173187

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