Making sense of paediatric sepsis

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The release of the Phoenix Criteria for paediatric sepsis and septic shock earlier this year marked a milestone for global child health. Derived from a clinical dataset of more than 3·5 million paediatric hospital encounters at ten sites in five countries, these criteria provide the first age-specific operational definition of paediatric sepsis as infection-associated, life-threatening organ dysfunction. These criteria can help to standardise research, benchmarking, and quality improvement—crucial steps towards reducing the burden of sepsis, which leads to 3 million deaths in children each year. In this context, we present a four-paper Series on paediatric sepsis by a diverse and multidisciplinary group of leading, global critical care experts in *The Lancet Child & Adolescent Health* and *The Lancet Digital Health*.

Half of all sepsis cases globally are in children younger than 19 years, with the highest incidence in the under-5 age group. With Paper 1 of the Series, we are given insight into the most recent estimates of the burden across country-income levels, the microbiological aetiologies and their relation to therapeutic approaches, and the long-term, multidomain, and often life-altering impact of the experience on survivors and their families. Paediatric sepsis has long been a leading cause of childhood morbidity and mortality, not because it is unusually hard to prevent or treat, but because historically, expert opinion and sometimes inaccurate generalisations—rather than data-driven evidence—have tarnished the lens through which the symptomatic child with suspected or confirmed infection was seen upon first encounter. Paper 2 dives into the immunopathology of paediatric sepsis and explores the cellular responses to infection within the context of a young, developing immune system. Biochemical, cell biological, and mouse model research is beginning to resolve the intricacies of the dysregulated host response to infection that leads to life-threatening organ dysfunction. The critical care community is capitalising on these advances: protein biomarkers and host gene expression signatures are just two examples of tools showing potential to expand the clinical management landscape of paediatric sepsis.

It is crucial to remember that sepsis itself and poor outcomes of sepsis in children are often preventable. Suboptimal quality of care, inadequate health infrastructure, poor infection prevention and control measures, late diagnosis, and inadequate clinical management across the care continuum are some of many interwoven reasons—especially in countries with resource-limited health-care systems—that sepsis still affects so many young children. Paper 3 is a proposal by global stakeholders to build sustainable and scalable systems of care through quality improvement programmes. We are reminded that sepsis is a disease of systemic failures to learn. From prevention to post-discharge support, the failures are rooted in pervasively insular attitudes to education, health-care investment, and collaboration shaped by decades of poor political priorities. A unified roadmap for strengthening sepsis quality improvement programmes is instructive and invaluable, but instrumental to its success will be unwavering government investment in the health of children.

The Series sends a strong message: honouring the 2030 World Sepsis Declaration will take transdisciplinary allyship and commitment to a research roadmap that closes the evidence gap for paediatric sepsis and improves survival and long-term quality of life in children affected by sepsis. From international networks to harmonised data-capture systems and agile platform trials, a resounding theme across much of this Series is the growing intersection of digital health and paediatric critical care. Aptly, Paper 4 highlights how digital technology is benefitting real-time decision support tools in paediatric sepsis care. Digital structures could also have a role in reducing global health disparities in care, but only if developed, tested, and deployed equitably.

We stand at the cusp of a new era for paediatric sepsis research that holds much promise. A decade of global collaborative work by the paediatric critical care community has resulted in tangible advances. But we must remember that sepsis starts with an infection that can be prevented and contained early on. Coordinated efforts must therefore involve clinicians in all health-care settings, researchers across disciplines, and policy makers—particularly in infection prevention and control, tackling antimicrobial resistance, implementing universal health coverage, and raising public health awareness—to reduce the burden of sepsis on children, families, and society. ■ *The Lancet Child & Adolescent Health*

For the **Phoenix Criteria for paediatric sepsis and septic shock** see *JAMA* 2024; **331:** 665–74

For the **Series on paediatric sepsis** see www.thelancet.com/series/paediatric-sepsis

For the **2030 World Sepsis Declaration** see https://www.worldsepsisday.org/declaration

For more on **protein biomarkers** see **Articles** *Lancet Child Adolesc Health* 2024; **8:** 358–68

For more on **host gene expression signatures of sepsis** see **Articles** *Lancet Child Adolesc Health* 2024; **8:** 325–38

For more on **antimicrobial resistance** see **Editorial** *Lancet Child Adolesc Health* 2024; **8:** 545