Society for Maternal-Fetal Medicine

Maternal sepsis

Consult Series #67

In the US, sepsis is the **second leading cause of maternal death**

Sepsis	life-threatening organ dysfunction* caused by dysregulated host response to infection
	*defined as an acute increase ≥ 2 points in the SOFA score (table 1)
Septic shock	underlying circulation and cellular/metabolic abnormalities are profound enough to substantially increase mortality
	Clinically: Persistent hypotension requiring vasopressors to maintain MAP ≥ 65 mm Hg and a serum lactate > 2 mmol/L despite adequate volume resuscitation

Fever is neither necessary nor sufficient to determine whether sepsis is present!

We recommend that clinicians consider the diagnosis of sepsis in pregnant or postpartum patients with otherwise unexplained end-organ damage in the presence of a suspected or confirmed infectious process, regardless of the presence of fever

TABLE 1
Sequential Organ Failure Assessment score[18]

	Score				
Organ system	0	1	2	3	4
Respiratory					
PaO_2/FiO_2	≥400 mm Hg (53.3 kPa)	<400 mm Hg (53.3 kPa)	<300 mm Hg (40 kPa)	<200 mm Hg (26.7 kPa) with respiratory support	<100 mm Hg (13.3 kPa) with respiratory support
Coagulation					
Platelets	≥150×10³/μL	<150	<100	<50	<20
Hepatic					
Bilirubin	<1.2 mg/dL (20 μmol/L)	1.2–1.9 mg/dL (20–32 μmol/L)	2.0–5.9 mg/dL (33–101 μmol/L)	6.0–11.9 mg/dL (102–204 μmol/L)	>12 mg/dL (204 μmol/L)
Cardiovascular					
MAP	≥70 mm Hg	<70	Dopamine <5 μg/kg/min, or any dose of dobutamine	Dopamine 5.1–15 μg/kg/min, or epinephrine ≤0.1 μg/kg/min, or norepinephrine ≤0.1 μg/kg/min	Dopamine >15, or epinephrine >0.1, or norepinephrine>0.1
Central nervous system: Glasgow Coma Scale score	15	13–14	10–12	6–9	<6
Renal	Serum creatinine <1.2 mg/dL (110 μmol/L)	Serum creatinine 1.2–1.9 mg/dL (110–170 μmol/L)	Serum creatinine 2.0–3.4 mg/dL (171–299 μmol/L)	Serum creatinine 3.5–4.9 mg/dL (300–440 μmol/L) OR Urine output <500 mL/d	Serum creatinine >5.0 mg/dL (440 μmol/L) OR Urine output < 200 mL/d

FiO_2, fraction of inspired oxygen; *MAP*, mean arterial pressure; PaO_2, partial pressure of oxygen.
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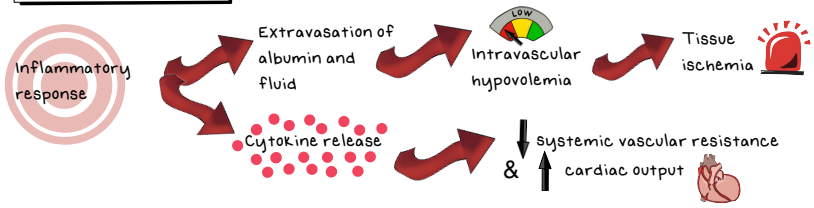
PATHOPHYSIOLOGY

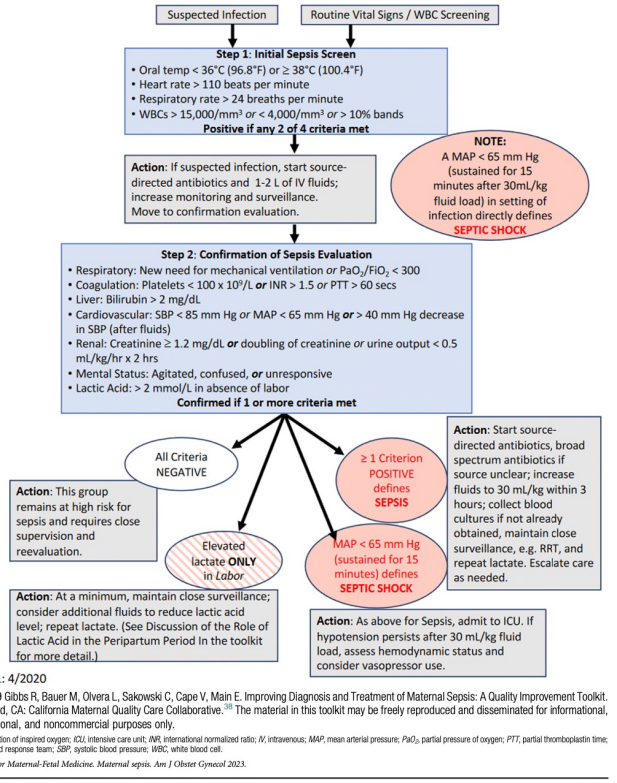


RECOGNITION

We recommend that sepsis and septic shock in pregnancy be considered medical emergencies and that treatment and resuscitation begin immediately

Each tool has significant limitations as a single screening tool

FIGURE 1
California Maternal Quality Care Collaborative 2-step system for diagnosis of maternal sepsis[38]



Rev1: 4/2020

FiO_2, fraction of inspired oxygen; *ICU*, intensive care unit; *INR*, international normalized ratio; *IV*, intravenous; *MAP*, mean arterial pressure; PaO_2, partial pressure of oxygen; *PTT*, partial thromboplastin time; *RRT*, rapid response team; *SBP*, systolic blood pressure; *WBC*, white blood cell.
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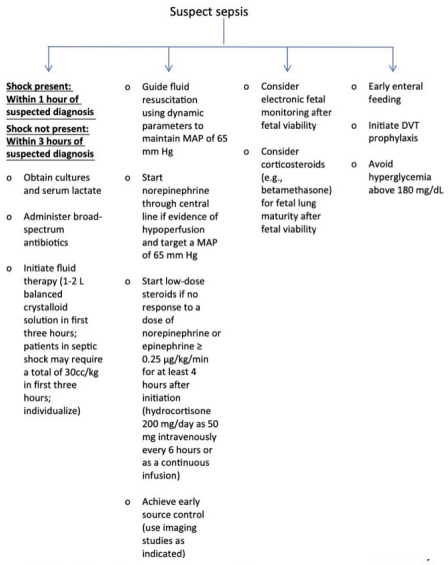
INITIAL MANAGEMENT

FIGURE 2
Initial treatment of sepsis during pregnancy



DVT, deep venous thrombosis; *MAP*, mean arterial pressure.
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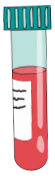

Lab evaluation commonly includes:
- CBC with diff
- cultures (blood, sputum, urine, etc.)
- serum lactate levels*
- CMP (renal and hepatic function)
- coagulation studies with INR
- ABG
- peripheral blood smear

*although lactate levels >2 mmol/L suggest possible sepsis, intrapartum lactate elevations of >2 mmol/L are typical

We recommend rapid identification or exclusion of an anatomical source of infection and emergency source control when indicated

Assess for and treat conditions that can mimic sepsis!
(eg, diabetic ketoacidosis, adrenal crises, pancreatitis, anaphylaxis, cardiomyopathy, etc.)

COMMON INFECTIOUS ETIOLOGIES

TABLE 3
Common sources of infection in sepsis

Sources	Antepartum	Postpartum
Obstetrical	Septic abortion	Endometritis
	Chorioamnionitis	Wound infection
Nonobstetrical	Urinary tract infection	Urinary tract infection
	Pneumonia	Pneumonia
	Appendicitis	Gastrointestinal

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Most frequently isolated:
E coli
Group A Strep
Group B Strep

30% of cases have no source identified

In pregnant or postpartum patients with septic shock or a high likelihood of sepsis, we recommend administration of empiric broad-spectrum anti microbial therapy, ideally within 1 hour of recognition

TABLE 4
Proposed broad-spectrum empiric antibiotic coverage in sepsis complicating pregnancy

Source infection	Recommended antibiotics
Community-acquired pneumonia	Cefotaxime, ceftriaxone, ertapenem, or ampicillin plus azithromycin, clarithromycin, or erythromycin.[59]
Hospital-acquired pneumonia	Low-risk patients may be treated with ceftriaxone, ampicillin-sulbactam, ertapenem, meropenem, imipenem, or cefepime. Patients at high risk of mortality may need double coverage for *Pseudomonas* (beta lactam plus an aminoglycoside or a quinolone) and MRSA coverage with vancomycin or linezolid.[56,57]
Chorioamnionitis	Ampicillin plus gentamicin.[59] Add anaerobic coverage with clindamycin or metronidazole if cesarean delivery required.
Endomyometritis	Ampicillin, gentamicin, and metronidazole (or clindamycin). Alternatively, may use cefotaxime or ceftriaxone plus metronidazole.[59]
Urinary tract infections	Gentamicin with ampicillin Alternatively, may use monotherapy with a carbapenem or piperacillin-tazobactam.[60]
Abdominal infections	Ceftriaxone, cefotaxime, ceftazidime, or cefepime plus metronidazole.[61] Complicated cases may require monotherapy with a carbapenem or piperacillin-tazobactam.
Skin and soft tissues (necrotizing)	Vancomycin plus piperacillin-tazobactam.[62] If group A *Streptococcus* or *Clostridium perfringens* are present, use penicillin G plus clindamycin.

MRSA, methicillin-resistant Staphylococcus aureus.
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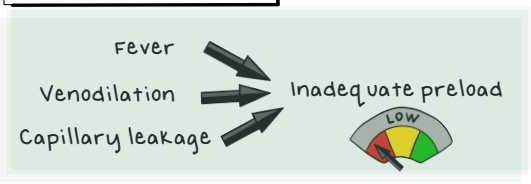
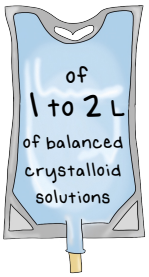
ROLE OF FLUID THERAPY



We recommend ongoing, detailed evaluation of the patient's response to fluid resuscitation guided by dynamic measures of preload

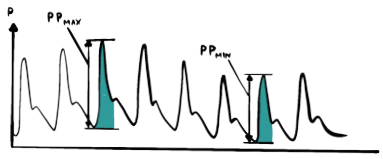
We recommend **early administration (within 3 hours)** of **1 to 2 L** of balanced crystalloid solutions in sepsis complicated by **hypotension** or suspected **organ hypoperfusion**



We recommend the use of a balanced crystalloid solution as a first-line fluid for resuscitation in pregnant and postpartum patients with sepsis or septic shock

We recommend against the use of starches or gelatin for resuscitation in pregnant and postpartum patients with sepsis or septic shock

Pulse-pressure variation

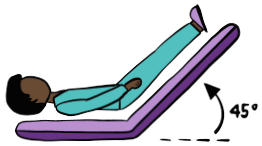


Accomplished by analyzing the waveform of an arterial line

If pulse pressure varies >13% with the respiratory cycle, the patient is volume-responsive

Only reliable in:
- Sedated individuals receiving positive pressure, controlled mechanical ventilation
- Those in sinus rhythm

Passive leg raising



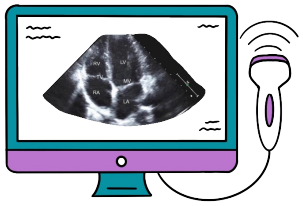
Passive leg raise to 30- 45 degrees causes autotranfuion of ~300mL of blood

After 2-3 min of passive leg raising, fluid responders will have an ↑ in cardiac output

Can be used in patients breathing spontaneously or not in sinus rhythm

*may not be useful to assess cardiac output after passive leg raising in third trimester because of uterine compression of the inferior vena cava; can instead consider administering 250-500 mL bolus of fluid

Echocardiography



Point-of-care ultrasound to measure the diameter of the inferior vena cava with respiration, determine stroke volume variation, and assess the hemodynamic response of the carotid artery to autotransfusion

Inferior vena cava diameter <1.5 cm with significant variation in caliber with the respiratory cycle predicts fluid responsiveness

VASOPRESSORS AND ISOTROPES

Used to increase blood pressure and cardiac contractility in hypotensive patients who are not fluid-responsive or not candidates for further fluid resuscitation (eg, patients with pulmonary edema)

We recommend **norepinephrine as the first-line vasopressor** during pregnancy and the postpartum period with septic shock

TABLE 5
Common vasopressors and inotropes used to treat septic shock during pregnancy and the postpartum period[78]

Vasopressor/ inotrope	Mechanism of action	Effects	Comments
Norepinephrine	Potent alpha-1 and beta-1 adrenergic receptor agonist	Increases the mean arterial pressure with a minimal impact on heart rate	• Lower mortality and lower risk of arrhythmias vs dopamine[79] • First-line agent for septic shock[15]
Vasopressin	Endogenous peptide hormone produced by the hypothalamus and stored and released by the posterior pituitary gland	Vasoconstrictive activity through binding of V_1 receptors on vascular smooth muscle resulting in increased arterial blood pressure	• Higher doses associated with cardiac, digital, and splanchnic ischemia[80] • Theoretical interaction with oxytocin receptors has been hypothesized[63]
Epinephrine	Potent β-1 adrenergic activity and moderate β-2 and α-1 adrenergic receptor activity	Lower doses (action on β-1 adrenergic receptors): • increase CO • decrease SVR • variable effects on MAPHigher doses: increase SVR and CO	• May be used alone in patients with septic shock and myocardial dysfunction[15] • Potential adverse effects include arrhythmias and impaired splanchnic circulation[78,81] • May increase aerobic lactate production via stimulation of skeletal muscle β-2 adrenergic receptors, making the use of serum lactate to guide resuscitation challenging[17]
Dobutamine	Inotrope that stimulates β-1 receptors of the heart	• Increases CO output and oxygen transport • Increases tissue performance • Improves acidosis and hyperlactatemia	Add to norepinephrine for patients with myocardial dysfunction who persist in septic shock[15]

CO, cardiac output; *MAP*, mean arterial pressure; *SVR*, systemic vascular resistance.
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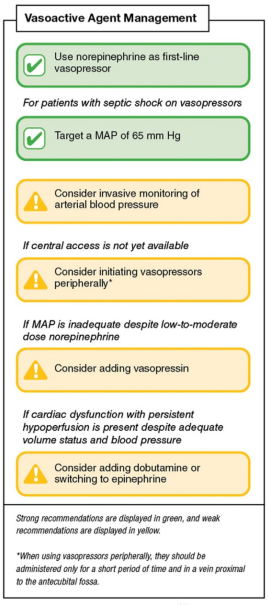
FIGURE 3
Summary of vasoactive agents for sepsis[17]



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MAP, mean arterial pressure.
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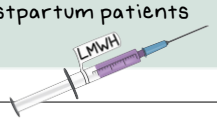
ADDITIONAL THERAPIES

We suggest using IV corticosteroids in pregnant or postpartum patients with septic shock who continue to require vasopressor therapy

We suggest initiating insulin therapy at a glucose level >180 mg/dL in critically ill pregnant patients with sepsis

Because of an increased risk of VTE in sepsis and septic shock, we recommend the use of pharmacologic VTE prophylaxis in pregnant and postpartum patients in septic shock



DELIVERY

If a uterine source for sepsis is suspected or confirmed, we recommend prompt delivery or evacuation of uterine contents to achieve source control, regardless of gestational age

MATERNAL AND PERINATAL OUTCOMES

Because of an increased risk of physical, cognitive, and emotional problems in survivors of sepsis and septic shock, we recommend ongoing comprehensive support for pregnant and postpartum sepsis survivors and their families