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Inclusion Criteria: Any patient at NCH and NCMC, including those > 18 yr old.

Exclusion Criteria:

- Patients already *in extremis*
- NICU patients

Early recognition

Timely evaluation, monitoring and management

Improved outcomes

Early Recognition Process: 2-step screen + treatment bundle

Treatment Bundles: [Suspected sepsis/sepsis](#) [Septic Shock](#)

This guideline covers timely recognition of children with suspected sepsis, sepsis, and septic shock. Current published guidelines for pediatric sepsis focus on early recognition and aggressive treatment of sepsis and septic shock to decrease the morbidity and mortality associated with this continuum of disease.

If any exclusion criteria are met, this guideline may be consulted but should not determine the extent of the user's evaluation and management of the patient. *Excluded patients may require additional testing, monitoring, and interventions. Management of excluded patients must be individualized.*

Using the guideline

1. A stop sign signals to exit the guideline and proceed with care specific to the needs of the patient.
2. Words or phrases in different colored font and underline indicate a hyperlink. Click on the words/phrases to learn more about the topic.
3. The blue boxes at the bottom of the page assist in navigating to specific pages in the guideline without having to scroll.

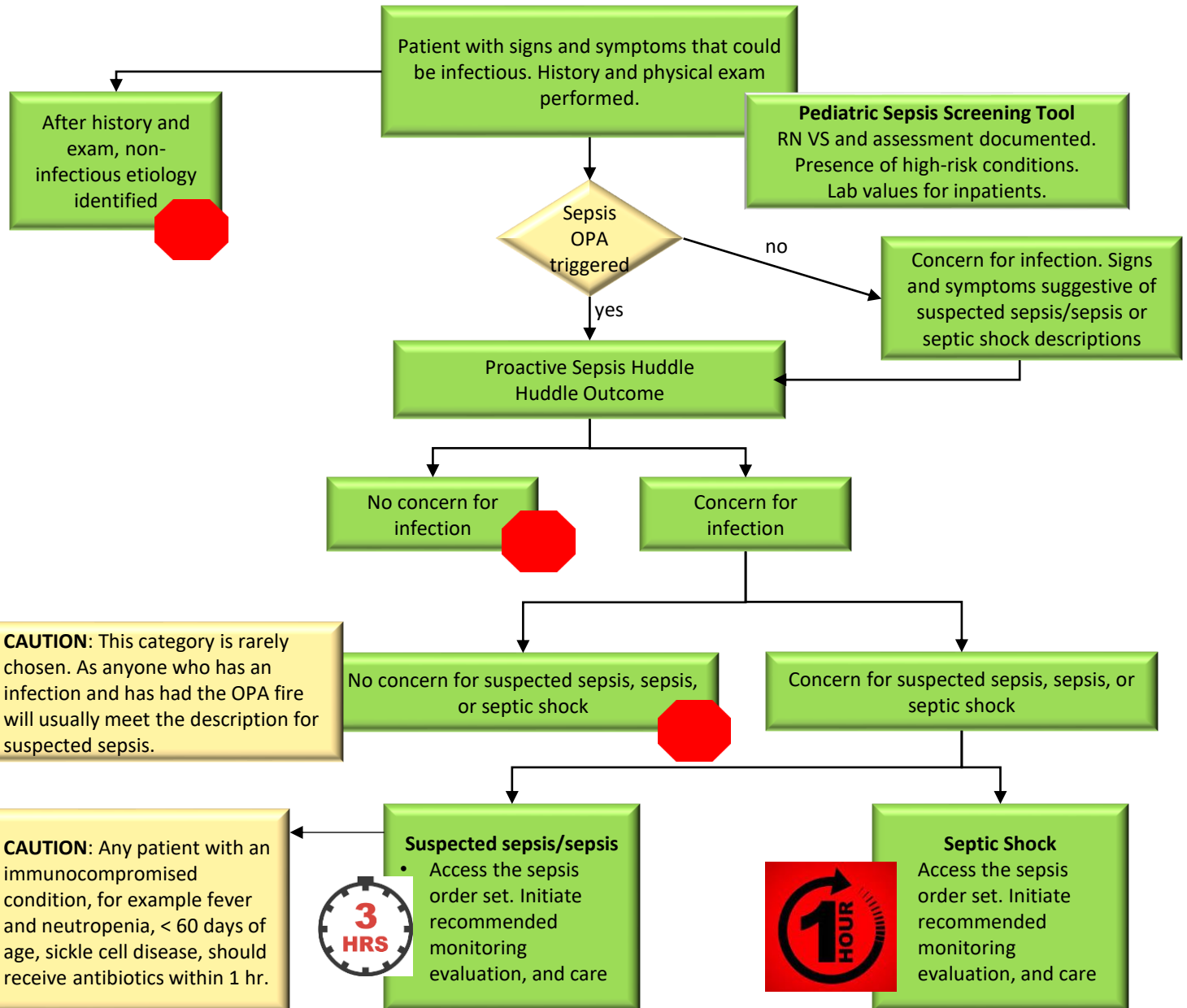
Key terms and descriptions

1. [Epic Pediatric sepsis screening tool](#): a multivariable algorithm continuously running in the background that triggers the OPA to fire when the trigger threshold is reached.
2. [OPA](#): new acronym for BPA. It stands for Our Practice Advisory Alert. The firing of the OPA is step 1 in our 2-step sepsis early recognition.
3. [Proactive sepsis huddle](#): This is the step 2 of our sepsis early recognition and is a tool for diagnostic excellence. It consists of review of the Epic Pediatric Sepsis Navigator and the discussion guide for conducting the huddle. The huddle outcome will be documented within this navigator.

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Pediatric Sepsis: Early Detection, Monitoring, and Care Overview

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Sepsis and Septic Shock Treatment Bundles
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Suspected sepsis/sepsis

For white hot and red hot patients, the time frame for 1 hour antibiotic administration still applies.

If patient deteriorates, move to septic shock care.

***CAUTION:** Any patient with an immunocompromised condition, for example fever and neutropenia, < 60 days of age, sickle cell disease, should receive antibiotics within 1 hr.


Evaluation

Recommended labs; CBC, CMP, Procalcitonin and/or CRP, lactate, blood culture.
 Consider additional tests based on severity of patient's illness: PT, INR, PTT, Fibrinogen, D-dimer, UA and/or culture, CXR

Monitoring

- Continuous HR, RR, pulse oximetry
- VS and mental status assessment q1hr x 3 hr
- Physician/APP reassessment q1-2 h x 3 hours

Treatment

- Order single dose of appropriate antibiotics or broaden current coverage
- *Complete administration of ordered antibiotics
- 1 – 2 isotonic fluid bolus(es), each infused over 30 – 60 minutes


Evaluation

Recommended labs; CBC, CMP, Procalcitonin, lactate, blood culture, PT, PTT, INR, Fibrinogen, D-dimer
Consider additional tests based on severity of patient's illness: UA and/or culture, CXR, ECHO

Monitoring

- Continuous HR, RR, pulse oximetry
- VS and mental status assessment q1hr
- Physician/APP reassessment q1 h

Treatment

- Establish adequate vascular access
- Supplemental oxygen
- Order single dose of appropriate antibiotics or broaden current coverage
- Complete administration of ordered antibiotics
- 1 – 3 isotonic fluid bolus(es), each infused over 10-20 min
- Initiation of epinephrine infusion if fluid refractory shock or severe hypotension

Septic Shock

- If patient deteriorates, transition to standard resuscitation care including establishment of a secure airway, placement of appropriate vascular devices
- Activate code or RRT team if indicated

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Sepsis Screen Outcome Based Care[Approvals and Bibliography](#)[Summary of Version Changes](#)[Medical and restriction disclaimers](#)**No concern for infection****ED:**

Exit Pediatric Sepsis and Septic Shock guideline. Continue to evaluate, monitor, and care for patient as indicated.

Inpatient:

- If patient warrants a higher level of care, activate the RRT (NCH) or arrange for transfer to a higher level of care.
- Exit Pediatric Sepsis and Septic Shock Guideline.
 - If you are not a member of the patient's primary team, update a member of the primary team about the proactive sepsis huddle and turn over further evaluation and care to the primary team.
 - If you are a member of the patient's primary team, continue to evaluate, monitor and care for the patient as indicated.

**Concern for infection.
No concern for
suspected sepsis, sepsis,
or septic shock****ED:**

Exit Pediatric Sepsis and Septic Shock guideline. Continue to evaluate, monitor, and care for patient as indicated.

Inpatient:

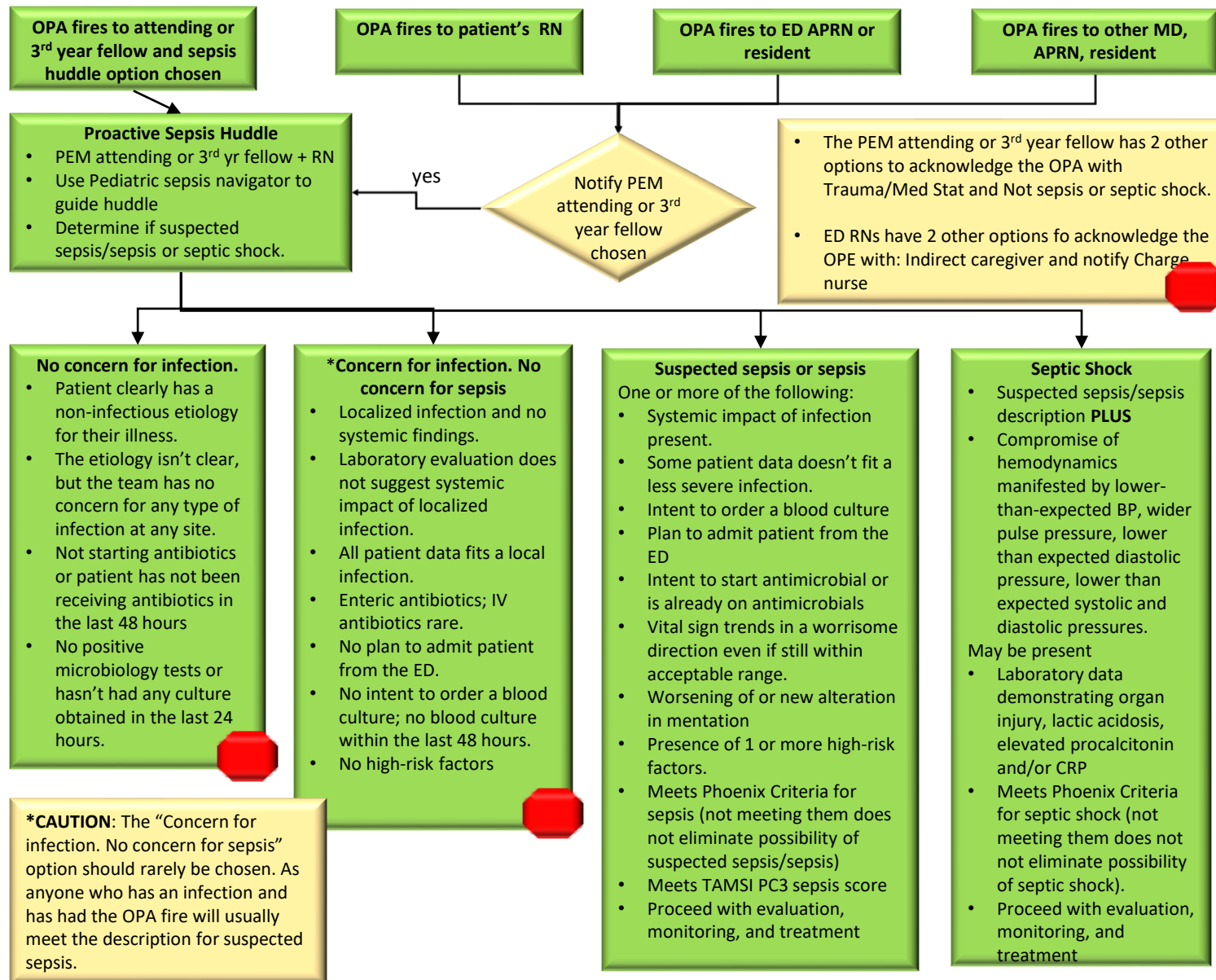
- If patient warrants a higher level of care, activate the RRT (NCH) or arrange for transfer to a higher level of care.
- Exit Pediatric Sepsis and Septic Shock Guideline.
 - If you are not a member of the patient's primary team, update a member of the primary team about the proactive sepsis huddle and turn over further evaluation and care to the primary team.
 - If you are a member of the patient's primary team, continue to evaluate, monitor and care for the patient as indicated.

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ED Sepsis Screen Process

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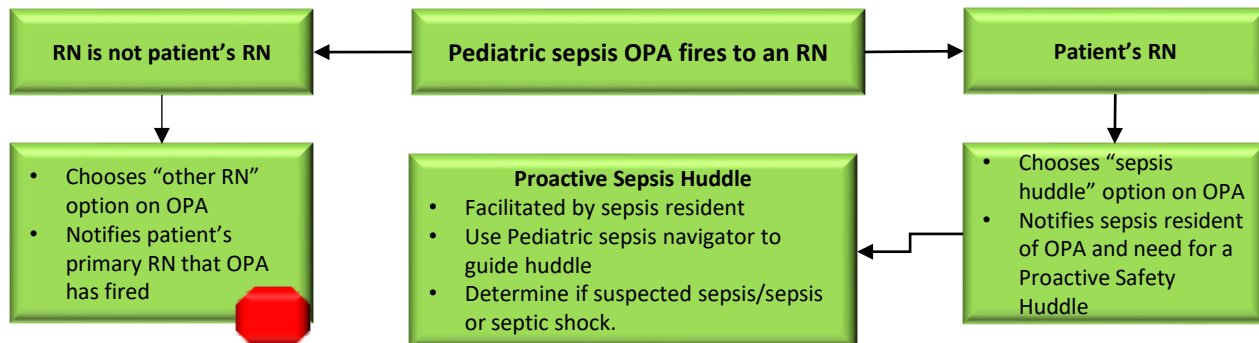
CAUTION: The sepsis OPA only occurs on small percent of patients in the ED – an average of 2 per day in the NCH ED, approximately 2 per week in NCH inpatient; less at NCMC and NWC. Think about these patients differently than you think about patients who didn't trigger the OPA.

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Inpatient Sepsis Screen Process

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No concern for infection.

- Patient clearly has a non-infectious etiology for their illness.
- The etiology isn't clear but the team has no concern for any type of infection at any site.
- Not starting antibiotics or patient has not been receiving antibiotics in the last 48 hours
- No positive microbiology tests or hasn't had any culture obtained in the last 24 hours.

*Concern for infection. No concern for sepsis

- Localized infection and no systemic findings.
- Laboratory evaluation does not suggest systemic impact of localized infection.
- All patient data fits a local infection.
- Enteric antibiotics; IV antibiotics rare.
- No plan to admit patient from the ED.
- No intent to order a blood culture; no blood culture within the last 48 hours.
- No high-risk factors

Suspected sepsis or sepsis

One or more of the following:

- Systemic impact of infection present.
- Some patient data doesn't fit a less severe infection.
- Intent to order a blood culture or has had a blood culture within the last 48 hours
- Plan to admit patient from the ED or is already an inpatient.
- Intent to start antimicrobial or is already on antimicrobials
- Vital sign trends in a worrisome direction even if still within acceptable range.
- Worsening of or new alteration in mentation
- Presence of 1 or more high-risk factors.
- Meets Phoenix Criteria for sepsis (not meeting them does not eliminate possibility of suspected sepsis/sepsis)
- Proceed with evaluation, monitoring, and care

Septic Shock

Suspected sepsis/sepsis description **PLUS**

- Compromise of hemodynamics manifested by lower than expected BP, wider pulse pressure, lower than expected diastolic pressure, lower than expected systolic and systolic pressure.
- May be present:
 - Laboratory data demonstrating organ injury, lactic acidosis, elevated procalcitonin and/or CRP
 - Meets Phoenix Criteria for septic shock (not meeting them does not eliminate possibility of septic shock).
 - Proceed with evaluation, monitoring, and care

***CAUTION:** The "Concern for infection. No concern for sepsis" option should rarely be chosen. As anyone who has an infection and has had the OPA fire will usually meet the description for suspected sepsis.

Remember that a call for a Proactive Sepsis Huddle only occurs for very few patients (approximately 2 per day in the NCH ED, approximately 2 per week in NCH inpatient; less at NCMC and NWC). Thus, a patient that is sick enough to trigger the Pediatric Sepsis OPA is different than the average patient with fever, tachycardia and tachypnea. Think about these patients differently than you think about calls about patients who didn't trigger the OPA.

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Proactive Sepsis Huddle (Step 2 of Screening Process)

1. Examine patient, paying particular attention to mental status, HR, RR, BP, quality of pulses, skin temperature, cap refill. If parent present, have they noticed any change in their child's interactions, thinking (slow, cloudy, confused, unable to concentrate). If child verbal, ask the child age-appropriate questions.

2. Review the pediatric sepsis navigator content, vital sign trends, laboratory data.

3. Does the patient have a known infection of any type, at any location or is there a concern that this patient might have an infection? If yes, proceed with huddle Q4. If no, close huddle and complete the appropriate steps.

4. Are there any patient factors present that increase the likelihood of sepsis or progression to septic shock?

5. If the patient "looks good" at the time of the huddle, are there treatments such as fluid boluses, analgesics, and antipyretics, that could be masking a more serious illness such as sepsis (This is why the sepsis OPA incorporates a look back period).

6. When considered collectively, could the vital signs, vital sign trends, cap refill, pulses, mental status, and lab data be indicative of systemic effects of an infection? Are there any findings or data that don't seem to fit the current working diagnosis(es)? Is the illness trajectory consistent with the working diagnosis?

7. While there are false positives, the OPA only fires on a small percent of febrile children. If the team does not believe that the child has suspected sepsis, sepsis, or septic shock, how does the team explain the firing of the sepsis BPA on this patient?

8. Based on huddle discussion, click on the appropriate outcome button. If suspected sepsis/sepsis or septic shock, access the sepsis order set to initiate the appropriate evaluation, monitoring, and care algorithm.

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Pediatric Sepsis Severity Scoring (not screening) Tools

Ped SOFA	LqSOFA	Pediatric Septic Shock Screening Score (qPS4)	Phoenix Criteria
Patient with confirmed or suspected infection			
It is designed to measure organ dysfunction. Adaptation of Sepsis-3 definitions (adult) for organ dysfunction to children. SOFA and pSOFA intended to predict in-hospital mortality. Primary utilization is in the intensive care unit.	Intended to predict which febrile children are at risk for critical care admission and sepsis-related mortality	Intended to predict septic shock and not early recognition of sepsis.	Intended to reliably identify children with sepsis/septic shock for the purpose of clinical care, benchmarking, quality improvement, epidemiology, and research. Identify life-threatening organ dysfunction due to infection. Not designed to serve as a screening tool
Adaptation of SOFA to children	Replaced SOFA BP with HR Eliminated labs	Enhancement of the LqSOFA	Replaced SIRS as the diagnostic criteria
Age adjusted thresholds P/F ratio or S/F ratio Platelet count Bilirubin MAP/vasoactive infusion GCS Serum creatinine	Age adjusted thresholds HR RR Mental status (alert, Voice, Pain, Unresponsive scale) Capillary refill time	TAMSI - calculated RR – derived from database Mental status (GCS) Capillary refill time $\text{TAMSI} = \frac{\text{HR} - (\text{T} - 37) * 10}{\text{MAP}}$	P/F, S/F Vasoactive medications Lactate Age adjusted MAP Platelets, INR, D-dimer, Fibrinogen GCS
Each variable scored 0 – 4 Range 0 – 24 point scale	0 – 4 point scale	0 – 4 point scale Score ≥ 2 predictive of septic shock developing within the next 2 – 3 hours	0 – 16 point score Sepsis: suspected infection + sepsis score ≥ 2 Septic Shock: sepsis definition with ≥ 1 cardiovascular point
Good predictor of mortality in critically ill children admitted to a PICU.	Good predictor of need for critical care admission within 48 hours compared to qSOFA, PEWS, NICE.	Good sensitivity, lower specificity especially for the older child (12 yr and older). Good predictor of septic shock, admission to higher level of care.	NA
Validated comparing it to other pediatric organ dysfunction scores such as PELOD-2, PRISM III and adult SOFA; critically ill children.	Validated in a pediatric ED population.	Validated in a pediatric ED in a cohort of children 1 month – 18 yrs	Validated for any location Replaced SIRS for differentiating between sepsis and septic shock.

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pSOFA Score

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pSOFA

Adaptation and Validation of a Pediatric Sequential Organ Failure Assessment Score and Evaluation of the Sepsis-3 Definitions in Critically Ill Children. Matics et al. JAMA Pediatrics. doi:10.1001/jamapediatrics.2017.2352

This scoring tool was developed to determine if modification of the SOFA score (adults) for children admitted to a Pediatric Intensive Care Unit would align with Sepsis-3 definitions in patients with confirmed or suspected infection. It is an organ dysfunction score. It is not a screening tool. It serves mostly as a tool to identify severity of sepsis and septic shock and risk of mortality. It requires BP and labs to calculate. Performs similarly to PELOD, PELOD-2 and PRISM III.

Sepsis-3 definitions (adult) were published in 2016.

Sepsis-life-threatening organ dysfunction caused by a dysregulated host response to infection.

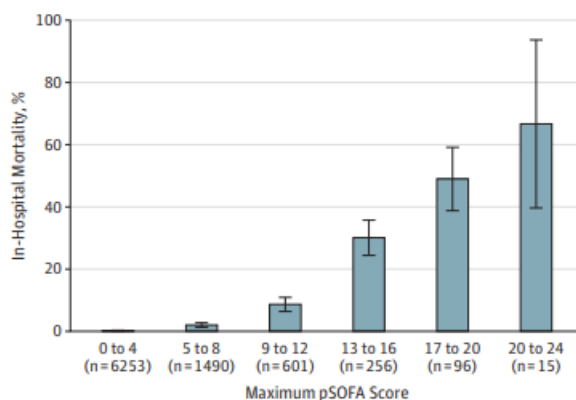
Organ dysfunction-identified as an acute change in total SOFA score (≥ 2) consequent to the infection. A SOFA score ≥ 2 reflects an overall mortality risk of approximately 10% in a general adult hospital population with suspected infection.

Septic Shock-subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality. These patients can be identified with a clinical construct of sepsis with persisting hypotension requiring vasopressors to maintain MAP ≥ 65 mmHg and having a serum lactate level >2 despite adequate volume resuscitation. Patients with these criteria had a hospital mortality in excess of 40%.

Table 1. Pediatric Sequential Organ Failure Assessment Score

Variables	Score ^a				
	0	1	2	3	4
Respiratory					
Pao ₂ :Fio ₂ ^b or SpO ₂ :Fio ₂ ^c	≥400	300-399	200-299	100-199 With respiratory support	<100 With respiratory support
	≥292	264-291	221-264	148-220 With respiratory support	<148 With respiratory support
Coagulation					
Platelet count, ×10 ³ /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 (any)	Dopamine hydrochloride >5 or epinephrine ≤0.1 or norepinephrine 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			
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

Figure. In-Hospital Mortality Rate Based on the Maximum Pediatric Sequential Organ Failure Assessment (pSOFA) Score



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LqSOFA Modified for Children

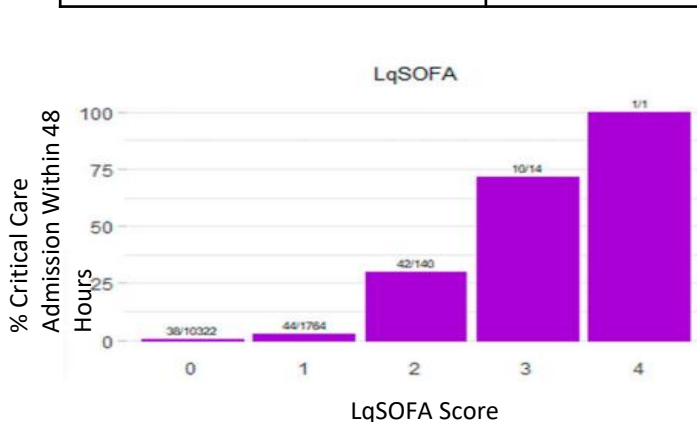
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LqSOFA Modified for Children

Accuracy of a Modified qSOFA Score for Predicting Critical Care Admission in Febrile Children. Romaine et al. Pediatrics. 2020.

This scoring tool is for identifying febrile children in a Pediatric Emergency Department who are at risk for critical care admission within 48 hours and sepsis-related mortality. It has been used as a scoring tool for predicting septic shock. It is NOT a screening tool for early sepsis. It may be used to inform disposition of febrile children in an emergency department. The higher the score, the more likely critical care admission will be needed within 48 hours. This score requires no BP or laboratory values to use.

Criteria	1 point	0 points
Capillary refill time	≥ 3 sec	< 3 sec
Mental status using AVPU (alert, responds to voice, responds to pain, unresponsive)	VPU	Alert
HR	> 99 th percentile Bonafide* et al age-specific thresholds	≤ 99 th
RR	> 99 th percentile Bonafide et al age-specific thresholds	≤ 99 th



Age	HR	RR
0-<3mo	➤ 186	➤ 76
3-<6mo	➤ 182	➤ 71
6-<9mo	➤ 178	➤ 67
9-<12mo	➤ 176	➤ 63
12-<18mo	➤ 173	➤ 60
18-<24mo	➤ 170	➤ 57
2-<3y	➤ 167	➤ 54
3-<4y	➤ 164	➤ 52
4-<6y	➤ 161	➤ 50
6-<8y	➤ 155	➤ 46
8-<12y	➤ 147	➤ 41
12-<15y	➤ 138	➤ 35
15-<18y	➤ 132	➤ 32

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qPS4 Score[Approvals and Bibliography](#)[Summary of Version Changes](#)[Medical and restriction disclaimers](#)**qPS4 Score: Screen for Septic Shock**

Development of a New Screening Tool for Pediatric Septic Shock. Gerogette et al. Ann Emerg Med 2024. doi.org/10.1016/j.annemergmed.2024.06.026.

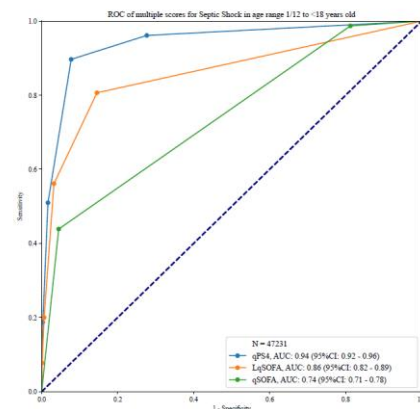
This scoring tool was developed as a screening tool for pediatric septic shock in Pediatric Emergency Departments. The patients ranged in age from 1 mo to 18 yr. It utilized the 4-point Liverpool quick Sequential Organ Failure Assessment (LqSOFA) tool. The authors modified the HR category by creating a derived variable using HR and temperature. This variable is called the Temperature and Age-adjusted Mean Shock Index (TAMSI). They replace the RR thresholds with thresholds derived empirically from the study cohort. No changes were made to the Altered mentation or capillary refill time variables.

Table 1. Score criteria for the quick Pediatric Septic Shock Screening Score (qPS4), range 0 to 4.

Criteria*	Score = 0	Score = 1
Altered mentation	Alert or GCS=15	Not alert or GCS<15
Respiratory rate		
1-11 mo	≤55	>55
1-2 y	≤47	>47
3-5 y	≤33	>33
6-11 y	≤25	>25
12-17 y	≤21	>21
TAMSI		
1-12 mo	≤2.64	>2.64
1-2 y	≤2.29	>2.29
3-5 y	≤1.96	>1.96
6-11 y	≤1.68	>1.68
12-17 y	≤1.54	>1.54
Capillary refill time	<3 s	≥3s

*This was adapted from the LqSOFA with empirically derived respiratory rate cutoffs and replacement of age-based tachycardia with TAMSI. The "worst" value during observation is used to compute the score.

$$\text{TAMSI} = \frac{\text{HR} - (T - 37) * 10}{\text{MAP}}$$

**Figure 2.** ROC curve for qPS4, LqSOFA, and qSOFA for outcome of septic shock (prevalence=0.003) in the validation cohort (N=47,231). The dots along the ROC curves indicate the values for each of the scores. The blue dashed diagonal indicates the line of no information.

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Phoenix Criteria for Diagnosis of Sepsis and Septic Shock

Phoenix Criteria are not a screening tool. They are not designed to help with early detection but rather provide a standard for categorizing pediatric sepsis and septic shock.

Variable	0 points	1 Point	2 Points	3 Points
Respiratory 0 – 3 points	PaO ₂ :FiO ₂ ≥400 or SpO ₂ :FiO ₂ ≥292 if SpO ₂ <97%	PaO ₂ :FiO ₂ <400 on any respiratory support or SpO ₂ :FiO ₂ <292 on any respiratory support	PaO ₂ :FiO ₂ 100-200 and IMV or SpO ₂ :FiO ₂ 148-220 and IMV	PaO ₂ :FiO ₂ <100 and IMV or SpO ₂ :FiO ₂ <148 and IMV
Cardiovascular 0 – 6 points	No vasoactive meds Lactate <5mmol/L	1 point each up to 3 1 vasoactive med Lactate 5-10 mmol/L	2 points each up to 6 ≥vasoactive med Lactate ≥11 mmol/L	
Age based mean arterial pressure				
<1 mo	>30	17-30	<17	
1 to 11 mo	>38	25-38	<25	
1 to <2y	>43	31-43	<31	
2 to <5y	>44	32-44	<32	
5 to <12y	>48	36-48	<36	
12 to ≥17 yr	>51	38-51	<38	
Coagulation 0 – 2 points	Platelets ≥100x10 ³ /μL INR ≤1.3 D-dimer ≤2 mg/L FEU Fibrinogen ≥100 mg/dL	1 point each up to 2 points Platelets <100x10 ³ /μL INR >1.3 D-dimer >2 mg/L FEU Fibrinogen <100 mg/dL		
Neurological 0 – 2 points	GCS >10 Pupils reactive	GCS ≤10	Fixed pupils bilaterally	

Sepsis and Septic Shock based on Phoenix sepsis criteria

Sepsis	Suspected infection AND Phoenix Sepsis Score ≥2 points
Septic shock	Sepsis with ≥1 cardiovascular point(s)

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ED RN

- Click on the Notify physician acknowledge button in the alert. This pauses the alert for 30 minutes for all RNs.
- Notify the PEM attending when the OPA fires.
- Document notification of the attending.
- Meet attending at bedside for a huddle.
- Participate in the huddle.
- No further documentation required.

Inpatient RN

- Click on the Notify physician acknowledgement button in the alert. This pauses the alert for 30 minutes for all RNs.
- Notify the sepsis physician when the OPA fires.
- Document notification of the sepsis physician.
- Meet attending at bedside for a huddle.
- Participate in the huddle.
- No further documentation required.

ED or Inpatient RN: Indirect caregiver

- Notify patient's primary nurse or charge nurse. This pauses the alert for you for the rest of the patient's encounter.

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Physician actions when the sepsis OPA fires
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PEM Attending

- Click on the appropriate acknowledgement reason. The options are RN notified for huddle (pauses the alert for 1 hour for all RNs and physicians), Trauma or Med stat patient (pauses alert for all for the rest of the encounter).
- If Notify RN selected, proceed to patient's bedside for a proactive sepsis huddle.
- Utilize the pediatric sepsis navigator to guide the huddle discussion.
- At the conclusion of the huddle, document the outcome. This step pauses the OPA for the rest of the ED encounter.
- If either of the sepsis outcomes selected, proceed to the PEDS ED Treatment: initial pediatric sepsis care order set.
- As more data is available for the patient, the final outcome for the patient can be documented in the encounter note.

Physician/APP member of PEM team

- Click on the Notify physician acknowledgement button in the alert. This pauses the alert for 30 minutes for all physicians/APPs
- Notify the PEM attending that the sepsis OPA fired.
- Meet PEM attending at bedside for a huddle.
- Participate in the huddle.
- No further documentation required.

Physician/APP AND not a member of the PEM team

- Click on the Not a PEM team member acknowledgement reason. This will pause the OPA for firing again for the rest of the patient's ED encounter whenever you open the patient's Epic chart.

The inpatient sepsis OPA does not fire to physicians.

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Comparison of 3 EPIC Peds Sepsis Models

Factor	ED	Sensitive	Specific	Comments
Population	All ED patients	Inpatient/Observation who do NOT have a high risk condition	Inpatient/Observation, presence of high risk condition, static encephalopathy	
Maximum score	15	26	26	
Score that triggers BPA to fire for RN	6 or higher	10 or higher	11 or higher	
Temperature	2	2	1	Looks back for 24 hrs for any temperature outside the parameter
High Risk Condition	2	3	2	Looks for qualifying condition or medication documented in EMR
HR	2	1	2 (have to meet HR and RR trigger to get the 2 points)	Looks back for any HR outside the parameter for age ED is 4hr lookback. Specific and Sensitive is 24hr lookback
RR	2	1		Looks back for any HR outside the parameter for age ED is 4hr lookback. Specific and Sensitive is 24hr lookback
Systolic BP Abnormality	3	2	3	Looks back for any HR outside the parameter for age ED is 4hr lookback. Specific and Sensitive is 24hr lookback
Pulse Exam	1	2	NA	Looks at last documented for the current encounter
Capillary Refill	2	1	1	Last documented for the current encounter
Skin exam abnormality	1	1	1	Last documented for the current encounter
Peds Mental Status Exam	NA	1	3	Looks back for 24 hours (for mental status exam or PEWS Behavioral) for value outside of parameter
PEWS Behavioral score of 2 or 3	NA	3	3	
High risk condition and PEWS cardiovascular of 2 or 3	NA	2	NA	Looks back 24 hours for value outside of parameter, both must be met
ALT	NA	1	1	Looks back 24 hours for value outside of the parameter
Neutrophil bands	NA	2	2	Looks back 24 hours for value outside of the parameter
WBC	NA	2	2	Looks back 24 hours for value outside of the parameter
Procalcitonin	NA	NA	2	Looks back 24 hours for value outside of the parameter
Lactate	NA	NA	2	Looks back 24 hours for value outside of the parameter
Length of stay less than 12 hours	NA	3	1	

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ED Pediatric Sepsis Model		
Parameter	Details	
High risk condition	<ul style="list-style-type: none"> • Oncology diagnosis • Asplenia • Sickle Cell Disease • Transplant • Central venous line, PICC, urethral catheter • Immunosuppressive medication(s) • Immunocompromised / Immunodeficiency 	
Temperature	Looks back 24 hours of current encounter for a temperature that is 96.8 or lower or 100.4 degrees or higher <ul style="list-style-type: none"> • Same for all ages 	
Heart rate	Looks back 4 hours of current encounter for a HR that meets definition <ul style="list-style-type: none"> • Less than 90 days old: greater than 205 • 91 days to 2 yr old: greater than 190 • More than 2 yr and less than 10 yr: greater than 140 • 10 yr or older: greater than 100 	
Respiratory rate	Looks back 4 hours of current encounter for a RR that meets definition <ul style="list-style-type: none"> • Less than 1 yr: RR greater than 60 • More than 1 yr and less than 4 yr: RR greater than 40 • More than 4 yr and less than 6 yr: RR greater than 34 • More than 6 yr and less than 13 yr: RR greater than 30 • 13 yr or older: RR greater than 24 	
Systolic BP	Looks back 4 hours of current encounter for a systolic BP that meets definition <ul style="list-style-type: none"> • Less than 30 days old: SBP less than 60 • Less than 1 year old: SBP less than 70 • Less than 2 years old: SBP less than 72 • Less than 3 years old: SBP less than 74 • Less than 4 years old: SBP less than 76 • Less than 5 years old: SBP less than 78 	<ul style="list-style-type: none"> • Less than 6 years old: SBP less than 80 • Less than 7 years old: SBP less than 82 • Less than 8 years old: SBP less than 84 • Less than 9 years old: SBP less than 86 • Less than 10 years old: SBP less than 88 • Patient is 10y/o and up: SBP less than 90
Pulse exam	Looks for last documented assessment of current encounter: absent, weak, or bounding	
Capillary refill	Looks for last documented assessment of current encounter: absent or more than 3 sec	
Skin abnormalities	Looks for last documented assessment of current encounter: dusky, flushed, hot, cool, cyanotic	

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Inpatient Sensitivity and Specificity Pediatric Sepsis Model		
Parameter	Details	
High risk conditions	<ul style="list-style-type: none"> Oncology diagnosis Asplenia Sickle Cell Disease Transplant 	<ul style="list-style-type: none"> Central venous line, PICC, urethral catheter Immunosuppressive medication(S) Immunocompromised / Immunodeficiency
Temperature	Looks back 24 hours of current encounter for a temperature that is 96.8 or lower or 100.4 degrees or higher. Same criteria for all ages	
Heart rate	Looks back 24 hours of current encounter for a HR that meets definition <ul style="list-style-type: none"> Less than 90 days old: greater than 205 91 days to 2 yr old: greater than 190 More than 2 yr and less than 10 yr: greater than 140 10 yr or older: greater than 100 	
Systolic BP	Looks back 4 hours of current encounter for a systolic BP that meets definition <ul style="list-style-type: none"> Less than 30 days old: SBP less than 60 Less than 1 year old: SBP less than 70 Less than 2 years old: SBP less than 72 Less than 3 years old: SBP less than 74 Less than 4 years old: SBP less than 76 	<ul style="list-style-type: none"> Less than 5 years old: SBP less than 78 Less than 6 years old: SBP less than 80 Less than 7 years old: SBP less than 82 Less than 8 years old: SBP less than 84 Less than 9 years old: SBP less than 86 Less than 10 years old: SBP less than 88 Patient is 10y/o and up: SBP less than 90
Capillary refill	Looks back for last documented assessment of current encounter: absent or more than 3 sec	
Skin abnormalities	Looks back for last documented assessment of current encounter: dusky, flushed, hot, cool, cyanotic	
Mental status exam OR Behavior-PEWS	Looks back for 24 hours: eyes do not open to stimulus, lethargic, non-responsive to stimulation, comatose OR Looks back 24 hours for PEWS Behavior score of 2 or 3	
ALT lab result	Looks back for 24 hours <ul style="list-style-type: none"> 90 days old or less: greater than 156 More than 90 days old: greater than 72 	
Neutrophil bands	Looks back for 24 hours for bands greater than 10%	
Procalcitonin	Looks back for 24 hours: any abnormal value	
Lactate	Looks back for 24 hours: higher than 2	
WBC	Looks back for 24 hours: <ul style="list-style-type: none"> Less than 8 days old: WBC more than 34 Less than 31 days old: WBC more than 19.5 Less than 2 years old: WBC more than 17.5 	<ul style="list-style-type: none"> Less than 6 years old: WBC more than 15. Less than 13 years old: WBC more than 13.5 13+ years old: WBC more than 11
Length of stay	Patient admitted for less than 12 hours	

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- Sepsis is a top 10 leading cause of death in US children ≤ 14 years old.
- Reported hospital mortality varies from 8 – 25% in pediatric patients with severe sepsis and septic shock
- 28% of sepsis survivors are discharged with new, mild functional disability; 17% have new moderate disability.
- About 1 in 3 children with severe sepsis will be rehospitalized within 90 days, most commonly due to scheduled chemotherapy, complications of indwelling devices, or recurrent sepsis.
- Using Pediatric Overall Performance Category (POPC), 34% of survivors have decline in their functional status at 28 days; 18% of these have poor functional outcome. (Farris et al)
- 21% of patients with severe sepsis develop acute kidney injury (AKI). 64% of patients with severe AKI died compared to 30% of patients with mild or no AKI. (CCM. 2016;44:2241-2250)

Findings that increase mortality include:^{4,7}

- Age < 1 year
- Underlying malignancy or immunodeficiency
- Underlying hematologic disorder
- Hyperchloremia
- Underlying cardiovascular disease
- Elevated serum lactate level
- Acute kidney injury
- Multiple organ dysfunction

Causes of death in pediatric sepsis

- Refractory shock (34%)
- Multiple organ dysfunction after shock recovery (27%)
- Neurologic injury (19%)
- Pulmonary failure (9%)

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Review of Sepsis and Septic Shock
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One of the most crucial elements of the care of a patient with sepsis/septic shock is early recognition and timely care. A high index of a suspicion for sepsis in a patient can lead to prompt treatment and even reversal of an otherwise worrisome trajectory. Thus, it is of utmost importance for every bedside caregiver to quickly be able to recognize the clinical signs and symptoms of suspected sepsis, sepsis, and septic shock.

Suspected sepsis, sepsis, and septic shock are part of the clinical spectrum in a patient who presents with suspected or known infection. For instance, patients may have a simple ear infection with no other concerns other than a low-grade fever and earache. In this revision of the Sepsis and septic shock guideline, clinical constructs for each of these categories were developed based on the IPSO study.

By definition, shock is an inability to maintain adequate perfusion or oxygen delivery to vital organs within the body – with septic shock being no different. Clinical manifestations of inadequate oxygen delivery depend on the organ systems affected. Vital sign abnormalities are often seen when evaluating a patient with presumed sepsis/septic shock. Patients may have hypo- or hyperthermia (fever), tachypnea and brady- or tachycardia. It is important to note that blood pressure may be normal in a child with any form of shock as compensatory mechanisms help maintain normotension until later in the clinical course. Patients in shock may present with altered mental status, agitation, fussiness, lethargy and inconsolable crying. Finally, shock is suggested in a patient with urine output less than 1 ml/kg/hour.

Unlike adults who generally present with vasodilatory/vasoplegic shock when septic, children can present with shock that is manifested by vasodilatation or vasoconstriction. In vasodilatory shock, more common in those with central line-associated sepsis (Brierly 2008), patients are often flushed with bounding pulses, flash capillary refill of less than 1 second and wide pulse pressure. In vasoconstriction shock, more likely in community-acquired sepsis (Brierly 2008), patients are noted to be cool and mottled with weak pulses and delayed capillary refill greater than 2 seconds.

Additionally, several risk factors may increase the likelihood of sepsis or septic shock that caregivers should be aware. These include, but are not limited to, malignancy, asplenia, sickle cell disease, bone marrow or solid organ transplant, central line or other indwelling catheter, severe global developmental delay or cerebral palsy, and immunodeficiency, immunocompromised or immunosuppressed state, and higher risks of UTIs (neurogenic bladder for example).

In a patient with suspected or proven infection, suspected sepsis, sepsis, and septic shock are generally diagnosed based on clinical suspicion with no single sign or symptom serving as confirmation. Currently there are no biochemical tests that will confirm the diagnosis. While there are septic shock scoring tools, screening tools for suspected sepsis are limited. Electronic medical record systems may have sepsis screening tools. At NCH, our pediatric sepsis screening tool is embedded in Epic. Some studies suggest that lactate (free-flowing venous sample) when elevated on initial measurement may be useful to evaluate presence of shock (Davis ACCM 2017). Additional laboratory tests to support the diagnosis may include complete blood count, procalcitonin, bacterial cultures, blood gas and metabolic profiles. In no case should treatment be delayed in order to obtain labs. Various sepsis tools are also available to assist with predicting those children with an infection who are at risk of needing critical care or dying as a result of sepsis.

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The Improving Pediatric Sepsis Outcomes Collaborative

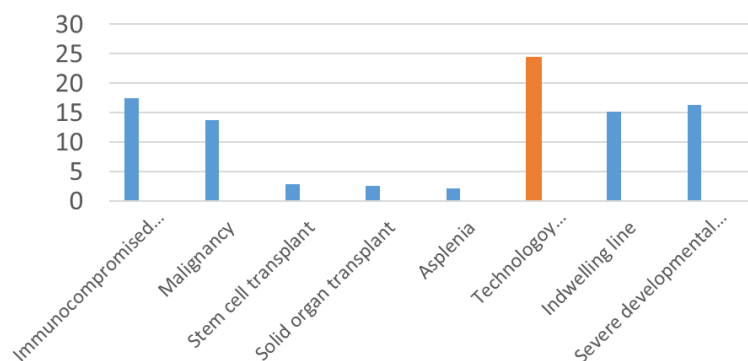
Bundled Care to Reduce Sepsis Mortality: The Improving Pediatric Sepsis Outcomes (IPSO) Collaborative. Paul et al. Pediatrics. 2023;152:e2022059938

This study represents a landmark study funded and supported by the Children's Hospital Association. The study results demonstrated that screening for sepsis and utilization of a treatment bundle significantly improved sepsis attributable mortality.

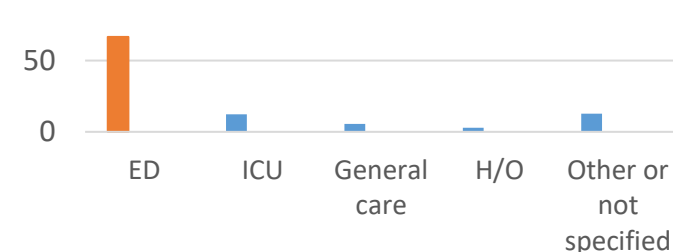
Key findings:

- Early recognition + treatment bundle improved outcomes in the emergency department and inpatient settings in children's hospitals.
- Early recognition was achieved by utilizing a 2-step screen: screening tool + bedside huddle.
- A treatment bundle and timeline for delivery of care existed for each group.
- Clinical constructs were developed and used to categorize patients into suspected sepsis and critical sepsis.
- There was an 80% decrease in mortality in the suspected sepsis group.
- There was a 47% decrease in mortality in the critical sepsis group.

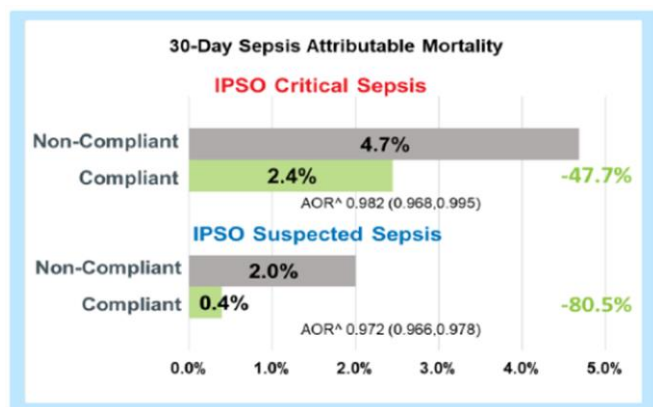
High Risk Conditions (%)



Location at Time of Recognition (%)



- 40 children's hospitals
- Median bed count of 238
- 37,330 cases of suspected infection
- Suspected sepsis: 24,518
- Critical sepsis: 12,821
- Iterative implementation of improvement over about 7-8 years



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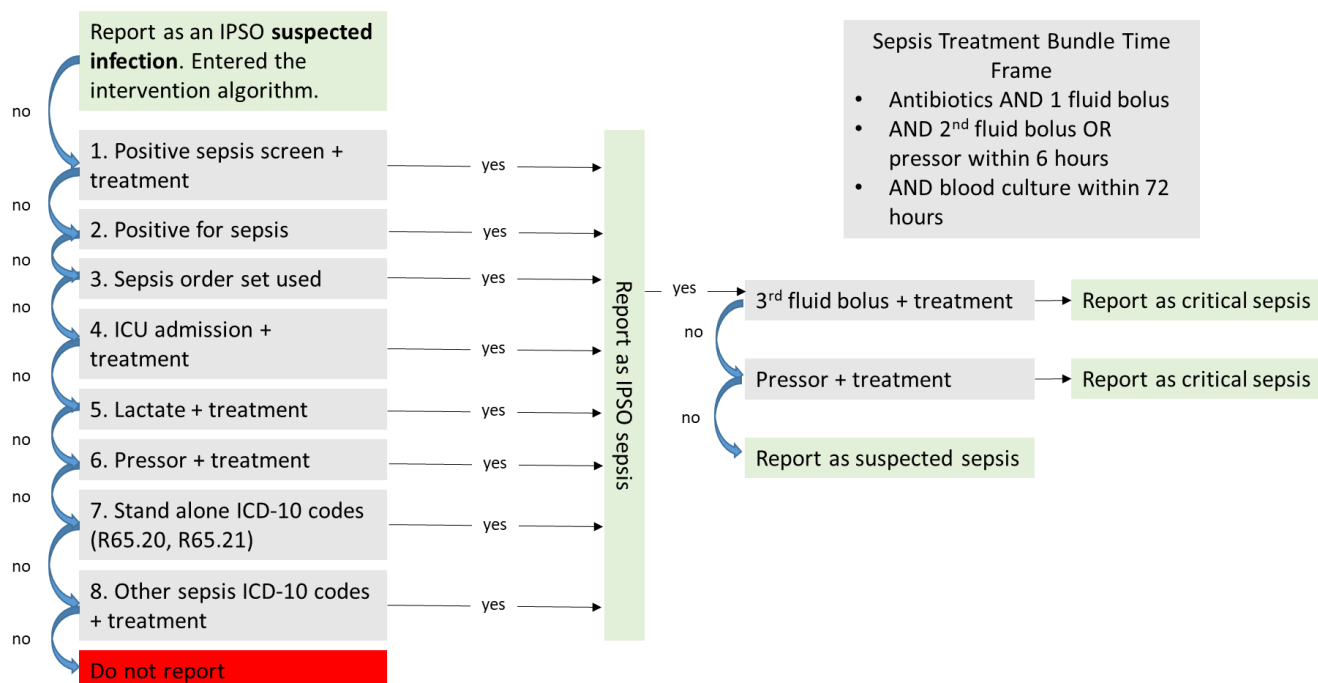
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Algorithm for assigning to the 2 groups



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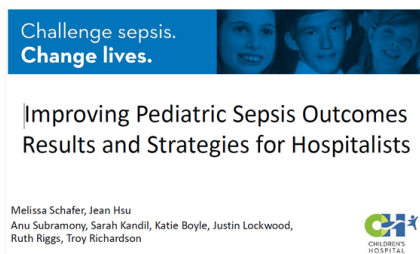
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IPSO Inpatient Population Analysis

This study is a secondary analysis of the IPSO study. The authors focused on children who had onset of sepsis as an inpatient. They evaluated outcomes as well as differences between emergency department and inpatient outcomes and patient characteristics. 2254 patients were included in this study.

Key findings:

- Inpatients have higher sepsis-attributable mortality (2% vs 1.4%)
- Longer length of stay (9 vs 5 days)
- More intensive care admissions (57.6% vs 54.1%)
- Greater average vasopressor use (18% vs 13.6%)
- >40% of inpatient cases were recognized within 12 hours of admission. 21% of cases were identified at >96 hours.
- Adherence to the sepsis treatment bundle was associated with improved 30-day sepsis attributable mortality. As bundle compliance improved, 30-day sepsis –attributable mortality decreased.



Mortality improves with compliance: Inpatient only

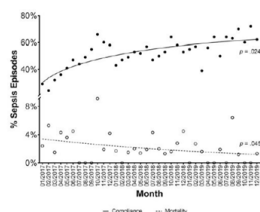


FIGURE 5 Improved bundle compliance leads to improved 30-day sepsis-attributable mortality for inpatients with sepsis.

Inpatient compared to ED

Inpatient vs ED clinical characteristics

- 10% of ED volume
- 18% vs **33.5% IPSO critical sepsis**
- 18% vs 6% originated from a referring hospital
- 37% vs 43% with comorbidities or medical complexity.
- 21% vs 20% technology dependence
- 16% vs 15% with severe cerebral palsy, intellectual disability
- 12% vs 21% immunocompromised/suppressed
- LESS likely to require 3rd fluid bolus or pressor
- **Longer time to recognition**
- Similar time to fluid bolus
- **Longer time to antibiotic**

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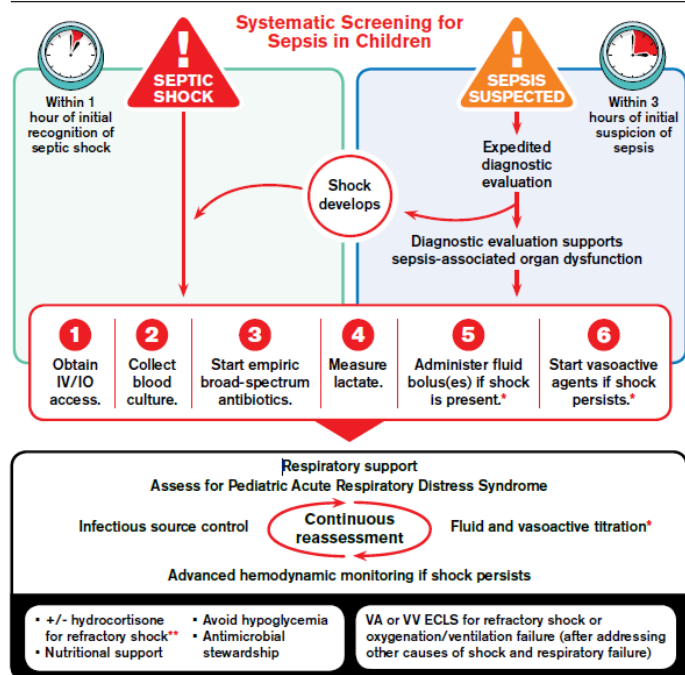
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Society of Critical Care Medicine Initial Resuscitation Algorithm for Children

Initial Resuscitation Algorithm for Children

Surviving Sepsis Campaign

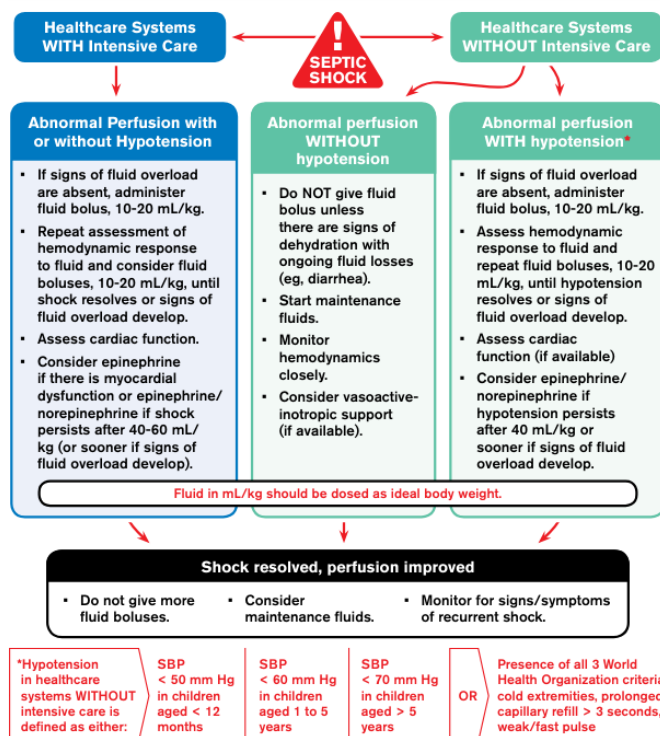


*See fluid and vasoactive algorithm. Note: Fluid bolus should be omitted from bundle if a) fluid overload is present or b) it is a low-resource setting without hypotension. Fluid in mL/kg should be dosed as ideal body weight.

**Hydrocortisone may produce benefit or harm.

Fluid and Vasoactive-Inotrope Management Algorithm For Children

Surviving Sepsis Campaign



www.sccm.org/SurvivingSepsisCampaign/Guidelines/Pediatric-Patients

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Fluid resuscitation remains a cornerstone in the initial treatment of pediatric septic shock. This tenant draws from the basic pathophysiology of sepsis in which a systemic inflammatory response leads to peripheral vasodilation and increased capillary permeability. This causes third spacing and decreased circulating intravascular volume. Fluid administration increases the total intravascular volume, thus increasing venous return, or preload. This, according to the Frank-Starling curve improves cardiac output and perfusion to vital organs.

Multiple studies have demonstrated the efficacy of timely administration of fluids. A landmark paper by Carcillo et al evaluated 90 pediatric patients with severe sepsis (a term no longer used) and septic shock. Of these, patients who received <20mL/kg of volume within the first hour had a markedly increased mortality compared to those who received >40mL/kg of volume within the first hour (73% vs 33%, p=0.03). Additionally, mortality trended up with increased length of time to volume infusion. Controlling for PIM score, early fluid resuscitation was associated with a 3-fold reduction in the odds of death. (Carcillo, 2008) There was no increased risk of ARDS or cardiogenic pulmonary edema in this study. This finding was mirrored in a study of 91 pediatric patients presenting to community hospital with septic shock, demonstrating a 9-fold increased odds of survival with rapid fluid resuscitation (Hann, 2003)). Similarly, In 2015, Akcan et al. implemented a fluid resuscitation bundle for children in the ED suspected to have septic shock or severe sepsis, which allowed for more timely administration of fluids. In the post-implementation group, there was significantly decreased incidence of acute kidney injury (29% vs 54% in pre-implementation group, p=0.04) as well as decreased PICU and hospital length of stay and decreased mortality (10 vs 3%, p=0.037 (Cruz)).

However, there is no doubt that fluid overload can be quite problematic. Chen et al demonstrated that early fluid overload (>5% fluid accumulation in the 1st 24 hours of PICU admission) was an independent risk factor for mortality (Chen). Additionally, Wong et al risk stratified patients by initial mortality risk (high, intermediate and low) and found that those with initial low mortality risk had worse outcomes with positive fluid balance. Thus, high volumes of fluids (generally >60mL/kg) should be used with cautions. Additionally, it is important to identify fluid-refractory shock early to prevent ongoing fluid resuscitation when it is ineffective. Fluid responsiveness should be based on clinical indicators, including heart rate, capillary refill, peripheral pulse character and mental status. If a child is in fluid-refractory septic shock, transition to vasopressors should be undertaken, ideally within 60 minutes of resuscitation.

The choice of initial fluid resuscitation is somewhat controversial. Theoretically, colloids may increase blood oncotic pressure and restore intravascular volume more efficiently than crystalloid. This, however, does not pan out in the literature, where actual volumes of colloid used for resuscitation are comparable to volumes of crystalloid used (Long). This may be because the capillary leak inherent to septic shock allows for diffusion of these more oncotic proteins into the interstitial space, thus worsening interstitial edema.. Head on evaluation of colloid vs crystalloid in the SAFE trial, which randomized 6997 adults to resuscitation with either 4% albumin or 0.9% NS, demonstrated no difference in mortality or other secondary endpoints.

In general, crystalloid is favored as the initial fluid of choice in resuscitation. Traditionally, 0.9% NS has been used, though this practice has been questioned as it can lead to a profound hyperchloremic metabolic acidosis. For this reason, many have begun to advocate for resuscitation with balanced crystalloid such as LR. However, a recent matched analysis of data from 12,529 patients <18 years of age with sepsis at 328 hospitals compared patients resuscitated with NS only to those resuscitated with any or only LR. Outcomes, including mortality, were no different between NS and LR-any or LR-only groups. Thus, no strong evidence for one type of crystalloid over another exists. Martin et al describes their practice of using any readily available crystalloid for initial resuscitation and switching to a more balanced solution, such as LR, if the pH falls below 7.2 or the serum chloride rises above 110.

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Integral to the management of sepsis and septic shock is the early administration of the appropriate, broad spectrum antibiotic(s). As a core element of the resuscitation bundle of the Surviving Sepsis Campaign, patients with septic shock should have administration of an empiric IV antibiotic(s) within one hour of shock recognition. Treatment should not be delayed by obtaining labs or studies, including a blood culture (Simmons). The adult literature has demonstrated increased mortality with delayed treatment of sepsis (Ames, Hans studies).

Sepsis can be the result of an infection with any microorganism, including bacteria, viruses, fungi, or protozoans. Bacteria are the most common etiology and account for >90% of cases. It is imperative that empiric treatment be broad and directed at many different bacteria species (Simmons, et al). If the primary site of infection is known at the time of recognition, then therapy can be tailored to cover the most likely pathogen.

Gram positive bacteria are the leading cause of sepsis in all patients, accounting for greater than fifty percent of cases. The most common organisms include: *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Staphylococcus epidermidis*, and other coagulase negative staphylococci, and *Enterococcus* species. Increasing resistance, particularly MRSA and vancomycin resistant *Enterococcus* species is a growing problem (Simmons). Coagulase negative staphylococci are commonly associated with central line infections, or infected intravascular devices.

Gram negative organisms are less common causes of sepsis, but tend to result in greater morbidity and mortality. *Escherichia coli* is the most implicated organism. Also included in this group are: *Klebsiella*, *Pseudomonas*, *Proteus*, *Serratia*, and *Enterobacter*. *Pseudomonas* infections are common in immunocompromised and neutropenic patients, and is overall responsible for more sepsis-related mortality than any other organism (Simmons).

In a study by Ames et al, ED patients admitted for septic shock, bacterial infection was identified in 48% of patients (streptococcus – 42 cases, staphylococcal – 24 cases, E. coli – 19 cases, and other gram negative species – 46, presumed bacterial infection in 16%, viral infection in 16% (rhinovirus – 17, rsv – 10, enterovirus – 1, and CMV 1), and no source of infection identified in 21%. Patients without an identified infectious etiology were more likely to have a complex chronic condition. 72% of isolated bacterial pathogens were sensitive to ceftriaxone.

Empiric antibiotics in the treatment of sepsis should be broad enough to cover the most likely organisms, as well as have adequate tissue penetration into the presumed primary source of infection. Clinicians should also be aware of emerging resistance patterns in their hospitals and communities. Bactericidal antimicrobial agents are preferred over bacteriostatic agents in the management of sepsis. The most common classes of antibiotics used empirically include: Beta lactams, aminoglycosides, fluoroquinolones, and vancomycin (Simmons).

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Antibiotic Choices for Sepsis and Septic Shock. It may be appropriate to change subsequent empiric antibiotic choices based on patient data and clinician concerns

Patient Population	Preferred Empiric Antibiotics	Alternatives and/or Additional Antibiotic(s)
< or equal to 28 days	Vancomycin + Ceftazidime	<u>Concern for HSV</u> Add Acyclovir <u>Cephalosporin and Vancomycin</u> <u>Anaphylaxis</u> Not applicable, If question consult pharmacy
> 28 days	Vancomycin + Ceftriaxone	<u>Cephalosporin Anaphylaxis</u> Levofloxacin <u>Vancomycin Anaphylaxis (not Red Man)</u> Linezolid IV
Pre-existing central line BMT/Oncology Patient Hospital Admission in Past 60 days	Vancomycin + Cefepime	<u>Cephalosporin Anaphylaxis</u> Levofloxacin <u>Vancomycin Anaphylaxis (not Red Man)</u> Linezolid IV
Febrile, neutropenia AND septic shock (hemodynamically unstable)	Vancomycin + Meropenem	<u>Cephalosporin Anaphylaxis</u> Levofloxacin <u>Vancomycin Anaphylaxis (not Red Man)</u> Linezolid IV
Short Gut Syndrome Concern for Anaerobes	Vancomycin + Cefepime + Metronidazole	<u>Cephalosporin Anaphylaxis</u> Levofloxacin for Cefepime <u>Vancomycin Anaphylaxis (not Red Man)</u> Linezolid IV

Antibiotic coverage for patient populations not addressed in this table needs to be individualized.

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Fluid Refractory Shock and Cardiovascular Drug Support
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Fluid-refractory shock may develop in children who remain in a state of decreased perfusion despite volume resuscitation with up to 60 ml/kg of isotonic fluids within the first 60 minutes of resuscitation (1). This includes patients who continue to have any of the following: delayed capillary refill (<2 seconds) or flash capillary refill (>2 seconds), weak or bounding peripheral pulses, heart rate outside of appropriate norms for age, cool/pale/mottled skin, narrow or widened pulse pressure, and altered mental status (1). By implementing the ACCM/PALS therapies, Carcillo et al reported a 40% mortality odds ratio reduction if these hemodynamic aberrancies were reversed (2). Therefore, in patients with fluid-refractory shock, vasoactive infusions may be indicated in an attempt to achieve adequate perfusion and restore appropriate hemodynamics. The choice of vasoactive infusions depends both on the patient's hemodynamic status and the subsequent effects the medication will have on systemic vascular resistance (SVR), heart rate (chronotropy), and contractility (inotropy).

Epinephrine is the recommended first line choice for fluid-refractory septic shock especially for patients with vasoconstriction (high SVR state with delayed capillary refill, cool extremities, faint pulses) (1). The primary effects of low doses of epinephrine (0.05 - 0.2 µg/kg/min) are increased contractility via β_1 adrenergic stimulation and mild vasodilation in the peripheral vasculature via β_2 adrenergic stimulation (3). This improves cardiac output and helps reduce SVR to improve perfusion. Higher infusion ranges (≥ 0.2 µg/kg/min) will introduce a vasopressor effect by increasing SVR due to stimulation of α receptors (3).

Norepinephrine may be used instead of epinephrine if the patient has evidence of vasodilatory shock (low SVR state with wide pulse pressure, bounding pulses, flash capillary refill), norepinephrine is recommended (1). Norepinephrine's action is primarily through its vasoconstriction effect via α_1 adrenergic receptor stimulation (4). This results in improvement in systemic perfusion in this hyperdynamic state of septic shock.

Vasopressin can be added in a catecholamine-resistant state when a patient has persistent hypotension despite volume resuscitation and vasopressor infusion (1). It acts to increase systemic vascular resistance and mean arterial pressure through its stimulation of vasopressin-specific receptors (4).

Dobutamine can also be used as an adjunctive agent to augment cardiac contractility, which improves cardiac output (1). It can decrease SVR; therefore, it is more appropriate for a patient with normal blood pressure or who is adequately supported with norepinephrine or high-dose epinephrine (1).

Milrinone is a phosphodiesterase inhibitor type III, which causes increased contractility, decreased SVR, and improved diastolic relaxation (4). This may be used as an adjunct in normotensive patients with epinephrine-resistant shock (1). It has a long elimination half-life and is affected by renal and liver dysfunction (1).

Phenylephrine

Children with septic shock require frequent reassessment due to a potentially labile hemodynamic state. Response to cardiovascular infusions must also be evaluated often in order to ensure a trajectory towards resolution of septic shock.

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Cardiovascular Drug	Primary Indication	Dosing Range
First-line Drugs		
Epinephrine	Any shock presentation	0.05 – 1 mcg/kg/min Quickly escalate to achieve improved hemodynamics and organ function
Norepinephrine	May be used instead of epinephrine for vasodilatory Shock	0.05 – 1 mcg/kg/min Quickly escalate to achieve improved hemodynamics and organ function
Second-line Drugs		
Vasopressin	Catecholamine Resistant Shock, especially if vasoplegic shock	< 40 kg: 18 – 80 milliunits/kg/hr 40 kg or greater: 1800 milliunits/hr
Dobutamine	Cardiogenic Shock with adequate BP or adjunct to epinephrine	5 – 20 mcg/kg/min
Milrinone	Catecholamine refractory cardiogenic shock if BP normal	0.25 – 1 mcg/kg/min
Phenylephrine	Alternative for vasoplegic shock with good cardiac function	0.1 – 1 mcg/kg/min

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Patients with septic shock that is refractory to fluids, antibiotics and pressors may benefit from one or several treatment adjuncts. Commonly employed therapies include steroids for catecholamine-resistant shock, methylene blue, continuous renal replacement therapy (CRRT) for fluid overload and acute kidney injury (AKI), extra-corporeal membrane oxygenation (ECMO) for respiratory failure, arrest, or severe multiple organ dysfunction syndrome (MODS), and therapeutic plasma exchange (TPE) for coagulopathy and MODS. In addition, glycemic control with maintenance of blood glucose levels 70-180 and prevention of wide variation, normalization of ionized calcium levels, transfusion to maintain hemoglobin levels >10 (>7 once shock has resolved), correction of significant electrolyte abnormalities and thyroid hormone deficiency all play a role in management of severe sepsis and refractory septic shock.

STEROIDS:

Routine use of steroids in septic shock is not recommended in pediatric or adult patients. Pediatric patients with known or suspected adrenal insufficiency and those on chronic or recurrent steroids prior to presentation are candidates for early use of hydrocortisone. In addition, pediatric patients with shock that is refractory to fluid and catecholamine therapy may benefit from hydrocortisone therapy. If possible, cortisol levels should be obtained prior to initiation of steroid therapy. ACTH-stimulation testing is not necessary prior to steroid administration.

EXTRACORPOREAL THERAPIES:

Multiple modalities utilize procedures whereby blood is diverted from the patient's circulation, some process(es) are performed on the blood, and the blood is then returned to the patient's circulation. Any one of these therapies can be utilized alone or in combination with one or both of the others.

Veno-arterial (VA) ECMO provides cardiac output, oxygenation and ventilation and has been shown in multiple studies to improve mortality for patients with septic shock who suffer full arrest or have severe/refractory respiratory failure. ECMO has also been utilized for patients with fluid and catecholamine-resistant shock and those with shock-associated MODS. Some studies suggest higher flows (>150mL/Kg/minute) are associated with improved outcomes. Both CRRT and TPE can also be performed through the ECMO circuitry for patients with fluid overload, AKI, thrombocytopenia and/or MODS.

Continuous Renal Replacement Therapy (CRRT) is a slow, continuous extracorporeal process whereby fluid and toxins are removed from the patient's blood, simulating the function of the kidneys; CRRT avoids the more rapid fluid shifts associated with typical hemodialysis. Fluid overload is associated with increased mortality in patients with septic shock; multiple studies have shown that use of CRRT prior to 10-20% fluid overload is associated with increased survival. CRRT allows for prevention or management of fluid overload and AKI, clearance of lactate and organic acids, removal of inflammatory mediators, and reversal of coagulopathy.

Total Plasma Exchange (TPE) attenuates the inflammatory response by removal of cytokines and cytotoxins present in plasma, replenishes proteins and enzymes which help balance the pro- and anti-thrombotic milieu, aids in organ system recovery (particularly hematologic and renal systems) and aids in reversal of coagulopathy. Some studies demonstrate improved outcomes if TPE is instituted earlier (<30 hours after recognition of sepsis).

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- **Inpatient: Initial treatment of suspected sepsis, sepsis, and septic shock order set [New]**
- **PEDS ED Treatment: Initial treatment of suspected sepsis, sepsis and septic shock [revised existing order set and added Septic Shock to name [1605030243]**
- Retire Severe Sepsis and Septic Shock order set [3040530399]
- PEDS Rule Out Infection for Patients Less than 2 Year of Age Admit [Rename of 3040530129- replaced the word sepsis with infection; sepsis will not be a search word for this order set.]
- PEDS ED Treatment Febrile Infant Work Up for Patient Age 0/Birth to 60 Days [Rename of 1605030263-removed the word sepsis from the title; sepsis will not be a search word for this order set.]

Bolded order sets are the preferred way to order evaluation, monitoring, and treatment orders for suspected sepsis, sepsis and septic shock. Please avoid using single orders or other order sets.

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Section Title: Must Read Articles
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Guidelines must have a mini review by the owner every 2 years and a major review by the writing group every 4 years. If there has been attrition of members during the interval, the owner may decide to move forward with the remaining members or add new members. If substantive changes are required, new members should be added as there may need to be a formal implementation plan to assure that the changes are incorporated into the care of patients. Any associated order sets, policies, and procedures will need to be updated.

Version	Date	Guideline Owner	Summary of Edits	Next Revision Due
1		Vicki Montgomery, MD	NA	August 2021
2	June 2025	Vicki Montgomery, MD	Numerous based on IPSO collaborative results, retiring SSASS as a construct for decision making, and shifting focus to early recognition.	June 2029

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