Answering Questions about the COVID-19 Vaccine

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Q1: Don't you think it's strange that the vaccine is ready despite the fact that it has not even been one year since the outbreak of COVID-19? Doesn’t vaccine development generally take several years?

A: This is the result of a concentrated investment of funds and the latest technology. No corners were cut.

① Following outbreaks of emerging diseases such as SARS (severe acute respiratory syndrome) and MERS (Middle East acute respiratory syndrome), scientists have been preparing prototypes of new vaccines, such as mRNA vaccines and adenovirus vector vaccines, in preparation for a new global epidemic. After an infectious disease occurred in China and the gene sequence of the virus causing the COVID-19 disease was revealed, researchers quickly used this information to develop a vaccine. The mRNA vaccine against the COVID-19 (Pfizer Biontec, Inc., and the Allergy and Infectious Diseases Research Institute Moderna, Inc.) and the vaccine using the adenovirus vector (AstraZeneca K.K., Oxford University) are based on these basic researches.

② A large amount of money was invested in a short period of time, and the phase I and II studies from animal testing were completed in a short period of time. From late July to August to the end of October 2020, approximately 30,000 volunteers (Moderna, Inc.) and 45,000 volunteers (Pfizer Biontec) participated in the Phase III study, completing 2 vaccinations by the end of November. Of these, 4.6% and 4.3% were Asians, respectively, and the differences in efficacy and side effects among race, age, and sex are being studied.

③ Due in part to the increased prevalence of COVID-19 in Europe and the U.S., scientists were able to determine the efficacy of the vaccine in preventing COVID-19 infection and preventing severe cases, which was the target of the Phase III trials, by December. The results of the animal experiments and the Phase I/II and Phase III trials of these vaccines have been reported in peer-reviewed scientific and medical journals, and are available for anyone to read.

④ Based on this scientific knowledge, the WHO and regulatory authorities in the UK, the U.S., and Europe approved the emergency use of mRNA vaccines last December.

Q2. What is an mRNA vaccine?

A: Messenger RNA (mRNA) is a type of genetic molecule strand that carries the sequence

information of proteins produced in the cell. The new mRNA vaccine is a human-made version of mRNA that contains the genetic sequence information of the spike protein, which is the structure used as a “hook” for the new coronavirus to enter human cells. The mRNA vaccine is designed to produce a large amount of spike protein from the new coronavirus once it has been introduced into the muscle cells. The spike protein produced in this way is recognized as a foreign substance by T cells and B cells, and induces an immune response. As a result, various antibodies, including neutralizing antibodies that prevent infection and eliminate viruses (humoral immunity), and antigen-specific helper T cells and killer T cells (cellular immunity) are produced.

mRNA is fragile and sensitive to its environment, thus after entering human cells, it degrades after temporarily synthesizing its instructed protein. This means that the genetic material from the mRNA vaccine does not remain in the human body.

Q3. How effective is the mRNA vaccine?

A: The results of Phase III trials of Pfizer-BioNTech and Moderna's mRNA vaccine were published in a leading medical journal in December last year. The former was 95% effective in preventing infection, while the latter was 94.1% effective in preventing infection. According to the data from Pfizer-BioNtech, infection prevention was observed from around 12 days after the first dose of the vaccine. Although a small number of cases occurred among the patients who received the vaccine, the vaccination did not cause serious illness and all serious cases among the participants in the Phase III study were among those who received the placebo. No differences in adverse effects or efficacy have been observed among different races.

Q4. If I get the mRNA vaccine, will it make me less likely to infect other people as well as make me less susceptible to the effects of COVID-19?

A: After the first vaccination, it takes about two weeks for an immune response to develop. Until then, there is a possibility of transmitting the virus to others if infected with COVID-19. In addition, even after vaccination, there is a certain percentage of people who have a low immune response due to their physical constitution (genetic factors). These people are at risk of contracting and spreading the virus when infected. Please do not think that vaccination is a perfect solution, but continue to take basic measures to protect yourself from infection such as washing your hands, wearing a mask, and avoiding crowded places.

Q5. What are the risks of mRNA vaccines?

A: Allow me to explain the initial adverse reactions that have been reported in Phase III studies and at the time of vaccination of about 1.9 million people in the U.S. There are two types of adverse reactions: injection site adverse reactions and nevovoviral adverse reactions. Injection site side-effects include pain (around 70%), redness and swelling (less than 10%). The side effects are more severe after the second injection. These symptoms subside within a few days after injection. General adverse reactions include fever, malaise, muscle pain, joint pain, etc., and are noted in 50% to 70% of patients after the second injection. These symptoms also subside within a few days after the injection. However, if these symptoms are troublesome to the patient, it is possible to use analgesic and antipyretic drugs. These reactions are caused by the immune response to the vaccine, and there is no need to be concerned.

The medium-term side effects suspected to be caused by vaccination are considered to be the same as those of other vaccines.

According to statistics from the Centers for Disease Control and Prevention (CDC), the vaccinations in the U.S. started on December 14, 2020, and by December 23, 2020, approximately 1.9 million people had received the first round of the Pfizer-BioNTech mRNA vaccine. Among them, 21 cases of anaphylaxis, a serious allergic reaction, have been observed. The frequency of anaphylaxis is 11 cases per million, which is about 10 times higher than that of ordinary vaccines. It seems to be more common in people with a history of anaphylaxis, but it also occurs in people without such a history. The onset of symptoms typically occurs 15 to 30 minutes after vaccination and can be treated without sequelae via epinephrine injection (or EpiPen® self-injection).

Q6. I have various allergies. Can I get an mRNA vaccine?

A: Patients who experience allergic reactions to mRNA vaccines are suspected to be allergic to polyethylene glycol 2000 (PEG2000), a component of the nanoparticles used to protect the mRNA and facilitate its uptake by cells. People who are allergic to polysorbate, which has a similar antigenic structure to PEG2000, are also considered to be at high risk. The CDC has defined contraindications and cautions for mRNA vaccination as follows

Contraindications: 1) Those who experienced anaphylaxis after the first mRNA vaccination, 2) Those who experienced early onset of symptoms such as urticaria or asthma after the first mRNA vaccination, 3) Those who have a history of allergy to PEG or polysorbate with a similar antigenic structure.

Caution Required: those who have experienced anaphylaxis from other vaccines, consult your doctor.
Acceptable: those with a history of allergies to food, oropharyngeal drugs, pollen, bees, latex, etc.

Q7. How long will the effect of the mRNA vaccine last?

A: In a follow-up study of patients who were infected with COVID-19 and cured, their IgG antibodies gradually decreased but remained sufficient even after six months. The concentration of IgG neutralizing antibodies in the blood is higher in mRNA vaccine recipients than in COVID-19 infected and cured patients, and even after three months of observation, the decrease is still minimal.
Vaccination produces immune cells such as memory B cells and memory T cells that can survive for a long time (acquired immunity). Even if IgG antibodies decrease after a certain period of time and the patient is reinfected, the secondary immune response will start up quickly and IgG antibodies will be produced from the beginning of the infection, thus preventing severe disease.

Q8. There is a rumor that the current vaccine will not work in the future because COVID-19 has demonstrated an ability to mutate.

COVID-19 is a member of the RNA family of viruses, and it is known to mutate frequently. On the other hand, in terms of the characteristics of the immune response, researchers do not believe that the vaccine will become 100% ineffective. In fact, the antibodies in the serum of those who have been inoculated with the mRNA vaccine will not only contain the virus types isolated in Wuhan, but also those isolated in the UK.

This is a bit technical, but I will explain. For simplicity, we will use the antigenic structure (epitope) on the Wuhan-type spike protein. The antigenic structure (epitope) on the Wuhan type spike protein is epitope A, and the antigenic structure in the mutated UK strain of the virus is epitope B. When a person is vaccinated with the Wuhan strain, he or she expresses an antigen receptor (membrane immunoglobulin) that binds to epitope A. When vaccinated with the Wuhan type vaccine, a variety of B cells expressing the antigen receptor (membrane immunoglobulin) that binds to epitope A begin to proliferate selectively. When they mature, they secrete immunoglobulin as antibodies. Some of them express not only epitope A but also cross-reactivity. Some of these antibodies can bind weakly to epitope B by cross-reacting with epitope A, while others bind strongly to epitope B. Some antibodies bind weakly to epitope A, while others bind

strongly to epitope B.

In addition, the epitope to which B cells bind and the sequence on the spike protein to which helper T cells bind are different. Even if the virus mutates, if the sequence to which the helper T cells bind remains unchanged, a new epitope will be generated. Even if the virus mutates, if the sequence to which the helper T cells bind remains unchanged, the B cells that can bind the new epitope C will be selectively stimulated by the helper T cells. B cells that can bind to the new epitope C will be selectively stimulated by helper T cells, and antibodies with high binding power to epitope C will be quickly produced. Thus, as the virus mutates, the immune system adapts and produces new antibodies, as long as the mutation is not extreme in antigenic structure. In this way, as long as the mutation is not an extreme mutation of the antigenic structure, the immune system will adapt and become immune to the virus with the new epitope.

Q9. Can I get an mRNA vaccine while pregnant or breastfeeding?

The Pfizer and Moderna Phase 3 studies did not include pregnant or lactating women. There is a lack of data on the safety of pregnant and lactating women after vaccination. In the U.S., pregnant and lactating women are offered the opportunity to be vaccinated, but the vaccination is voluntary. In the U.K., vaccination is recommended for pregnant women who work in an occupation where there is a high risk of infection with the new coronavirus, or who have a chronic illness where there is a high risk of serious illness if infected. Nursing mothers with or without occupational or medical concerns can be vaccinated with the mRNA vaccine; pregnancy after mRNA vaccination is not a problem as the vaccine does not contain the virus.