Surviving the Sepsis Guidelines
GOLDILOCKS AND THE PANEL OF BEARS
GOLDILOCKS AND THE PANEL OF BEARS

Surviving Sepsis

Not too little….Not too much…

..........just the right amount
MY FOCUS

• Sepsis is a HUGE topic

  A. Physiology - everyone knows macrocirculation, so my focus is microcirculation.

  B. Quick and dirty summary of the 2017 guidelines for treatment
YOUR FOCUS

• Time is the-issue

• You will see sepsis in it’s early stages

• Post-op: bacteremia is unleashed in surgery

• Pre-op: people who have surgery tend to have something wrong with them.
EARLY TREATMENT

- Recognize sepsis - hypotension, tachycardia, tachypnia, fever, malaise, fatigue, confusion
- Look for suspected source of infection
- Non-specific, so not diagnostic
- Fix it while waiting for the physician
SURVIVING SEPSIS GUIDELINES

• Guidelines first published in 2004

EVIDENCE VS. GUIDELINES

• Evidence - outcomes from actual studies. $$$, labor intensive, involves ethics and boards, controlled numbers and types of patients. Perfect, if you live in a fairytale, Goldilocks.

• Guidelines - turning evidence into real world scenarios. Done by panels of bears, none of whom like the same thing.
HOW GUIDELINES ARE MADE

1. Determine the scope of guidelines
2. Selection of panel members
3. Topics and questions prioritization
4. Formulation of PICO questions and outcome prioritization
5. Systematic review
6. Certainty of evidence assessment
7. Recommendation formulation
8. Voting on final recommendations
MAKING GUIDELINES

• You will need a committee oversight group, the guidelines committee groupheads, the methodology group, the conflict of interest chair and the panel members.

• Then all you need is 80% agreement!
2017 GUIDELINES

We recommend the protocolized, quantitative resuscitation of patients with sepsis-induced tissue hypoperfusion. During the first 6 hours of resuscitation, the goals of initial resuscitation should include all of the following as a part of a treatment protocol:

a) CVP 8–12 mm Hg  
b) MAP ≥ 65 mm Hg  
c) Urine output ≥ 0.5 mL/kg/hr  
d) Scvo2 ≥ 70%.
PHYSIOLOGY OF SEPSIS

- NOT determined by a panel
- if you know physiology, you can roll with the changing guidelines
DEFINITION OF SEPSIS

Sepsis = life threatening organ dysfunction caused by dysregulated host response to infection

Septic Shock = subset of sepsis with circulatory and cellular/metabolic dysfunction associated with higher risk of mortality

Just like life - Host response to infection is the key!
PHYSIOLOGY OF SEPSIS

KEY POINTS

• Source of infection

• Bacteria - release endotoxin that trigger vasodilitation and leaky capillaries

• Viral - more complicated

• Host Response

• My focus - Hypoperfusion of the macro and microcirculation
MACRO**CIRCULATION

• Familiar. Tangible. Visible.

• CPR, art line, BP cuff, foley catheter, Swan-ganz catheter, vent, pulm edema, imaging studies, rectal tube, chest tube, jp drain, wound-vac, echo, surgery, level of alertness, physical exam….etc.
MACHINES THAT MEASURE MICROCIRCULATION

• None!
Microvascular Disarray - pathogenic factors of sepsis affects almost every cell - endothelial cells, smooth muscle cells; white, red and plasma blood cells; tissue cells.

If not corrected, disarray in the microvasculature will lead to “respiratory distress” or mitochondrial dysfunction in tissue cells which triggers a cascade that ends in organ destruction.
BLOOD VESSELS

- Tone - not too little
- Flow - not too much
- Patency - clots and leaks at the same time
ENDOTHELUM

- Endo - inside
- Thelium - layer of cell tissue
  - e.g. Onion skin

= cells that line every blood vessel in the body.
CAPILLARIES

- microcirculatory system

- blood vessels with walls that are one cell thick.

- any inflammation or loss of tone creates a leak

- low flow and low velocity - prone to leaking and clotting
Capillaries

Walls made up of one thin layer of cells which allow for rapid diffusion of materials from blood to surrounding tissue.

Materials exchanged:
- Gases: oxygen, carbon dioxide
- Nutrients & waste
Severe capillary leak

Early major clinical manifestations
- Hypotension, shock
- AKI
- +/- pleural effusion, pulmonary edema

**Treatment**
- Volume resuscitation with crystalloids utilizing a bolus approach to provide the minimum effective volume
- No response
  - Vasopressors
  - Consider albumin
  - Refractory shock
  - Hetastarch or pentastarch

**Supportive care**
- Disease-specific therapy
- Spontaneous recovery

Recovery phase or mild capillary leak

Clinical manifestations
- Stable blood pressure
- Systemic edema
- Pulmonary edema, pleural effusions
- Ascites

**Treatment**
- Loop diuretics
- Inadequate response
- Loop diuretics + 25% albumin
- Inadequate response
- Renal replacement therapy
MEASURING MICRO**CIRCULATION

- oxygen, CO2, lactate, SvO2, procalcitonin, CRP, white blood cell #, H/H, electrolytes, troponin leak - basically, send some labs.

- response of macro organs - looking for signs of end organ dysfunction

- Goal is to treat **BEFORE** we reach end organ dysfunction
MICROVASCULAR DISARRAY

- mitochondrial distress syndrome
  - = an organelle that lives in almost every cell and makes energy
- leaky capillaries
MIGHTY MITOCHONDRIA MOTOR

Mitocondria

Healthy Cell
- Produces LOTS of Energy
- Produces very FEW harmful Free Radicals

Un-healthy Cell
- Produces LITTLE Energy
- Produces LOTS of harmful Free Radicals
SURVIVING SEPSIS GUIDELINES
2017 TOPICS

1. Fluids
2. Lactate
3. Vasopressors
4. Hospital based policy of response
5. Steroids
6. Blood cultures and antibiotics
7. Mechanical ventilation
8. Glucose control
9. Bicarb use
10. Transfusion goal
11. Stress ulcer prophylaxis
EARLY TREATMENT

• Focus: #1 fluids #2 lactate and #3 vasopressors

• First line responders - you can give fluid and pressors and affect the early microvasculature cascade!!!!!
TIME IS THE-ISSUE

• 2004 guidelines set the goal of treatment within 6 hours (early goal directed therapy)

• Prevent end organ dysfunction

• Don’t wait 6 hours to address hypoperfusion!
  Fix it now.
#4 HOSPITAL BASED POLICY

Time is tissue

- Patient care and reimbursement $$$$
- Mortality rate - 20 years ago, used to be 30-50%, now it’s less
- Hospital death rate - 1 in 3 patients who die in a hospital have sepsis (says the CDC)
  - lung infection such as pneumonia 35%
  - kidney or UTI 25%
  - intestinal 11%
  - skin 11%
#1 FLUIDS

- **Pre** Surviving Sepsis: levophed was “leave ‘em dead” because we did not fluid resuscitate.

  ....... too little

- **2004** - early goal directed therapy was the buzz phrase, and it included a lot of fluid.

  ....... too much

- Revisions, including **2016** - give fluid and measure their fluid responsiveness

  .......just the right amount
#1 FLUIDS

- **Flow:** leaky capillaries = 3rd spacing, peripheral edema, ascites, pleural effusion, insensible losses (emesis, sweating, fever, increased metabolic demand). We are losing fluid, so we need more.

- **Tone:** bacterial endotoxin causes vasodilatation. Decreased tone means we need more fluid to fill the space.

- **Patency** - do not want thick blood, dilute is a little better
#1 FLUIDS

- by far the most complicated part of treating sepsis
- CVP was supposed to measure fluid status. It doesn’t.
- Goal is to limit hypoperfusion - both macro and micro
- SS Guideline Recs: 30cc/kg bolus over 3 hours (about 2L)
- Dilemma - we can’t see the micro, so bring in the lactate!
#1 FLUID RESPONSIVENESS

- **Too much?** hypoxia, pulm edema, increased work of breathing, swelling

- **Too little?** you have not fixed the hypoperfusion

- Just the right amount - you fix the hypotension, tachycardia, tachypnia, fever, malaise, fatigue, confusion
#2 LACTATE

- a measure of hypoperfusion of the microcirculation (patient care)
- a tangible that insurance companies can track (hospital reimbursement)
- don’t forget our other micro measures - send the labs!
- Elevated lactate can have many causes - it is NOT diagnostic
- higher lactate does correlate with higher chance of dying
- Recs: make sure the number is decreasing
#2 LACTATE

- to see a trend, you must have 2 points at least! If you order one lactate, order another.
#3 VASOPRESSORS

- 2 ways to fix hypoperfusion - fluids and vasopressors
- according to insurance, one way to measure it - the lactate!
#3 VASOPRESSORS

- **Tone**: bacteria cause vasodilatation. Fluid alone will not fix it.

- **Flow**: a large, floppy tube will have low flow - vessels need to be filled (fluid) and pressed.
CARDIAC OUTPUT

• Early phase of sepsis is INCREASED cardiac output, til it wears itself out.

• Decreased output is an example of end organ damage (we would like to prevent this with our early treatment!)
#3 VASOPRESSORS

- Physiology: alpha-receptors are located on blood vessels, beta-receptors are located on heart tissue. In sepsis, you need to increase tone (alpha) and increase cardiac output (beta, inotrope, chronotrope).

- Vasopressors are catecholamines (flight and fight)

- **Too little?** you must overcome the vasodililation response in sepsis

- **Too much?** you risk catecholamine toxicity and increased afterload
#3 VASOPRESSORS

- **Levophed/norepinephrine** = alpha and beta
- **Neosymphehrine/phenylephrine** = alpha
- **Vasopressin** = different mechanism, part of neurohormonal response. Synergistic.
- **Epinephrine** = lots of alpha and beta (bazooka)

  - Dopamine is not a pressor - it binds dopamine receptors. Dopamine receptors are mostly on the heart and just make it go faster.
  - Dobutamine is beta, so it is often helpful in the low cardiac output phase of sepsis = later phase.
#3 VASOPRESSORS

- Catecholamine toxicity - tachycardia, cardiac irritability, takustubo syndrome, troponin leak
#3 VASOPRESSORS

- Multi-modal therapy, *Synergistic*, limit toxicity
- Just like Hypertension - using more than one agent to raise MAP is better
- My preference - when levophed @ 10mcg/kg/min, add vasopressin
#3 VASOPRESSORS

- MAP goal is 65.

- Bad things happen if MAP < 55.

- “Permissive hypotension” was invented by surgeons, because patients bleed less.

- Exceptions:
  - dialysis - I will tolerate MAP 60.
  - chronic hypertensive - they probably need >> 65
ANTIBIOTICS

• Antibiotics should be given within ONE hour.

• do NOT delay treatment to order a test

• However, if antibiotics are given one minute before cultures, then the insurance companies can FAIL you and not pay for the entire treatment of sepsis.
STEROIDS

• constant discussion and disagreement

• Consensus - only use them if you really have to, i.e if all the above things aren’t working.

• Steroids are usually at least several hours into the treatment, so should be physician directed.
TRANSFUSION

- **Patency**: capillaries are low flow, low velocity so giving thick, cold blood is not ideal.

- Blood in a bag has little oxygen carrying capacity

- The dysfunction in sepsis is not the blood, or the lack of oxygen, it’s the endothelium and the tissue cells.

- Historically - heparin was trialed, then Xigris to deal with micro-clotting

- SS Guideline Recs: transfuse if Hb < 7
BICARB

• Guidelines say ok to give if pH < 7.15
• Common sense says pH < 7 would be better
• Bandaid - short lived, no overall benefit, masks the true acidosis which is how we measure our treatment goals
• Ok to give if you are in a pinch (it will bump the MAP while you get pressors)
• It will cause potassium shifts and it is hypertonic 8.3%
OTHER GUIDELINE RECS

• Mechanical Vent - use ARDSnet goal of 6ml/kg and plateau pressure < 30

• Glucose - goal < 180.

• Stress Ulcer prophylaxis - if on the vent > 48 hrs

• DVT prophylaxis - sepsis is a high risk, inflammatory state.
TREATING SEPSIS

1. Give fluids - not too much, not too little
   - official rec - 30 cc/kg bolus over 3 hours

2. Give pressors - earlier pressors in CHF, ESRD, later pressors in drunk, dehydrated, homeless person.
   - Peripheral line is ok until you have better access- minutes, not hours!
   - MAP > 65
   - levophed, vasopressin

3. Track the lactate for insurance companies and as a measure of your microcirculation

4. Time is the-issue: MAP< 55 is bad, for any time. Antibiotics within an hour!
TREATING SEPSIS

- Recall physiology - sepsis is disarray of microvasculature system - decreased tone of blood vessels, leaky capillaries, poor flow, poor patency — this is what causes the end organ damage

- End organ damage is at the end!

- Remove the source (often not possible, unless it’s a line infection or surgical emergency)