The New "1-Hour" Sepsis Bundle…

Key Article

- *Levy M, Evans LE, Rhodes A. The Surviving Sepsis Campaign Bundle: 2018 Update. Crit Care Med 2018; 46:997-1000.*

Background

- Even though they were developed separately from the guidelines, "bundles" have been central to the implementation of the SSC even from the very first publication in 2004
- Bundles were designed to be updated as new evidence was published on the care of patients with sepsis
- Current evidence has demonstrated *an association* with bundle compliance and improved survival in sepsis and septic shock
- In the US, bundles adopted by the NQF, NY State Department of Health, and CMS
- In response to the SSC 2016 Update, a revised **1-hour bundle** has been developed

Important Points

- The 3-hour and 6-hour bundles have been combined into the 1-hour bundle
- "Time zero" is the time of triage in the ED!
- Evaluation and resuscitation should begin "immediately"
- May take more than 1 hour to complete resuscitation but should begin immediately

1-Hour Bundle

- Measure lactate level. Re-measure if initial lactate is > 2 mmol/L
- Obtain blood cultures prior to antibiotic administration
- Administer broad-spectrum antibiotics
- Begin rapid administration of 30 ml/kg crystalloid for hypotension or lactate >= 4 mmol/L
- Apply vasopressors if patient is hypotensive during or after fluid resuscitation to maintain MAP >= 65 mm Hg

2016 SSC Bundle Elements with Strength of Recommendations and Level of Evidence

- Measure lactate level. Re-measure if initial lactate > 2 mmol/L: **Weak** recommendation with **low** quality of evidence
- Obtain blood cultures prior to ABX: **Best practice statement**
- Administer broad-spectrum ABX: **Strong** recommendation with **moderate** quality of evidence

- Rapidly administer 30 ml/kg crystalloid for hypotension or lactate >= 4 mmol/L: **Strong** recommendation with **low** quality of evidence
- Apply vasopressors: **Strong** recommendation with **moderate** quality evidence

Lactate

- Not a direct measure of tissue perfusion but can serve as a surrogate
- RCTs have demonstrated reduction in mortality with lactate-guided resuscitation
- If elevated, should be followed every 2 to 4 hours to normalize lactate
- More to come…(below)

Blood Cultures

- Sterilization of cultures can occur within minutes of first dose of appropriate ABX
- Cultures "must be" obtained before ABX to optimize identification of pathogens and improve outcomes
- Try to get at least 2 sets (aerobic and anaerobic)

Broad-Spectrum Antibiotics

- Link between early administration of ABX for suspected infection and antibiotic stewardship remains critical aspect of sepsis care
- Give broad-spectrum ABX to cover all likely pathogens
- Should not be delayed in order to obtain appropriate cultures

Fluids

- Crucial for stabilization of sepsis-induced hypotension or septic shock
- Some evidence indicates a sustained positive fluid balance during the ICU stay is harmful, fluids beyond initial resuscitation requires careful assessment that patient remains fluid responsive

Vasopressors

- If BP not restored after initial fluid resuscitation, then pressors should be started within the first hour to achieve a MAP of >= 65 mm Hg

Our Thoughts…

- Does this make sense?
- Supported by the evidence?
- Feasible within 1 hour of ED triage?

Lactate Clearance…

Key Article

- *Hernandez G, Bellomo R, Bakker J. The ten pitfalls of lactate clearance in sepsis. Intensive Care Med. 2018. Epub online 5/12/18.*

Marker of severity

- Evidence that lactate is a marker of illness severity in situations of physiologic stress is overwhelming
- In sepsis, shown to be a powerful predictor of mortality
- Those with isolated hyperlactemia had 1.7 times the risk of 90-day mortality and were less likely to be DC'd from the ICU and hospital

Hyperlactemia - 4 Possibilities

- Anaerobic glycolysis in hypoperfused territories
- Stress-related adrenergic-induced aerobic glycolysis
- Impaired hepatic lactate clearance
- Mitochondrial dysfunction limiting pyruvate metabolism

- Aggressive resuscitation in non-hypoperfusion-related cases might lead to over-resuscitation

Production vs. Clearance

- Changes in lactate over time are generally thought to reflect changes in production
- Important to consider that ongoing hyperlactemia may actually be a decrease in clearance rather than increased production

Glucose Metabolism

- Lactate is a byproduct of glucose and pyruvate metabolism
- Any increase in glucose metabolism or decrease in pyruvate metabolism will increase lactate levels
- In sepsis, the inflammatory response appears associated with an increase in glycolysis and impaired pyruvate dehydrogenase
- The stress response alone increases glucose metabolism and lactate generation

Liver Dysfunction

- Liver is responsible for 60% of systemic lactate metabolism
- Liver is a vulnerable organ during sepsis-related acute circulatory dysfunction
- Contribution of the liver to hyperlactemia may be higher than previously thought

Resuscitation Fluids

- IV administration of LR doe not increase circulating lactate levels in hemodynamically stable adults, nor worsen metabolic acidosis
- Only when infusing large volumes (180 ml/kg/hr) may lactate levels rise slightly

A Substrate

- Lactate may also serve as a substrate for metabolism – provides a source of cellular energy

- Lactate released by muscle is taken up by the liver to enter the Cori Cycle to generate glucose, which through glycolysis may generate lactate
- May be metabolized by the kidney, accounting for up to 50% of lactate metabolism
- Lactate can be an important energy substrate for the brain; may be more important than glucose

Other Confounders

- Use of catecholamines in septic shock, lactate buffered continuous hemofiltration, and lung lactate production may increase levels
- Use of select medications (metformin, NRTIs for HIV, steroids) may increase levels, along with toxins such as ethylene glycol and methanol