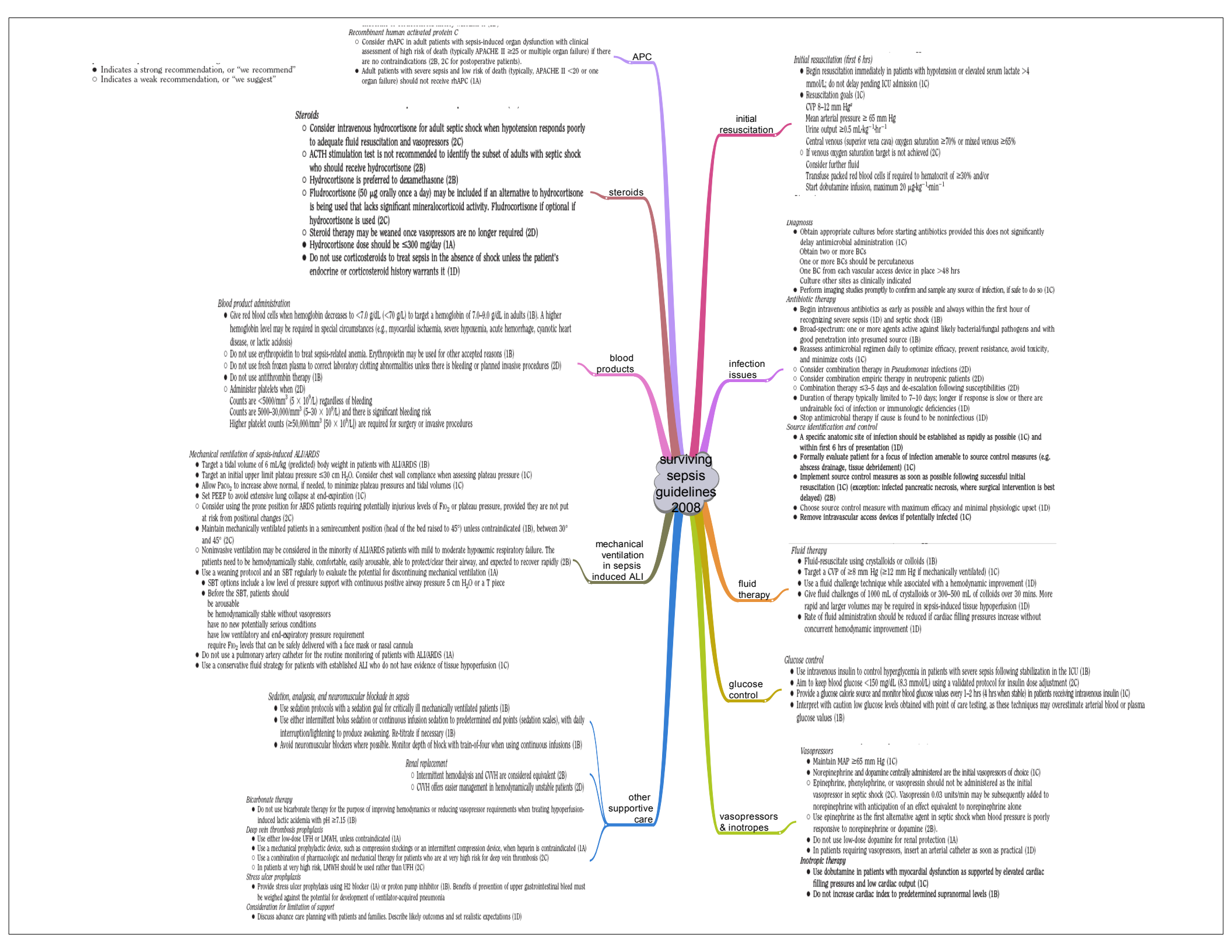
● Indicates a strong recommendation, or "we recommend"
○ Indicates a weak recommendation, or "we suggest"



Recombinant human activated protein C
- ○ 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 postoperative patients).
- ● Adult patients with severe sepsis and low risk of death (typically, APACHE II <20 or one organ failure) should not receive rhAPC (1A)

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 μg orally once a day) may be included if an alternative to hydrocortisone is being used that lacks significant mineralocorticoid activity. Fludrocortisone if 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)

Blood product administration
- ● Give red blood cells when hemoglobin decreases to <7.0 g/dL (<70 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 (e.g., myocardial ischaemia, 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 × 10^9/L) regardless of bleeding
  - Counts are 5000–30,000/mm^3 (5–30 × 10^9/L) and there is significant bleeding risk
  - Higher platelet counts (≥50,000/mm^3 [50 × 10^9/L]) are required for surgery or invasive procedures

Mechanical ventilation of sepsis-induced 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 cm H_2O. Consider chest wall compliance when assessing plateau pressure (1C)
- ● Allow $Paco_2$ to increase above normal, if needed, to minimize plateau pressures and tidal volumes (1C)
- ● Set PEEP to avoid extensive lung collapse at end-expiration (1C)
- ○ Consider using the prone position for ARDS patients requiring potentially injurious levels of Fio_2 or plateau pressure, provided they are not put at risk from positional changes (2C)
- ● Maintain mechanically ventilated patients in a semirecumbent position (head of the bed raised to 45°) unless contraindicated (1B), between 30° and 45° (2C)
- ○ Noninvasive ventilation may be considered in the minority of ALI/ARDS patients with mild to 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 an 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 H_2O 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 Fio_2 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)

Renal replacement
- ○ Intermittent hemodialysis and 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 hypoperfusion-induced lactic acidemia with pH ≥7.15 (1B)

Deep vein thrombosis prophylaxis
- ● Use either low-dose UFH or LMWH, unless contraindicated (1A)
- ● Use a mechanical prophylactic device, such as compression stockings or an intermittent compression device, when heparin is contraindicated (1A)
- ○ Use a combination of pharmacologic and mechanical therapy for patients who are at very high risk for deep vein thrombosis (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 gastrointestinal 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)

Initial resuscitation (first 6 hrs)
- ● Begin resuscitation immediately in patients with hypotension or elevated serum lactate >4 mmol/L; do not delay pending ICU admission (1C)
- ● Resuscitation goals (1C)
  - CVP 8–12 mm Hg[a]
  - Mean arterial pressure ≥ 65 mm Hg
  - Urine output ≥0.5 mL·kg^{-1}·hr^{-1}
  - Central venous (superior vena cava) oxygen saturation ≥70% or mixed venous ≥65%
- ○ If venous oxygen saturation target is not achieved (2C)
  - Consider further fluid
  - Transfuse packed red blood cells if required to hematocrit of ≥30% and/or
  - Start dobutamine infusion, maximum 20 μg·kg^{-1}·min^{-1}

Diagnosis
- ● Obtain appropriate cultures before starting antibiotics provided this does not significantly delay antimicrobial administration (1C)
  - Obtain two or more BCs
  - One or more BCs should be percutaneous
  - One BC from each vascular access device in place >48 hrs
  - Culture other sites as clinically indicated
- ● Perform imaging studies promptly 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, and minimize costs (1C)
- ○ Consider combination therapy in *Pseudomonas* infections (2D)
- ○ Consider combination empiric therapy in neutropenic patients (2D)
- ○ Combination therapy ≤3–5 days and de-escalation following susceptibilities (2D)
- ● Duration of therapy typically limited to 7–10 days; longer if response is slow or there are undrainable foci of infection or immunologic deficiencies (1D)
- ● Stop antimicrobial therapy if cause is found to be noninfectious (1D)

Source identification and control
- ● A specific anatomic site of infection should be established as rapidly as possible (1C) and within first 6 hrs of presentation (1D)
- ● Formally evaluate patient for a focus of infection amenable to source control measures (e.g. 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 is 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 mm Hg (≥12 mm Hg if mechanically ventilated) (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 mins. 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)

Glucose control
- ● Use intravenous insulin to control hyperglycemia in patients with severe sepsis following stabilization in the ICU (1B)
- ● Aim to keep blood glucose <150 mg/dL (8.3 mmol/L) using a validated protocol for insulin dose adjustment (2C)
- ● Provide a glucose calorie source and monitor blood glucose values every 1–2 hrs (4 hrs 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)

Vasopressors
- ● Maintain MAP ≥65 mm Hg (1C)
- ● Norepinephrine and 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)