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Brief Summary

GUIDELINE TITLE

Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2008.

BIBLIOGRAPHIC SOURCE(S)

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] PubMed

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Dellinger RP, Carlet JM, Masur H, Gerlach H, Calandra T, Cohen J, Gea-Banacloche J, Keh D, Marshall JC, Parker MM, Ramsay G, Zimmerman JL, Vincent JL, Levy MM. Surviving sepsis campaign guidelines for management of severe sepsis and septic shock. Crit Care Med 2004 Mar;32(3):858-73.

** 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.

- December 3, 2008, Innohep (tinzaparin): The U.S. Food and Drug Administration (FDA) has requested that the labeling for Innohep be revised to better describe overall study results which suggest that, when compared to unfractionated heparin, Innohep increases the risk of death for elderly patients (i.e., 70 years of age and older) with renal insufficiency. Healthcare professionals should consider the use of alternative treatments to Innohep when treating elderly patients over 70 years of age with renal insufficiency and deep vein thrombosis (DVT), pulmonary embolism (PE), or both.
- July 31, 2008, Erythropoiesis Stimulating Agents (ESAs): Amgen and the U.S. Food and Drug Administration (FDA) informed healthcare professionals of modifications to certain sections of the Boxed Warnings, Indications and Usage, and Dosage and Administration sections of prescribing information for Erythropoiesis Stimulating Agents (ESAs). The changes clarify the FDA-approved conditions for use of ESAs in patients with cancer and revise directions for dosing to state the hemoglobin level at which treatment with an ESA should be initiated.
- February 28, 2008, Heparin Sodium Injection: The U.S. Food and Drug Administration (FDA) informed the public that Baxter Healthcare Corporation has voluntarily recalled all of their multi-dose and single-use vials of heparin sodium for injection and their heparin lock flush solutions. Alternate heparin manufacturers are expected to be able to increase heparin production sufficiently to supply the U.S. market. There have been reports of serious adverse events including allergic or hypersensitivity-type reactions, with symptoms of oral swelling, nausea, vomiting, sweating, shortness of breath, and cases of severe hypotension.
- November 8, 2007 and January 3, 2008 Update, Erythropoiesis Stimulating Agents (ESAs): The U.S. Food and Drug Administration (FDA) notified healthcare professionals of revised boxed warnings and other safety-related product labeling changes for erythropoiesis-stimulating agents (ESAs) stating serious adverse events, such as tumor growth and shortened survival in patients with advanced cancer and chronic kidney failure.

BRIEF SUMMARY CONTENT

Go to the Complete Summary

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

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

Management of Severe Sepsis

A. Initial Resuscitation

1. The guideline committee recommends the protocolized resuscitation of a patient with **sepsis**-induced shock, defined as tissue hypoperfusion (hypotension persisting after initial fluid challenge or blood lactate concentration equal to or greater than 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 hours of resuscitation, the goals of initial resuscitation of **sepsis**-induced hypoperfusion should include all of the following as one part of a treatment protocol:

    - Central venous pressure (CVP): 8–12 mm Hg
    - Mean arterial pressure (MAP) ≥65 mm Hg
    - Urine output ≥0.5 mL/kg/hour
    - Central venous (superior vena cava) or mixed venous oxygen saturation ≥70% or ≥65%, respectively

    (Grade 1C)

2. The guideline committee suggests that during the first 6 hours of resuscitation of severe **sepsis** or septic shock, if central venous oxygen saturation ($S_{CV}O_2$) or mixed venous saturation (SvO_2) of 70% or 65% respectively is not achieved with fluid resuscitation to the CVP target, then transfusion of packed red blood cells to achieve a hematocrit of ≥30% and/or administration of a dobutamine infusion (up to a maximum of 20 micrograms/kg/min) be utilized to achieve this goal. **(Grade 2C)**

B. Diagnosis

1. The guideline committee recommends obtaining appropriate cultures before antimicrobial therapy is initiated if such cultures do not cause significant delay in antibiotic administration. To optimize identification of causative organisms, the committee recommends at least two blood cultures be obtained prior to antibiotics with at least one drawn percutaneously and one drawn through each vascular access device, unless the device was recently (less than 48 hours) inserted. 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 antibiotic therapy if not associated with significant delay in antibiotic administration. **(Grade 1C)**
2. The guideline committee recommends that imaging studies be performed promptly in attempts to confirm a potential source of infection. Sampling of potential sources of infection should occur as they are identified; however, some patients may be too unstable to warrant certain invasive procedures or transport outside of the ICU. Bedside studies, such as ultrasound, are useful in these circumstances. **(Grade 1C)**

C. Antibiotic Therapy

1. The guideline committee recommends that intravenous antibiotic therapy be started as early as possible and within the first hour of recognition of septic shock **(Grade 1B)** and severe **sepsis** without septic shock **(Grade 1D)**. Appropriate cultures should be obtained before initiating antibiotic therapy, but should not prevent prompt administration of antimicrobial therapy. **(Grade 1D)**

2a. The guideline committee recommends that initial empirical anti-infective therapy include one or more drugs that have activity against all likely pathogens (bacterial and/or fungal) and that penetrate in adequate concentrations into the presumed source of **sepsis**. **(Grade 1B)**

2b. The guideline committee recommends that the antimicrobial regimen be reassessed daily to optimize activity, to prevent the development of resistance, to reduce toxicity, and to reduce costs. **(Grade 1C)**

2c. The guideline committee suggests combination therapy for patients with known or suspected *Pseudomonas* infections as a cause of severe **sepsis**. **(Grade 2D)**

2d. The guideline committee suggests combination empiric therapy for neutropenic patients with severe **sepsis**. **(Grade 2D)**

2e. When used empirically in patients with severe **sepsis**, the guideline committee suggests that combination therapy should not be administered for more than 3 to 5 days. De-escalation to the most appropriate single therapy should be performed as soon as the susceptibility profile is known. **(Grade 2D)**

3. The guideline committee recommends that the duration of therapy typically be 7 to 10 days; longer courses may

be appropriate in patients who have a slow clinical response, undrainable foci of infection, or who have immunologic deficiencies including neutropenia. **(Grade 1D)**

4. If the presenting clinical syndrome is determined to be due to a noninfectious cause, the guideline committee recommends antimicrobial therapy be stopped promptly to minimize the likelihood that the patient will become infected with an antibiotic resistant pathogen or will develop a drug related adverse effect. **(Grade 1D)**

Source Control

1a. The guideline committee recommends that a specific anatomic diagnosis of infection requiring consideration for emergent source control- for example necrotizing fasciitis, diffuse peritonitis, cholangitis, intestinal infarction – be sought and diagnosed or excluded as rapidly as possible **(Grade 1C)** and within the first 6 hours following presentation **(Grade 1D)**.

1b. The guideline committee further recommends that all patients presenting with severe **sepsis** be evaluated for the presence of a focus of infection amenable to source control measures, specifically the drainage of an abscess or local focus of infection, the debridement of infected necrotic tissue, the removal of a potentially infected device, or the definitive control of a source of ongoing microbial contamination **(Grade 1C)** (see Appendix A in the original guideline document for examples of potential sites needing source control).

2. The guideline 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 non-viable tissues has occurred. **(Grade 2B)**

3. The guideline committee recommends that when source control is required, the effective intervention associated with the least physiologic insult be employed, for example, percutaneous rather than surgical drainage of an abscess. **(Grade 1D)**

4. The guideline committee recommends that when intravascular access devices are a possible source of severe **sepsis** or septic shock, they be promptly removed after establishing other vascular access. **(Grade 1C)**

D. **Fluid Therapy**

1. The guideline committee recommends fluid resuscitation with either natural/artificial colloids or crystalloids. There is no evidence-based support for one type of fluid over another. **(Grade 1B)**

2. The guideline committee recommends fluid resuscitation initially target a CVP of at least 8 mm Hg (12 mm Hg in mechanically ventilated patients). Further fluid therapy is often required. **(Grade 1C)**

3a. The guideline committee recommends that a fluid challenge technique be applied, wherein fluid administration is continued as long as the hemodynamic improvement (for example, arterial pressure, heart rate, urine output) continues. **(Grade 1D)**

3b. The guideline committee recommends fluid challenge in patients with suspected hypovolemia be started with at least 1000 mL of crystalloids or 300 to 500 mL of colloids over 30 minutes. More rapid administration and greater amounts of fluid may be needed in patients with **sepsis** induced tissue hypoperfusion (see *initial resuscitation* recommendations). **(Grade 1D)**

3c. The guideline committee recommends the rate of fluid administration be reduced substantially when cardiac filling pressures (CVP or pulmonary artery balloon-occluded pressure) increase without concurrent hemodynamic improvement. **(Grade 1D)**

E. **Vasopressors**

1. The guideline committee recommends mean arterial pressure (MAP) be maintained ≥65 mm Hg. **(Grade 1C)**

The guideline committee recommends either norepinephrine or dopamine as the first choice vasopressor agent to correct hypotension in septic shock (administered through a central catheter as soon as one is available). **(Grade 1C)**

3a. The guideline committee suggests that epinephrine, phenylephrine, or vasopressin should not be administered as the initial vasopressor in septic shock. **(Grade 2C)** Vasopressin .03 units/min may be subsequently added to norepinephrine with anticipation of an effect equivalent to norepinephrine alone.

3b. The guideline committee suggests that epinephrine be the first chosen alternative agent in septic shock that is poorly responsive to norepinephrine or dopamine. **(Grade 2B)**

5. The guideline committee recommends that low dose dopamine not be used for renal protection. **(Grade 1A)**

6. The guideline committee recommends that all patients requiring vasopressors have an arterial line placed as soon as practical if resources are available. **(Grade 1D)**

F. **Inotropic Therapy**

1. The guideline committee recommends a dobutamine infusion be administered in the presence of myocardial dysfunction as suggested by elevated cardiac filling pressures and low cardiac output. **(Grade 1C)**
2. The guideline committee recommends against the use of a strategy to increase cardiac index to predetermined supranormal levels. **(Grade 1B)**

G. **Corticosteroids**

1. The guideline committee suggests intravenous hydrocortisone be given *only* to adult septic shock patients after blood pressure is identified to be poorly responsive to fluid resuscitation and vasopressor therapy. **(Grade 2C)**
2. The guideline committee suggests the adrenocorticotropic hormone (ACTH) stimulation test *not* be used to identify the subset of adults with septic shock who should receive hydrocortisone. **(Grade 2B)**
3. The guideline committee suggests that patients with septic shock should *not* receive dexamethasone if hydrocortisone is available. **(Grade 2B)**
4. The guideline committee suggests the daily addition of oral fludrocortisone (50 micrograms) if hydrocortisone is not available and the steroid that is substituted has no significant mineralocorticoid activity. Fludrocortisone is considered optional if hydrocortisone is used. **(Grade 2C)**
5. The guideline committee suggests clinicians wean the patient from steroid therapy when vasopressors are no longer required. **(Grade 2D)**
6. The guideline committee recommends doses of corticosteroids comparable to >300 mg hydrocortisone daily *not* be used in severe **sepsis** or septic shock for the purpose of treating septic shock. **(Grade 1A)**
7. The guideline committee recommends corticosteroids *not* be administered for the treatment of **sepsis** in the absence of shock. There is, however, no contraindication to continuing maintenance steroid therapy or to using stress-dose steroids if the patient's endocrine or corticosteroid administration history warrants. **(Grade 1D)**

H. **Recombinant Human Activated Protein C (rhAPC)**

1. The guideline committee suggests that adult patients with **sepsis** induced organ dysfunction associated with a clinical assessment of high risk of death, most of whom will have Acute Physiology and Chronic Health Evaluation II (APACHE II) $\geq$25 or multiple organ failure, receive recombinant human activated protein C (rhAPC) if there are no contraindications **(Grade 2B except for patients within 30 days of surgery where it is Grade 2C)**. Relative contraindications should also be considered in decision making.
2. The guideline committee recommends that adult patients with severe **sepsis** and low risk of death, most of whom will have APACHE II <20 or one organ failure, *do not* receive rhAPC. **(Grade 1A)**

I. **Blood Product Administration**

1. Once tissue hypoperfusion has resolved and in the absence of extenuating circumstances, such as myocardial ischemia, severe hypoxemia, acute hemorrhage, cyanotic heart disease, or lactic acidosis (see recommendations for initial resuscitation), the guideline committee recommends that red blood cell transfusion occur when hemoglobin decreases to <7.0 g/dL (<70 g/L) to target a hemoglobin of 7.0 to 9.0 g/dL (70 to 90 g/L) in adults. **(Grade 1B)**
2. The guideline committee recommends that erythropoietin *not* be used as a specific treatment of anemia associated with severe **sepsis**, but may be used when septic patients have other accepted reasons for administration of erythropoietin such as renal failure-induced compromise of red blood cell production. **(Grade 1B)**
3. The guideline 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 guideline committee recommends *against* antithrombin administration for the treatment of severe **sepsis** and septic shock. **(Grade 1B)**
5. In patients with severe **sepsis**, the guideline committee suggests that platelets should be administered when counts are <5000/mm^3 (5 × 10^9/L) regardless of apparent bleeding. Platelet transfusion may be considered when counts are 5,000 to 30,000/mm^3 (5 to 30 × 10^9/L) and there is a significant risk of bleeding. Higher platelet counts ($\geq$50,000/mm^3 (50 × 10^9/L) are typically required for surgery or invasive procedures. **(Grade 2D)**

Supportive Therapy of Severe Sepsis

A. **Mechanical Ventilation of Sepsis-Induced Acute Lung Injury (ALI)/Acute Respiratory Distress Syndrome (ARDS)**

1. The guideline committee recommends that clinicians target a tidal volume of 6 mL/kg (predicted) body weight in patients with acute lung injury/acute respiratory distress syndrome (ALI/ARDS). **(Grade 1B)**

2. The guideline committee recommends that plateau pressures be measured in patients with ALI/ARDS and that the initial upper limit goal for plateau pressures in a passively inflated patient be ≤30 cm H_2O. Chest wall compliance should be considered in the assessment of plateau pressure. **(Grade 1C)**

3. The guideline committee recommends that hypercapnia (allowing partial pressure of arterial carbon dioxide [$PaCO_2$] to increase above its pre-morbid baseline, so-called permissive hypercapnia) be allowed in patients with ALI/ARDS if needed to minimize plateau pressures and tidal volumes. **(Grade 1C)**

4. The guideline committee recommends that positive end-expiratory pressure (PEEP) be set so as to avoid extensive lung collapse at end-expiration. **(Grade 1C)**

5. The guideline committee suggests prone positioning in ARDS patients requiring potentially injurious levels of fraction of inspired oxygen (F_IO_2) or plateau pressure who are not at high risk for adverse consequences of positional changes in those facilities who have experience with such practices. **(Grade 2C)**

6a. Unless contraindicated, the guideline committee recommends mechanically ventilated patients be maintained with the head of the bed elevated to limit aspiration risk and to prevent the development of ventilator-associated pneumonia. **(Grade 1B)**

6b. The guideline committee *suggests* that the head of bed is elevated approximately 30 to 45 degrees. **(Grade 2C)**

7. The guideline committee suggests that noninvasive mask ventilation (NIV) only be considered in that minority of ALI/ARDS patients with mild-moderate hypoxemic respiratory failure (responsive to relatively low levels of pressure support and PEEP) with stable hemodynamics who can be made comfortable and easily arousable, who are able to protect the airway, spontaneously clear the airway of secretions, and are anticipated to recover rapidly from the precipitating insult. A low threshold for airway intubation should be maintained. **(Grade 2B)**

8. The guideline committee recommends that a weaning protocol be in place, and mechanically ventilated patients with severe **sepsis** undergo spontaneous breathing trials on a regular basis 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) F_IO_2 requirements that could be safely delivered with a face mask or nasal cannula. If the spontaneous breathing trial is successful, consideration should be given for extubation (see Appendix E in the original guideline document). Spontaneous breathing trial options include a low level of pressure support, continuous positive airway pressure (approximately 5 cm H_2O) or a T-piece. **(Grade 1A)**

9. The guideline committee recommends *against* the routine use of the pulmonary artery catheter for patients with ALI/ARDS. **(Grade 1A)**

10. To decrease days of mechanical ventilation and ICU length of stay the guideline committee recommends a conservative fluid strategy for patients with established acute lung injury who do not have evidence of tissue hypoperfusion. **(Grade 1C)**

B. **Sedation, Analgesia, and Neuromuscular Blockade in Sepsis**

1. The guideline committee recommends sedation protocols with a sedation goal when sedation of critically ill mechanically ventilated patients with **sepsis** is required. **(Grade 1B)**
2. The guideline committee recommends intermittent bolus sedation or continuous infusion sedation to predetermined end points (e.g., sedation scales) with daily interruption/lightening of continuous infusion sedation with awakening and retitration if necessary for sedation administration to septic mechanically ventilated patients. **(Grade 1B)**
3. The guideline committee recommends that neuromuscular blocking agents (NMBAs) be avoided if possible in the septic patient due to the risk of prolonged neuromuscular blockade following discontinuation. If NMBAs must be maintained, either intermittent bolus as required or continuous infusion with monitoring the depth of blockade with train-of-four monitoring should be used. **(Grade 1B)**

C. **Glucose Control**

1. The guideline committee recommends that, following initial stabilization, patients with severe **sepsis** and hyperglycemia who are admitted to the ICU receive intravenous (IV) insulin therapy to reduce blood glucose levels. **(Grade 1B)**
2. The guideline committee suggests use of a validated protocol for insulin dose adjustments and targeting glucose levels to the <150 mg/dL range. **(Grade 2C)**
3. The guideline committee recommends that all patients receiving intravenous insulin receive a glucose calorie source and that blood glucose values be monitored every 1 to 2 hours until glucose values and insulin infusion rates are stable and then every 4 hours thereafter. **(Grade 1C)**
4. The guideline committee recommends that low glucose levels obtained with point-of-care testing of capillary blood be interpreted with caution, as such measurements may overestimate arterial blood or

plasma glucose values. **(Grade 1B)**

D. **Renal Replacement**

1. The guideline committee suggests that continuous renal replacement therapies and intermittent hemodialysis are equivalent in patients with severe **sepsis** and acute renal failure. **(Grade 2B)**
2. The guideline committee suggests the use of continuous therapies to facilitate management of fluid balance in hemodynamically unstable septic patients. **(Grade 2D)**

E. **Bicarbonate Therapy**

1. The guideline committee recommends *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 1B)**

F. **Deep Vein Thrombosis Prophylaxis**

1. The guideline committee recommends that severe **sepsis** patients receive deep vein thrombosis (DVT) prophylaxis with either (a) low-dose unfractionated heparin (UFH) administered twice daily or three times daily or (b) daily low-molecular weight heparin (LMWH) unless there are contraindications (i.e., thrombocytopenia, severe coagulopathy, active bleeding, recent intracerebral hemorrhage). **(Grade 1A)**
2. The guideline committee recommends that septic patients who have a contraindication for heparin use receive mechanical prophylactic device such as graduated compression stockings (GCS) or intermittent compression devices (ICD) unless contraindicated. **(Grade 1A)**
3. The guideline committee suggests that in very high-risk patients such as those who have severe **sepsis** and history of DVT, trauma, or orthopedic surgery, a combination of pharmacologic and mechanical therapy be used unless contraindicated or not practical. **(Grade 2C)**
4. The guideline committee suggests that in patients at very high risk, LMWH be used rather than UFH as LMWH is proven superior in other high-risk patients. **(Grade 2C)**

G. **Stress Ulcer Prophylaxis (SUP)**

1. The guideline committee recommends that stress ulcer prophylaxis (SUP) using H_2 blocker **(Grade 1A)** or proton pump inhibitor **(Grade 1B)** be given to patients with severe **sepsis** to prevent upper gastrointestinal (GI) bleed. Benefit of prevention of upper GI bleed must be weighed against potential effect of an increased stomach pH on development of ventilator-associated pneumonia.

H. **Selective Digestive Tract Decontamination (SDD)**

1. The guideline committee was evenly split on the issue of selective digestive tract decontamination (SDD), with equal numbers weakly in favor and against recommending the use of SDD (see Appendix H of the original guideline document). The committee therefore chose not to make a recommendation for the use of SDD specifically in severe **sepsis** at this time. The final consensus on use of SDD in severe **sepsis** was achieved at the last nominal committee meeting and subsequently approved by the entire committee.

I. **Consideration for Limitation of Support**

1. The guideline committee recommends that advance care planning, including the communication of likely outcomes and realistic goals of treatment, be discussed with patients and families. **(Grade 1D)**

Pediatric Considerations in Severe Sepsis

A. **Antibiotics**

1. The guideline committee recommends antibiotics be administered within one hour of the identification of severe **sepsis**, after appropriate cultures have been obtained. **(Grade 1D)**

B. **Mechanical Ventilation**

The guideline committee has no graded recommendations.

C. **Fluid Resuscitation**

1. The guideline committee suggests initial resuscitation begin with infusion of crystalloids with boluses of 20 mL/kg over 5 to 10 minutes, titrated to clinical monitors of cardiac output, including heart rate, urine output, capillary refill, and level of consciousness. **(Grade 2C)**

D. **Vasopressors/Inotropes (should be used in volume loaded patients with fluid refractory shock)**

1. The guideline committee suggests dopamine as the first choice of support for the pediatric patient with hypotension refractory to fluid resuscitation. **(Grade 2C)**
2. The guideline committee suggests that patients with low cardiac output and elevated systemic vascular

resistance states (cool extremities, prolonged capillary refill, decreased urine output but normal blood pressure following fluid resuscitation) be given dobutamine. **(Grade 2C)**

E. **Therapeutic End Points**

1. The guideline committee suggests that the therapeutic end points of resuscitation of septic shock be normalization of the heart rate, capillary refill of <2 seconds, normal pulses with no differential between peripheral and central pulses, warm extremities, urine output >1 mL/kg/hour, and normal mental status. **(Grade 2C)**

F. **Approach to Pediatric Septic Shock**

Figure 1 in the original guideline document shows a flow diagram summarizing an approach to pediatric septic shock.

G. **Steroids**

1. The guideline committee suggests that hydrocortisone therapy be reserved for use in children with catecholamine resistance and suspected or proven adrenal insufficiency. **(Grade 2C)**

H. **Protein C and Activated Protein C**

1. The guideline committee recommends *against* the use rhAPC in children. **(Grade 1B)**

I. **DVT Prophylaxis**

1. The guideline committee suggests the use of DVT prophylaxis in post-pubertal children with severe **sepsis**. **(Grade 2C)**

J. **Stress Ulcer Prophylaxis**

The guideline committee has no graded recommendations.

K. **Renal Replacement Therapy**

The guideline committee has no graded recommendations.

L. **Glycemic Control**

The guideline committee has no graded recommendations.

M. **Sedation/Analgesia**

1. The guideline committee recommends sedation protocols with a sedation goal when sedation of critically ill mechanically ventilated patients with **sepsis** is required. **(Grade 1D)**

N. **Blood Products**

The guideline committee has no graded recommendations.

O. **Intravenous Immunoglobulin**

1. The guideline committee suggests that immunoglobulin may be considered in children with severe **sepsis**. **(Grade 2C)**

P. **Extracorporeal Membrane Oxygenation (ECMO)**

1. The guideline committee suggests that use of extracorporeal membrane oxygenation (ECMO) be limited to refractory pediatric septic shock and/or respiratory failure that cannot be supported by conventional therapies. **(Grade 2C)**

Definitions:

Grades of Evidence

Grade A: Randomized controlled trial (RCT)

Grade B: Downgraded RCT or upgraded observational studies

Grade C: Well-done observational studies

Grade D: Case series or expert opinion

Levels of 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.

CLINICAL ALGORITHM(S)

An algorithm is provided in the original guideline for the "Approach to Pediatric Shock."

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EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

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

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IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

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] PubMed

ADAPTATION

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

DATE RELEASED

2004 (revised 2008 Jan)

GUIDELINE DEVELOPER(S)

Society of Critical Care Medicine - Professional Association

SOURCE(S) OF FUNDING

The Surviving **Sepsis** Campaign (SSC) is partially funded by unrestricted educational industry grants, including those from Edwards LifeSciences, Eli Lilly and Company, and Philips Medical Systems. SSC also received funding from the Coalition for Critical Care Excellence of the Society of Critical Care Medicine. The great majority of industry funding has come from Eli Lilly and Company.

Current industry funding for the Surviving **Sepsis** Campaign is directed to the performance improvement initiative. No industry funding was used for committee meetings. No honoraria were provided to committee members. The revision process was funded primarily by the Society of Critical Care Medicine, with the sponsoring professional organizations providing travel expenses for their designated delegate to the guidelines revision meeting where needed.

GUIDELINE COMMITTEE

2008 Surviving **Sepsis** Campaign (SSC) Guidelines Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Authors: R. Phillip Dellinger; Mitchell M. Levy; Jean M. Carlet; Julian Bion; Margaret M. Parker; Roman Jaeschke; Konrad Reinhart; Derek C. Angus; Christian Brun-Buisson; Richard Beale; Thierry Calandra; Jean-Francois Dhainaut; Herwig Gerlach; Maurene Harvey; John J. Marini; John Marshall; Marco Ranieri; Graham Ramsay; Jonathan Sevransky; B. Taylor Thompson; Sean Townsend; Jeffrey S. Vender; Janice L. Zimmerman; Jean-Louis Vincent

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FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

For both the 2004 and the 2006/2007 efforts there were no members of the committee from industry, no industry input into guidelines development, and no industry presence at any of the meetings. Industry awareness or comment on the recommendations was not allowed. No member of the guideline committee received any honoraria for any role in the 2004 or 2006/2007 guidelines process. The committee considered the issue of recusement of individual committee members during deliberation and decision making in areas where committee members had either financial or academic competing interests; however, consensus as to threshold for exclusion could not be reached. Alternatively, the committee agreed to ensure full disclosure and transparency of all committee members' potential conflicts at time of publication (see following):

Dr. Dellinger has consulted for AstraZeneca, Talecris, and B Braun. He has received honoraria from Eli Lilly (2), Brahms (2), INO Therapeutics (1), Pulsion (1), and bioMerieux (1). He has also received grant support from AstraZeneca and Artisan.

Dr. Levy has received honoraria from Eli Lilly and Edwards Lifesciences. He has also received grant support from Phillips Medical Systems, Edwards Lifesciences, Phillips Medical Systems, Novartis, Biosite, and Eisai.

Dr. Carlet has consulted for Forrest, Wyeth, Chiron, bioMerieux, and GlaxoSmithKline. He has also received honoraria from Eli Lilly, Becton Dickinson, Jansen, Cook, AstraZeneca, Hutchinson, Bayer, Gilead, MSD, and Targanta.

Dr. Bion has not disclosed any potential conflicts of interest.

Dr. Parker has consulted for Johnson & Johnson.

Dr. Jaeschke has received honoraria from AstraZeneca, Boehringer, Eli Lilly, GlaxoSmithKline, and MSD.

Dr. Reinhart has consulted for Eli Lilly and Edwards Lifesciences. He has also received honoraria from B Braun and royalties from Edwards Lifesciences.

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Dr. Calandra has consulted for Baxter, received honoraria from Roche Diagnostics, and grant support from Baxter and Roche Diagnostics. He also served on the advisory board for Biosite.

Dr. Dhainaut has consulted for Eli Lilly and Novartis. He has also received honoraria from Eli Lilly.

Dr. Gerlach has not disclosed any potential conflicts of interest.

Ms. Harvey has not disclosed any potential conflicts of interest.

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Dr. Vincent has consulted for AstraZeneca, Biosite, bioMerieux, Edwards Lifesciences, Eli Lilly Eisai, Ferring, GlaxoSmithKline, Intercell, Merck, Novartis, NovoNordisk, Organon, Pfizer, Phillips Medical Systems, Roche Diagnostics, Spectral Diagnostics, Takeda, and WyethLederle. He has also received honoraria from Eli Lilly, Edwards Lifesciences, Eisai, GlaxoSmithKline, Novartis, NovoNordisk, and Pfizer.

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, Carlet JM, Masur H, Gerlach H, Calandra T, Cohen J, Gea-Banacloche J, Keh D, Marshall JC, Parker MM, Ramsay G, Zimmerman JL, Vincent JL, Levy MM. Surviving **sepsis** campaign guidelines for management of severe **sepsis** and septic shock. Crit Care Med 2004 Mar;32(3):858-73.

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, 701 Lee Street, Suite 200, Des Plaines, IL 60016; Phone: (847) 827-6869; Fax: (847) 827-6886; on-line through the SCCM Bookstore.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Dorman T, Angood PB, Angus DC, Clemmer TP, Cohen NH, Durbin CG Jr, Falk JL, Helfaer MA, Haupt MT, Horst HM, Ivy ME, Ognibene FP, Sladen RN, Grenvik AN, Napolitano LM. Guidelines for critical care medicine training and continuing medical education. Crit Care Med 2004 Jan;32(1):263-72.

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The following are also available:

- Guidelines for the management of severe **sepsis** and septic shock. Pocket guide. 2008 Jan. Electronic copies: Available in Portable Document Format (PDF) from the Surviving **Sepsis** Campaign Web site.
- Guidelines for the management of severe **sepsis** and septic shock. Wall poster. 2008 Jan. Electronic copies: Available in Portable Document Format (PDF) from the Surviving **Sepsis** Campaign Web site.

Additional implementation tools, including quality indicators, measures, screening tools, a tool for Personal Digital Assistants (PDAs), and a chart review database, are available from the Surviving **Sepsis** Campaign Web site. Several of the tools are available in Chinese, as well as English.

PATIENT RESOURCES

The following is available:

- **Sepsis**: what you should know. Information about **sepsis** for individuals and families. Available from the Surviving **Sepsis** Campaign Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

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