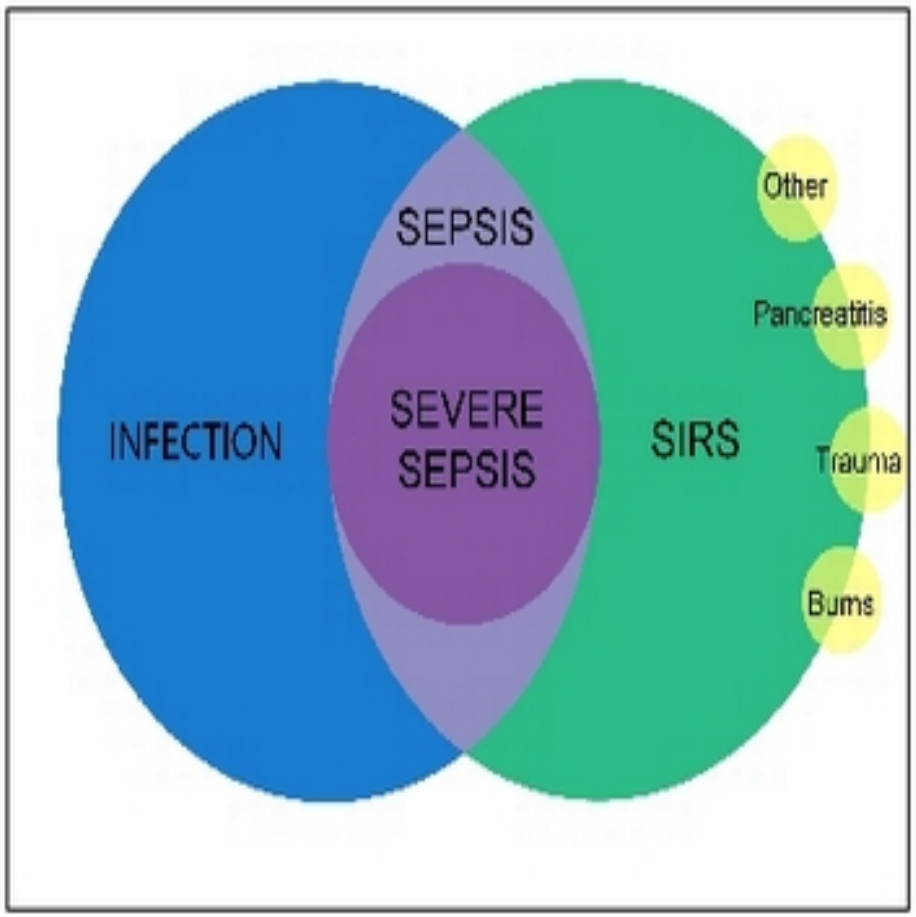
Sepsis, Severe Sepsis, and Septic Shock

Surviving Sepsis Campaign

Diagnosis: The Sepsis Continuum

- SIRS criteria:
  - 36°C < T > 38°C
  - RR > 20
  - HR > 90
  - 4,000 < WBC >

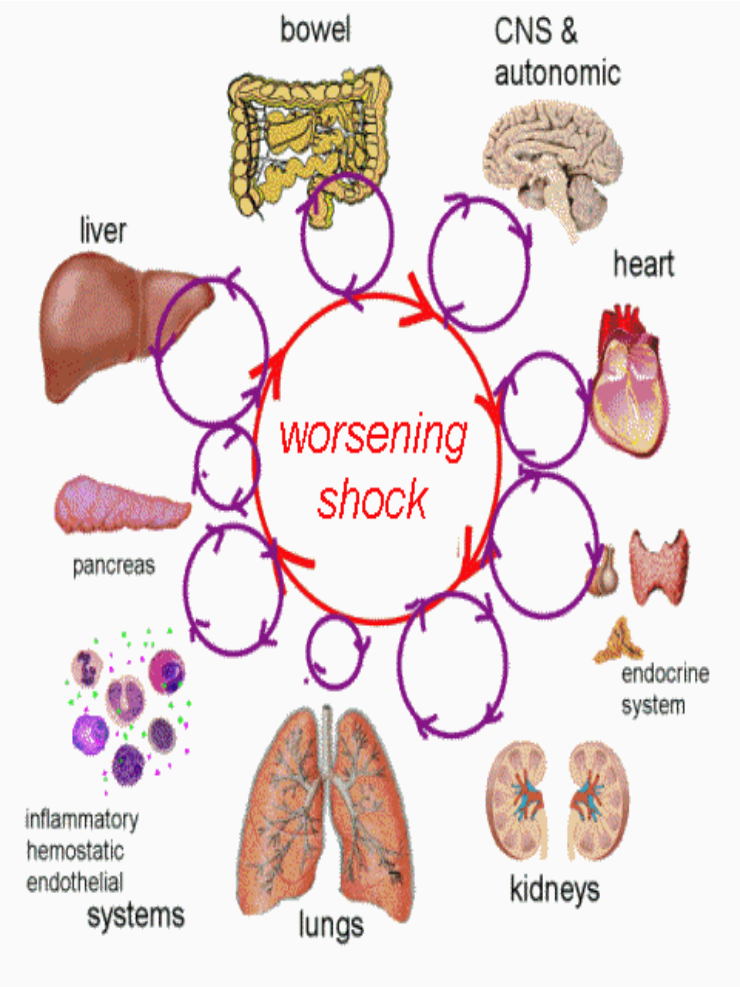


Severe Sepsis = Sepsis + Organ Dysfunction

- **Brain:** Encephalopathy
- **Lung:** Hypoxemia (P:F < 250 w/o PNA, P:F < 200 w/ PNA)
- **Cardiovascular:** Hypotension, elevated lactate, decreased capillary refill/mottling
- **Kidney:** Acute oliguria
- **GI:** Ileus, hyperbilirubinemia, liver dysfunction
- **Heme/Onc:** Coagulopathy, thrombocytopenia
- **Endo:** Hyperglycemia, adrenal insufficiency
- **Inflammatory markers:** Elevated procalcitonin or CRP

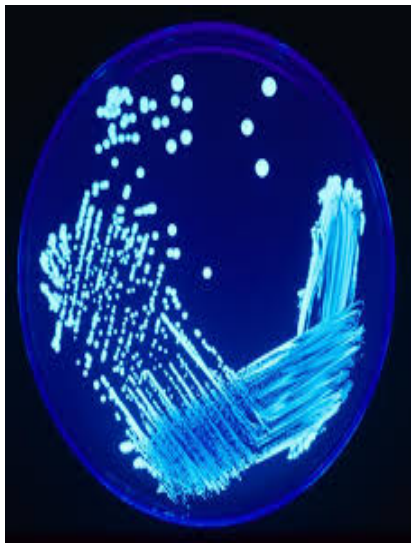
Septic Shock and Multi Organ Failure

- Septic shock can spiral out of control from the overwhelming inflammatory response and quickly progress to multi organ failure
- **Early infection control** is key to effective treatment, before refractory shock and complete cardiovascular collapse



Infection Control: Cultures and Imaging

- Cultures should be drawn before abx if this does not delay abx administration
  - Blood cultures
    - Percutaneous + each central line > 48h old
    - Anaerobic and aerobic
  - UA/culture, sputum, CSF, wound, pleural/peritoneal culture if indicated
  - Consider rapid influenza antigen testing during flu season
- Imaging studies to promptly confirm potential sources of infection



Infection Control: Empiric Antibiotics

- **Load** broad spectrum abx within **1 hour**
  - **Antibacterial: cover MRSA and GNR**
    - Consider resistance to extended-spectrum beta-lactams as well as carbapenems (both have surfaced in our hospital)
  - **Antifungal: high dose fluconazole or echinocandin**
    - Consider echinocandin if patient recently on antifungals, if Candida glabrata on previous cultures, or fungemia
    - Remember that echinocandins do not concentrate in the urine
  - **Antiviral: oseltamivir or zanamivir; acyclovir**
    - If Influenza A/B, start oseltamivir or zanamivir
    - If VZV or HSV, start acyclovir
    - If CMV – role in active infection causing organ injury is unclear without biopsy, but if present it is a bad prognosticator

Infection Control: Combination Therapy

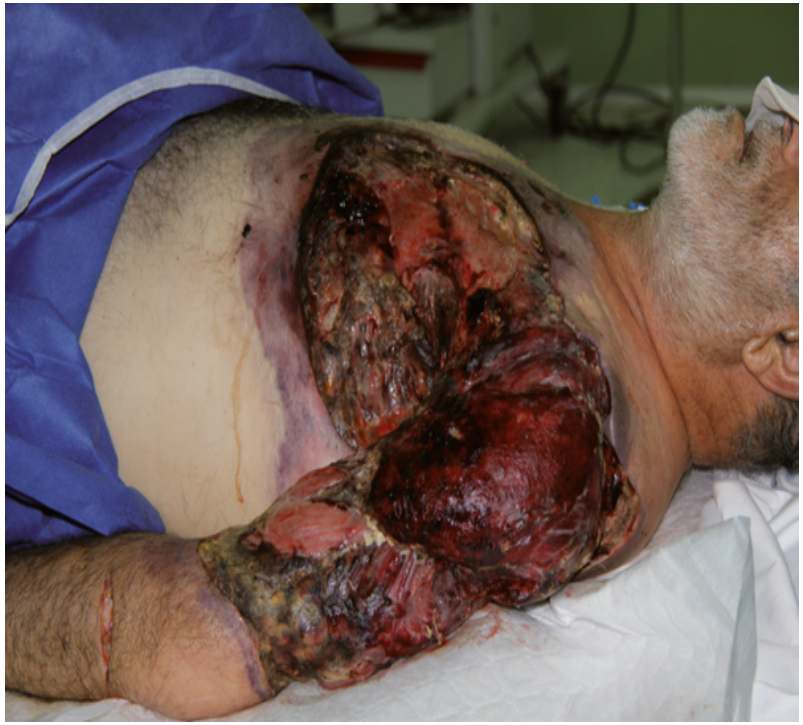
- In **neutropenic** patients with severe sepsis or MDR bacterial pathogens like **Acinetobacter** or **Pseudomonas**, start with **combination empirical** therapy
  - Increase the chance that your antibiotic will be sensitive to the microbe by using combination therapy
- In those with respiratory failure and septic shock with bacteremia
  - Pseudomonas: start combination empiric therapy with extended spectrum beta-lactam + AG or FQ active against Pseudomonas
  - Strep pneumo: start combination empiric therapy with beta-lactam + macrolide

Infection Control: Antibiotic Deescalation

- Reassess daily for de-escalation
  - **Deescalate to single therapy** when susceptibilities known (3-5d)
    - Except monotherapy with aminoglycosides for Pseudomonas
  - Treat for **7-10 days** unless there is slow clinical response, undrainable foci of infection, S aureus bacteremia, neutropenia, or some fungal/viral infections
- Do not give abx if SIRS is determined to be non-infectious
  - But keep in mind that 50% of the time, blood cultures will be negative despite bacterial or fungal infections being present
- May use low procalcitonin levels to support lack of infectious source
  - Procalcitonin has been used as a tool to d/c unnecessary abx

Infection Control: Source Control

- If there is an abscess, get imaging promptly and have it drained within 12 hours if possible
  - Use the least invasive route (percutaneous vs surgical)
  - Surgical intervention for necrotizing soft tissue infections and intestinal infarcts
  - Drainage of septic joints, empyemas (VATS)
- If central line is a possible source, start another line and remove the old one



Early Goal Directed Therapy

- Within the first **3 hours**:
  - Measure **lactate**
  - Obtain cultures prior to abx if possible
  - **Start broad spectrum abx (within 1 hour)**
  - Fluid resuscitation **30mL/kg crystalloids** if hypotensive or lactate ≥ 4
- Within the first **6 hours**:
  - Start vasopressors to keep **MAP ≥ 65** after IVF
  - If septic shock persists or initial lactate ≥ 4
    - Measure **CVP and ScvO2**
  - Trend lactates if initially elevated until normalized

Initial Resuscitation: What Kind of Fluid?

- Crystalloids vs colloids
  - Use crystalloids initially
  - **Do not use hetastarch**
  - Use albumin when need for crystalloids is substantial
- Blood products
  - If no tissue hypoperfusion, active MI, severe hypoxemia, or acute hemorrhage, **do not transfuse unless Hgb < 7**
  - If no bleeding or planned invasive procedures, **do not give FFP**
  - Give platelets prophylactically if
    - < 10 and not bleeding
    - < 20 and there is risk of spontaneously bleeding
    - < 50 if there is active bleeding, planned surgery or invasive procedures

Initial Resuscitation: How Much Fluid?

- Give up to **30 mL/kg of IVF** to replete hypovolemia and improve tissue perfusion
- Fluid challenges can be repeated as long as hemodynamics improve
  - Dynamic: pulse pressure or stroke volume variation
  - Static: SBP or HR
- Keep **UOP ≥ 0.5 ml/kg/hr**
- **Normalize lactate (10% every hour = 10% decreased mortality)**
- **CVP 8-12** (12-15 if intubated)

Hemodynamic Therapies: Vasopressors

- What type of vasopressor?
  - Start **NOREPINEPHRINE FIRST**
    - Add **EPINEPHRINE SECOND** (or substitute for NE) if NE not working
    - Add **VASOPRESSIN 0.03 u/min** to lower NE dose or if NE not working
  - **DO NOT**
    - Use DA instead of NE unless bradycardic
    - Use DA for “renal protection”
    - Use vasopressin by itself
    - Use phenylephrine by itself
- How much vasopressor?
  - Titrate to keep **MAP ≥ 65**

Hemodynamic Therapies: Inotropes

- How about inotropes?
  - Indicated for **myocardial dysfunction**
  - Indicated for **ongoing signs of hypoperfusion** despite adequate IVF and MAP
- What kind?
  - If you don't have a CO monitor, **add EPINEPHRINE**
  - If you have a CO monitor, **add DOBUTAMINE**
  - If RV dysfunction/pulm HTN/arrhythmias**, add MILRINONE**
- How much?
  - Titrate to **keep ScvO2 ≥ 70%**
  - Do not increase cardiac index to supranormal levels

Supplemental Therapies: Hydrocortisone

- Steroids can be used if **shock is refractory** to IVF and vasopressors – give **200 mg hydrocortisone infusion daily**
- Do not obtain ACTH stimulation test in those with septic shock to identify need for steroids
  - Random cortisol < 18 identifies those with absolute/primary adrenal insufficiency
- When pressors are weaned off, taper the steroids off
  - Study protocols differ in duration of treatment and taper, so no specific recommendations

Supplemental Therapies

- Mechanical ventilation will be discussed in ARDS topic
- Do not use IVIG or selenium, and recombinant APC is off the market
  - PROWESS study in 2011 showed no benefit
- Sedation, analgesia, and neuromuscular blockade
- Blood sugar control
  - Use a protocol to keep BS < 180 and start an infusion if BS > 180 x 2
  - Check BS on infusion every hour until stable, then every 4h
- Bicarbonate therapy if **pH < 7.15**

Supplemental Therapies

- Renal replacement therapy
  - CRRT and IHD are equivalent in AKI
- DVT prophylaxis
  - Use daily LMWH if good renal function or TID heparin
  - If CrCl < 30 ml/min, use dalteparin or heparin
- Stress ulcer prophylaxis
  - PPI is preferred, but H2 blockers ok
  - Risk factors: coagulopathy, mechanical ventilation > 48h, hypotension
- Nutrition
  - Start trophic feedings as tolerated within 48 hours x 1 week
  - Use D5 and tube feeds instead of TPN in the first week

Etomidate and Adrenal Insufficiency

- Etomidate is frequently selected for RSI in hemodynamically compromised patients
- Even after one dose, 11-β-hydroxylase is inhibited, leading to adrenal insufficiency by inhibiting conversion of 11-deoxycortisol to cortisol, which can have a particularly pronounced effect in septic shock
  - Lasts 72 hours and is reversible
  - Decreases cortisol, but is this clinically relevant?

Etomidate and Adrenal Insufficiency

- Bottom line: we need a good, high powered RCT with definitive evidence showing that etomidate increases mortality
- Uncertainty remains regarding the clinical significance because steroid replacement did not improve mortality
  - May suggest that increased mortality is not related to adrenal insufficiency
- In the mean time, it may be reasonable to continue using etomidate for its hemodynamic profile
- If the patient is already severely hypotensive and septic, it may be prudent to use ketamine or small doses of midazolam to secure the airway

Putting it All Together: Preop Assessment

- Identify the **etiology and severity** of sepsis using lactate, presence of organ dysfunction, and refractory hypotension
- Ensure that **proper antibiotics** have been given
- Ensure adequate ventilation, oxygenation, and hemodynamic support of patient during transport
- Ensure proper availability of IV pumps and monitors
- Confirm vascular access or prepare for placement
- Impress your attending with your robust plan

Putting it All Together: Intraop Plan

- Obtain adequate vascular access for IVF and vasoactives
- Initial **30ml/kg IVF** resuscitation
- Remember to use **dynamic measures** to evaluate fluid resuscitation/responsiveness as well as **ScvO2 and lactate**
- Remember to **start norepinephrine first, followed by epinephrine and/or vasopressin**
- Add **steroids** if shock still refractory
- Slow down IVF when fluid resuscitated with normal SVV, lactate, and ScvO2
- Keep UOP adequate and **do not give diuretics** if in shock
- Hold off on loading that epidural for now

Putting it All Together: Intraop Plan

- Remember, patients who are at risk for or already have ARDS should have some PEEP on board
  - Will discuss other ARDS management later
- If the blood sugar is > 180, treat it with insulin, and if still uncontrolled in one hour, start an insulin drip and check sugars every hour to avoid hypoglycemia
- Make sure that antibiotics scheduled to be given while in the OR do not get missed
- Update your attending frequently

Putting it All Together: Postop Care

- Is your patient better now, just as sick or worse – is the source now controlled?
- Consider safe transport of patient including ventilator, pressors/pumps (don't leave them in the OR), monitors, and emergency supplies
- Give good sign out to the ICU resident because the surgery resident probably has no idea what happened
- Ask your attending nicely to help you transport ☺