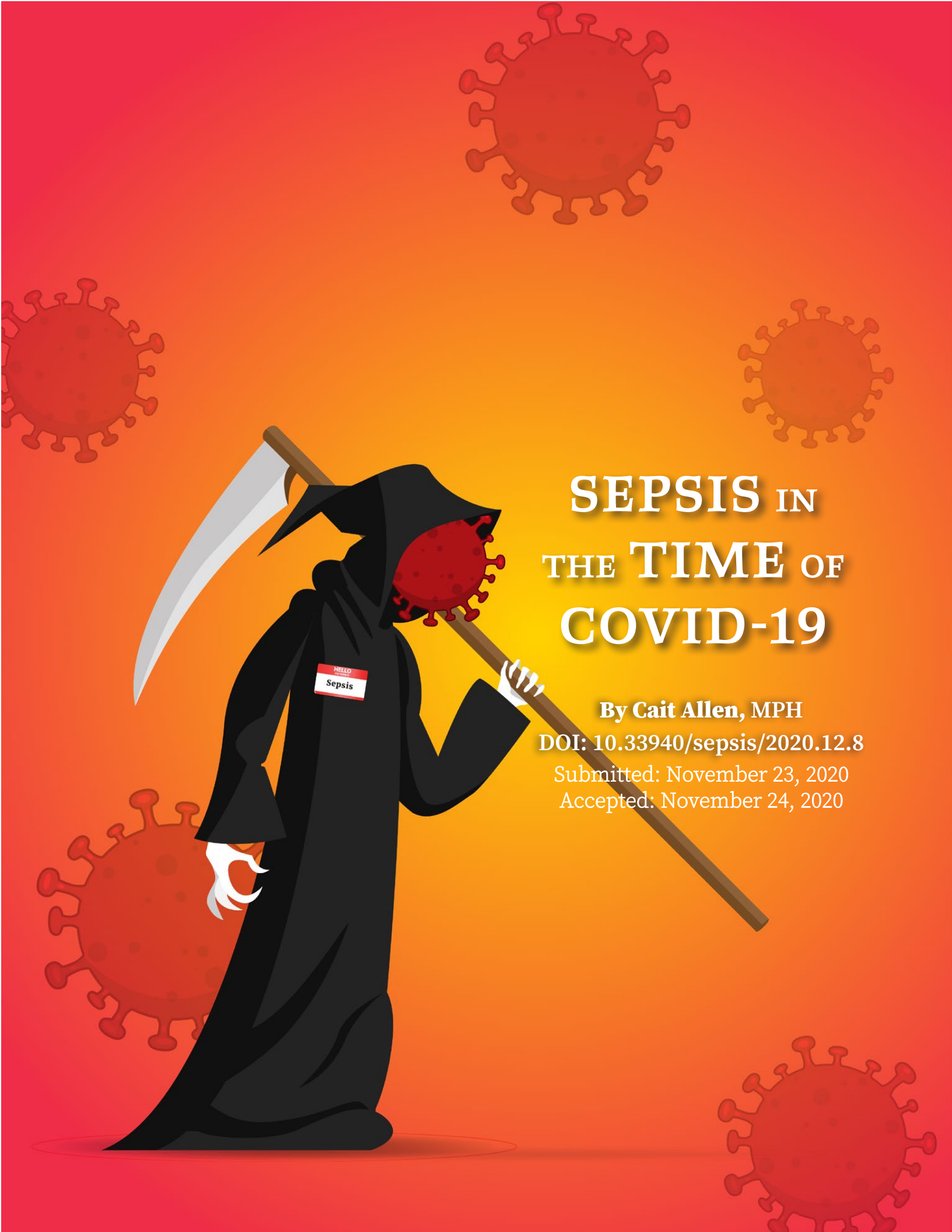

SEPSIS IN THE TIME OF COVID-19

By Cait Allen, MPH

DOI: 10.33940/sepsis/2020.12.8
Submitted: November 23, 2020
Accepted: November 24, 2020

This year, almost 2 million adults will contract this condition, and 270,000 will die as a result. Not COVID-19, sepsis. I sat down with Dr. David F. Gaieski, emergency medicine physician and director of Emergency Critical Care at Jefferson Health, to understand what sepsis is, its relationship with COVID-19, and how we can—and must—prevent both.

Cait Allen: What is sepsis?

Dr. David Gaieski: Sepsis is a reaction of the body to an infectious stimulus, which can be a virus, a fungus, a parasite, or most commonly bacteria. The body is mounting an immune response to try to fight off the infection. Sepsis as it's defined now is a dysregulation of that immune response: a dysregulated inflammatory response where the body is injuring itself, causing acute organ dysfunction, through its attempts to get rid of the pathogen that's causing an infection.

Why is this something that we should care about?

Because it's common. There are at least a million cases a year in the United States, probably significantly more than that. And the mortality from sepsis cases is somewhere in the 20% range; when patients also have shock—inadequate oxygen delivery to meet the metabolic needs of the cells—the mortality goes up over 30%. It affects all age groups. Young kids can get sepsis, adults can get sepsis, geriatric patients can get sepsis. It's also important because the more we know about it both as a lay public and as physicians and other healthcare workers, the better we can take care of it. People need to know the warning signs of sepsis, and they need to know how to get proper care when they are starting to develop sepsis.

What are some of those warning signs?

That's part of the problem, because sepsis isn't like a heart attack or a stroke, where you typically know exactly when things started or have a good idea of when things started because the person was normal, and now, for example, they're slurring their speech and they can't move one side of their body. But sepsis grows slowly in a lot of cases, and the initial symptoms are not unlike the symptoms of a cold or a mild case of the flu. It's a continuum. You can have sepsis from the flu, and the easiest way to think about the difference is that a lot of people who get the flu may feel achy and have some nausea and a stuffy nose and a fever. But their heart keeps working right, their oxygen level doesn't drop, their kidneys keep working right.

But some people get really sick with the flu, most commonly by having hypoxia—a low oxygen level in their blood. The problem is that sometimes it's hard to know when you just have the flu that you can treat at home with fluids and Tylenol, versus the flu that you need to go into the hospital for. A lot of the symptoms of sepsis are the same as the symptoms of less severe infections: fever, aches, nausea, decreased appetite. The concerning signs are when people start to feel confused, really weak, or short of breath like "I can't get enough air in" and they have a sense of air hunger, or have severe pain, or their urine output drops. Those are all things that can be pointing to a more severe case of infection and sepsis.

What things do clinicians typically look for to determine whether it's sepsis?

When someone comes into the emergency department, the first thing we ask them is, "Why are you here?" They might say, "I have a fever. I have a cough. I have belly pain." Then right off the bat we're going to get a set of vital signs. Is their blood pressure low or is it normal but significantly lower than where they usually are because they have baseline hypertension? What's their temperature? Is it high or low? What's their heart rate? Is it fast? What's their respiratory rate? Is it higher than 20? They're breathing very fast, are they taking really deep respirations? What's their mental status? Are they confused or sluggish or slow to respond?

We use something called the Glasgow Coma Scale, which gives us a 3 to 15 range, with 15 being totally normal. People with sepsis will often be confused and not answer questions appropriately. Then we'll look at their pulse ox, which is where you check the oxygen level in the blood through a sensor that's put on their finger.

We also check the patient's lactate level in most cases of possible sepsis. Our blood flow is all about bringing oxygen to cells so they can run the engines of life. If there's not enough oxygen delivery, then we shift into what's called anaerobic metabolism, where we use up the energy that's already been produced instead of being able to continually produce more energy. When that happens, the lactate level goes up. A normal lactate is typically less than 2 mmol/L. What research has shown is that as the lactate level goes above 2, the mortality starts to increase in sepsis, and it heads upward in a stepwise fashion, depending upon the lactate level. We check that early to help us risk stratify patients, to start therapy earlier, and it's considered an organ dysfunction by the different committees that have tried to codify what sepsis is and make uniform definitions.

What can make sepsis so difficult to diagnose?

It's not always obvious where the infection is, or even if there is an infection. It's not hard to diagnose sepsis when someone comes in with a cough and say "I think I have pneumonia' and you get a chest X-ray, and they have an obvious pneumonia on their chest X-ray. Or they come in and they say, "I have pain in my back, and I've been urinating a lot." Then you get a urine sample and they have an obvious kidney infection. Or if they have cellulitis and they have a big area of redness on their arm. But it can be much harder to diagnose in people who present confused and don't have something obvious on their physical exam, or in people who primarily have bacteremia. The bacteria have gotten into their blood and it's circulating around, but you don't know exactly where it came from. You don't have an obvious source.

There's also a lot of overlap with other diseases. For example, we often go down the pathway of, is this pneumonia, or is this a pulmonary embolism? Is this a kidney stone or is this diverticulitis? There are things that look like each other, some of which are infectious and some of which aren't. The speed with which you need to diagnose sepsis in general is faster than some other disease entities.

People can know that something's going on, but it can be harder for us to find. That's a lot of the reason. Then some of it too is that we don't have the optimal systems in a lot of emergency departments to take someone who has some screening criteria that raise a concern for possible sepsis, put them in a treatment space, and systematically work them up until we've ruled in or ruled out sepsis. If they're fairly stable, they may float around the ED and have a circuitous path to their diagnosis. But 25 years from now, maybe we'll be able to do bedside immunologic panels and tailor therapy to the way people respond to their infection.

Could there be a genetic predisposition to sepsis?

It's certainly being looked into. I'm not an immunologist, but there are known conditions in patients, for example those with meningococcemia and meningococcal sepsis, where they have certain genetic polymorphisms, which put them at a higher risk. Some of the overwhelming cases of meningococcal sepsis that you see will be in people who have a genetic defect in one of the factors that would help them to fight off infection.

Would it be better to take a more aggressive approach for treating sepsis, for instance, assuming that any patient could be or could become septic and ruling out sepsis as part of the standard differential?

Sure. The standard of care in most emergency departments when you see most patients is that you're evaluating them for exactly that and systematically ruling sepsis in or out. It might be as simple as you go to see someone who sprained their ankle and you say, "Tell me what happened." Big difference when it's a 25-year-old kid who says, "I was playing basketball and I stepped on someone's foot and I rolled my ankle," versus some older person who says, "I don't know really what happened. I went into the bathroom and I just twisted my ankle." Then the next question I always ask is, "How were you feeling when you went into the bathroom?" If they say, "Doc, I was feeling great." You say, "Have you been sick at all?" "No." So then you assume they probably just sprained their ankle.

But if they say, "I'm just feeling run down and not feeling great," then your suspicion that it could be something else goes up a little bit. You start to think maybe I need to figure out why they fell or why they sprained their ankle. I think we do this in all patients we see, it's just a question of whether we do it as systematically and as thoroughly as possible.

Is there any national registry for sepsis like what exists for cancer patients? Is this something that you think would be worthwhile?

There is no national registry, but I think it would be great to have one. If we were able to have a better sense of how many cases of sepsis there are a year, we would maybe be able to dedicate more resources to treating it and have, epidemiologically, a lot more sense of the syndrome and who it's affecting, and where and when it occurs most frequently, and stuff like that.

The Sepsis Alliance has been proposing to have a national sepsis registry. I don't know where they are in the process of that, but they were meeting with some government officials to try and talk through how to build one. That would be a heavy lift to get an actual registry where say 90% of the sepsis cases were tracked; you'd need a lot of resources dedicated to it.

But it would be great to have a registry. I'm not going to hold my breath because there isn't even a national cardiac arrest registry in America. Many countries in Europe and Asia have national cardiac arrest registries.

For example, in Japan, they know within a dozen patients a year probably how many cardiac arrests there are, because by law they have to enter them into a database within 24 hours of the cardiac arrest occurring, and the EMS [emergency medical services] providers do just that. In the U.S., we don't have anything like that. We just guess that there's 350,000 out-of-hospital cardiac arrests a year. But in Japan they know there's 109,452—I am making this number up but it is close to their real number—because they have it worked out as an epidemiologic tool. But I think it would be very helpful to have one, I would love to see it come along.

What are some of the long-term effects of sepsis?

When someone's hospitalized, they are often focused on recovery from that episode and going home. I think the longer-term effects are less appreciated. With sepsis, there's a lot of overlap with many other critical illnesses, something called post-intensive care syndrome. That has some well-defined things that happen to people, and bad sepsis cases have a lot of the same things. People have more depression afterwards. They have accelerated dementia if they already had it. They have earlier onset of other kinds of aging-related neurologic conditions. They're physically deconditioned. People who had a bad episode of sepsis fall more often, break hips more often, end up getting subdural hematomas. They may also get sepsis again.

A significant percentage of patients who had bad sepsis get readmitted within 30 days. Sometimes it's for another sepsis event that's related to the one they had, because they didn't get rid of it. But oftentimes it's just another event of sepsis that's different, because their immune system is not working well, and they're more at risk of infection in general for a period of time. The repercussions of sepsis are huge. Some places even have multidisciplinary sepsis follow-up clinics with PT/OT [physical therapy/occupational therapy], nutrition, and things like that. Some places do neurocognitive functioning tests down the road to see how people are doing after sepsis.

This just reinforces why everyone should care about this. Not only is sepsis challenging, but so is everything that happens afterwards. What can people do to prevent sepsis?

Wear their masks, so that they don't get COVID and then viral sepsis. They can wash their hands. They can get their vaccines, that's probably the most important thing if you're in a high risk category, or if you're old enough to be in a high risk category, you should be getting your strep pneumonia vaccine. You should get your flu vaccine, even if the flu vaccine for that year isn't a great vaccine as far as its match. Because in general if you've had your flu vaccine and you do get flu, you're going to get a less severe case of flu. Basic stuff like that. Basic first aid, you cut yourself you clean it off, and you pull out a splinter if it's there, and things like that. Most of it is common sense, but right now, the number one way to prevent sepsis is social distancing and wearing a mask.

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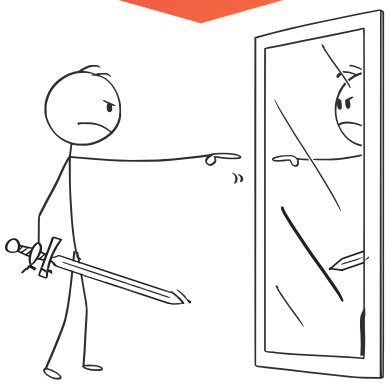
Sepsis Fast Facts

Sepsis is when the body starts attacking itself when trying to **fight an infection.**



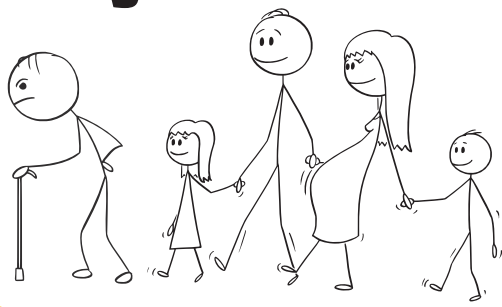
Long-term effects:

Early onset of age-related diseases like dementia

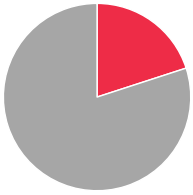
Depression

Increased risk of falls and infections

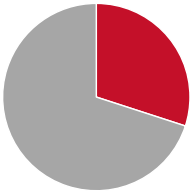
Anyone can get sepsis.



Sepsis must be treated in a **medical facility.**



20%
of people with sepsis die.



30%
of people with septic shock die.

Symptoms include:

Aches

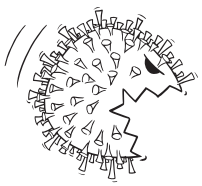
Fever/chills

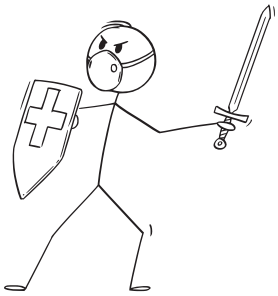
Nausea/decreased appetite

Shortness of breath

Feeling weak

The best way to prevent sepsis is to prevent infection.





Source: Patient Safety Authority

You mentioned that sepsis can stem from any kind of infection. Over the course of your career what have been some of the more surprising sources of infection that you've seen?

One interesting case I had was a young person who had acute HIV, seroconversion to HIV, and was diagnosed when we took care of him in the hospital. He presented with classic sepsis, a markedly elevated lactate level, and hypotension that required a lot of fluids, and then a vasopressor, and had kidney injury and liver injury as well. Every other diagnostic test was negative in him. The only thing that we found was that he did have acute HIV. The infectious disease doctors that saw him thought that's what was causing his sepsis syndrome.

Then things like septic foreign bodies, septic miscarriages. A young woman, who had just moved to the U.S. from a malaria-prone part of Africa, had falciparum malaria, which is the most dangerous kind of malaria. She was in septic shock with that. There are a lot of questions about how you should resuscitate people with malaria because of some of the issues with brain swelling. It was interesting to treat someone with that as their cause of septic shock and think through how to best manage her care.

How do sepsis and COVID relate to each other? Are you more likely to contract COVID following sepsis or vice versa?

Some people would debate this, but there's general consensus that bad COVID is sepsis. Because if you look at the body's response toward COVID and what COVID does to different organs in the body—kidneys, heart, and especially the lungs—it's clear that there's an inflammatory response to COVID. The body's trying to get rid of it, and that is, in part, what damages the tissues and organs,. But some people don't agree with that.

If someone is hypoxic or hypotensive, or someone has acute kidney injury, and they have sepsis, we need to try to recover the acutely damaged organs and treat the person with systematic supportive care, and try to make sure nothing else goes wrong for them. The same is true for critically ill COVID patients.

I think people get into big debates about whether COVID is sepsis, because there isn't the same antibiotic therapy. Remdesivir helps a bit in the sicker patients. But there isn't the whole array of broad-spectrum antibiotics to target to the patient's specific source of infection and which should be administered as soon as possible. Regardless, the basic principles of management of patients are very similar with any kind of viral sepsis.

As far as whether after you have sepsis you're at more risk for COVID, if you have had a lower respiratory infection like pneumonia, you're probably a little more at risk for being exposed and then contracting a virus. Your immune system's not as good for a period of time after you've been sick, and your mucosal barriers where you're going to get exposed to COVID aren't going to be intact in the same way. After sepsis, you're probably a little more at risk for getting COVID, because you're a little more immunocompromised.

Then after you have COVID, are you at risk of getting sepsis? I would say similar things. We haven't seen that much co-infection with bacteria and COVID at the same time. We've seen co-infections with COVID and other viruses more frequently. But after any major episode of critical illness you're at increased risk for another infection. That's one of the things people get readmitted with after they have COVID—a urinary tract infection or a bed sore that gets infected or pneumonia. All these things are related to what state the immune system is in and your ability to fight off another infection.

How difficult is it to distinguish between sepsis, COVID, and the flu? What should clinicians look for, and what can patients do to help get an accurate diagnosis?

They can be very hard to tell apart. The level of hypoxia that we see with COVID when people otherwise look pretty good suggests that it's not a bacterial pneumonia, for example. When you have bacterial pneumonia and your oxygen level is only 70% on room air, people look horrible, they feel horrible. We saw it more at the beginning of the COVID pandemic then we're seeing now, but when patients come in with COVID with pulse oxes of 60, 70, 72%, they often say, "No, I don't feel short of breath. I feel fine." There's a lot of theories about why that is. There's some neuro input from the lungs to the brain, and then the damage that COVID does to the olfactory area. There are some thoughts that this is all linked together, that our brain's perception of hypoxia is altered by COVID the same way our sense of smell is and this is what produces "happy hypoxia."

I'm not sure that's correct, but I saw one presentation on it that was very convincing to me. If I go climb Mount Kilimanjaro and I'm at 20,000 feet on Kilimanjaro, I'm going to have a pulse ox of 70% or 75% or so if I'm not using any supplemental oxygen. I'm going to know that I'm short of breath. I'm not going to be saying I feel perfectly fine. I might still be able to climb up the mountain, but I will have a sense of hypoxia and shortness of breath. These people coming in who aren't nearly in as good shape as your average person climbing Kilimanjaro don't even know that they're hypoxic.

It's interesting. But there's a ton of overlap and that's one thing people are really concerned about, the overlap in symptomatology between the flu and COVID and bacterial pneumonia.

Now, are we going to get people who don't know whether they have the flu or COVID, and they don't know whether they should come in or not? Or are they going to come in with both infections and then they're going to be sicker than they would have if they had one or the other? That's what we'll find out when flu season comes.

Sepsis versus those is different than with a localized infection. If I have a septic knee, my knee hurts. If I have cellulitis, my arm hurts where the cellulitis is. If I have an infected kidney stone or gallbladder, things are localized there, at least in the beginning. There's a lot more overlap between bacterial pneumonia and COVID or bacterial pneumonia and influenza than there is between some of those other bacterial causes of sepsis.

What should you do if you think you have sepsis? Can you treat it yourself or should you seek medical attention?

For most infections you need to get medical attention. Essentially, with the definition of sepsis now being infection and acute organ dysfunction, what we used to call severe sepsis, no one should be taking care of that on their own at home. Most of the time you need some IV fluid. Most cases require antibiotics unless it's caused by a viral source or a fungus or something, and many of those still require an antiviral or antifungal drug. Most of the time you need to be monitored and watched in a hospital setting. Sometimes it's only for a day or two to get the antibiotics going and make sure the person's stable and responding.

But it's not something you should manage on your own. The problem is many things that we feel like are "just a virus" or "just feeling run down" could be sepsis. People that are postoperative who start to feel flu-like symptoms, have a fever, achiness, etc., should be concerned about those symptoms. They should call their surgeon or go to the ED for evaluation. Odds-wise it's more likely that nothing serious is going on, but there's a decent chance that it's a complication of their surgery and that should be evaluated. Then the warning signs we talked about earlier, trying to really sort through, "Do I just have strep throat or an ear infection? Or do I have something more serious?" People need to have some medical literacy so they can sort through some of those things on their own and know what to go to the emergency department for versus what to go to an urgent care for versus what to call their doctors about the next day.

What can someone do to gain that medical literacy?

For patients at home trying to figure out what they should do, it is important that they know concerning symptoms. "I feel short of breath, I have pain in my rib cage when I take a deep breath and I've been coughing a lot. My urine output has dropped off, I feel fuzzy-headed and cannot think clear. Am I running a fever?" I think every person is capable of counting their pulse, counting their respiratory rate. People should know what normal vital signs are and people should really think about doing that—checking their vital signs when they don't feel good. Just look at a clock with a second hand, know where your radial pulse is and count your heart rate. If you feel like you're fighting off an infection and you are tachycardic that's a different scenario from if your heart rate is normal. No one of these things is definitive, but people can get some more medical literacy and really think through the question, "Do I need to be seen or not?"

A 30–year–old woman who's had three bladder infections can call her primary care doctor or go on to a video visit and describe her symptoms, and say, "My heart rate's 62 and I don't have a fever, and I feel fine, but I feel like I can't empty my bladder, like I have to urinate again as soon as I just went, and no I don't have any kidney pain. No, I haven't had chills or anything." That person can be treated with an antibiotic prescription over the phone or over the video connection. Being able to differentiate that from, "I have flank pain and I feel like I'm not peeing as much as I normally do, and my temperature's 102 and my heart rate's 110," is crucially important.

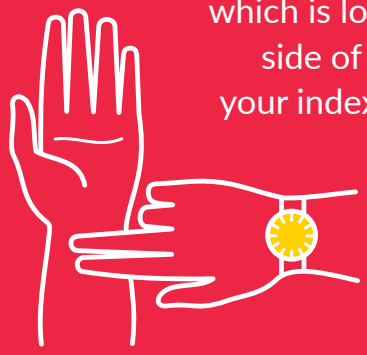
With that information, you can tell them to go to the emergency department so someone can check their vital signs there, lay a stethoscope on them and figure out what's going on, and get a urine sample and probably some lab work to further evaluate the situation. That's the kind of literacy people can have to help them know whether they should go in to the ED or not.

David F. Gaieski, MD, is a professor, vice chair for Resuscitation Services, and director of Emergency Critical Care in the Department of Emergency Medicine at the Sidney Kimmel Medical College of Thomas Jefferson University. His clinical and research expertise focuses on cardiopulmonary resuscitation, post-cardiac arrest syndrome (PCAS), extracorporeal CPR, and protocolized care for severe sepsis and septic shock. Dr. Gaieski has lectured and published extensively on the optimal clinical management of patients with PCAS and severe sepsis. In addition, he has used large national and international databases to study cardiac arrest and sepsis incidence and mortality.

Be Your Own Advocate: How to Measure Your Heart Rate

60 to 100
beats per minute:
normal resting heart rate for adults

To measure your heart rate, start by checking your pulse. Place two fingers between the bone and the tendon over your radial artery — which is located on the thumb side of your wrist. Or place your index and middle fingers on your neck to the side of your windpipe.



When you feel your pulse, count the number of beats in 15 seconds. Multiply this number by four to calculate your beats per minute.

x4
=BPM

Source: Mayo Clinic