UPDATE
on the Novel Coronavirus

From **Aaron E. Glatt**, MD, Mount Sinai South Nassau

Information regarding the novel coronavirus is a rapidly changing landscape. As soon as new data surfaces, assumptions made by the scientific community shift. Armed with the most up-to-date information at press time, Aaron E. Glatt, MD, Chair of the Department of Medicine, Chief of Infectious Diseases and Hospital Epidemiologist at Mount Sinai South Nassau, answers an important question about vaccine development.

Aaron E. Glatt, MD

What progress is being made in the development of a safe and effective COVID-19 vaccine?

Dr. Glatt: *The New England Journal of Medicine* published an open-label trial of 45 healthy adults, ages 18 to 55, who received two doses of the Moderna vaccine candidate, mRNA-1273, in their arm, 28 days apart. Fifteen participants each received a "low," "medium," or "high" dose of the vaccine. After the second vaccination, serum-neutralizing activity was detected in all participants, with values generally similar to those in the upper half of control convalescent serum specimens. Adverse events occurred in more than half of the participants and included fatigue, chills, headache, myalgia, and pain at the injection site. Systemic adverse events were more common after the second vaccination, and particularly with the highest dose. These safety and immunogenicity findings support further development and advancement of this mRNA-1273 vaccine, which is partially funded by the National Institute of Allergy and Infectious Diseases, to later-stage

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clinical trials. The strong neutralization response coupled with an improved adverse effects profile makes the "medium" dose more favorable than the "high" dose. A Phase II trial of mRNA-1273 in 600 healthy adults, evaluating doses of 50 ug ("low") and 100 ug ("medium") is already underway, and a large Phase III trial of the 100 ug dose began on July 27.

A University of Oxford Phase I/II vaccine trial involving 1,077 healthy adult volunteers, testing against a meningitis vaccine in the control group, was published in *The Lancet*. This vaccine alters the genes of a common chimpanzee adenovirus (cold virus), which mimics COVID-19, and is intended to induce a COVID-19 immune response in its recipients. And indeed, their vaccine induced a powerful immune response, yet caused few serious side effects. While recipients had minor side reactions, such as fever, chills, and muscle pain, more often than those who got the control meningitis vaccine, there were no serious side effects. A Phase III test involving 30,000 participants in the U.S. began in late July, along with a similar test of the Moderna vaccine.

In the same issue of *The Lancet*, Chinese researchers published a study on their own experimental COVID-19 vaccine in approximately 500 volunteers. The researchers used a technique similar to the one the Oxford scientists used, except their vaccine is produced with a human cold virus. China's government actually gave approval for its military to use this vaccine while it continues experimental trials on it in Abu Dhabi and other locations.

Vaccines BNT162b1 and BNT162b2, manufactured by Pfizer and Biopharmaceutical New Technologies, were granted fast-track regulatory approval by the FDA. Researchers enrolled up to 30,000 subjects in a Phase 2b/3 trial in July. If the ongoing studies are successful, they claim they can manufacture up to 100 million doses by the end of 2020 and 1.2 billion doses by the close of 2021.

Health and Human Services Secretary Alex Azar reported there are currently six vaccines under contract with the U.S. government with good safety profiles and with studies documenting neutralizing antibodies at a level at or above what people recovering from COVID-19 produce in their own bodies. Very good news, indeed, with the hope that one or more of these vaccines will receive emergency use authorization from the FDA before year's end. In addition, large clinical trials of a COVID-19 vaccine are underway in China, Russia, Pakistan, and other countries.

Many people have expressed a concern that any vaccine approval will be rushed and therefore, not as safe as our vaccines usually are. To address this, FDA officials will use the regular tried and tested guidelines whether and when a vaccine can be made available. Commissioner Stephen Hahn, MD, and other senior FDA officials insisted that they would maintain "unwavering regulatory safeguards" in evaluating COVID-19 vaccines. Before any approvals are granted, they promised the agency will convene its vaccines advisory committee to review candidates while ensuring a vaccine meets traditional standards for efficacy and safety.

According to an AHRQ-funded modeling study in the *American Journal of Preventive Medicine* that simulated the spread of the COVID-19 virus in the nation, 75 percent of the U.S. population would need to get vaccinated to end the pandemic without implementation of social distancing and other measures. This does not take into account natural immunity, and obviously depends on vaccine efficacy and the long-term immunity it generated.

We at Mount Sinai South Nassau, in conjunction with Mount Sinai under the leadership of Principal Investigator Dr. Judy Aberg, are moving forward with vaccine trials. More information to follow.

To date, more than 30 candidate vaccines for COVID-19 have reached human trials. This is very positive news. As I have said on multiple occasions, it is my belief that we will return to normal, unmasked, and socially closer lives when a safe and effective vaccine is available.

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