COVID: Two Years Later

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It's been two years since the COVID-19 pandemic changed our lives forever. Luckily, we're in a much better place now thanks to cutting-edge scientific discoveries and expert knowledge. In this episode, learn what experts now know about COVID-19 and how it affects the arthritis community, including disease severity and outcomes, vaccine effectiveness, risk factors for long COVID, treatments and more. Also, learn what experts predict about the future of the pandemic, including when restrictions can loosen and how the daily living might evolve.

This episode's guest expert, Dr. Michael Saag, is an infectious disease expert who's done pioneering work in HIV. He has participated in many studies of antiretroviral therapy and novel treatments for opportunistic infections. He has published over 260 articles in peer reviewed journals, including the first description of the rapid dynamics of viral replication, and directed the 'first-in- patient' studies of 7 of the 25 antiretroviral drugs currently on the market. Dr. Saag currently serves as an Editor of the Sanford Guide for Antimicrobial Agents, and recently served on the Board of Directors of the American Board of Internal Medicine (and as Chair of the Infectious Disease Subspecialty Board).

Additional resources:

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PODCAST OPEN:
You're listening to the Live Yes! With Arthritis podcast, created by the Arthritis Foundation to help people with arthritis — and the people who love them — live their best lives. If you're dealing with chronic pain, this podcast is for you. You may have arthritis, but it doesn't have you. Here, learn how you can take control. Our host is Rebecca Gillett, an arthritis patient and occupational therapist, who is joined by others to help you live your Yes.

MUSIC BRIDGE
Rebecca Gillett:
Thanks for joining us on the Live Yes! With Arthritis Podcast. I cannot believe that I'm saying this, but we are going to talk about COVID two years later and what perhaps the future might bring. It's been a very scary time to navigate and a lot of unknowns, but I think we know a lot more than we did two years ago. And so, I'm happy to have Dr. Michael Saag join me today as our guest expert.

He is a renowned infectious disease expert who's done pioneering work in HIV. He's participated in many studies around viral therapy and novel treatments for it and has published over 500 articles in peer review journals. He is currently serving as editor of the Sanford Guide for Antimicrobial Agents and recently served on the board of directors of the American Board of Internal Medicine and as chair of the infectious disease subspecialty board. Dr. Saag, thank you so much for joining me today to give us an update on what's going on with COVID.

Dr. Mike Saag:
Great to be with you.

Rebecca:
Can you just give us a little background on the work you're doing right now as it relates to COVID?

Dr. Saag:
Most of the work I've done on COVID started when I had COVID myself back in March of 2020. I was exposed on Friday the 13th in March and had a pretty rough go of it and didn't have to go to the hospital. Afterwards I felt like one of those video game characters that blinked 'cause it's got a cloak of invincibility.

Rebecca: (laughs)

Dr. Saag:

So, I started taking care of patients on the brink of needing hospitalization, and we did what we could in terms of keeping them out of the hospital. As time moved on, we initiated monoclonal antibody therapies, then expanded our role to doing even more in the way of prevention. And to the point of this podcast, a lot of our patients were immunocompromised patients who needed to come in for monoclonals or for other preventative types of approaches.

Rebecca:
What do we know about the severity for our population of patients?

Dr. Saag:
It really depends on a lot of the details. Like all infectious diseases, the infection is usually worse based on inoculum. So, if you're in a room with one person who's infected and they're breathing in a very close space with you, and you breathe in a lot of virus, right off the bat you're gonna have a worse outcome simply because of the amount of virus you're exposed to.

The second thing is what's your host status? If you're totally unvaccinated, even if you're not immunocompromised in any way, you're at very high risk for bad things to happen. We now know that someone who gets significant infection and needs to come in the hospital, the mortality rates for people unvaccinated is twentyfold.

Rebecca:
Wow.

Dr. Saag:
Not just one time, two times — this is 20 times more likely to die than someone who is fully vaccinated. So, getting vaccinated is important. And then finally, people who are on immunosuppressive drugs, like a lot of people if not most people with rheumatologic disorders, their response to vaccines is variable. If they're on drugs like Rituxan to block antibody production, then their responses are generally not as robust as somebody who say is on methotrexate or on low doses of prednisone or something.

So, it's highly variable; it depends on the individual situation. But, as you said at the outset, we know so much more about COVID right now. And we're putting that information to good use every day, and I think saving a lot of lives right now.

Rebecca:
Are you seeing now with the omicron variant that patients in our community are having milder cases if they are contracting it? Or are you still seeing some severe cases?

Dr. Saag:

I think it's very fair to say that omicron as a variant is less virulent. And what I mean by that is that once somebody gets it, there's less likelihood that they're gonna go on to have advanced cases and potentially go on a ventilator and die. That said, it's also much more transmissible, which means that many, many more people get the infection.

There are about four to five times as many people who've had omicron as had delta, yet there are just about as many deaths now with omicron as there was back in the summer and early fall with delta because there are so many cases. Even with a smaller percentage of people having severe disease, the aggregate number is pretty high.

Rebecca:
And taking those immunosuppressant type drugs that some of us might be on, how does that affect the response?

Dr. Saag:
It's variable, but even having had the vaccine, which helps enormously, generally speaking people who are on immunosuppressive drugs, have more trouble with COVID as a rule than people who are vaccinated and are not on immunosuppressive drugs.

Rebecca:
Yeah. And also more easily able to contract COVID, correct?

Dr. Saag:
In some ways. But if you do the mitigating things, like wearing a mask, avoiding large crowds, you can protect yourself against exposure and infection in the first place. And of course, that's what we recommend. Before everybody gets all demoralized from listening to me, let me tell you what you can do, the most important thing: Monitor yourself for symptoms, especially during these surges and spikes.

When you sense that you might have been exposed and infected with COVID, get tested right away. Get your diagnosis as early as possible. Call your rheumatologist or your doctor, and they will get you monoclonal antibody or antiviral therapy in that first two days after onset of symptoms. I think that's the number one take-home point for everybody listening: Get diagnosed early and get on an antiviral as soon as possible after onset of symptoms.

Rebecca:
Yeah. And I know personally. I had COVID about a year ago. And I actually am recovering again from contracting COVID a second time earlier this year, fully vaccinated. But I still contracted it, and I was not able to get any monoclonal antibodies because of supply. What do you have as far as knowledge about supply?

Dr. Saag:
Before there was omicron, we had ample supplies of the Lilly monoclonal antibody product and the Regeneron monoclonal antibody products. And they worked extraordinarily well for alpha variant, for the regular initial virus and also for delta. Omicron came along and neither the Lilly nor Regeneron product works. So, the third product, Sotrovimab, which is made by GSK, was in very small supply because the government had been buying those other two products and not really purchasing the Sotrovimab because they didn't need it. Of course, we're making more Sotrovimab, and Omicron right now, this is as of February 2022, seems to be going away for the moment.

Rebecca:
Well, one of the questions I had when I called my rheumatologist is: Who qualifies to get the monoclonal?

Dr. Saag:
Anybody who's got a rheumatologic disorder would qualify. There's other conditions like diabetes, obesity, older age. But anybody who has an autoimmune disorder would qualify. I should say also that there are other antivirals that don't require IV therapy. The first drug is molnupiravir. You might know that as the Merck drug. The better drug is one that's called Paxlovid; that's a Pfizer product. We have to pair it up with another drug called ritonavir, 'cause it inhibits the metabolism of the drug so the levels go higher.

When people use Paxlovid, it's already pre-packaged with ritonavir. They're both given over five days, but they're orally bio available. Again, the take home-point: You want to get it early. Both of those drugs initially were in short supply. We had a kind of a perfect bad storm of omicron spiking, the monoclonals that we used to use not working, the antivirals not quite there yet, and now we're coming out of that. So, fortunately, from this point forward, I think we'll be in much better shape.

Rebecca:
Well, that's good news. One of the things that I know there's a lot of confusion on is people understanding what immunocompromised versus immunocompetent mean. So, can you explain that difference and how they apply to COVID and would affect our community?

Dr. Saag:
Well, let's just start with immunocompetent. What that basically means is somebody with a normal immune system, full stop. A large number of your listeners have autoimmune diseases or arthritis that has gotten to the point that led to a rheumatologist visit. And that rheumatologist will give medicines to calm the immune system down. Any effort to do that makes that individual immunocompromised, so they're not immunocompetent fully. But the trick, and the difficulty for everyone, including the

doctors, is understanding to what degree is the immune system compromised. And the immune system, as everyone knows, is very complex.

Even if one part of the immune system may be suppressed, the other part may be fully competent. So, the antibody production may be down, but the T-cell immunity may be OK, or vice versa. The details matter, and it's gonna be darn near impossible for any patient, or for that matter, a lot of doctors when they're using new medicines, to know fully with regard to COVID how much of the immune system is impaired in its response. But I think as a rule, we can consider anyone on any immunomodulator to be relatively immunocompromised compared to somebody who's not on any of those drugs and has a normal immune system.

Rebecca:
I know CDC just released different recommendations for people who are immunocompromised on boosters. What are the current recommendations for people with rheumatic diseases?

Dr. Saag:
Well, right now we recommend everyone to get the initial series. So, I'm hopeful that everybody listening has gotten their first shot and has followed that up with a second shot. Then about four to five months after that first series, it's time for really everyone to get their third shot. Regarding a fourth shot, I think the jury's still out; the data are still coming in. But for a lot of the patients that I'm following who are immunocompromised, I'm starting to encourage folks to get their fourth shot. I feel comfortable from a safety standpoint so far recommending that and probably from an efficacy standpoint.

Even though a second infection can happen, it's usually much less severe because the immune system is more efficient in its approach to managing it. Here's a way to think about it: Think of the immune system as an army, and it's out there ready to fight whatever it's called upon. When it gets a signal that there's an invader like COVID, it wakes up and goes and attacks. But along the way, it has to learn about the enemy, and that knowledge isn't there upfront when it's back say March of 2020.

You get it, you get sick and your immune system has to learn as it goes. What the vaccines do is they say, "Here's what this looks like." Think about it as military intelligence. "When you see this, this is what you're gonna attack, and this is how you're gonna do it." The immune system is much more knowledgeable and efficient in attacking COVID after a vaccine, or for that matter, after an initial infection, than it would be had it not seen any of that before.

Rebecca:
Right. I love that analogy. Can we guess from the data that the effectiveness of the booster only has an efficacy of… maybe it's... is it four or five months for somebody who's immunocompromised? How do we know how long it leads for protection?

Dr. Saag:
To continue that analogy just a bit further: It's not that, after three or four or five months, the immune system forgets about it, ignores it. What happens, though, is that it just stands down. Your immune system can't be on alert all the time for everything 24/7. It has what's called memory, literally memory.

And so, when it encounters that thing again, even after four or five months, it may not rev up like within 12 hours; it might take 24 to 36 hours. But as it revs up, it's much more efficient. You can get reinfected, you can develop symptoms, but as that immune system revs up, the duration and severity of the infection is much less than it was initially or in somebody who's never had COVID or a vaccine before.

If you get a vaccine, you're protected against the probability or the likelihood that you're gonna have a severe illness or that you're gonna die. But it's not gonna protect you necessarily against a brief, small symptomatic episode.

Rebecca:
Yeah. A vaccine isn't a cure, right? It is to protect us. So…

Dr. Saag:
It is worth a pound of cure.

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Whenever you need help, the Arthritis Foundation's Helpline is here for you, now offering support in Spanish and other languages. Whether it's about insurance coverage, a provider you need help from or something else, get in touch with us by phone, toll-free, at 800-283-7800. Or send us an email at https://www.arthritis.org/i-need-help.

Rebecca:
What is the evidence on mixing and matching these vaccines, especially in regard to those with immunocompromised systems? Is it smart to mix and match? Should you?

Dr. Saag:
There's a great study that was published in October or so of 2021 that showed that the intensity of the immune response was much better mixing and matching. So, if you have the Moderna product up front and then for your booster you use Moderna, it's basically seeing the same thing exactly as it saw four to six months before. If you use Pfizer, all of a sudden it's similar, but it's not the same. And your immune system uses that information to broaden its response. It's basically giving it more information.

Rebecca:
Dr. Saag, what would you tell people who received the J&J vaccine that are worried they might not be getting adequate protection?

Dr. Saag:
I think it's good to vary the vaccines because you get a broader immune response. If I got J&J initially, I would not continue with J&J. I would be switching over to Pfizer or Moderna, and then following the recommendations of boosters for that as time goes on. I'm a big advocate of mixing and matching. Giving the immune system a wider array of types of COVID viruses, to respond to different variants, the smarter the immune system becomes, and the more efficient it becomes at knocking it out.

Rebecca:
Is there a harm in getting more vaccine doses than what is recommended?

Dr. Saag:
There's a potential of harm, yes. I wouldn't get too far out in front of the data. Everyone, all of us, have to keep in mind that this is something the world has never seen before. We're making educated guesses, but we can't have absolute answers to things we don't fully understand yet.

Rebecca:
Right.

Dr. Saag:
Look at what's happened in two years of COVID. We had a vaccine within one year. That is a miracle. When we see the empiric evidence that having a vaccine reduces mortality by twentyfold, you can't ask anymore of any vaccine, much less one that was put together in a very strategic, logical way; tested impeccably with the best technologies that we've learned over the last 30 years; and now it's in our hands and there's ample supply of it. That is something to embrace and celebrate.

Rebecca:
Absolutely. We didn't start from scratch. And so many people are like, "How did they come up with this vaccine so fast?"

Dr. Saag:
We always are building on the shoulders of giants and the shoulders of work that has come before. I take a lot of this back to HIV, but it was also Ebola where we learned a lot about virology and the immune system response. We also developed new technologies, not just live and activated viruses

and protein products. We started looking over 12 years ago at the concept of an mRNA virus vaccine. And so all that converged in January of 2020.

This is a fascinating story, where the NIH, Tony Fauci and the group at the national Vaccine Research Center saw the sequence that was released out of Wuhan, the full length of the virus, the full sequence, 30,000 base pair. They knew from prior work with SARS-CoV-1, like you were talking about, where the spike protein region is. They saw it, they knew where the most conserved epitopes were likely to be.

They identified that. Within two days, they modeled and developed the construct of a first mRNA vaccine. Within a week, they had developed this construct in physical form, started testing it in animals and then ended up putting it into humans within two months. And then that developed onto the phase two and three studies, such that by November/December though — this was the Moderna vaccine —that was developed in two days. Two days…

Rebecca:
Days.

Dr. Saag:
…after the sequence was released.

Rebecca:
Based on prior knowledge and years and years of research. There's a lot of talk out there in the media that: Is COVID going to turn into an endemic? Can you explain what that even means?

Dr. Saag:
When transmissibility or transmission of a pathogen is confined to a local area but not widespread, that's an endemic infection. When it spreads to multiple local areas in one region, that's an epidemic. And when it goes across the entire globe, that's a pandemic. So, we're in a pandemic state right now with regard to SARS-CoV-2. As we start to develop more people who've had an immune system that recognizes it and responds hopefully, mostly through vaccine, to some degree through prior infection, the infection will ease in terms of its ability to cause bad infection.

There'll still be transmission, but a lot of it may be asymptomatic, and that's no big deal assuming that people have a robust immune response. And then you'll see hot pockets popping up here and there. And that's what we're probably going to see occurring over the next year to year and a half, assuming that another highly transmissible unique variant doesn't emerge. No way to predict that. I just think we've been through the worst of it at this point, in my opinion.

Rebecca:

Let's hope so. Does that mean that we'll probably need boosters or extra doses going forward? Are COVID vaccines here to stay?

Dr. Saag:
I think they are, for at least the next three to five years, and how often we give them we'll just discover literally together as we go. I would strongly suggest we listen to the experts like Tony Fauci and others. But I think logically it makes sense that we all be getting boosters at least on the order of six months, and maybe we can stretch it out to 12 months as time goes by.

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Rebecca:
Let's talk about antibody testing. I know a lot of listeners are concerned that they may not have produced meaningful antibodies to protect themselves against COVID after vaccination. So, what do those tests mean?

Dr. Saag:
Before we do any tests, we have to ask ourselves: What are we gonna do with the result one way or the other? To be honest, I don't know what to do with the result, so I wouldn't order the test to begin with. Complicating this: An antibody test is just one antibody test is not another is not another. The details matter in terms of what antibody that test is testing for. Is it just an antibody that we might have had in our body because of a prior cold, nothing to do with COVID?

Could it be there was a cross reactive antibody that doesn't do much for COVID but might do the common cold? You need neutralizing antibodies to be tested, not just antibodies. And neutralizing antibody tests are very expensive and requires more sophistication in the lab.

The final thing is that even if antibodies are impaired in terms of production, it doesn't mean that your whole immune system is impaired. Other parts of the immune system can respond. I would tap the brakes on antibodies for the foreseeable future until we have robust data that tells us what it means and what to do with the information.

Rebecca:
OK, that's helpful. Now what about long COVID? Who's most at risk for long COVID? What's causing it? Does vaccination minimize the likelihood of developing what long COVID is?

Dr. Saag:

Well, first let's define it for folks who don't know. Long COVID is a syndrome of symptoms that either come back or persist at least 28 days after the initial COVID illness. Take out of the equation those who have been in the ICU because their symptoms might be related to other things. I'm talking about somebody maybe had COVID at home and then their symptoms persist for well more than a month after they had their initial illness. Or worse, come back about two to three months after they had their initial COVID. And it's not a reinfection; it's not a new infection. It's actually persistent symptoms.

Think of long COVID as some sort of autoimmune disease. That's how it's behaving. And it can involve the major organ systems: the lungs, of course, heart, brain, gut. Those are the main areas. A recent study that just came out two or three days ago said the people who are at most risk for developing that are: One, people who had very high amounts of virus in that initial phase, so that's a risk factor for long COVID. People who have type two diabetes, for reasons that are unclear. The third is people who have had, during the course of their COVID illness, reactivation of Epstein-Barr virus. And then finally, those people who, during their COVID illness, produce a lot of autoantibodies. So, it could be like a rheumatologic illness, in a sense, where autoantibodies are produced, this time sparked by the COVID virus. It could be that we put people on immunosuppressive drugs, just like we do for rheumatologic diseases. But we just aren't there yet.

Rebecca:
A lot of states and areas are starting to lift restrictions and lift mandates. I know that the American College of Rheumatology recently updated their COVID guidelines for people with arthritis. What are some of those key updates that we should be concerned with? And what do they mean for our community?

Dr. Saag:
During the spike of omicron, it's important to retrench back into masking and reduction of numbers of people at events and that type of thing. Basically, this is all just common sense. As we come out of COVID, we can relax. The number to follow, in my opinion, is the relative rate of infections on a daily basis. And that metric is a number of new cases per hundred thousand in the population. It's really about your local environment and knowing what your number is and following your health officials and guidance.

Rebecca:
The risks are gonna change based on where you are and what the rates are, right? It's on us to make that personal choice of how you are going to protect yourself?

Dr. Saag:
We're gonna have to get used to the notion that COVID's gonna be with us in some form or fashion over the next several years. And so, what we're gonna have to do is get used to risk calculating what

our current environment is. And monitor ourselves for symptoms, especially for those on immunomodulating drugs. If we get symptoms that suggest COVID, get tested right away. Call your doctor. And now we have multiple interventions that can get us out of this personally and protect us from getting very sick and dying from COVID.

Rebecca:
How do we continue to protect ourselves when restrictions are being lifted if we're immunocompromised?

Dr. Saag:
I would generally still try to avoid very large crowds. If I'm in a large crowd, I'm gonna make sure, if I can, that it's outdoors and that I'm wearing a good mask, an N95 or KN95. That's the best you can do.

One thing I haven't said yet that's very important for immunocompromised individuals, especially on some treatments that impair antibody response: There's another monoclonal that's an injectable Sub-Q and it's long lasting — it's not an IV — that is called Evusheld. It's a monoclonal. It's active against omicron and it's just coming out, and it lasts for about six months. Talk to your rheumatologist in particular about whether you're eligible for that, to give extra protection to you on top of your vaccine or, in your case, your vaccine and two episodes of prior COVID.

Rebecca:
We have a lot of listeners, too, who might have kids with arthritis. For the child with juvenile arthritis or some form of rheumatic condition, or for a parent with a child in a public school: Should they continue to mask? Should they continue to be vigilant and practice social distancing and masking?

Dr. Saag:
It depends. And I go back to what I said before on how much transmission there is in the community. Right now I would think, at least where I live, when there are a hundred cases per a hundred thousand, yeah, kids should be masked in school. Kids should be vaccinated. Right now, only 20% of our kids from age 5 to 12 are vaccinated.

There are data that support that masks reduce transmission at least three- to eightfold in a school setting. But as the numbers come down, we will be able to relax, return to normal and just be watching out for any new variants, or any new endemic wildfire that might spring up, and then we call our troops in and we do what we have to do to clean it up.

PROMO:

Learn the latest about how COVID may impact people with arthritis, and get the answers you need, including information about the vaccines and boosters and how to keep yourself and your family safe and healthy. Visit our Care and Connect Center at https://www.arthritis.org/care-connect.

Rebecca:
Before we go, I wanted to see: What are your top takeaways from our conversation today?

Dr. Saag:
Number one, be informed. These podcasts and other things help. Use reliable sources and be vigilant about what's going on in your neck of the woods in terms of spikes or surges in cases and protect yourself. Two, use the science. Get vaccinated, test early if you have symptoms and get treatment for the virus, which will reduce your duration and severity of symptoms. And three, celebrate the science. Holy smokes. I mean, this is a miraculous time.

Rebecca:
Well, thank you, Dr. Saag. I really appreciate your perspective and your expertise. One thing for me about this whole pandemic that is a silver lining is: I feel like, for the rheumatology world, we've learned so much about the immune system that could only bring us better treatments for our chronic diseases and, you know, maybe closer to a cure one day. But to me, it's very hopeful. So, thanks so much for sharing your knowledge with us, and we appreciate you joining us.

Dr. Saag:
It was joyful to be with you.

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