



## MAYO and TGen Q&A - Transcript

The question is, and it's a two part question. Most vaccines take much longer for approval. Do these current COVID vaccines have enough data to determine whether they are safe or not?

And the second part is if you can, please explain the history behind the mRNA technology that has gone over decades and really we will save that. See that same mRNA technology help treat a laundry list of cancers. In the very near future.

So in a nutshell, Dr. Ohrenstein, if you can touch on the overall safety of the vaccines and the history of the mRNA technology.

Well, thank you for inviting me to speak about this and also maybe to clear up some misconceptions.

So the mRNA vaccines that we're currently using really have evolved out of a platform that was developed many years ago in anticipation of trying to find new vaccines. So these platforms have existed for things like Ebola vaccine, Zika vaccine, Chikungunya vaccine, all of which really didn't have the need or the demand until we ran into COVID-19 where there was an immediate demand for us to develop a rapid vaccination that could be tested quickly and determined to be there, safe and/or effective.

So the platforms existed because of this technology, it's relatively simple to choose a target. And use the messenger RNA to deliver that particular target, and so you can develop vaccines quite rapidly. The challenge in vaccines is mostly been delivering those into clinical trials. Getting enough participants in the clinical trials to show that the vaccine are safe and/or effective, and we were fortunate that we were again in the middle of a large epidemic worldwide, so that the companies that had made these vaccines were able to take them from the laboratory and start clinical trials rapidly and roll a large number of patients and determine whether they were safe and effective.

So those initial trials run by Pfizer and Moderna each involved about 40,000 patients, 20,000 or so receiving a placebo, the other 20,000 receiving the vaccines, and from those studies we learned about the effectiveness. Of the vaccines and their safety. Now that's only 80,000 people or so, but we have now seen this vaccine, or this group of vaccines used in over a billion people worldwide, probably more than any other vaccine in the history of mankind.

And so we know a lot about the safety of the vaccines. We know a lot about their effectiveness, both in the short term now and in the long term. As far as vaccines are concerned, typically vaccine safety is usually established, excuse me, within the first couple months. Because that's the period of time when most of the complications related to these vaccines have arisen, and so from both the studies and the follow up of people who've been vaccinated throughout the world, you know, we understand what the side effects of these vaccines are and what the risks are, and many of the concerns that people have had or read about are really not those concerns.

Does the COVID vaccine cause the patient to fall ill from COVID-19?

I think this is a question that we frequently get - one of the most frequently asked questions.

A couple of things. One, these COVID vaccines do not cause COVID. They're not live vaccines. We've talked. We've heard from Doctor Ornstein on the mechanism of the mRNA and how it works within the system.

That said, all vaccines can cause some form of immune response and that's what we're looking for and this immune response can elicit itself in ways of mild symptoms. These symptoms are not necessarily considered life threatening, or some people may have no symptoms at all. The most common effects that we see are feeling tired, headache, low grade fever, pain at the injection site, and muscle or joint pains. I think a lot of us can say that's what it sort of feels like when we have a flu, like symptoms, right? These symptoms generally happen the day after vaccination and resolve within 24 hours.

Can you spread COVID after receiving the vaccine?

Yeah, the short answer to that is yes. Depending upon how much virus you're infected with after you've been vaccinated, so many of you might have heard this concern right when CDC released a bunch of information about an outbreak in Provincetown, MA.

The problem there is that these individuals were very close to each other. There's a lot of hugging and close contact, and so it's possible in those situations to transmit the virus if you're infected.

The vaccines are predominantly developed to prevent disease, so they are to prevent you from getting sick, hospitalized, and dying. They're not really designed. In fact, we were all excited with the efficacy when they first came out because it was so high, but they're really not designed to prevent infection.

They're designed to prevent disease, and so if you think about how your immune system works, if you're exposed to somebody who has a lot of viral particles you get exposed to those your immune system has to wake up and recognize those, and that may take a little bit of time before you can do that, because the vaccines that we give stimulate immunity within the bloodstream but not necessarily within our nose within our mouth. And so it takes a little while for those parts of our immune system to wake up recognize they're seeing the virus again and clear it.

So yes. You potentially can get infected if you've been vaccinated, but the risk is much, much less than if you run vaccinated.

This has been a popular question among our tire techs and store employees and simply put, does the mRNA vaccine platform change your DNA?

No, so you know.

One of the challenges is if you haven't been through biochemistry, makes it a little bit difficult to understand the mechanism by which some of these agents work, but essentially mRNA is a messenger and that messenger is carrying a message to the host cell to produce something. Usually that's a protein.

In the case of these vaccines, we know that the way the virus binds to human cells is through, it's called the spike protein. So what the chemists have done is they've engineered the spike protein signal to this messenger RNA that then gets delivered into your muscle and then your body recognizes that picks up the signal and allows you to recognize the protein.

But the messenger RNA actually degrades quite quickly, usually within days of the time that it's injected, and so there's no opportunity for that messenger RNA to get transcribed and become part of the host DNA that is not been seen in either humans or an animal models with these types of vaccines. So though there's obviously concern about that, that has not been seen.

Last question for now is, in your opinion, what COVID vaccine is most effective and safe?

A great question, and another one that we frequently get.

I think the best vaccine is the vaccine that you have offered, available and in your arm. They'll all protect you from the most serious effects of COVID-19.

None of them have been directly compared side by side to see which is better. There is some new information suggesting that perhaps the Pfizer and Moderna vaccines may provide a bit better booster response than the Johnson and Johnson.

Next question is, I think this is an important question.

Knowing our internal data and the fact that our hospitalizations, our intubations, patients experiencing chronic symptoms after their initial COVID infection really becoming a long hauler.

Looking at that, all of these patients internally have been unvaccinated, so the question is, if I had COVID in the past. Why do I need the vaccine or the booster? Because I should have some type of natural antibodies that would protect or help me fight against another COVID infection, so it simply put, if I had COVID in the past, why do I need the vaccine and booster if I already have antibodies?

Yeah, that's also a good question, and we know that coronaviruses don't often produce long term immunity and what we know now, having been through several years now of the pandemic, those individuals that got the coronavirus infection do have immunity, but that immunity is boosted significantly by getting the vaccine.

So the best thing you can do is to get the vaccine after you've had the infection. The second best thing is if you ended up getting the infection after you were vaccinated, you'll have immunity that way and the third way is to get the vaccine and get the booster if you need it, because that will also give you additional immunity.

I guess I would look at it like a tire, right? So you get a puncture wound in your tire. You know the tires running, but it's not quite flat. So what do you do? You patch it. And you know you get the patch in there and the tire runs a little bit better and maybe you get a long term solution out of that. So it's an improvement upon, you know what naturally occurred.

Many people think because they had natural immunity that they have more antibodies and they're better protected and that has not been shown to be the case. What is the cases if you get that infection and then you get the booster of the vaccine, you're much better protected than if you just go based on your original infection.

Next question, Mr. Boetcher is who should not get the COVID vaccine.

Yeah, and so this is really an extremely short list right now. It's children who are too young to be eligible at this time. I think. Good news here as we expect that the FDA will be approving shortly for younger children by the end of the year.

We hope to be able to offer vaccines to them people who are allergic to any component of the vaccine, like propylene or polyethylene glycol or Polysorbate. And then people who had a severe reaction or anaphylaxis to their first shot. These folks did not get the subsequent dose, and this, however, is very rare.

Some people have concerns about allergic reactions with other vaccines, and if they should get the COVID vaccination as well. This is not a reason not to get the COVID vaccination. If there is any anxiety surrounding this, I would suggest talking with your doctor and really talking about becoming vaccinated and maybe a more medically supervised environment than one of the pop up tents.

Our allergists here at Mayo Clinic have successfully been working with many patients who have had these concerns and have been able to help them be able to get the vaccine without problems.

I know our Discount Tire population would absolutely appreciate an answer from you on this question. So what exactly is the breakdown of effectiveness of the vaccine overtime and how long does immunity antibodies last after receiving the vaccine?

Yeah, and this is another great question, I think to a doctor.

Ornstein used the tire analogy earlier and maybe that applies here a little bit. Right tire should get 70,000 mile warranty right? Well you're probably not going to quite get 70,000 depending on how you drive the car you may get 50 to 70,000.

So the answer here is that it really varies from person to person. We're all unique. Our bodies responses are unique as well. The vaccine protection as we know it today appears to wane at 6 to eight months after initial vaccination and earlier in certain patient populations, the way these vaccines work.

I think Dr. Ornstein did a great job of describing that, but it's by injecting these antigens and again it's not the virus itself, it's an antigen that's recognizable into the body. The immune system can safely learn to recognize them as hostile invaders, provide antibodies, and remember them for the future.

Our bodies are all individual and they remember some remember better than others. And really keep in mind that those that are older than 65, those that are on certain medications or with certain health conditions that weaken the immune system may see their protection wane a little bit sooner, and that's why we saw the recommendation or the additional third shot with our immune suppressed population and why the CDC has recommended booster shots for some of these other groups earlier than others.

If I have already had COVID and suffering from long term side effects, chronic symptoms after my initial COVID infection, months after my initial COVID infection, will the vaccine help improve these overall symptoms? There's a lot of studies out there, there's a lot of long hauler facilities that are using the vaccine to reverse a lot of these symptoms. Do you have any feedback on that?

Yeah, I think that's a question that we don't know the answer to.

There have been some anecdotal reports that individuals with symptoms of prolonged COVID infection have gone on to develop improvement when they've been vaccinated, but we don't really have the answer to that.

You know, my feeling is that, again, if you had the illness, then you should get the vaccine to protect you from developing another infection with COVID-19. Certainly we know when you get COVID-19, not only can you get you know a mild respiratory illness, but you can develop a severe respiratory illness and you can develop these long term side effects and so even if you've had it before, you're potentially at risk of getting the illness again, and therefore the vaccine makes sense from that perspective, even if it doesn't prevent some of these complications called long COVID.

For those Discount Tire employees that remain hesitant on receiving the vaccine, a large majority of these people fear the same thing. And the question is, what are some of the long term effects from receiving the vaccine that use the mRNA platform?

Yeah, I guess the question really is what are the long term effects versus the long term adverse effects.

The long term effects are protection against this virus and reduction in hospitalizations and reductions in death. That's really so far the long term effect of the vaccine.

The long term adverse effects are unknown, but I must say that if you look at all vaccine technology, most of the adverse events occur within a two month window, and so once you get beyond several months and now for these we're, you know, beyond a year, it looks like these are very safe and do not have any sort of long term adverse effects.

You know, most of the effects were picking up in the first eight weeks or so. You've heard of things like myocarditis, Guillain barre, and these are very rare side effects, but they almost always occur early, not years after the vaccine and as we talked about earlier, these do not change your DNA, so there's not going to be a risk of genetic abnormalities or increases in cancers because of that. Because this does not get into your DNA.

So why does the mRNA vaccine change a woman's menstrual cycle for a short period of time and the second part of that is, does the COVID vaccine cause infertility in women?

Yeah, also a very good question to which we don't yet know the answer.

We know that some vaccines have been associated with alterations in women's menstrual cycles. Good example is vaccine that's been used for many years now for human papilloma virus. We know that that sometimes alters cycles

We think the reason for that is that the immune system wakes up and some of these immune cells travel to the uterus and they may interfere with the cycle. Usually it's for a very short period of time and then the cycle returns to normal.

What we do know is that has no effect on fertility, and in fact we could go at one of the OB GYN meetings. There were three abstracts looking at different populations of women undergoing in vitro fertilization to see in a group of people. We were vaccinated versus unvaccinated. Whether there was any effect on fertility and those three studies all showed no effect on fertility of women who were vaccinated.

One of the questions that also popular is: Will having the vaccine give me some level of immunity to the different strains that are coming our way, post Delta variant, after the delta bearing.

Yeah again, great question. We don't know the answer to that, but what we do know is that the vaccines we currently use were really designed for the original strain of COVID-19, and there's been emergence of a variety of strains, not just delta, but the beta strains, the alpha strains, and these vaccines still work against those. They are less effective, but they still work, so the anticipation is that as new strains emerge, depending upon what the target of those strains are, how have they changed, and how does the binding of antibodies affect the ability of that virus to infect, you will determine whether the older vaccines still retain affect.

It's anticipated and one of the advantages of the mRNA technology is that you can adapt these platforms to the development. Of new vaccines as new strains emerge. So if we identify a strain that's becoming predominant and we see that the current vaccines were using are less effective, we have the ability fairly rapidly to develop new vaccines that are targeted against that. Many people have asked why don't we do that now with Delta, and the reason for that is primarily that the current vaccines still work quite effectively at preventing significant illness. Even from Delta currently, even though it's not as good as it was against the other strains.

If you are fully vaccinated with one of the mRNA vaccines, can you receive a booster from a different manufacturer? So if you originally vaccinated with Pfizer? Would that population be able to receive the Moderna booster?

So you're right, there was new information that just came out from the FDA and CDC this week that has suggested that is acceptable to mix and match these vaccines. This means it's OK to get a booster that is a different brand from your first shots.

Really, we still recommend that you get the same shot that you received before. That's probably, that's still a good choice today, but again, if you're in a situation where those other vaccines aren't available or the vaccine that you originally had your initial shot with is not available, you could safely get one of the other vaccines. I would also recommend that you bring your vaccine card with you to your booster appointments just to keep good records. Your vaccines that you are receiving.

If someone had received the monoclonal antibody infusion, when and should they get vaccinated?

So the two monoclonal or three monoclonal antibodies we're currently utilizing have relatively short half lives, meaning that they're in your body for a period of between 30 and 90 days, and during that time period you have plenty of antibodies, so there's no reason to get vaccinated. During that time period, in fact, it might limit your vaccine response because you already have circulating antibodies. That holds true for the ones we're using today.

There is a vaccine that was recently studied that actually lasts many months, and so when that monoclonal antibody becomes available and starts getting used, then that window of time to get vaccinated will be much longer. If we use that monoclonal and that one is the one that is being looked at from AstraZeneca.

The two that are currently available are the one that is from Glaxo and the Regeneron ones, and Willy ones that we've been using. Those it's usually recommended for 90 days after you receive it.

Is there any way you can shed some light on the B & T cell immunity and how it relates to the COVID vaccine? It would help a lot of people that are simply confused on that question?

Yeah, so your immune system as a variety of parts to it. The one we classically think about is the production of antibodies. Those antibodies are made by B cell and the other part of your immune system that often functions in the background and protects you against what we call opportunistic infections are your T cells.

Those T cells are important because they present antigen or the foreign invader to the B cells. They say here it is again, you know, recognize it and take care of it. And so when you get these vaccines, you stimulate both B cell immunity and T cell immunity. And not only do you get immunity from both of them, but there are long lived cells that are in your bone marrow that are memory cells, so they're the ones that Doctor Boetcher talked about that then show up later as a response to hey, here's this infection again, you know, wake up and start producing antibodies.

And so these long live cells, both T&B cells, are really important in the immune response, and that's why it's been so difficult to try to figure out whether people are protected after these antibody levels in your blood drop, because we know that happens naturally.

With every vaccine and every infection, but we don't always boost ourselves every time that our antibody levels fall, we expect that our memory immune system. will wake up when we're re exposed and trigger the production of those antibodies again to fight infection.