

# Covid-19 Vaccines: Current Evidence and Clinical Considerations

Institute of Functional Medicine (IFM), February 17, 2021

Notes written and compiled by Cynthia Li, MD

Freely accessible 90-minute webinar: [COVID-19 Vaccines: Current Evidence and Clinical Considerations, video](#) and [video transcript](#)

## Panelists

- [Heather Zwickey, PhD](#), immunologist, Yale post-doc and professor, currently National University of Natural Medicine in Portland, OR, doing NIH-funded research on natural therapies and nutrition on immunology
- James Carter, Jr, MD, triple boarded Internal Medicine, cardiology, vascular medicine, expert on social determinants of disease
- Patrick Hanaway, MD, IFM faculty, family medicine, head of medical education and former head of Cleveland Clinic's FM center
- Joel Evans, MD, IFM faculty, OB-gyn, expert on hormones and the immune system

## Nuggets

Hanaway summarized the evidence from the current vaccines: [COVID-19 Vaccines in Phase 3 Trials](#)

- Zwickey: vaccines stimulate multiple parts of the immune system.
- Antibodies (Abs), measurable
- T-cells, a very important part, not measurable by standard labs; so even if someone doesn't generate a strong Ab, it doesn't mean the vaccine didn't generate a strong response; T-cell response seems more important in protection
- Cytokines, responsible for the fatigue and fever (IL<sup>1</sup>-1), and aches (IL-6, TNF<sup>2</sup>-a) post-vaccine
- Circadian rhythm of cortisol (highest in AM) may effect vaccine response; the earlier in the day, the more likely to have less of a reaction (this could mean fewer side effects, but may also mean less of an immune response)

Difference in effect between infection with wild-type virus vs vaccine:

- Infection has a smaller inoculum but the concentration will grow; vaccine is a larger inoculum but there is no growth

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<sup>1</sup> IL=Interleukin

<sup>2</sup> TNF=Tumor Necrosis Factor

- Both stimulate IgM<sup>3</sup>—>IgG
- Usually a greater Ab response from wild-type infection

IFM's hypothesis based on biologic plausibility: pre-emptive improvement of immune function, inflammation, and lifestyle factors will help improve the effectiveness of vaccines and decrease the severity of side-effects.

“ATMs” (antecedents, triggers, mediators)

Antecedents: genetics, epigenetics, and methylation

\*improve methylation before vaccine—lots of leafy greens + 5-MTHF [Methyltetrahydrofolate] form of folate supplement

Triggers: delay vaccination during an active infection

Mediators (perpetuators): examples include dementia, obesity, smoking—try to address them before vaccination to improve the response to vaccination

## Systems Optimization

### Digestion

Fiber intake, supporting healthy gut flora--> these positively influence the immune system

### Defense & Repair

Reduce inflammation, avoiding vaccination during an uncontrolled autoimmune flare

### Communication (hormones)

Testosterone (Testosterone Replacement Therapy, TRT, in men can decrease vaccine responsiveness in influenza vaccines) and estrogen (Estrogen Replacement Therapy, ERT, in women can increase vaccine responsiveness in influenza vaccines)

### Mental, emotional, and spiritual factors

affect both the vaccine and immune response

### Lifestyle factors

Sleep duration pre-vaccination—a good night's sleep for the 2-3 days pre-vaccine, as well as after the vaccine

Physical fitness can help improve response to the vaccine

Nutrition—correcting undernutrition is very important for immune health and may help with the immune response

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<sup>3</sup> Ig=Immunoglobulin

Any acute stressor—much less robust response to vaccines (research: caregivers of dementia patients)

Relationships—loneliness affects the response to vaccines

## **Options to improve physiological function**

(\*means to consider for conditions of hypertension, diabetes, cardiovascular disease, dyslipidemia, autoimmunity, obesity)

- Curcumin
- Resveratrol
- Quercetin
- Melatonin
- Green tea extract\*
- Glutathione or NAC<sup>4</sup>\*
- Andrographis\*
- Berberine\*

## **Options to support immune function**

- Vitamins A, C, D3, E, B6, B12
- Folate
- Iron, zinc, copper, selenium
- Mushrooms
- Beta-glucans
- Echinacea
- Quercetin
- Resveratrol

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<sup>4</sup> NAC=N-Acetyl Cysteine

Simplified chart (From [Pandemic Pre-Vaccination Protocol](#))



## Pandemic Pre-Vaccination Protocol

Interventions that may Improve the Immune Response to Vaccination

### Patient waiting to receive vaccination

**Public Health Measures:**

- Masks
- Distancing
- Hand washing

**Address Comorbid Conditions (From CDC List):**

**Address Lifestyle Factors:**

- Sleep
- Exercise
- Nutrition
- Stress
- Relationships

Gut health (IFM's "DIGIN" and "5R")

**Options to Improve Physiological Function:**

- Curcumin
- Resveratrol
- Quercetin
- Melatonin
- \*Green Tea Extract
- \*Glutathione or
- \*N-acetylcysteine
- \*Andrographis
- \*Berberine

\*For conditions below, consider agents above with asterix:

- Hypertension
- Diabetes
- CVD
- Hypertriglyceridemia
- Hyperinsulinemia
- Autoimmunity
- Obesity

**Options to Support Immune Function:**

- Vit A, C, D, E, B6, B12, Folate, Fe, Zn, Cu, Se
- Mushrooms
- Beta glucans
- Echinacea
- Quercetin
- Resveratrol

**If vaccination is weeks to months away:**

- Enhance immune function
- Address inflammation
- Smoking cessation
- Weight loss
- Stress management
- Physical fitness
- Mind/body therapies
- Dietary fiber
- Optimize microbiota
- Address autoimmunity
- Address hormone balance

**If vaccination is imminent within days:**

- Avoid acute stressors
- Obtain adequate sleep
- Avoid anti-inflammatory agents 2 days pre- & post
- If active infection, postpone vaccination

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## Question and Answer Segment

Note: Q and A starts at 63 minutes in the video. [This link](#) to the video is cued up to that section (note that it will take a few minutes to upload) The transcript of the Q and A session is at the end of this document.

## Dr. Li's summary of the Q & A session

**Do you need a vaccine if you've already had Covid-19 illness or test + for Abs?**

--Coronaviruses don't seem to follow the same rules as many other infections where you're infected, then you're done. With the previously circulating 4 coronaviruses, even for +Ab or past

illness, ~50% of people develop memory responses, and of those people, they can still get re-infected multiple times a year. We don't know if this current coronavirus behaves the same way, so the recommendation is still to get the vaccine.

--If you already had the infection and have a very strong reaction to the first vaccine, that acts like a booster shot. You probably don't need a second vaccine; you've had your second dose.

--If you've just had Covid illness within the last 1-2 months, wait to get a vaccine. The CDC recommends to wait 90 days. IFM (Dr. Heather Zwickey, PhD) recommends 90 days to 6 months.

### **Should we delay the 2nd dosage for people?**

--The reason the vaccines are spaced out the way they are is because that's how the clinical trials were done. They were rushed for the pandemic and didn't have time to wait for other trials. What we know from other vaccine trials, like the Hepatitis B vaccine, is that you can push that 2nd dose out 6 months and still get a strong immune response. The general sense right now is that these vaccines are behaving like Hep B vaccines. We just don't have the data yet.

### **Vaccine and pregnancy?**

Not a lot of data. ACOG (American College of Obstetrics and Gynecology) and SMFM (The Society for Maternal Fetal Medicine) have strong statements that say the vaccine should not be withheld, but that it's also important to have a discussion with each patient. WHO says the vaccine should be withheld unless the patient has a high risk of exposure.

What we know is that in animal studies, there's no toxicity.

In women who are pregnant when they contract Covid-19, they have a higher risk of severe infection and death.

Several videos suggesting there's a shared sequence of amino acids in the part of the mRNA that would take the spike protein and embed it into the envelope of the virus, and that this small piece encodes a 4 amino acid sequence is actually shared with the syncytium protein on the trophoblast. However, this sequence is too short to stimulate an immune response; it's too small to generate an Ab response. There's no evidence that it has ever happened.

The vaccine does not appear to affect fertility for men or women.

### **Do I still need a vaccine if I take good care of myself, take various vitamins, do all the right things, maybe even take ivermectin prophylactically?**

--Dr. Joel Evans: there is no data to say with certainty that any of these measures, or these measures taken together, give 95% protection against Covid 19. Biological plausibility (of lifestyle factors and immune optimization) is different than studies that show 95% efficacy.

Drs. Carter, Hanaway, and Evans have all chosen and gotten the vaccine.

### **How do we respond to patients who are worried or hesitant about the vaccines? How do you counsel them? (Drs. Carter & Hanaway)**

--Take the time to hear their stories. It's not appropriate to rush people into a decision.  
--Then he shares with them his process and what the risks were for him as well as for those around him.  
--Vaccines also decrease hospitalizations and disease severity and mortality (especially in places like Israel, where 40% of the population has already been vaccinated)

Covid long-haulers now make up 40% of patients who had moderate to severe Covid illness. There's no data yet on Covid long-haulers and whether the vaccines can reduce this.

**How long does the mRNA stick around? And the adenovirus vaccine--how long does that stick around? Are there concerns for the mRNAs sticking around for a long time?**

--mRNA itself is unstable. If you just have normal mRNA, it will be degraded within 20 minutes. The lipid that is around the mRNA in the vaccines offers protection and also allows it to be taken into cells. Goes into macrophages in the tissues--> lymph nodes--> T-cell immune response--> all of the mRNA appears to be killed as the macrophages are killed.

--in animal models, within 2-3 days, all of the synthetic mRNA is gone.

--it's different for the adenovirus vaccines (i.e. AstraZenca, Sputnik V and the Johnson & Johnson vaccines). Taken up into the macrophage into the lymph nodes--these cells are also going to be killed. But because the adenovirus is a live viral vector, it may stick around for 7 days. In some immunosuppressed people, it may stick around for 3 weeks or longer (data from dengue trials; similar vaccines; the longest duration is 6 months).

**If I just finished cancer treatment or if I have cancer, is the vaccine going to be somehow problematic and promote recurrence or worsening?**

Joel Evans: the real issue is that these patients may not have a robust immune response to the vaccine. Most oncologists are recommending patients wait until their treatment period is over (2-3 months). Right now, there is no concern about the vaccine making cancer worse.

**Autoimmune disease and vaccine risk**

Yes, while people with autoimmune disease are at higher risk for having an adverse reaction to the vaccine, they're also more at risk for having moderate to severe Covid-19 illnesses.

If people have uncontrolled systemic autoimmunity or having frequent inflammatory flares (SLE, RA, MS)-- the likelihood of vaccination influencing a flare is very high. INF<sup>5</sup>-gamma can exacerbate autoimmune disease. For people with controlled autoimmunity, like if they're on biologics or methotrexate, there is less concern about vaccination. Rheumatologists have been saying for a year now that they're concerned about Covid leading to long-term consequences. Vaccination seems to be less likely to lead to autoimmunity than Covid, since it's 1 spike protein vs an entire viral molecule.

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<sup>5</sup> IFN=interferon

## More Information

For a practical summary and guidance on preparing for vaccination to share with your patients, please see the following COVID Strategies/BCCT blog post. Note that this post includes other IFM resources for specific diet, lifestyle, and nutritional supplementation guidance: [Preparing to Be Vaccinated: An Integrative Approach](#)

## About the Author

Dr. Cynthia Li is a Functional Medicine physician and author of [Brave New Medicine](#). Dr. Li is a regular contributor to [BCCT](#), including her writings on Intuition in [Cancer Diagnosis and Treatment](#) and her eBook [How to Shield Yourself against COVID-19: Science-Based, Integrative Medicine Strategies for a Once-in-a-Century Pandemic](#)



## IFM Webinar Question & Answer Transcript

### **Patrick Hanaway, MD:**

Great, thank you so much, Robert. I would say that we have had over 300 questions that came in before the talk today, before the webinar. We've had hundreds of more questions come in during the time of the talk and we appreciate it. We obviously won't be able to get to all of them, we're going to spend more time at the next webinar as well. But I'm going to go through and sort of in a round-robin style, asking our experts questions related to their expertise. So let's start off with Dr. Zwickey. And a common question that's been asked is if you've tested positive for the SARS-CoV-2 virus, or if you've had the COVID infection, should you still get the vaccine? Do you need to get the vaccine? Does it matter whether it was a mild or severe infection?

### **Heather Zwickey, PhD:**

Yeah, that's a great question. So for many types of infections, if once you've had the wild-type infection, you've got a solid immune response and you probably wouldn't need vaccination. However, coronaviruses are a little different. And so we know from the four coronaviruses that circulate regularly, that roughly 50% of people develop memory responses. And even those who do develop memory responses are able to get reinfected multiple times a year. So we're not sure if this coronavirus is going to behave like those coronaviruses, which is why vaccination is being recommended even if you've already had an infection. Now, if you have a very strong immune response to the first vaccine, that acts as your booster shot, so you probably don't need two injections at that point. If you've already had an infection and you have a strong reaction to the vaccine, you've had two reactions and likely you'll generate immunological memory. But that's why vaccination is still being recommended post COVID infection. That said, I would also say just as we're recommending through IFM that you don't get vaccinated while you have an infection, if you've just had a COVID infection within the month, wait to get vaccinated. And I believe the current recommendation that the CDC has is wait 90 days, and I would say anywhere from 90 days to six months. And so we're seeing that, that indication that there is protection and it's really good up to about 12-week period of time before you get that secondary booster.

### **Patrick Hanaway, MD:**

There's been a question also about, more of a public health kind of question, but should we delay the second dosage for people? What are your thoughts on that Dr. Zwickey?

### **Heather Zwickey, PhD:**

Yeah, again, it's a really good question. So what we're seeing, the reason that the vaccines are spaced the way they are is simply because that's what was done in the clinical trials. And the clinical trials were done quickly so that the vaccines could hit the market fast. So they didn't wait to see how long out you could go and vaccinate and still get that secondary response. If we look at other vaccines for historical evidence, what we can see with things like the Hep B vaccine, is you can push that second dose out six months and still get a very strong immune response to it. So the idea is that these vaccines are behaving like Hep B vaccines. We could push them out, we don't currently have the data showing exactly how far out they can be pushed.

### **Patrick Hanaway, MD:**

Okay, so let me ask a similar related question to Dr. Carter, and that is, what is the issue, why do they think that every single person should be vaccinated, regardless of whether they've already got immunity? Can't they be protected by the herd immunity without having to get vaccinated themselves?

### **James Carter, MD:**

Well, there are a number of elements to that question. I think that we always have to be concerned about those who have a mild case being able to infect others and they may not have large symptoms, but others near



them might be more vulnerable to have a worst case. And as you mentioned, herd immunity is the goal, we're trying to decrease the likelihood of that type of community spread. We also cannot predict who have low risk. What we would look at as low risk might have a severe infection. And that includes from pediatric all the way through to adults. And we have many adults who are physically fit and don't consider themselves to be at high risk, who have long-term effects to having COVID-19 infection.

**Patrick Hanaway, MD:**

And so, as we talk about that, Dr. Evans, as an OB-GYN, a number of people have raised questions about pregnancy, about infertility issues. Can I get the vaccine if I'm pregnant? If I get the vaccine, how long should I wait before I get pregnant?

**Joel Evans, MD:**

So this absolutely is a huge question. And unfortunately we really can't use a lot of data to guide us with an answer because there's absolutely no data on the use of these vaccines in pregnancy. And even though that's the case, ACOG the American College of OB GYN, and SMFM, Society of Maternal-Fetal Medicine, have very strong statements that say the vaccine should not be withheld. And that a discussion with the patient should be held. Now the World Health Organization, however, has a different recommendation, which says that the vaccine should be withheld unless the patient has a high risk of exposure. And so it's very difficult for a woman who's pregnant or thinking about getting pregnant to decide what to do when there's no data and there's conflicting information from the professional societies. So what we have to do is look at what we do know. And so what we do know is that in animal studies, there's no toxicity. We know that women that are pregnant, if they do contract COVID-19, they have a much higher risk of severe illness and a much higher risk of death. So this sort of tells us that we always have to be, when we look at the extremes, which is if you get it, if you're likely to get it, if you're out there, if you're not able to safely isolate, if you're a frontline worker, it really can make a difference with your risk of death. And so that's why it's important to individualize, women have to decide what their own risks are, what their risk tolerances are, and then make the decision, are they going to wait until after they deliver, or maybe wait for a more traditional vaccine if they are pregnant. As far as the fertility question goes, this does not impact fertility in any way for men or for women.

**Patrick Hanaway, MD:**

Dr. Zwickey, could you just elaborate on that for a moment? There has been a concern raised that there is a component within the mRNA that correlates with the syncytium that is a part of the trophoblast in the placenta. And that's raised a concern amongst some people that even though there is no evidence as Dr. Evans just said, that there may be some on toward risk.

**Heather Zwickey, PhD:**

Yeah, there's been several videos that have gone out. There is no data showing risk, but there's been several videos going out that suggests that there's a shared sequence of amino acids in the specifically the part of the mRNA that would take the viral spike protein and anchor it into the envelope of the virus. And that little piece of mRNA, encodes a four amino acid sequence that anchors the spike protein into the virus. And that four amino acid sequence is actually shared with this syncytium protein on the trophoblast. However, this sequence is too short to stimulate an immune response. It doesn't bind to an MHC molecule and it's too small to actually stimulate an antibody response. So while there could be a remote possibility of this happening, there's actually no evidence that it has ever happened. And the likelihood it happens because that amino acid sequence is so short is very, very, very small.



**Patrick Hanaway, MD:**

Okay. Dr. Evans, back to you on looking at people who say, "Well, if I just enhance my immune system and sleep well and eat right, and do all the right things, maybe even take ivermectin preventatively, why should I get a vaccine?"

**Joel Evans, MD:**

Well, first of all, we have data on the effectiveness of these vaccines and none of the regimens that you talked about, can we say with certainty gives you 95% reduction of getting COVID. And especially if you are someone that has co-morbidities or increased risk from getting COVID, you need that 95% assurance. But again, it is a personalized decision, but the important thing is that we're talking about biological plausibility, which is different than saying 95% risk reduction.

**Patrick Hanaway, MD:**

So I would acknowledge to everybody that the three of us, Dr. Evans, Dr. Carter and myself, who are all seeing patients directly, all have chosen to receive the vaccine ourselves. But and Dr. Carter, what do you do when you have a patient who comes in expressing those concerns, both from the historical concerns relative to how they've been treated as experimental subjects, i.e. this vaccine is experimental at this point in time, even though we've seen it now in the clinical trials given to over 100,000 people and in practice given to millions and millions of people. How do you counsel them? How do you listen to them? What's your approach with that?

**James Carter, MD:**

Our approach is to take the time to hear their story. I think it's very, very important, and I do not think it's appropriate to rush people to a decision. This is part of the reason I had concern about some of the rollouts where certain communities were given 48 hours, for example, to respond, whether they wanted to have the vaccine or not. I don't think that that's appropriate given this context. But I do think that every individual story requires listening and putting it into context. And then after I hear their story, I share mine, I share my personal experiences and the journey I took, that what I described in the talk is real. At first, I actually checked off the box that I wasn't going to get vaccinated yet. And then when I thought about the risk for me and the risk for those around me, I decided that 95% effectiveness of such a large trial was something I felt comfortable with compared to the unknown of getting COVID-19 infection.

**Patrick Hanaway, MD:**

Thank you. So people have asked me what's really the goal of this vaccination program? And we see that the vaccines are useful to be able to decrease the development of symptoms of COVID, but we also see them decreasing hospitalizations and decreasing mortality. The data is there initially in smaller, we'll call them smaller trials of 40,000 people. But we're seeing that data bearing itself out now in a place like Israel, where 40% of the population has already received the vaccine. Interestingly, the second highest vaccine rate in the world is in the United States. So while we wish it were faster, it's actually moving along pretty well. And we are seeing changes in the hospitalization, in the death rate and in the overall infection rate that's going on, and this is not due to a decrease in testing that's there. As I think that one of the other big reasons for the vaccine program from my perspective, is that I'm taking care of patients with post COVID syndrome, some 12, or even 36 weeks out from being infected who are still very seriously affected by the post infectious sequelae of that. And working with them has led me to look at the data where 40% or more of the patients who've had



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moderate to severe COVID have long-term post COVID, long COVID, "long hauler" symptoms that go on. And so I feel like the vaccine is important if we can decrease the degree of severity of illness through the vaccine, and we can decrease that post COVID syndrome. That would be great. Now that said, we don't yet have data on exactly does it do that? We're making inferences around that, and we're going to be clear about what we know and what we don't know with the data overall. So back to you Dr. Zwickey, there've been questions about the mRNA. Both the mRNA vaccine that's given and how fast it degrades or sticks around. And then with the adenovirus vaccine such as the one from Johnson and Johnson that I mentioned, where it's incorporated into the nucleus, and then mRNA is produced, how long does it stick around? And is there a concern for the long-term presence of that messenger RNA?

**Heather Zwickey, PhD:**

Sure, let's start with the mRNA vaccines. So with mRNA vaccines, mRNA itself is unstable. And if you just have normal mRNA, it's usually gonna be degraded very quickly, like within 20 minutes. The lipid that is going around the mRNA and these vaccines is providing protection, but it's also helping it being taken up into cells. It doesn't go into germ cells, so it's not going into sperm or eggs. It actually doesn't really even go into muscle cells. It goes into macrophages in the tissue. And those macrophages now carry it off to the lymph node where they're going to stimulate a T-cell response, and they're going to be killed. We can see in the animal models that within two days, 48 hours, all of the mRNA is gone.

**Patrick Hanaway, MD:**

Even though it's synthetic, even though it is a modified or synthetic mRNA?

**Heather Zwickey, PhD:**

Absolutely, yeah. Even the modified mRNA is gone in 48 hours. So we're not worried about long-term consequences of mRNA sticking around in your body. It's a little different for the adenovirus vaccines. As you mentioned, the adenovirus vaccine is taken up again, usually into macrophages and carried off to the lymph node. That's how we're going to stimulate the immune response. And then those cells are also going to be killed. However, because the adenovirus is a live viral vector, it may stick around as much as seven days. It may, in some individuals who are immunocompromised or immunosuppressed or going through immunosenescence, stick around for as long as three weeks. And we know this from data that we have from the dengue trials, because this is a similar vaccine that we've used for dengue fever. It doesn't stick around for, well, the longest they've gone in four to six months, and it's not there at six months. It's probably not there at 12 weeks. It may be there for a week or two. But again, all of the cells that get infected are going to be killed. That's why it's a good stimulus of the immune response. If the immune system is doing its job, it's just going to go kill that adenovirus and any adenovirus infected cell.

**Patrick Hanaway, MD:**

Thank you. So and Dr. Evans, in addition to your work as an OB-GYN, you've done a lot of work with cancer and worked and counseled and supported cancer patients through your practice for a long period of time. People are asking questions about, if I have cancer, does that mean I should be concerned about the role of getting a vaccine or not? And are there any relationships between the safety of vaccines in patients who have received cancer therapy? And of course you can build into that sort of the current recommendations around vaccinations, as it relates to people who are actively receiving chemotherapy.

**Joel Evans, MD:**



So it's interesting Dr. Hanaway, because what you just described is what most people are concerned about, which is, "If I have cancer, if I've just finished cancer treatment, is the vaccine somehow going to be problematic for having cancer and promote recurrence?" The real interesting thing here is the real concern is that somebody undergoing cancer treatment will have a less effective response to the vaccine. So the issue here is that people with cancer and people undergoing chemotherapy or treatment for cancer are less likely to have an effective response. And therefore, most oncologists are recommending, waiting until active treatment is completed. However, this again, becomes a multifactorial decision about exposures and risks, et cetera. But there's really no concern about the vaccine making cancer worse.

**Patrick Hanaway, MD:**

And then in the subset of patients who have finished active treatment chemotherapy, the recommendations relative to any of the different kinds of vaccines, where do you sit?

**Joel Evans, MD:**

I said that it's a good thing. All my patients as you said, I do have many patients that are involved in the cancer treatment process and they were waiting three months, two to three months after post treatment. However, for patients that are receiving monoclonal antibody treatment for their cancer, that's not a problem with lowering the effectiveness of the immune response.

**Patrick Hanaway, MD:**

Great, thank you. Dr. Zwickey, there were many questions about autoimmune disease and I just like to give you sort of the closing timeframe of a couple of minutes here for you to speak about autoimmune disease and risk. And we've talked about those patients who have uncontrolled autoimmune disease. Can you help to elaborate on that a little bit for our listeners? And I'm sure we'll have an opportunity to talk about that again next month.

**Heather Zwickey, PhD:**

Sure, so as you had in your chart so eloquently, if people have uncontrolled un-autoimmune disease, meaning they are not being controlled by medication, they're having frequent flares. The likelihood that vaccination could influence a flare can be very high. And when I say autoimmune disease, I'm talking about systemic autoimmune disease, talking about things like rheumatoid arthritis, lupus, multiple sclerosis. Why do we think that? Well, these vaccines in the preclinical trials and in the phase one and phase two trials have been shown to stimulate the production of interferon gamma. And interferon gamma can exacerbate autoimmune disease, we know that. So could this cause a flare? It could. For people who have controlled autoimmune disease, whether they're on something like methotrexate or they're on a biologic, the biologics will actually help control any flares that a vaccine might stimulate. So if your autoimmune disease is under control, we're less worried about vaccination. If the autoimmune disease is not under control, then we tend to worry. But let's also remember that rheumatologists have been saying for months now, in fact, almost a year now, that we're worried about COVID leading to long-term autoimmune disease. So if we're looking at relative risk of vaccination versus COVID, vaccination is much less likely to lead to autoimmune disease because we're looking at one protein, a spike protein, as opposed to an entire viral molecule. And we have quite a lot of data showing that infections using multiple different mechanisms can lead to autoimmune disease, molecular mimicry, bystander effect, et cetera. So what I want to make really clear is this is a might. This is dependent on somebody having T-cells and B-cells escaping central tolerance in the thymus and the bone marrow getting into the periphery, having the right HLA background to have an autoimmune disease, and then getting



stimulated at exactly the right time with the right peptide in order to lead to autoimmune disease. The likelihood is very, very small, but it's there. So I don't want to deny that it exists, but I also want to say that our likelihood of getting hit by a car on our way home is higher. Not that I want anyone to get hit by a car.

**Patrick Hanaway, MD:**

And to just, if you could also make a comment about the biologics that are currently used for a number of autoimmune diseases and what their relative risk factor is for those patients who are getting vaccinated?

**Heather Zwickey, PhD:**

Yeah, so I think one of the things that's interesting is that the biologics that are being used for autoimmune diseases are actually in clinical trials to be tested for COVID, because they seem to help reduce the cytokine storm. So the biologics are perfectly safe to be administered with the vaccine. We're not worried about that at all. And in fact, the MS Society has a statement saying that, for MS patients who are controlled, it should be safe for them to be vaccinated.

**Patrick Hanaway, MD:**

Thank you. I know there are many, many more questions and we will have an opportunity to answer those questions in our next webinar, which will be on March the 16th. I appreciate that if you go to the website and look at the information that we have on the dashboard that we put up, it will also contain the pre vaccination protocol that Dr. Evans showed you as well as you can find those things that will help with prevention and early treatment. So Dr. Luby, you want to take us home?

**Robert Luby, MD:**

Thank you, Dr. Hanaway, yes. Indeed, we will be making this recording of the webinar available this Friday, February 19th. There'll be further communication about that and how to sign up for the webinar on March 16th, which will be free, please mark it on your calendars. Also, how to submit questions for that webinar. And as Dr. Hanaway mentioned, we will be updating the vaccine dashboard. So your questions about the vaccine formulations. Also, we will be having the author of a landmark article, just published on how to improve your immune response to the vaccines. We will also provide you any evidence and outcomes that are emerging from chronic COVID or post COVID syndrome as well, and any further developments on the pre vaccination protocol that we've already developed. So we'd like to close with a special thanks to those of you who are new to functional medicine for joining us tonight. And another special thanks to those of you who are on the path to certification, who will be attending our Immune Advanced Practice training module, 36 hours from now. We'll see you very soon. So on behalf of the entire staff at the Institute for Functional Medicine, we'd all like to thank you for joining us tonight. And we hope next month, March 16th, have a good evening, everyone.

**James Carter, MD:**

Good evening.

**Patrick Hanaway, MD:**

Thanks.