- Altered pharmacokinetics and dynamics with anticonvulsants: Resistance to neuromuscular blockers and opioids with chronic therapy.
- Routine preop monitoring of serum anticonvulsant levels is indicated only in pts with poor seizure control or those who are critically ill.
- Caution with intraop IV phenytoin or fosphenytoin (hypotension, rate of 50 and 150 µg/min, respectively).
- Delayed emergence.

Overview

- Periop seizures: First episode or with known seizure disorder.
- Often self-limiting, trauma to head or extremities is common if precautions are not taken (padded hospital bed). May progress to SE, a life-threatening condition requiring rapid and emergent intervention to terminate attack before cerebral damage results (30–60 min). Subtherapeutic anticonvulsant serum levels and alcohol withdrawal most commonly provoke SE.
- During seizures and postictally, airway reflexes are typically preserved; intubation is not indicated unless aspiration is strongly suspected.
- Postictally, enhancement of a previous neurologic motor deficit is common (Todd paralysis) for hours after seizure.

Etiology

- Idiopathic; Leading cause (30%).
- Acquired: Secondary to congenital syndromes, perinatal asphyxia, developmental disorders, trauma, CNS infection, cerebrovascular disease, intracranial tumor, drug withdrawal (commonly alcohol), metabolic (glucose, Na^+, Ca^{2+}, Mg^{2+}), renal or hepatic failure.
- Periop factors that might precipitate seizure in a pt with a known seizure disorder include NPO status, noncompliance with anticonvulsants, sleep deprivation, fatigue, stress, surgical pain, adverse drug reactions, and interactions between anticonvulsants and anesthetic agents.

Usual Treatment

- For one seizure, no therapy required. Check serum anticonvulsant levels if there is a Hx of epilepsy.
- Rule out hypoxia, STAT determination of serum glucose, electrolytes, and serum Ca^{2+}.
- Treatment includes IV benzodiazepines like lorazepam 0.1–0.2 mg/kg, midazolam 0.2 mg/kg, diazepam 0.15–0.2 mg/kg. Alternatively, thiopental 1–2 mg/kg, propofol 1 mg/kg. To prevent recurrence, load with phenytoin/fosphenytoin, or levetiracetam.
- IV levetiracetam often used in intraop settings owing to lack of hemodynamic disturbance and limited drug-drug interactions.
- Refractory seizures: Consider midazolam, thiopental 2–3 mg/kg, propofol 1–2 mg/kg boluses followed by infusion. May require ventilator assistance. IV magnesium and inhalational agents (isoflurane) are other options.
- EEG required if neurologic status does not return to baseline after 10 min following seizure.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
HEENT	Gingival hyperplasia (phenytoin) Seizure-induced oral trauma		Oral exam	
CV	Drug-induced SIADH (carbamazepine) Hypoglycemia, hypocalcemia, Thrombocytopenia, bone marrow suppression (several drugs)			CBC, lytes
RESP	Hypoxia Aspiration pneumonia	Need for supplemental O_2 SOB, fever	Auscultation	ABGs, O_2 sat CXR, sputum culture
GI	Poor absorption of anticonvulsant Drug-induced increase of hepatic P450 Drug-induced transaminase elevation	Low serum levels Increase dosage requirement of various drugs		Drug levels
CNS	Postictal somnolence Nonconvulsive SE Possible multiple CNS abnormalities	 Developmental Hx	Disturbed sensorium Delayed emergence Cognitive, motor deficits	 EEG
MS	Seizure-induced focal injury			

Key References: Brophy GM, Bell R, Claassen J, et al.: Guidelines for the evaluation and management of status epilepticus, *Neurocrit Care* 17(1):3–23, 2012; Perks A, Cheema S, Mohanraj R: Anaesthesia and epilepsy, *Br J Anaesth* 108(4):562–571, 2012.

Perioperative Implications

Preoperative Preparation

- Continue anticonvulsants on the day of surgery. Confirm availability of parenteral preparations.
- Ensure therapeutic anticonvulsant levels.
- Avoid triggers.
- Provide protection from injury should seizure occur.

Monitoring

- Routine
- Depth of anesthesia monitors
- EEG if poor emergence is observed

Airway

- Evaluate for past seizure-induced oral trauma.
- Gingival hyperplasia (phenytoin).

Induction (General Anesthesia)

- Standard induction drugs provide anticonvulsant action.
- Benzodiazepines are a useful adjunct.
- Sevoflurane induction in conjunction with hypocapnia can produce epileptiform spikes and seizure activity, especially in children.
- Avoid etomidate and ketamine; they lower the seizure threshold.

Maintenance

- Interaction between NMBs and anticonvulsants.
- CV changes may indicate seizures.

Extubation

- Delayed emergence could be due to sedation from periop anticonvulsant use, postictal state, and nonconvulsive SE.

Regional Anesthesia

- Check coagulation profile
- In pts predisposed to seizures, use lowest effective LA dose.
- Avoid transarterial injections.

Postoperative Period

- Postop seizures should be differentiated from conditions mimicking seizures (e.g., postop shivering, myoclonic and dystonic reactions, psychogenic nonepileptic seizures).
- Anticonvulsants should be restarted as soon as possible.
- Avoid meperidine for analgesia or postop shivering.
- EEG if level of arousal not as expected.

Anticipated Problems/Concerns

- Seizure on induction or emergence (risk of injury and aspiration).
- Intraop seizure with consequent delayed emergence.
- Subclinical or convulsive SE.

Sepsis, Severe Sepsis, and Septic Shock

Justin D. Ramos | Peter M. Schulman

Risk

- Incidence of sepsis within USA: Approximately 1 million per year and increasing. Severe sepsis and septic shock are associated with high morbidity and mortality, and septic shock is the most common cause of death among critically ill pts in noncoronary ICUs.
- Although in-hospital mortality rates are very high, they have been declining. With prompt and appropriate treatment, approximate mortality from septic shock is 20–30%.
- Increased prevalence with advanced age, male gender, nonwhite ethnic origin, comorbid diseases (COPD, cancer, chronic renal and liver disease, DM).

Perioperative Risks

- Hemodynamic and respiratory instability
- Thrombocytopenia and DIC
- End-organ ischemia and worsening multisystem organ dysfunction

Worry About

- Rapid hemodynamic deterioration following induction of anesthesia secondary to limited physiologic reserve
- Blunted response to vasopressors and inotropes
- Early and appropriate initiation of antibiotics
- Multidrug-resistant bacteria (in up to 25% of cases of severe sepsis and septic shock)
- Multisystem organ failure (mortality increases with each successive organ failure)

Overview

- Syndrome is a continuum from sepsis to severe sepsis to septic shock, resulting in worsening inflammation and widespread tissue injury, ultimately leading to multisystem organ dysfunction.
  - SIRS: Dx based on alterations in temperature, HR, RR, and WBC count; should prompt evaluation for sepsis.
  - Sepsis: Infection (documented or suspected) and its systemic manifestations.
  - Sepsis-induced hypotension: SBP <90 mm Hg, MAP <70 mm Hg, or SBP decrease >40 mm Hg in adults (or less than two standard deviations below normal).
  - Severe sepsis: Sepsis plus sepsis-induced tissue hypoperfusion or organ dysfunction.
  - Septic shock: Severe sepsis plus hemodynamic instability (hypotension not reversible with fluid resuscitation).
- Prompt diagnosis and appropriate treatment are critical for survival (highest chance of survival occurs when therapies are initiated within 6 h of recognition, and preferably sooner).
- Signs and symptoms of septic shock are nonspecific; presentation is based on initial source of infection.

Etiology

- Environmental factors (exposure to infecting pathogen) plus possible genetic predisposition result in abnormal immune, coagulation, and inflammatory responses.
- Gram-positive bacteria (MRSA, VRE, *Streptococcus*) have become the most common causative pathogens. Other causative pathogens are gram-negative bacilli (*Escherichia coli*, *Pseudomonas*), and fungi (*Candida*).
- Most common site of infection is the respiratory tract (pneumonia). Other common sites are the genitourinary system, abdominal organs, skin and soft tissue, devices (central lines), CNS, and heart (endocarditis).
- Also consider noninfectious causes of SIRS (burns, acute pancreatitis, trauma, thromboembolism, surgery).

Usual Treatment

- Speed and appropriateness of treatment affects outcome.
- General approach is triad of broad-spectrum antimicrobial therapy (ideally within 1 h of Dx), hemodynamic resuscitation to maintain adequate perfusion pressure and optimize O_2 balance, and source control.
- Key considerations:
  - Obtain blood cultures prior to initiation of broad-spectrum antibiotics.
  - Imaging studies if warranted to confirm potential source of infection.
  - Initial fluid resuscitation with crystalloid (30 mL/kg) for hypotension or hyperlactemia.
  - Vasopressors to maintain MAP ≥65 for hypotension not responsive to initial fluid resuscitation.
  - Target normal lactate (remeasure within 6 h if initially elevated).
  - Repeat clinical examination to reassess volume status and tissue perfusion. Consider other methods to assess fluid responsiveness and tissue perfusion, including cardiac ultrasound, CVP, $SCVO_2$, passive leg raise, and additional fluid challenge.
- Other considerations:
  - Fluid resuscitation with crystalloid is preferred. Albumin may be considered if significant amounts of crystalloid are required, but hydroxyethyl starches should be avoided.
  - Restrictive approach to blood transfusion (target transfusion trigger of 7 g/dL). A higher transfusion threshold may be appropriate in the setting of acute coronary syndrome, acute hemorrhage, or tissue hypoperfusion.
  - Lung protective ventilation strategy with PEEP if pt is mechanically ventilated.
  - Daily reassessment of antibiotic therapy to narrow coverage when appropriate.
  - Stress-dose steroids (200 mg/d via hydrocortisone infusion) only for refractory septic shock (BP not responsive to fluid and vasopressor therapy) for up to 7 d or until vasopressors are no longer needed.
  - First-choice vasopressor is norepinephrine.
  - Addition of low-dose vasopressin infusion (0.03 U/min) to augment MAP or reduce norepinephrine dose in refractory septic shock.
  - Recommended target blood glucose range 110–180.

Assessment Points

System	Effect	Assessment by Hx	PE	Test
NEURO	Altered mental status	Level of consciousness, delirium	Somnolent, obtunded, confused	CT of the head if there is a focal deficit
CV	Vasodilation, hypovolemia, acidosis, hypercontractility or hypocontractility, circulatory failure	Signs of end-organ hypoperfusion	Tachycardia, hypotension, wide pulse pressure, warm (or cold) extremities, low SVR, high or low CI, low SVO_2	Invasive hemodynamic monitoring, ECHO
PULM	Hypoxemia, hyperventilation, respiratory failure	Tachypnea, dyspnea	Use of accessory muscles, rapid shallow breathing, cyanosis	CXR, ABG
RENAL	Oliguria, acute kidney injury, ATN	UO	Signs of hypovolemia, rising, Cr, BUN	UO, Cr, BUN, urine lytes, UA
ID	Infection	Fever, chills, rigors	Hyperthermia or hypothermia	WBC with differential, cultures, radiographic imaging
HEME	Hemolysis, thrombocytopenia, DIC		Bleeding	CBC, D-dimer, INR, PTT, fibrinogen

Key References: Dellinger RP, Levy MM, Rhodes A, et al.: Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012, *Crit Care Med* 41(2):580–637, 2013; Mouncey PR, Osborn TM, Power S, et al.: Trial of early, goal-directed resuscitation for septic shock, *N Engl J Med* 372(14):1301–1311, 2015.

Perioperative Implications

Preoperative Preparation

- Septic pts are often extremely unstable and have limited physiologic reserve.
- Surgery should be postponed until sepsis is treated unless underlying cause requires surgical intervention (source control).
- If surgery is urgent, consider whether pt's condition may be optimized before proceeding to the OR.

Intraoperative

- Goal for induction is hemodynamic stability.
- Invasive monitoring is generally indicated.
- Inotropes and vasopressors should be readily available.
- Target goal: Directed resuscitation to MAP >65, CVP 8–12, adequate UO, normal pH, normal lactate, SVO_2 >70.
- Consider steroids for refractory shock.
- Consider need for pt to remain intubated postprocedure.

Postoperative Period

- Need for ICU care and possible prolonged mechanical ventilation

Anticipated Problems/Concerns

- Hemodynamic and respiratory instability
- Worsening metabolic acidosis, low central or mixed venous O_2 sat
- Altered coagulation/DIC
- Multisystem organ dysfunction
- Prolonged ICU stay
- High morbidity and mortality