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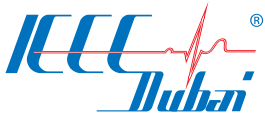
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1st Asia-African Conference of the World Federation of Societies of Intensive and Critical Care Medicine

GUIDELINES FOR MANAGEMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

Initial resuscitation (first 6 hours)

Begin resuscitation immediately in patients with hypotension or elevated serum lactate ≥ 4 mmol/L; do not delay pending ICU admission. ^(1C)

Resuscitation goals: ^(1C)

- Central venous pressure (CVP) 8–12 mmHg*
- Mean arterial pressure ≥ 65 mmHg
- Urine output ≥ 0.5 mL.kg⁻¹.hr⁻¹
- Central venous (superior vena cava) oxygen saturation $\geq 70\%$, or mixed venous $\geq 65\%$

If venous O₂ saturation target not achieved: ^(2C)

- consider further fluid
- transfuse packed red blood cells if required to hematocrit of $\geq 30\%$ and/or
- dobutamine infusion max 20 μ g.kg⁻¹.min⁻¹

* A higher target CVP of 12–15 mmHg is recommended in the presence of mechanical ventilation or pre-existing decreased ventricular compliance.

Diagnosis

Obtain appropriate cultures before starting antibiotics provided this does not significantly delay antimicrobial administration. ^(1C)

- Obtain two or more blood cultures (BCs)
- One or more BCs should be percutaneous
- One BC from each vascular access device in place ≥ 48 hours
- Culture other sites as clinically indicated

Perform imaging studies promptly in order to confirm and sample any source of infection if safe to do so. ^(1C)

Antibiotic therapy

Begin intravenous antibiotics as early as possible, and always within the first hour of recognizing severe sepsis ^(1D) and septic shock. ^(1B)

- Broad-spectrum: one or more agents active against likely bacterial/fungal pathogens and with good penetration into presumed source. ^(1B)
- Reassess antimicrobial regimen daily to optimize efficacy, prevent resistance, avoid toxicity, & minimize costs. ^(1C)
- Consider combination therapy in Pseudomonas infections. ^(2D)
- Consider combination empiric therapy in neutropenic patients. ^(2D)
- Combination therapy no more than 3–5 days and de-escalation following susceptibilities. ^(2D)
- Duration of therapy typically limited to 7–10 days; longer if response slow, undrainable foci of infection, or immunologic deficiencies. ^(1D)
- Stop antimicrobial therapy if cause is found to be non-infectious. ^(1D)

Source identification and control

A specific anatomic site of infection should be established as rapidly as possible. ^(1C) and within the first 6 hours of presentation. ^(1D)

- Formally evaluate patient for a focus of infection amenable to source control measures (eg: abscess drainage, tissue debridement). ^(1C)
- Implement source control measures as soon as possible following successful initial resuscitation. ^(1C)
- Exception: infected pancreatic necrosis, where surgical intervention best delayed. ^(2B)
- Choose source control measure with maximum efficacy and minimal physiologic upset. ^(1D)
- Remove intravascular access devices if potentially infected. ^(1C)

Fluid therapy

- Fluid-resuscitate using crystalloids or colloids. ^(1B)
- Target a CVP of ≥ 8 mmHg (≥ 12 mmHg if mechanically vent-ilated). ^(1C)
- Use a fluid challenge technique while associated with a hemodynamic improvement. ^(1D)
- Give fluid challenges of 1000 mL of crystalloids or 300–500 mL of colloids over 30 minutes. More rapid and larger volumes may be required in sepsis-induced tissue hypoperfusion. ^(1D)
- Rate of fluid administration should be reduced if cardiac filling pressures increase without concurrent hemodynamic improvement. ^(1D)

Vasopressors

- Maintain MAP ≥ 65 mmHg. ^(1C)
- Norepinephrine or dopamine centrally administered are the initial vasopressors of choice. ^(1C)
- Epinephrine, phenylephrine, or vasopressin should not be administered as the initial vasopressor in septic shock. ^(2C)
- Vasopressin 0.03 units/min may be subsequently added to norepinephrine with anticipation of an effect equivalent to norepinephrine alone.

- Use epinephrine as the first alternative agent in septic shock when blood pressure is poorly responsive to norepinephrine or dopamine. ^(2B)
- Do not use low-dose dopamine for renal protection. ^(1A)
- In patients requiring vasopressors, insert an arterial catheter as soon as practical. ^(1D)

Inotropic therapy

- Use dobutamine in patients with myocardial dysfunction as supported by elevated cardiac filling pressures and low cardiac output. ^(1C)
- Do not increase cardiac index to predetermined supranormal levels. ^(1B)

Steroids

- Consider intravenous hydrocortisone for adult septic shock when hypotension responds poorly to adequate fluid resuscitation and vasopressors. ^(2C)
- ACTH stimulation test is not recommended to identify the subset of adults with septic shock who should receive hydrocortisone. ^(2B)
- Hydrocortisone is preferred to dexamethasone. ^(2B)
- Fludrocortisone (50 μ g orally once a day) may be included if an alternative to hydrocortisone is being used which lacks significant mineralocorticoid activity. Fludrocortisone is optional if hydrocortisone is used. ^(2C)
- Steroid therapy may be weaned once vasopressors are no longer required. ^(2D)
- Hydrocortisone dose should be 300 mg/day. ^(1A)
- Do not use corticosteroids to treat sepsis in the absence of shock unless the patient's endocrine or corticosteroid history warrants it. ^(1D)

Recombinant human activated protein C (rhAPC)

- Consider rhAPC in adult patients with sepsis-induced organ dysfunction with clinical assessment of high risk of death (typically APACHE II ≥ 25 or multiple organ failure) if there are no contraindications. ^(2B; 2C for post-operative patients)
- Adult patients with severe sepsis and low risk of death (eg: APACHE II ≥ 20 or one organ failure) should not receive rhAPC. ^(1A)

Blood product administration

- Give red blood cells when hemoglobin decreases to ≥ 7.0 g/dL (≥ 7.0 g/L) to target a hemoglobin of 7.0 – 9.0 g/dL in adults. ^(1B) A higher hemoglobin level may be required in special circumstances (eg: myo cardiac ischemia, severe hypoxemia, acute hemorrhage, cyanotic heart disease, or lactic acidosis)
- Do not use erythropoietin to treat sepsis-related anemia. Erythropoietin may be used for other accepted reasons. ^(1B)
- Do not use fresh frozen plasma to correct laboratory clotting abnormalities unless there is bleeding or planned invasive procedures. ^(2D)
- Do not use antithrombin therapy. ^(1B)
- Administer platelets when: ^(2D)
 - counts are $<5000/mm^3$ (5 X 10⁹/L) regardless of bleeding.
 - counts are 5000 to 30,000/mm³ (5–30 X 10⁹/L) and there is significant bleeding risk.
 - Higher platelet counts $\geq 50,000/mm^3$ (50 X 10⁹/L) are typically required for surgery or invasive procedures.

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

- Target a tidal volume of 6 mL/kg (predicted) body weight in patients with ALI/ARDS. ^(1B)
- Target an initial upper limit plateau pressure ≤ 30 cmH₂O. Consider chest wall compliance when assessing plateau pressure. ^(1C)
- Allow PaCO₂ to increase above normal, if needed, to minimize plateau pressures and tidal volumes. ^(1C)
- Positive end expiratory pressure (PEEP) should be set to avoid extensive lung collapse at end expiration. ^(1C)
- Consider using the prone position for ARDS patients requiring potentially injurious levels of FIO₂ or plateau pressure, provided they are not put at risk from positional changes. ^(2C)
- Maintain mechanically ventilated patients in a semi-recumbent position unless contraindicated. ^(1B)
- Suggested target elevation 30 – 45 degrees. ^(2C)
- Noninvasive ventilation may be considered in the minority of ALI/ARDS patients with mild-moderate hypoxemic respiratory failure. The patients need to be hemodynamically stable, comfortable, easily arousable, able to protect/clear their airway, and expected to recover rapidly. ^(2B)
- Use a weaning protocol and a spontaneous breathing trial (SBT) regularly to evaluate the potential for discontinuing mechanical ventilation. ^(1A)

○ SBT options include a low level of pressure support with continuous positive airway pressure 5 cm H₂O or a T-piece.

○ Before the SBT, patients should:

- > be arousable
- > be hemodynamically stable without vasopressors
- > have no new potentially serious conditions
- > have low ventilatory and end-expiratory pressure requirement
- > require FIO₂ levels that can be safely delivered with a face mask or nasal cannula

■ Do not use a pulmonary artery catheter for the routine monitoring of patients with ALI/ARDS. ^(1A)

■ Use a conservative fluid strategy for patients with established ALI who do not have evidence of tissue hypoperfusion. ^(1C)

Sedation, analgesia, and neuromuscular blockade in sepsis

- Use sedation protocols with a sedation goal for critically ill mechanically ventilated patients. ^(1B)
- Use either intermittent bolus sedation or continuous infusion sedation to predetermined end points (sedation scales), with daily interruption/ lightening to produce awakening. Re-titrate if necessary. ^(1B)
- Avoid neuromuscular blockers where possible. Monitor depth of block with train-of-four when using continuous infusions. ^(1B)

Glucose control

- Use IV insulin to control hyperglycemia in patients with severe sepsis following stabilization in the ICU. ^(1B)
- Aim to keep blood glucose ≤ 8.3 mmol/L (150 mg/dL) using a validated protocol for insulin dose adjustment. ^(2C)
- Provide a glucose calorie source and monitor blood glucose values every 1–2 hours (4 hours when stable) in patients receiving intravenous insulin. ^(1C)
- Interpret with caution low glucose levels obtained with point of care testing, as these techniques may overestimate arterial blood or plasma glucose values. ^(1B)

Renal replacement

- Intermittent hemodialysis and continuous veno-venous hemofiltration (CVVH) are considered equivalent. ^(2B)
- CVVH offers easier management in hemodynamically unstable patients. ^(2D)

Bicarbonate therapy

- Do not use bicarbonate therapy for the purpose of improving hemodynamics or reducing vasopressor requirements when treating hypo perfusion-induced lactic acidemia with pH ≥ 7.15 . ^(1B)

Deep vein thrombosis (DVT) prophylaxis

- Use either low-dose unfractionated heparin (UFH) or low-molecular weight heparin (LMWH), unless contraindicated. ^(1A)
- Use a mechanical prophylactic device, such as compression stockings or an intermittent compression device, when heparin is contra indicated. ^(1A)
- Use a combination of pharmacologic and mechanical therapy for patients who are at very high risk for DVT. ^(2C)
- In patients at very high risk LMWH should be used rather than UFH. ^(2C)

Stress ulcer prophylaxis

- Provide stress ulcer prophylaxis using H₂ blocker ^(1A) or proton pump inhibitor. ^(1B) Benefits of prevention of upper GI bleed must be weighed against the potential for development of ventilator-acquired pneumonia.

Consideration for limitation of support

- Discuss advance care planning with patients and families. Describe likely outcomes and set realistic expectations. ^(1D)

With Best Compliments from

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Strength of recommendation and quality of evidence have been assessed using the GRADE criteria, presented in brackets after each guideline.

For added clarity:

- Indicates a strong recommendation or “we recommend”
- Indicates a weak recommendation or “we suggest”