

Episode 61: The cost of uncertainty: Infection, antibiotics and the race to prevent sepsis

Josh Casey: Hi, I'm Josh Casey. Welcome to *QuidelOrtho Science Bytes*, your trusted source for diagnostic insights and innovations. Sepsis is now one of the leading causes of death in U.S. hospitals. At least one in five adults and one in ten children who contract sepsis die or go into hospice care. Delayed diagnosis, as well as a one-size-fits-all approach that leads to over-resuscitation of patients with sepsis also drives up organ dysfunction and mortality rates. But there are new guidelines and awareness initiatives currently underway to help improve outcomes and care standards for sepsis patients.

The surviving sepsis campaign guidelines from the Society of Critical Care Medicine and European Society of Intensive Care Medicine highlights the need for rapid diagnostics and biomarkers, and the CDC's Hospital Sepsis Program Core Elements released earlier this year supports hospitals in improving patient recovery from this life-threatening emergency.

Joining us today to discuss this important topic is medical education liaison, Chris Sanchez. As an experienced medical science liaison and clinical specialist, Chris has deep expertise in advancing technological competencies and championing antimicrobial stewardship initiatives. His experience spans the gamut, from guiding hospitals and implementing diagnostic strategies to providing specialized care for critically ill patients.

Chris, thank you for being here today.

Chris Sanchez: Hey Josh, happy to be here. Thanks for having me.

Josh Casey: Of course. First question: Why is distinguishing bacterial from viral infections such a persistent clinical challenge? And what are the consequences when clinicians don't have enough information to make the distinction confidently?

Chris Sanchez: Yeah, good question. Distinguishing bacterial from viral infections remains difficult because many patients present with overlapping signs and symptoms such as fever, cough, elevated heart rate, inflammation, fatigue and abnormal laboratory findings. Early in the disease course, clinical presentation alone often doesn't clearly identify the underlying cause, and traditional microbiology cultures can take days, and even rapid diagnostics can take hours, to provide definitive answers.

When clinicians lack confidence about the infection type, they must balance two competing risks. Delaying antibiotics in patients with a bacterial infection can allow progression to severe infection, organ dysfunction, sepsis or septic shock, and conversely, prescribing antibiotics unnecessarily for viral illnesses exposes many patients to medication-related adverse events, increases healthcare costs and contributes to antimicrobial resistance.

This diagnostic uncertainty is one of the greatest challenges in both emergency and inpatient care. The guidelines established by the IDSA or Infectious Disease Society of America, help drive provider treatment decisions. Antibiotic delay can lead to worsening patient condition in many instances, so they're stuck on the fence of whether or not to provide the antibiotics or not to provide the antibiotics.

Josh Casey: So how can tests like procalcitonin, or PCT, help clinicians determine whether an infection is likely bacterial or viral? And how does that influence treatment decisions in emergency department and hospital settings?

Chris Sanchez: Well, first of all, PCT is the biomarker that rises in response to many bacterial infections while generally remaining low or stable in viral infections due to differences in the body's immune response. As a result, PCT can provide objective information that complements clinical assessment, imaging, cultures and other laboratory findings. In the emergency department, a low PCT result may increase confidence that a patient's symptoms are unlikely to be caused by a significant bacterial infection, supporting observation, further evaluation or avoidance of unnecessary antibiotics. Whereas an elevated procalcitonin can strengthen suspicion of bacterial processes and support more timely initiation of antimicrobial therapy. It's another tool in a clinician's toolbox.

In hospitalized patients, PCT serves as an additional decision support tool that helps clinicians determine the likelihood of bacterial infection, helps stratify risk and guide treatment decisions while awaiting definitive microbiological results, and to see the benefits of PCT, one of the main challenges is that it needs to be started in the emergency department. If a bacterial infection was caught in the early phases of systemic infection, PCT may not be significantly elevated. This is why empiric antibiotic therapy, when high clinical suspicion exists, remains in the guidelines. So a lot of times if there's high clinical suspicion, the patient's going to receive antibiotics regardless, depending on the guidelines, the treatment guidelines, but it's still an additional tool and serial draws are necessary approximately twenty-four to forty-eight hours later to determine if it truly is a bacterial cause of infection.

Josh Casey: Turning now to antibiotic stewardship, this remains a top priority for healthcare systems, and with good reason. How can PCT-guided care help reduce unnecessary antibiotic use while ensuring patients with bacterial infections receive timely treatment?

Chris Sanchez: PCT-guided care helps clinicians make more informed antibiotic decisions by adding biological evidence to the clinical picture. When PCT levels are low and consistent with a low probability of bacterial infection, clinicians may feel more comfortable withholding or shortening antibiotic therapy when clinically appropriate. When procalcitonin levels are elevated, clinicians can more confidently initiate treatment in patients who may benefit from antibiotics. This approach supports the core goals of antibiotic stewardship: getting the right antibiotic to the right patient at the right time and for the right duration. By reducing unnecessary exposure to antibiotics while maintaining rapid treatment for patients with true bacterial infections, healthcare organizations can improve patient care and support stewardship objectives simultaneously.

Josh Casey: That's interesting. So it's a bit of a balancing act then. But what is the connection between misuse of antibiotics, antimicrobial resistance and the growing threat of multidrug-resistant organisms, or MDROs for short?

Chris Sanchez: Every exposure to antibiotics creates selective pressure on microorganisms. When antibiotics are used unnecessarily, used for too long or used inappropriately, susceptible bacteria are eliminated while resistant organisms survive and proliferate. Over time, this process contributes to antimicrobial resistance and the emergence of multidrug-resistant organisms, which are significantly more difficult and costly to treat. Resistant infections are associated with longer hospital stays, higher healthcare costs, increased morbidity and greater mortality risk. The rise of antimicrobial resistance also complicates sepsis management because clinicians may have fewer effective treatment options when resistant pathogens are responsible for severe infections. Even with current technology and improved testing, such as rapid tests and PCR, that are not always one hundred percent, it is important to know that there's genotypic and phenotypic resistance,

and procalcitonin is a good tool to help clinicians and ID pharmacists both decide whether or not they're comfortable with either de-escalating antibiotic therapy or the need to escalate antibiotic therapy.

Josh Casey: Got it. Then connecting the dots here a bit, how can serial PCT testing help clinicians assess treatment response and determine when antibiotics can be safely de-escalated or discontinued?

Chris Sanchez: The value of PCT extends beyond initial diagnosis. Serial measurements allow clinicians to observe trends over time rather than relying on a single result. In patients receiving treatment for bacterial infection, declining procalcitonin levels may indicate that an infection is responding to therapy and the bacterial burden is decreasing. When clinical improvement aligns with the falling PCT values, clinicians may have greater confidence to narrow, de-escalate or discontinue antibiotic therapy earlier than they otherwise would.

This trend-based approach can help reduce unnecessary antibiotic days while maintaining patient safety, supporting both clinical outcomes and stewardship goals. There are published studies that show that a peak procalcitonin level reduced by eighty percent equals safety in discontinuing antibiotics.

Josh Casey: We know sepsis can develop quickly when bacterial infections go unrecognized or undertreated. How can earlier identification of bacterial infection and more targeted intervention help prevent progression to severe infection, organ dysfunction or fully developed sepsis?

Chris Sanchez: Sepsis is the body's life-threatening dysregulated response to infection and can rapidly progress to organ failure if not recognized and treated properly. Earlier identification of patients likely to have bacterial infections enables clinicians to initiate appropriate therapy sooner, including antibiotics, source control, fluid resuscitation and close monitoring when needed. The earlier the clinicians can distinguish patients who require urgent antimicrobial treatment from those who do not, the greater the opportunity to interrupt the disease progression before severe infection, organ dysfunction, septic shock or death occurs. Rapid recognition and treatment remain fundamental principles of modern sepsis care.

Josh Casey: From an operational perspective now, how can earlier differentiation between viral and bacterial infections improve triage decisions, patient flow, hospital resource utilization and ultimately healthcare costs?

Chris Sanchez: Earlier diagnostic clarity can have significant operational benefits across the healthcare system. When clinicians can more quickly differentiate likely bacterial from viral infections, they can make faster and more competent triage decisions, including determining the appropriate level of care, need for admission, isolation requirements and urgency of treatment. This can reduce unnecessary admissions, avoid excessive diagnostic testing and shorten time to definitive treatment plans.

Improved decision-making can also enhance patient flow through emergency departments, reduce hospital length of stay, optimize use of critical care resources and lower overall healthcare expenditures. At the same time, it's important to know, that more targeted antibiotic use can reduce pharmacy cost and the downstream cost associated with antimicrobial resistance and adverse drug events such as *C. diff* infections.

Josh Casey: With all the apparent upside to PCT testing, what barriers exist to implementing PCT-guided protocols and what are some of the maybe best practices you've seen work for successful adoption?

Chris Sanchez: Yeah, this is a good question. Several barriers can affect implementation. Variability in clinician familiarity and comfort with PCT-guided decision-making, such as how procalcitonin is cleared from the body, for such in those patients with renal disease. In these patients, it's very important that initial draw in the emergency department is collected. So this is why protocolization of utilizing procalcitonin seems to be the most effective strategy.

Some physicians do not understand the caveats and limitations of procalcitonin. And also, procalcitonin when looked at post-ER admission. Many clinicians are not very comfortable because there was not an initial procalcitonin collected. And this can impact decision-making in patients with poor renal function.

Concerns about relying too heavily on a biomarker without considering the full clinical picture is a barrier. Differences in institutional workflows and electronic health record integration, cost considerations and laboratory resource constraints, as well as lack of standardized protocols or education can also be a barrier.

And successful adoption typically includes strong leadership support and multidisciplinary collaboration among the antimicrobial stewardship team to include ID pharmacists, ID physicians, ER physicians and hospitalists.

Clear evidence-based protocols defining how PCT results should inform treatment decisions, integration into clinical pathways, order sets and decision support tools, ongoing clinician education and performance feedback, and monitoring of outcomes such as antibiotic utilization, length of therapy, sepsis metrics and patient outcomes. Organizations that align PCT implementation with broader sepsis and antimicrobial stewardship initiatives generally achieve the greatest success.

It's important to know in my personal experience, the biggest barrier is typically the fact that procalcitonin oftentimes is not ordered at the point of entry. And this is when it's most useful in being able to look at a serial measurement and not just a singular measurement a day or two after the patient is admitted and already on antibiotic therapy, thus having a baseline to compare against when looking at performing antimicrobial stewardship.

Josh Casey: Makes sense. Looking ahead now, what role do you see PCT playing in the future of infection management, antibiotic stewardship and sepsis prevention?

Chris Sanchez: Yes, PCT is likely to continue evolving as an important component of precision infection management. Rather than replacing clinical judgment, it can serve as a valuable biomarker that helps clinicians make faster, more individualized decisions across the continuum of care. As healthcare systems increasingly prioritize earlier sepsis recognition, antimicrobial stewardship and evidence-based resource utilization, procalcitonin can help support more targeted treatment decisions, reduce unnecessary antibiotic exposure and improve monitoring of treatment response. Combined with advances in rapid diagnostics, clinical decision support and sepsis programs, PCT has the potential to play an increasingly important role in improving patient outcomes while helping healthcare systems address the growing challenges of antimicrobial resistance and sepsis.

Josh Casey: A recurring theme we hear on the podcast is the need for time-critical diagnostic and intervention tools, particularly in busy ER settings. Nowhere is that more apparent than in sepsis cases, where every moment counts. I'd like to thank Chris Sanchez for joining today and sharing his first-hand insights and technical expertise in the latest testing regimens. These advances are aiding urgent care providers in making decisions that can improve survival rates.

And thanks, everyone for listening today. If you enjoyed the discussion, we invite you to subscribe to *QuidelOrtho Science Bytes*, our monthly podcast sponsored by QuidelOrtho Corporation, where we are advancing the power of diagnostics for a healthier future for all.

Until next time, take care, everyone.

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