



COVID-19: Focus on Pediatric Bone Marrow Failure Patients

Webinar Summary

(Transcribed from the AAMDSIF webinar on March 21, 2020 with Dr. David Margolis from Children's Hospital of Wisconsin and Dr. Inga Hofmann from American Family Children's Hospital in Wisconsin, edited for clarity and brevity)

Q: If a pediatric aplastic anemia patient comes down with COVID-19 symptoms, do they go to the hospital where they are being treated, or should they go to the local hospital? And if the local hospital, how should a parent explain the underlying issues?

A: Don't go anywhere without calling your treating hematologist/oncologist or pediatrician/family doctor first. We want to talk things through and then make a decision about going to the ER. Have your healthcare team call ahead to the ER and coordinate the care. What we're learning is that sometimes the best and safest thing to do is to stay home, which goes against what we usually think. Staying home limits exposure. If you have a cold, communicate with your pediatrician/family doctor. If you have a cold and fever, communicate with your hematologist/oncologist.

Q: If a child gets sick, who is currently taking Cyclosporine, is it even possible to keep them safe? How do you isolate the child living in the same household?

A: It depends on your home situation and circumstances. What we want you to do and what the general recommendation is in the current coronavirus pandemic is that if there is a person in the household that now has symptoms or confirmed COVID-19, especially if there's a confirmed case, that you self-isolate in the house. If you have a spare room, or if it's either your child or another family member, a sibling or a parent, that you isolate in the house and keep distance. If you have the luxury of having an extra bathroom, than you restrict basically using any common spaces. Vigilant hand washing routines are important. Many of you probably have masks at home, and I would say to use them. People say to basically try to isolate for 14 days at home, because that's the estimated time when people are sick and thought to shed virus. To really prove that somebody is basically cleared after, or if they had a confirmed COVID-19 infection, the only way to prove that they were safe, and not shedding virus and risking to infect somebody else is actually having to negative test. I think in practicality, that is probably a challenge due to the testing still not be able to widespread be available. Find creative ways to keep that person away from the rest of the family members so it doesn't go around in the household.

Q: Since COVID-19 appears to attack the lymphocytes and drops CD4 counts, will this impact post bone marrow transplant patients that still have a less than normal CD4 count and become positive with COVID-19?

A: The intricate details of that we don't know. What we've seen in patients or what's being described in the reports is that one common theme in laboratory results is a drop in the white blood cell and lymphocyte count. After your transplant, your white blood cell count and the lymphocyte count is going to be low in many cases depending on how early you are in that transplant process. In general, any patient that is immunocompromised is at risk for this disease more than others. What we're hearing from colleagues in Europe is that this is an ever-changing situation. We have heard from some doctors in Italy that maybe the chance of getting it are not quite as high for bone marrow failure disease patients as we were initially worried and it could be because perhaps you are already doing the right things and have been doing them for a long time. You have already self-isolated and take precautions. We just don't have enough information yet, though.

Q: Every day that goes by, we learn more about COVID-19. Based on what has been discovered, when do you think the severity will lessen in the US?

A: Dr. Margolis: The honest answer is we don't know. I think that there are certain countries where there has been a curve that had a shorter period of time, and there are some countries where it's had a longer period of time and we don't know yet where the United States is. I think for the foreseeable future if you are aplastic anemia, bone marrow failure or PNH patient, the recommendation is going to be stay at home as much as you can. I totally agree with Dr. Hoffman, our patients were uniquely prepared for this. It's sort of like everybody else is joining us in this way of dealing with certain things. My personal view, is to try to keep buying more time, because I am hopeful that we will understand and have better treatments for this sooner rather than later.

A: Dr. Hofmann: Yeah, I agree. I think it is impossible to predict for sure because it so in flux. Most of us believe it's probably going to get worse before it gets better. I think that's maybe not a bad approach to think about things and have a prepared mindset. How long are we going to be in this situation? It's hard to know and I keep on reinforcing to families they are well equipped more than anybody else, and that might be your secret superpower right now that nobody else has to handle this. I have seen families post amazing comments all across social media, and you have over the years collectively found ways to creatively take care of your child because you have always had to worry about germs.

Q: Is the progression of COVID-19 any different in patients who are immunocompromised such as a PNH patient or anyone else can become infected?

A: We've been scouring the literature and communicating with colleagues in China, in Italy and other areas of Europe. The honest answer is we don't know yet, and actually my personal opinion is that's actually a hopeful sign. I keep reminding my patients, this coronavirus is similar to our immune compromised hosts with any virus, which means a virus can hurt any one of our patients. Every season, I worry about influenza and RSV. And the issue

is, most healthy people walk around and say, "Oh, I get a cold." The fact that we're not seeing in the literature a lot yet about extraordinary natural histories in immune compromised hosts, I'm going to take a little bit of a ray of hope. Our immune compromised hosts are battling through this, like any other patient who doesn't have an immune system to fight it. But that doesn't mean I'm not taking it into account when I'm making medical decisions. My hope is that every one of our patients can have as many immune cells as humanly possible. The cells that are going to fight this, we think are primarily lymphocytes, and most of our bone marrow failure patients have lymphocytes.

Q: If a person tends to be sick twice as often as most people, how long then do you isolate if someone gets sick in the house, or the immunocompromised person gets sick? Does it need to be longer than 14 days?

A: I think it's hard to know that perfect scientific answer. I would say that 14 days is a good hard and fast rule, realizing that if people are still asymptomatic post the period and are still coughing and having symptoms, then probably it needs to be extended. That would be my best answer. Again, we don't know the trajectory of that, if you have truly been infected by the virus and get COVID, if your trajectory in healing process in your specific situation will be different or not than for other people. We don't know because there's not enough numbers to tell us this answer. There has not been sort of an onslaught of cases that we hear, especially in our population. I, too, take that as a positive sign as a sign of hope. For whatever reason, it doesn't seem exponentially worse. And again, it might be because of all the precautions you already took way ahead of time.

Q: Is there anything behind the news reports about ibuprofen? What can bone marrow failure patient take safely?

A: The way ibuprofen works as a fever reliever is it acts on some of the proteins that can cause a fever. Fever by itself is not a bad thing. Fever is the Mother Nature's way to help fight a bug. Tylenol, or acetaminophen does not change the proteins that are part of our immune system when it controls fever. It works more centrally in your brain. I've said for a long time that ibuprofen should not be used when you have a fever because you're sick, because you're crippling your body's way natural defenses. Aspirin and ibuprofen attack a similar pathway in your body. Do not stop taking aspirin without talking to your healthcare provider. And if you're on ibuprofen for other reasons, do not stop taking it without talking to your healthcare provider. But I do think that fighting a fever associated with the virus is best done with Tylenol or acetaminophen, not ibuprofen. Because in my mind, when you use ibuprofen, you're somewhat hurting your body's ability to fight against that virus.

Q: After a child has undergone ATG with a full response, if that child becomes infected, do you think it could cause reoccurrence in their bone marrow failure?

A: Dr. Hofmann: Honestly, we don't know for this particular virus because we have never been in the situation ever before. Have people wondered about having had an immune response or a good response towards immunosuppression, and that may be lost or responds

again, after exposure to some diseases or viruses? People have wondered about that in the medical community. On an anecdote basis, I would say, probably Dr. Margolis, can think about patients where he asked himself that question. I asked myself that question on probably one or two patients over the time of my career. But again, it is not. If you think about it viruses are very, very common and our kids get them all the time. It is not that every time a kid gets a virus, our immune response that we had from IST is lost. We don't know the specific answer for this virus.

A: Dr. Margolis: I don't know. If this was a mom or dad that was in front of me, some of my response would be, how long ago was the ATG and how good was the response? I always worry about every virus, but I don't particularly worry about this virus more than any other virus that's stimulating the immune system. I've been swabbing kids noses for years, and I've seen coronavirus after coronaviruses, just this one happens to be one that is new. I would treat it with the respect that I would give any other virus, but I would not give it any more panic than any other virus. The bottom line is we don't know yet.

Q: How would an RN working in an adult oncology clinic protect their child if that child become infected with COVID-19? Child had a related transplant from older sibling, 96% whole blood donor and t-cell line is 84% donor.

A: My heart goes out to you because you're on the front lines and have a patient at home, or a family member at home who you're worried about. I think you do the best in stringent conditions you can to protect yourself, and to be extremely mindful of that and avoid exposures. I would be very honest with your employers. I think that people need to be creative. Your child is at a higher risk. He's got a T-Cell count that's under 200, and he's had two bone marrow transplants. I would social isolate as best I can. I would be very honest with your supervisors, and try to be creative about limiting your exposure to other humans. Obviously, it's easy to keep them in the house. But you're saying the same thing I've said for years, we can keep our patients in the house, but when their siblings or parents are in the real world, there's always a risk. And usually it's an influenza risk, or usually, it's an RSV risk, but this year it's a coronavirus risk.

Q: Were there any cases when SARS was around relating to Aplastic Anemia?

A: I just used our search engine that we use for medical literature, which is PubMed. I typed in SARS and Aplastic Anemia, and got zero results.

Q: Can increasing your IgG (immunoglobulin) level help fight against COVID-19 if the patient were to get infected? My doctor has said stay above 400 and others say about 600?

A: Dr. Hofmann: IgG is pooled immunoglobulin and it responds to what our bodies have been exposed to. Currently, we're dealing with a brand new virus that has never occurred in human species to our knowledge. So, we must assume that any IgG we currently have, which was produced before this probably started is not providing immunity against COVID-19. We recommend that you follow the general advice of your treating hematologist/oncologist

about the appropriate IgG levels related to your particular situation. A lot of people use 400 as a cutoff, for example, after a transplant or in an immunocompromised patient. So, we would still supplement with IgG. If it's under 400 for all the other risks that are there besides COVID-19, but it is highly unlikely that IgG would protect you against COVID-19. That would be a good answer for all of us. Because it is a new virus, our people have not formed immunity against it.

A: Dr. Margolis: Medical teams are now working throughout the world to find people who have tested positive and recovered. My hunch is they will become plasma donors sooner rather than later, and we will try to use their antibodies. I keep saying we should just try to social distance, try to limit exposure and try to avoid it. I am hopeful that our biomedical sciences will catch up with this in fast order. I've seen a number of communications within the last week on ways to test to see if you've had the virus, because there are a lot of asymptomatic people. Those are the people that we would love to tap into their plasma, so stay tuned.

Q: What do we know about blood transfusions? Are they being screened and has anyone become infected due to a blood transfusion with COVID-19?

A: Dr. Margolis: I'll take that one because I was just as part of the public Milwaukee Area blood drive campaign at a press conference. The head of transfusion medicine at the University of Wisconsin publicly stated that no other coronavirus has ever been known to be a blood borne pathogen, which in real people's terms means you can't get it from blood. Assuming that this coronavirus is similar to other coronaviruses, and it is. It's biologically a coronavirus, the blood supply should be very safe.

Q: What type of masks patients should be wearing when they go out in the community? Not all masks are created equal.

A: The recommendation on masks changes on an hourly basis from the CDC. And so, instead of going out, my recommendation would be to not go out. I would really, really, really try to avoid going out because I'm not convinced the mask will solve the problem. But the data is if you're just passing people, there's no data that the mask will do anything. If you're a healthcare worker and you're on top of somebody trying to manage somebody's airway, yeah, a mask is necessary. And for those, an n95 mask is what is being used. But for face-to-face for community transmission, my personal recommendation, and I'm doing this every day on rounds. I'm six foot, so that means my wingspan is six feet. I don't let anybody come within my wingspan.

Q: Should a RN who is 8 years post-transplant for aplastic anemia take additional precautions?

A: Dr. Margolis: My personal view is if you're well enough to work as a nurse and you've gotten through influenza and RSV seasons in the past, my hope is that you would do well with this. The caveat to that is knowing what your lung function is and if you've had chronic Graft

versus Host Disease (GVHD). If you've been a smoker or have lung dysfunction, that would be my concern. Eight years post-transplant means your immune system is pretty darn good. I'm going to assume you've been immunized and re-immunized so that tells you you've got a coordinated immune response. What we're learning about this disease is the danger is attacking the lungs. I have seen some data that people that are smokers are at higher risk, and that makes sense, so their lungs have a previous injury. Knowing what your lung function is now would be how I would approach that.

Q: If a patient were to become infected with COVID-19, would this change the therapeutic level of medication such as cyclosporine? Do we expect that the levels would drop and changes to medications need to be made?

A: I don't think we would expect the levels to change.

Q: Do we know if a patient were to become infected with COVID-19, would we expect to see a change in their disease? For instance, if you have a mild case of Aplastic Anemia, would we expect to see the disease progress to a more severe level, therefore then needing treatment?

A: Dr. Hoffman: I think that goes back to the questions somebody asked earlier about, could the disease recur after you had a decent response? I think like Dr. Margolis mentioned earlier, the true answer is we don't know. We certainly think about any virus that has the potential to change immune responses. We don't know anything specific for this virus.

Q: What treatments are currently for COVID-19? And would you expect to possibly see some new treatments being brought forth?

A: There's no evidence-based treatments yet, but there are healthcare professionals throughout the country banding together to try clinical trials. If somebody does get coronavirus, they should work with their healthcare provider to see what clinical trials are available.

Q: What precautions should a post-transplant patient take that has been vaccinated but some inoculations are not taking hold?

A: I would follow post-transplant precautions. If some of the vaccinations haven't worked yet, that tells me that the immune system isn't quite at 100%. Maintain social distancing and the self-quarantine to avoid exposure would be my medical recommendation as it would be for anybody else even when they got a good immune system.