Going Viral: Testing, Diagnosis and Treatment of COVID-19

with

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EPISODE 2: RISK STRATIFICATION

ANGELA LECLERC: Hello, and thank you for joining us today. My name is Angela Leclerc. I'm a PA working in critical care in Portland, Maine. You are tuning into the Going Viral, Testing, Diagnosis and Treatment of COVID-19 podcast series developed by the American Academy of Physician Associates and supported by an independent education grant from Pfizer. The goal of this series is to provide education and tools to assist PAs and other clinicians in providing patient-centered care in the early recognition, diagnosis, and management of patients presenting in the outpatient setting with symptoms of COVID-19.

The COVID-19 pandemic is now entering its third year, and while cases are abating, new variants continue to emerge, along with the threat of new surges in infections. In addition to having three effective and approved vaccines in the United States, new therapeutics have arrived in the clinic that have the goal of preventing serious illness, hospitalization, and death.

Throughout the pandemic, PAs have played a critical role in helping combat COVID-19. As diagnosis and treatment shifts to the outpatient setting, PAs are ready to meet the challenge on the front line. This is the second episode in a five-part podcast series focused on risk stratification, early treatment, and coordination of patient care. I'm proud to be joined by Steph Podolski, who is a PA working in hospital medicine in Augusta, Maine, with a Master's of Public Health, and Dr. Sam Wijesinghe, who is a PA and Clinical Assistant Professor of Medicine at Stanford University with a Doctorate in Health Sciences. Welcome, Sam and Steph.

Our first topic this episode centers around risk stratification of COVID-19 patients. This is particularly important as the pandemic has led to an increased demand for healthcare resources and a shortage of medical equipment and staff. Prioritization of testing and resource allocation for patients at highest risk is crucial. Steph, what factors are considered when risk stratifying patients with acute COVID-19 infection?

STEPH PODOLSKI: So, severe illness means that a person with COVID-19 may require hospitalization, intensive care, or a ventilator to help them breathe or else they may die. People of any age and with certain underlying medical conditions are at increased risk for severe illness from the SARS-CoV-2 infection. There have been many multivariable models that have looked at many risk factors. The risk factors that put patients at greatest risk for severe infection include unvaccinated status, age greater than 65 years, specific ethnic backgrounds or race, diabetes mellitus, immunosuppression, chronic kidney disease, chronic liver disease, chronic neurological

disease, chronic cardiac disease, and chronic pulmonary disease. There are some studies out there that suggest that male sex increases risk for severe illness, whereas female sex increases risk for individuals to have long COVID-19 symptoms post-acute illness.

Additional factors to consider are the social determinants of health for an individual patient, which are the economic and social conditions that influence individual and group differences in health status. Healthy People 2030 organizes the social determinants of health around five key domains: economic stability, education, health and healthcare, neighborhood, and built environment. The last one would be social and community context. Individuals that live in poverty, who don't have access to healthy food or water, or don't have access to housing are at increased risk for adverse health outcomes in general. Differences in health are striking in communities with poor social determinants of health, such as unstable housing, lack of transportation, low income, unsafe neighborhoods, or substandard education. And all these factors have been shown to increase the risk of severe outcome associated with an acute COVID-19 infection.

It's important to mention that there are special populations that we have noted as healthcare providers throughout the course of the pandemic that put people at increased risk. These include pediatrics, pregnant individuals, immunocompromised folks or transplant patients. And I'd like to mention a few things about each here briefly.

Most children continue to do fairly well with the acute COVID-19 infection, thankfully. However, the pediatric population is at risk for multisystem inflammatory syndrome, also known as MIS-C. Multisystem inflammatory syndrome in children, which is what the C stands for in MIS-C, is a condition where different body parts can become inflamed, including the heart, lungs, kidneys, brain, skin, eyes or gastrointestinal organs. There's ongoing research about the cause of this syndrome specifically. However, there's a known link between COVID-19 and this syndrome specifically. Most children who have been diagnosed with MIS-C have done fairly well and improved with supportive medical care. However, it has been documented that there have been children who have died.

Moving on to pregnancy, pregnancy alone is a risk factor for severe COVID-19 illness. Pregnancy increases hypercoagulability, and COVID-19 also is a risk factor for hypercoagulability. COVID-19 acute infection during pregnancy increases the risk of delivering a preterm or stillborn infant. And preterm in this context is defined as earlier than 37 weeks. People with COVID-19 during pregnancy may also be more likely to have other pregnancy-related complications.

And the last population I'd like to touch on under the special population section is transplant patients or immunocompromised patients. These folks are at risk for severe illness just because of their medical comorbidities. Medications needed for transplant of certain conditions blunt the immune response, and some of these medications would include chemotherapeutic agents, anti-rejection medications for transplant patients, chronic steroid use, or medications needed for autoimmune or rheumatological

conditions. The known immune response for COVID-19 vaccination may actually also not be as strong in this population, which is why these folks are still at high risk for severe outcome or severe infection.

ANGELA LECLERC: That was a really great, thorough review of the considerations when risk stratifying patients, particularly the special populations. Thank you, Steph. Sam, are there any validated tools that primary care providers may use to assist with risk stratification?

DR. SAM WIJESINGHE: You know, personally, I see many patients that I have taken care of for many years. Most of my patients, I have been taking care of them for like 5 to 12 years. So therefore, I know their history, not only their past medical history, but also their social determinants of health. You know, things like transportation issues, housing, their culture, financial barriers, education, and then access to healthcare. So, I try considering all these elements when I'm determining my treatment plan. I know that many primary care providers deal with COVID-19 patients virtually. So, that is a challenging situation, especially we had a challenging situation at the beginning of the pandemic. But I think for primary care providers, having a very comprehensive HPI is the most vital part when they are taking care of patients virtually.

ANGELA LECLERC: Great. Thank you, Sam. After you've performed your risk stratification, which patients should a primary care provider send to the emergency department to be considered for hospitalization?

DR. SAM WIJESINGHE: Yeah, we run into this situation a lot. So during the initial assessment, we can often determine which patients are appropriate for self-care at home and then which patients may be eligible for treatment with the COVID-19 specific therapy. In other words, supportive care plus antiviral. And finally, which patients warrant an urgent emergency department evaluation so we can assist that during the initial visit, and then we will go from there.

ANGELA LECLERC: Are there challenges that you face when assessing patients for the severity of their COVID-19 infection, either in an office visit or via telehealth?

DR. SAM WIJESINGHE: Yes, certainly we do. I just want to give you a little bit background about my practice setting. We do manage patients with COVID exclusively, virtually, so we don't really bring any patients with those symptoms into the clinic. The reason for that is that we take care of many patients with the immunocompromised and geriatric population, and they continue to come to the clinic. So as a result, we manage our COVID patients exclusively virtually.

So, when we manage patients virtually, that is challenging. This is not something we learn in PA school. When you practice medicine, you get to know how unreliable some of the information that your patients provide. You know, for example, someone might say, I had high fever. And then when you ask what's the temperature like; she or he might say it was 99. And you and I, you know we know 99 Fahrenheit is not febrile. So,

you have to be very careful when you are managing your patients virtually, to assist them carefully, because what you are hearing is probably not very reliable at times. I also should add that we do virtual visits via phone and video. And while video is more helpful, because then we can see the patients, not all the patients are educated with the technology and they are not able to do the video. So, we have to do quite a bit phone virtual visit, which is another limitation because we cannot even see how patient appears during the visit. And then now, we have been dealing with many COVID patients virtually for over 2 years. So, we have developed some experience within the last 2 years plus - but now, we have some experience with that. But it was very challenging at the beginning of the pandemic to take care of these patients virtually.

ANGELA LECLERC: Yeah. That's a good point, Sam. I can't imagine having to assess a patient over the phone, never mind the challenges of the 2D world. But actually, just talking to them over the phone would be another layer of challenge, trying to decide what the best disposition is for that patient.

OK, well, now that we have identified high risk patients, assessment tools for risk stratification, and which patients should be referred to the hospital, Sam, how can providers identify and mitigate barriers for patients who will remain home during the course of their illness?

DR. SAM WIJESINGHE: That's an excellent question, Angie, thank you for asking. You know, I would say close follow up. We need to continue to follow up these patients. So when they are home, maybe on antiviral, doing supportive care. And then I ask them to follow up with me so that we can continue to evaluate how things are going with these patients. And then there are some cases that we have a very full schedule and it's very hard to do follow ups. And then I sometimes ask my nurse to give a call to these patients and find out how they're doing. And then sometimes, even medical assistant, they do a follow up. So basically, when they're at home, and then we try our best to monitor them, how they are doing. And then also, we encourage them to do frequent follow-ups as needed.

ANGELA LECLERC: Sam, what about the patients who perhaps are undergoing cancer treatment or regularly follow up with a transplant specialist and are immunosuppressed? Are you calling those specialists and coordinating care for those patients?

DR. SAM WIJESINGHE: Yeah. Thank you for asking that question. I think that's another very important thing. When I have a patient with COVID-19 and if the patient has a terminal illness, for example, let's say malignancy, I try to coordinate with the oncologist, and then make sure that what I'm trying to do with the patient is okay with the oncologist. And so, coordination of care is very important. So, I really like to make sure that we are all on the same page when we come up with the treatment plan. So, I make sure to coordinate with those specialists. At the same time, in my case, I am a HIV specialist too. So there are some other primary care providers reach out to me and if somebody has HIV, and then they want to make sure it is okay for them to start some

of the new antiviral treatment for COVID, I appreciate that. I think that coordination of care is important and we should team up and take care of patients together.

ANGELA LECLERC: Great, Sam. Thank you. I'm sure your patients all appreciate that you're coordinating their care for them like that. Staying with the theme of the in-person versus telehealth, Sam, when and how is it recommended that providers follow up with their patients who have COVID?

DR. SAM WIJESINGHE: So, I want to say, depending on the severity of the illness, for example, if I have a young, healthy patient with a negative past medical history with mild cough, I might say, "Please follow up if symptoms are not improving or worsening." And then if I have a patient with HIV/AIDS with the same symptom, for example, mild cough, I will sure to have a follow up because of their immunity is compromised. And then, of course, if there is a patient with moderate to severe symptoms, we will continue to follow up. That may be an ER follow up or hospital follow up. So, in general, we try to follow up these patients, almost all our patients unless they are doing very well and they don't have symptoms. And then also, based on the resources we have, if we have enough providers, we would like to follow up everyone. But sometimes, we have to make some decisions who we should follow up and maybe some to follow up only as needed.

ANGELA LECLERC: Something that you said piqued my interest, Sam. You mentioned follow up in the emergency department. Can you tell me more about that? Is it a primary care patient who doesn't actually need emergency care but is just doing a regular COVID follow up with an ED provider?

DR. SAM WIJESINGHE: You know, actually, the reason I say that... Let's say I talk to a patient, I take care of the patient virtually, then I feel like patient should go to the emergency room. I send the patient to the emergency room, but I tell the patient, please follow up with me after your ER visit. So that's what I meant by that. So, maybe patient was evaluated at the ER setting, and then I will follow up the patient after discharge from the ER.

ANGELA LECLERC: Okay. Great. Thanks for that clarification. So, part of coordinating patient care is ensuring that the patients are receiving the right treatment to keep them out of the hospital. Let's move over to you, Steph. Which patients do you recommend prescribing steroids to?

STEPH PODOLSKI: So, the guidelines are pretty clear on this for acute COVID-19 infection. At this point in the course of the pandemic, steroids should only be used for patients requiring oxygen. The standard of care for steroid treatment is dexamethasone, prescribed at a dose of 6 mg for up to 10 days, not to exceed 10 days, but could be prescribed for less, and that is only for the period of time in which that patient is requiring oxygen. There is some data that notes that prednisone could be used at an equivalent dose of 40 milligrams, however, it's been studied and noted that

this steroid is not as effective as dexamethasone in the treatment for acute COVID-19 infection.

ANGELA LECLERC: And Steph, what about oxygen? If you have a patient with new oxygen requirements, do they have to be hospitalized or can they receive oxygen at home?

STEPH PODOLSKI: That's a great question. And the answer is they do not always have to be hospitalized. And I would like to mention here that oxygen can be established at home, although there are many barriers to getting this set up, one of which specifically is qualifying a patient for oxygen so that their insurance company will pay for it. A few other barriers include financial barriers and supply chain issues. There was a period in time geographically where it was difficult to get oxygen because of the demand across the country, because so many people were requiring oxygen.

And so, there are some qualification tests that are needed that can be performed in an office setting or even emergency department, including a hallway ambulation study where somebody ambulates with a patient with a pulse oximeter, determines if there is hypoxia, at which time oxygen would be required to maintain a certain oxygen level for the patient based on that individual patient and their health comorbidities. And that would qualify a patient for home oxygen for insurance purposes, which means that their insurance company would pay for it. And it's a very easy and inexpensive test to complete. Another test that is not as easy to perform, that often is performed on the inpatient setting, is an overnight oximetry study to see if oxygen is needed at night. But again, the hallway ambulation would be a study that's easy to complete and would help qualify that patient for home oxygen and prevent hospitalization.

ANGELA LECLERC: Yeah, I agree. There were such challenges with the supply and demand of oxygen during the height of the pandemic. I'm going to go back to you Steph again one more time. Could you comment on the use of prophylactic antibiotics? Are they recommended to decrease the risk of bacterial pneumonia in COVID-19 patients?

STEPH PODOLSKI: That's a really great question, Angie. In general, I would say the answer is no. This is a viral respiratory illness. And if possible, antibiotics should be avoided. Antibiotic stewardship continues to be a priority in healthcare, and clinicians should be extra cautious and only consider antibiotics when it's felt to be truly indicated. In the mainstay of treatment, for patients with mild to moderate symptoms related to acute COVID-19 infection, who are at high risk for severe disease, is oral antivirals and supportive care. There are some exceptions to this, although in general, I would say the answer is no.

ANGELA LECLERC: Steph, do you see any downside to prescribing prophylactic antibiotics as outpatient? What's the risk?

STEPH PODOLSKI: I do see many downsides. The risk would be increasing that individual patient's future risk for bacterial resistance to antibiotics, increased risk of C. difficile colitis infections, potential side effects related to the type of antibiotic being used such as cardiac arrhythmias or even tendon rupture, which are well-known with many antibiotics, and the list goes on. And so, I would say the risk of antibiotic prophylaxis is actually much greater than the benefit.

ANGELA LECLERC: Steph, we already established that prophylactic antibiotics for possible superimposed bacterial pneumonia are not recommended. When would you consider antibiotics for patients with COVID-19?

STEPH PODOLSKI: That's a great question, Angie. Thank you. There are certain populations where antibiotics should be considered for a superimposed bacterial pneumonia. And these populations include patients who are significantly immunocompromised, cancer patients with febrile neutropenia, where their immune system is unable to fight off any sort of insult or infection. Individuals with moderate to severe COPD who have an acute exacerbation of their COPD in the setting of an acute COVID-19 infection, and then those who have true findings of community-acquired aspiration or even ventilator-acquired pneumonia on imaging. And these folks also should have a high-risk score for pneumonia. And so, the score we use is the CURB-65 risk calculator. And I think we'll be talking a little bit more about special populations in our next episode. And at that time, we can highlight a little bit more specifics. And I would still like to say in general, antibiotics should not be used for the majority of patients with acute COVID-19 infections, about 80% to 90% of our patients who are at home managing their viral illness.

ANGELA LECLERC: Yeah, that's helpful, Steph. Thank you. I completely agree with that. Sam, could you please discuss which patients are prescribed antivirals such as nirmatrelvir-ritonavir?

DR. SAM WIJESINGHE: Yes. So, I actually look at a few important things. I look at their age, then comorbidities. And then if they are compromised, immunocompromised or not. So, patients are recommended antiviral based on their risk profile. That's how I make a recommendation. And furthermore, I look at whether there are medication interactions, and then if they have – if they got the vaccine or not, you know, I look at those factors as well before I make that determination to start antiviral.

That being said, I like to go back to what Steph was talking about, antibiotic use. Steph, thank you for bringing that up. I like to share what we experience in primary care setting, it has been a challenge. Most of the time, when we manage patients with COVID, that is the first thing they ask. "Can you prescribe me an antibiotic?" So, I think it's a teachable moment, that we have to teach these patients antibiotic is not going to do anything for your COVID-19 and show the difference between the viral infections and bacterial infection. But it is a constant battle, but we try our best to teach patients regarding antibiotic resistance.

ANGELA LECLERC: Yeah, Sam. I think that we've all run across a lot of teaching moments the past 3 years with our patients who have never been so interested in how science works. Steph, what else could providers take into consideration when deciding whether or not to prescribe antivirals?

STEPH PODOLSKI: So, there are many things to consider with the medications, the oral antiviral treatments for COVID-19. Medication interactions is a big consideration, kidney function, liver function and immunosuppression. So, ritonavir is a strong cytochrome P450, and a 3A4 inhibitor, and a P-glycoprotein inhibitor. And the co-administration with the nirmatrelvir is to increase the blood concentration of nirmatrelvir. And so, it thereby is making it effective against the SARS-CoV-2 virus.

So interestingly enough, with the combination of these two medications into one oral antiviral agent, is that there are many, many medication interactions. And so, when you are considering prescribing this agent or any of the oral antiviral agents, medication interaction with a home med list is vitally important. I think it's important to mention here, and a lot of people are not aware of this: There is a recommendation by the manufacturer that there's a 2- to 3-day hold on certain medications that a patient may be taking if prescribing ritonavir /nirmatrelvir. And these medications include anticoagulants such as rivaroxaban, lipid modifying agents, specifically all of the statins, erectile dysfunction medications, respiratory medications, migraine medications, including the triptans, cardiovascular agents, neuropsychiatric agents, and other things that we use regularly for conditions like gout, one of which is colchicine. That's the list of medications that is recommended to be held for 2 to 3 days if prescribing ritonavir /nirmatrelvir.

There is a list of additional medications that should be considered as medications that could increase an adverse reaction when prescribed in combination with oral antiviral agents. The list of medications, and I'll just be giving you some examples here, that should be considered as potential medications that could cause an adverse reaction in combination with the oral antiviral treatment for acute COVID-19 infection include anticonvulsants, cardiovascular agents, such as amiodarone and clopidogrel, immunosuppressants, anti-infective agents, multiple neuropsychiatric agents, and some pulmonary hypertension medications. And so, my comments here are that we, in general as clinicians need to be very careful at looking at home medication lists and kidney function, liver function, other medical comorbidities before prescribing antivirals. And at times, the risk of the antiviral course may actually outweigh the benefit of the agent.

ANGELA LECLERC: Thank you for sharing that. It sounds like it's a real balance of risk and benefit in terms of medication interactions and the indication for prescription for other medications, such as anticoagulants and antiepileptic drugs.

DR. SAM WIJESINGHE: Angie and Steph, if you have a moment, there is another thing I would like to highlight really quick. We had an observation study done recently, and then we were looking at what medications might make things worse when

somebody has COVID-19. I can share one example. We looked at, if somebody has GERD, if the patient is on omeprazole, actually, things can be worse. When we compare to antiacid such as famotidine and other PPIs, they are okay. But if the patient is on omeprazole, the severity of COVID-19 can get worse. So, I thought that was an interesting thing to share. And so, providers, look at the current medications that your patients are on and then continue to review materials and guidelines, because things can change rapidly, and also, ultimately, our goal is to take care of our patients as best as we can. So, I just wanted to share that as well.

ANGELA LECLERC: That's great, Sam. Thank you for sharing that. It's very important for us to continue to review and evaluate each patient individually and stay up to date as much as we can with these medications.

ANGELA LECLERC: This has been a really great review for episode two of risk stratification for COVID-19 patients, and also some of the challenges with telehealth, and office visits, and follow up. In addition to that, we reviewed some information about oral antivirals and other possible treatments for high-risk patients. We'll review these in more details in the future, as Steph pointed out.

This concludes Episode 2 of our five-part series. Thank you, Steph and Sam, for joining the discussion about COVID-19 risk stratification, early treatment and coordination of patient care. I also want to thank our listeners for joining us. Please join us for Episode 3, where we will discuss current treatments available to outpatients, including steroids and antivirals.

RESOURCES

For Providers

- COVID-19 Treatment Guidelines: Special Populations (NIH)
- Underlying Medical Conditions (CDC)
- COVID-19 Drug Interaction Checker (University of Liverpool)
- Drug-Drug Interactions Between Ritonavir-Boosted Nirmatrelvir (Paxlovid) and Concomitant Medications (NIH)
- Healthy People 2030 (HHS)

For Patients

- Specific Groups of People at Increased Risk (CDC)