EARLY RECOGNITION AND MANAGEMENT OF PEDIATRIC SEPSIS

OBJECTIVES

Upon completion of the presentation the learner will:

• Discuss the continuum of sepsis including Systemic Inflammatory Response Syndrome (SIRS), sepsis, severe sepsis and septic shock in the pediatric patient
• Explore new adult definitions of sepsis and how that may impact pediatrics
• Analyze lab results that are used to identify the severity and adequacy of treatment of sepsis/septic shock
• Summarize an evidence based recommended treatment plan for septic shock in the pediatric patient.

WE CAN MAKE A DIFFERENCE

07/11/2012
Source:
New York Times Online
About New York: An Infection, Unnoticed, Turns Unstoppable

EPIDEMIOLOGY

• Sepsis data may be incomplete for pediatric patients
• Globally it is estimated that infection causes about 60% of deaths in children under age 5.
• Severe sepsis in children continues to be a significant problem in US with over 72,000 annual hospitalizations
• Tenth leading cause of death in children in the US

EPIDEMIOLOGY

• Pediatric sepsis is usually community acquired (57%)
• Occurs most often in toddlers with median age of 3
• Most common infection site is respiratory
• 5-30% of pediatric patients with sepsis will develop septic shock
• Overall mortality rate is 4%-10% and as high as 24% for PICU admission

WE ARE MAKING A DIFFERENCE

In 1963, before the advent of neonatal and pediatric critical care medicine, a study of 900 infants at the University of Minnesota reported a 97% mortality rate in infants with gram-negative sepsis and septic shock.

In 1985, the Children's National Medical Center reported a 57% mortality rate in children with septic shock.

In 1991 the same center reported a 12% mortality rate when aggressive volume resuscitation was used.

2004-2012 data collected by CHA N= 636,842 pediatric patients, sepsis prevalence was 7.7% and mortality rate was decreased from 18.9% to 12% during that time period.
CASE PRESENTATION

3 yo male first presented to PCP with complaints of fever times 2 days, no evident source of infection. T-max 102, HR 122, RR 22 irritable. Strep neg, urinalysis WNL, diagnosed with viral syndrome. Sent home with instructions for viral syndrome (patient and his twin both have history of abscess MRSA+) no symptoms of abscesses currently. By evening patient still very irritable and febrile, father took to an outside ED (mom is out of town on a business trip) who then transferred to a local children's hospital related to fever/tachycardia and unknown source of infection. Presents by EMS from OSH with complaint of fever of 103, "sore all over" especially r shoulder. Patient has no other medical problems. Has had no noted injuries, has no co-morbidities. Upon arrival patient's vital signs were T 39.2, HR 124, RR 24, and B/P 106/70. Pt is alert but irritable with complaints of body hurting when asked to stand on scale. Capillary refill is < 2 seconds, skin flushed and peripheral pulses are 2+.

DEFINITIONS

- The definitions of sepsis and the continuum from infection through septic shock are evolving.
- The adult definitions were revised in 2016.
- Pediatric definitions have not yet been revised and still rely on the 2005 paper from Brill & Goldstein. Definitions will not change how we treat the disease but how we track, trend and research.

Evidence of infection includes positive findings on clinical exam:
- OR imaging or laboratory tests
  - white blood cells in a normally sterile body fluid
  - perforated viscus
  - chest radiograph consistent with pneumonia
  - petechial or purpuric rash or purpura fulminans

DEFINITIONS

- The 2016 task force recognized that sepsis is a syndrome without, at present, a validated criterion standard diagnostic test.
- Adult definitions (eliminated SIRS)
  - Sepsis - a life threatening organ dysfunction caused by a dysregulated host response to infection
  - Organ dysfunction - an acute change in total SOFA score > 2 points consequent to the infection
  - Septic Shock - A subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality
- Today we will use the current pediatric definitions of infection, sepsis, severe sepsis and septic shock.
- Will discuss the continuum from infection to septic shock.
**Systemic Inflammatory Response Syndrome (SIRS)**

- Occurs when the body’s inflammatory state is “revved up” in response to an insult.
- For SIRS must have the presence of at least two of the following 4 criteria (*one of them must be abnormal temp or leukocyte count).
  - Core temp of > 38.5 or < 36.
  - Tachycardia (or for children < 1 yo bradycardia).
  - Tachypnea (Respiratory rate > 2SD above normal for age)
  - Leukocyte count elevated or depressed for age (not due to immunosuppression therapy).

- SIRS is not always caused by infection may be attributed to non infectious processes such as trauma/burns/autoimmune responses.

**FEVER AND HEART RATES**

- How does fever affect heart rates in children?
- A study by Davies on 21,033 patients showed that for children the HR increased on average 10 BPM for each °C of temperature above normal.
- A study by Hanna et al on 490 patients < 1 year showed that in children 2mo-1 year the HR increased on average 9.6 BPM for each °C of temperature above normal.
- A study by Brent et al. showed that fever was a poor predictor of serious bacterial infection, however elevated HR had a stronger correlation.

**WHAT IS AN NORMAL HEART RATE?**

- PAL/APLS define tachycardia as a heart rate greater than or equal to the 98th percentile for age, as described in the Harriet Lane Handbook.

<table>
<thead>
<tr>
<th>AGE</th>
<th>Heart Rate</th>
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<tbody>
<tr>
<td>0-7 days</td>
<td>95-160</td>
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<tr>
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<td>50-110</td>
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<tr>
<td>&gt; 19 yrs</td>
<td>60-110</td>
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**PEDIATRIC SIRS VITAL SIGNS AND LAB VALUES**

The term sepsis is derived from the Greek word sepsis, which means to putrefy or make rot. SIRS- symptoms of the systemic inflammatory response syndrome (SIRS) that are attributable to documented or suspected infection. There are two components necessary, therefore, for the diagnosis of sepsis:

- Recognition of SIRS+ infection (suspected or definite).
CASE PRESENTATION

Does our patient meet the criteria for sepsis? Why or why not?

Reminder

WBC 20,000, platelets 160,000.

T- 38.6 (101.5), HR 138, RR 32 112/70. Patient quiet in bed answers questions readily

Sepsis = Recognition of SIRS+ infection

Ø Core temp of > 38.5 or < 36.
Ø Tachycardia (or for children < 1 yo bradycardia).
Ø Tachypnea (Respiratory rate > 2SD above normal for age)
Ø *Leukocyte count elevated or depressed for age (not due to immunosuppression therapy).

INFECTION SIRS Sepsis

Higher Risk for Sepsis

• Neonates, infants, and children who are hospitalized
• Those with indwelling devices or prosthetic material and other breaches in barrier protective function
• Serious Injuries (major trauma, penetrating wounds)
• Chronic debilitating medical condition
• Large surgical incisions
• In children the most common infections related to sepsis are respiratory and blood stream.
• In adults the four most common infections related to sepsis are pneumonia, GI track, skin and urinary tract

How would you assess for organ dysfunction (hypoperfusion)?

Goldstein Criteria for Organ Dysfunction

Cardiovascular
Despite administration of isotonic IV fluid bolus [AL Recru < 1.5 Hypotension (> 5% for age or systolic < 2 SD below normal) OR Need for vasodilator drug to maintain blood pressure in the normal range OR Two of the following: Metabolic acidosis Elevated arterial lactate > 2x upper limit of normal (2-18 years: 1.0-2.4 mmol/L) Oliguria Prolonged capillary refill time]

Respiratory
PaO2/FiO2 < 300 OR PaCO2 > 45 or 20 mm Hg above baseline OR Need for > 50% FiO2 to maintain oxygen saturation > 92% OR Need for non-elective mechanical ventilation

Neurologic
Glasgow Coma Scale ≤ 11 OR Acute change in mental status

Hematologic
Platlet count < 80,000/microliter OR A decline of 50% from the highest value recorded over the previous three days OR Disseminated intravascular coagulopathy

Renal
Serum creatinine > 2 times upper limit OR Need for dialysis therapy at presentation

Hepatic
Total bilirubin > 4 mg/dL OR Serum glutamic pyruvic transaminase > 2 times upper limit Lottstein (2001)

Severe Sepsis- Suspected or present infection, PLUS at least two out of four SIRS criteria (= sepsis) PLUS organ system dysfunction (per Goldstein criteria).
In other words Sepsis + Organ hypoperfusion
Must have two or more organ dysfunctions or cardiovascular dysfunction alone.

Organ Dysfunction-

• Renal
• Respiratory
• Hepatic
• Hematological
• Central nervous system
• Unexplained metabolic acidosis
• Cardiovascular
Clinical characteristics that relate to the severity of sepsis include:

- Host response to infection
- Site and type of infection
- Timing and type of antimicrobial therapy
- Offending organism (virulence)
- Development of shock
- Underlying disease
- Patient's long-term health condition
- Number of failed organs.

**CASE PRESENTATION**

Our patient now has the following vital signs/assessment:

- T-40 (104), HR 150 RR 36  B/P 102/58

He is irritable, crying his “body hurts” does not want to watch television and does not calm with father. He has an IV that was placed with the labs has received no other interventions. The nurse approaches the physician for more medications for pain and fever.

(by the way it is a VERY busy day in the ED)

**CARDIOVASCULAR DYSFUNCTION INDICATING SEPTIC SHOCK**

- Hypotension,
- Reliance on vasoactive drug administration to maintain a normal blood pressure

Or two of the following:

- Prolonged capillary refill,
- Oliguria,
- Metabolic acidosis,
- Elevated arterial lactate

**FACT**

- Refractory shock is the most common cause of death in severe pediatric sepsis (34%), followed by multiple organ dysfunction syndrome (MODS) after shock recovery (27%), neurologic injury (19%) and respiratory failure (9%).

- Septic Shock: Meet Severe Sepsis Criteria (Suspected or present infection, PLUS at least two out of four SIRS criteria (= sepsis) PLUS organ system dysfunction (per Goldstein criteria).

- PLUS has clinical signs of inadequate cardiac system function including inadequate tissue perfusion and/or hypotension despite fluid resuscitation.
WARM SEPTIC SHOCK

Septic shock is different than other shock states in that it initially appears as a “warm shock” state. Warm shock occurs as a result vasodilation due to release of compounds such as histamine and bradykinins which are produced during the inflammatory response.

The patient may have an elevated temperature, warm flushed skin, bounding pulses and profound diuresis.

COLD SEPTIC SHOCK

• As shock progresses and the body’s compensatory mechanisms fail, cardiac output fails, and stage of cold shock occurs. Hypo-perfusion leads to profound hypotension.

• This is an ominous sign

BODY’S RESPONSE TO SHOCK

VASCULAR RESPONSE

Hypotension is a late sign of shock in children.

Narrowing or widening pulse pressure, may be subtle earlier signs.

The formula for the lowest acceptable limit of systolic blood pressure in children 2 and older is 70+ (2x age in years).
VASCULAR RESPONSE

As volume decreases the peripheral blood vessels vasoconstrict. The arterioles constrict to increase total peripheral resistance and, ultimately blood pressure. The venous system vasoconstricts to improve venous return to the right atrium. This is what you would normally expect in a SHOCK state, However…

CEREBRAL RESPONSE

As shock progresses
• Primary goal of the body is to maintain perfusion of the brain, heart, and lungs.
• Alteration in LOC is a late sign of shock
  – May have decreased Glasgow coma score
  – Response to environment will change
    • Irritable, lethargic, agitated

ADRENAL RESPONSE (FIGHT OR FLIGHT)

• Adrenal glands are stimulated by the sympathetic nervous system.
• Increase in epinephrine and norepinephrine.
• Causes an increase in heart rate and to a small extent in children an increased in the force of cardiac contraction.

ADRENAL RESPONSE

Epi and Norepi cause vasoconstriction and ultimately increase blood pressure and perfusion. The signs of shock resulting from adrenal gland stimulation are:
• Tachycardia, increased anxiety, sweating
  “fight or flight”

PULMONARY RESPONSE

Anaerobic metabolism leads to lactic acidosis

Acidosis will be a stimulus for the lungs to increase the respiratory drive and rate of ventilation to maintain acid-base balance.
Toxins release by the offending organism may also cause profound tachypnea
LET’S TALK

What are some warning signs that pt may be at risk for or developing severe sepsis/septic shock?

- Recent history of trauma/illness
- Warmth, swelling, and/or erythema of an extremity or joint suggestive of osteomyelitis and/or septic arthritis
- Fever, tachycardia, and/or tachypnea
- History of HROD
- High risk populations
- Sickle cell
- Oncology
- Chronic illness
- Central lines
- Tachycardia not responsive to intervention (persistent tachycardia)
- Change in LOC or behavior
- BP with narrowed or widened pulse pressure

LET’S TALK

What are some typical symptoms/presentation for sepsis/severe sepsis? What would YOU recognize as severe sepsis?

- Fever
- Tachycardia
- Delayed capillary refill or flash refill
- Weak or bounding pulses
- Decreased LOC
- Mottled
- Petechiae

LET’S TALK

What are some atypical symptoms/presentation for severe sepsis/septic shock? What symptoms might not be on the radar?

- Irritable
- Change in personality
- Argumentative
- Inappropriate behavior for age
- "Just not acting right"
- Hypothermia
- Babies cry with holding or movement (Cry de Chat)
- Cold extremities vs warm core
- Symptoms of warm shock: widening pulse pressure, bounding pulses, flushed skin, flash refill
- Mucosal erythema with mucosal changes (eg, strawberry tongue and conjunctival injection) suggestive of toxic shock syndrome

CASE PRESENTATION

- The nurse reassesses the patient (has now been 4 hours since arrival)
  - HR 180, RR 40, B/P 88/40
  - Cap refill 4 seconds
  - Patient is seeing “pink elephants” and crying irritable.
- Physician is called to the room and patient is transferred to the critical care area
- Fluid resuscitation and antibiotic therapy is begun
- Pt is transferred to ICU and has a cardiac arrest after arrival
  - Is intubated and placed on ECMO
CASE PRESENTATION

Patient's blood culture grows MRSA after 4 hours (patient has history of an abscess with MRSA)

After 3 weeks in ICU and another week in inpatient our patient is discharged from the hospital. He is one of the lucky ones.

LABORATORY EVALUATIONS WITH SEPSIS/SEPTIC SHOCK

- “Recommended that early recognition of pediatric septic shock is by clinical examination, not biochemical tests”.
- There is no singular biomarker that has been determined to be diagnostic of sepsis

LABORATORY EVALUATIONS

- Blood Cultures
- CBC with diff
- VBG
- Electrolytes
- iCA and glucose
- Lactate
- Lytes

LABORATORY EVALUATIONS FOR OUR PATIENT

First laboratory evaluation from OSH Red Flags
Venous blood gas
pH 7.34
pO2 venous-45
pCO2 28
HCO3 20
BE -5
Serum Lactate- 2.6
CBC
WBC-6000
Hgb/hct- 11/33
Platelets 175,000

Second laboratory evaluation.
Venous blood gas
pH 7.02
pO2 venous 38
pCO2 33
HCO3 13
BE -10
Serum Lactate- 3.0
CBC
WBC-18,000
Hgb/hct- 10.5/30
Platelets 165,000
GOAL DIRECTED THERAPY

Resuscitation guided by goals
- Once septic shock has been recognized, the goals for the management of septic shock are:
  - Airway, oxygenation, and ventilation (increase oxygen delivery to the tissues)
  - Circulation
  - Threshold heart rate (i.e., heart rate that is neither too low nor too high to ensure adequate cardiac output)
  - Treat the underlying infection


GOAL DIRECTED THERAPY

Strive for
- B/P at 5th % for age 70+ 2X years in age
- Improving heart rate
- Capillary refill of <2 seconds
- Normal pulses with no differential between peripheral and central pulses
- Warm extremities
- Urine output >1 mL/kg/hr
- Normal mental status
- Superior vena cava or mixed venous oxygen saturation >70%
- Decreased lactate and increased Base deficit

Survival after Adjustment for Patient Severity

Every hour without appropriate resuscitation and restoration of capillary refill <2 s and normal blood pressure increases mortality risk by 40%! (Han et al Pediatrics 2003)

The transition from sepsis to septic shock occurs most often during the first 24 hours of hospitalization. It carries with it an increase not only in morbidity but also in mortality: 20%–46%

EVIDENCE BASED TREATMENT

TIME ZERO

Recognize decreased mental status and perfusion (cold, delayed cap refill, weak or bounding pulses) Begin High flow O2 and establish IV/IO access
Begin fluid resuscitation with 20 mL/Kg of isotonic crystalloids (up to 60 mL/Kg in one hour) until perfusion improves or rales/hepatomegaly occurs. Correct hypoglycemia or calcemia and begin antibiotics.

Blood pressure is not an adequate measure for assessment of adequate resuscitation. Treatment should be titrated by improved perfusion measured by increased urine output, level of consciousness, and capillary refill without inducing hepatomegaly or rales.

The first line of defense against septic shock is aggressive fluid resuscitation.

WHERE IS THE EVIDENCE?

**FLUID RESUSCITATION**

Fluid Resuscitation for pediatric septic shock is supported by few small studies. Most of the support is consensus based.

- **FLUID RESUSCITATION**
  - Rapid fluid resuscitation in excess of 40 mL/kg in the first hour following emergency department presentation was associated with improved survival, decreased occurrence of persistent hypovolemia, and no increase in the risk of cardiogenic pulmonary edema.

WHERE IS THE EVIDENCE?

**FLUID RESUSCITATION**

There have been questions of late by both adult and pediatric researchers about aggressive fluid resuscitation and the impact on morbidity and mortality for septic shock.

- **2015 version of PALS has this statement:** In specific settings, when treating pediatric patients with febrile illnesses, the use of restrictive volumes of isotonic crystalloids leads to improved survival. This contrasts with traditional thinking that routine aggressive volume resuscitation is beneficial.

WHERE IS THE EVIDENCE?

**VASOACTIVE AGENTS**

Double-Blind Prospective Randomized Controlled Trial of Dopamine Versus Epinephrine as First-Line Vasoactive Drugs in Pediatric Septic Shock.

Consecutive children who are 1 month to 15 years old and met the clinical criteria for fluid-refractory septic shock. Dopamine was associated with an increased risk of death and healthcare-associated infection. Early administration of peripheral or intraosseous epinephrine was associated with increased survival in this population. Limitations should be observed while interpreting these results.

WHERE IS THE EVIDENCE?

**ANTIBIOTICS FIRST HOUR**

Impact of time to antibiotics on survival in patients with severe sepsis or septic shock in whom early goal-directed therapy was initiated in the emergency department.

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Impact of time to antibiotics on survival in patients with severe sepsis or septic shock in whom early goal-directed therapy was initiated in the emergency department.
WHERE IS THE EVIDENCE? ANTIBIOTICS FIRST HOUR

Timing of Antibiotic Administration in Pediatric Sepsis.

Retrospective chart review for children 18 or younger presenting to tertiary care children’s ED over a period of 4 years that were ultimately diagnosed with septic shock. N=135. Conclusion - Children with criteria for sepsis who subsequently progressed to septic shock who received antibiotics within 1 hour of meeting sepsis criteria had increased mortality, length of stay and organ dysfunction.

REMEMBER

Not all patients who present with fever, tachycardia will spiral down to severe sepsis or septic shock. Early recognition and appropriate referral and treatment are key.

Always be aware of:
- Persistent tachycardia
- Changes in mental status
- Changes in perfusion
- Lack of response to therapy

PREVENTION

How can you help prevent sepsis?

Timely recognition and evidence-based interventions (within one hour) is the single most crucial step in sepsis management.

- Identify your high risk patients
- Prevent infection by following infection control practices
  - Hand hygiene,
  - Prevention of HACs
- Educate patients and families on sepsis and importance of completing antibiotic therapy
- Antibiotic prophylaxis
  - GBS

PREVENTION

- Immunizations
  - Rubella (German measles)
  - Varicella (chicken pox)
  - Haemophilus influenzae type b (Hib)
  - Pneumococcal vaccine

- We Can make a difference by prevention, recognition and timely intervention.

WHAT’S NEXT?

- Research is currently being conducted for pediatric sepsis
  - Definitions
  - Treatment
- Expected publication to be released soon through Surviving Sepsis Campaign
  - International Guidelines for Management of Sepsis and Septic Shock in Children

REFERENCES


REFERENCES


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