

Sepsis for the anaesthetist

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Abstract

Sepsis is as a dysregulated systemic response to infection. Morbidity and mortality of the syndrome are very high world-wide. Recent definitions have redefined criteria for sepsis. The new definition (Sepsis-3) classifies sepsis as infection with organ dysfunction (the old 'severe sepsis'). Septic patients are at risk for secondary injuries, thus aggressive source control, resuscitation, and antibiotic therapy are the mainstays of management. Central to sepsis physiology is vasodilated shock. Many patients respond to i.v. fluid therapy. Pathophysiology also includes energy failure, or a cellular inability to oxidize fuel, and immune incompetence, often manifest by susceptibility to superinfections. Sepsis treatment is optimized by timely resuscitation and control of infection. Early recognition and resuscitation are associated with improved outcomes, although no single resuscitation end point is as good as overall patient assessment. Dynamic resuscitation metrics might be useful to avoid overinfusion of fluid therapies. Antibiotics should treat likely pathogens, with broader coverage for sicker patients (e.g. those with septic shock). Avoidance of iatrogenic injury, such as ventilator-induced lung injury from large tidal volumes, helps to prevent subsequent tissue damage and worsened systemic response. Single-agent therapies to block the systemic response have not fulfilled promise in sepsis, probably because part of the complex syndrome is adaptive. However, early aggressive care based on bundles is associated with improved outcomes. Research opportunities include understanding the role of neurological, endocrine, immune, and metabolic pathophysiology in the syndrome.

Key words: resuscitation; sepsis; shock

Sepsis, a dysregulated systemic response to infection,¹ afflicts >1 million patients annually in the USA;² severe sepsis accounts for ~27% of critical care admissions in the UK³ and >30 million patients worldwide.⁴ Of those afflicted, between 30 and 50% die.^{5–6} Comparatively, sepsis is not only a leading cause of death, but is also responsible for more deaths than several major cancers combined. In spite of this, advances in sepsis management have been limited.

Sepsis care is an opportunity for the anaesthetist. Septic patients come to the operating room regularly, and they need resuscitation and source control. Perioperative sepsis is deadly; 40% of cardiac arrests in the perioperative period were associated with sepsis, and these patients had a mortality of 77%.⁷ Some of these deaths might be preventable, as early recognition and treatment are associated with improved mortality.⁸ This is

where perioperative specialists can make a difference. Monitoring, resuscitation, and most importantly, facilitating timely source control through procedural interventions can make a difference.

Defining sepsis

Consensus definitions of sepsis are still imperfect, but help to establish guidelines for appropriate care and inform the research agenda. Recent efforts have produced a new consensus definition, known as 'Sepsis-3'.¹ This definition is nimble and flexible, but does not capture every patient with sepsis. Providing ideal care requires good clinical judgement and a high level of suspicion.

Editor's key points

- Sepsis is a systemic inflammatory response to infection that is associated with organ dysfunction.
- Sepsis is a global problem with high morbidity and mortality.
- Treatment requires early recognition, goal-directed cardiovascular resuscitation, and control of infection source.

Sepsis requires the presence of infection, which in the perioperative environment is not necessarily obvious. Patients with surgical pathology, such as a perforated viscus or undrained abscess, need urgent surgical intervention to avoid worsening infection and an overwhelming systemic response. Bacteria, fungi, and viruses can all cause sepsis, but the latter two can easily be missed. Sources, such as acalculous cholecystitis or even pneumonia, can be occult. Vigilance for sepsis should be a part of anaesthetists' care of surgical patients. Combining the concepts of infection and host response means a diagnosis can be made from one perspective or the other. On the one hand, the systemic signs in these definitions should prompt a search for infection. On the other hand, the presence of a known infection leads the clinician to ask, 'Is my infected patient septic?' The sepsis definition, as a screening tool, performs differently depending on this perspective.

The response to sepsis shares features with the systemic response to tissue injury.⁹ The non-specific nature of this systemic response impedes timely diagnosis and confounds consensus as to disease definitions. A challenge of maintaining sensitivity (a low false-negative rate of diagnosis) at the cost of lower specificity (some patients will be incorrectly treated for sepsis) underscores older and newer definitions. Sepsis-3

replaces the old Systemic Inflammatory Response Syndrome (SIRS) criteria in favour of a discriminator for more severe disease. Whereas SIRS defined a population with a systemic response to infection (severe infection), the new criteria specify a population with organ dysfunction, as indicated by a change in the Sequential [Sepsis-related] Organ Failure Assessment (SOFA) score of 2 points or more (Table 1). Such reclassification means that a sicker population can be tracked and studied. Both criteria emphasize the multiple ways that sepsis affects the patient, and both leverage readily available, albeit non-specific data to characterize a patient subset that is likely to have a potentially correctable yet deadly illness. Subtle elements, such as lethargy (or other mental status changes), hyperglycaemia (blood glucose >6.66 mmol litre⁻¹), and ileus, can serve as early warning markers for worsening infection and incipient sepsis.

The SIRS criteria included two or more of the following: elevated (or depressed) leucocyte count (e.g. >12 000 or <4000 cells litre⁻¹), tachypnoea (>20 bpm), tachycardia (>90 breaths min⁻¹), and fever (or hypothermia). These correlated with increased odds of having sepsis, but missed one in eight septic patients in a large review.¹³ A new and easier to use clinical score, qSofa, uses mental status changes, tachypnoea, and low arterial blood pressure in the setting of suspected infection to establish a new screening tool for sepsis, one that appears to perform better than SIRS plus infection, identifying 68% of decedents at a cut-off of two or more criteria.¹² Although there are substantive differences between the two definitions, both follow the overall concept of sepsis as a dysregulated host response to infection. Future research will enhance the new definitions.

Sepsis is no longer defined simply as serious infection. One substantive change in the Sepsis-3 definitions is the application of 'sepsis' to mean organ dysfunction in the presence of infection and host response. Previously, this subgroup was called 'severe sepsis', a term that is absent from the new definitions. Clinicians will continue to use this terminology as long as it continues to be a diagnostic code. It is a part of historical sepsis

Table 1 Criteria for sepsis. The SOFA scores range from 0 to 4 points for each criterion. ICU, intensive care unit; PaCO₂, partial pressure of carbon dioxide; PaO₂/FI_{o2}, ratio of partial pressure of arterial oxygen to fraction of inspired oxygen

Scale	Criteria	Comments
Systemic Inflammatory Response Syndrome (SIRS)	i. Temperature >38.0 or < 36.0 °C ii. Heart rate >90 beats min ⁻¹ iii. Respiratory rate >20 bpm or PaCO ₂ <4.3 kPa iv. White blood cell count >12 000 or < 4000 µl ⁻¹ , or > 10% band forms	Non-specific, misses one in eight patients with severe sepsis, ⁹ and positive in > 50% of inpatients at least once during their hospitalization ¹⁰
Sequential [Sepsis-Related] Organ Failure Assessment (SOFA) Score ¹¹	i. PaO ₂ /FI _{o2} , respiratory support ii. Platelet count (<150 × 10 ³ µl ⁻¹ abnormal) iii. Bilirubin (>1.2 mg dl ⁻¹ abnormal) iv. Mean arterial pressure, use of dobutamine, epinephrine, norepinephrine v. Glasgow Coma Scale score vi. Serum creatinine, urine output	Scores range from 0 to 24. An increase in SOFA of ≥ 2 is used to signify organ dysfunction in Sepsis-3 definition. A cut-off of 2 or more SOFA points captured 68% of decedents outside the ICU and 98% of decedents in the ICU ¹²
Quick SOFA (qSOFA) criteria	i. Respiratory rate ≥22 bpm ii. Altered mentation iii. Systolic blood pressure ≤100 mm Hg	Simple; does not require laboratory testing. Outperforms SOFA score in non-ICU populations; slightly less predictive in the ICU
Septic shock	i. Criteria for sepsis ii. Mean arterial pressure <65 mm Hg or need for vasopressors iii. Serum lactate >2 mmol litre ⁻¹	Definition assumes the absence of hypovolaemia

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