

**Norepinephrine**



**Vasopressin**

**Crystalloids**



**Colloids**

**CVVHD**



**IHD**

**Epinephrine**



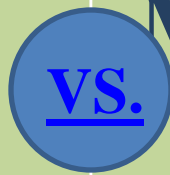
**Phenylephrine**

**NIPPV**



**IPPV**

**Single antibiotic  
Rx**



**Multiple antibiotics  
Rx**



# SURVIVING SEPSIS CAMPAIGN

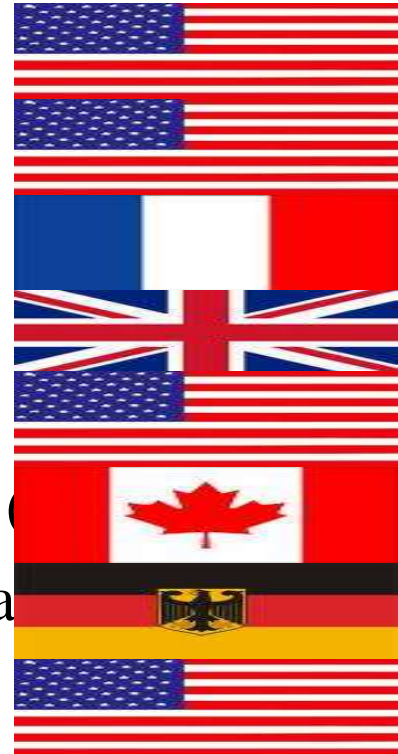
Ammar Alhakim M.D.

SAMA Lecture

8 May 2010

# Citation

- Cooper University Hospital, Camden, NJ (RPD)
- Rhode Island Hospital, Providence, RI (MML)
- Hospital Saint-Joseph, Paris, France (JMC)
- Birmingham University, BirminghamUK (JB)
- SUNY at Stony Brook, Stony Brook, NY (MMP)
- McMaster University, Hamilton, Ontario, Canada
- Friedrich-Schiller-University of Jena, Jena, Germany
- University of Pittsburgh, Pittsburgh, PA (DCA)



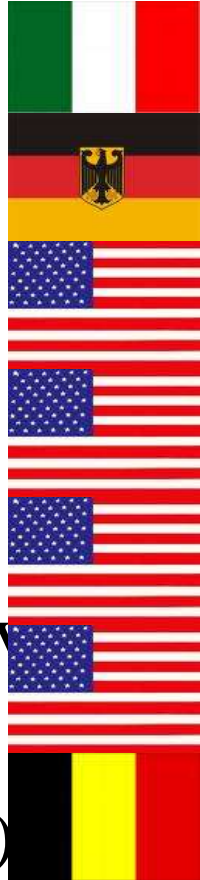
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- Guy's and St Thomas' Hospital Trust, London, UK (RB)
- Centre Hospitalier Universitaire Vaudois, Lausanne, Switzerland (TC)
- French Agency for Evaluation of Research and Higher Education, Paris, France (JFD)
- Vivantes-Klinikum Neukoelin, Berlin, Germany (HG)
- Consultants in Critical Care, Inc, Glenbrook, NV (ME)
- University of Minnesota, St. Paul, MN (JJM)
- St. Michael's Hospital, Toronto, Ontario, Canada (JM)



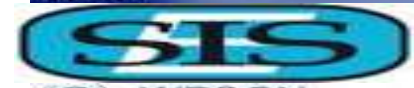
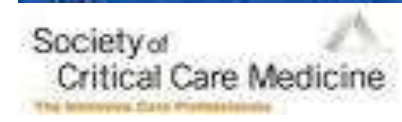
# Citation

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- Rhode Island Hospital, Providence, RI(ST)
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- The Methodist Hospital, Houston, TX (JLZ)
- Erasme University Hospital, Brussels, Belgium (JLV)



# Sponsoring organizations

- Japanese Association for Acute Medicine
- Japanese Society of Intensive Care Medicine
- Society of Critical Care Medicine
- Society of Hospital Medicine
- Surgical Infection Society
- World Federation of Critical Care Nurses
- World Federation of Societies of Intensive and Critical Care Medicine
- Participation and endorsement by the German Sepsis Society
- Latin American Sepsis Institute



# Sponsoring organizations

- American Association of Critical-Care Nurses
- American College of Chest Physicians
- American College of Emergency Physicians
- Canadian Critical Care Society
- European Society of Clinical Microbiology and Infectious Diseases
- European Society of Intensive Care Medicine
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- Indian Society of Critical Care Medicine
- International Sepsis Forum



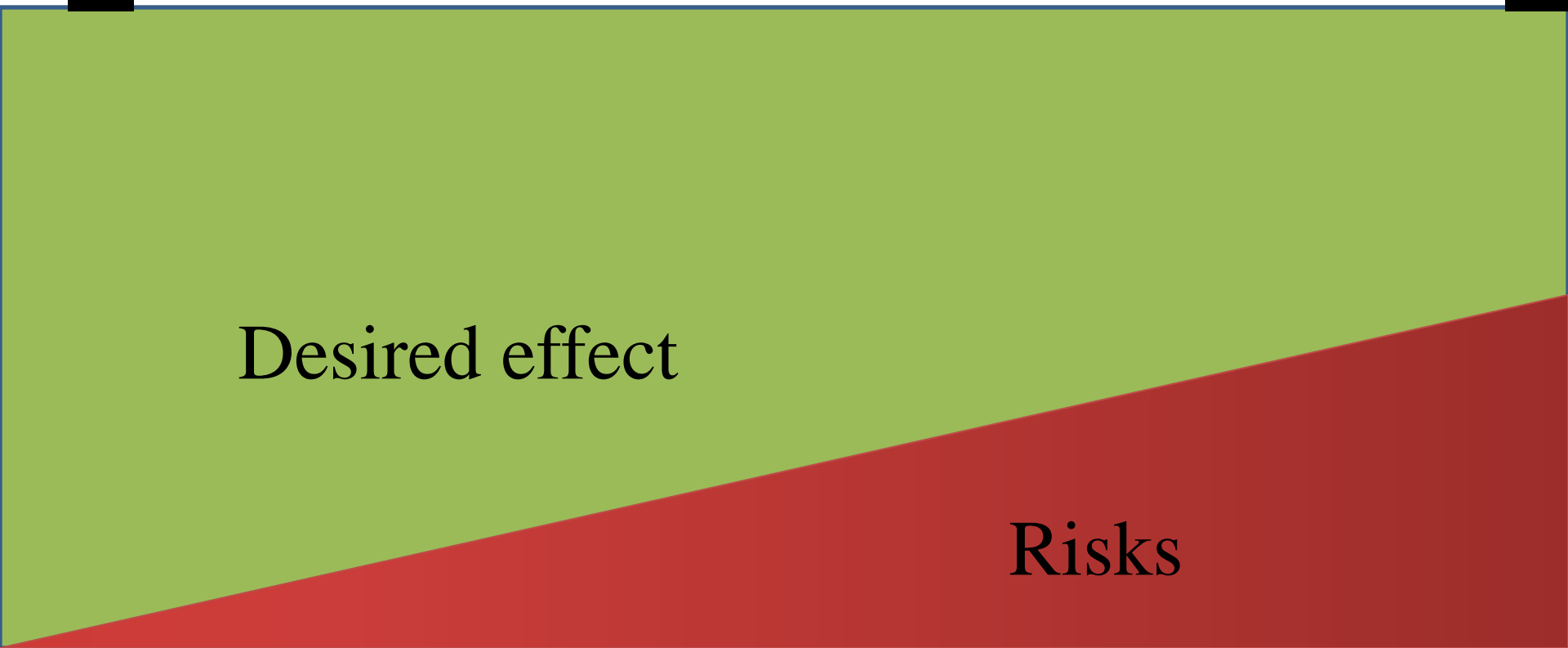
# Strength of recommendations

**1**

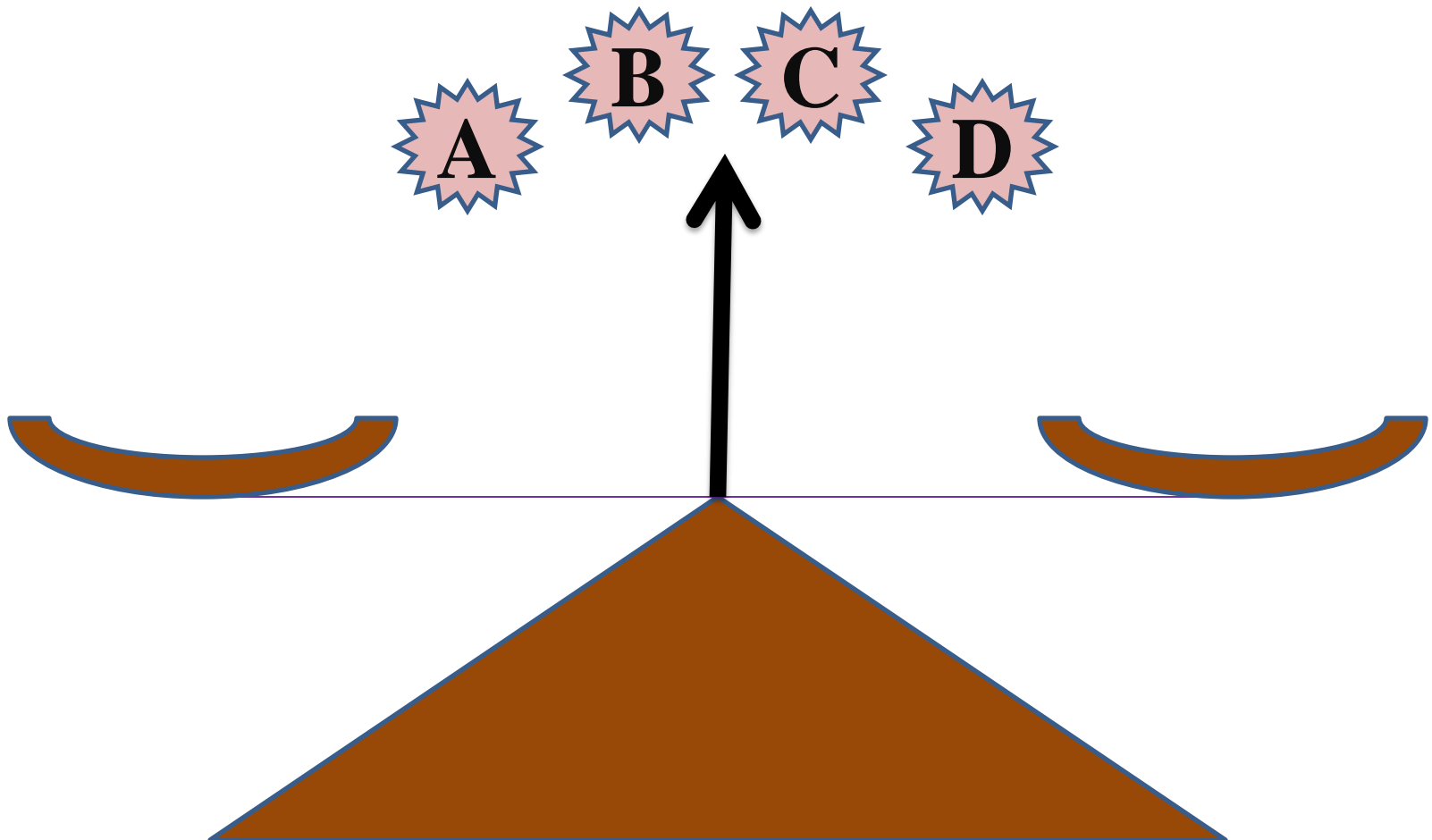
**2**

Desired effect

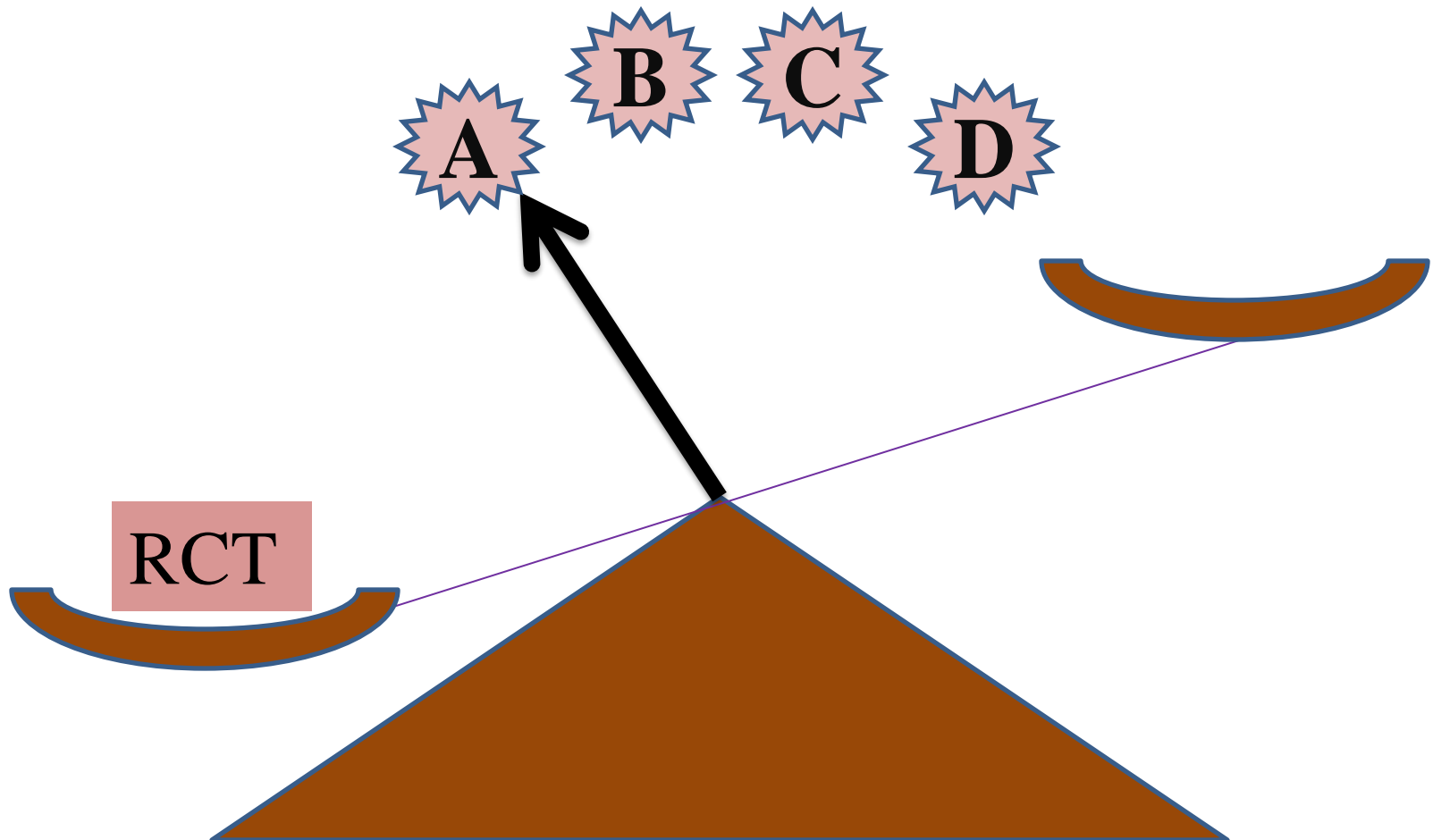
Risks



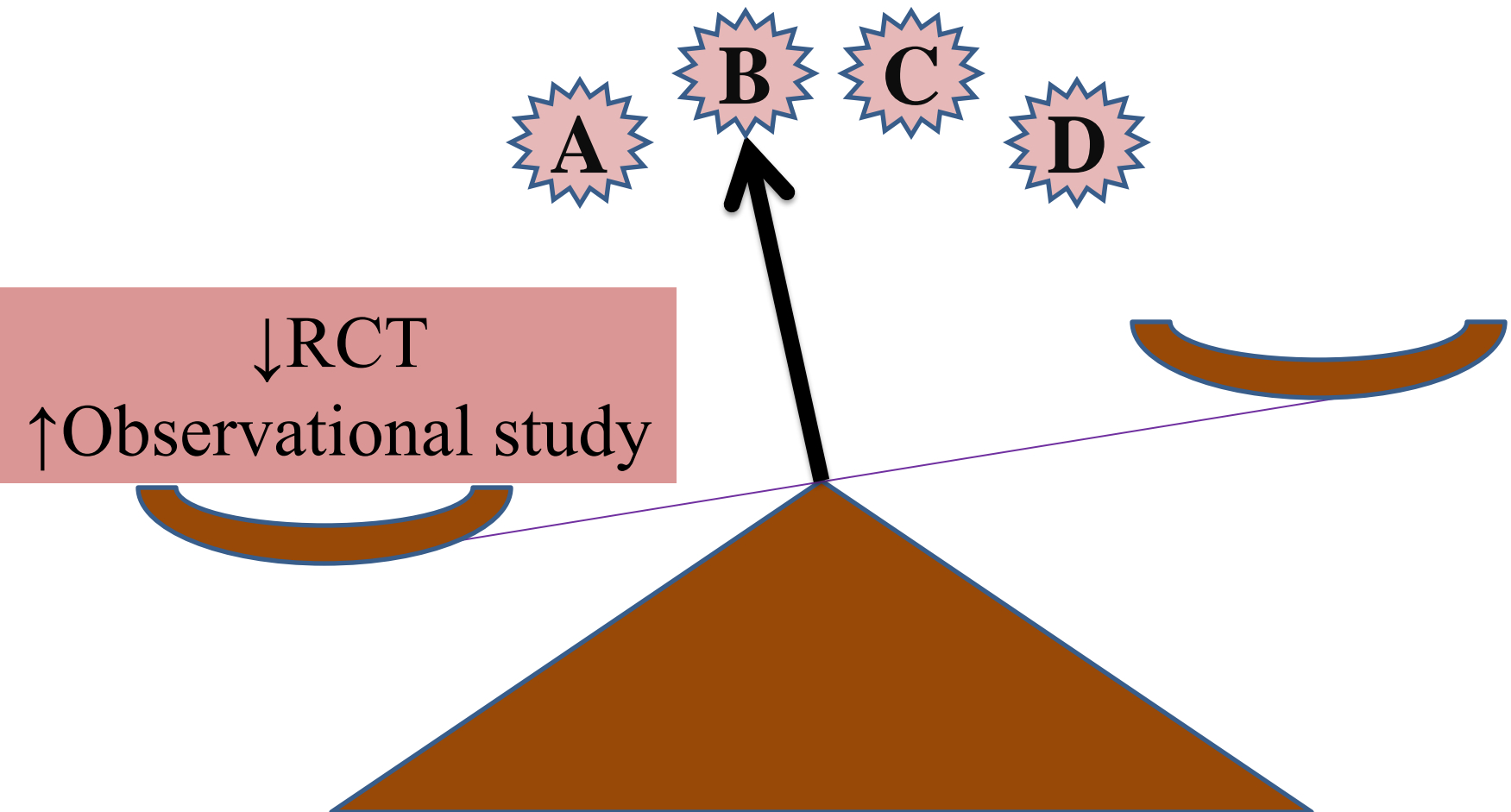
# GRADE



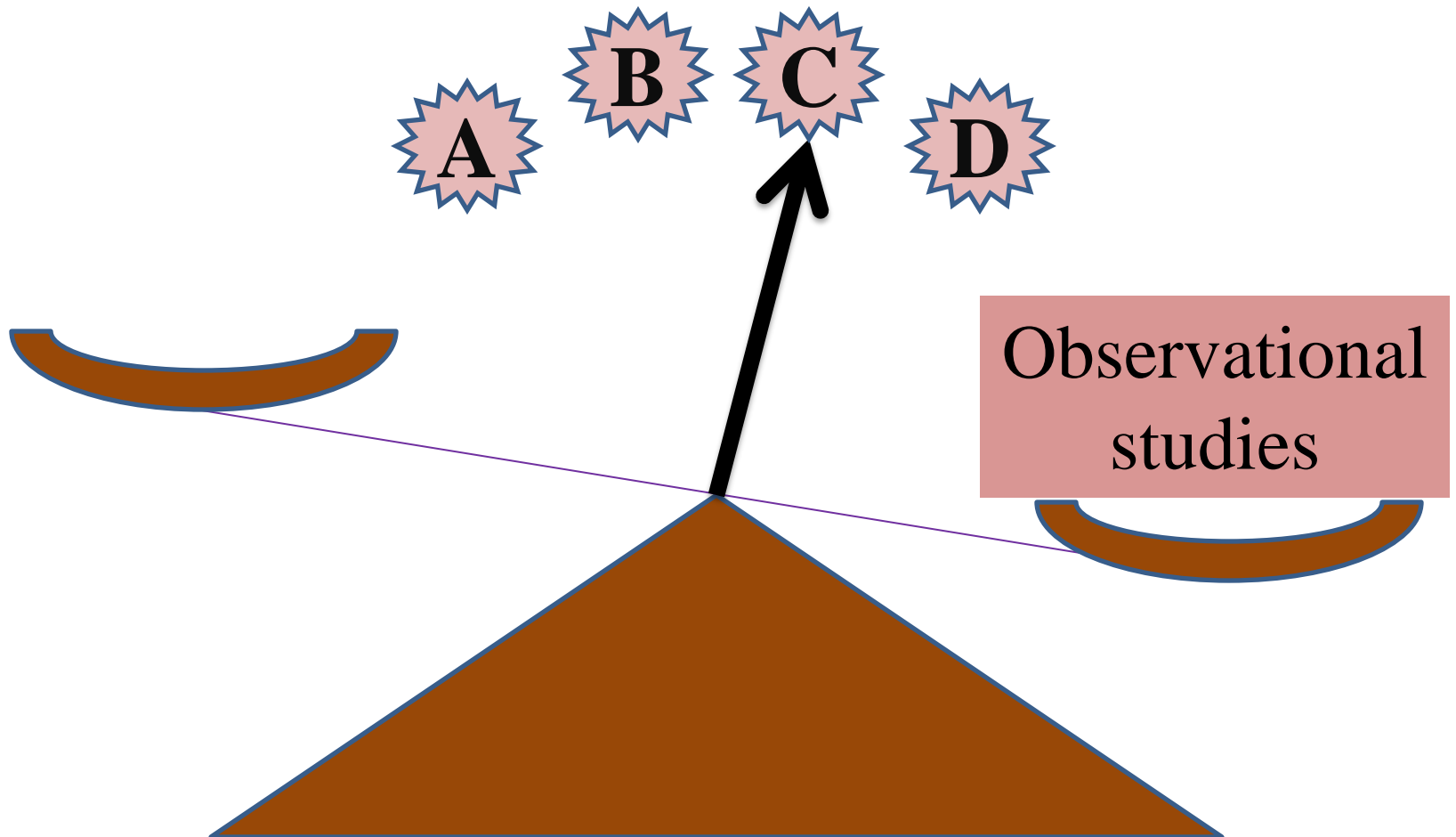
# GRADE



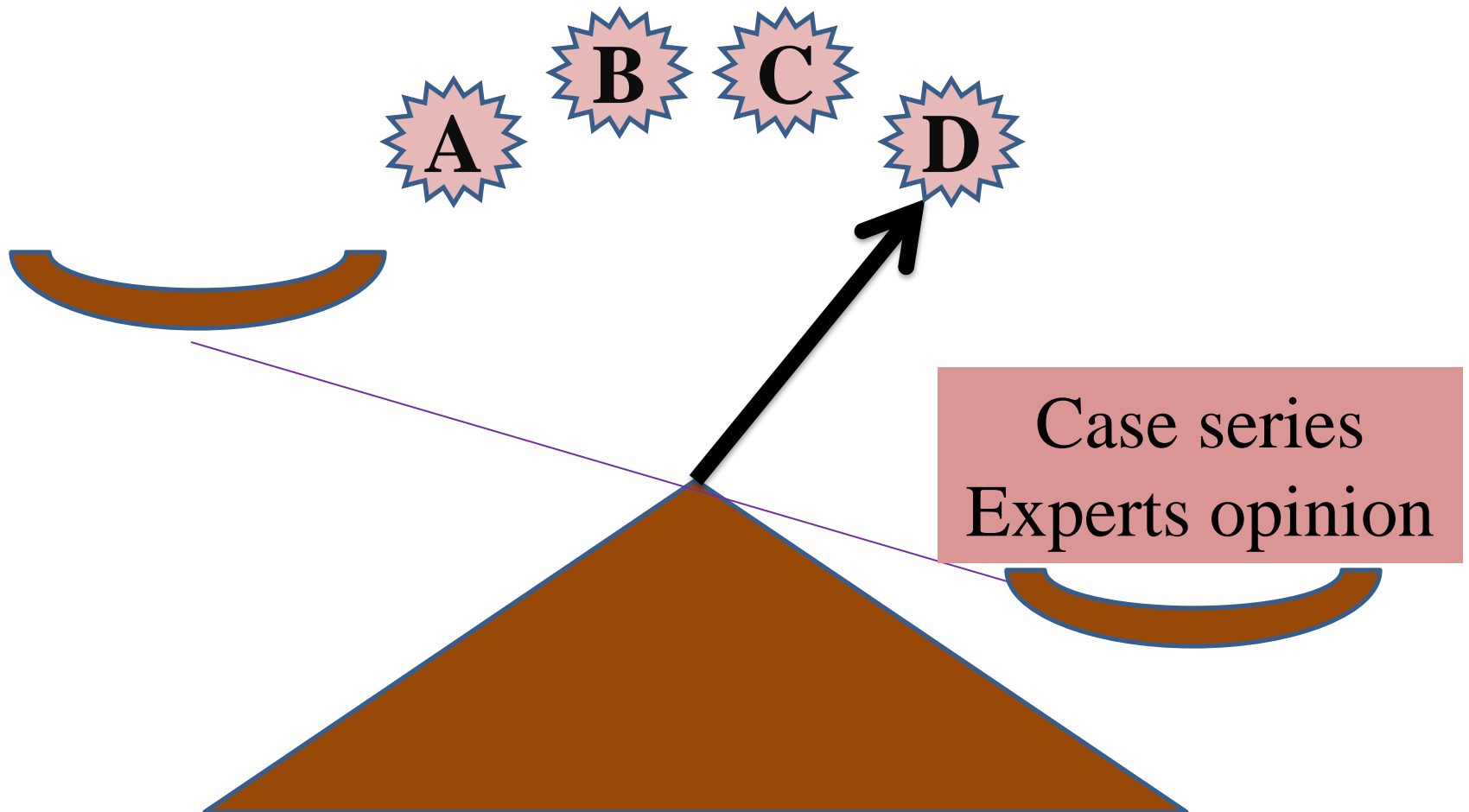
# GRADE



# GRADE



# GRADE



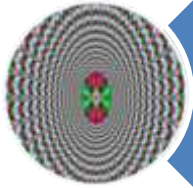
# Resuscitation and infection control

- *Initial resuscitation (first 6 hrs)*
- *Diagnosis*
- *Antibiotic therapy*
- *Source identification and control*

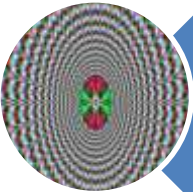
# Initial resuscitation (first 6 hrs)

- ● Begin resuscitation immediately in patients with
  - Hypotension
  - Elevated serum lactate 4 mmol/L
- Do not delay pending ICU admission (1C)

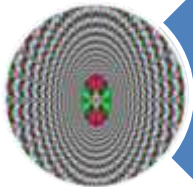
# Initial resuscitation (first 6 hrs)



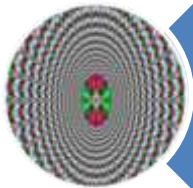
## • Resuscitation goals (1C)



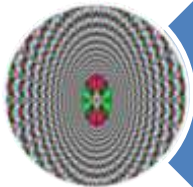
CVP 8–12 mm Hg



Mean arterial pressure 65 mm Hg

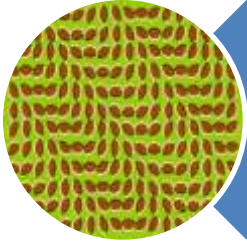


Urine output 0.5 mL.kg/hr

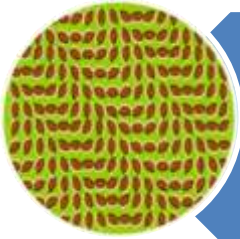


Central venous (superior vena cava) oxygen saturation 70% or mixed venous 65%

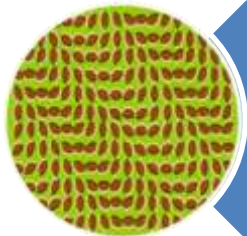
# Initial resuscitation (first 6 hrs)



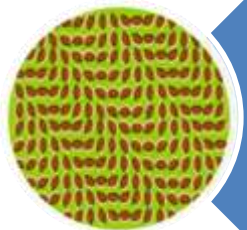
If venous oxygen saturation target is not achieved



Consider further fluid (2C)



Start dobutamine infusion, maximum 20  $\mu\text{g.kg/min}$



Transfuse packed red blood cells if required to hematocrit of 30%

# 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)

# 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)

# 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)

Combination therapy 3–5 days and de-escalation following susceptibilities (2D)

Consider combination therapy in *Pseudomonas infections* (2D)

Consider combination empiric therapy in neutropenic patients (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)

# Hemodynamic support and adjunctive therapy

- *Fluid therapy*
- *Vasopressors*
- *Inotropic therapy*
- *Steroids*
- *Recombinant human activated protein C*

# 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)

# Pediatric considerations

- Early intraosseous access
- Infuse crystalloids with boluses of 20 mL/kg over 5–10 mins
- Titrate to clinical monitors (2C)
  - Cardiac output
  - Heart rate
  - Urine output
  - Capillary refill, and level of consciousness
- Blood pressure by itself is not a reliable end point for assessing the adequacy of resuscitation.
- Hepatomegaly occurs in children who are fluid overloaded and can be a helpful sign of adequacy of fluid resuscitation

# 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)

# Pediatric considerations

0-5  
minutes

Recognize decreased mental status and perfusion  
ABC's according to PALS

Push fluids 20cc/kg up o 60cc/kg  
Correct hypoglycemia and hypocalcemia  
Administer Antibiotics

15  
minutes

**Fluids refractory shock**

Establish Central venous line access  
Begin Dopamine or Dobutamine Rx  
Establish arterial line monitoring

**Fluids refractory- Dopamine/ Dobutamine resistant shock**

Titrate Epinephrine for cold shock  
Titrate Norepinephrine for warm shock

# Pediatric considerations

## Catecholamine-resistant shock

60  
minutes

Begin hydrocortisone if at risk of relative adrenal insufficiency

Normal blood pressure  
Cold Shock  
SVO<sub>2</sub> < 70%

Add vasodilator  
Phosphodiesterase  
inhibitor III  
With volume loading

Low blood pressure  
Cold Shock  
SVO<sub>2</sub> < 70%

Titrate volume &  
Epinephrine

Low blood pressure  
Warm Shock  
SVO<sub>2</sub> ≥ 70%

Titrate volume &  
Norepinephrine

# Pediatric considerations

## Persistent catecholamine-resistant shock

Start Cardiac output measurements

Direct volumes, inotrope, vasopressor, vasodilator, hormonal Rx to attain  
Cardiac index  $CI > 3.3$  and  $< 6$  L.min/m<sup>2</sup>

## Refractory shock

Consider ECMO

# 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 is optional if hydrocortisone is used (2C)

Fludrocortisone (50 µg orally once a day) may be included if an alternative to hydrocortisone is being used that lacks significant mineralocorticoid activity

Steroid therapy may be weaned once vasopressors are no longer required (2D)

- Hydrocortisone dose should be  $\leq 300$  mg/day (1A)

# Pediatric considerations

- Hydrocortisone therapy be reserved for use in children with catecholamine resistance and suspected or proven adrenal insufficiency (2C)
- Steroids should not be used in children who do not meet minimal criteria for adrenal insufficiency
  - random total cortisol concentration  $18 \mu\text{g/dL}$  ( $496 \text{ nmol/L}$ )
  - Post 30- or 60-min ACTH stimulation test increase in cortisol of  $9 \mu\text{g/dL}$  ( $248 \text{ nmol/L}$ )

# 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)

# Pediatric considerations

- We recommend against the use rhAPC in children (1B).

# supportive therapy of severe sepsis

- *Blood product administration*
- *Mechanical ventilation of sepsis-induced ALI/ARDS*
- *Sedation, analgesia, and neuromuscular blockade*
- *Glucose control*
- *Deep vein thrombosis prophylaxis*

# supportive therapy of severe sepsis

- *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)
- *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*

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# Pediatric considerations

- CVVH or other renal replacement therapy should be instituted in children with anuria/severe oliguria before significant fluid overload occurs
- Children with less fluid overload before CVVH had better survival

# Blood product administration

- Give red blood cells when hemoglobin decreases to 7.0 g/dL to target a hemoglobin of 7.0–9.0 g/dL in adults (1B)

A higher hemoglobin level may be required in special circumstances

Myocardial ischaemia

Severe hypoxemia

Acute hemorrhage

Cyanotic heart disease

Lactic acidosis

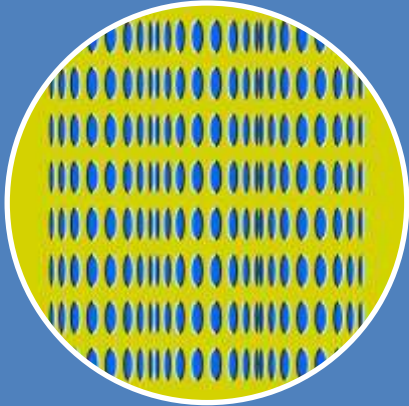
# Blood product administration

- Do not use erythropoietin to treat sepsis-related anemia. (1B)

Do not use fresh frozen plasma to correct laboratory clotting abnormalities unless there is bleeding or planned invasive procedures (2D)

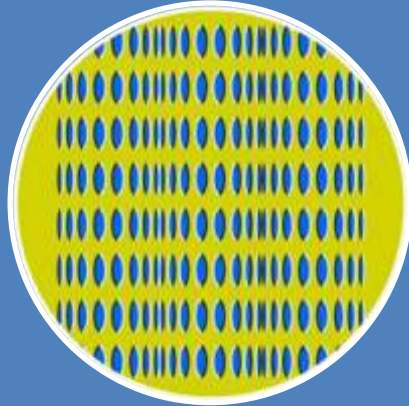
- Do not use antithrombin therapy (1B)

# Blood product administration



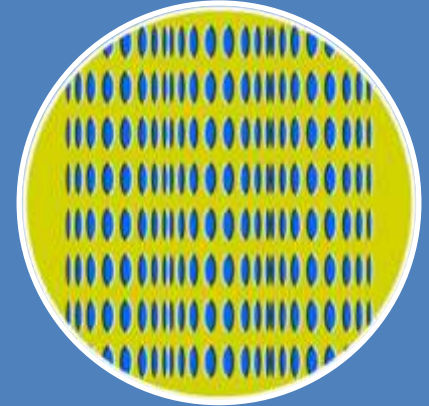
5000/mm<sup>3</sup>

- Regardless of bleeding



5000–30,000/mm<sup>3</sup>

- For significant bleeding risk



>50,000/mm<sup>3</sup>

- For surgery or invasive procedures

Administer platelets when (2D)

# Pediatric considerations

- We suggest that immunoglobulin be considered in children with severe sepsis (2C)

# Mechanical ventilation of sepsis-induced ALI/ARDS

- Maintain mechanically ventilated patients in a semirecumbent position (head of the bed raised to  $45^{\circ}$ ) unless contraindicated (1B), between  $30^{\circ}$  and  $45^{\circ}$  (2C)

# Mechanical ventilation of sepsis- induced ALI/ARDS

- Set PEEP to avoid extensive lung collapse at end-expiration (1C)

# Mechanical ventilation of sepsis- induced ALI/ARDS

- Target a tidal volume of 6 mL/kg (predicted) body weight in patients with ALI/ARDS (1B)

# Mechanical ventilation of sepsis- induced ALI/ARDS

- Target an initial upper limit plateau pressure 30 cm H<sub>2</sub>O. Consider chest wall compliance when assessing plateau pressure (1C)

# Mechanical ventilation of sepsis- induced ALI/ARDS

- Allow PaCO<sub>2</sub> to increase above normal, if needed, to minimize plateau pressures and tidal volumes (1C)

# Mechanical ventilation of sepsis-induced ALI/ARDS

- Consider using the prone position for ARDS patients requiring potentially injurious levels of FIO<sub>2</sub> or plateau pressure, provided they are not put at risk from positional changes (2C)

# Mechanical ventilation of sepsis-induced ALI/ARDS

- Noninvasive ventilation may be considered in minority of ALI/ARDS patients with (2B)
  - 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

# Mechanical ventilation of sepsis- induced ALI/ARDS

- Use a weaning protocol and an SBT regularly to evaluate the potential for discontinuing mechanical ventilation (1A)

# Mechanical ventilation of sepsis-induced ALI/ARDS

- ● SBT options include
  - low level of pressure support with CPAP 5 cm H<sub>2</sub>O
  - T piece Before the SBT
- patients should be
  - Arousable
  - Hemodynamically stable without vasopressors
  - low ventilatory, end-expiratory pressure and FIO<sub>2</sub> requirements

# Mechanical ventilation of sepsis- induced ALI/ARDS

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

# Mechanical ventilation of sepsis- induced ALI/ARDS

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

# Pediatric considerations

- Due to low functional residual capacity, young infants and neonates with severe sepsis may require early intubation
- Etomidate in children with meningococcal sepsis because of adrenal suppression effect

# Sedation, analgesia, and neuromuscular blockade

- 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)

# Pediatric considerations

- Propofol should not be used for long term sedation in children because of the reported association with fatal metabolic acidosis

# 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)

# 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)

# Pediatric considerations

- We suggest the use of DVT prophylaxis in postpubertal children with severe sepsis (2C)

# Pediatric considerations

- We suggest that use of ECMO be limited to refractory pediatric septic shock and/or respiratory failure that cannot be supported by conventional therapies ( 2C)
- Children with sepsis on ECMO do not perform worse than children without sepsis at long-term follow-up

