Agency for Healthcare Research and Quality
Advancing Excellence in Health Care

NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012.

Bibliographic Source(s)

Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, Sevransky JE, Sprung CL, Douglas IS, Jaeschke R, Osborn TM, Nunnally ME, Townsend SR, Reinhart K, Kleinpell RM, Angus DC, Deutschman CS, Machado FR, Rubenfeld GD, Webb SA, Beale RJ, Vincent JL, Moreno R, Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med. 2013 Feb;41(2):580-637. [636 references] PubMed

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Dellinger RP, Levy MM, Carlet JM, Bion J, Parker MM, Jaeschke R, Reinhart K, Angus DC, Brun-Buisson C, Beale R, Calandra T, Dhainaut JF, Gerlach H, Harvey M, Marini JJ, Marshall J, Ranieri M, Ramsay G, Sevransky J, Thompson BT, Townsend S, Vender JS, Zimmerman JL, Vincent JL. Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008. Intensive Care Med 2008 Jan;34(1):17-60. [341 references]

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- November 6, 2013 – Low Molecular Weight Heparins: The U.S. Food and Drug Administration (FDA) is recommending that health care professionals carefully consider the timing of spinal catheter placement and removal in patients taking anticoagulant drugs, such as enoxaparin, and delay dosing of anticoagulant medications for some time interval after catheter removal to decrease the risk of spinal column bleeding and subsequent paralysis after spinal injections, including epidural procedures and lumbar punctures. These new timing recommendations, which can decrease the risk of epidural or spinal hematoma, will be added to the labels of anticoagulant drugs known as low molecular weight heparins, including Lovenox and generic enoxaparin products and similar products.

Recommendations

Major Recommendations

The grades of evidence (A-D) and levels of recommendations (1-2) are defined at the end of the "Major Recommendations" field.

Note: These clinical practice guidelines are a revision of the 2008 Surviving Sepsis Campaign (SSC) guidelines for the management of severe sepsis and septic shock. The initial SSC guidelines were published in 2004 and incorporated the evidence available through the end of 2003. The 2008 publication analyzed evidence available through the end of 2007. The most current iteration is based on updated literature search incorporated into the evolving manuscript through fall 2012.

Management of Severe Sepsis

Initial Resuscitation and Infection Issues

A. Initial Resuscitation
   1. The committee recommends the protocolized, quantitative resuscitation of patients with sepsis-induced tissue hypoperfusion (defined in this document as hypotension persisting after initial fluid challenge or blood lactate concentration ≥4 mmol/L). This protocol should be initiated as soon as hypoperfusion is recognized and should not be delayed pending intensive care unit (ICU) admission. During the first 6 hrs of resuscitation, the goals of initial resuscitation of sepsis-induced hypoperfusion should include all of the following as a part of a treatment protocol (Grade 1C):
      a. Central venous pressure (CVP) 8–12 mm Hg
      b. Mean arterial pressure (MAP) ≥65 mm Hg
      c. Urine output ≥0.5 mL·kg·hr
      d. Superior vena cava oxygenation saturation ($ScvO_2$) or mixed venous oxygen saturation (SvO_2) 70% or 65%, respectively
   2. The committee suggests targeting resuscitation to normalize lactate in patients with elevated lactate levels as a marker of tissue hypoperfusion (Grade 2C).

B. Screening for Sepsis and Performance Improvement
   1. The committee recommends routine screening of potentially infected seriously ill patients for severe sepsis to increase the early identification of sepsis and allow implementation of early sepsis therapy (Grade 1C).
   2. Performance improvement efforts in severe sepsis should be used to improve patient outcomes (UG).

C. Diagnosis
   1. The committee recommends obtaining appropriate cultures before antimicrobial therapy is initiated if such cultures do not cause significant delay (>45 minutes) in the start of antimicrobial(s) administration (Grade 1C). To optimize identification of causative organisms, the committee recommends obtaining at least two sets of blood cultures (both aerobic and anaerobic bottles) before antimicrobial therapy, with at least one drawn percutaneously and one drawn through each vascular access device, unless the device was recently (<48 hours) inserted. These blood cultures can be drawn at the same time if they are obtained from different sites. Cultures of other sites (preferably quantitative where appropriate), such as urine, cerebrospinal fluid, wounds, respiratory secretions, or other body fluids that may be the source of infection, should also be obtained before antimicrobial therapy if doing so does not cause significant delay in antibiotic administration (Grade 1C).
   2. The committee suggests the use of the 1,3 β-d-glucan assay (Grade 2B), mannan and anti-mannan antibody assays (Grade 2C) when invasive candidiasis is in the differential diagnosis of infection.
   3. The committee recommends that imaging studies be performed promptly in attempts to confirm a potential source of infection. Potential sources of infection should be sampled as they are identified and in consideration of patient risk for transport and invasive procedures (e.g., careful coordination and aggressive monitoring if the decision is made to transport for a computed tomography [CT]-guided needle aspiration). Bedside studies, such as ultrasound, may avoid patient transport (UG).

D. Antimicrobial Therapy

> 1. The administration of effective intravenous antimicrobials within the first hour of recognition of septic shock (Grade 1B) and severe sepsis without septic shock (Grade 1C) should be the goal of therapy. *Remark*: Although the weight of the evidence supports prompt administration of antibiotics following the recognition of severe sepsis and septic shock, the feasibility with which clinicians may achieve this ideal state has not been scientifically evaluated.
>
> 2a. The committee recommends that initial empiric anti-infective therapy include one or more drugs that have activity against all likely pathogens (bacterial and/or fungal or viral) and that penetrate in adequate concentrations into the tissues presumed to be the source of sepsis (Grade 1B).

> 2b. The antimicrobial regimen should be reassessed daily for potential de-escalation to prevent the development of resistance, to reduce toxicity, and to reduce costs (Grade 1B).
>
> 3. The committee suggest the use of low procalcitonin levels or similar biomarkers to assist the clinician in the discontinuation of empiric antibiotics in patients who appeared septic, but have no subsequent evidence of infection (Grade 2C).
>
> 4a. Empiric therapy should attempt to provide antimicrobial activity against the most likely pathogens based upon each patient's presenting illness and local patterns of infection. The committee suggests combination empiric therapy for neutropenic patients with severe sepsis (Grade 2B) and for patients with difficult-to-treat, multidrug-resistant bacterial pathogens such as *Acinetobacter* and *Pseudomonas* spp. (Grade 2B). For selected patients with severe infections associated with respiratory failure and septic shock, combination therapy with an extended spectrum beta-lactam and either an aminoglycoside or a fluoroquinolone is suggested for *P. aeruginosa* bacteremia (Grade 2B). Similarly, a more complex combination of beta-lactam and a macrolide is suggested for patients with septic shock from bacteremic *Streptococcus pneumoniae* infections (Grade 2B).
>
> 4b. The committee suggests that combination therapy, when used empirically in patients with severe sepsis, should not be administered for longer than 3 to 5 days. De-escalation to the most appropriate single-agent therapy should be performed as soon as the susceptibility profile is known (Grade 2B). Exceptions would include aminoglycoside monotherapy, which should be generally avoided, particularly for *P. aeruginosa* sepsis, and for selected forms of endocarditis, where prolonged courses of combinations of antibiotics are warranted.
>
> 5. The committee suggests that the duration of therapy typically be 7 to 10 days if clinically indicated; longer courses may be appropriate in patients who have a slow clinical response, undrainable foci of infection, bacteremia with *S. aureus*; some fungal and viral infections, or immunologic deficiencies, including neutropenia (Grade 2C).
>
> 6. The committee suggests that antiviral therapy be initiated as early as possible in patients with severe sepsis or septic shock of viral origin (Grade 2C).
>
> 7. The committee recommends that antimicrobial agents not be used in patients with severe inflammatory states determined to be of noninfectious cause (UG).

E. Source Control
   1. The committee recommends that a specific anatomical diagnosis of infection requiring consideration for emergent source control (e.g., necrotizing soft tissue infection, peritonitis, cholangitis, intestinal infarction) be sought and diagnosed or excluded as rapidly as possible, and intervention be undertaken for source control within the first 12 hours after the diagnosis is made, if feasible (Grade 1C).
   2. The committee suggests that when infected peripancreatic necrosis is identified as a potential source of infection, definitive intervention is best delayed until adequate demarcation of viable and nonviable tissues has occurred (Grade 2B).
   3. When source control in a severely septic patient is required, the effective intervention associated with the least physiologic insult should be used (e.g., percutaneous rather than surgical drainage of an abscess) (UG).
   4. If intravascular access devices are a possible source of severe sepsis or septic shock, they should be removed promptly after other vascular access has been established (UG).

F. Infection Prevention

> 1a. The committee suggest that selective oral decontamination (SOD) and selective digestive decontamination (SDD) should be introduced and investigated as a method to reduce the incidence of ventilator-associated pneumonia (VAP); this infection control measure can then be instituted in healthcare settings and regions where this methodology is found to be effective (Grade 2B).
>
> 1b. The committee suggest oral chlorhexidine gluconate (CHG) be used as a form of oropharyngeal decontamination to reduce the risk of VAP in ICU patients with severe sepsis (Grade 2B).

Hemodynamic Support and Adjunctive Therapy

G. Fluid Therapy of Severe Sepsis
   1. The committee recommends crystalloids be used as the initial fluid of choice in the resuscitation of severe sepsis and septic shock

(Grade 1B).

2. The committee recommends against the use of hydroxyethyl starches (HES) for fluid resuscitation of severe sepsis and septic shock (Grade 1B). (This recommendation is based on the results of the VISEP [Brunkhorst et al., 2008], CRYSTMAS [Guidet et al., 2012], 6S [Perner et al., 2012], and CHEST [Myburgh et al., 2012] trials. The results of the recently completed CRYSTAL trial were not considered.)
3. The committee suggests the use of albumin in the fluid resuscitation of severe sepsis and septic shock when patients require substantial amounts of crystalloids (Grade 2C).
4. The committee recommends an initial fluid challenge in patients with sepsis-induced tissue hypoperfusion with suspicion of hypovolemia to achieve a minimum of 30 mL/kg of crystalloids (a portion of this may be albumin equivalent). More rapid administration and greater amounts of fluid may be needed in some patients (see Initial Resuscitation recommendations) (Grade 1C).
5. The committee recommends that a fluid challenge technique be applied wherein fluid administration is continued as long as there is hemodynamic improvement either based on dynamic (e.g., change in pulse pressure, stroke volume variation) or static (e.g., arterial pressure, heart rate) variables (UG).

H. Vasopressors

1. The committee recommends that vasopressor therapy initially target a MAP of 65 mm Hg (Grade 1C).
2. The committee recommends norepinephrine as the first-choice vasopressor (Grade 1B).
3. The committee suggests epinephrine (added to and potentially substituted for norepinephrine) when an additional agent is needed to maintain adequate blood pressure (Grade 2B).
4. Vasopressin (up to 0.03 U/min) can be added to norepinephrine with the intent of raising MAP to target or decreasing norepinephrine dosage (UG).
5. Low-dose vasopressin is not recommended as the single initial vasopressor for treatment of sepsis-induced hypotension, and vasopressin doses higher than 0.03–0.04 U/min should be reserved for salvage therapy (failure to achieve an adequate MAP with other vasopressor agents) (UG).
6. The committee suggests dopamine as an alternative vasopressor agent to norepinephrine only in highly selected patients (e.g., patients with low risk of tachyarrhythmias and absolute or relative bradycardia) (Grade 2C).
7. Phenylephrine is not recommended in the treatment of septic shock except in the following circumstances: (a) norepinephrine is associated with serious arrhythmias, (b) cardiac output is known to be high and blood pressure persistently low, or (c) as salvage therapy when combined inotrope/ vasopressor drugs and low-dose vasopressin have failed to achieve the MAP target (Grade 1C).
8. The committee recommends that low-dose dopamine not be used for renal protection (Grade 1A).
9. The committee recommends that all patients requiring vasopressors have an arterial catheter placed as soon as practical if resources are available (UG).

I. Inotropic Therapy

1. The committee recommends that a trial of dobutamine infusion up to 20 µg/kg/min be administered or added to vasopressor (if in use) in the presence of: a) myocardial dysfunction, as suggested by elevated cardiac filling pressures and low cardiac output, or b) ongoing signs of hypoperfusion, despite achieving adequate intravascular volume and adequate MAP (Grade 1C).
2. The committee recommends against the use of a strategy to increase cardiac index to predetermined supranormal levels (Grade 1B).

J. Corticosteroids

1. The committee suggests not using intravenous hydrocortisone as a treatment of adult septic shock patients if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability (see goals for Initial Resuscitation). If this is not achievable, the committee suggests intravenous hydrocortisone alone at a dose of 200 mg per day (Grade 2C).
2. The committee suggests not using the postadrenocorticotropic hormone (ACTH) stimulation test to identify the subset of adults with septic shock who should receive hydrocortisone (Grade 2B).
3. The committee suggests that clinicians taper the treated patient from steroid therapy when vasopressors are no longer required (Grade 2D).
4. The committee recommends that corticosteroids not be administered for the treatment of sepsis in the absence of shock (Grade 1D).
5. When low-dose hydrocortisone is given, the committee suggests using continuous infusion rather than repetitive bolus injections (Grade 2D).

<u>Supportive Therapy of Severe Sepsis</u>

K. Blood Product Administration

1. Once tissue hypoperfusion has resolved and in the absence of extenuating circumstances, such as myocardial ischemia, severe hypoxemia, acute hemorrhage, or ischemic coronary artery disease, the committee recommends that red blood cell transfusion occur

when the hemoglobin concentration decreases to <7.0 g/dL to target a hemoglobin concentration of 7.0 to 9.0 g/dL in adults (Grade 1B).

2. The committee recommends not using erythropoietin as a specific treatment of anemia associated with severe sepsis (Grade 1B).
3. The committee suggests that fresh frozen plasma not be used to correct laboratory clotting abnormalities in the absence of bleeding or planned invasive procedures (Grade 2D).
4. The committee recommends against antithrombin administration for the treatment of severe sepsis and septic shock (Grade 1B).
5. In patients with severe sepsis, the committee suggests that platelets be administered prophylactically when counts are $\leq 10{,}000/mm^3$ ($10 \times 10^9/L$) in the absence of apparent bleeding, as well when counts are $\leq 20{,}000/mm^3$ ($20 \times 10^9/L$) if the patient has a significant risk of bleeding. Higher platelet counts ($\geq 50{,}000/mm^3$ [$50 \times 10^9/L$]) are advised for active bleeding, surgery, or invasive procedures (Grade 2D).

L. Immunoglobulins

1. The committee suggests not using intravenous immunoglobulins in adult patients with severe sepsis or septic shock (Grade 2B).

M. Selenium

1. The committee suggests not using intravenous selenium to treat severe sepsis (Grade 2C).

N. History of Recommendations Regarding Use of Recombinant Activated Protein C (rhAPC)

The drug was withdrawn from the market and is no longer available, negating any need for a recommendation regarding its use. A history of the evolution of Surviving Sepsis Campaign (SSC) recommendations as to rhAPC is provided in the original guideline document.

O. Mechanical Ventilation of Sepsis-Induced Acute Respiratory Distress Syndrome

1. The committee recommends that clinicians target a tidal volume of 6 mL/kg predicted body weight in patients with sepsis induced acute respiratory distress syndrome (ARDS) (Grade 1A vs. 12 mL/kg).
2. The committee recommends that plateau pressures be measured in patients with ARDS and that the initial upper limit goal for plateau pressures in a passively inflated lung be ≤ 30 cm H_2O (Grade 1B).
3. The committee recommends that positive end-expiratory pressure (PEEP) be applied to avoid alveolar collapse at end expiration (atelectotrauma) (Grade 1B).
4. The committee suggests strategies based on higher rather than lower levels of PEEP for patients with sepsis-induced moderate to severe ARDS (Grade 2C).
5. The committee suggests recruitment maneuvers in sepsis patients with severe refractory hypoxemia due to ARDS (Grade 2C).
6. The committee suggests prone positioning in sepsis-induced ARDS patients with a partial pressure of oxygen in arterial blood/fraction of inspired oxygen (PaO_2/FiO_2) ratio ≤ 100 mm Hg in facilities that have experience with such practices (Grade 2B).
7. The committee recommends that mechanically ventilated sepsis patients be maintained with the head of the bed elevated between 30 and 45 degrees to limit aspiration risk and to prevent the development of VAP (Grade 1B).
8. The committee suggests that noninvasive mask ventilation (NIV) be used in that minority of sepsis-induced ARDS patients in whom the benefits of NIV have been carefully considered and are thought to outweigh the risks (Grade 2B).
9. The committee recommends that a weaning protocol be in place and that mechanically ventilated patients with severe sepsis undergo spontaneous breathing trials regularly to evaluate the ability to discontinue mechanical ventilation when they satisfy the following criteria: a) arousable; b) hemodynamically stable (without vasopressor agents); c) no new potentially serious conditions; d) low ventilatory and end-expiratory pressure requirements; and e) low FiO_2 requirements which can be safely delivered with a face mask or nasal cannula. If the spontaneous breathing trial is successful, extubation should be considered (Grade 1A).
10. The committee recommends against the routine use of the pulmonary artery catheter for patients with sepsis-induced ARDS (Grade 1A).
11. The committee recommends a conservative fluid strategy for patients with established sepsis-induced ARDS who do not have evidence of tissue hypoperfusion (Grade 1C).
12. In the absence of specific indications such as bronchospasm, the committee recommends against the use of β2-agonists for treatment of patients with sepsis-induced ARDS (Grade 1B).

P. Sedation, Analgesia, and Neuromuscular Blockade in Sepsis

1. The committee recommends that either continuous or intermittent sedation be minimized in mechanically ventilated sepsis patients, targeting specific titration endpoints (Grade 1B).
2. The committee recommends that neuromuscular blocking agents (NMBAs) be avoided if possible in the septic patient without ARDS due to the risk of prolonged neuromuscular blockade following discontinuation. If NMBAs must be maintained, either intermittent bolus as required or continuous infusion with train-of-four monitoring of the depth of blockade should be used (Grade 1C).

3. The committee suggests a short course of an NMBA (≤48 hours) for patients with early, sepsis-induced ARDS and PaO_2/FiO_2 <150 mm Hg (Grade 2C).

Q. Glucose Control
1. The committee recommends a protocolized approach to blood glucose management in ICU patients with severe sepsis, commencing insulin dosing when two consecutive blood glucose levels are >180 mg/dL. This approach should target an upper blood glucose level ≤180 mg/dL rather than an upper target blood glucose ≤110 mg/dL (Grade 1A).
2. The committee recommends blood glucose values be monitored every 1 to 2 hrs until glucose values and insulin infusion rates are stable, then every 4 hrs thereafter (Grade 1C).
3. The committee recommends that glucose levels obtained with point-of-care testing of capillary blood be interpreted with caution, as such measurements may not accurately estimate arterial blood or plasma glucose values (UG).

R. Renal Replacement Therapy
1. The committee suggests that continuous renal replacement therapies and intermittent hemodialysis are equivalent in patients with severe sepsis and acute renal failure because they achieve similar short-term survival rates (Grade 2B).
2. The committee suggests the use of continuous therapies to facilitate management of fluid balance in hemodynamically unstable septic patients (Grade 2D).

S. Bicarbonate Therapy
1. The committee recommend against the use of sodium bicarbonate therapy for the purpose of improving hemodynamics or reducing vasopressor requirements in patients with hypoperfusion-induced lactic acidemia with pH ≥7.15 (Grade 2B).

T. Deep Vein Thrombosis Prophylaxis
1. The committee recommends that patients with severe sepsis receive daily pharmacoprophylaxis against venous thromboembolism (VTE) (Grade 1B). The committee recommends that this be accomplished with daily subcutaneous low-molecular weight heparin (LMWH) (Grade 1B versus unfractionated heparin [UFH] twice daily and Grade 2C versus UFH given thrice daily). If creatinine clearance is <30 mL/min, the committee recommends use of dalteparin (Grade 1A) or another form of LMWH that has a low degree of renal metabolism (Grade 2C) or UFH (Grade 1A).
2. The committee suggests that patients with severe sepsis be treated with a combination of pharmacologic therapy and intermittent pneumatic compression devices whenever possible (Grade 2C).
3. The committee recommends that septic patients who have a contraindication to heparin use (e.g., thrombocytopenia, severe coagulopathy, active bleeding, recent intracerebral hemorrhage) not receive pharmacoprophylaxis (Grade 1B). Rather the committee suggests they receive mechanical prophylactic treatment, such as graduated compression stockings or intermittent compression devices (Grade 2C), unless contraindicated. When the risk decreases, the committee suggests starting pharmacoprophylaxis (Grade 2C).

U. Stress Ulcer Prophylaxis
1. The committee recommends that stress ulcer prophylaxis using H_2 blocker or proton pump inhibitor be given to patients with severe sepsis/septic shock who have bleeding risk factors (Grade 1B).
2. When stress ulcer prophylaxis is used, the committee suggests the use of proton pump inhibitors rather than H_2 receptor antagonists (H_2RA) (Grade 2C).
3. The committee suggests that patients without risk factors should not receive prophylaxis (Grade 2B).

V. Nutrition
1. The committee suggests administering oral or enteral (if necessary) feedings, as tolerated, rather than either complete fasting or provision of only intravenous glucose within the first 48 hrs after a diagnosis of severe sepsis/septic shock (Grade 2C).
2. The committee suggests avoiding mandatory full caloric feeding in the first week, but rather suggest low-dose feeding (e.g., up to 500 kcal per day), advancing only as tolerated (Grade 2B).
3. The committee suggests using intravenous glucose and enteral nutrition rather than total parenteral nutrition (TPN) alone or parenteral nutrition in conjunction with enteral feeding in the first 7 days after a diagnosis of severe sepsis/septic shock (Grade 2B).
4. The committee suggests using nutrition with no specific immunomodulating supplementation in patients with severe sepsis (Grade 2C).

W. Setting Goals of Care
1. The committee recommends that goals of care and prognosis be discussed with patients and families (Grade 1B).
2. The committee recommends that the goals of care be incorporated into treatment and end-of-life care planning, utilizing palliative care principles where appropriate (Grade 1B).

3. The committee suggests that goals of care be addressed as early as feasible, but no later than within 72 hrs of ICU admission (Grade 2C).

Pediatric Considerations in Severe Sepsis

A. Initial Resuscitation
   1. The committee suggests starting with oxygen administered by face mask or, if needed and available, high-flow nasal cannula oxygen or nasopharyngeal continuous positive airway pressure (CPAP) for respiratory distress and hypoxemia. Peripheral intravenous access or intraosseous access can be used for fluid resuscitation and inotrope infusion when a central line is not available. If mechanical ventilation is required, then cardiovascular instability during intubation is less likely after appropriate cardiovascular resuscitation (Grade 2C).
   2. The committee suggests that the initial therapeutic endpoints of resuscitation of septic shock be capillary refill of ≤2 secs, normal blood pressure for age, normal pulses with no differential between peripheral and central pulses, warm extremities, urine output >1 mL/kg/hr, and normal mental status. Thereafter, $ScvO_2$ saturation greater than or equal to 70% and cardiac index between 3.3 and 6.0 L/min/m^2 should be targeted (Grade 2C).
   3. The committee recommends following the American College of Critical Care Medicine-Pediatric Advanced Life Support guidelines for the management of septic shock (Grade 1C).
   4. The committee recommends evaluating for and reversing pneumothorax, pericardial tamponade, or endocrine emergencies in patients with refractory shock (Grade 1C).

B. Antibiotics and Source Control
   1. The committee recommends that empiric antimicrobials be administered within 1 hour of the identification of severe sepsis. Blood cultures should be obtained before administering antibiotics when possible, but this should not delay initiation of antibiotics. The empiric drug choice should be changed as epidemic and endemic ecologies dictate (e.g., H1N1, methicillin- resistant *S. aureus*, chloroquine-resistant malaria, penicillin-resistant pneumococci, recent ICU stay, neutropenia) (Grade 1D).
   2. The committee suggests the use of clindamycin and antitoxin therapies for toxic shock syndromes with refractory hypotension (Grade 2D).
   3. The committee recommends early and aggressive infection source control (Grade 1D).
   4. *C. difficile* colitis should be treated with enteral antibiotics if tolerated. Oral vancomycin is preferred for severe disease (Grade 1A).

C. Fluid Resuscitation
   1. In the industrialized world with access to inotropes and mechanical ventilation, the committee suggests that initial resuscitation of hypovolemic shock begin with infusion of isotonic crystalloids or albumin, with boluses of up to 20 mL/kg for crystalloids (or albumin equivalent) over 5 to 10 mins. These should be titrated to reversing hypotension, increasing urine output, and attaining normal capillary refill, peripheral pulses and level of consciousness without inducing hepatomegaly or rales. If hepatomegaly or rales develop, inotropic support should be implemented, not fluid resuscitation. In children with severe hemolytic anemia (severe malaria or sickle cell crises) who are not hypotensive, blood transfusion is considered superior to crystalloid or albumin blousing (Grade 2C).

D. Inotropes/Vasopressors/Vasodilators
   1. The committee suggests beginning peripheral inotropic support until central venous access can be attained in children who are not responsive to fluid resuscitation (Grade 2C).
   2. The committee suggests that patients with low cardiac output and elevated systemic vascular resistance states with normal blood pressure be given vasodilator therapies in addition to inotropes (Grade 2C).

E. Extracorporeal Membrane Oxygenation (ECMO)
   1. The committee suggests ECMO in children with refractory septic shock or with refractory respiratory failure associated with sepsis (Grade 2C).

F. Corticosteroids
   1. The committee suggest timely hydrocortisone therapy in children with fluid-refractory, catecholamine-resistant shock and suspected or proven absolute (classic) adrenal insufficiency (Grade 1A).

G. Protein C and Activated Protein Concentrate
   See section, "History of Recommendations Regarding Use of Recombinant Activated Protein C" in the original guideline document.

H. Blood Products and Plasma Therapies
   1. The committee suggests similar hemoglobin targets in children as in adults. During resuscitation of low superior vena cava oxygen

saturation shock (<70%), hemoglobin levels of 10 g/dL are targeted. After stabilization and recovery from shock and hypoxemia, then a lower target >7.0 g/dL can be considered reasonable (Grade 1B).
2. The committee suggests similar platelet transfusion targets in children as in adults (Grade 2C).
3. The committee suggests the use of plasma therapies in children to correct sepsis-induced thrombotic purpura disorders, including progressive disseminated intravascular coagulation, secondary thrombotic microangiopathy, and thrombotic thrombocytopenic purpura (Grade 2C).

I. Mechanical Ventilation
   1. The committee suggests providing lung-protective strategies during mechanical ventilation (Grade 2C).

J. Sedation/Analgesia/Drug Toxicities
   1. The committee recommends use of sedation with a sedation goal in critically ill mechanically ventilated patients with sepsis (Grade 1D).
   2. The committee recommends monitoring drug toxicity labs because drug metabolism is reduced during severe sepsis, putting children at greater risk of adverse drug-related events (Grade 1C).

K. Glycemic Control
   1. The committee suggests controlling hyperglycemia using a similar target as in adults (≤180 mg/dL). Glucose infusion should accompany insulin therapy in newborns and children (Grade 2C).

L. Diuretics and Renal Replacement Therapy
   1. The committee suggests the use of diuretics to reverse fluid overload when shock has resolved and if unsuccessful, then continuous venovenous hemofiltration or intermittent dialysis to prevent greater than 10% total body weight fluid overload (Grade 2C).

M. Deep Vein Thrombosis (DVT) Prophylaxis
   1. The committee makes no graded recommendations on the use of DVT prophylaxis in prepubertal children with severe sepsis.

N. Stress Ulcer Prophylaxis
   1. The committee makes no graded recommendations on stress ulcer prophylaxis.

O. Nutrition
   1. Enteral nutrition should be used in children who can tolerate it, parenteral feeding in those who cannot (Grade 2C).

<u>Definitions</u>:

Determination of Quality of Evidence

Grade A (High): Randomized controlled trial (RCT)

Grade B (Moderate): Downgraded RCT or upgraded observational studies

Grade C (Low): Well-done observational studies with control RCTs

Grade D (Very Low): Downgraded controlled studies or expert opinion based on other evidence

Factors that may decrease the strength of the evidence:

1. Poor quality of planning and implementation of available RCTs suggesting high likelihood of bias
2. Inconsistency of results (including problems with subgroup analyses)
3. Indirectness of evidence (differing population, intervention, control, outcomes, comparison)
4. Imprecision of results
5. High likelihood of reporting bias

Main factors that may increase the strength of evidence

1. Large magnitude of effect (direct evidence, relative risk [RR]>2 with no plausible confounders)
2. Very large magnitude of effect with RR>5 and no threats to validity (by two levels)
3. Dose response gradient

Strength of the Recommendations

Grade 1 (Strong): A recommendation in favor of an intervention reflects that the desirable effects of adherence to a recommendation (beneficial health outcomes, less burden on staff and patients, and cost savings) will clearly outweigh the undesirable effects (harms, more burden and greater costs).

Grade 2 (Weak): A recommendation in favor of an intervention indicates that the desirable effects of adherence to a recommendation probably will outweigh the undesirable effects, but the panel is not confident about these tradeoffs – either because some of the evidence is low-quality (and thus there remains uncertainty regarding the benefits and risks) or the benefits and downsides are closely balanced.

UG: Ungraded

Clinical Algorithm(s)

An algorithm for time sensitive, goal-directed stepwise management of hemodynamic support in infants and children is provided in the original guideline.

Scope

Disease/Condition(s)

Severe sepsis
Septic shock

Guideline Category

Management

Treatment

Clinical Specialty

Critical Care

Emergency Medicine

Internal Medicine

Nursing

Pediatrics

Intended Users

Advanced Practice Nurses

Emergency Medical Technicians/Paramedics

Health Care Providers

Hospitals

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

- To provide an update to the most recent version of the Surviving Sepsis Campaign clinical management guidelines, "Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock," published in 2008
- To provide guidance for the clinician caring for a patient with severe sepsis or septic shock

Target Population

Adult and pediatric patients in intensive care unit (ICU) and non-ICU settings with severe sepsis or septic shock

Interventions and Practices Considered

1. Initial resuscitation
2. Diagnostic studies, as indicated
    - Blood culture and cultures from other sites, such as urine, cerebrospinal fluid, wounds, respiratory secretions, or other body fluids, as indicated
    - 1,3 β-d-glucan assay
    - Mannan and anti-mannan antibody assays
    - Imaging studies, such as ultrasound, computed tomography-guided needle aspiration as indicated
3. Antimicrobial therapy
    - Antibiotics (single agent, combination therapy)
    - Antiviral therapy
    - Measurement of biomarkers (procalcitonin)
4. Source identification and control measures
5. Infection prevention (selective oral decontamination and selective digestive decontamination, oral chlorhexidine gluconate)
6. Fluid therapy
    - Natural or artificial colloids or crystalloids
    - Fluid challenge in patients with suspected hypovolemia
7. Vasopressor therapy (norepinephrine, dopamine, vasopressin, epinephrine)
8. Inotropic therapy (dobutamine infusion)
9. Corticosteroids (hydrocortisone)
10. Blood product administration (red blood cells, erythropoietin*, fresh frozen plasma*, antithrombin*, platelets, immunoglobulins [intravenous]*)
11. Mechanical ventilation of sepsis-induced acute lung injury/acute respiratory distress syndrome (ALI/ARDS)
12. Sedation, analgesia, and neuromuscular blockade
13. Glucose control (intravenous [IV] insulin, blood glucose monitoring)
14. Renal replacement
15. Bicarbonate therapy*
16. Deep vein thrombosis prophylaxis (low-dose unfractionated heparin [UFH], low-molecular weight heparin [LMWH], mechanical prophylactic devices)
17. Stress ulcer prophylaxis (H_2 blockers, proton pump inhibitors [PPIs])
18. Nutrition (oral feeding, enteral feeding, IV glucose)
19. Selenium*
20. Setting goals of care
21. Considerations for pediatric patients

*Guideline developers considered but did not recommend these interventions.

Major Outcomes Considered

- Survival of patients with severe sepsis and septic shock
- Length of stay in intensive care unit (ICU)
- Sepsis-related mortality and morbidity

- Other outcomes such as renal function, blood glucose, arrhythmias

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Search Techniques

A separate literature search was performed for each clearly defined question. The committee chairs worked with subgroup heads to identify pertinent search terms that were to include, at a minimum, sepsis, severe sepsis, septic shock, and sepsis syndrome crossed against the subgroup's general topic area, as well as appropriate key words of the specific question posed. All questions used in the previous guidelines publications were searched, as were pertinent new questions generated by general topic-related searches or recent trials. The authors were specifically asked to look for existing meta-analyses related to their question and search a minimum of one general database (i.e., MEDLINE, EMBASE) and the Cochrane Library (both The Cochrane Database of Systematic Reviews [CDSR] and Database of Abstracts of Reviews of Effectiveness [DARE]). Other databases were optional (ACP Journal Club, Evidence- Based Medicine Journal, Cochrane Registry of Controlled Clinical Trials, International Standard Randomized Controlled Trial Registry [http://www.controlled-trials.com/isrctn/] or metaRegister of Controlled Trials [http://www.controlledtrials.com/mrct/]). Where appropriate, available evidence was summarized in the form of evidence tables.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Determination of the Quality of Evidence

Grade A (high): Randomized Control Trials (RCTs)

Grade B (moderate): Downgraded RCTs or upgraded observational studies

Grade C (low): Well-done observational studies with control RCTs

Grade D (very low): Downgraded controlled studies or expert opinion based on other evidence

Factors that may decrease the strength of the evidence:

1. Poor quality of planning and implementation of available RCTs suggesting high likelihood of bias
2. Inconsistency of results (including problems with subgroup analyses)
3. Indirectness of evidence (differing population, intervention, control, outcomes, comparison)
4. Imprecision of results

5. High likelihood of reporting bias

Main factors that may increase the strength of evidence

1. Large magnitude of effect (direct evidence, relative risk [RR]>2 with no plausible confounders)
2. Very large magnitude of effect with RR>5 and no threats to validity (by two levels)
3. Dose response gradient

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Authors were advised to follow the principles of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system to guide assessment of quality of evidence from high (A) to very low (D) and to determine the strength of recommendations. The Surviving Sepsis Campaign (SSC) Steering Committee and individual authors collaborated with GRADE representatives to apply the system during the SSC guidelines revision process. The members of the GRADE group were directly involved, either in person or via e-mail, in all discussions and deliberations among the guidelines committee members as to grading decisions.

The GRADE system is based on a sequential assessment of the quality of evidence, followed by assessment of the balance between the benefits and risks, burden, and cost, leading to development and grading of a management recommendation. Keeping the rating of quality of evidence and strength of recommendation explicitly separate constitutes a crucial and defining feature of the GRADE approach. This system classifies quality of evidence as high (grade A), moderate (grade B), low (grade C), or very low (grade D). Randomized trials begin as high-quality evidence but may be downgraded due to limitations in implementation, inconsistency, or imprecision of the results, indirectness of the evidence, and possible reporting bias. Examples of indirectness of the evidence include population studied, interventions used, outcomes measured, and how these relate to the question of interest. Well-done observational (nonrandomized) studies begin as low-quality evidence, but the quality level may be upgraded on the basis of a large magnitude of effect. An example of this is the quality of evidence for early administration of antibiotics. References to supplemental digital content appendices of GRADEpro Summary of Evidence Tables appear throughout the original guideline document (also see the "Availability of Companion Documents" field).

Methods Used to Formulate the Recommendations

Expert Consensus (Consensus Development Conference)

Expert Consensus (Nominal Group Technique)

Description of Methods Used to Formulate the Recommendations

The selection of committee members was based on interest and expertise in specific aspects of sepsis. Co-chairs and executive committee members were appointed by the Society of Critical Care Medicine and European Society of Intensive Care Medicine governing bodies. Each sponsoring organization appointed a representative who had sepsis expertise. Additional committee members were appointed by the co-chairs and executive committee to create continuity with the previous committees' membership as well as to address content needs for the development process. Four clinicians with experience in the Grading of Recommendations Assessment, Development and Evaluation (GRADE) process application (referred to in this document as GRADE group or Evidence-Based Medicine [EBM] group) took part in the guidelines development.

The guidelines development process began with appointment of group heads and assignment of committee members to groups according to their specific expertise. Each group was responsible for drafting the initial update to the 2008 edition in their assigned area (with major additional elements of information incorporated into the evolving manuscript through year-end 2011 and early 2012).

With input from the EBM group, an initial group meeting was held to establish procedures for literature review and development of tables for evidence analysis. Committees and their subgroups continued work via phone and the Internet. Several subsequent meetings of subgroups and key

individuals occurred at major international meetings (nominal groups), with work continuing via teleconferences and electronic- based discussions among subgroups and members of the entire committee. Ultimately, a meeting of all group heads, executive committee members, and other key committee members was held to finalize the draft document for submission to reviewers.

Significant education of committee members on the GRADE approach built on the process conducted during 2008 efforts. Several members of the committee were trained in the use of GRADEpro software, allowing more formal use of the GRADE system. Rules were distributed concerning assessing the body of evidence, and GRADE representatives were available for advice throughout the process. Subgroups agreed electronically on draft proposals that were then presented for general discussion among subgroup heads, the Surviving Sepsis Campaign (SSC) Steering Committee (two co-chairs, two co-vice chairs, and an at-large committee member), and several selected key committee members who met in July 2011 in Chicago. The results of that discussion were incorporated into the next version of recommendations and again discussed with the whole group using electronic mail.

Throughout the document are a number of statements that either follow graded recommendations or are listed as stand-alone numbered statements followed by "ungraded" in parentheses (UG). In the opinion of the committee, these recommendations were not conducive for the GRADE process.

The GRADE system classifies recommendations as strong (grade 1) or weak (grade 2). The factors influencing this determination are presented in Table 4 in the original guideline document. The assignment of strong or weak is considered of greater clinical importance than a difference in letter level of quality of evidence. The committee assessed whether the desirable effects of adherence would outweigh the undesirable effects, and the strength of a recommendation reflects the group's degree of confidence in that assessment. Strong recommendations are listed as "recommendations" and weak recommendations as "suggestions."

Draft recommendations were distributed to the entire committee and finalized during an additional nominal group meeting in Berlin in October 2011. Deliberations and decisions were then recirculated to the entire committee for approval. At the discretion of the chairs and following discussion, competing proposals for wording of recommendations or assigning strength of evidence were resolved by formal voting within subgroups and at nominal group meetings.

Rating Scheme for the Strength of the Recommendations

Strength of the Recommendations

Grade 1 (Strong): A recommendation in favor of an intervention reflects that the desirable effects of adherence to a recommendation (beneficial health outcomes, less burden on staff and patients, and costs savings) will clearly outweigh the undesirable effects (harms, more burden and greater costs).

Grade 2 (Weak): A recommendation in favor of an intervention indicates that the desirable effects of adherence to a recommendation probably will outweigh the undesirable effects, but the panel is not confident about these tradeoffs-either because some of the evidence is low-quality (and thus there remains uncertainty regarding the benefits and risks) or the benefits and downsides are closely balanced.

UG: Ungraded

Cost Analysis

The guideline developer reviewed published cost analyses.

Method of Guideline Validation

Peer Review

Description of Method of Guideline Validation

The manuscript was edited for style and form by the writing committee with final approval by subgroup heads and then by the entire committee. To satisfy peer review during the final stages of manuscript approval for publication, several recommendations were edited with approval of the Surviving Sepsis Campaign (SSC) executive committee group head for that recommendation and the Evidence-Based Medicine (EBM) lead.

Evidence Supporting the Recommendations

References Supporting the Recommendations

Brunkhorst FM, Engel C, Bloos F, Meier-Hellmann A, Ragaller M, Weiler N, Moerer O, Gruendling M, Oppert M, Grond S, Olthoff D, Jaschinski U, John S, Rossaint R, Welte T, Schaefer M, Kern P, Kuhnt E, Kiehntopf M, Hartog C, Natanson C, Loeffler M, Reinhart K, German Competence Network Sepsis (SepNet). Intensive insulin therapy and pentastarch resuscitation in severe sepsis. N Engl J Med. 2008 Jan 10;358(2):125-39. PubMed

Guidet B, Martinet O, Boulain T, Philippart F, Poussel JF, Maizel J, Forceville X, Feissel M, Hasselmann M, Heininger A, Van Aken H. Assessment of hemodynamic efficacy and safety of 6% hydroxyethylstarch 130/0.4 vs. 0.9% NaCl fluid replacement in patients with severe sepsis: The CRYSTMAS study. Crit Care. 2012 May 24;16(3):R94. PubMed

Myburgh JA, Finfer S, Bellomo R, Billot L, Cass A, Gattas D, Glass P, Lipman J, Liu B, McArthur C, McGuinness S, Rajbhandari D, Taylor CB, Webb SA, CHEST Investigators, Australian and New Zealand Intensive Care Society Clinical Trials Group. Hydroxyethyl starch or saline for fluid resuscitation in intensive care. N Engl J Med. 2012 Nov 15;367(20):1901-11. PubMed

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Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the Major Recommendations field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate management of patients with severe sepsis and septic shock

Potential Harms

- Heparin increases the risk of bleeding. Patients receiving heparin should be monitored for development of heparin-induced thrombocytopenia.
- The use of low-dose hydrocortisone in septic shock patients may increase hyperglycemia and hypernatremia.
- Drugs used for sedation have important side effects in pediatric patients and put them at greater risk of toxicity and adverse events.
- Source control interventions may cause further complications such as bleeding, fistulas, or inadvertent organ injury.

Contraindications

Contraindications

- Hypercapnia is contraindicated in patients with high intracranial pressure.
- Thrombocytopenia, severe coagulopathy, active bleeding, and recent intracerebral hemorrhage are contraindications to the use of heparin.

Qualifying Statements

Qualifying Statements

The recommendations in this document are intended to provide guidance for the clinician caring for a patient with severe sepsis or septic shock. Recommendations from these guidelines cannot replace the clinician's decision-making capability when he or she is presented with a patient's unique set of clinical variables. Most of these recommendations are appropriate for the severe sepsis patient in the intensive care unit (ICU) and non-ICU settings. In fact, the committee believes that the greatest outcome improvement can be made through education and process change for those caring for severe sepsis patients in the non-ICU setting and across the spectrum of acute care. Resource limitations in some institutions and countries may prevent physicians from accomplishing particular recommendations. Thus, these recommendations are intended to be best practice (the committee considers this a goal for clinical practice) and not created to represent standard of care. The Surviving Sepsis Campaign (SSC) Guidelines Committee hopes that over time, particularly through education programs and formal audit and feedback performance improvement initiatives, the guidelines will influence bedside healthcare practitioner behavior that will reduce the burden of sepsis worldwide.

Implementation of the Guideline

Description of Implementation Strategy

The Surviving Sepsis Campaign (SSC) partnered with the Institute for Healthcare Improvement (IHI) to incorporate its "bundle concept" into the diagnosis and treatment of patients with severe sepsis and septic shock. Those involved with the SSC believe that improvement in the delivery of care should be measured one patient at a time through a series of incremental steps that will eventually lead to systemic change within institutions and larger health care systems. Information about the LEADER implementation strategy can be found at the Surviving Sepsis Campaign Web site .

Implementation Tools

Chart Documentation/Checklists/Forms

Clinical Algorithm

Pocket Guide/Reference Cards

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

IOM Domain

Effectiveness

Timeliness

Identifying Information and Availability

Bibliographic Source(s)

Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, Sevransky JE, Sprung CL, Douglas IS, Jaeschke R, Osborn TM, Nunnally ME, Townsend SR, Reinhart K, Kleinpell RM, Angus DC, Deutschman CS, Machado FR, Rubenfeld GD, Webb SA, Beale RJ, Vincent JL, Moreno R, Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med. 2013 Feb;41(2):580-637. [636 references] PubMed

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2004 (revised 2013 Feb)

Guideline Developer(s)

European Society of Intensive Care Medicine - Professional Association

Society of Critical Care Medicine - Professional Association

Source(s) of Funding

The "Surviving Sepsis Campaign Guidelines for Management of Severe Sepsis and Septic Shock" guideline revision process was funded through a grant from the Gordon and Betty Irene Moore Foundation.

Guideline Committee

Surviving Sepsis Campaign (SSC) Guidelines Committee

Composition of Group That Authored the Guideline

Authors: R. Phillip Dellinger, MD; Mitchell M. Levy, MD; Andrew Rhodes, MB BS; Djillali Annane, MD; Herwig Gerlach, MD, PhD; Steven M. Opal, MD; Jonathan E. Sevransky, MD; Charles L. Sprung, MD; Ivor S. Douglas, MD; Roman Jaeschke, MD; Tiffany M. Osborn, MD, MPH; Mark E. Nunnally, MD; Sean R. Townsend, MD; Konrad Reinhart, MD; Ruth M. Kleinpell, PhD, RN-CS; Derek C. Angus, MD, MPH; Clifford S. Deutschman, MD, MS; Flavia R. Machado, MD, PhD; Gordon D. Rubenfeld, MD; Steven A. Webb, MB BS, PhD; Richard J. Beale, MB BS; Jean-Louis Vincent, MD, PhD; Rui Moreno, MD, PhD; and the Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup*

*See Appendix A in the original guideline document for members of the 2012 Surviving Sepsis Campaign (SSC) Guidelines Committee and Pediatric Subgroup.

Financial Disclosures/Conflicts of Interest

A formal conflict of interest policy was developed at the onset of the process and enforced throughout. The entire guidelines process was conducted independent of any industry funding.

Conflict of Interest (COI) Policy

Since the inception of the Surviving Sepsis Campaign (SSC) guidelines in 2004, no members of the committee represented industry; there was no industry input into guidelines development; and no industry representatives were present at any of the meetings. Industry awareness or comment on the recommendations was not allowed. No member of the guidelines committee received honoraria for any role in the 2004, 2008, or 2012 guidelines process.

A detailed description of the disclosure process and all author disclosures appear in Supplemental Digital Content 1 in the supplemental materials to this document. Appendix B of the original guideline document shows a flowchart of the COI disclosure process. Committee members who were judged to have either financial or nonfinancial/academic competing interests were recused during the closed discussion session and voting session on that topic. Full disclosure and transparency of all committee members' potential conflicts were sought.

On initial review, 68 financial COI disclosures and 54 nonfinancial disclosures were submitted by committee members. Declared COI disclosures from 19 members were determined by the COI subcommittee to be not relevant to the guidelines content process. Nine who were determined to have COI (financial and nonfinancial) were adjudicated by group reassignment and requirement to adhere to SSC COI policy regarding discussion or voting at any committee meetings where content germane to their COI was discussed. Nine were judged as having conflicts that could not be resolved solely by reassignment. One of these individuals was asked to step down from the committee. The other eight were assigned to the groups in which they had the least COI. They were required to work within their group with full disclosure when a topic for which they had relevant COI was discussed, and they were not allowed to serve as group head. At the time of final approval of the document, an update of the COI statement was required. No additional COI issues were reported that required further adjudication.

Guideline Endorser(s)

German Sepsis Society - Disease Specific Society

Latin American Sepsis Institute - Disease Specific Society

Guideline Status

This is the current release of the guideline.

This guideline updates a previous version: Dellinger RP, Levy MM, Carlet JM, Bion J, Parker MM, Jaeschke R, Reinhart K, Angus DC, Brun-Buisson C, Beale R, Calandra T, Dhainaut JF, Gerlach H, Harvey M, Marini JJ, Marshall J, Ranieri M, Ramsay G, Sevransky J, Thompson BT, Townsend S, Vender JS, Zimmerman JL, Vincent JL. Surviving Sepsis Campaign: International guidelines for management of severe sepsis and septic shock: 2008. Intensive Care Med 2008 Jan;34(1):17-60. [341 references]

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the Society of Critical Care Medicine (SCCM) Web site .

Print copies: Available from the Society of Critical Care Medicine, 500 Midway Drive, Mount Prospect, IL 60056; Phone: (847) 827-6869; Fax: (847) 827-6886; on-line through the SCCM Bookstore .

Availability of Companion Documents

The following is available:

- Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. Supplemental digital content. Available in Portable Document Format (PDF) from the Society of Critical Care Medicine (SCCM) Web site .

Additional information and tools, including sample screening tools and a pocket card, are available from the Surviving Sepsis Campaign Web site .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI on June 22, 2004. The information was verified by the guideline developer on August 9, 2004. This summary was updated by ECRI on November 14, 2006, following the U.S. Food and Drug Administration (FDA) advisory on Xigris. This summary was updated by ECRI on January 29, 2007, following the U.S. Food and Drug Administration advisory on erythropoiesis stimulating agents. This summary was updated by ECRI Institute on June 22, 2007 following the U.S. Food and Drug Administration (FDA) advisory on heparin sodium injection. This summary was updated by ECRI Institute on July 9, 2007, following the FDA advisory on erythropoiesis stimulating agents. This summary was updated by ECRI Institute on February 26, 2008 following the U.S. Food and Drug Administration advisory/voluntary market withdrawal of the liquid formulation of Leukine (sargramostim). This summary was updated by ECRI Institute on March 13, 2008 following the updated FDA advisory on heparin sodium injection. This summary was updated by ECRI Institute on March 21, 2008 following the FDA advisory on Erythropoiesis Stimulating Agents. This summary was updated by ECRI Institute on August 15, 2008 following the U.S. Food and Drug Administration advisory on Erythropoiesis Stimulating Agents (ESAs). This NGC summary was updated by ECRI Institute on June 11, 2008. The updated information was verified by the guideline developer on August 15, 2008. This summary was updated by ECRI Institute on December 26, 2008 following the FDA advisory on Innohep (tinzaparin). This summary was updated by ECRI Institute on April 1, 2010 following the U.S. Food and Drug Administration advisory on Erythropoiesis-Stimulating Agents (ESAs). This summary was updated by ECRI Institute on July 26, 2010 following the U.S. Food and Drug Administration (FDA) advisory on Proton Pump Inhibitors (PPI). This summary was updated by ECRI Institute on July 27, 2010 following the FDA drug safety communication on Heparin. This NGC summary was updated by ECRI Institute on May 14, 2013. The updated information was verified by the guideline developer on June 17, 2013. This summary was updated by ECRI Institute on October 25, 2013 following the U.S. Food and Drug Administration advisory on Fluoroquinolone Antibacterial Drugs. This summary was updated by ECRI Institute on March 10, 2014 following the U.S. Food and Drug Administration advisory on Low Molecular Weight Heparins.

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