Transcript

Kendal Williams, MD (Host): Welcome everyone to the Penn Primary Care Podcast. I'm your host, Dr. Kendal Williams.

So, we have done two sessions— two podcasts on COVID. But given what's happening in the world right now, we thought it appropriate to do another session.

And as we started to think about a guest for this session, a wonderful document came into my email from the Department of Medicine Leadership. Dr. Michael Parmacek and Dr. Charles Abrams have been sending Department of Medicine Briefings on the COVID pandemic since the beginning of the pandemic, and these have come out on a regular basis. They have a wonderful tone of collegiality and support for everyone working on the front lines.

But they also have provided an enormous amount of information. And so we really have gotten direct information about what's happening in a very practical way throughout the pandemic from our Department of Medicine Leadership. So, I asked Dr. Parmacek and Dr. Abrams to come on the podcast. And I'd like to introduce them now.

And then we're going to talk about this Omicron wave, what it means, and talk about some of the practical issues for the frontline clinicians. So, let me introduce everyone.

Dr. Michael Parmacek is the Frank Wister Thomas Professor of Medicine at the University of Pennsylvania and Perlman School of Medicine. He is the Chair of the Department of Medicine. Dr. Parmacek is a Cardiologist and was the Chief of Cardiology at Penn before becoming the Chair of Medicine at Penn. Mike, thanks so much for.

Michael Parmacek, MD (Guest): Oh, it's a pleasure being on. And I look forward to this.

Kendal Williams, MD (Host): It's exciting to you here, Mike. I hope in the future we can do more with, I think all of our guests so far have been in within to your department. So, it's really a pleasure to have you on. Dr. Charles Abrams is the Francis C. Wood Professor of Medicine and the Vice Chair for Research and the Chief Scientific Officer in the Department of Medicine. He is a Hematologist Oncologist by training and the Director of the Penn-CHOP Blood Center of patient care and discovery. Charles, thank you so much.

Charles Abrams, MD (Guest): Thanks for the invitation Kendall.

Kendal Williams, MD (Host): And we, again, bring back Dr. Steve Gluckman.

Steve, as many of you may know from the previous podcasts is the Full Professor of Medicine in the Division of Infectious Diseases at Penn. He's been a storied educator of many generations of residents and students, and really has given us a lot of wonderful perspective on what we've been experiencing with the COVID pandemic.

Steve, thanks so much for coming.

Stephen J. Gluckman, MD (Guest): Thanks Kendal. And also as a reader of this, I appreciate regular information Mike and Charles send out. It's good reading and it's well up to date.

Dr. Parmacek: Well, again, credit to Charles on that one. Cause he's the major writer. I'm just the suggester of ideas and minor editor.

Host: Well, they've been terrific. And I've been meaning to send you both an email about that, but we're going to be able to call some of that knowledge and spread it out to the broader Penn community through this podcast.

So, let me set the stage of our current situation. Before Omicron, we had Delta of course, and that had produced a wave over the summer that didn't hit us terribly hard here.

We have a situation now where a lot of the U.S. population has some immunity to COVID. So 70% of US adults are vaccinated with two doses, 23% with the booster. That's estimated that 90% of adults likely have some immunity to COVID from either vaccination or prior infection.

Unfortunately, despite the availability of vaccines to kids, there's a low rate of vaccination in children, 17% of five to 12 year olds have been vaccinated. But it's higher for teenagers at 54%, for 12 to 17 year olds.

So, so that was sort of the situation before Omicron hit us.

Omicron itself, we know now, is a highly transmissible variant. To give a sense of this, case test positivity rates for the early part of the pandemic where maybe three and a half, 4%. Now we're seeing numbers in range of 30 to 40% of people who are tested are testing positive. So, it's really out there. It does appear to be less virulent. We'll talk about how much less. I saw 25% in one study, but we're getting information on this all the time. There's less length of stay when patients are hospitalized and less ICU transfers.

It does seem to have Omicron, a somewhat different clinical presentation. The data suggests more sore throat and less effect on taste and smell. But the sheer volume of transmission has led to a dramatic increase in hospitalizations. New York City reported half of its hospitalizations were for COVID a couple of weeks ago.

And at Penn, hospitalization numbers appear roughly double what they were in the spring of 2020. So that's just some broad sketches of where we're at right now.

I'm going to now sort of put the question out there and I'm going to start with Mike.

How are we doing at Penn here now, Mike?

Dr. Parmacek: Well, things are better this week than they were last week.

It's fair to say that this is not how I wanted to spend my holiday week vacation. Unfortunately, what we really saw happen could not have happened at a more challenging time.

Prior to this wave of COVID, you all heard about the great resignation and our staffing has been impacted dramatically across the nation.

The statistics show that the healthcare industry, not surprisingly, has been disproportionately impacted by the great resignation and our staffing for nurses, respiratory therapists, infusion techs, has really been dramatically impacted, reducing our capacity to care for patients.

On top of that, literally in Philadelphia, the numbers started rising the day or two before Christmas and continued to rise until about a week ago.

The week between Christmas and New Years, we were seeing an increase at our three downtown hospitals 40 to 50 patients, inpatients, per day. And this was really challenging to accommodate, but as I told everybody, I've never been prouder of our department and our health system because people really stepped up in a big way.

And it was really the residents that were the heroes of this, the APPs, the hospitalists. And the intensive care doctors, as well as a number of specialists, ID doctors, pulmonary, critical care. It's amazing.

And I am so proud that we have always accommodated and cared for the patients. And when I compare our outcomes data for what it's worth, to other systems across the country, they're at least as good if not better. And I attribute that to a remarkably talented and dedicated staff.

Now to your exact question: The numbers seem to have peaked about a week ago, and we've been reducing the number of inpatients, interestingly, differentially across the health system. Pennsylvania Hospital has come down rather dramatically in terms of the number of inpatients, HUP has come down more slowly as has Penn Presbyterian.

But we are seeing declines at all three places and we're in a much better place than we were a year ago. Now a lagging indicator has been the number of admissions in the intensive care units. That number has not come down significantly and is pretty flat. That's consistent with all the other waves. The number of really sick patients tends to lag and tends to be prolonged leading to longer length of stay for those patients. Our hope is that, that will start to decline.

If I had to predict, although I've learned every time, I predict I'm wrong, my guess is it will start to decline in the next week or two in the intensive care units. But we still have a lot of patients at our three downtown hospitals. It's just a lot better than it was a week ago.

Host: I wonder if some of the differences are due to the hospitals who do the patient populations they serve. I think Presbyterian's a little older population and so we might be seeing them lag a little bit more and getting placements back into the home and so forth.

Dr. Parmacek: Well, as Charles knows, we actually debated this. What was the cause of this? And our best theory is that the number of patients that were hospitalized and vaccinated, Pennsylvania Hospital was higher than it is at HUP and Presbyterian. And at HUP in particular, we have a high number of immunosuppressed patients.

So, we think that to your point, the patient populations define it, but vaccination, I can't stress this enough, it's the most important thing everyone can take away from this is it's important to get vaccinated and boosted, if at all possible. That reduces your risk of being seriously ill, more than anything else.

Dr. Gluckman: Many people have called this, the epidemic of the unvaccinated. It's true. And I guess immunosuppressed, but that's a small number. If you look at the population of people in all hospitals, the vast majority are people that are not, have not been vaccinated. And our numbers have dropped. They've dropped by about 25% in the last week. Actually. That's pretty impressive.

Host: So, what do you see as the short term? Let's just talk about the short term issues of this, we're peaking and now we're coming down. Nobody has a crystal ball, but do we think the next four to six weeks, we'll be seeing this kind of slowly coming down or how are we thinking about this?

Dr. Parmacek: Well, I'll let Steve or Charles, they are much more on top of the epidemiology. They may want to make their predictions. Every time I predict I've been wrong.

Dr. Abrams: Through that, if you look at initially South Africa and then you took a look at the UK and in the states, you took the look at New York and Boston, and more recently DC, it went up like a straight wall. And have been coming down pretty fast. None of those locations that I've mentioned have come down to the baseline, the number of cases they had before the epidemic came.

But it does look like Omicron is unless we call it a wave or a sheer face, but looks like it goes up and comes down faster than the other waves that we've seen. And so I think hospitalizations are down. The number of cases in the area are down. Mike's right. We're probably going to see a continued rise in ICU cases for a little while, but I think this is all gonna play out over the next couple of weeks. And I think we'll get a respite for a while.

The big question is really, what's it look like beyond that? Or are we in store for more waves or are things going to kind of settle down for a while?

Dr. Gluckman: Yeah, I'll put my nickel down. It's going down. It's going to continue to drop rather dramatically. And unless we have another problematic variant, I think, things will be much better in several months. The problem is this variant.

Dr. Abrams: You know, Steve, I think you're hitting on the right point as to is there going to be another variant or did Omicron immunize enough people? That it's gonna kind of settled things. You know, Mike and I had this discussion a couple of days ago. And I think Omicron was kind of a fluke. A prize that a milder variant took over so much when the virus was spreading so easily without having the advantage of a milder variant and people going and

spreading the virus.

And so, there will be more mutants. The question is, will they look more like Omicron or are they going to look like Delta or something that we've never even heard of before? And so, predicting the future, it's just really tough.

Dr. Gluckman: I know we're preaching to the choir here, but the way you don't get mutants is to not have the virus replicate. And that means vaccinations.

Dr. Parmacek: And let me, Steve, let me just say the real opportunity is young people. Now, the statistics that Kendall gave out with young people really under 20% vaccinated, that's the real opportunity. And just as a side note, one of the biggest challenges we faced, our faculty who have called in because they've been either sick or exposed and the preponderance of those exposures, are when people are exposed to their own kids who are infected. So, we should really concentrate on getting kids and teenagers vaccinated. It's really important.

Dr. Abrams: Yeah. Well, I agree with you, Mike, but this is a worldwide problem and I think it's 40% of the world has gotten at least one dose of one vaccine, but we're nowhere where we need to be.

Dr. Parmacek: No, your point's well taken. We have to distribute the vaccine to the world and we have to concentrate on that. Your point is well taken.

Dr. Abrams: Yeah, I mean, I don't want to blame any country, but all of these mutants are coming from all over the place. And yet some came from California and we have some that looked like they may have come from our area, but this is a worldwide problem.

Host: So, let me ask a question that you addressed in one of your recent briefings and that is this issue of sort of natural immunity that develops after infection and whether Omicron is going to be immunizing those who didn't get immunized through the vaccine. And whether or not that could be one of the forces that improves our situation.

Dr. Abrams: Yeah, well, I'd be happy to start the discussion on that and say that I don't think any of us really know. I mean, there is evidence that people that received their immunity from COVID infection have a decent amount of immunity probably approaching that of vaccination. And so there's been this wish that maybe Omicron induced immunity will be like Delta or alpha immunity. And I don't think we know that. I mean, clearly Delta immunity was not enough to protect you from Omicron. And so, what will the next wave look like?

Will it look like Omicron, and if that's the case, then all those people that got Omicron should be in really good shape. But if it looks like something else, they may not have all that much protection.

Now I do think that when we talk about immunity, a lot of the times we're talking about the antibodies. And those are very sensitive to the mutant they have, but we do have T-cell immunity and that tends to kick in a little bit later in the infection process.

And that's much more resistant to the mutations. And so it's possible that people that have some immunity will be protected against hospitalizations or death but not so much against

getting infections that make them symptomatic but out of the hospital.

Dr. Gluckman: Another way to emphasize that, and patients ask us this, we really don't have a good way to determine how protective somebody is. An individual, we don't, we can't measure enough to give them the reassurance they need. We can just encourage them to get vaccinated because that's the best we can do at the moment.

Dr. Parmacek: Yeah. And Steve, just to highlight that, one of the greatest misperceptions in the community, even in the medical community is that in vitro antibody levels are what determines immunity. And there's a lot more to it than that.

And in fact is, as Charles just pointed out, the T-cell response in terms of the memory cells, in terms of recognizing different variants may be equally or more important. And that's very difficult to measure.

Host: So, the most positive thing that I've seen in data in the last several months has been the overall effectiveness of the vaccines for Omicron in prevention of severe disease. And how well actually the population seems to be, that the vaccinated population seems to be doing in relation to Omicron because of the vaccine.

And we highlighted this a little bit in our last podcast, going over the risks of death, if you were vaccinated versus unvaccinated, versus some of the other risks that we face in our world. But the data continues to come in about the extraordinary effectiveness of the vaccines.

I found some humor in or some insight from a comment from the Alberta study that was done in Canada that said in summary of their data, they said that vaccinated 80 year olds had lower rate of hospitalization than unvaccinated teenagers and young adults in their population that they studied compared vaccinated to unvaccinated. And we're really just, you know, I've seen so many of these graphs. I don't even need to look at another one where you look at deaths or hospitalizations or any measure of severity, And you know, they're going up with unvaccinated individuals and they're sort of, you know, trickling along, the X axis in vaccinated individuals.

So, there's a dramatic difference. It does appear that the effectiveness of the vaccines and even COVID infection itself wanes over time. So we know, the Pfizer vaccine for instance, was 90% effective, a couple of weeks after getting both shots. And then at six months was 60% effective in reducing symptomatic disease. But that with the booster went back up to over 90% to 93, 95%. And Moderna, and Pfizer were very similar. Moderna appeared to do a little better actually, but both with boosters were hitting 95% in terms of reducing symptomatic infection. So, that's been, I think one of the most positive things about this. Would you all agree?

Dr. Parmacek: I don't think you can emphasize enough how important vaccination is.

And one thing, as long as I'm on the podcast and I can put on my Cardiology hat, one of the most misrepresented arguments against vaccination has been the risk of vaccine induced myocarditis. And that risk in very well controlled studies, the best possibly being an Israeli study is the risk of vaccine induced myocarditis is about two cases, per hundred thousand

people vaccinated. Moreover the disease is almost always mild, reversible and really of little consequence.

The chance of having myocarditis following COVID infection is close to 150 cases, per hundred thousand people infected with COVID. So, it's about a 75 to one ratio in favor of getting vaccinated to reduce the risk of myocarditis. So, that argument that I don't want to subject somebody to myocarditis is just a flawed argument because the risk of getting myocarditis is much, much higher if you're infected with the virus.

Dr. Gluckman: Agreed. In fact, you could say that about every occasional complication of the vaccine. The risk of getting that problem from the disease itself is much higher. It doesn't matter what complication you pick.

Host: So we now have four populations of people in the world really. We have the unvaccinated, we have the vaccinated with two doses, the vaccinated with three doses and the immunocompromised, and there seems to be, you know, almost an increased risk with each of those.

Although I think Steve, we need to talk about the immunocompromised because that's a major concern of our patients who are on immunocompromising drugs or have immunocompromising conditions.

How are you thinking about the risk for the immunocompromised who have been vaccinated and maybe even fully boosted?

Dr. Gluckman: Well, the first thing to remind people that being immunocompromised is not an all or none phenomenon. An easy example is HIV.

If you have HIV, but your CD4 count is 800, you're really not immunocompromised. And if your CD4 count is eight, you absolutely are. But what if your CD4 count is 208? You're a little bit immunocompromised. So, it is not an all-in-one phenomenon. And we do use that.

The people that we're most worried about are the people that we have the proper, I think perception are severely immunocompromised, the bone marrow transplant patients, people with liquid malignancies. Solid organ transplant for that matter. And that's different than somebody with a CD4 count of 208 or 250. So, it requires some clinical judgment. And until we have enough of treatment options for everybody, that clinical judgment is clinically relevant.

On the other hand, there's absolutely no concern about potential side effects, vaccinating somebody who's immunocompromised. These are not live vaccines. They may not work, or they may not work as well as you like, but there's no downside. So same thing, get vaccinated.

Host: Charles in your population, you know, you're a Hematologist Oncologist, because of the nature of the diseases, but also the nature of some of the treatments, you see a lot of patients who have immune system compromise. What are you seeing in your population?

Dr. Abrams: Well, I am trained as an Oncologist as well as Hematologist, but my practice is purely Hematology. But I see many patients that ask me this question. A lot of them are immunocompromised. They're not as severely immunocompromised as those that are cared for by my colleagues who are bone marrow transplanters.

But patients who gets rituximab and other B-cell toxic drugs are definitely worried. I have not seen a huge group of those patients who have even gotten COVID end up in the hospital. And so that would be consistent with what Steve was saying earlier that there are degrees of being immunosuppressed.

But this is a disease that can affect everyone no matter how careful you are. And so, we're just going back to what Steve's emphasized before, that we just need to vaccinate everyone who's willing to be vaccinated.

Host: So those who are immunocompromised, won't be exposed to people who have a high level of viral replication.

Dr. Parmacek: Yeah, vaccination helps the community.

Dr. Gluckman: It's public health. It's not politics.

Host: So, the next question I think that we'll be facing here in the next couple months is the question about whether or not we should be boosting with a fourth dose.

Israel has gone forward with the vaccination program to boost with a fourth dose in their most vulnerable. And I think we're starting to get some data from the results of that. But what do you all think about that?

Dr. Abrams: Well, you know, there was two articles that made it seem like boosting may do some good. But just as recently as yesterday, there was another report, that the effects are really quite transient.

So, our colleague, John Wherry, who's head of Pharmacology has some very interesting data that has looked at the immune response after the first dose, after the second dose. And then after a third dose. And if you recall there both T-cells and B-cells and B cells are the ones that make the antibodies and this T-cell response goes up really it just sort of peaks about two months after you get that first dose, pretty much stays up for months and looks pretty stable after that. The antibodies go up, then they start to come down slowly and you get another shot.

And it goes up higher and it starts to come down slowly and they continue to go down over the next couple months like they do with every other vaccine that we give. And then if you give a booster shot, they go up and they start to come down slowly again at the same rate that they were coming down after the first two shots. And so if you're not going to be able to give a vaccine where you give a third shot, a forth shots and that's it, and you're set for life, this is not. You're just not going to be able to give a vaccine that's going to keep the antibodies up and so what that means, you're not going to get a vaccine where you're going to be able to prevent people from having very mild infections from ever getting infected.

I'm paraphrasing Ali Guevara's Paul Offit from CHOP. And Paul said, if your goal is to give boosters, to keep people from ever getting infected at all, you're going to be boosting till the day they die. I think for now, anyways, three shots, like it's good enough. And maybe once a year we'll be getting a shot with whatever variant's around, just like with the flu. But right now, I don't think there's sufficient evidence to suggest a fourth booster shot.

Dr. Gluckman: Yeah, we might be boosting for variants sort of analogous to flu. But as you properly said, Charles, when you vaccinate somebody, the antibodies drop afterwards. You know, in general, nice animestric responses, you're not left unprotected. You just have levels which are lower or occasionally even below what you can measure, but it doesn't mean they're not going to bounce back up.

Hepatitis B is a good example of that. A lot of people who've been properly vaccinated, they don't have measurable levels, but the presumption is they're still fully protected. And I think it was emphasized all of our eggs in the antibody basket, it's something to measure, but that's not the be all and end all of this.

Dr. Parmacek: Just to call out to our colleague, Drew Weissman and Katalin Karikó, who also was at Penn who developed the mRNA technology, that both the Pfizer BioEnTech and Moderna have used for their vaccines. There is the opportunity to more quickly adapt a new vaccine to a variant than there ever was in the past using older methodologies.

And just to the audience, one of the really exciting things is Drew is currently working on a panCoronavirus vaccine that hopefully would work against future variants, but that's just a work in his lab at this point. We'll see if he can pull it off.

Host: So, new thing that's happened in the last few months has been the appearance of new therapeutics for COVID-19 infection. The big one is Paxlovid, the Pfizer drug, but there are others out there.

Let me just go over these quickly and then we'll talk about them. Actually, there was a wonderful Department of Medicine brief, just put out this week that goes into great detail on this, but Paxlovid, it is Pfizer drug five days of PO treatment at a cost of $700 led to an 89% reduction in hospitalization.

Currently, it's not very available. It's approved, but the production of it has not kept up with the need, which is enormous, obviously. It'll take six months to make 10 million doses is the estimate.

And then of course we have the other one the molnupiravir, the Merck drug which is not as good as the Pfizer drug, but we can address that. There's also remdesivir, which we've been using for inpatients and have some benefit is now in a New England Journal Study has been shown to have some value in outpatients as well. So, three days of remdesavir, that's IV did reduce the risk of hospitalization 87%.

And then, you know, we also have the issue of the monoclonal antibodies, which were limited in Omicron because of their lack of effectiveness. But now we're starting to get ones that can be used for Omicron.

So, what is your perspective on all of the therapeutics that are now out there? Charles, maybe I'll start with you.

Dr. Abrams: I think it's amazing how many new drugs come out and have shown activity. And even when new mutants come out, how many more drugs are coming out and there's more in the pipeline.

Something that looks very promising is asubavex, which is a new class of drugs called a DARPin type of drug. And what that does is it binds to the spike protein, just like an antibody would and gums it up so that it can't attack a cell.

So, that's currently being requested for emergency use authorization at the FDA. I think it's astounding. I mean, we have antivirals, we have antibodies, some of them can treat an acute infection. Some of them last a very long time, perhaps six months. And can be used prophylactically in high risk patients.

And so the pandemic has been awful and it's done so many terrible things, but science and our colleagues have really stepped up to the plate and everyone's trying to help here.

Dr. Gluckman: I agree. We have now several very encouraging treatment options and one prophylaxis option. But each one has its issues and the generalizable issue, is it just very, very hard to find them. Now hopefully over the next month, two or three, that part will go away.

Paxlovid looks spectacular. And it is effective against Omicron. At the moment because it's not an FDA approved drug just as an EUA, it's not allowed to be used in the hospital, nor is it allowed to be used for prophylaxis. So, it is a drug that will clearly markedly the decrease the hospitalization risks in somebody with clinical. Monupiravir is probably not going to be the drug. It's not as good. And it has serious concerns in pregnant women and in children with teratogenicity. Remdisivir, which is the only FDA approved drug on the whole list. Hence it could be used off-label without getting in trouble but it is only IV and that means you have to have a really robust.

If you're really going to try to use this on a lot of symptomatic patients, you need a very robust setup to give intravenous infusion and it's three days. So, it's not a one dose deal.

Monoclonal citrozimab, is the only monoclonal that is effective against COVID. The prior monoclonals are no longer effective and in fact, they're not an option at Penn, at least, but citronomab is theoretically, just a few doses basically. And it's a very limited supply and it is also IV, but it's only one dose. And then there's also a prophylaxis option for people that have either pre or post exposure, but have not gotten sick.

And that's Evusheld. It also looks very good, but there's incredibly little of it around. And there is at least, I don't know if Mike has a comment and there is at least been a wrinkle of a concern about increased risks of MI and heart failure. I don't have any idea if any of that's true or not.

Dr. Abrams: You know, all of these antibodies have been clouded a little bit about whether it's in ICU patients, whether they could increase your risk for MIs.

I think Evusheld is, it's like this fascinating, long-lasting antibody that's tantalizing. It's not as active, at least in the test tube against Omicron as it is against the Delta and the Alpha, but it does still have some activity.

Citrozimab though does look very active against the Omicron variant.

Dr. Gluckman: It's not for prophylaxis at the moment because it has an EUA and you can't do it legally. You can't give it for prophylaxis. In fact, can't even give it as an inpatient legally.

Dr. Abrams: Yeah. And it has usual short half-life, but it hasn't been modified like Evusheld.

Dr. Parmacek: Just to again as the not qualified to comment on this person, I will, anyways, and to me, Paxlovid seems like a game changer, if we can make enough of it. The one issue though that I don't think has gotten enough press and Charles brought this to everybody's attention, is because it's metabolized by the cytochrome P450 system, there is a huge number of drug interactions.

And in fact, Charles and I were talking to Lee Goldberg who runs our heart transplant program. And Lee pointed out that they'd already had complications in immunosuppressed patients who had taken Paxlovid.

So, just a cautionary note, and it's not just rare drugs. It's things like statins. So, drug interactions are critically important to think about before you prescribe Paxlovid when it becomes available.

Dr. Gluckman: It's the ritonovir component primarily.

Dr. Abrams: Yeah. Yes. But you know, a big issue that we touched on is the disparity of this whole situation. I mean, here we're talking about drugs that are very hard to get and some people are getting them and most are not. And so Paxlovid could be a game changer throughout the world. But I'm not sure it ever will.

Host: Steve, you may have answered a question I had about Paxlovid because from a public health perspective, if it's such an effective drug, you would think that you should give it to the portals where they have the sickest patients, you should give it to emergency departments and other places, not to commercial pharmacies where there's no gatekeepers to who's really getting it.

You may have patients who've been boosted and vaccinated who just have the sniffles, so are getting Paxlovid, whereas other sick people are not. And, but I guess that's just the nature of the FDA approval, right? That it has to be outpatient.

Dr. Gluckman: That's correct. And it's only been given so far to commercial pharmacies and I echo what Charles is getting at that makes me very nervous that the people who are going to get to the front of the line are people who aren't necessarily the most needy. They're the people who have the resources. And that's just not good. That's not what we should espouse in this country.

Dr. Abrams: I agree with you, Steve. You know, I think moving it to the pharmacies wanted to widen the distribution. So, in a sense, you could argue, well that should increase access and it's not just people associated with elite institutions that are going to get their medications.

But the problem is that when there's not much of the drug to go around, some people are just have ways of working the system better than us. And so it a terrible situation.

Host: It's like the early days of the vaccination program that people who would be up till three in the morning, looking for a spot, would find a spot, but the average person was having trouble.

So, Steve, just to close the loop on the monoclonal antibodies effectively, there's no program at Penn right now for them to be done as outpatients. Is that correct?

Dr. Gluckman: No, that's not true. Sotrovimab, there is a program at Penn. It can only be given to outpatients and it's given to people with mild disease. Has to be given within five days of onset and where they have a terrible, underlying other problem, like a bone marrow transplant. There's precious little of it. And there's actually a panel of experts that sit in judgment and decide if somebody is sotrovimab worthy. Which sounds terrible, but I don't know that anybody else here is old enough. That was exactly the way renal dialysis was originally done that there wasn't enough. So, hospitals had panels that would decide this person is dialysis worthy, and this person, we don't have the room.

So, Penn theoretically has the drug. I don't know how many doses, but not much. So, if you have a patient who's has mild disease and is markedly immunosuppressed it's worth pursuing.

Dr. Abrams: I heard that it's sort of a weighted lottery system and so people are judged, but…

Dr. Gluckman: That's exactly right. It's a double thing. You get judged and then you get thrown in a lottery. It's the best you can do. There's no criticism about that. It's just not very much of it. And I've been told, I've not experienced this, that the actual paperwork involved in this is incredibly onerous, hours' worth of paperwork.

Host: So, it's probably not practical to even give guidance to a primary care audience on how this could be done. This would be mostly through the subspecialists that are caring for those patients that would get some experience in ordering it, right?

Dr. Gluckman: Oh, I don't think a primary care, should they have something else to do, I think they don't have the time to do that, but they're going to identify these people probably because you're looking for, you can only be given as an outpatient. You're looking for somebody who has mild disease, but it has condition which, puts you at great fear that they're going to progress.

So, it might be somebody who walks into a primary care office although I suspect, as you said, most of these people are already being followed by specialists. And hopefully the patient will find one or the other either the specialist or in the primary care person. The actual getting of it is going to be, I think the specialists.

Host: So, we've talked about the new therapeutics. There are some of these repurposed drugs that have been used obviously, internationally azithromycin, hydroxychloroquine, ivermectin and, you know, we're starting to get some data in it. It does look like fluvoxamine may have some value. I know there was a study in Brazil.

Steve, you may have seen that and have some thoughts on that, that suggested that drug may have some value.

Dr. Gluckman: I agree with what you said. One study may have some value. I get a lot of phone calls about it. I'll tell you that. I'm not, I've not prescribed it.

Host: In the last minute here, let's just talk about the new CDC guidelines on getting out of isolation. Right. And they were somewhat controversial. The CDC standard now is five days. If you have had clinical improvement and no fever, you do not need testing to complete isolation after infection with Omicron. Steve, any thoughts on..

Dr. Gluckman: It's based on science. How's that? Yeah, and I totally agree with not doing testing because these tests, which of course, whether you're doing the rapid test, PCR, don't represent live intact virus and they can stay positive in some people for many, many weeks. And in somebody that doesn't understand that, these patients can be continued in isolation or deprived from going back to work and those sorts of things.

So, the simple way to avoid that is if you got better, you're done. You don't get retested. Now I realize some institutions require it. That's a different issue, but if it's not required, you just going to complicate your life if you get retested.

Host: And Mike, our standard here at Penn for employees who become positive is just that standard?

Dr. Parmacek: Well, that's the standard, but there are the vast majority of people actually are getting retested whether that's required or not depends on their particular job, but I can tell you unequivocally that almost all of our house staff who have gone out, have wanted to be retested and have gotten retested. And the only thing I would say about that, cause Steve's right, is you can be test positive for a variety of reasons is at least the antigen test, the rapid test is a little bit less sensitive to that. And if you're going to be retested, that's the one to be retested with.

Host: So, at the end of our podcast, we always put it out there for any closing thoughts to the primary care audience from each of you, any closing thoughts on where we're at with the pandemic?

Dr. Parmacek: Well, Charles and I are like Frick and Frack. Charles points out the stark reality and the science of the whole thing. And I am a unblinded optimist. So, I want to believe that once we get beyond this wave that it's not going away. I'm not that blind, but that things will get markedly better. And that if a new variant doesn't emerge, which again, I don't know with certainty it won't, that by the late spring, life should be getting a lot more back to normal, but that's just my perspective. Charles may want to take the other side of that.

Dr. Abrams: I hope you're right, but I'll say during this pandemic, medicine has been an experience that reminded me of why I went into medicine to begin with and the way my

colleagues have marched into work every day to do what had to be done even during those early days, when everyone was truly scared about what this is going to mean for me, has just been remarkable. And it's been a moment where you realize that medicine is really a noble profession.

Dr. Gluckman: Well said. By the way, I agree with

Host: I agree with them too. And I emphasize that point. I've never been so proud as I've been the last year and a half to be a doctor. I think that what we're seeing in terms of the therapeutics and the vaccination is really a triumph of science akin to anything that science has ever accomplished. So, there's a lot of very positive lights that are coming out of this pandemic.

And so hopefully we will, in a few months, be out of this thing and for those who would get infected, we'll have effective therapeutics and it'll become just like any other disease we treat. So, let's hope we're there by summer.

So, with that, I want to thank you all for joining. It's been a wonderful discussion and to the audience please send me any questions that you have or any concerns or any issues that you'd like to be addressed on future podcast.

Thank you all for joining.