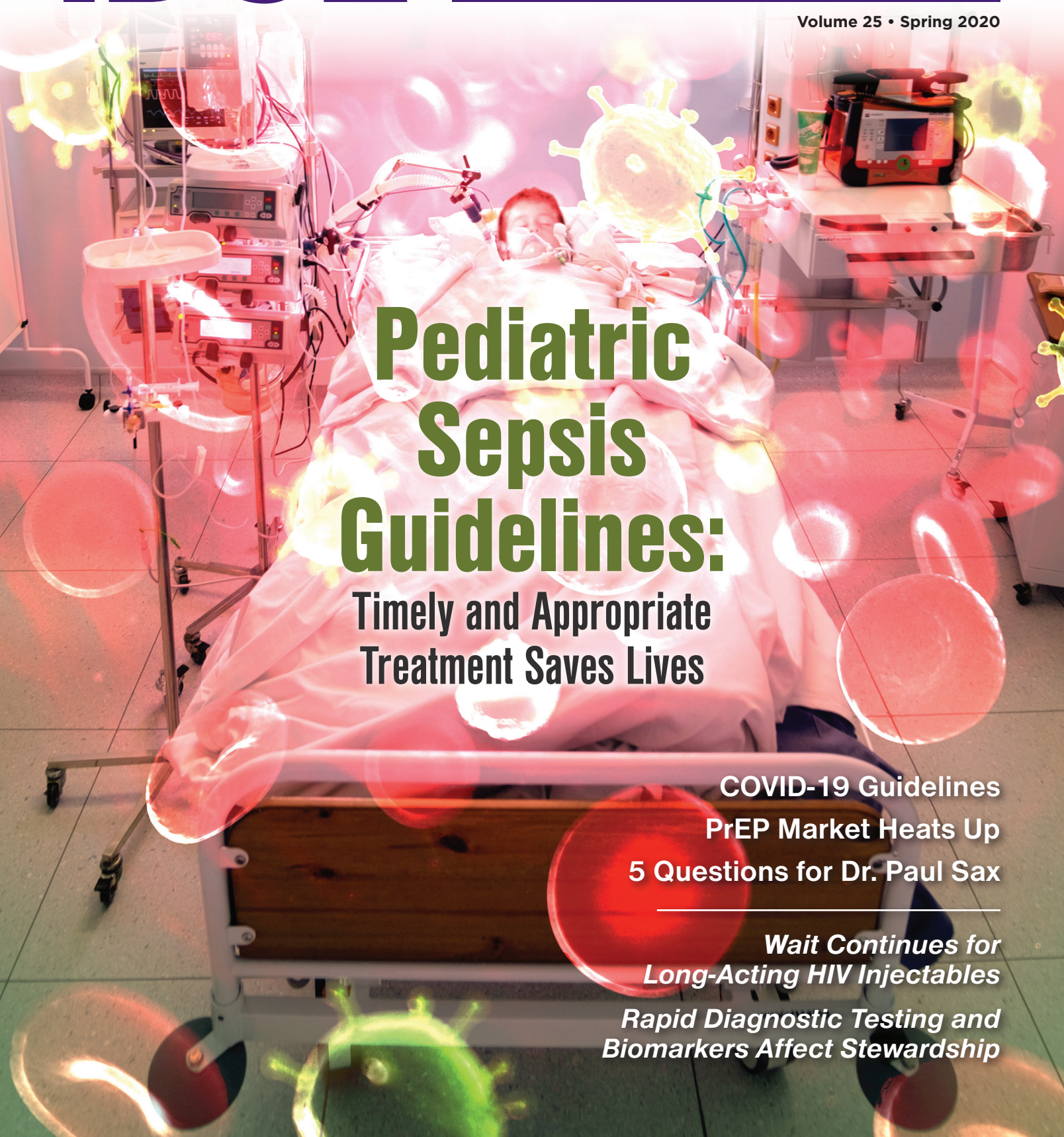
IDSE Infectious Disease SPECIAL EDITION

Volume 25 • Spring 2020



Pediatric Sepsis Guidelines:

Timely and Appropriate Treatment Saves Lives

COVID-19 Guidelines

PrEP Market Heats Up

5 Questions for Dr. Paul Sax

Wait Continues for Long-Acting HIV Injectables

Rapid Diagnostic Testing and Biomarkers Affect Stewardship

Pediatric Sepsis Guidelines:

Timely and Appropriate Treatment Saves Lives

By Marie Rosenthal, MS

With an estimated 7,000 U.S. children dying from septic shock every year, recognizing and responding quickly to sepsis—when a response can have the most benefit—is challenging because symptoms, such as high fever and general fatigue, are common presentations for many pediatric conditions.

However, until now, there has been no comprehensive sepsis guideline from the Surviving Sepsis Campaign (SSC) specifically focused on children to help clinicians on the front lines make this critical diagnosis (*Pediatr Crit Care Med* 2020;21[2]:e52-e106; *Intensive Care Med* 2020;46[suppl 1]:10-67). The SSC is a joint initiative of the Society of Critical Care Medicine and the European Society of Intensive Care Medicine, which are committed to reducing death and disability from sepsis worldwide.

More than 75,000 U.S. children develop sepsis or sepsis-associated organ dysfunction each year, and the numbers are increasing by about 8% per year, according to the Sepsis Alliance. Around the world, the numbers are staggering. An estimated 25 million children develop sepsis or sepsis-associated organ dysfunction, and up to 4 million die each year, according to Niranjan "Tex" Kissoon, MD, FRCP(C), FAAP, MCCM, FACPE, the vice president of medical affairs at British Columbia Children's Hospital and Sunny Hill Health Centre for Children, in Vancouver.

"Most of these deaths occur very early on. If we can get care as quickly as possible, we have a better chance of making inroads in outcome and survival," said Dr. Kissoon, who was the co-chair of the new SSC guidelines.

"Children are not simply small adults, and the signs of sepsis and its treatment differ, so they need to be assessed and managed differently," added Scott Weiss, MD, MSCE, FCCM, an intensivist at Children's Hospital of Philadelphia, and the co-vice chair of the guidelines, which "provides a road map for improving outcomes and saving lives."

The guidelines recommend each institution implement protocols to facilitate timely recognition and treatment for septic children. Health care providers should consider assessments of abnormal blood flow beyond blood pressure in children, including pulse strength, capillary refill time, and hand and foot temperature. "We suggest implementing systemic screening for timely recognition of septic shock and other sepsis-associated organ dysfunction," Dr. Weiss said, "and we recommend implementing a protocol for the management of children with septic shock and other sepsis-associated organ dysfunction based on these guidelines, which is a best-practice statement."

Infectious Response

Although adult sepsis guidelines recommend all patients begin antimicrobial therapy within one hour of recognizing sepsis, the pediatric guidelines recommend a two-phase process for assessing which children should receive immediate antibiotics. Those with septic shock should be started on antimicrobial therapy within one

hour of shock recognition. Those who do not have septic shock symptoms may require more evaluation to confirm the differential, and if positive, started on therapy within three hours of the initial suspicion for sepsis—or sooner if shock develops. This evaluation should include blood cultures, according to Dr. Weiss, as long as this will not delay antibiotics.

"This is a best-practice statement for children who have septic shock that is clinically identified," he said. "We recommend starting antimicrobial therapy as soon as possible and ideally within one hour of recommendation.

"In contrast for children who have sepsis but without shock, we suggest starting antimicrobial therapy as soon as possible after appropriate evaluation and within three hours of the initial suspicion of sepsis," he said.

When making this two-tiered recommendation, the panel considered the potential adverse events of antibiotics, as well as the development of resistance.

"To balance the competing priorities of being able to accurately administer antibiotics to those who need it, for children *who do not have shock*, we recommend an expedited diagnostic evaluation to confirm sepsis rather than blindly treating all children who may, or may not, have sepsis," he said.

For immunocompetent children or those without a high risk for multidrug-resistant (MDR) pathogens, the panel recommends empiric broad-spectrum monotherapy that covers all likely pathogens. For those who are immunocompromised or at risk for MDR pathogens, the panel recommends choosing multidrug therapy.

The reason: "Several studies have demonstrated increased adverse effects associated with routine use of multidrug therapy," Dr. Weiss said. "As an example, vancomycin and piperacillin-tazobactam combination is associated with an increased risk of acute kidney injury in children.

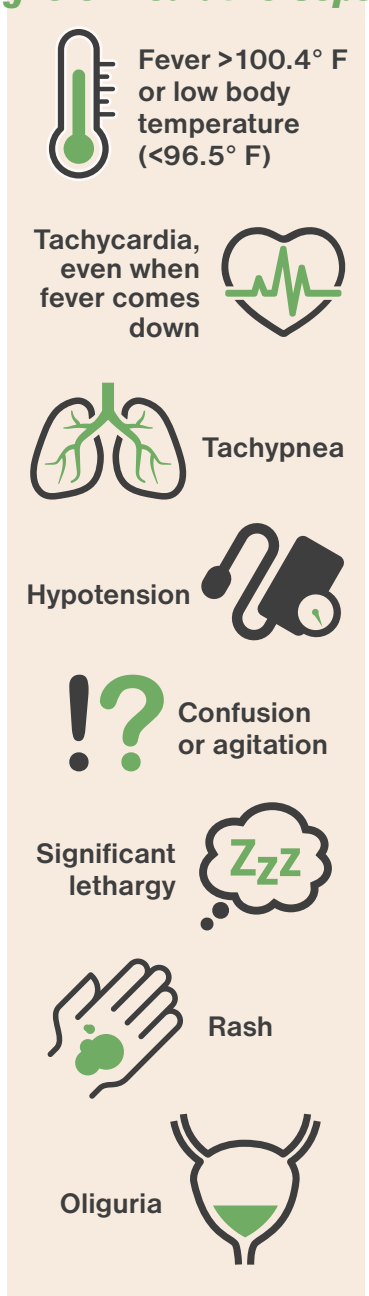
"If there's a high risk of antimicrobial resistance in the community or the hospital in which you're treating the patient, you might consider expanding your coverage to include a glycopeptide like vancomycin, or an aminoglycoside."

He added the level of resistance that would be concerning is unclear, but he suggested a level around 10% would be reasonable to start thinking about MDR coverage.

Narrow therapy once the specific pathogens have been identified, he said, and the need for de-escalation should be assessed daily. Along those stewardship lines, the panel recommends that the length of antimicrobial therapy should be based on the individual patient, rather than a set period.

The panel also recommends quickly instituting source-control procedures, including the removal of intravascular devices that are confirmed to be the source of sepsis.

Signs of Pediatric Sepsis



Cardiac Response

When evaluating the need for fluids and vasopressors, it's time to move away from the "cold" and "warm" shock categorizations and use hemodynamic variables, such as trends in blood lactate levels, suggested Pierre Tissieres, MD, PhD, the director of the pediatric neonatal intensive care unit at Paris South University Hospitals.

Based on cardiac output, children who are being treated in hospitals with ICUs should be given up to 40 to 60 mL/kg of bolus fluids over the first hour of treatment if shock is present. But fluids should be discontinued if the child exhibits signs of fluid overload, according to Dr. Tissieres, a co-chair of the guidelines. If the health care system is without the resources to manage fluid overload—either locally or via transfer to another facility—do not administer a bolus of fluid unless the child's blood pressure is very low. Instead, provide maintenance fluid.

The guidelines recommend using buffered crystalloids rather than 0.9% saline for the initial resuscitation of children with sepsis or septic shock. Starches and gelatin should not be used.

continued on page 64

Pediatric Sepsis continued from page 11

"Fluid administration should be guided by frequent reassessment of clinical markers, such as blood lactate levels [in addition to clinical signs]," Dr. Tissieres said.

Epinephrine or norepinephrine, rather than dopamine, to treat hypotension should be started if the child continues to show signs of shock despite appropriate fluid therapy, according to Dr. Tissieres. They could not recommend initiating vasoactive agents through peripheral access in children in shock. "In our practice, we administer a dilute concentration of the initial vasoactive medication through a peripheral vein, if central venous catheterization is not available," Dr. Tissieres said.

Intubation

The panel was unable to make a recommendation about when to intubate children with fluid-refractory, catecholamine-resistant shock. "When the decision is made to intubate, we suggest not to use etomidate as an indoctrination agent," Dr. Weiss said. "We further suggest trying noninvasive mechanical ventilation in children with sepsis-induced pediatric acute respiratory distress [PARDS] without a clear indication for intubation and who are responding to initial resuscitation."

The panel recommends against the routine use of inhaled nitric oxide in all children with PARDS, "but we suggest trialing inhaled nitric oxide as a rescue therapy in a subset of children who have refractory hypoxemia after other oxygenation strategies have been optimized," Dr. Weiss said.

Nutrition

Enteral nutrition is the preferred method of feeding, according to the guidelines. The panel is against the routine use of selenium, glutamine, arginine, zinc, thiamine, and vitamins C and D, as current evidence does not yet support benefit of these nutritional supplements.

The panel provided comprehensive recommendations for managing sepsis in children following the GRADE methodology and released the guidelines at the 2020 Critical Care Congress in Orlando, Fla. For more information, visit bit.ly/3bn8NVUidse. ■