Sepsis and Septic Shock in the Emergency Department

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Disclosure

I have no financial interests or relationships to disclose.
Objectives

- Review the definitions of sepsis and septic shock
- Review the pathophysiology of sepsis
- Understand the clinical presentation of a septic patient
- Review screening tools used in the ER to identify potential septic patients
- Understand the immediate evaluation/management of a septic patient
- Understand the necessary diagnostic tests (labs/imaging) to diagnose sepsis and identify source.
- Review a case study

How we need to think about sepsis...

SEPSIS IS A MEDICAL EMERGENCY
ANY INFECTION CAN LEAD TO SEPSIS
Sepsis

Sepsis-3 (Out with SIRS and in with SOFA)

- Sepsis-2 defined 2 or more SIRS criteria (fever/hypothermia, tachycardia, tachypnea, leukocytosis/leukopenia) plus a source of infection
  - Not specific/sensitive enough
  - In 2016, this definition was changed to Sepsis-3
- Sepsis is now defined as life-threatening organ dysfunction caused by dysregulated host response to infection
  - Nebraska Medicine: Suspected/confirmed infection and evidence of new end organ dysfunction.
    - Lactate >2
    - Bilirubin >2
    - Creatinine >2
    - Platelet count < 100

Septic Shock

Sepsis-3

- Septic shock is defined as sepsis with circulatory and cellular/metabolic dysfunction associated with higher risk of mortality
  - Nebraska Medicine: Sepsis 3 criteria plus
    - Lactate ≥ 4 or
    - Hypotension (SBP <90, MAP <65)

- Mortality with sepsis is approximately 10 percent but when shock present it increases to approximately 40 percent.
### Pertinent Facts

**Sepsis Alliance (sepsis.org)**

- Sepsis is the leading cause of death in US hospitals.
- 270K patients die from sepsis every year in the US – one every 2 minutes.
- Mortality from sepsis increases by as much as 8% for every hour that treatment is delayed. As many as 80% of sepsis deaths could be prevented with rapid diagnosis and treatment.
- Approximately 6% of hospital admissions are due to sepsis and 35% of all deaths in-hospital are due to sepsis.
- More than 75K children develop severe sepsis each year and 6800 of these children die, more than from pediatric cancers.
- More than 40% of US adults have NEVER heard of sepsis.

### Pathophysiology

- The normal immune response to an infection is a balance between proinflammatory mediators and anti-inflammatory mediators. This inflammatory process kills the invading bacteria, removes the remaining debris from injured tissue and if anti-inflammatory mediators are in balance, healing begins, and homeostasis is restored.

- Sepsis occurs when the release of proinflammatory mediators in response to infection exceeds the boundaries of the local environment which leads to a more generalized inflammatory response.
Pathophysiology

The over exaggerated response

• The pathogen (bacteria, virus, fungi) invades the body, and an immune response is activated.
  • Macrophage, monocytes, neutrophil activation
  • As the immune cells are fighting off the pathogen, they release cytokines and inflammatory mediators.
  • These inflammatory mediators and cytokines act on the endothelium to cause vasodilation and increased vascular permeability.
    • Endothelium releases nitric oxide (Vasodilation)
    • Intravascular fluid leaks into interstitial space (Hypovolemia)
    • Vasodilation + Hypovolemia = Hypotension
  • Inflammatory mediators/cytokines activate the coagulation and fibrinolytic system which become imbalanced.
    • Widespread thrombin form in microcirculation which impede blood flow.
  • This all results in decreased perfusion and oxygenation of tissues and end organs.
  • Organ dysfunction begins and eventual organ failure develops if the process is not intervened.
Pathophysiology

NO organ system is protected from the effects of sepsis.

- Circulation
  - Hypotension due to vasodilation and redistribution of intravascular fluid.
  - Cardiac output initially increases to help compensate for decreased oxygen supply, but cardiac output will begin to fail as shock sets in.
  - Inability to appropriately distribute systemic blood flow among organ systems.
  - Decreased function of capillaries leading to inability to extract oxygen efficiently and remove carbon dioxide.
Pathophysiology

Organ system effects from sepsis

- Lungs
  - Pulmonary vascular injury negatively impacts capillary blood flow and enhances permeability resulting in pulmonary edema.
  - ARDS
- GI
  - Circulatory abnormalities can possibly depress the gut’s normal barrier function. This can lead to translocation of bacteria and endotoxin into systemic circulation worsening sepsis.

Pathophysiology

Organ system effects from sepsis

- Liver
  - Liver dysfunction can lead to inability to detoxify and eliminate bacteria and endotoxin from the gut.
  - Impairment in the coagulation system leading to bleeding and DIC. When DIC is present, mortality increases significantly.
- Kidney
  - Acute renal failure is often seen in sepsis. Causes may be multifactorial including hypotension, direct renal vasoconstriction and release of inflammatory mediators.
Pathophysiology

Organ system effects from sepsis

- Nervous system
  - The most common CNS complication is encephalopathy and can be seen before signs of organ failure.
  - The blood brain barrier is most likely impaired allowing exposure of proinflammatory and toxic mediators.
  - Possible hypoxic injury due to coagulopathy.
  - Parasympathetic nervous system may be a mediator of systemic inflammation during sepsis.
Risk Factors

Anyone affected by an infection can progress to sepsis, but these patients are at higher risk:
- Older patients (65 or older)
- Hospitalized patients (ICU patients)
- Patients with a history of sepsis
- Patients with autoimmune disorders (i.e. diabetes, etc.)
- Patients with cancer
- Patients on immunosuppressive medications
- Pregnant or recently pregnant patients
- Patients with kidney disease, cirrhosis, or who have had their spleen removed
- Patients with HIV/AIDS
- Children younger than 1

Screening Tools for the ED

Early identification of sepsis using systemic screening tools can be helpful in early diagnosis and rapid intervention.

Screening tools have been studied and all have been shown to have benefits and limitations. However, along with sound clinical judgement, using a combination of the screening tools available can be very effective.
Screening Tools for the ED

qSOFA (quick Sequential Organ Failure Assessment)

- This is a modified version of the SOFA that is typically used in the ICU setting.
- The qSOFA is quick and easy and incorporates only 3 components. A score of 2-3 is associated with poor outcomes due to sepsis
  - Respiratory rate ≥ 22 breaths/minute
  - Altered mentation (GCS ≤ 13)
  - Systolic BP ≤ 100 mmHg
- It can also be repeated serially when there is change in clinical condition
- Used on patients ≥ 18 years of age

Screening Tools for the ED

SIRS criteria (Systemic Inflammatory Response Syndrome)

- SIRS is a clinical syndrome from dysregulated inflammation and can be seen in noninfectious conditions including autoimmune disorders, pancreatitis, thromboembolism, burns or surgery
- A score of ≥ 2 meets SIRS criteria (along with a suspected infection source would indicate sepsis)
  - Temp > 38°C or < 36°C
  - Heart rate > 90
  - Respiratory rate > 20 or PaCO2 < 32
  - WBC > 12,000 or < 4000 or > 10% bands
Screening Tools for the ED

**NEWS (National Early Warning Score)**

- Can be used for initial assessment and serial monitoring
- Used on patients ≥ 16 years of age
- This is an aggregate scoring system looking at 6 parameters:
  - Respiration rate
  - O2 SAT
  - SBP
  - Heart rate
  - Level of consciousness
  - Temperature
- 0-4 (low risk), 5-6 (medium risk), 7 or more (high risk)

Screening Tools for the ED

**SEWS (Sepsis Early Warning System)**

- At Nebraska Medicine, integrated in our EMR is a BPA (best practice alert) that analyzes numerous data points in a patient’s chart to identify patients who are at elevated risks of developing sepsis/septic shock. An alert is made to the patient’s nurse who is then directed to follow the appropriate protocols including notifying the physician/APP.
Clinical Presentation

- Symptoms and signs specific to an infectious source
- Hypotension
- Temperature > 38.3 or < 36 C
- Heart rate > 90 BPM or more than two standard deviations above normal value for age
- Tachypnea, respiratory rate > 20 breaths/minute
- Signs of end-organ damage
  - Pale skin, decreased capillary refill, mottling
  - Altered mental status
  - Oliguria/anuria
  - Ileus

Surviving Sepsis Campaign (SSC)

From the SSC website

- SSC is a joint initiative of the Society of Critical Care Medicine and the European Society of Intensive Care Medicine, who are committed to reducing mortality and morbidity from sepsis and septic shock worldwide.

- The SSC is led by multidisciplinary international experts committed to improving time to recognition and treatment of sepsis and septic shock, which are leading causes of death worldwide.

- The SSC published a revision to the bundle based on the 2016 guidelines. The bundle changed from 3 hours and 6 hours to Hour-1 to encourage more rapid interventions for adult patients with sepsis and septic shock.
  - Shortening the time to treatment acknowledges the urgency that exists for patients with sepsis and septic shock.
  - Not all elements may be accomplished in 1 hour
Immediate Evaluation/Management

- ACLS protocol
- Stabilize respiration
  - Supplemental oxygen
  - Consider intubation/mechanical ventilation if there are signs of increased work of breathing or if their level of consciousness is so that they are unable to protect their airway.
- Establish venous access
- Obtain an initial brief history and examination which will help determine suspected source of infection and direct empiric antibiotics and additional testing.

Immediate Evaluation/Management

*Do not let this delay resuscitative efforts*

- While venous access is being established, obtain labs.
  - CBC with differential, CMP and coagulation studies. These will help to determine severity of sepsis and provide a baseline to follow how therapy is working.
  - Serum lactate – an elevated lactate (>2) may indicate severity of sepsis and is used to follow response to therapy.
  - Peripheral blood cultures (aerobic/anaerobic from 2 different sites) which will focus in antibiotic treatment
  - ABG – will identify hypoxemia or hypercapnia and may reveal acidosis
  - Procalcitonin
  - Coagulation studies (INR, D-dimer, TEG, etc.)
  - Later labs after patient is stabilized could include UA with culture, wound cultures and CSF.

- Obtain appropriate imaging for suspected site of infection (X-ray, CT, ultrasound, etc.)
Initial Therapy

IV fluids

- IVF are crucial in the initial management of sepsis to correct hypovolemia and help improve tissue perfusion.
- Crystalloid fluids (typically lactated ringers or normal saline) should be given at 30 mL/kg and started within the first hour of presentation.
- Fluid therapy should be administered in well defined, rapidly infused boluses (500mL or 1000mL)
  - Closely monitor hemodynamic response to boluses as well as signs of pulmonary edema. A MAP of ≥ 65 is ideal.
- Example: Your patient weighs 70 kg (30 ml/kg)
  - 30 x 70 = 2100 mL
  - Administer 2100 mL of crystalloid fluid rapidly starting within the 1st hour.

Initial Therapy

Application of Fluid Resuscitation in Adult Septic Shock

Sepsis-induced hypotension or lactate ≥ 4 mmol/L

- Pneumonia or AU with high flow oxygen requirements
- ESRD on hemodialysis or CRF

No high flow oxygen and No ESRD on dialysis or CRF

- Liquid infusion of 30 mL/kg crystalloid

Consider intubation/mechanical ventilation to facilitate rapid crystalloid infusion

- Indicated/ mechanically ventilated
- Rapid infusion of 30 mL/kg crystalloid

Considerations post 30mL/kg crystalloid infusion

1. Continue to balance fluid resuscitation and vasopressor dose with attention to maintain tissue perfusion and minimize ileal edema
2. Implement care coordination of the ICU to ensure a full resuscitation course that may include additional fluid or vasopressor therapy
3. Consider monitoring for heart rate response
4. Urine output
5. Cardiac output (ultrasound)
6. CRP, SOFA
7. Pulse pressure variation
8. Lactate clearance/hemoglobinization
9. Dynamic measurement such as response of flow to fluid bolus or passive leg raise

Total of 30 mL/kg with frequent reassessment of maintenance
Initial Therapy

What if initial fluid resuscitation fails?

- If patient is not responding to adequate fluid resuscitation and hypotension persists or if pulmonary edema develops, vaspressors should be added to the treatment. Don’t hesitate to start a vasopressor!
- The typical first agent used is norepinephrine.
- Vasopressin or phenylephrine if the patient has persistent tachyarrhythmia that may worsen their medical condition.
- Epinephrine and dopamine is an option if the patient has significant bradycardia.
- Multiple vasopressors may be needed
- Vasopressor use can be started in a peripheral IV typically at lower doses, but prolonged use of vasopressors will need to run through a central line. Also, an arterial line will need to be placed to monitor hemodynamics.

Initial Therapy

Antibiotics

- Empiric antibiotics need to be started within the first hour of presentation based on the suspected site of infection.
- Other considerations when choosing antibiotics include; prior culture results, recent antibiotic use, comorbidities of the patient, community v. healthcare-acquired, immune deficiency and allergies.
- The antibiotics need to be broad spectrum and should cover gram negative and positive bacteria as well as anaerobes. Usually, more than one antibiotic is used from a different class.
- Consider antifungal coverage if it is highly suspected or if neutropenia is present.
- Utilize the Hospital Pharmacist! They are a great resource!
Initial Therapy

Antibiotic regimen based on source at Nebraska Medicine

• Intra-abdominal: Piperacillin/tazobactam or Cefepime plus Metronidazole +/- Gentamycin
  • If severe beta-lactam allergy: Vancomycin plus Aztreonam plus Metronidazole
• Urinary tract: Ceftriaxone +/- Gentamicin
  • If severe beta-lactam allergy: Aztreonam plus Gentamicin
• Skin/Soft infection: Vancomycin or if MRSA is not suspected Oxacillin/nafcillin
• Necrotizing skin/soft tissue infection: Vancomycin plus piperacillin/tazobactam +/- Clindamycin (only if shock present)
  • If severe beta-lactam allergy: Vancomycin plus Aztreonam plus Metronidazole +/- Clindamycin (only if shock present)

Initial Therapy

Antibiotic regimen based on source at Nebraska Medicine

• CAP: Ceftriaxone plus Azithromycin
  • If severe beta-lactam allergy: Levofloxacin
• CAP with risk factors for resistance: Cefepime plus Azithromycin +/- Vancomycin
  • If severe beta-lactam allergy: Levofloxacin plus Aztreonam +/- Vancomycin +/- Tobramycin
• HAP: Vancomycin plus Cefepime +/- Tobramycin
  • If severe beta-lactam allergy: Vancomycin plus Aztreonam +/- Tobramycin
• Unknown source/Catheter related: Vancomycin plus Cefepime +/- Tobramycin
  • If severe beta-lactam allergy: Vancomycin plus Aztreonam +/- Tobramycin
Initial Therapy

Other considerations

- It is important to be thinking early in the course of treatment on where your patient will need to go when leaving the ER (ICU v step down v floor) and what consults will be needed to address the source of infection especially if a procedure/surgery is needed (Interventional Radiology, General Surgery, GI, Urology, etc.)

- If you are in a critical access hospital, most likely you will need to start think about transferring your patient to a hospital with the resources necessary to treat your patient as well as how you will transfer your patient (ground v air, time needed to get a transfer completed, etc.)

Other considerations

- Source control (physical measures to eradicate a focus of infection and prevent spread) should be done in a timely manner. This is important to keep in mind when contacting consults.
- Source of infection may not respond to antibiotics alone and will need to be drained, debrided or surgically removed
- Examples of some surgical/procedures
  - Soft tissue debridement or amputation (necrotizing fasciitis)
  - Abscess drainage (empyema, infected joint, cutaneous abscesses, intraabdominal abscess, etc.)
  - Removal of infected implantable devices/hardware and vascular access lines
  - ERCP
  - Cholecystectomy
  - Bowel resection for obstruction or perforation
  - Decompression for obstructing nephrolithiasis
Initial Therapy

Targets of resuscitation in the ER

- Successful completion of 1-hour bundle
- MAP ≥ 65 with fluid resuscitation +/- vasopressor
- Improvement in heart rate
- Broad spectrum antibiotics started within 1 hour of presentation
- Urine output at > 0.5 mL/kg/hour, reassuring but not necessarily a reliable indicator
- Good mental status/improved mental status

Pediatric systemic inflammatory response syndrome vital signs and laboratory values by age

Pediatric SIRS when ≥ 2 of these parameters are met

<table>
<thead>
<tr>
<th>Age group</th>
<th>Heart rate (beats/minute)</th>
<th>Respiratory rate (breaths/minute)</th>
<th>Leukocyte count (leukocytes x 10^3/mm^3)</th>
<th>Systolic blood pressure (mmHg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Newborn (0 days to 1 week)</td>
<td>&gt;180 &gt;120 &lt;50 &gt;54</td>
<td>&lt;50</td>
<td>≥10.5 or &lt;5</td>
<td>&lt;59</td>
</tr>
<tr>
<td>Neonate (1 week to 1 month)</td>
<td>&gt;180 &gt;120 &lt;40 &gt;19.5 or &lt;5</td>
<td>&lt;40</td>
<td>≥10.5 or &lt;5</td>
<td>&lt;79</td>
</tr>
<tr>
<td>Infant (1 month to 1 year)</td>
<td>&gt;180 &lt;90 &lt;14 &gt;17.5 or &lt;5</td>
<td>&lt;14</td>
<td>≥10.5 or &lt;5</td>
<td>&lt;75</td>
</tr>
<tr>
<td>Toddler and preschool (&gt;1 to 5 years)</td>
<td>&gt;140 NA &lt;22 &gt;15.5 or &lt;6</td>
<td>&lt;22</td>
<td>≥10.5 or &lt;6</td>
<td>&lt;74</td>
</tr>
<tr>
<td>School age (&gt;5 to 12 years)</td>
<td>&gt;120 NA &lt;18 &gt;13.5 or &lt;4.5</td>
<td>&lt;18</td>
<td>≥10.5 or &lt;6</td>
<td>&lt;90</td>
</tr>
<tr>
<td>Adolescent (&gt;12 to &lt;18 years)</td>
<td>&gt;110 NA &lt;14 &gt;11 or &gt;4.5</td>
<td>&lt;14</td>
<td>≥10.5 or &lt;6</td>
<td>&lt;90</td>
</tr>
</tbody>
</table>
Immediate Evaluation/Resuscitation

- As with adults, evaluation and treatment (airway, IV/IO access, fluid resuscitation, labs, broad spectrum empiric antibiotics, etc.) needs to be completed within the first hour of presentation.
  - Additional labs include POC blood glucose for hypo/hyperglycemia and serum ionized calcium. Replace if low. Neonates ≤ 28 days will need CSF
  - Fluid resuscitation with LR (or NS) at 10-20 ml/kg infused over 10 minutes. Monitor for hemodynamic response and signs of pulmonary edema after each bolus. May require 60mL/kg in the first hour. If not responsive, may require vasoactive therapy (epinephrine or norepinephrine)
  - Consult pediatric intensivist immediately!

Case Study

A 68-year-old male presents to the ER by EMS for complaints of weakness and poor appetite for the last 4 days. He lives at home with his son and the son told EMS that his dad seemed a little confused over the last day. Pt states he had recently stopped a 40-day course of antibiotics for a “gut infection”. He has a h/o COPD and has had 2 exacerbations over the last year requiring antibiotics. In addition, patient endorses subjective fever, chills and mild testicular pain. No other complaints. Other medical history includes HTN. Patient smokes a pack a day and drinks about a 6-pack of beer daily.

Vitals on arrival: T 101.4 (38.6 C), SBP 98, HR 110, RR 22, SAT 94% GCS 15

Before your physical exam, what are your initial thoughts? qSOFA? SIRS criteria? Initial interventions?
Case Study cont.

On physical exam, the patient appears pale and cachectic. Lungs sounds rhonchi throughout, heart rate is tachycardic, but regular, capillary refill is 2 seconds, abdomen is benign, genital area shows an erythematous and swollen scrotum extending in the perianal area, neuro is intact.

Ok, so now what?
• What interventions do you want to start immediately?
• What labs and imaging do you want to help with diagnosis and further management?
• Is it time to start thinking about potential consults? Or transfer if you are in critical access hospital? What if you are in an Urgent Care?

Case Study cont.

• Labs: CBC shows an elevated WBC of 16 with 8 percent bands and platelet count of 98. Lactate is elevated at 3.6. Creatinine is 2.1 (baseline 1.3), BUN elevated but otherwise CMP is unremarkable. INR at 1.1. ABG shows slightly decreased PaO2 at 70, but otherwise normal. Urine shows no signs of infection but noted to be concentrated.
• Imaging/EKG: Chest X-ray shows no evidence of infection or edema. CT abdomen/pelvis shows evidence of necrotizing fasciitis and Fournier’s gangrene and a perirectal abscess. EKG shows sinus tachycardia, no ST changes
• Blood cultures have been drawn, what antibiotics do you want to start?
• Who would you like to consult? Is this patient in need of an ICU?
• Our patient’s blood pressure is dropping to 85 systolic despite fluid resuscitation at 30 mL/kg. What should we do?
Case Study cont.

A few takeaways…..

• Make sure this patient is a high priority in the ER. Constant reassessment by nursing and yourself, q 15-minute vitals, telemetry, O2 SAT, etc.
• Make sure this patient is gowned during nursing assessment. Helps with a full body examination.
• Treating a septic patient is a team effort! EMS, nurses, aids/techs play a vital role!
• Suspecting sepsis is the first major step towards early recognition.
• Even if the primary admitting team has seen and admitted this patient, the patient is still yours until they leave the ER.

Nebraska Medicine Videos

On the NOW website under Sepsis Resources

https://vimeo.com/155851219 Suspect Sepsis

https://vimeo.com/262048721 Give’em 30
Sources


Nebraska Medicine Now Sepsis Resources Website https://now.nebraskamed.com/resources/sepsis/


Sources