COVID 19 pandemic is here. What to expect?

COVID 19 is now a global pandemic.The cases of coronavirus are increasing rapidly across the world with the count crossing 246,005 globally and increasing every day. The virus, which originated from China, has rapidly spread to about 160 countries.

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This is a critical time for information, support and reassurance that science and evidence can offer.

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We are talking to infectious disease expert Dr. Steven Pergam on where we stand and what to expect in terms of safety for immunocompromised patients, effectiveness of social distancing, preparing and responding to the pandemic in our daily lives.

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Full Transcript:

Priya Menon: Good afternoon everyone and welcome to CureTalks. I'm Priya Menon and your host. Today on CureTalks we are discussing COVID-19 pandemic and what to expect with infectious disease specialist Dr. Steven Pergam from Fred Hutchinson Cancer Research Center. Talking to Dr. Pergam on the patient panel are patient advocates Gary Petersen, Jack Aiello, Cynthia Chmielewsky and Yelak Biru. Now to get the discussion started, we have with us Dr. Steven Pergam, associate member of Vaccine and Infectious Disease division and Clinical Research at Fred Hutchinson Cancer Research Center, Dr. Pergam, first of all, I want to thank you for coming on our show to inform and educate us today.

Dr Steven Pergam: Well, thank you so much for the invitation. Really appreciate it and hope we can be helpful.

Priya: Dr. Pergam, as we all know, we have a pandemic on us and we are scrambling. So there is no current proven treatment or cure for COVID-19 and scientists around the world are working to find one. So what are some of the drug names that are floating around and what do we know about them?

Dr Steven Pergam: Yeah, that's a great question. So one that has been talked about probably the most in the media recently is the drug hydroxychloroquine. Hydroxychloroquine is a drug that's usually used for Systemic Lupus Erythematosus and rheumatoid arthritis amongst others. It's also a drug that's used in its chloroquine form more frequently for prevention of malaria. It's been a drug that has had some evaluations in the past for other viral diseases. And it looks really good in vitro meaning in sort of the lab, but actually in

clinical scenarios, maybe not quite as dramatic. And so I think many people are kind of waiting for major clinical trials to sort of come together to determine if this is really effective. There's been some concern, as there's been some national media that have really promoted this as a potential pathway. And I think what we don't want is we don't want people to rush out and buy this at the pharmacy.

And there's a really interesting trial that's going to be happening here at the University of Minnesota, in the United States where they're actually evaluating this and people that have either been exposed or have early symptoms amongst normal otherwise healthy people to see if that actually has a benefit but I think it's still an unproven therapy unfortunately. There is a small study on comparing people that did get hydrochloroquine and with the addition of a drug called azithromycin. It was done by Didier Raoult and colleagues in France. It's a small study of about 30 patients and it looked like there was potentially a benefit of that combination trial, but I would caution anyone to believe that that's the definitive answer. I think we need really good randomized clinical trials to really identify what's going on. But the example I've given in other situations is the drug called Kaletra, which is a combination therapy for HIV was thought to potentially be effective in the lab and got rolled out in many locations around the country, and people were scrambling to get the drug.

But a recent clinical trial came to us through China that did not show us effectiveness. So that's kind of fallen out of favor. So I think we need to be cautious about all these different agents that are talked about early. The ones that I think are most potentially exciting is there's a drug called Remdesivir which is a drug that's produced by Gilead. And there is an ongoing randomized clinical trial for patients with some more severe disease, they have to be hospitalized and on oxygen to be eligible for that trial. Previously it was being given, you could get it through a couple of different mechanisms. But now it's only through the NIH trial. And that I think the early data looked promising in that, but that, again, is still ongoing. So we'll be waiting to see what the results look like from that.

There's a new drug and that is being investigated in Japan, which is not currently available. There have only been some early reports in the news media about it, but none of us have seen actual data. And I believe the name is (not-audible). I am probably mispronouncing that in this delegate, but there's too many names out there. But that's another one that's being discussed on a couple of different levels, but we haven't actually seen much of that data yet. And then there are some other aspects that are interesting. So there's a drug called Tocilizumab which is an IL-6 inhibitor that's used primarily in cancer therapy that has potentially some have thought that this might be beneficial in preventing some of the really severe pulmonary complications late in disease. But again, very small studies, need more data and it's an incredibly expensive drug, so very hard at the moment to consider that as a worldwide usage. And I think not enough data to suggest that it's useful for all patient populations, and certainly not for the person at home.

And then I think what's most probably the most promising of all is people with convalescent serum. So what you can do in patients who have been exposed, those who've had COVID-19, if documented, COVID-19 have recovered, their serum and then do passive transfer of that serum to patients who are really ill, that provides an opportunity to potentially treat patients with preformed antibodies, and that might really help them. And there's been a lot of data with other viral diseases that has shown a lot of benefit from that regard. So that is probably the most exciting. There are another group of agents that are being worked on and those are specific monoclonal antibodies that people are focusing on specifically for treatment, they're being developed to target the virus. There are other agents that are out and being discussed which are sort of homologues for ACE2, which is the primary receptor on in the body for COVID-19. But those are all early in the process. And none of those are really at a place where they can have widespread use. So really, the answer is we don't have a proven drug yet. And so the best approach to prevent COVID-19 is to not to really work on social distancing, washing your hands and then staying away from getting it in the first place.

Priya: So, Dr. Pergam, how long do you think it's going to take for an effective treatment to come through at your optimist best, that is, and I will also want to plug this with one of the audience questions that came in asking which antiviral vaccines may be available if this returns next fall?

Dr Steven Pergam: So let me take the first question first, how soon can we have a trial that shows an effect? I think that there's so many cases that are developed around the world at the moment, clinical trials are enrolling rapidly. That's a matter of getting those trials analyzed and presenting your data on a national level and an international level. And what's been really wonderful about the experience if there is one good thing that's come out of this is how much research has been produced around COVID19 so quickly. So the rapid dissemination of information through preprint articles and word of mouth has been very important. And so I think some of those early data will be quickly presented. Journals like the Lancet, or the New England Journal or JAMA are really ready and prepared and getting fast turnaround for reviews to get these trials into public record so that people can use them to make treatment decisions.

My hope is that sometime by maybe the end of April, early June, we'll have some early results from some of the data from China regarding the rest of the trials that they've done, there will be additional data on hydroxychloroquine and other combination therapies or combination therapies including Remdsivir and hydrochloroquine that will be coming out from China and other locations like Italy. There are a lot of ongoing trials in those areas where there's a large amount of disease and hopefully some of those will help inform what we're doing for the next few months. So that would be potentially the best case scenario, it might take longer than that. But that I think is what many of us are really hoping that we'll get some, some hint of what might be effective. I will warn people, it's possible that all of these therapies that we've been talking about at the end of the day don't show much benefit. Antivirals are more difficult to produce than antibacterials in many ways. And so it does take a little more time and a little more, a little more effort to sort of put them together. So it may not be immediate.

In terms of vaccines, I think most would argue that in a best case scenario, we might have a vaccine in maybe a year or a year and a half. There is at least one vaccine trial that is ongoing. There are others that are planned, on there's a company called Moderna, which is doing a vaccine trial with an RNA based vaccine But a lot of these are very early in the phases. Vaccine trials in general are incredibly time consuming because they have to demonstrate efficacy. They have to demonstrate safety and there's a rigorous process to get vaccines approved. So my expectation is a best case scenario with a vaccine is a year and a half, and that would be moving the process quickly. So I think we need to be focusing on prevention – again, because that's going to be really important. So I would love to have something earlier than that. I think that's probably being realistic.

Priya: Thank you, Dr. Pergam. I'm so I'm just going to hand this over to Gary Petersen so he can start with the patient panel as well. Gary, you're on air, please ask your questions.

Gary Petersen: Yes. Thank you, Doctor very much for a couple of things. The first of which is – The first patient actually landed from China to Seattle Tacoma International Airport on January 15. So you have the longest experience and all of us on this panel have defeated to some extent a terminal cancer and as a result we have immune systems that are very, very badly compromised. So I would like to know if you had a lot of experience with the Seattle Cancer Care Alliance with people with immune systems that have been compromised. And given that are there things that can be done for that set of people who get the disease that can help them improve?

Dr Steven Pergam: So that's an important question. Some of our goals in the way we treat patients here is we have a really robust system of infection prevention, to hope that we don't get patients that are infected in the first place. And although we've had cases that probably have been in the community, and there's been some spread at some level, a lot of what initially happened was it was not detected. So we had a patient come in January, but we were not seeing large components of community spread in the early phases. So only recently in the past four weeks or so, we've really been in a situation where there's been community transmission more prominently. At the moment, we have not had a large number of cancer patients who've been infected and we've seen so far a variance in what they look like. We've had some that have come in very ill.

We've had some that have come in with mild symptoms, and we've had some that have recovered. So it

kind of depends a lot, as you can imagine, cancer is not one particular illness. It's a varied mix. It's the people on therapy. It's people who've read recovery. It's people that have transplants, it's people that have hematologic or bone marrow cancers, and so it's quite different. And the level of immune suppression is varied amongst those groups. So it may be very different. The other thing that clearly we know is a risk factor is not only having potentially a cancer, a malignancy, is also the things that come along with it. So often, we see this in people that are older, people that fit the age criteria that would put them at higher risk for developing complications from COVID19, being 65 and older for sure, people that have another organ dysfunction.

So either lung disease or heart disease or kidney disease can also increase your risk. So I think the combination in my view is really what puts cancer patients at most at risk is that common combination of comorbid problems, things that they have in their health history, beyond their cancer, the addition of immune suppression or the cancer itself, and then age which oftentimes is associated. So I think, right now, unfortunately, my colleagues in New York are probably seeing a lot more of these cases and have more experience about the variety of what they're seeing, because it's transmitting much more prominently in those areas. But I think for us, it's been really trying to identify these patients early and watching them very closely. What we do know is that patients who develop this particular illness can present with mild symptoms initially. So it's important to reach out to your physicians and talk to people ahead of time to call ahead to your clinics.

If you have fever, if you have a cough, notice shortness of breath. If you have, you know, a new onset diarrhea that's really unexpected and not related to one of the medications you're on. Or if you are developing a sort of general sort of muscle aches and really profound fatigue that is not expected. We've seen some patients present with headaches and there's a whole variety of complications, but usually a couple of those symptoms together would be something that we would recommend at least telling your team, I think I might have something going on and let them sort of walk them through the next steps because sometimes the best thing to do is not go directly to your clinic, but to stay at home and see how those symptoms progress. If it's really important for you to be seen, your cancer doctors can advise you the best way to do that safely. So if you are infected, you don't infect others during your arrival on your evaluation in the clinic or in hospital space.

And if you are feeling sick enough that you're feeling very short winded, and you're really concerned, you have a fever and you don't have adequate cells to fight infection. And that would be a time when you want to call ahead to the emergency room or your care team and say I need to be seen right away, and they can help you sort of sort through that process. So there's a lot of different ways to do that. But I think, our estimations and our thoughts are that patients who have cancer who developed this will develop more severe complications. Because, in general, what we've seen is that if you're older in your 70s and 80s, and you develop complications, we know that people as they age, develop more immune deficits. There's a particular condition called immune senescence, where your immune system is a little, it's sort of ages along with you, and so it doesn't fight infections as well. And our assumption is that, if that's true, that that's the population that's getting very ill, that it might be that as people who don't have adequate immune systems get these illnesses, they will get more sick.

So I think the key pieces, again, is just sort of watching yourself, watching your symptoms, talking to your teams, and letting people know ahead of time before you come into the clinic. I think those are really important concepts to get across. And we can talk about prevention strategies in a moment. But I think those are some things that I think are the most advantageous and what we're really worried about is people developing pulmonary complications. We've seen some patients develop heart involvement or myocarditis, or inflammation of the heart has been described across the world and in patients who develop this complication. And the other thing that we've seen a little more frequently in these patients is thrombotic complications where they get blood clots in their veins. And that seems to be from the inflammatory process itself. So those are some of the early findings that I think that people are describing in patients and the data on cancers, actually not very deep at the moment.

There's a small paper in Lancet Hematology that describes 18 patients. There's bits and pieces in some of the Chinese literature, but there's not been much that is really sort of separated out into different groups and what their complications are, they're usually lumped together which makes it hard to sort of advise people about what we should expect to see. Again, we've been really lucky, a knock on wood, that we have not seen in a large number of cases, but we're fully expecting to see more in our system as it spreads in the community more and more.

Gary Petersen: Recently, we've at least a small, I guess about probably 50 people in our IMF support group in the last two weeks have seen two people come down with infection, one of which was, "an unknown virus" and passed away very quickly with pneumonia, double pneumonia, that type of thing. And that's the kind of thing that just happens to us, we get sick. And it just happened, it overcomes us, our immune system is lower. So, one of the things that I've read recently, it might have been a similar article to yours was that this is caused by some, the lung damage is caused by a cytokine storm. And we see the cytokine storm ourselves from CAR-T and the same thing happens to us in CAR-T. But everybody has now at least the myeloma folks have found ways to prevent the CAR-T from creating the cytokine storm that kills us. So I was wondering if something like that might be applicable. And I'm just asking this because I just read an article and it just made all the sense in the world to me.

Dr Steven Pergam: Yeah. So there is a drug for CAR-T cell therapy, there's a drug called Tocilizumab which is an IL-6 inhibitor and IL-6 seems to be a primary driver of a lot of this cytokine storm. And there's actually a lot of interest in that being a potential therapeutic option. The problem with socialism as its cost, so it makes it hard to sort of widely use it. Yeah, well, nobody cares about cost, right. We have to focus on that, I guess. But I think the important thing is it's actually a little bit of a shortage because people have been using it around the world to try it as a potential therapy. So I think there's a lot of interest in that, that if you could turn off this inflammatory response from the virus, is that enough to protect patients? We don't know. We do know that involvement in the virus itself can cause damage to the lungs. So it may not be sufficient. But it could slow down the process and allow people to recover.

There have also been descriptions of this being used to prevent people from needing to go to the ICU and to need to be on a ventilator. But again, because there isn't really a lot of data yet about it, we've been looking at it and I think, have even used it in a couple of situations but it has it right now we just we just don't know enough about the best way to use it. My colleagues who I spoke to, in detail about this in Italy are doing studies with this now and one of the comments that they made to me was they said, you don't want to do it too early, because if you give it too early, you don't get the benefit. And you don't want to get it too late because then it's too late to help people. So trying to find that sweet spot where it might be helpful is part of the challenge. But I think it's a great point and one thing that we're looking at closely. The other, compared to that which is a little more of a blunt instrument is something like prednisone or systemic steroids, which is sometimes being used in people with really severe lung disease.

And there's a lot of debate about whether that is beneficial or not, because usually that weakens the immune system further. And it may help the short term process but doesn't help the long game. So it's unclear that that's beneficial. And again, those are studies that are ongoing. I'll say this. I can understand the frustration from a cancer patient. You want to hurry up and get these studies done and figure this out. It is super important and I know everyone is focusing highly on what are effective therapies. This is a process that is necessary. If we run too fast, and we put all of our eggs in one basket and try to figure out that that is the solution, then we find that it doesn't work. We've really sent patients down a negative pathway that hasn't been beneficial to them. So I think all of us need to be cautious about stepping up to new treatments, but we're looking around the corners, we're pulling up new agents, they're out there, communicating with pharmaceutical companies on a regular basis for products that they think might be helpful.

And there's been a lot of support from the cancer community with different ideas. And one thing we are doing is we're talking on a regular basis with our transplant community, both in Europe and in the United States to try to understand what are the best therapies that people are seeing and what the results so that might be beneficial. Those calls are happening at least once a week so that we can quickly update

guidelines and give people new information depending on what people are seeing. So we're all talking through different channels about what they see and what you're finding effective. It's been really helpful from that perspective to talk about that. But the tocilizumab is interesting. And I think there's a lot of people that would like to see more about this, but I think those trials are coming.

Gary Petersen: Okay, well, thank you so much, doctor. We have a time scheduled for this and I think I just ran over mine and it's 10 minutes per person. I am going to hard break right now for Jack. .

Jack Aiello: Thanks, Gary. And thank you, Dr Pergam for being on this call. I wanted to ask a couple of questions. Some patients are dependent on blood products, any chance of transmitting the virus via blood transfusions of any kind?

Dr Steven Pergam: Not that we're aware of. There are specific blood transfusion organizations that have come up with some specific guidelines for when and if you can donate blood. So there's a lot of work being done in that space, to better identify that. We are not aware that that's a particular pathway of infection. This is a primary respiratory infection and usually respiratory infections are not transmitted through blood. So for flu as an example, we don't necessarily expect that if somebody had the flu the day before and you collected blood and gave it to someone that they wouldn't necessarily develop the flu. The organism itself has attachment points at places that are primarily focused in the airways and in the lungs, although there are many other locations in the body as well. And so, I think for most individuals, we don't think that that's a primary method and there is going on in that space.

The problem is, is that some of the tests we use to identify the virus are these PCR polymerase chain reaction and then what we find is parts of the virus. But we can't tell whether it's alive or dead. And so and I think in a lot of situations, they're just being cautious about how blood donations are happening. There have been new regulations that have been put in place to help protect against that. So I think blood transfusions, I would not worry about, there's a lot of work and a lot of people that are in that space trying to protect patients who are getting blood transfusions. I would say one of the challenges that has come up that was a surprise to us was that blood transfusions have been difficult to get. So getting an adequate blood supply was something that was unexpected, because as all these social distancing efforts have taken place in Seattle, it got harder to bring people in to do blood donations.

So there's been a lot of work here to expand that. And even a lot of our staff at the Seattle Cancer Care Alliance went in and donated blood because we wanted to make sure there was adequate supply and I think we're in good shape now, but that's been something that's happened naturally, which was a bit of a surprise. And it makes sense in retrospect, it wasn't something we'd planned around.

Jack Aiello: How reliable is the COVID19 testing? Are there a higher than normal percentage of false positives or false negatives?

Dr Steven Pergam: Well, there's a bunch of different assays out there. The WHO assay, there was an assay that was developed in China. And there are a number of other assets. We have one here that was developed in our own lab. It's hard to know exactly the performance characteristics of these lab tests. What we've seen is that people that are positive clearly are infected, have symptoms that are consistent. There's been reports of false negatives where initially someone is negative and then they develop more prominent symptoms and they're tested again and are positive. It may be that people are tested at time points where there's not a lot of virus in the nose or in the nasal pharynx where these nasopharyngeal swabs go. So it may just be a timing issue, rather than the amount of virus that's there. Sometimes it's also a sampling issue that these nasopharyngeal swabs are kind of uncomfortable, if you've ever had one, they kind of poke in the back and kind of almost go to the back of your throat.

And so if they're not done correctly, you may not get enough of the virus. So there's, it's not clear, we've not seen a lot of false positives, ones that repeated negative right away. I can't say that I can tell you, if any. And generally, what we've seen is we've seen if the test is positive, it's positive. I can only think of one

case out of all of the patients we've seen here that was negative initially, and then had a test that was positive later. And that might have been somebody that had a late exposure, and then developed more complications and had more development of disease. So my sense is that false positives on our site at least have been relatively infrequent. Excuse me, false negatives have been relatively infrequent. But I think what's been reported, at least in many places is about 20%. And that's not at least what we're seeing. But I think it really depends on the performance characteristics of the assay itself and since there's a bunch of them out there, it is really dependent.

My general take on this is there may be patients that have really severe pneumonia that don't have a lot of virus in their nose. But I don't think the data supports that at the moment. It looks like the nose and the nasopharynx are places where there should be plenty of virus. So it may be related to testing, it may be related to the specific assay. But I think as time goes on, these assays are going to get better and better. And they're going to be more specific. So I think the issues with false positives is probably going to be something that will dissipate over time and certainly false negatives. We hope that will dissipate as well.

Jack Aiello: And then just maybe a quick response to the question that I'm going to follow up with Gary's, we talked about immunocompromised patients. And you indicated that there's a lot of heterogeneous there in terms of not all cancer patients are the same. Are there any kind of lab markers, we're getting blood tests all the time that we should look at to determine our level of immune compromised?

Dr Steven Pergam: Yeah, I mean, there are some things that are helpful, I guess. So, first of all, there's no great single marker that I can send on anyone that tells me your level of immune compromise. So there is no perfect assay that will tell me that you're at risk for x infection or our y virus. It's just not easy to do. Our immune systems are incredibly complex. And we've seen this with cancer therapies where when you knock out a component of the immune system, you're at risk for complications that we would never have expected. Certain infections that are rare in most populations, but show up because of the way the immune system has been affected that's targeted to one small aspect of it. But what we look at generally is I would think that patients who are getting treatment for cancers that involve the hematologic system, so particularly people that have weaknesses in their immune cells, so if you look at your neutrophil count, if it's really low, if you're below 500, we would expect that you would probably be at increased risk.

Patients that have low lymphocyte counts, so very low, what we typically assume are agents that are fighting against most viral infections, those are low, those potentially put patients at risk. And then patients who are getting therapies that might weaken their ability to produce antibodies against a viral infection might make it so that they have more complications too. So a drug like Rituxan which is used a lot of times in patients with lymphoma might either lead to a prolonged shedding of the virus because you don't produce adequate antibodies or potentially more complications. It's entirely possible and we don't know this for sure, but that some of these therapies may actually not be all bad. It is possible that certain components of these immune therapies or the treatments that patients are on may limit the immune response and may help you to prevent getting severe inflammatory conditions in the lung.

What we're not sure is whether that's all good because it could be damaged as the virus continues to replicate to the lung specifically from, the virus might not be in the best interest. So there may be two different ways that the virus can cause problems. So in general, those are the things that didn't get the most easy to look at for most patients. So they look at their complete blood count, and look at the levels. If their neutrophils are low or their lymphocytes are low, that's probably a good predictor. And if they are getting immune globulin or are told their immunoglobulin levels are low, that might be another potential indication that they might be at increased risk. And generally, it's people with bone marrow cancers or cancers that involve the immune system itself, that I think are probably going to be at the highest risk.

Jack Aiello: Thanks so much. I'll turn it over to Cindy Chmielewski.

Cynthia Chmielewski: So thank you so much for spending your time and I was just following up a little bit with Jack's question. Most of the patients listening to this show would be myeloma patients and myeloma is

a cancer of the immune system. So I guess we're pretty much at risk. But also, in our, like monthly labs, we usually get our immunoglobulins checked IgG or IgA or IgM. Now if those levels are basically within the range, would you consider it not being as immune compromised as someone whose levels may be off range?

Dr Steven Pergam: Well, I think myeloma is a particularly challenging group, because the disease itself involves the plasma cell. And what we've known for a long time is that myeloma patients tend to be at higher risk for developing viral complications. And for a lot of you, I'm sure and you're also on if you've had an auto transplant or you've gotten CAR-T cell therapy, many of you are on maintenance therapies with things like bortezomib or lenalidomide and so we don't know exactly how those long-term agents might affect you. So my expectation is that if you have a normal immunoglobulin level, that's good, that doesn't hurt you for sure. But not having an immunoglobulin level, that's low does not mean you're necessarily protected. So I wouldn't imagine your immunoglobulin levels are necessarily predictive of safety. I just worry about people who don't have adequate immunoglobulin levels that their body's not producing enough immunoglobulin by their B cells and some of the other immune processes that work in that way. And that would be and that's probably more of my issue from that perspective. So I don't think having a normal immunoglobulin level means you're not at risk. So keep in mind that myeloma patients are probably at increased risk because they have an involvement of the immune system itself in how we address infections.

Cynthia Chmielewski: Okay, so consider increased risk we need to take increased precautions, I guess. But many of us are still in treatment and I have to travel to our treatment centers, what precautions should be taken, should we be wearing masks? Do you think we should be talking to our colleges about maybe for a few months trying to do an oral therapy? Should we skip the dex for a while what types of recommendations would you make for myeloma patients in treatment?

Dr Steven Pergam: Yeah, it's a really important question. I think the way that I focus on this first is it's really important to talk to your oncologist and to keep in mind that they're the ones that are going to give you the best advice about how your disease needs to be treated. For some of myelomas, they're in a position where they can go on oral therapy, and they can be monitored from a distance. They don't need to be seen every week. And it might be an opportunity to talk about telehealth where you could be calling in or video chatting about your current symptoms and how you're feeling and if you could avoid coming into the clinic that might be fantastic. For others, you have to come in to get infusions, you have to come in to get blood products, you might have to come in for dialysis if your kidney has been involved with myeloma. And so the realistic pieces here are that you need to be seen for your disease.

So whenever possible, if it's possible, talk to your teams about what are options so that you can do therapy where you don't need to be sort of on campus. I would say we're in the cancer center itself. But remember that many cancer centers are incredibly focused on trying to protect you the best they can so even when you do come in they're doing all they can. So in our particular situation in Seattle, everyone who comes in the door goes through intense screening and anyone who is symptomatic gets swabbed for COVID19. For those who don't need to have appointments, we send them on to others, we try to reschedule them at different times. But for those who really need to come in, we see them in precautions. And then anyone who has a diagnosis of COVID19, we follow very closely. We try not to bring them into the clinic whenever possible, so we can follow them closely and monitor their symptoms, we call them basically twice daily to make sure they're doing okay.

And if they do develop more complicated problems, we have them call ahead and go to an ER or we directly admit them for management in hospital. So, what I typically tell people is a couple of things is, there's a lot you can do in your life, to sort of protect yourself. And many of you do this anyways, because cancer patients, they don't always feel the best so they're not out in public places as much. You're also often advised during flu season to not only do your flu shot, but to try to distance yourself from people in general who are sick. So I think certainly staying at home as much as you can, avoiding many activities out in the community, if you can, that are going to be high density. That doesn't mean you have to live as a hermit. Many people have to go get groceries, they need to get supplies for themselves. What if you have a delivery

service with your local grocery and they can deliver to your house even better.

Just less contact. So think about every person you connect with and every time you're going someplace, if you work and you're at an office where there's a bunch of people around, talk to your boss and see if it's a possibility that you could work from home because that'd be a good opportunity. Tell them why you are at risk for developing a major complex and have that conversation one on one to let them know that not only do you want to protect your other employees by not bringing in something yourself, but that you are really worried that somebody might expose you to something. And be very clear to family and friends that if they are ill, they should not come to see you. Even somebody with a mild cough or somebody who has a little bit of a sore throat or they're not sure they tell you it's their allergies, just say please don't come see me during those time frames when you're having illness. Use lots of hand sanitizer when you're out in the community. But masking in general, it's not clear that a surgical mask wearing every day is going to be necessarily super protective.

So I would talk to your individual doctors about whether they think that's valuable. And certainly if you have symptoms, you should wear a mask if possible, when going to any appointments or going out into the community. So if you're having symptoms at home, if you have a mask that you can wear, and when you go out into a public space because you have to and that's important and I would really recommend that people with active symptoms not go out into public as possible. And then finally, with your family members, just make sure they know that if they develop symptoms, and it's hard to do this for some people, but to kind of isolate themselves from you, if possible, and to go get tested and if they do have an infection defined, if possible, another place where they could be. That's not always super easy. And there are a lot of issues with how to manage that. But as much as you can stay apart and wash your hands very carefully, that can be helpful, I think, to potentially prevent transmission in the household.

Cynthia Chmielewski: Thank you so much. And since we're on limited time, Yelak why don't you go ahead with your questions?

Yelak Biru: Thanks again for time with us today and give us a little bit more information about what's going on with this virus. Can you go back to the basics and explain the difference between bacteria, fungus and virus and if we have a broad spectrum antibiotic why don't we have a broad spectrum antiviral?

Dr Steven Pergam: Yeah. So let's talk about that. Those are really different conditions. So bacteria are bigger organisms. Our intestinal proponents of stool are full of bacteria, our mouth is full of bacteria. They live sort of symbiotically with us. And we actually have some types of viruses that live with us that are called bacteriophages naturally, in fact, sort of transmit information between bacteria as well. There are also some viruses that live in our system. Some of you may have had complications with a virus called CMV, or shingles would be another. That's the chickenpox virus. Some viruses that after exposure, we sort of have latently that live in our systems. And so there's a variety of different ways that those can be. But the largest of those groups is fungi. So molds like Aspergillus, and those are ones that really prominently cause an illness mostly in the lung. In patients who have low neutrophil counts, and most prominently in patients who are getting bone marrow transplant and patients that have types of leukemia, where they have very low neutrophil counts for an extended period of time.

And that usually presents as cough and pneumonia and often fever. Sometimes the patients will cough up blood, and those typically are treated with antifungal agents which take often months to clear up. Those are often diagnosed either by blood tests or by doing a bronchoscopy where you go down in the lung and wash the lung with some fluid and then send it to the lab for identification. So fungi are more often exposed in the community. So you're breathing fungi everywhere. So they're, anything that's like bread, mold and things like that are possibilities if you leave anything out for too long it'll, molds are important to break down things in the environment. But I think they are important infections in our populations. Tyria typically leads to things like bacteremia, where you are told you have E.coli in your bloodstream.

Those can cause shaking, chills and fever, something called sepsis where you get really sick and need to go

to the ICU. And that can also lead to things like pneumonia or urinary tract infections, and some bacteria can also involve the intestinal lining. Something like C.diff can do that. But those are organisms that we have particular agents for as well. So we've got the antibacterials that target components of those organisms. And it's a little easier when you have a bigger organism like a fungus or a bacteria to identify a particular target. Viruses tend to be small, they replicate very quickly. And for some, they can develop resistance more easily to an antiviral. So we have a couple of antivirals that work really well for specific conditions. So we have a treatment for CMV. We have a number actually at this point in time that are treatments.

We have treatment for influenza, but for most common respiratory viruses like respiratory syncytial virus or metapneumovirus or parainfluenza we don't have particular treatments for those. So we've struggled, they're just harder to find good targets for them. And because they change a little bit every year, they're a little bit harder to find. So with viruses, we really like vaccines. And because they tend to re-target something that is an area of the virus that is conserved, meaning it sort of stays with the virus through all of the generations of change. That's critically important to the virus. And if we can target that with a vaccine and an antibody that can take that out, then that's a great way to prevent infections.

So I think, in general, we have a lot more vaccines for viruses that work really well. Things like measles and rubella have been really effective and are great ways for prevention. And so I think, viral treatments are just harder to develop in. In general, we've had less success with antiviral therapies than we have with vaccines. So Ebola is a great example, where we tried a bunch of different antiviral therapies. And it wasn't clear that any were perfect. But once there became a vaccine that was available, it's really had a big effect in certain parts of the world with Ebola is more of a problem. And that's our hope with this as we get to a point where we can slow this down enough that we have vaccines that are available, and I think Corona virus and some of the coronavirus sort of lineage, particularly this type of Coronavirus has the potential for being a vaccine.

There might be a vaccine that could be used here and there's a number of people that have been working on some vaccines like this, unrelated to SARS, or other related coronavirus infections. So there's already been some preliminary work and those people have really ramped up their efforts to find that but antivirals in general are just a little bit harder to develop. Because these viruses are small, they have fewer targets, and they can mutate more quickly because they replicate so fast. So that is sometimes challenging.

Yelak Biru: Okay, thank you so much for that one. Can we talk about the immune compromised area, like most myeloma patients or patients on chemotherapy or other immune compromising therapies, in general have low absolute neutrophil counts, white blood cells and lymphocytes and IVIG. Will the patients benefit from Neupogen shots or IVIG infusion or other immune boosting methods specifically for this disease or avoid opportunistic infections?

Dr Steven Pergam: Yeah, I think so for the first point Neupogen, I don't think so. And we don't think then neutrophils themselves provide a huge amount of immune response to Coronavirus. I think it's more the lymphocytes. What we see is that people who are neutropenic or have low neutrophil counts that tends to predict a general immune compromise rather than just that particular component. So neutrophils are really important for bacterial and fungal infections but not as critical for viral infections. One of the reasons with bone marrow transplant, we see a lot of fungal infections earlier post transplant is because your neutrophils are low, and then as you go further out as your immune system takes a while to recover viral infections tend to continue to be problems for long periods. So I don't think getting Neupogen shots is going to necessarily help in this particular situation. That's a great thought. And then IVIG, I think there's possibilities that that could be eventually beneficial.

The problem is, at the moment, there's not enough community immunity to this particular virus in the United States and in other parts of the world. There's not a lot of people who have that we know that they've been exposed to this and so collecting immunoglobulin, we don't think we have enough of the antibody that would potentially protect you if you're given that particular strain. So, as an example, with measles after an exposure, we have measles specific antibodies that we can give to people that focus. We know there's

enough measles antibody in that, that we can potentially give it to you and protect you from getting measles complications. With this, we don't know that yet. And some of the work around what's called serology or identifying people who have been infected is really progressing rapidly.

And I think that'll be very helpful because once we identify who those people are, we can start collecting more immune globulin and having more targeted immunotherapies like immunoglobulin that has higher titers of this antibody against coronavirus that might be beneficial for people who are at risk. So I think eventually that could be something that's developed over time. And what I'm really excited about is thinking about it in a different way is thinking about, like monoclonal antibodies that we use for a lot of treatments for cancers like rituximab, could there be a monoclonal antibody that is directed against coronavirus that identifies it and can help the immune system fight it off. So there's real interest in that area as a therapeutic. But unfortunately, there are no immune boosting strategies. I will tell you a couple of things that I think do help though. And these seem very basic, but getting exercise walking around your neighborhood and keeping fit is important. Eating healthy.

So eating a really well balanced diet and making sure you're taking in good nutrition can help your immune system function better, and then frankly, getting enough sleep. So if you're spending your nights worrying about getting coronavirus, you might actually be putting yourself at risk, sleep as much as you can. These seem like really basic things, but they do really help. And then I think having a conversation with your oncologist specifically about what could be changed in your therapy, to maybe lessen your immune suppression a little bit, is something that is totally worthwhile if you're concerned and that's a conversation that's really important because we don't want to change your immune responses and make your cancer worse. What we want to do is to do something that makes sense that can protect you. It's a balance, it's a really, really tightrope that we're that we're walking. We don't want to put you in a situation where your disease gets worse and you need additional therapy, but we also want to help protect you against immune suppression as possible. And that's why I always recommend talking to your oncologist to really be experts in that area.

Yelak Biru: Excellent. Yeah, I will yield my last question I am thinking has been answered around telemedicine, home infusion and modifying treatments. So I understand there are more questions in the pipeline. So I will yield back my question.

Priya: So we have Dana Holmes dialing in. Dana, please ask your question.

Dana Holmes: Yes. Hi, Priya. Thank you so much. Hi, Dr. Pergam:. My name is Dana Holmes and I'm in New York City. I'm in the COVID epicenter of the United States right now. And I'll be honest with you, it's just been mind numbing what's been going on. With our current spread, I cannot help but believe that this virus was well rooted in New York City before that first confirmed case was reported in early March. Obviously, we're just not testing then. In your opinion, do you think that this is really just our first wave or might we see some relief as the warmer weather sets in? I'm hearing that could be a potential relief for us for at least a small portion of time.

Dr Steven Pergam: Yeah. I would love to give you a more optimistic response to that. I'm not sure if that's going to be true. I think first of all, I think you're right on your first point. I think Corona virus has likely been in New York for longer than expected. I mean, if you just think about travel patterns and how people move back and forth across the world, I mean, the fact that we had someone who'd been to Wuhan, China who ended up coming back to Seattle, or close to Seattle. It shows you that there's a ton of travel patterns. And actually, one of the direct flights from Wuhan is to, I believe, to JFK. So the assumption was it probably was introduced at some point in time with some mild infection. I think it probably has been in your community for longer than expected. It is an issue that we didn't have adequate testing and we didn't know I think everyone in New York was working really hard to change that but there were some issues in terms of how the testing was made available.

I know Governor Cuomo has really been instrumental and putting a real robust attack and trying to take this

on. I know my colleagues who are in the centers in New York are working diligently to protect patients. So I think it's really important that there's a lot of work being done there. What worries me a little bit about the summer component to this and it may be true that maybe it lightens a little bit. But Peter Hotez, he's an expert and is actually from Texas Children's he's worked in vaccines, actually trying to look at coronavirus vaccines, has been a little bit skeptical that it's gonna be true. With a novel virus like this that spreads really well, we're really no one who has never seen, none of us have seen this before so all of us are at risk for getting it. It makes it easier to transmit. And sunlight can break down viruses a little better with UV rays.

But what we've seen is there's a lot of transmission going on in Florida and Florida it's 80 degrees now. And so I don't imagine that the summertime is going to be a period of relief, unfortunately, what I expect is that New York will peak at some point in time with a large amount of disease. And then there will be at some point in time, like all what we would call epidemic curves, they will start to come down as there's more community transmission, and there's more people that are previously infected, that have recovered, so that the transmission is harder for the virus.

Dana: But it's like a wildfire right now. It's really mind numbing, it's just incredibly mind numbing.

Dr Steven Pergam: And I think that, this is a virus that's really targeted towards places where there's lots of people together and the density is hard, because even if you want to do social distancing in New York, that's harder to do. And so I really empathize with you. So please be safe out there.

Dana: Yeah. Well, thank you. I have a question, you mentioned lymphopenia as a risk and I've also read that It's listed as a common lab value in COVID patients. Is it the virus, which is also causing this? Or is it the infected patients already just have this?

Dr Steven Pergam: Yeah, so I think it's probably both. So probably some people have lymphopenia because of their disease, and because of your inability, because you have low lymphocyte counts, and you're more at risk for getting this particular complication and leading to complicated disease. But I think for sure, we've seen this with other respiratory viruses that in normal people, not people that are with cancer is when their lymphocytes really dropped. It tells us that there's like a large component of viral infection that's being engaged in that and so some people think that is a predictor for the development of more complications. So lymphocyte counts that are low are often a predictor of this and typically mean you have a viral infection. So that's not surprising. So I think it's probably a combination of both.

Dana: And regarding the antibody process, do you believe that all COVID infected and recovered patients will develop them? Or will immunocompromised patients such as myeloma patients will develop a more limited antibody protective level?

Dr Steven Pergam: Yeah, we're trying to figure that out. Generally, when you look at things like the flu vaccine, you don't really get as good of a response to the flu vaccine. So my assumption is that your immune response to this virus will not quite be as good. But I don't know if that means that potentially you could get it multiple times in the season. I think that's probably less likely. But we don't know. And we actually don't know a ton about the immune response. Even in people that are normal hosts who recover this may be a virus that you get an immune response that's present for a period of time and then disappears. And then you're eligible to get it again the next season, similar to influenza.

I don't think it's gonna be exactly the same. I think it may be that some of these antibodies are not really visible. But if you re-expose someone, they increase, we just don't know. So that's an outstanding question. There's been some rumors that there is transmission that there's been people that have received this twice or gotten infected twice. But I haven't seen any real reports that indicate that that's true. These are all kind of word of mouth. And so until I see more data about that and I'm still pretty convinced that our immune systems are pretty smart, and they can develop immune responses to a virus like this. But we don't know. And I think that's something that'll be coming in the future. But I think that question about immunocompromised patients, my assumption is being your responses will not be as robust.

Priya: Thank you, Dana. Dr. Pergam and we have a few more questions from the audience. And we're almost at the end of the hour. But if you have a few more minutes, it'd be really helpful to just some quick responses, I'm not going to pick up questions that we've already covered on immunocompromised patients, multiple myeloma patients being immunocompromised, as well as healthcare regimens. What I'm going to ask is, from one of our audience members who's listening says, what medicines should we have if they become infected with the disease?

Dr Steven Pergam: Yeah, okay. That's a good question. So I think probably, if you are getting a fever, having Tylenol is great because if you're having a high fever, it's great to try to prevent you from developing and it's uncomfortable to have a fever for a long portion of the day. I think Tylenol is your best choice. There's a question about whether things like ibuprofen or other non-steroidal anti inflammatory drugs could cause more complications. I think the jury's still out about that a little bit. But I would probably focus on Tylenol if you can. And that's probably a good thing for your fever and to follow the directions that you don't take too much. Don't take it so that you can hide your fever all the time, because you want to know when your fever is gone. But if you're feeling feverish, and you take your temperature and it's up, make sure you tell your doctor and then you can take some Tylenol to help relieve the symptoms related to that fever.

Some people like to carry cough drops around, it can really help with the cough that might be associated with it. Some people who develop long coughs and a lot of complications after they've recovered, need something like an inhaler for something like albuterol that can help them with that sort of bronchitis that can develop after an infection like that. And then I think, for a lot of this is, it's mostly just things that make you feel better when you have a normal cold. So get a bunch of Kleenex in the house, have some wipes that you can wipe down and clean up spaces where you are. And if you have other symptoms related to this, talk to your doctor about what they can give you, that can help relieve some of those. But there's not a lot of great things, it's mostly symptomatic care more than anything else. So I think having a little Tylenol at home can be helpful. And whatever else makes you feel good when you have when you have a cold or flu.

One other real quick comment, people who do have medications that they get regularly, make sure you have enough of them at home. So what I do suggest to people who can't go out and get enough medications for a couple of months that they have them in stocks enough to go to the pharmacy. And that's often also helpful when you're ill that you can continue to take the medicines you need to for your treatment. It's also really important if you do develop symptoms, and you think you might have this to talk to your doctor about, should you stop some of those treatments for a short period of time, that can be really helpful, but making sure you have your own normal medicines can be really helpful, particularly if you have pain medications or things that you're using on a regular basis. Make sure you have enough because you don't want to have to go to the pharmacy when you're sick.

Priya: So as a follow up, like if you had contracted COVID and you're cured, do you think treatment should be continued for a couple of weeks until the new cases of corona starts to decline?

Dr Steven Pergam: So you're cured, should it continue? Should your treatment continue? We don't think so. I mean, I think if you're cured and the virus is resolved, I think we would stop therapy and we've had a number of those patients who've been treated and have come out on the other side and we've been able to either send them out of the ICU or they have recovered. And we wouldn't continue therapy at that point in time, there's no reason to. So what we would do is we would, still maintaining the way you were taking care of yourself at home, talk to your doctor about what you need to do for continued social distancing. Eventually, I hope when people start getting this, that we can check antibody responses and see what you look like on the other side of the infection, to see if you're really, if you've had a good adequate immune response, but I again, I'm not sure that we're going to have evidence that people are going to get infected multiple times. I think that seems less likely. We just don't know yet.

Priya: And thank you, Dr. Pergam. The next question is how or by what mechanism is a virus destroyed over time? And he says not without washing with soap and water and what temperatures if any destroys a virus?

Dr Steven Pergam: Yeah, so these are enveloped viruses. So they have like a fatty layer on the outside. So using soap and water is a great way to break them down so they can't survive. You can use alcohol and hand sanitizer as well, that works well. In terms of other things that break it down is time. So UV light over an extended period of time will break it down. And it doesn't survive well, it survives well on surfaces, but not for an extended period. So if you have something where it's been exposed, it can last on plastic for a little longer metal, some cardboard but, if you leave these things out for a day or so that usually is enough for the virus to not be able to survive. If you've got things like that, that you're worried might have had an exposure and if you wipe them down with things like bleach, and bleach mixes with water, and that can be sufficient to clean it. So any sort of standard antibacterial wipe will usually work pretty well to break down this virus. In terms of temperature when washing your hands doesn't really matter, I think it's really the friction and the soap. But do make sure you don't burn your hands, because I know a lot of new myeloma patients do get some neuropathy, so be careful about that.

Priya: So Dr. Pergam, we did talk about clinical trials, right in the beginning. There is a follow up on that. What is available through compassionate use, are there and are these available in local hospitals?

Dr Steven Pergam: Well, Remdesivir was initially offered as a compassionate use, but they've removed that because they had so many requests. So it's only available by clinical trial, but they're working on getting a protocol open that you could open individual centers that would allow people to get that drug and that's just in process. There are agents some of these agents I talked about are already approved agents that were using, like chloroquine and hydrochloroquine that are available. But there are no other agents that I know right now that are available for compassionate use specifically. There are People that are working on these immune sera that could be given this passive transfer. So that is ongoing work and I think will eventually become available as well. But at the moment, there are no other compassionate use trials that I'm aware of.

Priya: Thank you, Dr. Pergam. And I think I'm going to wrap up with that one. And thank you very much for your time and the extra time too. Gary, Jack, Cindy and Yelak – thanks for participating. On March 11, the World Health Organization officially designated the novel Coronavirus outbreak as a pandemic, defined as a worldwide spread of a new disease such a declaration. This was the first to be made since 2009 when H1N1 swine flu was declared a pandemic. So as of now, there have been approximately for more than 400,000 confirmed cases of the COVID-19 disease and this is increasing as we speak, and this has resulted in more than 21,000 deaths worldwide. This is a critical time for information, support and reassurance that science and evidence can offer. Majority of us are under lockdown in our countries, counties and states. So let's follow social distancing. Wash your hands and do our best to flatten the curve. We can definitely overcome this if we stay together. So stay home and stay safe. On that note. Thank you everybody. The talk will be available on curetalks.com. Thank you everyone. Have a great day.