





Recognition and Treatment of Pediatric Sepsis

Pediatric Emergencies: Early Assessment & Treatment of Children

Rhea Vidrine, MD 9/28/21

The Joint Heart Program, a collaboration of Kentucky Children's Hospital and Cincinnati Children's, is jointly ranked by *U.S. News and World Report*.



Objectives

- At the end of this presentation, learners will be able to:
 - Appreciate the difficulty in defining and recognizing pediatric sepsis
 - Acknowledge the importance of standardized screening and management in pediatric sepsis
 - Initiate appropriate treatment in potentially septic patients



Adult Sepsis-3 Definitions

- Life-threatening organ dysfunction caused by a dysregulated host response to infection
 - Sequential Organ Failure Assessment (SOFA) change of ≥ 2 indicates organ dvsfunction
- Septic shock is the state in which profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone.
 - Clinical indicators include hypotension and hyperlactatemia

Clinical Features

Potential source of infection OR NEWS ≥4?

- Pneumonia
- Meningitis
- · Skin/soft tissue infection

- Empyema
- Infective endocarditis
- Bone/joint infection · Wound infection

- UTI
- CVC infection
- Other

- Acute abdomen
- New signs or symptoms of infection? TWO or more of the
- following:
- Temperature >38.3°C
- · Heart Rate >90bpm Altered mental state
- WBC <4x10⁹/L

- Temperature <36°C Respiratory Rate >20 bpm
- WBC >12x10⁹/L
- Blood glucose >7.7mmol/L
- Evidence of organ dysfunction remote to the site of infection? ONE of the following or SOFA ≥2 (see opposite):
- · Lactate >2mmol/L
- Systolic blood pressure <90mmHg OR Mean arterial pressure <65mmHg
- Systolic blood pressure >40mmHg below baseline
- Creatinine >175mmol/L OR urine output 0.5ml/kg/hour for more than 2 hours
- · Bilateral pulmonary infiltrates PLUS O2 required to keep O2 saturations >92%
- Bilateral pulmonary infiltrates PLUS PaO2/FiO2 ratio <300*
- Bilirubin > 34 mmol/L
- Coagulopathy INR >1.5 OR APTT >60 seconds
- Platelet count <100x10⁹/L

If YES to questions 1+2+3 = criteria for SEPSIS

Note: *PaO2 measured in mmHg (1kPa = 7.5mmHg), FiO2 as % converted into a decimal e.g. 32% = 0.32

Adapted from: Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock www.survivingsepsis.org

Schlapbach LJ, Kissoon N. Defining Pediatric Sepsis. JAMA Pediatr. 2018; 172(4):312-314.

What is Pediatric Sepsis?

- Pediatric sepsis definitions (2005)
 - <u>Sepsis</u> SIRS associated with infection (2/4 criteria, one of which must be abnormal temperature or leukocyte count):
 - Core temperature of > 38.5°C or < 36°C
 - Tachycardia or for children <1 yr old: bradycardia
 - Tachypnea
 - Leukocyte count elevated or depressed for age (not secondary to chemotherapy-induced leukopenia) or >10% immature neutrophils.
 - Infection: A suspected or proven infection caused by any pathogen OR a clinical syndrome associated with a high probability of infection.
 - <u>Severe sepsis</u> sepsis + cardiovascular dysfunction OR ARDS OR <u>></u>2 other organ dysfunction
 - <u>Septic shock</u> sepsis with cardiovascular dysfunction

2017 Pediatric sepsis updates

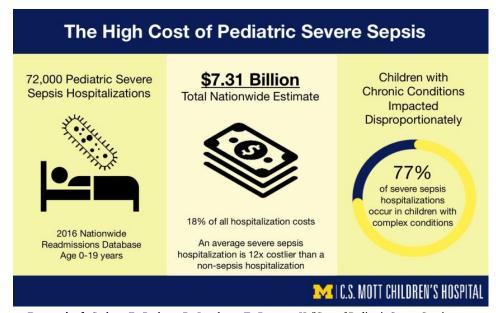
- Adult definitions attempted to be applied but never formally adopted
- Adaptations to create pSOFA
- >8 points associated with increased mortality



| | Score ^a | | | | | |
|---|--------------------|---------|---|----------------------------------|--|--|
| Variables | 0 | 1 | 2 | 3 | 4 | |
| Respiratory | | | | | | |
| Pao ₂ :Fio ₂ ^b or | ≥400 | 300-399 | 200-299 | 100-199 With respiratory support | <100 With respiratory support | |
| Spo ₂ :Fio ₂ ^c | ≥292 | 264-291 | 221-264 | 148-220 With respiratory support | <148 With respiratory support | |
| Coagulation | | | | | | |
| Platelet count, ×10³/μL | ≥150 | 100-149 | 50-99 | 20-49 | <20 | |
| Hepatic | | | | | | |
| Bilirubin, mg/dL | <1.2 | 1.2-1.9 | 2.0-5.9 | 6.0-11.9 | >12.0 | |
| Cardiovascular | | | | | | |
| MAP by age group or vasoactive infusion, mm Hg or µg/kg/min ^d | | | | | | |
| <1 mo | ≥46 | <46 | Dopamine hydrochloride ≤5 or dobutamine hydrochloride hydrochloride (any) hydrochloride >5 or epinephrine bitartrate ≤0.1 | | Dopamine hydrochloride >15 or epinephrine >0.1 or norepinephrine bitartrate >0.1 | |
| 1-11 mo | ≥55 | <55 | | | | |
| 12-23 mo | ≥60 | <60 | | | | |
| 24-59 mo | ≥62 | <62 | — (ally) | bital trate 20.1 | bital trace > 0.1 | |
| 60-143 mo | ≥65 | <65 | | | | |
| 144-216 mo | ≥67 | <67 | | | | |
| >216 mo ^e | ≥70 | <70 | | | | |
| Neurologic | | | | | | |
| Glasgow Coma Score ^f | 15 | 13-14 | 10-12 | 6-9 | <6 | |
| Renal | | | | | | |
| Creatinine by age group, mg/dL | | | | | | |
| <1 mo | <0.8 | 0.8-0.9 | 1.0-1.1 | 1.2-1.5 | ≥1.6 | |
| 1-11 mo | < 0.3 | 0.3-0.4 | 0.5-0.7 | 0.8-1.1 | ≥1.2 | |
| 12-23 mo | <0.4 | 0.4-0.5 | 0.6-1.0 | 1.1-1.4 | ≥1.5 | |
| 24-59 mo | <0.6 | 0.6-0.8 | 0.9-1.5 | 1.6-2.2 | ≥2.3 | |
| 60-143 mo | <0.7 | 0.7-1.0 | 1.1-1.7 | 1.8-2.5 | ≥2.6 | |
| 144-216 mo | <1.0 | 1.0-1.6 | 1.7-2.8 | 2.9-4.1 | ≥4.2 | |
| >216 mo ^e | <1.2 | 1.2-1.9 | 2.0-3.4 | 3.5-4.9 | ≥5 | |

Why is Sepsis Important?

- Sepsis is leading cause of pediatric mortality worldwide¹
 - 25% mortality rate for patients admitted to PICU
- Prevalence of severe sepsis has increased to 7.7%²
- 1/5th of sepsis survivors have a moderate disability¹
- Severe sepsis accounts for \$7.31 billion in healthcare costs³



Paper cited: Carlton, E., Barbaro, R., Iwashyna, T., Prescott, H. "Cost of Pediatric Severe Sepsis Hospitalizations" *JAMA Pediatrics*. DOI: :10.1001/jamapediatrics.2019.2570

What Does Pediatric Sepsis Look Like?

- Fever or hypothermia (<36°C or >38°C)
- Tachycardia or bradycardia if < 1yo
- Tachypnea
- Altered perfusion

 delayed capillary refill, mottled, poor pulses OR bounding pulses, flash capillary refill, flushed
- Hypotension → LATE SIGN

Pediatric sepsis can look like many other disease processes



Standardizing Pediatric Sepsis Care

Treating Pediatric Sepsis 2020

- Panel of 49 international experts provided 77 statements on management and resuscitation of children with septic shock and other sepsis-associated organ dysfunction
 - "In children who present as acutely unwell, we suggest implementing systematic screening for timely recognition of septic shock and other sepsis-associated organ dysfunction (weak recommendation, very low quality of evidence)."
 - "We recommend implementing a protocol/guideline for management of children with septic shock or other sepsis-associated organ dysfunction (BPS)."

Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children

Standardizing Pediatric Sepsis Care

- Surviving Sepsis Campaign and American College of Critical Care Medicine (ACCM) recommend implementing sepsis bundles to
 - Improve sepsis recognition
 - Increase efficacy of treatment
- Standardized care throughout the institution → improved recognition and treatment



Standardize Care for Sepsis: Sepsis Bundles

| Bundle | Elements |
|--------------------------------------|---|
| Recognition Bundle | Implementation of sepsis screening tool Rapid identification Prompt assessment |
| Resuscitation & Stabilization Bundle | Blood culture collection Prompt antibiotic administration Early rapid fluid bolus with crystalloid Early lactate measurement |
| Performance Bundle | Monitor and measure processesContinued improvement and sustainability |

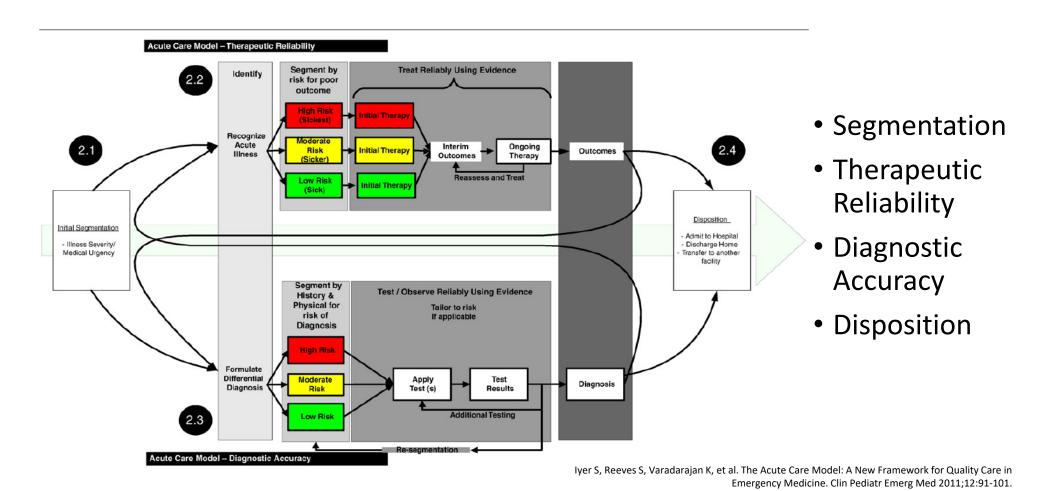
Why standardize care?

- Healthcare delivery has many characteristics of high-risk processes that increase the risk of failure:
 - Variable input
 - Complexity
 - Inconsistency
 - Tight coupling
 - Human intervention
 - Tight time constraints
 - Hierarchical culture

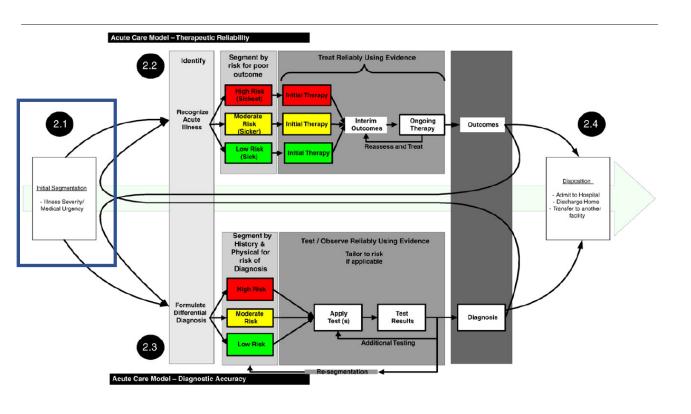


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Acute Care Model

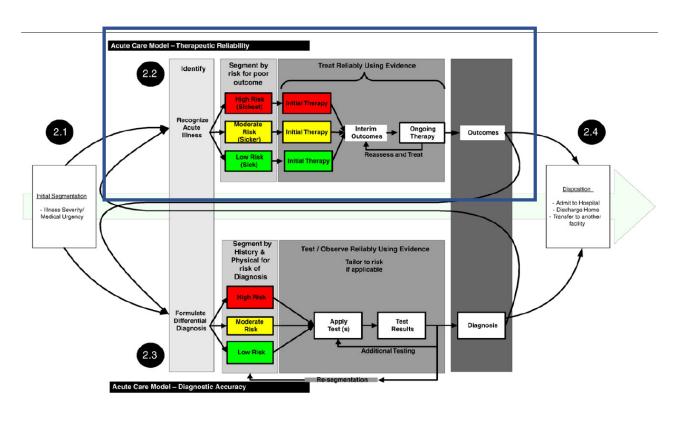


Acute Care Model – Segmentation



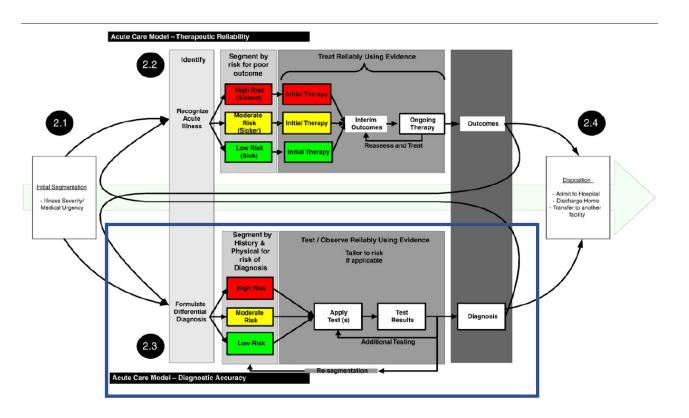
- Occurs at onset
- Repeated as new results/outcomes arise

Acute Care Model – Therapeutic Reliability



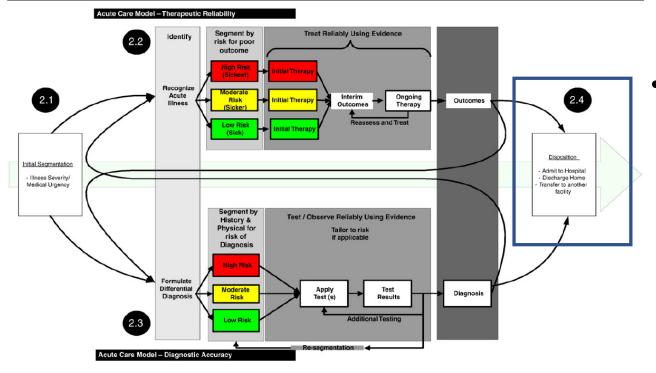
- Minimal diagnostic uncertainty
- Standardized therapeutic approach

Acute Care Model – Diagnostic Accuracy



- Undifferentiated illness
- Custom approach to diagnosis
- Testing tailored to risk category

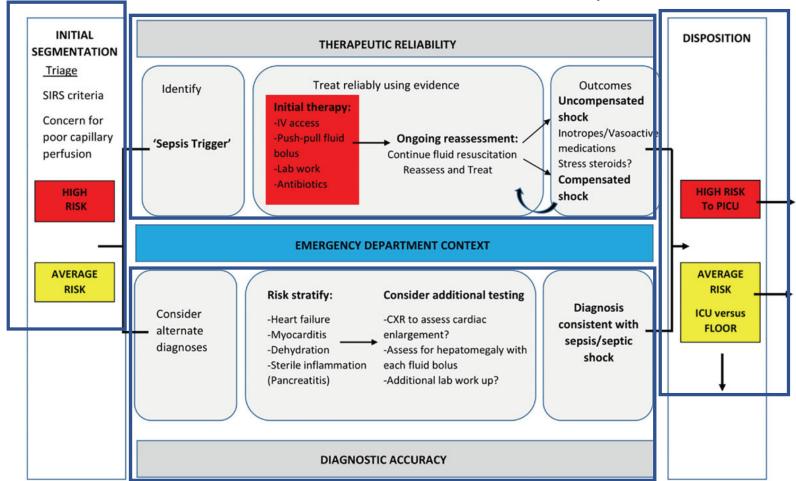
Acute Care Model – Disposition



 Assess outcome of pathway to decided disposition

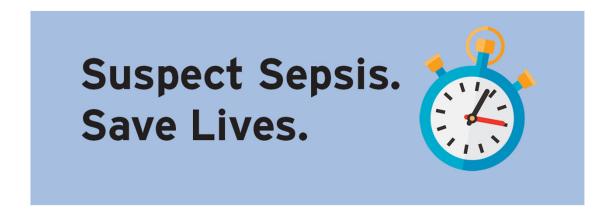
Iyer S, Reeves S, Varadarajan K, et al. The Acute Care Model: A New Framework for Quality Care in Emergency Medicine. Clin Pediatr Emerg Med 2011;12:91-101.

Acute Care Model for Pediatric Sepsis



Vidrine R, Atreya MR, Stalets EL. Continuum of care in pediatric sepsis: a prototypical acute care delivery model. Transl Pediatr 2018;7(4):253-261. doi: 10.21037/tp.2018.10.01 Zackoff MW, lyer S, Dewan M. An overarching approach for acute care delivery: extension of the acute care model to the entire inpatient admission. *Transl Pediatr*. 2018;7(4):246-252. doi:10.21037/tp.2018.09.14

"To ensure seamless delivery of care across different care contexts, an institutional approach to pediatric sepsis care is needed"



JAMA | Original Investigation

Association Between the New York Sepsis Care Mandate and In-Hospital Mortality for Pediatric Sepsis

Idris V. R. Evans, MD, MSc; Gary S. Phillips, MAS; Elizabeth R. Alpern, MD, MSCE; Derek C. Angus, MD, MPH; Marcus E. Friedrich, MD; Niranjan Kissoon, MD; Stanley Lemeshow, PhD; Mitchell M. Levy, MD; Margaret M. Parker, MD; Kathleen M. Terry, PhD; R. Scott Watson, MD, MPH; Scott L. Weiss, MD, MSCE; Jerry Zimmerman, MD, PhD; Christopher W. Seymour, MD, MSc

- Previous studies have shown that implementation of bundles reduces time to antibiotics and time to fluid bolus but no current studies on mortality
- To determine the association between completion of a sepsis bundle within 1 hour and risk adjusted in- hospital mortality for pediatric sepsis and septic shock

Study Design

- All NY hospitals are required to have pediatric sepsis protocols that include the following interventions within 1 hour:
 - Blood culture collected before antibiotics
 - Broad spectrum antibiotics
 - 20ml/kg fluid bolus

| | No. (%) | | | |
|--|---------------|------------------------|-----------------------------|----------------------|
| | All Patients | 1-h Bundle Completed i | 1-h Bundle Completed in 1 h | |
| Characteristica | | Yes | No | P Value ^b |
| Type of pathogen | | | | |
| Gram positive | 139 (11.8) | 47 (16.0) | 92 (10.4) | |
| Gram negative | 104 (8.8) | 27 (9.2) | 77 (8.7) | - 001 |
| Other ^e | 87 (7.4) | 4 (1.4) | 83 (9.4) | <.001 |
| None reported | 849 (72.0) | 216 (73.5) | 633 (71.5) | |
| Hospital with pediatric intensive care | 1031 (87.4) | 258 (87.8) | 773 (87.3) | .85 |
| Hospital length of stay, median (IQR), h | 235 (118-496) | 198 (101-358) | 244 (123-554) | <.001 ^d |
| In-hospital death | 139 (11.8) | 22 (7.5) | 117 (13.2) | .008 |

Abbreviations: HMO, health maintenance organization; IQR, interquartile range.

Evans, I. V. R. *et al.* Association Between the New York Sepsis Care Mandate and In-Hospital Mortality for Pediatric Sepsis. *JAMA* **320**, 358–367 (2018).

^a No data were missing among individual bundle elements, transfer status, age, payer, place of protocol initiation, septic shock, site of infection, platelet count at protocol initiation, chronic renal disease or liver failure, diabetes, mechanical ventilation prior to protocol initiation, mortality, and length of stay.

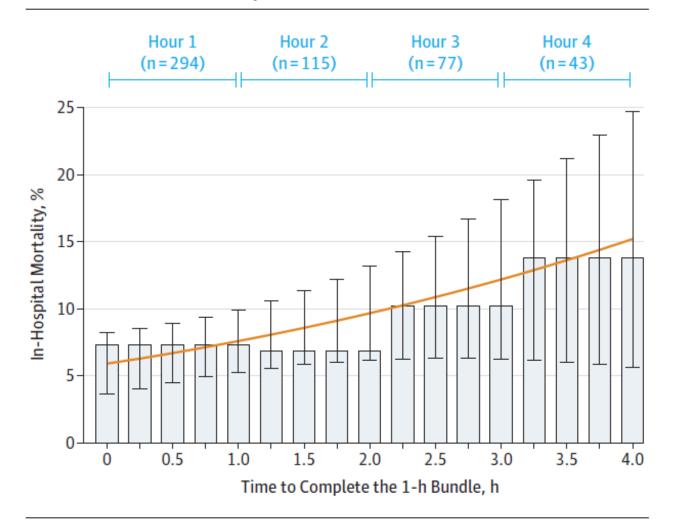
^b P values are based on Pearson χ² test unless otherwise noted.

^c P value based on Fisher exact test.

^d P value based on Wilcoxon rank-sum test.

^e Anaerobic bacteria, yeast, fungus, mixed pathogens, and viruses.

Figure 3. Crude In-Hospital Mortality and Predicted Risk of In-Hospital Death After the Time of Sepsis Protocol Initiation



Evans, I. V. R. *et al.* Association Between the New York Sepsis Care Mandate and In-Hospital Mortality for Pediatric Sepsis. *JAMA* **320**, 358–367 (2018).

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Completion of 1 hour sepsis bundle within 1 hour compared with not completing the bundle within 1 hour was associated with lower risk adjusted in-hospital mortality among patients with pediatric sepsis and septic shock

Published in final edited form as:

Ann Emerg Med. 2017 December; 70(6): 759–768.e2. doi:10.1016/j.annemergmed.2017.03.019.

Improving Recognition of Pediatric Severe Sepsis in the Emergency Department: Contributions of a Vital Sign Based Electronic Alert and Bedside Clinician Identification

Fran Balamuth, MD, PhD, MSCE^{1,2}, Elizabeth R. Alpern, MD, MSCE^{3,4}, Mary Kate Abaddessa, MSN, RN¹, Katie Hayes, BS¹, Aileen Schast, PhD⁷, Jane Lavelle, MD^{1,2}, Julie C. Fitzgerald, MD, PhD^{5,6}, Scott L. Weiss, MD, MSCE^{5,6}, and Joseph J. Zorc, MD, MSCE^{1,2}

- Compared 2 cohorts- pre and post sepsis alert
- Positive alert= tachycardia or hypotension, concern for infection, and at least one of the following: abnormal cap refill, abnormal mental status, or high risk condition
- Positive sepsis alert → team huddle and decision to place on sepsis protocol
- Alert sensitivity 86%, specificity 99%.
- Sepsis alert increased ED sepsis recognition from 83% to 96%

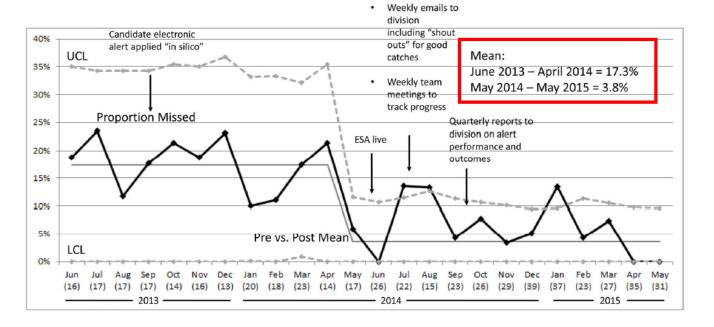


Figure 3.

Statistical process control chart demonstrating proportion of missed sepsis cases during the study. Black line is the proportion of missed cases during the study period. The total number of patients each month is indicated below the name of the month in parentheses. A missed case is a patient with severe sepsis in the PICU within 24 hours of their ED visit who was not treated with the ED sepsis protocol. The implementation of the ESA is marked with an arrow. Dashed lines are the upper and lower confidence limits defined as 2 standard deviations above and below the mean. Upper and lower control limits were recalculated each month, and a new mean was calculated when criteria were met for special cause variation. Aggregate proportions of missed cases for pre and post implementation period is indicated in the text box.

Balamuth, F. et al. Improving Recognition of Pediatric Severe Sepsis in the Emergency Department: Contributions of a Vital Sign Based Electronic Alert and Bedside Clinician Identification. Ann Emerg Med 70, 759-768.e2 (2017).

Alert fatigue??

No one alert is perfect

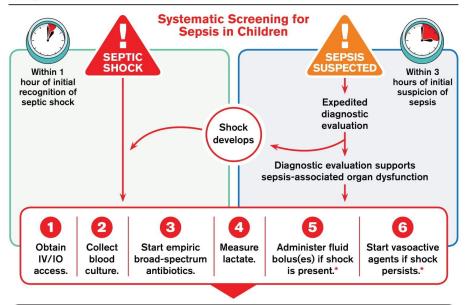
Alerts should be tailored to your population

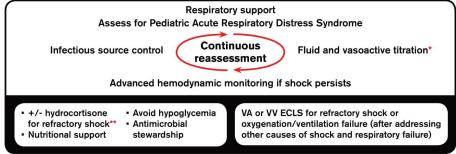


Management of Pediatric Sepsis

Initial Resuscitation Algorithm for Children







*See fluid and vasoactive algorithm. Note: Fluid bolus should be omitted from bundle if a) fluid overload is present or b) it is a low-resource setting without hypotension. Fluid in mL/kg should be dosed as ideal body weight.

Weiss, S. L. et al. Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children. Pediatric Critical Care Medicine | Society of Critical Care Medicine 21, e52 (2020).

^{**}Hydrocortisone may produce benefit or harm.

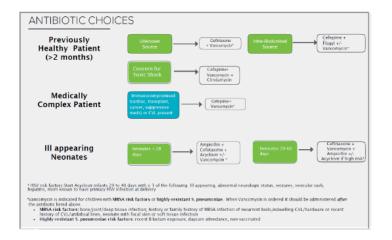
PEDIATRIC SEPSIS ALGORITHM



This algorithm/order set should NOT be used for the well appearing febrile neonate



| SEPSIS HUDDLE | | Huddle St | art Time: | | |
|---|---------------------|-------------------------------------|---------------|--|--|
| S What triggered sepsis huddle (review sepsis screen and concerns) What findings does this patient have which are concer sepsis? | | Rapid Fluid Bolus In (Goal time) | 20 minutes | | |
| B • What is the clinical background? • When did the change in clinical status occur? | | | Time: | | |
| What are the most recent vitals, labs, and exam? What do you think th problem is? | | Antibiotics Given | 60 minutes | | |
| R Should the sepsic algorithm be initiated? Does the patient needs additional monitoring or transf PICU? Should an RRT be called? | (Goal time) | | Time: | | |
| Open the sepsis order set | | | | | |
| Initial Diagnosis / Review of Previous Work | | | | | |
| Fluid resuscitation 20 mL/kg (unless signs of cardiac dysfunction) | Initial Sepsis Labs | | | | |
| Administer O ₂ (min of 10 L NRB) | ☐ CBC | ☐ i cal, POC glucose | | | |
| | ☐ Blood gas | _ | | | |
| Antibiotics | ☐ CMP | ☐ Urine cx (if foley) | 0 - 20 minute | | |
| Order/administer | □ Procal | ☐ Resp cx (if ETT/trach) | , | | |



□ Lactate

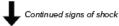
☐ Broaden if already on antibiotics

PEDIATRIC SEPTIC SHOCK ALGORITHM



At 20 minutes Reassess for ongoing signs of shock

- Persistent tachycardia for age
- Hypotension for age
- Poor perfusion



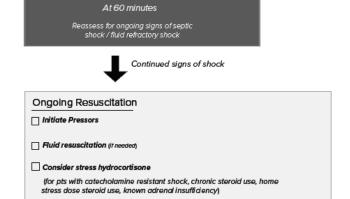
| | Fluid administration (unless signs of cardiac dysfunction) | Consider additional labs |
|------------|--|------------------------------|
| | □40 mL/kg | Coags (PT/INR, PTT, |
| ☐ 60 mL/kg | ☐ 60 mL/kg | Fibrinogen) |
| | ☐ Verify antibiotics ordered / given | ☐ ESR/CRP (concern for MIS-C |
| | \square Order pressors to bedside | ☐ Cortisol |
| | | |



20 - 60 minutes



Transfer to PICU for management of septic shock after 2nd fluid bolus and continued signs of shock





Adapted from the Cincinnati Children's Hospital Medical Center sepsis algorithm

Fluid Resuscitation

No ICU Care Available

- in the absence of hypotension, we recommend against bolus fluid administration while starting maintenance fluids (strong recommendation, high quality of evidence).
- if hypotension is present, we suggest administering up to 40 mL/kg in bolus fluid (10–20 mL/kg per bolus)

ICU Care Available

- we suggest administering up to 40-60 mL/kg in bolus fluid (10-20 mL/kg per bolus) over the first hour (weak recommendation, low quality of evidence).
 - Titrate to clinical markers of cardiac output
 - HR, BP, cap refill, level of consciousness, UOP, serial lactate, advanced monitoring
 - Discontinue if signs of fluid overload develop
 - Pulmonary edema, hepatomegaly

Fluid Resuscitation

- We suggest using balanced/buffered crystalloids, rather than 0.9% saline (weak recommendation, very low quality of evidence)
 - Hyperchloremia → metabolic acidosis, systemic inflammation, AKI, coagulopathy, and mortality when compared with resuscitation with more balanced/buffered crystalloids (LR, PlasmaLyte)

| Initial Diagnosis / Review of Previous Work | | |
|--|--|--|
| Fluid resuscitation 20 mL/kg (max 1L) (unless signsof cardiac dysfunction) | Initial Sepsis Labs (tube colors for labs) | |
| | ☐ CBC (purple) ☐ POC glucose | |
| ☐ Administer O₂ (min of 10 L NRB) | ☐ Blood gas ☐ Blood cx | |
| ☐ Antibiotics | \square CMP (mint gr) \square Urine cx (if foley) | |
| ☐ Order/administer | \square Procal _(mint gr) \square Resp cx (if ETT/trach) | |
| ☐ Broaden if already on antibiotics | ☐ Lactate (on blood gas) | |
| | | |

0 - 20 minutes

Antimicrobial Therapy

- In children with septic shock, we recommend starting antimicrobial therapy, within 1 hour of recognition (strong recommendation, very low quality of evidence)
- In children with sepsis-associated organ dysfunction but without shock, we suggest starting antimicrobial therapy, within 3 hours of recognition (weak recommendation, very low quality of evidence)

ANTIBIOTIC CHOICES Cefepime + **Previously** Ceftriaxone Intra-Abdominal Flagyl +/-+ Vancomycin* Healthy Patient Vancomycin* (>2 months) Cefepime+ **Toxic Shock** Vancomycin + Clindamycin Medically (cardiac, transplant, Cefepime+ **Complex Patient** Vancomycin* cancer, suppressive meds) or CVL present Ampicillin + Ceftriaxone + III appearing Vancomycin + Cefotaxime + Ampicillin +/-Acyclovir +/-**Neonates** Acyclovir if high risk+ Vancomycin *

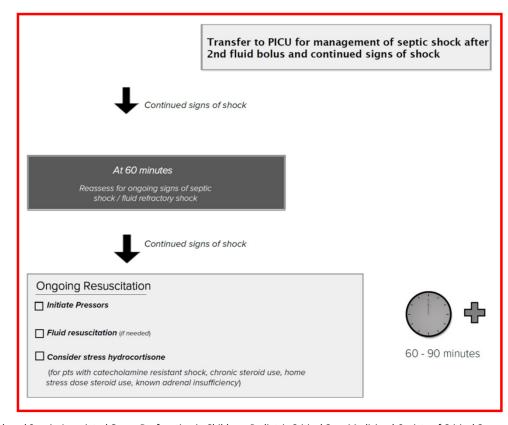
* HSV risk factors:Start Acyclovir infants 29 to 40 days with ≥ 1 of the following: Ill appearing, abnormal neurologic status, seizures, vesicular rash, hepatitis, mom known to have primary HSV infection at delivery

*Vancomycin is indicated for children with MRSA risk factors or highly-resistant S. pneumoniae. When Vancomycin is ordered it should be administered after the antibiotic listed above.

- MRSA risk factors: bone/joint/deep tissue infection; history or family history of MRSA infection of recurrent boils, indwelling CVL/hardware or recent
 history of CVL/umbilical lines, neonate with focal skin or soft tissue infection
- · Highly-resistant S. pneumoniae risk factors: recent B-lactam exposure, daycare attendance, non-vaccinated

Fluid Refractory Shock

- We suggest using epinephrine or norepinephrine, rather than dopamine, in children with septic shock (weak recommendation, low and very low quality of evidence, respectively).
- May be administered through a peripheral vein (or intraosseous, if in place) if central venous access is not readily accessible.



Weiss, S. L. et al. Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children. Pediatric Critical Care Medicine | Society of Critical Care Medicine | Medicine 21, e52 (2020).

Monitoring

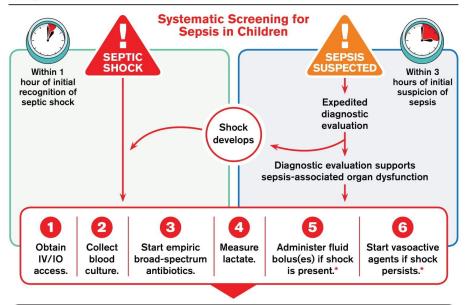
- We suggest using advanced hemodynamic variables, when available, in addition to bedside clinical variables to guide the resuscitation of children with septic shock or other sepsis-associated organ dysfunction (weak recommendation, low quality of evidence).
- We suggest using trends in blood lactate levels, in addition to clinical assessment, to guide resuscitation of children with septic shock and other sepsis-associated organ dysfunction (weak recommendation, very low quality of evidence).

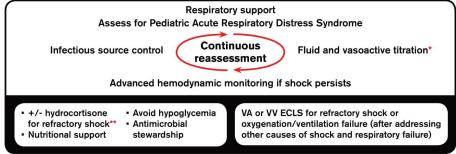
Catecholamine Refractory Shock

- We suggest against using intravenous hydrocortisone to treat children with septic shock if adequate fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability (weak recommendation, low quality of evidence).
- We suggest that either intravenous hydrocortisone or no hydrocortisone may be used if adequate fluid resuscitation and vasopressor therapy are not able to restore hemodynamic stability (weak recommendation, low quality of evidence).
- Patients with adrenal insufficiency?

Initial Resuscitation Algorithm for Children







*See fluid and vasoactive algorithm. Note: Fluid bolus should be omitted from bundle if a) fluid overload is present or b) it is a low-resource setting without hypotension. Fluid in mL/kg should be dosed as ideal body weight.

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^{**}Hydrocortisone may produce benefit or harm.

Take Home Messages

- Pediatric sepsis is often difficult to recognize
- Standardized care reduces variation, waste and error
- Sepsis bundles improve pediatric sepsis recognition and treatment

