بسم الله النور

Basic concepts & definition

TABLE 304-1 Definitions and Criteria for Sepsis and Septic Shock

CONDITION	DEFINITION	COMMON CLINICAL FEATURES	CRITERIA IN 1991/2003 ("SEPSIS-1"/"SEPSIS-2")	CRITERIA IN 2016 ("SEPSIS-3")
Sepsis	A life-threatening organ dysfunction caused by a dysregulated host response to infection	Include signs of infection, with organ dysfunction, plus altered mentation; tachypnea; hypotension; hepatic, renal, or hematologic dysfunction	Suspected (or documented) infection plus ≥2 systemic inflammatory response syndrome (SIRS) criteria[a]	Suspected (or documented) infection and an acute increase in ≥2 sepsis-related organ failure assessment (SOFA) points[b]
Septic shock	A subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities lead to substantially increased mortality risk	Signs of infection, plus altered mentation, oliguria, cool peripheries, hyperlactemia	Suspected (or documented) infection plus persistent arterial hypotension (systolic arterial pressure, <90 mmHg; mean arterial pressure, <60 mmHg; or change in systolic by >40 mmHg from baseline	Suspected (or documented) infection plus vasopressor therapy needed to maintain mean arterial pressure at ≥65 mmHg and serum lactate >2.0 mmol/L despite adequate fluid resuscitation

[a]SIRS criteria include 1 point for each of the following (score range, 0–4): fever >38°C (>100.4°F) or <36°C (<96.8°F); tachypnea with >20 breaths per min; tachycardia with heart rate >90 beats/min; leukocytosis with white blood cell count >12,000/μL; leukopenia (<4000/μL) or >10% bands. [b]SOFA score is a 24-point measure of organ dysfunction that uses six organ systems (renal, cardiovascular, pulmonary, hepatic, neurologic, hematologic), where 0–4 points are assigned per organ system.

TABLE 100-1 SCREENING FOR SEPSIS AND SEPTIC SHOCK

Step 1. Screen for sepsis using Quick SOFA (qSOFA):
One point is given for each adverse finding as follows:

1. Respiratory rate ≥22/minute
2. Altered mentation—Glasgow Coma Score less than 15
3. Systolic blood pressure ≤100 mm Hg

Step 2. Diagnose sepsis as a 2-point increase in SOFA as follows:
Sequential (Sepsis-related) Organ Failure Assessment (SOFA).
Step 3. Diagnose septic shock by the following:
Use of vasopressors (e.g., norepinephrine, epinephrine, phenylephrine) to maintain a mean arterial pressure ≥65 mm Hg
PLUS
Serum lactate >18 mg/dL (2 mmol/L) despite adequate volume resuscitation

SEQUENTIAL (SEPSIS-RELATED) ORGAN FAILURE ASSESSMENT SCORE

	SCORE				
SYSTEM	**0**	**1**	**2**	**3**	**4**
Respiratory (P_{AO_2}/F_{IO_2})	≥400	<400	<300	<200	<100
Coagulation (platelet count × $10^3/\mu L$)	≥150	<150	<100	<50	<20
Liver (bilirubin mg/dL [μmol/L])	<1.2 (20)	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	>12 (204)
Cardiovascular	MAP ≥70 mm Hg	MAP <70 mm Hg	Dopa <5 (or any dose dob*)	Dopa 5.1-15 or epi <0.1 or norepi ≤0.1	Dopa >15 or epi >0.1 or norepi >0.1
CNS GCS†	15	13-14	10-12	6-9	<6
Renal (creat mg/dL [μmol/L])	<1.2 (100)	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-400)	>5 (440)
Urine output, mL/d				<500	<200

Dob = dobutamine; Dopa = dopamine; epi = epinephrine; F_{IO_2} = fraction of inspired oxygen; MAP = mean arterial pressure; norepi = norepinephrine; P_{AO_2} = partial pressure oxygen.
*Catecholamine doses are given as μg/kg/minute for at least 1 hour.
†Glasgow Coma Scale scores range from 3 to 15; higher score indicates better neurological function.
Data from Vincent JL, Moreno R, Takala J, et al; Working Group on Sepsis-Related Problems of the European Society of Intensive Care Medicine. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure. *Intensive Care Med.* 1996;22(7):707-710.

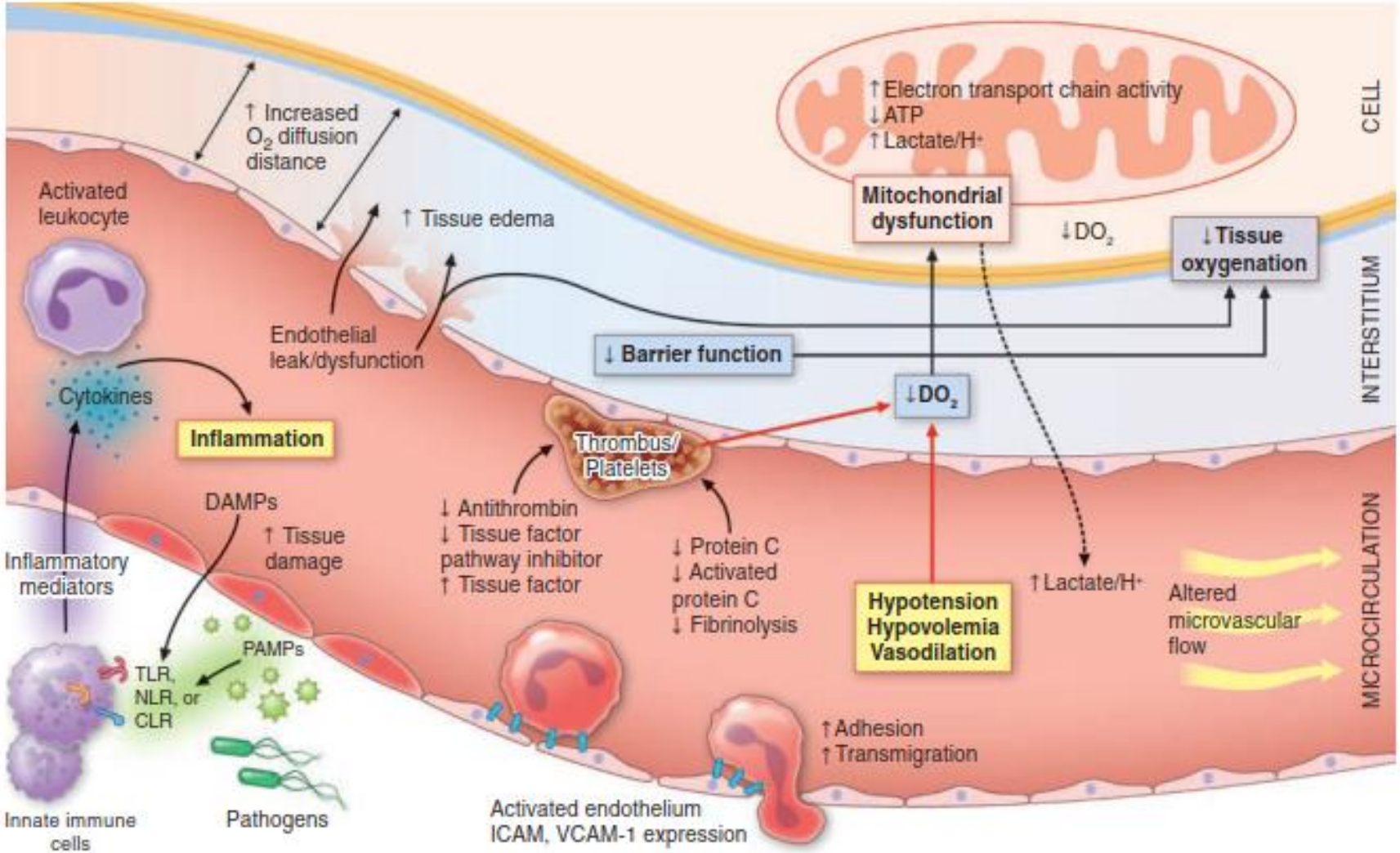

FIGURE 304-1 Select mechanisms implicated in the pathogenesis of sepsis-induced organ and cellular dysfunction. The host response to sepsis involves multiple mechanisms that lead to decreased oxygen delivery (DO_2) at the tissue level. The duration, extent, and direction of these interactions are modified by the organ under threat, host factors (e.g., age, genetic characteristics, medications), and pathogen factors (e.g., microbial load and virulence). The inflammatory response is typically initiated by an interaction between pathogen-associated molecular patterns (PAMPs) expressed by pathogens and pattern recognition receptors expressed by innate immune cells on the cell surface (Toll-like receptors [TLRs] and C-type lectin receptors [CLRs]), in the endosome (TLRs), or in the cytoplasm (retinoic acid inducible gene 1–like receptors and nucleotide-binding oligomerization domain–like receptors [NLRs]). The resulting tissue damage and necrotic cell death lead to release of damage-associated molecular patterns (DAMPs) such as uric acid, high-mobility group protein B1, S100 proteins, and extracellular RNA, DNA, and histones. These molecules promote the activation of leukocytes, leading to greater endothelial dysfunction, expression of intercellular adhesion molecule (ICAM) and vascular cell adhesion molecule 1 (VCAM-1) on the activated endothelium, coagulation activation, and complement activation. This cascade is compounded by macrovascular changes such as vasodilation and hypotension, which are exacerbated by greater endothelial leak tissue edema, and relative intravascular hypovolemia. Subsequent alterations in cellular bioenergetics lead to greater glycolysis (e.g., lactate production), mitochondrial injury, release of reactive oxygen species, and greater organ dysfunction.

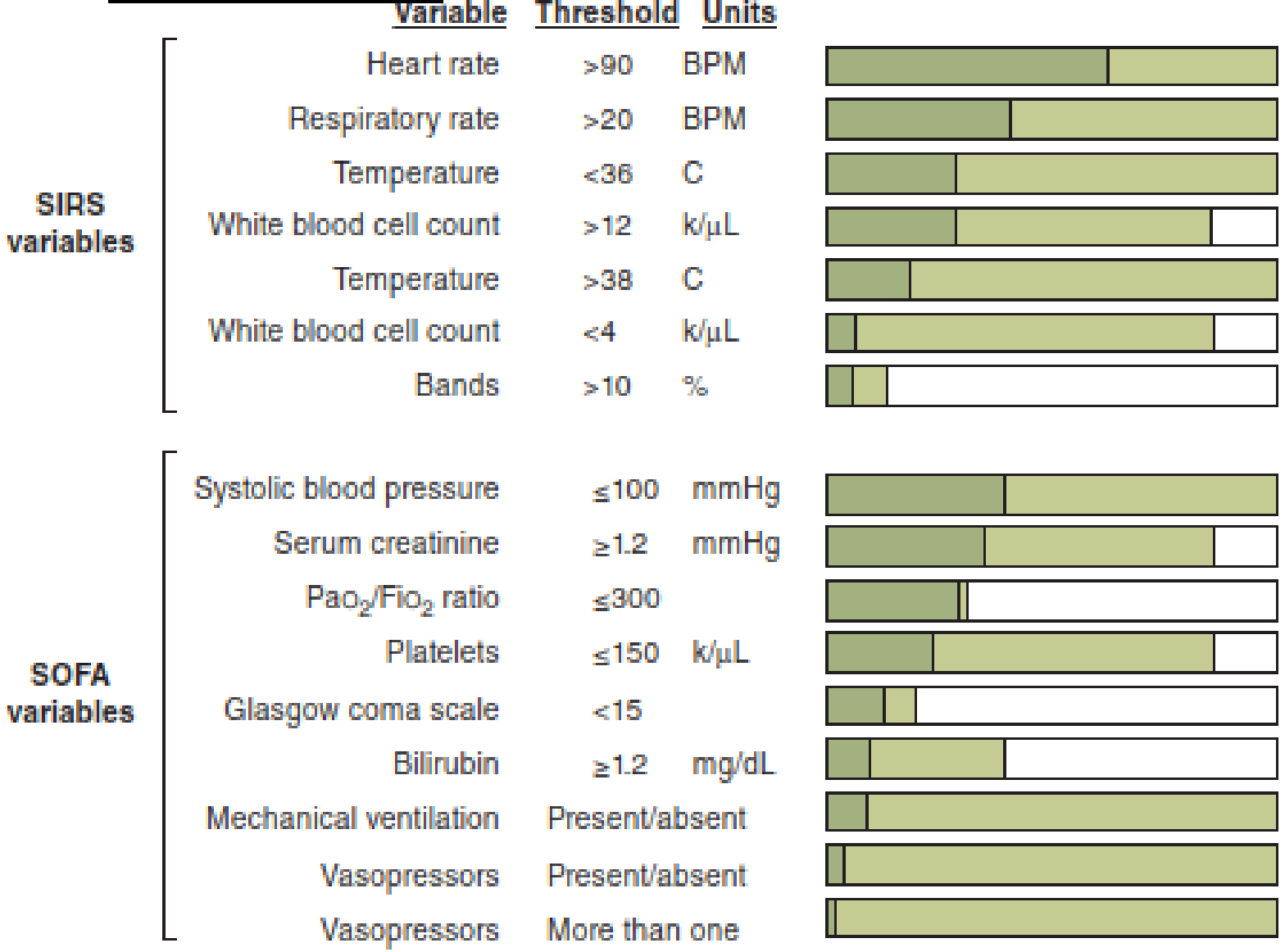

FIGURE 304-2 Distribution of systemic inflammatory response syndrome (SIRS) and sequential (or sepsis-related) organ failure assessment (SOFA) variables among infected patients at risk for sepsis, as documented in the electronic health record. Dark green bars represent the proportion of such patients with abnormal findings; light green bars, the proportion with normal findings; and white bars, the proportion with missing data. *(Adapted from CW Seymour et al: Assessment of clinical criteria for sepsis: For the Third International Consensus Definitions for Sepsis and Septic Shock [Sepsis-3]. JAMA 315:762, 2016.)*

TABLE 304-2 Elements of Care in Sepsis and Septic Shock: Recommendations Adapted from International Consensus Guidelines

Resuscitation
Sepsis and septic shock constitute an emergency, and treatment should begin right away.
Resuscitation with IV crystalloid fluid (30 mL/kg) should begin within the first 3 h.
Saline or balanced crystalloids are suggested for resuscitation.
If the clinical examination does not clearly identify the diagnosis, hemodynamic assessments (e.g., with focused cardiac ultrasound) can be considered.
In patients with elevated serum lactate levels, resuscitation should be guided toward normalizing these levels when possible.
In patients with septic shock requiring vasopressors, the recommended target mean arterial pressure is 65 mmHg.
Hydroxyethyl starches and gelatins are not recommended.
Norepinephrine is recommended as the first-choice vasopressor.
Vasopressin should be used with the intent of reducing the norepinephrine dose.
The use of dopamine should be avoided except in specific situations—e.g., in those patients at highest risk of tachyarrhythmias or relative bradycardia.
Dobutamine use is suggested when patients show persistent evidence of hypoperfusion despite adequate fluid loading and use of vasopressors.
Red blood cell transfusion is recommended only when the hemoglobin concentration decreases to <7.0 g/dL in the absence of acute myocardial infarction, severe hypoxemia, or acute hemorrhage.
Infection Control
So long as no substantial delay is incurred, appropriate samples for microbiologic cultures should be obtained before antimicrobial therapy is started.
IV antibiotics should be initiated as soon as possible (within 1 h); specifically, empirical broad-spectrum therapy should be used to cover all likely pathogens.
Antibiotic therapy should be narrowed once pathogens are identified and their sensitivities determined and/or once clinical improvement is evident.
If needed, source control should be undertaken as soon as is medically and logistically possible.
Daily assessment for de-esclation of antimicrobial therapy should be conducted.
Respiratory Support
A target tidal volume of 6 mL/kg of predicted body weight (compared with 12 mL/kg in adult patients) is recommended in sepsis-induced ARDS.
A higher PEEP rather than a lower PEEP is used in moderate to severe sepsis-induced ARDS.
In severe ARDS (Pao_2/Fio_2, <150 mmHg), prone positioning is recommended, and recruitment maneuvers and/or neuromuscular blocking agents for ≤48 h are suggested.
A conservative fluid strategy should be used in sepsis-induced ARDS if there is no evidence of tissue hypoperfusion.
Routine use of a pulmonary artery catheter is not recommended.
Spontaneous breathing trials should be used in mechanically ventilated patients who are ready for weaning.
General Supportive Care
Patients requiring a vasopressor should have an arterial catheter placed as soon as is practical.
Hydrocortisone is not suggested in septic shock if adequate fluids and vasopressor therapy can restore hemodynamic stability.
Continuous or intermittent sedation should be minimized in mechanically ventilated sepsis patients, with titration targets used whenever possible.
A protocol-based approach to blood glucose management should be used in ICU patients with sepsis, with insulin dosing initiated when two consecutive blood glucose levels are >180 mg/dL.
Continuous or intermittent renal replacement therapy should be used in patients with sepsis and acute kidney injury.
Pharmacologic prophylaxis (unfractionated heparin or low-molecular-weight heparin) against venous thromboembolism should be used in the absence of contraindications.
Stress ulcer prophylaxis should be given to patients with risk factors for gastrointestinal bleeding.
The goals of care and prognosis should be discussed with patients and their families.

Abbreviations: ARDS, acute respiratory distress syndrome; ICU, intensive care unit; PEEP, positive end-expiratory pressure.

Source: Adapted from A Rhodes et al: Surviving Sepsis Campaign: International guidelines for management of sepsis and septic shock: 2016. Crit Care Med 45:486, 2017.

TABLE 304-3 Initial Antimicrobial Therapy for Severe Sepsis with No Obvious Source in Adults with Normal Renal Function

CLINICAL CONDITION	ANTIMICROBIAL REGIMENS*
Septic shock (immunocompetent adult)	The many acceptable regimens include (1) piperacillin-tazobactam (4.5 g q6h), (2) cefepime (2 g q8h), or (3) meropenem (1 g q8h) or imipenem-cilastatin (0.5 g q6h). If the patient is allergic to β-lactam antibiotics, use (1) aztreonam (2 g q8h) or (2) ciprofloxacin (400 mg q12h) or levofloxacin (750 mg q24h). Add vancomycin (loading dose of 25–30 mg/kg, then 15–20 mg/kg q8–12h) to each of the above regimens.
Neutropenia (<500 neutrophils/μL)	Regimens include (1) cefepime (2 g q8h), (2) meropenem (1 g q8h) or imipenem-cilastatin (0.5 g q6h) or doripenem (500 mg q8h), or (3) piperacillin-tazobactam (3.375 g q4h). Add vancomycin (as above) if the patient has a suspected central line–associated bloodstream infection, severe mucositis, skin/soft tissue infection, or hypotension. Add tobramycin (5–7 mg/kg q24h) plus vancomycin (as above) plus caspofungin (one dose of 70 mg, then 50 mg q24h) if the patient has severe sepsis/septic shock.
Splenectomy	Use ceftriaxone (2 g q24h, or—in meningitis—2 g q12h). If the local prevalence of cephalosporin-resistant pneumococci is high, add vancomycin (as above). If the patient is allergic to β-lactam antibiotics, use levofloxacin (750 mg q24h) or moxifloxacin (400 mg q24h) plus vancomycin (as above).

*All agents are administered by the intravenous route. Beta-lactam antibiotics may exhibit unpredictable pharmacodynamics in sepsis; therefore, continuous infusions are often used.

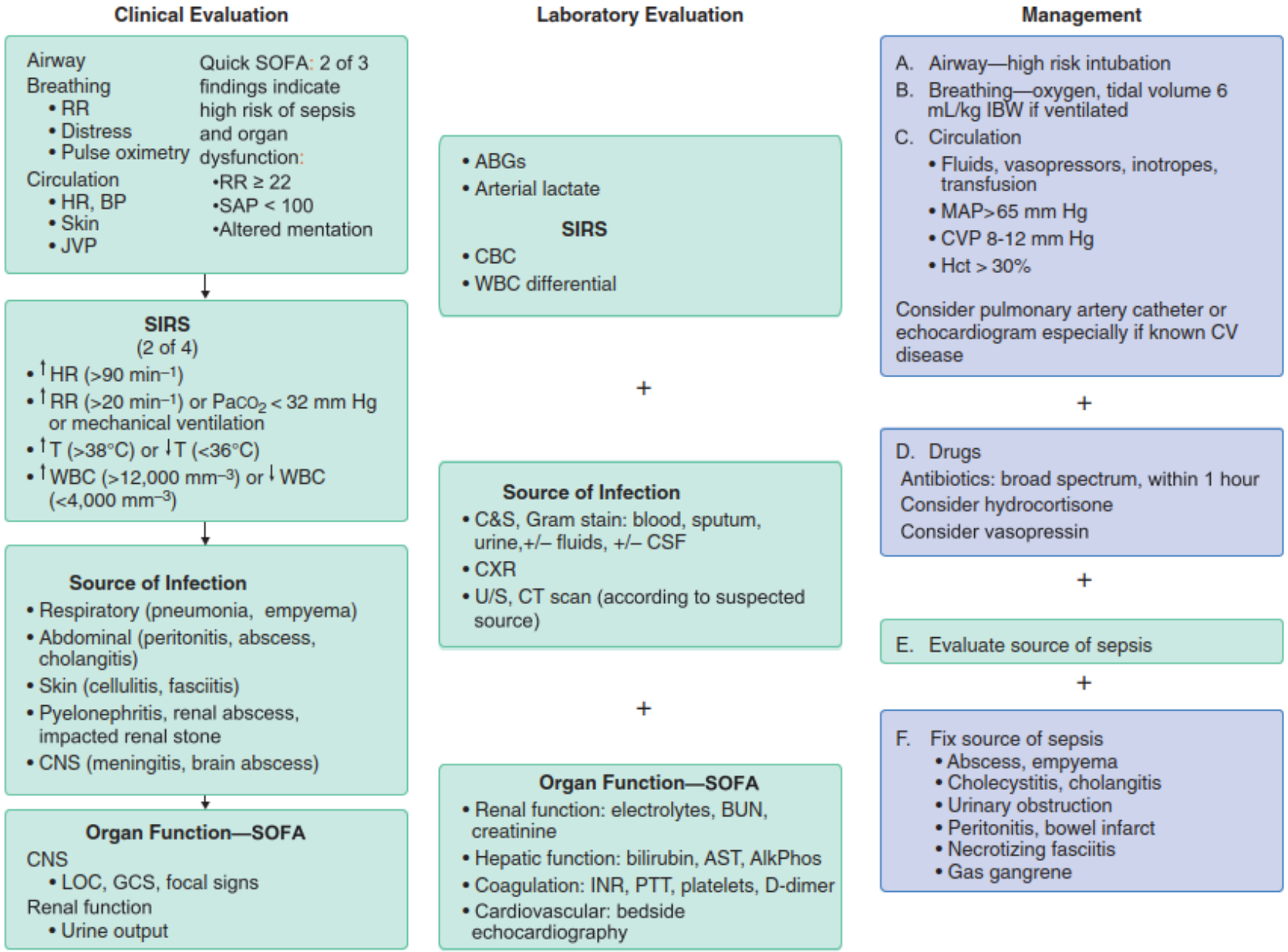

FIGURE 100-1. Algorithm for the clinical and laboratory evaluation and management of septic shock. ABGs = arterial blood gases; AlkPhos = alkaline phosphatase; AST = aspartate aminotransferase; BP = blood pressure; BUN = blood urea nitrogen; C&S = culture and sensitivity; CBC = complete blood count; CNS = central nervous system; CSF = cerebrospinal fluid; CT = computed tomography; CV = cardiovascular; CVP = central venous pressure; CXR = chest radiograph; Hct = hematocrit; HR = heart rate; IBW = ideal body weight; INR = international normalized ratio; JVP = jugular venous pressure; LOC = level of consciousness; MAP = mean arterial pressure; $Paco_2$ = partial pressure of carbon dioxide; PTT = partial thromboplastin time; RR = respiratory rate; $Scvo_2$ = central venous oxygen saturation; SIRS = systemic inflammatory response syndrome; T = temperature; U/S = ultrasound; WBC = white blood cell count.