# COVID-19 Vaccines with Dr. Benjamin Greenberg

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**GG deFiebre:** [00:00:00] So thank you for joining us today. To begin, do you mind just talking about what vaccines are likely to be available first for COVID-19? Yeah, if you want to start with that one.

**Dr. Benjamin Greenberg:** [00:00:13] Certainly. So, as everyone's aware, this is a hot topic today, and we want a safe and effective vaccine to be available as soon as possible.

[00:00:22] It's important to note that there are multiple different types of vaccines being developed. And within each type, multiple different companies, organizations working. And so there's upwards of 20 plus different vaccine development efforts currently underway internationally. And some of them, as we've heard in the news recently, have reported what are called top-line results, initial results.

[00:00:45] So, the first two to report results came out of a Pfizer collaboration with a small company, and the second one was a company called Moderna, each of which working on a very similar type of vaccine. By estimates, and all we have are the estimates that the companies provide, the first doses could be available in December on a limited quantity basis with a rollout of increasing dosages and administration going all the way through May.

[00:01:15] So we expect for the Moderna and the Pfizer vaccine, probably to be the first ones available if they indeed get FDA approval.

**GG deFiebre:** [00:01:23] Okay. And you mentioned that these two vaccines are similar. What kind of vaccines are they? Can you just talk a little bit about the type of vaccine?

**Dr. Benjamin Greenberg:** [00:01:31] Certainly. This is going to cause I think a lot of confusion, and it's important to take a step back and first talk about what a vaccine is meant to do and then these new strategies that have been employed to try and achieve that goal.

[00:01:44] So, the whole point of a vaccine is to prime our immune system against an infectious agent, such that when we encounter that agent in nature - when we walk through a restaurant and somebody sneezes on us and the virus comes into our system - our immune system is already primed and ready to block or defeat that virus from causing any issues in us.

[00:02:09] So the traditional ways, the old ways, if you will, of developing an immune response to a virus, for example, would be to either take dead viral particles - what's called inactivated viruses - and inject them into a human and, since the virus can't replicate, it's a safe way for your immune system to learn the virus and then develop a response to it without you actually getting infected with the virus.

[00:02:38] A second strategy, involved using what are called live attenuated viruses. So these are viruses that can replicate in a human being, but on a very low level and are not associated with causing illness in an individual, but it allows your immune system to see the virus, to see it replicating, and in a safe way, develop a response to it that is then protective against future exposures. Those have been the traditional ways for creating viral vaccines.

[00:03:09] Additionally, we have some vaccines that use protein subunits from an infectious agent to prime the immune system. So instead of giving the whole virus, albeit dead, to the immune system, we take one protein out and we show the immune system that one protein and you mount a response to that protein, such that when it comes back in the setting of a live virus, you're able to attack the virus.

[00:03:35] That's what's been available to us for years. And there are multiple companies working on those technologies to try and create a safe and effective COVID-19 vaccine.

[00:03:44] But what we've seen recently is the use of new technology that has not been available to us, for humans before. And that is by using DNA or RNA to induce an immune system response. So how does it work? [00:04:00] So the idea is to take genetic material that encodes for one of the proteins from the virus, inject it into muscle cell, and let our own cells express part of that protein and show it to the immune system. One of the things human cells do on a regular basis as proteins are being made in the cell is they take little pieces of every protein we make and they show it to the immune system. And they do that as a warning to the immune system of: this is a snapshot, a picture of what's going on in my cell. And a lot of those proteins are self, normal human proteins, so the immune system just ignores them. And the immune system is trained not to pay attention to those. But if a protein gets expressed on the cell surface, gets shown to the immune system that is a foreign protein, your immune system will get trained and activated to be on the lookout for and attack a foreign invader.

[00:05:04] So what new technologies have been developed for COVID-19 vaccines is to use DNA or RNA to inject into human cells and to get our own cell to make proteins from the virus transiently, and the Moderna vaccine and the Pfizer product are both examples of mRNA vaccination programs.

**GG deFiebre:** [00:05:28] Okay, thank you for that explanation. And so do these mRNA vaccines alter someone's DNA with, in how they're working?

**Dr. Benjamin Greenberg:** [00:05:38] Really good question. And the answer is no. In all of the studies that have been done in modeling and in experiments, we don't see mRNA altering our DNA. It doesn't go to the nucleus of the cell, it does not get incorporated, and we don't see genetic mutations resulting from the introduction of these molecules. There was a concern years ago for what's called a DNA vaccine, which is under development for COVID-19, where the DNA does go to the nucleus - that's what it's supposed to do - and then it gets translated into RNA and ultimately into protein. And that DNA, the fear was could it incorporate into human DNA and alter our genome.

[00:06:23] And in all of the preclinical safety work that's been done to date, I am not aware of any evidence of that DNA incorporating into the human genome. It stays separate but in the nucleus for transcription and translation, ultimately into proteins in order to elicit that immune response. So, so far, at least in the modeling, we don't see a safety signal.

[00:06:44] It is worth noting, these are new vaccine technologies, and we do not have any of the primary data from the clinical trials that Pfizer or Moderna have reportedly completed. They have filed their data with the FDA, but it has not been made public. So we are all waiting to see if there are any new insights or any new safety concerns around these vaccines once that data is made public.

**GG deFiebre:** [00:07:09] So although the data has not been made public yet, we do have some information from, for example, press releases or other information. What are the side effects that people have experienced and kind of the efficacy of these vaccines so far that we know of?

**Dr. Benjamin Greenberg:** [00:07:24] Yeah. So I know what you know, I know what CNN and MSN and Fox and websites report, and those come only from the press releases. And the language that's in there seems to suggest that there were what we would consider mild vaccine-related side effects in terms of sore arms or sore limbs or achiness after vaccination. And it's important to know why that happens because we get this question a lot with influenza vaccination. People will say, "well, I got the flu vaccine and it made me sick. It gave me the flu". It's actually not exactly what's happening. When we give a vaccination like a flu vaccine, or in this case a COVID-19 vaccine, we are trying to activate the immune system in the exact way it would be activated if you got the natural infection, but since the virus isn't replicating and isn't growing out of control, you get a modest immune response with very mild symptoms compared to what would happen with the natural infection. And so those symptoms we get after a vaccination are not a sign of inducing illness. It's actually a sign that we're activating the immune system and getting it primed just in case we see the natural infection. So when reading the press releases for these vaccinations, I get the sense that we see similar features that we do with other vaccines, but nothing unique, or at least nothing uniquely reported so far relative to these two products.

**GG deFiebre:** [00:08:50] Okay. And then talking additionally about safety. How are these vaccines, you know, potentially safe if this testing and approval process happened so quickly? And do we have any kind of a long-term safety data on these types of vaccines, these mRNA vaccines?

**Dr. Benjamin Greenberg:** [00:09:08] So we have no long-term data when it comes to mRNA or DNA vaccines in humans. This would actually be the first endeavor for using mRNA vaccines, either the Moderna or the Pfizer product would be a first for us. So there's, there's going to be no way to have long-term data, which is why, from all reports, the FDA and independent review groups that have been put together to review the data are looking very carefully at the clinical trials, which involved over 30,000 patients in each of these studies.

[00:09:41] And so what we're looking for are obvious safety signals that would be of a high enough incidence to appear in 30,000 people getting exposed. So if there were no serious adverse events, then we can say with a certain level of certainty that the risk of a serious event is quite low. There's no such thing as zero until we get more data prospectively.

[00:10:10] We don't have the same experience as we do with other vaccines that we have on the market, where we have an incredible safety database to rely on. These are new, but so far, the reporting suggests they're not seeing adverse events.

**GG deFiebre:** [00:10:24] And then are there any concerns in terms of kind of like the timeline of this happening? I know we've gotten some questions about it happening very quickly. Can you just talk a little bit about that?

**Dr. Benjamin Greenberg:** [00:10:34] Yeah, I know it seems quick. What's happened quickly, frankly, was the acceleration of the research development and initiation of the trials. The trials themselves have gone quickly not because things are being rushed, but because we have so much infection going on in the world.

[00:10:53] If I want to do a vaccine study for a rare infection, I'll give you an example, meningococcal disease, which causes meningitis. It's so rare for meningococcal meningitis to happen today. I have to vaccinate a lot of people, tens of thousands of people and follow them for years to show that the vaccine made a difference.

[00:11:14] But we're in the middle of a pandemic. There are a lot of people getting sick left and right. So they were able to do trials in a shorter amount of time because the risk of getting sick was so high, they could show a separation between the vaccinated and unvaccinated groups. So the actual trials themselves don't seem to have cut any corners.

[00:11:34] They seem to have enrolled appropriate numbers of patients. They seem to have had a placebo control arm. They seem to have, again, collected data appropriately based on what we know from the press releases, and I don't have any other insider information. But what was unique was how quickly we went from wanting to start a trial to actually starting it. And that was just due to resources being invested in a massive way to push things along. But when it comes to the trials themselves, I would not equate going quickly with a concern of cutting corners or safety.

**GG deFiebre:** [00:12:11] Got it. And then do we have any data on these vaccines in our patient population or for those maybe on acute immunosuppressant treatments, like for example, steroids or on maybe these longer-term treatments like rituximab, for example?

**Dr. Benjamin Greenberg:** [00:12:26] Yeah, it's a really good and important question. The answer is no. To my knowledge, special patient populations were not included in these clinical trials. But to be clear, I have not seen the full data.

[00:12:38] So it may be that in the publication that comes out or the data that gets released, a subset of those tens of thousands of patients were immunosuppressed in some way, whether they have an autoimmune disease or cancer or something that impacts the immune system. But to my knowledge, the impact in our unique population has not yet been studied.

[00:12:59] And this is going to get back to the different types of vaccines. So if we're talking about live attenuated vaccines, in general we avoid those in individuals who are immunosuppressed, as just a general rule. But for an RNA vaccine or a DNA vaccine or an inactivated virus vaccine or a protein subunit vaccine, in general we would consider those safe even in immunosuppressed individuals. And so we are not going to have a reason upfront to avoid vaccinating our patients with one of those. But there's one other piece to it and that is, individuals who are on immunosuppression in general mount less of a response to a vaccine then those who aren't. So while we may get to a place where we feel as though the vaccine is safe in our patients, we're not sure what the efficacy is going to be. And so it's still important for everyone to remember: prevention is critical as we're moving through these stages of the pandemic.

**GG deFiebre:** [00:14:00] Okay. Thank you. And then I know there was a lot of discussion in our community after the result that there was news about the AstraZeneca vaccine trial, where it was paused, and there were potential reports of someone being diagnosed with transverse myelitis. Do you know any kind of additional information about that? If you could just talk a little bit about that as well.

**Dr. Benjamin Greenberg:** [00:14:22] Yeah, again, I wish I did. But we've not been involved the AstraZeneca trial. We've not seen the primary data of what happened to that patient who was diagnosed with transverse myelitis, at least according to public records. I haven't looked at films. I haven't looked at the case history, so I don't have any additional information.

[00:14:40] We are keeping an eye on the safety data of that trial. They did complete their enrollment and their first look at efficacy, they just reported that in the last week. And so they too will be going in front of regulatory agencies and we look forward to being able to see that data in particular, to determine if there are any unique aspects.

[00:14:59] It is a different type of virus, excuse me, a different type of vaccine than what the Moderna and Pfizer products are.

**GG deFiebre:** [00:15:07] Okay, thank you. And then, you know, as we've talked about, this is just coming from press releases at this point, we're waiting for the dataset. So what else do we really need to know before we can make decisions about who should and shouldn't maybe get vaccinated in our community of those with rare neuro immune disorders?

**Dr. Benjamin Greenberg:** [00:15:27] So the way we're approaching it here at our institution and talking to colleagues is a recognition that the availability of the vaccine is going to come in waves. And so by all accounts, the first doses of vaccinations are going to target frontline workers, healthcare workers, first responders, and very unique, at-risk populations.

[00:15:51] And so, and those are going to be defined based on COVID-19. So it's probably going to be individuals over 65 with certain medical conditions. By the time there's enough vaccine available to be more generally available to our community, we're going to have several months of additional data and not just tens of thousands of patients vaccinated, but hundreds of thousands of individuals or even millions of individuals vaccinated.

[00:16:20] So it's going to give us a chance to look for any rare adverse events or rare, serious adverse events that would change our counsel relative to our patients. So, essentially, we're going to take the first responders and healthcare team, and we are going to be a national, massive guinea pig population, both to help protect ourselves, but also expand the number of people who get exposed to the vaccine and ensure there aren't surprises.

[00:16:48] So my expectation is, by the time we get to a point where the vaccine's readily available, say February, March, April range, somewhere in there, we'll have a lot more experience and data to reassure us about the safety. Assuming we don't hear reports of new serious adverse events once the first wave of vaccines hit frontline workers, first responders, etcetera, then it's going to give us a lot of reassurance that it's safe for our patients to take. Again, because the RNA vaccines at least are not a replicating entity, then the risk to an immunocompromised individual should be no different than the risk to somebody who has a normal immune system. And so as long as we don't see any surprises, and we'll keep our fingers crossed, we'll be able to say it's safe for our patients to take.

**GG deFiebre:** [00:17:41] Okay. And it seems like we will likely have multiple vaccine candidates available next year. How should someone choose kind of between this potentially, you know, menu of options that might exist?

**Dr. Benjamin Greenberg:** [00:17:56] So I think in general, if my patients are on an immunosuppression, I'm going to tell them to avoid the live attenuated vaccine, whenever it becomes available.

[00:18:05] And, other than that, the others, in general, should be considered safe unless we learn a unique safety issue along the way. What we don't know in terms of how this is all going to play out is, on the production side, I can imagine a world where vaccine number one is getting up to 50 million doses, vaccine number two is getting up to 50 million, vaccine number three 50 million, and we actually need to use all of them in order to achieve vaccination of the population as quickly as possible. And so it may be that regions get access or certain clinics get access to certain vaccines because they can handle the storage of them better than others. [00:18:46] We've heard the notes in the media about the Pfizer vaccine needed to be stored at ultra-low temperatures, something that most pharmacies aren't equipped to do, but medical centers like mine are equipped to be able to do that. So they may say, let's deploy resources in different ways. And so I think we

have to stay tuned about what the options are going to be, even as these vaccines get released. But in general, for the RNA vaccines, the DNA vaccines, and the inactivated vaccines, if we don't see a safety signal in the general population, I would not expect for our patients to have unique issues relative to those vaccines.

**GG deFiebre:** [00:19:23] Okay. And then with, you know, hand washing and social distancing being encouraged, masking, should someone still get a flu shot in our patient population?

**Dr. Benjamin Greenberg:** [00:19:36] I'm going to answer that question with my mask on. I'm alone in this office. I beg, plead, and will be happy to bribe: everybody out in public, if you have to be in public, even if you're just walking outside, just wear the mask. This should not be a controversial issue. If you're listening to people talking about it increasing spread or making it risky, it is factually incorrect. Everybody needs to wear a mask, and the people you are around need to wear a mask. You are protecting them, and they are protecting you. So please, we could put this all behind us if we were all wearing masks all the time. So, I know that wasn't the point of your question, but I couldn't, miss the opportunity to stand on my soapbox. Your question was about flu vaccine and the answer is, on the pleading and begging, for everybody to get their flu vaccine this year. We are really worried about having a simultaneous flu and COVID season happening at the exact same time. And so, as soon as possible, as early as possible, get the flu vaccine. Even with mask wearing, even with hand washing, every bit of protection makes a difference. And this is a combination of viruses we really need to avoid as a society, not just as individuals, but as a society.

**GG deFiebre:** [00:21:02] Great. Thank you. And then any last thoughts on this topic?

**Dr. Benjamin Greenberg:** [00:21:06] So, we're recording this just a couple of days before Thanksgiving. And for a lot of us, we're not doing our normal Thanksgiving routine. My mother is in a deep despair. This will be the first year in decades that the family isn't together on Thanksgiving.

[00:21:23] It was a heartbreaking decision to make but ultimately what we have to do. And what I want to remind people is, this has been a long process, we've got more time to go, but instead of focusing on everything we are sacrificing and everything we're losing, I'm hoping people will focus on what we can do together proactively. The social, the physical distancing, the hand-washing, the mask wearing works. And it allows us to get out of this sooner rather than later. So we are not powerless. We are quite powerful if we can get everybody around us to join in those efforts. The vaccine or vaccines will come. I am confident we will have a safe and effective option if not multiple. But in the meantime, there's a lot we can do and should do to try and lessen the spread of this really horrific condition. So, I hope in whatever ways people are celebrating that they have a good Thanksgiving, and next year will be better.

**GG deFiebre:** [00:22:23] Thank you. Yes. I think that's a great point. And I'm sure we'll continue this conversation, you know, as we get more information about these vaccines going forward, so thank you so much.

**Dr. Benjamin Greenberg:** [00:22:33] Absolutely. Thanks for being here.