

January 11, 2021

MMS RESPONSE TO COVID19-VACCINE:

Patients with mitochondrial disease and families have many questions about the new COVID-19 vaccine(s), including whether to take it? Whether they should be prioritized? And its potential risks and benefits.

Although we know we are continuing to learn more about COVID-19, there is still much uncertainty about risks of COVID-19 infection in people with mitochondrial disease. At this time, there are still few reported children and adults with mitochondrial disease who have had COVID-19 infection based on worldwide registries. While some of the few reported to have had COVID-19 may have had significant problems, we do not have any evidence to believe or suspect that the frequency of poor outcome following COVID-19 infection is out of proportion to that in the general population.

The Food and Drug Administration (FDA) has now cleared two vaccines designed to lessen the risk of acquiring COVID-19: the [BioNTech/Pfizer](#) and the [Moderna](#) COVID-19 vaccinations for emergency use. Both are [mRNA vaccines](#), a new type of vaccine to protect against infectious diseases. So far, European Medicines Agency (EMA) has approved the BioNTech/Pfizer and Moderna vaccines. This authorization follows a positive scientific [recommendation](#) based on a thorough assessment of the safety, effectiveness and quality of the vaccine by the European Medicines Agency and is endorsed by the Member States. The UK has also approved the [Oxford/AstraZeneca](#) vaccine which is an adenovirus vaccine.

In Phase 3 trials, the BioNTech/Pfizer vaccine showed a 95% efficacy rate, 7 days after the second dose was given in people 16 years and older (94% effective in adults >65 years old). The Moderna vaccine showed a 94% efficacy rate, 14 days after the second dose is received, in people 18 years and older. These results were consistent across gender, age, race and ethnicity. The Oxford/AstraZeneca vaccine given to people 18 years and older, showed an efficacy of 70.4% after 2 standard doses of the vaccine given 28 days apart.

At this time, vaccine availability is limited but it is hoped supplies will increase so that most of the global population can be vaccinated. The distribution of the vaccine in the US is being driven by [recommendations](#) put forth by the Centers for Disease Control and Prevention Advisory Committee on Immunization Practices, with slight local changes put forth by individual states. The overall strategy is to offer the vaccines to health care professionals and residents in long-term care facilities in the first phase of vaccination. This will then be extended to people at risk and in later stages, to the rest of the population. The European Commission planned a [centralized EU approach](#) to secure equitable access to the vaccine across EU. Under its [vaccines strategy](#), the Commission forged agreements with individual vaccine producers on behalf of EU countries. Once available, proven safe and effective, and authorized at EU level, all Member States will have access to COVID-19 vaccines at the same time and the distribution will be done on a per capita basis to ensure fair access.

It is very important to remember that even with vaccines becoming available in the US and elsewhere, the best measures to prevent COVID-19 spread remain the current infection control procedures - Keep wearing your mask, wash your hands, avoid large

gatherings, and remember social distancing and washing your hands. The vaccine is just another way of fighting the pandemic and **DOES NOT** replace these important safety measures. At this time it is not certain whether those vaccinated and immune to getting COVID-19 themselves can be vectors of COVID-19, meaning they may be able to spread the disease without acquiring it themselves.

How is the COVID-19 vaccine administered?

The COVID-19 vaccines are intramuscular (IM) injections. A second booster is necessary 3 weeks (BioNTech/Pfizer) and 4 weeks (Moderna, Oxford/AstraZeneca) after the initial injection. In some countries such as the UK, the second booster is being administered later than the 4 weeks per government recommendations to allow more people to get the first injection.

Are the COVID-19 vaccines recommended for mitochondrial disease patients?

Clinical trials have not been conducted in patients with rare diseases or children. Although knowledge concerning all the potential vaccine effects in mitochondrial disease is currently unknown, the safety profile of the vaccine so far suggests that the benefit of preventing COVID-19 infection outweighs the risk of vaccine reaction. We do expect patients with mitochondrial disease to have a similar response to the vaccine as the general population.

Are there any specific precautions that I need to take if I, or my child have a mitochondrial disease?

You should always discuss your health care with your doctor or nurse specialist. Patients who have immune deficiencies or other serious complications from their mitochondrial disease could be at risk of worsening of their mitochondrial disease symptoms if the side effects produce fever, loss of appetite, inability to hydrate, diarrhea or vomiting. The safety profile of the vaccines so far suggests that the benefit of preventing COVID-19 infection outweighs the risk of vaccine reactions. The knowledge of prior reactions and experiences with other vaccines such as the flu vaccine can be a helpful guide for making a plan if such side effects occur.

COVID-19 vaccines have not yet been approved for children. The youngest age tested in clinical trials has been 16 years old. Moderna has already started clinical trials in children aged 12- to 17-years-old. At present, only children at very high risk should be considered for vaccination.

If you or your child are immunosuppressed, immunocompromised or have received an organ transplant, please discuss the suitability of the vaccine with your health care team.

Can I get COVID-19 from a vaccine? Can I transmit it to other people?

No. The vaccines do not contain the full live SARS-CoV-2 virus and cannot cause COVID-19 infection. The BioNTech/Pfizer and Moderna vaccines contain non-infectious genetic material (mRNA) that is quickly destroyed by the body.

It typically takes a few weeks for the body to build immunity after vaccination. It is therefore possible that a person could become infected with COVID-19 just before or just after vaccination and become unwell. This is because the vaccine has not had enough time to provide protection. If this happens, please call your health care providers to discuss your management.

You also cannot pass COVID-19 to your family if you get vaccinated. If you become ill with COVID-19 in the days or first few weeks after vaccination and before the vaccine has time to become effective, then you could still transmit virus to your family or others you are in contact with. At this time, we still don't know if the vaccine prevents transmission, and therefore, you

should continue to practice the same precautions as you are now to prevent transmitting COVID-19 to family members who are not part of your immediate household.

What are the side effects from the vaccine?

The most common reported symptoms from the vaccine have been local reactions at the site of vaccination (pain, soreness), similar to the flu vaccine. Some systemic effects such as fatigue, headache, muscle pain, joint pain and chills have also been observed in some people and are generally of short duration (a few hours to a few days).

There are differences between injection reactions which can be mild to severe and mimic the COVID-19 infection and allergic reactions that may rarely be life threatening.

Allergic reactions to vaccines are very rare (about 1 in 1 million people will have an allergic reaction to a vaccine). Some reactions are mild (hives) but others can be severe (anaphylaxis). Allergic reaction symptoms start very quickly after the injection (within minutes to 4 hours of vaccination) and typically include diffuse skin hives; body part swelling (mouth, lips, tongue or throat); breathing difficulties (shortness of breath, wheezing, chest tightness); or low blood pressure or loss of consciousness. About half of allergic reactions to vaccines happen in the first 15 minutes after receiving the vaccination. For this reason, vaccines need to be administered in a controlled medical setting and the patient should be observed for at least 15 minutes after the injection to detect any possible allergic reaction needing urgent treatment.

These are the symptoms that may develop after the vaccination:

Injection reactions occurring within 3 days of the vaccination, counting the day of vaccination as day 1. These can last several days and although uncomfortable there is **no risk** of an allergic reaction with the next vaccination.

- 1) Local injection site reaction is quite common and expected to occur in 8 of 10 people. (i.e., redness, soreness or swelling at the injection site)
- 2) Mild post vaccination reaction, which is also common and including: feeling feverish with temperature less than 100°F/37.8°C, mild headache, new or worsening fatigue, mild muscle aches, and mild joint pains.
- 3) Moderate or severe symptoms are uncommon, including fever of 100°F/37.8°C or greater, moderate/severe headache, moderate/severe fatigue, moderate/severe muscle aches, moderate/severe joint pains. These can be associated with any of the following new or progressive symptoms consistent with COVID-19 such as sore throat, new cough, new nasal congestion, new runny nose, new loss of smell or taste or shortness of breath

Allergic reactions occurring within minutes to hours of the vaccination.

Different ingredients in vaccines, including gelatin, egg, and excipients (inactive ingredients such as polyethylene glycol (PEG) and polysorbates) can cause an allergic reaction. PEG is a water-soluble ingredient used in a variety of commercial products, medications and vaccines (> 1000 FDA approved medications). It is found in commonly used colonoscopy preparations (Golytely) or constipation treatment (Miralax), IV PEGylated medications, ultrasound gel and injectable steroid injections such as methylprednisolone acetate. Reactions to PEG are exceedingly rare but anaphylaxis has been reported.

Both the [BioNTech/Pfizer](#) and [Moderna](#) COVID vaccine contain PEG but do not contain gelatin, egg, or latex.

1) Mild allergic symptoms (i.e., itching, rash but NOT hives) are uncommon and occur after the initial observation period of 15 minutes post vaccine injection.

2) More severe allergic reactions are very rare and include hives, swollen lips, tongue, eyes, or face, wheezing, chest tightness, or shortness of breath. If you develop any of these symptoms, please call your national emergency telephone number or go to the nearest Emergency Department immediately.

If I had vaccine reactions in the past (with non-COVID-19 vaccines), are there any precautions I should take?

Some patients with mitochondrial disease may have developed high fevers and other symptoms with their routine vaccination. Before you receive your COVID-19 vaccine, you should discuss this with your treating health care provider to evaluate if certain precautions like taking acetaminophen (paracetamol) prior to the vaccine and up to 24 hours afterwards might be appropriate for you. Other interventions, if you develop vaccine reactions as described above, might be to make sure that supportive care is available for you and your child including appropriate hydration and caloric intake.

What if I have a history of severe allergy to a vaccine?

No serious allergic reactions to the vaccine were reported in the clinical trials and very few have been reported in the US and UK since the beginning of the vaccination campaign in December 2020. Anaphylaxis which is a severe allergic reaction that involves multiple body systems was observed in a few people who had a history of food or medication allergy. The United Kingdom Commission on Human Medicines (CHM) decided to pause vaccination of any person with a history of anaphylaxis to a vaccine, medicine, or food.

The United States Food and Drug Administration (FDA) and Health Canada (the Canadian version of the US FDA) recommend that only people with a history of **severe** allergic reaction to the vaccine or the ingredients in the vaccine should not be vaccinated. They do not recommend that people with food allergy or medication allergy should avoid receiving the vaccine.

The CDC also recommends that persons who have had a severe allergic reaction to any vaccine or injectable therapy (intramuscular, intravenous, or subcutaneous) discuss the risk of receiving the vaccine with their doctors and be monitored for 30 minutes afterward. This is because some of these injectable medications do contain PEG.

Are patients with mitochondrial disease considered “at risk patients” and can they get the vaccine in the first wave?

Immune deficiency is not a common feature of mitochondrial disease, and therefore most people with mitochondrial disease should not be at increased risk of contracting COVID-19 infection. However, those people who have immune deficiency because of or in addition to mitochondrial disease are, like anyone with immune deficiency, at increased risk of infection.

Patients with mitochondrial disease are not considered to be at high risk for a severe course of COVID-19 infection unless they have comorbidities that puts them at risk such as heart disease, diabetes, severe myopathy with respiratory involvement, or severe metabolic decompensation

with minimal stress. If you (or your child) have any of these comorbidities, please discuss the possibility of obtaining a COVID-19 vaccine as part of the earlier, high risk patients' group with your health care providers.

If I have had COVID-19, do I still need the vaccine?

Yes, even if you have had COVID-19 infection and developed symptoms from it, you should still be vaccinated.

How long will immunity last after I get vaccinated? Will I need to be vaccinated every year?

This information is still being investigated. At this time, we do not know how long the immunity conferred by the vaccine will last. We will have to wait for long-term data to become available to guide future vaccine protocols.

If I feel unwell or have side effects after getting the first dose, should I get the second dose?

If you have had mild side effects from the vaccine, these should resolve within a day or so and you should get your second dose as prescribed. If you have developed more severe side effects, you should be evaluated by your treating physicians to see if there are any contraindications to a second dose.

What happens if I only receive one dose of the vaccine and not both?

It is recommended to receive both doses of the vaccine to achieve maximum effectiveness. If you only receive one vaccine dose, the effectiveness may be reduced, and immunity to COVID-19 may not be guaranteed.

If I am unwell (sniffles, achy, cold symptoms...), should I still get the vaccine, or do I need to reschedule?

If you have any symptoms, you should stay home and contact your health care providers as you would normally do. Your vaccine will need to be rescheduled.

If I am exposed to COVID-19 infection between doses, what should I do?

There are no changes to definitions of exposure for vaccinated individuals. Exposure Investigations and Contact Tracing Policy following your state and public health guidelines will have to be followed regardless of vaccination status.

Could receiving the vaccine cause a false positive COVID-19 test?

No. The vaccine will not cause the standard COVID-19 tests (nasal swabs) to yield a false-positive response.

Is the vaccination safe for pregnant or breastfeeding women?

There is not enough data currently to answer this question because clinical trials for COVID-19 vaccines have excluded pregnant women. In general, vaccines that do not contain live virus such as the COVID-19 vaccine, are considered safe and a routine part of prenatal care. There is no clear safety data for pregnant patients at this time. Pregnant individuals will need to weigh their own risk for potential exposure to the virus, risk of severe illness from COVID-19 and the lack of available information about the vaccine. These decisions should be individualized and discussed with obstetric care providers.

Breastfeeding should not be considered a contraindication to receive the COVID-19 vaccine; as little mRNA from the maternal vaccine should make it into the breast milk and will likely be quickly inactivated in the baby's digestive tract.

Will the vaccine affect my chance of getting pregnant in the future?

Vaccination is not believed to impact fertility or future offspring.

Will there be other vaccines for COVID-19?

Additional COVID-19 vaccines are being developed worldwide. Some will be very similar to the commonly used vaccine for the seasonal flu and some will be different. Each vaccine will have to be individually reviewed to better understand the safety profile and efficacy.

Information and recommendations will evolve as more data are collected. Please obtain your information from scientific, trustworthy sources, such as those provided below.

Please see the newest COVID-19 updates here:

- 1) UMDF website: <https://www.umdff.org/coronavirus/>
- 2) MitoAction website: <https://www.mitoaction.org/coronavirus/>.
- 3) GOV.UK website: <https://www.gov.uk/coronavirus>
- 4) NHS Rare Mitochondrial Disorders website:
<https://mitochondrialdisease.nhs.uk/coronavirus/coronavirus-and-mitochondrial-disease/>
- 5) MITOCON website www.mitocon.it
- 6) ASMRM website: <http://asmrm.org/index.php>
- 7) CDC website: www.cdc.gov/coronavirus
<https://www.cdc.gov/coronavirus/2019-ncov/community/schools-childcare/checklist.html>
- 8) <https://www.ema.europa.eu/en/human-regulatory/overview/public-health-threats/coronavirus-disease-covid-19/treatments-vaccines-covid-19#authorised-medicines-section>
- 9) <https://ern-euro-nmd.eu>

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