Updates in sepsis management

On Oct 4, the Surviving Sepsis Campaign released updated global adult sepsis treatment guidelines. Ammara Mushtaq and Farooq Kazi report.

Sepsis and septic shock are leading causes of death worldwide. Improving sepsis management is critical in light of the COVID-19 pandemic. On Oct 4, the Surviving Sepsis Campaign released updated adult sepsis treatment guidelines. "The most important update, from my perspective as a stewardship researcher, is the introduction of nuance into the antibiotic timing and spectrum recommendations. The one size fits all, 1 h target for antibiotics has been replaced with a tiered approach that acknowledges both severity of illness (shock present or absent) and likelihood of sepsis as determined by the clinician", said Dr Michael Pulia, director of the Emergency Care for Infectious Diseases Research Program at the University of Wisconsin-Madison, WI, USA.

Early administration of appropriate antibiotics has been shown to reduce sepsis mortality. However, signs of infection or sepsis are often non-specific, and so the benefit of early administration of antibiotics should be balanced against the risk of adverse effects of antimicrobials—for example, hypersensitivity reactions, renal failure, *Clostridioides difficile* infection, and antimicrobial resistance. According to Dr Pulia, acknowledging the diagnostic uncertainty involved evaluating patients for potential sepsis is an important patient safety and antibiotic stewardship component of the guideline. He also pointed out that the diagnosis of sepsis when no infection is present drives overuse of antibiotics but also results in failure to identify the true cause of a patient's presentation. Encouraging clinicians to continue evaluating for alternative causes should prevent reflexive initiation of antibiotics and reduce the chance of early diagnostic closure errors that can occur when a patient is labelled as septic.

The strongest evidence for mortality reduction as a result of timely anti-biotics comes from a study in 149 hospitals in New York including 49 331 patients with septic shock. For each additional hour from emergency department arrival to administration of antimicrobials, there was a 1·04 (95% CI 1·05–1·09) increased odds of in-hospital death for patients requiring vasopressors and 1·01 (0·99–1·04) for patients not requiring vasopressor support. The new guidelines therefore recommend administration of anti-biotics within 1 h to patients with suspected septic shock. For those with suspected sepsis and without shock, a time-limited course of rapid investigation is recommended, and if suspicion of infection persists, administration of antibiotics within 3 h is recommended. For patients with a low likelihood of infection and without shock, deferring antimicrobials with close patient monitoring is suggested. According to Dr Pulia, the provision of a 3-h period of rapid and sequential evaluation will enable clinicians to refine their diagnosis and strike a good balance between timeliness and overuse concerns. "The inclusion of a recommendation to defer antimicrobials in stable patients with low likelihood of infection is an important step forward for stewardship and could dramatically curb overuse of antibiotics if it were to be incorporated into quality metrics such as the SEP-1", Dr Pulia said. Importantly, the guidelines recommend searching for alternative diagnoses in patients who are suspected to have sepsis (or septic shock), but in whom no source of infection has been found.

For patients with sepsis or septic shock who are at high risk for fungal infections, empirical antifungal therapy is suggested by the new guidelines. "There is definitely a narrow patient population, particularly those with profound neutropenia, that would likely benefit from empirical use of antifungals in a suspected sepsis scenario", said Dr Pulia. However, the exact criteria for this determination are poorly defined, and the evidence of benefit is lacking in more broad populations, hence the weak recommendation. Ultimately, the decision to include empirical antifungals is based on each individual patient's risk factor and clinical history. Sepsis and septic shock due to fungi are most commonly encountered in intensive care units and are associated with poor outcomes.

The updated guidelines also strongly stress individualised recommendations on the empirical use of meticillin-resistant *Staphylococcus aureus* (MRSA) coverage, one of the biggest drivers of patients receiving multiple antibiotics during sepsis care. MRSA coverage is recommended in patients at high-risk of infection with MRSA. Furthermore, for patients with sepsis or septic shock who are at high risk for multidrug-resistant organisms, empirical therapy using two antibiotics for Gram-negative bacteria is suggested. These antibiotics should be adjusted once the susceptibility of the causative bacteria is discovered. Given the increased prevalence of multidrug-resistant organisms and link between delays in active antibiotic therapy and adverse outcomes, this is considered a reasonable approach. "Similar to the change for MRSA and antifungal coverage recommendations, this approach involves a patient specific risk assessment and is more in line with the available data and stewardship principles", Dr Pulia said.

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