Anaesthetic management of patients with severe sepsis

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Key points

- Patients with sepsis often require surgical interventions.
- Anaesthesia can be hazardous in these cardiovascularily unstable patients.
- Preoperative optimization and intraoperative and postoperative care need to be planned before starting.
- Techniques that preserve cardiovascular and respiratory function are required.

Summary. Severe sepsis, a syndrome characterized by systemic inflammation and acute organ dysfunction in response to infection, is a major healthcare problem affecting all age groups throughout the world. Anaesthetists play a central role in the multidisciplinary management of patients with severe sepsis from their initial deterioration at ward level, transfer to the diagnostic imaging suite, and intraoperative management for emergency surgery. The timely administration of appropriate i.v. antimicrobial therapy is a crucial step in the care of patients with severe sepsis who may require surgery to control the source of sepsis. Preoperative resuscitation, aimed at optimizing major organ perfusion, is based on judicious use of fluids, vasopressors, and inotropes. Intraoperative anaesthesia management requires careful induction and maintenance of anaesthesia, optimizing intravascular volume status, avoidance of lung injury during mechanical ventilation, and ongoing monitoring of arterial blood gases, lactate concentration, haematological and renal indices, and electrolyte levels. Postoperative care overlaps with ongoing management of the severe sepsis syndrome patient in the intensive care unit. These patients are by definition, high risk, already requiring multiple supports, and require experienced and skilful decision-making to optimize their chances of a favourable outcome. Similar to acute myocardial infarction, stroke, or acute trauma, the initial hours (golden hours) of clinical management of severe sepsis represent an important opportunity to reduce morbidity and mortality. Rapid clinical assessment, resuscitation and surgical management by a focused multidisciplinary team, and early effective antimicrobial therapy are the key components to improved patient outcome.

Keywords: anaesthesia; emergency service; anaesthesia, general; infection; surgery; perioperative period

Epidemiology

Severe sepsis and septic shock are major healthcare problems with a reported incidence of 66–132 per 100 000 population in the USA and UK, respectively.1,2 In 2001, a consensus conference (Society of Critical Care Medicine, European Society of Intensive Care Medicine, American College of Chest Physicians, American Thoracic Society, and Surgical Infection Society) concluded that the basic definitions of systemic inflammatory response syndrome (SIRS), as originally described in 1992 by the American College of Chest Physicians and the Society of Critical Care Medicine,3 should remain largely unchanged4 (Table 1). Because of the limitations of the definitions of SIRS and infection, the 2001 consensus conference suggested an expanded list of possible signs of systemic inflammation that may be observed in ‘septic-looking’ patients (Table 2).

Severe sepsis occurs in 1–2% of all hospitalizations and accounts for as much as 25% of intensive care unit (ICU) bed utilization. It is common in elderly, immune-compromised, and critically ill patients and is a major cause of death in ICUs worldwide.5 Sepsis is the second leading cause of death in non-coronary ICU patients. Mortality remains high at 30–50% despite improved care in the past 10–15 yr.1,5,6

Causes of sepsis

Severe sepsis may have infective and non-infective causes (Table 3). Infections are common and amenable to treatment; therefore, in patients presenting with clinical signs of systemic inflammation (SIRS), an infective cause should be actively sought. Community-acquired infections in previously well patients are easier to recognize than nosocomial infections in debilitated hospitalized patients. Infections leading to sepsis include central nervous system (CNS) infections, for example, meningitis or encephalitis, cardiovascular infections (e.g. infective endocarditis), respiratory infections (e.g. pneumonia), gastrointestinal infections (e.g. peritonitis), or urinary tract infections (e.g. pyelonephritis).1,7 Although bacterial infections are the most common infective cause, viruses and fungi can also cause septic shock. Non-infective...
causes include severe trauma or haemorrhage and acute systemic disease, including myocardial infarction, pulmonary embolus, and acute pancreatitis. Table 4 summarizes the presentation of severe sepsis syndrome, the pathophysiology underpinning the symptoms and signs, and the organisms most commonly implicated.

### Pathophysiology of sepsis

A detailed discussion of the physiology of sepsis is beyond the scope of this review, but has itself been recently reviewed comprehensively. This review concentrates on anaesthetic management of patients with severe sepsis syndrome.

### Anaesthetic management

Anaesthetists are frequently involved in the care of severely septic patients in the emergency department, operating theatre, or ICU. Infection source control, involving surgical drainage of an abscess or debridement of necrotic tissue coupled with early effective antimicrobial therapy, is central to the successful treatment of a patient with severe sepsis. In high-risk surgical or trauma patients with sepsis, early haemodynamic optimization before the development of organ failure reduced mortality by 23% in comparison with those who were optimized after the development of organ failure. [9](#) [10](#)

### Preoperative assessment

Although not all patients with severe sepsis have an infective focus, it is prudent to examine patients systematically looking for a source of infection (Table 4). The primary source may be self-evident (e.g. trauma, burns, recent surgery) or may be more difficult to identify (e.g. empyema of the gall bladder, pancreatitis, gynaecological sepsis, soft tissue, and bony infections), particularly in agitated un-cooperative patients. The examination should focus on the severity of SIRS, the state of intravascular hydration, the presence of shock or multi-organ dysfunction, and the adequacy of haemodynamic resuscitation.

### Surviving Sepsis Campaign

Following an international process of consultation to standardize the management of critically ill septic patients, the Surviving Sepsis Campaign suggested that therapies be grouped or ‘bundled’ for particular subsets of patients. The concept is not unlike that of Advanced Trauma Life Support (ATLS), where somewhat didactic therapies are proposed in...
given clinical situations. Although its detractors point out that bundled therapies are not individualized to a particular patient’s needs, and the lack of evidence-based medicine to underpin its guidelines, there is nonetheless some evidence that the process of care and outcomes improved after educational programmes were instituted based on the Surviving Sepsis Campaign.\textsuperscript{11–13}

### Antibiotic therapy

It is imperative that i.v. antibiotics should be started as early as possible after the diagnosis of severe sepsis and septic shock. There is no evidence that delaying until the start of the surgical procedure or until microbiology culture results are available is beneficial. Appropriate samples should be obtained for culture before giving first-line anti-microbial therapy.\textsuperscript{14} Anti-microbial drugs are best given i.v. and in sufficient dosage to achieve therapeutic concentration. The choice of agents should be based on the clinical history, physical examination, likely pathogen(s), optimal penetration of anti-microbial drugs into infected tissues, and the local pattern of sensitivity to anti-microbial agents. Broad-spectrum agents should be used initially with one or more agents active against all likely bacterial/fungal pathogens.

### Haemodynamic resuscitation

The objective of preoperative resuscitation measures is to rapidly restore adequate oxygen delivery to peripheral tissues. If the patient is haemodynamically unstable, invasive arterial pressure monitoring, central venous access, and ICU or high dependency unit admission must be considered. Placement of a central venous catheter (CVC) will allow measurement of central venous pressure (CVP), mixed venous oxygen saturation ($S_{\text{VO}_2}$), administration of i.v. fluids, and vasopressor medication.\textsuperscript{15–17} Resuscitation measures begun in the emergency room can be continued even if the patient requires diagnostic imaging studies or admission to the ICU before transfer to the operating theatre. The first 6 h of resuscitation of septic patients, the so-called ‘golden hours’, are crucial and frequently coincide with the time for emergency surgery.\textsuperscript{11,18} There is little disagreement among clinicians that in the hypotensive septic patient with lactate $>3$ mmol litre$^{-1}$, volume resuscitation using crystalloids or colloids should be used initially, aiming to reach the following clinical endpoints: CVP 8–12 mm Hg, mean arterial pressure 65 mm Hg, urine output 0.5 ml kg$^{-1}$ h$^{-1}$, central venous oxygen saturation: $>70\%$ (Table 5). There is no evidence-based support for one type of i.v. fluid over another with regard to ICU stay, duration of mechanical ventilation, duration of renal replacement therapy, and 28 day outcome.\textsuperscript{11,16} Colloid with pentastarch therapy was associated with higher rates of acute renal failure and renal-replacement therapy than Ringer’s lactate and its toxicity is increased with accumulating doses.\textsuperscript{7}

Vasopressor support with norepinephrine may be considered even before optimal i.v. fluid loading has been achieved. Low-dose vasopressin (0.03 units min$^{-1}$) may be subsequently added to reduce the requirement for high-dose norepinephrine alone.\textsuperscript{10,18,19} Inotropes are added to volume resuscitation and vasopressors, if there is evidence of continued low cardiac output despite adequate cardiac filling and fluid resuscitation. The Surviving Sepsis Campaign recommends that dobutamine is the first-line inotropic therapy to be added to vasopressors in septic patients.\textsuperscript{11} However, a study in septic patients showed no difference in efficacy and safety with epinephrine alone compared with norepinephrine plus dobutamine (28 day mortality: 40\% vs 34\% respectively, $P=0.31$) in the management of septic shock.\textsuperscript{19} There is no evidence to support the use of dobutamine to achieve supernormal oxygen delivery in terms of improving outcomes.\textsuperscript{16–18} Resuscitation efforts should be continued as long as haemodynamic improvement accompanies each step in the process. Further i.v. fluid administration should be stopped when filling pressures are high and no further improvement seen in tissue perfusion is seen (e.g. serum lactate not decreasing). Transfusion of red blood cells may be considered if tissue oxygen delivery remains inadequate.\textsuperscript{20,21}

Levosimendan may be a useful adjunct to conventional inotropic therapy in cases of refractory myocardial dysfunction in sepsis. Its inotropic effect is attributable to increased cardiac troponin C sensitivity to calcium. The systemic and pulmonary vasodilator effect is attributable to its opening of ATP-dependent potassium channels.\textsuperscript{22} A single randomized controlled trial in 28 patients with septic shock and ejection fraction $<45\%$ persisting $>48$ h after conventional treatment found that cardiac index and renal function indices improved after levosimendan, compared with dobutamine.\textsuperscript{22,23} However, further larger clinical studies are required before levosimendan becomes a widely accepted therapy in septic shock.

Supplemental oxygen therapy is valuable in severely septic patients even if they do not have signs of respiratory distress. Immediate tracheal intubation and mechanical

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**Table 3** Aetiology of severe sepsis

<table>
<thead>
<tr>
<th>Infective causes</th>
<th>Non-infective causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS infections</td>
<td>Severe trauma</td>
</tr>
<tr>
<td>CVS infections</td>
<td>Haemorrhage</td>
</tr>
<tr>
<td>Respiratory infections</td>
<td>Complication of surgery</td>
</tr>
<tr>
<td>Renal infections</td>
<td>Complicated aortic aneurysm</td>
</tr>
<tr>
<td>GIT infections</td>
<td>Myocardial infarction</td>
</tr>
<tr>
<td>Skin and soft tissue infections</td>
<td>Pulmonary embolism</td>
</tr>
<tr>
<td>Bone and joint infections</td>
<td>Cardiac tamponade</td>
</tr>
<tr>
<td>Subarachnoid haemorrhage</td>
<td>Burns</td>
</tr>
<tr>
<td>Burns</td>
<td>Acute pancreatitis</td>
</tr>
<tr>
<td>Drug overdose/toxicity</td>
<td>Diabetic ketoacidosis</td>
</tr>
<tr>
<td>Adrenal insufficiency</td>
<td>Anaphylaxis</td>
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</tbody>
</table>
ventilation of the lungs can be considered if the patient's level of consciousness is low or if there is progressive distress and hypoxia. If there is an inadequate response to these resuscitation measures, it is important to consider the presence of an alternative diagnosis. The non-infective causes of SIRS or an iatrogenic complication, for example, tension pneumothorax after CVC placement, should also be considered (Table 3).

### Diagnostic imaging

Diagnostic imaging studies are increasingly important in confirming the site of infection, excluding alternative pathology and guiding radiological or surgical source control procedures. If diagnostic imaging studies are considered appropriate, it is important that all other therapeutic measures (e.g. i.v. fluid resuscitation, antimicrobial therapy, mechanical ventilation) are continued in a comprehensive manner. Computerized tomography is the most useful imaging modality for complex soft-tissue infections and deep-seated infections in the abdomen and thorax. Ultrasound imaging of the biliary and urinary tract may also be considered. Expert interpretation of all imaging studies should be sought to assist in planning the optimal management strategy.

<table>
<thead>
<tr>
<th>System affected</th>
<th>Signs and symptoms</th>
<th>Mechanism</th>
<th>Common system pathogens</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central nervous system</td>
<td>Confusion, drowsiness, irritability coma headache, neck stiffness, photophobia</td>
<td>Alteration in blood–brain barrier neurotransmitter levels; receptor function energy availability</td>
<td>Community-acquired pathogens: <em>Streptococcus pneumoniae</em>; <em>Neisseria meningitides</em>; <em>Listeria monocytogenes</em></td>
</tr>
<tr>
<td>Cardiovascular system</td>
<td>Hypovolaemia, impaired myocardial contractility, tachycardia, increased cardiac output, decreased systemic vascular resistance (SVR), impaired responsiveness to vasopressor agents, short of breath, orthopnoea, raised venous pressure</td>
<td>(a) Poor intake, inadequate replacement, excessive insensible losses</td>
<td>Nosocomial pathogens: <em>Pseudomonas aeruginosa</em>; <em>Escherichia coli</em></td>
</tr>
<tr>
<td>Respiratory system</td>
<td>Hypoxaemia, cyanosis, tachypnoea, use of accessory muscles, change in sputum: volume, purulence</td>
<td>(b) Increase in microvascular permeability and hypoaalbuminaemia</td>
<td>Major community-acquired pathogens: <em>Enterococcus</em>; <em>Streptococcus bovis</em>; <em>Streptococcus spp.</em>; coagulase-negative staphylococci; <em>Coxiella burnetii</em>; <em>Staphylococcus aureus</em>; <em>Campylobacter</em>; <em>E. coli</em>; fungus</td>
</tr>
<tr>
<td>Gastrointestinal system</td>
<td>Vomiting, diarrhoea, abdominal pain, tenderness, liver failure, cholestasis</td>
<td>(c) Myocardial depression</td>
<td>Major nosocomial pathogens: <em>Staphylococcus spp.</em>; <em>methicillin-resistant S. aureus</em>; <em>methicillin-resistant Staphylococcus epidermidis</em>; <em>methicillin-resistant coagulase negative Staphylococcus</em></td>
</tr>
<tr>
<td>GU system</td>
<td>(a) Frequency, dysuria, haematuria, flank pain, renal failure</td>
<td>(d) Down-regulation of adrenergic receptors heart valve dysfunction</td>
<td></td>
</tr>
</tbody>
</table>

Table 4 Common presentation, pathophysiology, and pathogens in severe sepsis

<table>
<thead>
<tr>
<th>Clinical parameter</th>
<th>Goal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Central venous pressure</td>
<td>8 - 12 mm Hg (≥ 8 mm Hg in spontaneously breathing patient, ≥ 12 mm Hg in ventilated patients)</td>
</tr>
<tr>
<td>Mean arterial pressure</td>
<td>Between 65 and 90 mm Hg</td>
</tr>
<tr>
<td>Central venous oxygen saturation</td>
<td>≥ 70 mm Hg</td>
</tr>
<tr>
<td>Urine output</td>
<td>≥ 0.5 ml kg⁻¹ h⁻¹</td>
</tr>
<tr>
<td>Haematocrit</td>
<td>≥ 30%</td>
</tr>
</tbody>
</table>

Table 5 Goal-directed therapy: a summary of clinical targets
Source control

Source control measures include drainage or debridement procedures and definitive correction of anatomical abnormalities leading to ongoing contamination of previously sterile tissue. Drainage procedures apply to well-circumscribed infections that can be drained either percutaneously under image-guidance or by an open surgical approach. Debridement refers to the physical removal of non-viable solid tissue usually by an open surgical approach. Definitive surgical interventions are indicated to correct anatomical abnormalities and prevent further contamination.

A surgeon with experience in dealing with complex infections in critically ill patients is best placed to be involved in the decision-making process regarding a particular source control procedure. The immediate goal is to achieve adequate control of the source of infection with the least physiological embarrassment. Source control intervention may cause further complications such as bleeding, fistulas, or inadvertent organ injury. The optimal timing of any surgical intervention depends on the diagnosis and the clinical course of the patient. In some patients, immediate surgery or within 1–2 h of presentation (e.g. upper airway infections leading to airway compromise, necrotizing fasciitis) is lifesaving. There are also a number of commonly occurring severe infections (intra-abdominal abscess, infections associated with intravascular or prosthetic device, infective endocarditis with structural heart damage leading to cardiogenic shock) which may require urgent surgical intervention. The exception to this rule is peripancreatic necrosis associated with acute pancreatitis, where percutaneous drainage and full supportive therapy facilitate delayed surgical intervention, which is associated with improved outcome.

Clear and timely communication between the anaesthetist, surgeon, microbiologist-infectious disease physician, and radiologist is essential for rapid implementation of an effective treatment plan, which can be discussed with the patient and their family. It is vital that the anaesthetist assumes a central role in the multidisciplinary team.

Intraoperative management

The primary goal of the anaesthetist during the intraoperative period is to provide safe and optimal care for critically ill septic patients so that they may benefit maximally from the surgical or radiological source control procedure. The majority of surgical source control procedures are optimally carried out in the operating theatre under general anaesthesia.

Before induction

Many source control procedures are done out of hours, so it is important that the anaesthetist has appropriate help available in the operating theatre. Some thought should be given early to whether the patient may require ICU management after operation. Awareness of the microbiological samples sent for culture, the anti-microbial agents which were started, and timing of the next scheduled dose is important to optimize type and timing of intraoperative antimicrobial therapy. Therapeutic concentrations of effective antimicrobial agents should be maintained throughout the perioperative period as the procedure itself may cause further bacteraemia and clinical deterioration. Invasive haemodynamic monitoring is likely to be indicated in addition to standard intraoperative monitoring. Serial measurements of arterial blood gases and lactate concentration should be readily available from near-patient testing equipment. If large volume loss is anticipated during the surgical procedure, it is worth considering placement of an appropriate volume resuscitation intravascular device.

Induction of anaesthesia and initiation of mechanical ventilation

Patients undergoing source control procedures are in an inherently unstable cardiovascular state due to the combined effects of sepsis, anaesthesia, intravascular volume loss, bleeding, and surgical stress. De-nitrogenation of the lungs, breathing 100% O2 through a tightly fitted facemask for up to 3 min, may be considered before induction of anaesthesia. Because many surgical procedures on severely septic patients occur on an emergency basis, a modified rapid sequence induction, perhaps using rocuronium rather than succinylcholine to facilitate tracheal intubation, may be required. Options for the induction technique are many, including ketamine, etomidate, and slow administration of more commonly used agents such as propofol. Most i.v. or inhalation anaesthetic agents cause vasodilation or impaired ventricular contractility. Induction of anaesthesia is ideally a deliberate step-wise process, using small doses of i.v. anaesthetic agents, titrated to clinical response. The choice of induction agent or narcotic is less important than the care with which they are administered. Ketamine or midazolam may provide a degree of haemodynamic stability and short-acting opioids such as fentanyl or alfentanil will enable a reduction in the dose of anaesthetic induction agent. With the exception of remifentanil, the effects and duration of action of i.v. opioids may be increased by impaired hepatic and renal perfusion. Remifentanil infusion, either as a primary agent or as a background adjunct to another induction drug, has much to recommend it in the setting of induction of anaesthesia in the septic, unstable patient. Although it can cause bradycardia, many of these patients are tachycardic, and its effects on myocardial contractility are minimal. Further, remifentanil avoids sudden reductions in systemic vascular resistance. Placement of a cuffed tracheal tube is facilitated by the use of neuromuscular blocking agents (preferably non-histamine releasing agents).

Continued volume resuscitation and incremental doses of vasopressors are helpful to counteract the hypotensive effect of anaesthetic agents and positive pressure mechanical ventilation. Options for the use of vasopressors include ephedrine, phenylephrine, and metaraminol, but there is no evidence base to support the use of any of these in preference to another. Norepinephrine infusion may be used for a more prolonged effect. The goal of mechanically
Ventilating patients with severe sepsis is to use sufficiently high fractional inspired oxygen concentration ($\text{FiO}_2$) to maintain adequate oxygenation ($\text{PaO}_2 > 12$ kPa). There is now strong evidence supporting a low tidal volume ventilatory strategy, to minimize the impact of positive pressure ventilation on the lung tissue itself, and also on venous return and cardiac output. Shear forces caused by high tidal volumes or high inspiratory pressures will exacerbate lung injury. Therefore, where oxygenation is adequate, the concept of ‘permissive hypercapnia’ has arisen, where low alveolar minute ventilation to minimize ventilatory lung damage inevitably results in a degree of hypercapnia (typically $\text{PaCO}_2 > 8–9$ kPa), which is tolerated and appears relatively safe in the short term (i.e. more than 3–4 days).

**Maintenance of anaesthesia**

There is no evidence to suggest an outcome benefit when anaesthesia is maintained by the inhalation or i.v. route. Options for maintaining anaesthesia include inhalation agents, i.v. agents, and opioids, for example, remifentanil infusion using 0.25–0.5 $\mu$g kg$^{-1}$ min$^{-1}$. The anaesthetist should choose the technique which they believe best fits with their assessment of the individual patient’s risk factors and co-morbidities, and their own experience and expertise. The MAC of inhalation anaesthetic agents is reduced in severe sepsis. In patients with significant lung dysfunction, maintenance of stable concentrations of anaesthetic agents in the brain may be more reliably achieved when using i.v. rather than inhalation agents. Whatever technique is used, the depth of anaesthesia achieved can be estimated using bispectral index monitoring. During surgery, the haemodynamic state may be further complicated by blood loss or systemic release of bacteria or endotoxins. Transfusion of blood products should proceed without delay if the surgical procedure is complicated by excessive blood loss.

Intravascular volume resuscitation should continue as indicated throughout the surgical procedure. Although a CVP of 8–12 cm H$_2$O is a commonly used haemodynamic goal in the initial resuscitation of septic patients, intraoperative CVP values may be increased by raised intra-thoracic and intra-abdominal pressure. Changes in dynamic markers (pulse pressure variation, stroke volume variation) have been shown to predict volume responsiveness more accurately than pressure-based estimates (CVP or pulmonary artery occlusion pressure). Changes in dynamic markers of volume responsiveness can be used intraoperatively to guide i.v. volume therapy, especially in patients with regular sinus heart rhythm and whose lungs are ventilated by controlled mechanical ventilation. Concurrent transoesophageal echocardiography or oesophageal Doppler may be used to define changes in stroke volume variation.

There are many devices available to monitor changes in cardiac output either continuously (pulmonary artery catheter, oesophageal Doppler, impedance plethysmography) or at discrete time intervals (trans-thoracic or trans-oesophageal echocardiography, or serial measurement of mixed-venous $\text{O}_2$ saturation). Throughout the surgical procedure, cardiovascular parameters (heart rate, cardiac filling pressures, inotropic state, systemic arterial pressure) can be adjusted to optimize tissue oxygen delivery rather than to achieve set values of cardiac output or arterial pressure. The adequacy of global oxygen delivery may be assessed by serum lactate <2 mmol litre$^{-1}$ and mixed-venous $\text{O}_2$ saturation >70%.

Oxygenation may be impaired by non-cardiogenic pulmonary oedema, which is caused by the increased capillary permeability in sepsis. Management options for hypoxaemia during maintenance of anaesthesia include increasing the inspired oxygen concentration and incrementally increasing PEEP. The inspired oxygen concentration can be increased until $\text{SaO}_2$ is at least 90% and the use of PEEP may be considered during the surgical procedure. The PEEP may be cautiously increased in haemodynamically stable patients if there is still hypoxia despite increasing the $\text{FiO}_2$. Hypercarbia should be avoided specifically in patients with increased intra-thoracic pressure or compensated metabolic acidosis, or the later stages of pregnancy. In all other circumstances, hypercarbia may be well tolerated and there is some evidence that permissive hypercapnia may have inherent protective effects.

Protective lung strategies are advisable for mechanical ventilation of the lungs. The difference between the pressure inside and outside the alveolar air space at end-inspiration is the transpulmonary pressure. Plateau airway pressure, measured during volume-control mechanical ventilation when an end-inspiratory pause has been applied, is an indicator of the maximal pressure applied inside the alveolar sac. The pressure outside the alveolar sac cannot be measured directly but is estimated clinically by assessing changes in pleural pressure. Extra-alveolar or pleural pressure can be abruptly increased by placing the patient in the Trendelenberg position or by the increased intra-abdominal pressure associated with inflation of a pneumoperitoneum for laparoscopic surgery. Pulmonary gas exchange may deteriorate if pleural pressure is increased and plateau pressure remains constant (i.e. a reduction in transpulmonary pressure). On the other hand, high transpulmonary pressures are associated with lung injury. In patients with early acute lung injury, the ventilatory strategy should aim to strike an expeditious balance between significant reduction in transpulmonary airway pressure (e.g. <20–25 cm H$_2$O, with associated reduction in alveolar ventilation), and excessive transpulmonary pressures (e.g. >25–30 cm H$_2$O, and the associated risk of barotraumas). Recruitment of collapsed alveoli by manually ventilating the patient to a peak airway pressure of 30–40 mm Hg for short periods may reduce shunt and improve intraoperative oxygenation. Caution is advisable in undertaking this manoeuvre in patients at risk of pneumothorax, such as patients with emphysematous bullae or severe chronic obstructive pulmonary disease. During the surgical procedure, regular near-patient testing of arterial blood gases, full blood count, coagulation screen, electrolytes, lactate, and glucose concentration is advisable. Every
Role of regional anaesthesia and nerve blocks in anaesthesia for septic patients

Peripheral nerve block may be effective at minimizing the sympathetic response to a painful stimulus, while avoiding the systemic effects of opioid and may be used if an individual assessment of the risk–benefit balance suggests that it may be justified in their particular circumstances. However, the presence of coagulopathy, local or systemic spread of infection, and the fact that local anaesthetics may not work properly in the presence of infection or acidosis may limit the application of regional techniques in septic patients. Neuraxial block (spinal and epidural anaesthesia) should be undertaken with caution, since the haemodynamic effects of these techniques in the setting of sepsis-induced cardiovascular compromise may be difficult to reverse. Recent blood tests confirming normal coagulation are essential.

More than 700 000 central neuraxial blocks are conducted annually in the UK. The incidence of permanent injury from CNB was 4.2 (95% CI 2.9–6.1) per 100 000 and that of paralysis or death was 1.8 (95% CI 1.0–3.1) per 100 000 cases. Of the 52 cases which were the focus of follow-up for permanent injury from CNB, 22 made a complete recovery from their serious complication within the follow-up period. Therefore, while epidural anaesthesia appears to have a very low risk of permanent neurological sequelae overall, severely septic patients may be at increased risk of this and other serious complications. Although there is no evidence that placement of an epidural catheter in severely septic patients increases the risk of epidural abscess or haematoma formation, a substantial proportion of clinical opinion would seem to believe that the risks associated with using it in the context of severe sepsis is not justifiable.

End of surgical procedure

At the conclusion of the surgical procedure, administration of further neuromuscular blocking agents to facilitate surgical closure of the abdomen or thorax may be considered. The rate of blood loss should be minimal before leaving the operating theatre. Supplemental doses of antimicrobial agents may be considered. In patients who will require further surgery and in all severely ill patients, analgesia, sedation, and mechanical ventilation are maintained at the conclusion of the surgery. Safe transfer of the patient to the ICU is essential. A focused hand-over report is helpful for the ICU colleagues which highlights the clinical presentation, response to resuscitation measures, antimicrobial agents used, details of the surgical procedure performed, blood products used intraoperatively, and any specific problems that should be anticipated in the postoperative period.

Postoperative management of patients with severe sepsis

It is important to note that pre-resuscitation measurements should be used to calculate the Intensive Care admission APACHE score and not those that have improved after resuscitation and the surgical procedure. Ongoing infusions of vasopressor medication should be adjusted to match the present intravascular volume and the new mechanical ventilator settings. Having secured the patient’s airway, mechanical ventilation settings can be decided, with the objective of minimizing ventilation-induced volutrauma and barotraumas to the lungs. This is most likely to be achieved using low-pressure settings, a high fractional inspired oxygen concentration ($F_{i\text{O}_2}$), and suitably set alarm limits. Low tidal volumes (up to 6 ml kg$^{-1}$ of the predicted body weight) and permissive hypercapnia may be considered, provided that arterial pH does not decrease below 7.20. The use of high PEEP (10–15 cm H$_2$O) may be limited by the degree of associated haemodynamic instability. The $F_{i\text{O}_2}$ can be decreased (i.e. $<60\%$) to achieve an $Sp_{\text{O}_2}$ of 93–95%.41

It is obviously important that antimicrobial therapy, which was started before operation, should be continued in the ICU and the time of the next scheduled dose was noted. Antibacterial regimens can be reassessed daily in light of microbiological results, and adjusted to ensure efficacy, prevent resistance, and to avoid toxicity.

Duration of therapy should be limited to 7–10 days. It has been shown that patients who had a restrictive red blood cell transfusion strategy (transfusion avoided unless Hb < 7 g d$^{-1}$) had a significantly lower mortality rate (22% vs 28%) than those who were transfused at higher Hb levels, with the possible exception of patients with acute myocardial infarction and unstable angina. Fresh-frozen plasma may be used to correct laboratory clotting abnormalities only if there is clinical bleeding or an invasive procedure is planned. Platelets are transfused if counts are $\leq 5000$ mm$^{-3}$ regardless of bleeding, or if between 5000 and 30 000 mm$^{-3}$ with significant bleeding risk. Deep venous thrombosis thromboprophylaxis should usually be considered when concerns about coagulopathy have abated. Recombinant human activated protein C (rhAPC) may be considered in adult patients with sepsis-induced organ dysfunction with clinical assessment of high risk of death (typically APACHE score $>25$ or multiple organ failure) if there are no contraindications to rhAPC. Adult patients with severe sepsis and low risk of death (typically, APACHE II $<20$ or one organ failure) should not receive rhAPC.

Continuation of adequate glycaemic control ($<$8.5 mmol litre$^{-1}$) is important in the control of the septic process. In
a large, international, randomized trial of ICU patients, there was no significant difference between strict glycaemic control (blood glucose 4–6 mmol litre\(^{-1}\)) and more liberal glycaemic control (blood glucose 6–10 mmol litre\(^{-1}\)) in the rate of death or the mean organ failure score. However, the rate of severe hypoglycaemia (glucose level \(\leq 2.2\) mmol litre\(^{-1}\)) was higher in the intensive-therapy group than in the conventional-therapy group (17% vs 4%, \(P=0.001\)), as was the rate of serious adverse events (11% vs 5%, \(P=0.01\)). Therefore, in severely septic patients, blood glucose should be maintained in the range 6–10 mmol litre\(^{-1}\).

Nutrition is one of the cornerstones of management in critically ill septic patients. Enteral nutrition via a nasogastric tube is the best choice to maintain enterocyte integrity and nourish the patient. Gastrointestinal protective measures (stress ulcer prophylaxis) and antiemetic drugs are also prescribed. Total parenteral nutrition (TPN) should be considered if there is a surgical contraindication to enteral nutrition or if nutritional requirements are not fully met by enteral nutrition alone. Patients may become rapidly hypoglycaemic if TPN or enteral nutrition is stopped during the perioperative period.

I.V. hydrocortisone may be considered when hypotension responds poorly to fluid resuscitation and vasopressors. A 7 day trial treatment with low doses of hydrocortisone and flu-drocortisone significantly reduced the risk of death in patients with septic shock and relative adrenal insufficiency without increasing adverse events \((P<0.05)\). In this study, there were 81 deaths (70%) in the placebo group and 66 deaths (58%) in the corticosteroid group at the end of ICU stay \(\text{relative risk (RR) } 0.82; 95\% \text{ CI } 0.68–1.00; \text{ adjusted odds ratio (OR) } 0.50; 95\% \text{ CI } 0.28–0.89; P=0.02\). Although this study was conducted in the ICU setting, it seems prudent to extrapolate the finding to appropriately selected patients in the perioperative period.

Hydrocortisone in a dose of 200 mg per day in four divided doses or as a continuous infusion in a dose of 240 mg per day \((10 \text{ mg h}^{-1})\) for 7 days is recommended for septic shock in the ICU setting. Whether administration of low-dose steroids during intraoperative management of the septic patient would improve haemodynamic stability or outcome is unknown and seems unlikely. The role of glucocorticoids in the management of patients with severe sepsis requires further investigation. In a multicentre, randomized, blinded, controlled trial of patients with septic shock who were treated with corticosteroids, there was significantly decreased mortality in patients who received vasopressin compared with norepinephrine \((36\% \text{ vs } 45\%, \text{ respectively}, P=0.03)\). In contrast, in septic patients who did not receive corticosteroids, vasopressin use was associated with increased mortality compared with norepinephrine \((34\% \text{ vs } 21\%, \text{ respectively}, P=0.05)\). There appears to be a benefit to the use of low-dose glucocorticoids (e.g. hydrocortisone 50 mg, four times daily, where normovolaemic septic patients seem refractory to vasopressor therapy to maintain major organ perfusion and haemodynamic stability).

Acute renal failure occurs in 23% of patients with severe sepsis. Renal replacement therapy may be initiated to correct acidosis, hyperkalaemia, or fluid overload and may be continued until acute tubular necrosis has recovered. Sodium bicarbonate is not recommended for correcting acidosis unless \(\text{pH }< 7.1\). Continuous veno-venous haemodiafiltration does not confer any survival benefit when compared with intermittent haemodialysis, the observed mortality being 67% for intermittent haemodialysis vs 65% for continuous haemodiafiltration, with an RR of 1.03 \((95\% \text{ CI } 0.94–1.14), P=0.54\). However, continuous renal replacement may be more practical in hemodynamic unstable patients. A study comparing daily with alternate-day haemodialysis found that daily haemodialysis resulted in better control of uraemia, fewer hypotensive episodes during haemodialysis, and more rapid resolution of acute renal failure \(\text{mean (so), 9 (2) vs 16 (6) days; } P=0.001\) than did conventional intermittent haemodialysis on alternate days.

Although the weight of current evidence suggests that higher doses of renal replacement may be associated with improved outcomes, these results may not apply specifically to patients with severe sepsis.

Analgesia and sedative medication is continued by infusion, but excessive use of sedation or neuromuscular blocking agents is not recommended. Finally where applicable, it is wise to raise the subject of advanced care planning with the patient and his family, and realistic expectations and outcomes targeted.

In conclusion, severe sepsis is a major healthcare issue, with a persistently high mortality. Patients with severe sepsis syndrome often require surgery for source of infection control. The anaesthetist has a crucially important role in coordinating and delivering resuscitation and therapeutic strategies to optimize patient survival outcome. Early i.v. administration of effective antimicrobial therapy is essential. Preoperative resuscitation, aimed at optimizing major organ perfusion, is based on judicious use of fluids, vasopressors, and inotropes. Intraoperative management requires careful induction of anaesthesia, using lowest effective doses of a range of agents. Maintenance of anaesthesia is challenging, requiring achievement of optimal volume status, avoidance of lung injury during mechanical ventilation, and ongoing monitoring of arterial blood gases, haematological and renal indices, and electrolyte levels. Postoperative care overlaps with ongoing management of the severe sepsis syndrome patient in the ICU. The care of critically ill septic patients requiring anaesthesia and surgery will be further enhanced by testing promising therapeutic strategies, e.g. use of levosimendan for intraoperative inotropic support, in well-designed clinical trials.

**Conflict of interest**

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