

# GUIDELINES FOR MANAGEMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

Surviving This is a summary of the Surviving Sepsis Sepsis Campaign Guidelines for Management of Campaign Severe Sepsis and Septic Shock condensed from Dellinger RP, Carlet JM, Masur H, et al: Surviving Sepsis Campaign: Guidelines for management of severe sepsis and septic shock. Intensive Care Medicine (2004) 30: 536-555. This version does not contain the rationale or appendices contained in the primary publication. Please refer to the guidelines for additional information at www.survivingsepsis.org.

Green italics indicate one of the goals chosen for implementation in the Institute of Healthcare Improvements change package, i.e. part of the "sepsis bundles."

#### THESE GUIDELINES HAVE BEEN ENDORSED BY

American Association of Critical-Care Nurses
American College of Chest Physicians
American College of Emergency Physicians
American Thoracic Society
Australian and New Zealand Intensive Care Society
European Society of Clinical Microbiology and Infectious Diseases
European Society of Intensive Care Medicine
European Respiratory Society;
Infectious Disease Society of America
International Sepsis Forum
Society of Critical Care Medicine
Surgical Infection Society



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#### Initial resuscitation

in patients with hypotension or elevated serum lactate.

#### Resuscitation goals:

- ◆ Central venous pressure: 8-12 mm Hg
- **♦** Mean arterial pressure ≥ 65 mm Hq
- ♦ Urine output  $\geq$  0.5 mL.kg-1.hr-1
- **♦** Central venous or mixed venous oxygen saturation ≥ 70%

If central venous oxygen saturation or mixed venous oxygen saturation of 70% is not achieved with a central venous pressure of 8-12 mm Hg, then transfuse packed red blood cells to achieve a haematocrit of  $\geq$  30% and/or administer a dobutamine infusion of up to a maximum of 20 µg.kg-1.min-1.

#### Diagnosis

Before starting antibiotics obtain two or more blood cultures. At least one blood draw should be percutaneous and one should be through each vascular assist device that has been in place longer than 48 hours. Obtain cultures from other sites as indicated - cerebrospinal fluid, respiratory secretions, urine, wounds, and other body fluids.

#### Antibiotic therapy

Begin intravenous antibiotics within first hour of recognition of severe sepsis.

Administer one or more drugs that are active against likely bacterial or fungal pathogens. Consider microorganism susceptibility patterns in the community and hospital.

Reassess antimicrobial regimen 48–72 hours after starting treatment with the objective of using a narrow spectrum antibiotic.

Consider combination therapy for neutropenic patients and those with Pseudomonas infections.

Stop antimicrobial therapy immediately if the condition is determined to be a non-infectious cause.

#### Source control

Evaluate patient for a focus of infection amenable to source control measures including abscess drainage or tissue debridement.

Choose the source control measure that will cause the least physiologic upset and still accomplish the clinical goal.

Institute source control measures as soon as an infection focus in need of source control has been identified.

Remove intravascular access devices that are a potential infection source promptly after establishing other vascular access.

#### **Vasopressors**

Start vasopressor therapy when fluid challenge fails to restore adequate blood pressure and organ perfusion, or transiently until fluid resuscitation restores adequate perfusion.

Either norepinephrine or dopamine administered through a central catheter is the initial vasopressor of choice.

Do not use low-dose dopamine for renal protection.

In patients requiring vasopressors, place an arterial catheter as soon as practical.

Consider vasopressin in patients with refractory shock despite adequate fluid resuscitation and high-dose conventional vasopressors.

Vasopressin is not recommended as a replacement for norepinephrine or dopamine as a first-line agent. Administer vasopressin at infusion rates of 0.01–0.04 units/minute in adults.

#### Inotropic therapy

Consider dobutamine in patients with low cardiac output despite fluid resuscitation.
Continue to titrate vasopressor to mean arterial pressure of 65 mm Hg or greater.

Do not increase cardiac index to achieve an arbitrarily predefined elevated level of oxygen delivery.

#### **Steroids**

Treat patients who still require vasopressors despite fluid replacement with hydrocortisone 200–300 mg/day, for 7 days in three or four divided doses or by continuous infusion.

#### Optional:

- Perform 250-microgram adrenocorticotropic hormone (ACTH) stimulation test and discontinue steroids in patients who are responders (increase in cortisol of >9 μg/dl).
- Decrease steroid dose if septic shock resolves.
- ◆ Taper corticosteroid dose at end of therapy.
- Add fludrocortisone (50μg orally once a day) to this regimen.

Do not use corticosteroids >300 mg/day of hydrocortisone to treat septic shock.

Do not use corticosteroids to treat sepsis in the absence of shock unless the patient's endocrine or corticosteroid history warrants.

#### Fluid therapy

See initial resuscitation timing

recommendations.

Use crystalloids or colloids.

Give fluid challenge to patients with suspected inadequate tissue perfusion at a rate of 500–1000 ml of crystalloids or 300–500 ml of colloids over 30 minutes and repeat if blood pressure and urine output do not increase and there is no evidence of intravascular volume overload.

### Blood product administration

Following resolution of tissue hypoperfusion, and in the absence of

significant coronary artery disease or acute haemorrhage, transfuse red blood cells when haemoglobin decreases to <7.0 g/dl (<70 g/L) to target a haemoglobin of 7.0 - 9.0 g/dl.

Do not use erythropoietin to treat sepsis-related anaemia.

Erythropoietin may be used for other accepted reasons.

Do not use fresh frozen plasma to correct laboratory clotting abnormalities unless there is bleeding or planned invasive procedures.

Do not use antithrombin therapy.

Administer platelets when counts are <5000/mm3 (5 x 109/L) regardless of bleeding. Transfuse platelets when counts are 5000 to 30,000/mm3 (5-30 x 109/L) and there is significant bleeding risk.

Higher platelet counts ( $\geq 50,000/mm3$  [50 x 109/L]) are required for surgery or invasive procedures.

### Sedation, analgesia, and neuromuscular blockade in sepsis

Use sedation protocols for critically ill mechanically

ventilated patients. Measure the sedation goal with a standardized subjective sedation scale.

Target sedation to predetermined end-points (sedation score).

Use either intermittent bolus sedation or continuous infusion sedation with daily interruption/lightening to produce awakening. Re-titrate if necessary.

Avoid neuromuscular blockers (NMBs), if at all possible.

If NMBs must be utilized for longer than the first 2 to 3 hours of mechanical ventilation, use either intermittent bolus as required or continuous infusion with monitoring of depth of block with train of four monitoring.

### Mechanical ventilation of sepsis-induced acute lung injury (ALI)/ARDS

Avoid high tidal volumes coupled

with high plateau pressures. Reduce tidal volumes over 1-2 hours to a low tidal volume (6 ml per kilogram of lean body weight) as a goal in conjunction with the goal of maintaining end-inspiratory plateau pressures <30 cm  $H_2O$ .

If necessary, minimize plateau pressures and tidal volumes by allowing PaCO<sub>2</sub> to increase above normal.

Set a minimum amount of positive end-expiratory pressure (PEEP) to prevent lung collapse at end expiration. Set PEEP based on severity of oxygenation deficit and guided by the FiO<sub>2</sub> required to maintain adequate oxygenation (ARDSnet guidelines) or titrate PEEP according to bedside measurements of thoracopulmonary compliance.

Prone ARDS patients requiring potentially injurious levels of  ${\rm FiO}_2$  or plateau pressure. Only prone patients not at high risk from positional changes.

To prevent ventilator-associated pneumonia maintain mechanically ventilated patients in a semi-recumbent position (head of bed raised 45 degrees), unless contraindicated.

Use a weaning protocol and have mechanically ventilated patients undergo a spontaneous breathing trial (SBT), at least daily, to evaluate for ventilation discontinuation.

SBT options include a low level of pressure support with continuous positive airway pressure 5 cm H<sub>2</sub>O or a T-piece. Prior to SBT, patients should:

- be arousable;
- be haemodynamically stable without vasopressors;
- have no new potentially serious conditions:
- have low ventilatory and end-expiratory pressure requirement; and
- require FiO<sub>2</sub> levels that can be safely delivered with a face mask or nasal cannula.

Consider extubation if SBT is successful.

#### Glucose control

Maintain blood glucose <150 mg/dl (8.3mmol/L) following initial stabilization. Use continuous insulin and glucose infusion. Monitor blood glucose every 30 - 60 minutes until stabilized, then monitor every 4 hours.

Include a nutritional protocol for glycaemic control.

### Recombinant human activated protein C (rhAPC)

rhAPC is recommended in patients at high risk of death

(APACHE II  $\geq$  25, sepsis-induced multiple organ failure, septic shock, or sepsis-induced acute respiratory distress syndrome) and with no absolute contraindication related to bleeding risk or relative contraindication that outweighs the potential benefit of rhAPC.

rhAPC is indicated for the treatment of adult patients with severe sepsis with multiple organ failure when added to best standard care.

#### Renal replacement

Intermittent haemodialysis and continuous veno venous haemofiltration (CVVH) are considered equivalent. CVVH offers easier management in haemodynamically unstable patients.

#### **Bicarbonate therapy**

Do not use bicarbonate therapy for the purpose of improving haemodynamics or reducing vaso-pressor requirements when treating hypoperfusion induced lactic acidaemia with pH  $\geq$  7.15.

### Deep vein thrombosis (DVT) prophylaxis

Use either low-dose unfractionated heparin or low-molecular weight

heparin. Use a mechanical prophylactic device, such as compression stockings or an intermittent compression device, when heparin is contraindicated.

Use a combination of pharmacologic and mechanical therapy for patients who are at very high risk for DVT.

## Stress ulcer prophylaxis

Provide stress ulcer prophylaxis.

The preferred agents are H<sub>2</sub> receptor inhibitors.

### Consideration for limitation of support

Discuss advance care planning with patients and families. Describe likely

outcomes and set realistic expectations.