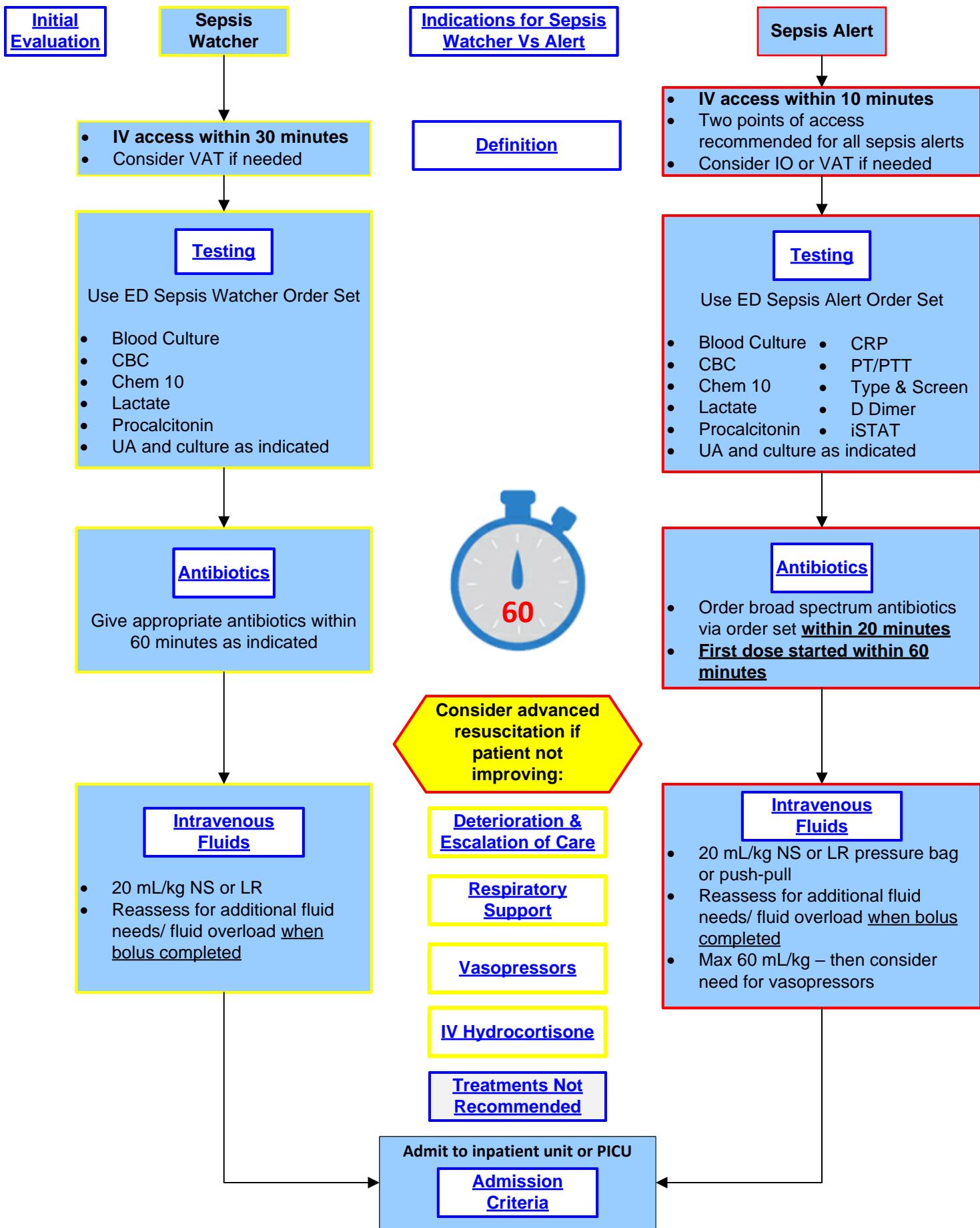


Management



Definition

Sepsis:

- Confirmed or suspected infection accompanied by life-threatening organ dysfunction.
- Also defined as suspected or confirmed infection along with at least 2 points for organ dysfunction from the Phoenix Sepsis score.

Septic Shock:

Subset of patients with sepsis with at least 1 point for cardiovascular dysfunction. This is associated with higher mortality.

Life-threatening Organ Dysfunction:

Defined by the novel Phoenix Sepsis Score, which is a composite of respiratory, cardiovascular, coagulation, and/or neurological dysfunction.

The Phoenix Sepsis Score:

Variables	0 Points	1 Point	2 Points	3 Points
Respiratory, 0-3 points	$\text{PaO}_2:\text{FIO}_2 \geq 400$ or $\text{SpO}_2:\text{FIO}_2 \geq 292^a$	$\text{PaO}_2:\text{FIO}_2 < 400$ on any respiratory support or $\text{SpO}_2:\text{FIO}_2 \geq 292$ on any respiratory support ^{a,b}	$\text{PaO}_2:\text{FIO}_2 100-200$ and IMV or $\text{SpO}_2:\text{FIO}_2 148-220$ and IMV ^a	$\text{PaO}_2:\text{FIO}_2 < 100$ and IMV or $\text{SpO}_2:\text{FIO}_2 < 148$ and IMV ^a
Cardiovascular, 0-6 points		1 Point each (up to 3)	2 Points each (up to 6)	
	No vasoactive medications ^c	1 Vasoactive medication ^c	≥ 2 Vasoactive medications ^c	
	Lactate $< 5 \text{ mmol/L}^d$	Lactate 5-10.9 mmol/L^d	Lactate $\geq 11 \text{ mmol/L}^d$	
Age based^e				
	Mean arterial pressure, mmHg ^f	Mean arterial pressure, mmHg ^f	Mean arterial pressure, mmHg ^f	
<1 mo	>30	17-30	<17	
1 to 11 mo	>38	25-38	<25	
1 to <2 y	>43	31-43	<31	
2 to <5 y	>44	32-44	<32	
5 to <12 y	>48	36-48	<36	
12 to 17 y	>51	38-51	<38	
Coagulation, 0-2 points				
		1 Point each (max 2 points)		
	Platelets $\geq 100 \times 10^3/\mu\text{L}$	Platelets $< 100 \times 10^3/\mu\text{L}$		
	International normalized ratio ≤ 1.3	International normalized ratio > 1.3		
	D-dimer $\leq 2 \text{ mg/L FEU}$	D-dimer $> 2 \text{ mg/L FEU}$		
	Fibrinogen $\geq 100 \text{ mg/dL}$	Fibrinogen $< 100 \text{ mg/dL}$		
Neurological, 0-2 points				
	Glasgow Coma Scale score > 10 ; pupils reactive	Glasgow Coma Scale score ≤ 10	Fixed pupils bilaterally	
Phoenix sepsis criteria				
Sepsis	Suspected infection and Phoenix Sepsis Score ≥ 2 points			
Septic shock	Sepsis with ≥ 1 cardiovascular point(s)			

Abbreviations: FEU, fibrinogen equivalent units; IMV, invasive mechanical ventilation; INR, international normalized ratio of prothrombin time; MAP, mean arterial pressure; $\text{PaO}_2:\text{FIO}_2$, arterial partial pressure of oxygen to fraction of inspired oxygen ratio; SpO_2 , oxygen saturation measured by pulse oximetry (only SpO_2 of $\leq 97\%$).

a $\text{SpO}_2:\text{FIO}_2$ ratio is only calculated if SpO_2 is 97% or less.

b The respiratory dysfunction of 1 point can be assessed in any patient receiving oxygen, high-flow, noninvasive positive pressure, or IMV respiratory support, and includes a $\text{PaO}_2:\text{FIO}_2$ ratio of less than 200 and a $\text{SpO}_2:\text{FIO}_2$ ratio of less than 220 in children who are not receiving IMV. For children receiving IMV with a $\text{PaO}_2:\text{FIO}_2$ less than 200 and $\text{SpO}_2:\text{FIO}_2$ less than 220, see criteria for 2 and 3 points.

c Vasoactive medications include any dose of epinephrine, norepinephrine, dopamine, dobutamine, milrinone, and/or vasopressin (for shock).

d Lactate reference range is 0.5-2.2 mmol/L . Lactate can be arterial or venous.

e Age is not adjusted for prematurity, and the criteria do not apply to birth hospitalizations, children whose postconceptional age is younger than 37 weeks, or those 18 years or older.

f Use measured MAP preferentially (invasive arterial if available or noninvasive oscillometric), and if measured MAP is not available, a calculated MAP ($1/3 \times$ systolic + $2/3 \times$ diastolic) may be used as an alternative.

Schlappbach LJ, Watson RS, Sorce LR, et al. International Consensus Criteria for Pediatric Sepsis and Septic Shock. *JAMA*. 2024;331(8):665-674. doi:10.1001/jama.2024.0179

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Differential Diagnosis

- Ingestion
- Hypoglycemia
- Environmental Hyperthermia/Heat Stroke
- Congenital Heart disease (Particularly in patients <2 weeks of age)
- Myocarditis
- Inborn Errors of Metabolism
- Congenital Adrenal Hyperplasia
- Intussusception
- Malrotation with volvulus
- Necrotizing enterocolitis
- Acute Gastroenteritis
- Hypovolemic shock
- Anemia
- New onset diabetes

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Sepsis Risk Score Calculator

Sepsis Risk Score Calculator:

- 3 points:
Hypotension
- 2 points:
Fever or concern for infection
Tachycardia (fever adjusted)
Tachypnea
Cap Refill abnormality
High risk condition*
- 1 point:
Peripheral pulse abnormality

BPA fires for score ≥ 6 with no exclusion criteria

*High Risk Conditions:

- Malignancy
- Asplenia (including SCD)
- Bone Marrow or
- solid organ transplant
- Central or indwelling line/catheter
- Significant neurologic impairment
- Immunodeficiency
- Immunocompromise
- Immunosuppression
- Chemotherapy either active or in last 6 months
- Bone marrow transplant in last 12 months

Sepsis Risk Score Exclusion Criteria:

Always excluded:

- Trauma Activations
- ESI Category 5
- Chief complaints:
Heart problem
Abnormal blood sugar
Intentional ingestion

Excluded unless high risk condition* present:

- Respiratory chief complaint: BPA fires for score ≥ 9
Asthma
Choking
URI symptoms
Croup-like symptoms
Flu-like illness
Respiratory distress
Shortness of breath
Wheezing
- Meds given/ ordered:
Albuterol
Prednisolone
Prednisone
Decadron
Keppra
Diazepam
Fosphenytoin

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High Risk Condition

High Risk Conditions:

- Malignancy
- Asplenia (including sickle cell disease)
- Bone Marrow or solid organ transplant
- Central or indwelling line/catheter
- Significant neurologic impairment
- Immunodeficiency
- Immunocompromise
- Immunosuppression
- Chemotherapy either active or in last 6 months or bone marrow transplant in last 12 months

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Indications for Sepsis Watcher vs Alert

Indications for sepsis watcher or alert include but are not limited to:

Watcher

- Worsening, persistent or unexplained tachycardia
- Concern or uncertainty regarding:
 - Mental status
 - Respiratory status
 - Perfusion
 - Purpura, petechia
 - Orthostasis or syncope

Alert

- Critically ill
- Hypotension
- Severe alterations in mental status or respiratory status
- Organ failure:
 - Lactate > 4
 - Acute Kidney Injury
 - Coagulopathy
 - Liver Dysfunction

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Testing

Sepsis Watcher:

- Blood culture x 1 (via port/indwelling catheter if present, otherwise via PIV)
- CBC
- chem 10
- lactate
- procalcitonin
- urinalysis and urine culture, as indicated

Sepsis Alert:

- Blood culture (via port/indwelling catheter if present, otherwise via PIV)
- CBC
- chem 10
- LFTs
- lactate,
- procalcitonin
- CRP
- Coagulation panel
- type and screen
- D-dimer
- VBG
- urinalysis and urine culture, as indicated

Blood Culture: We recommend obtaining blood cultures before initiating antimicrobial therapy in situations where this does not substantially delay antimicrobial administration.

Lactate level: Should be interpreted as part of a more comprehensive assessment of clinical status and perfusion. Trends in blood lactate levels, in addition to clinical assessment, may help guide resuscitation of children with septic shock or sepsis-associated organ dysfunction (weak recommendation, very low quality of evidence).

Procalcitonin: We recommend obtaining procalcitonin levels in all age groups for the purposes of risk stratification

Based on Best Practice Statement from SCCM Surviving Sepsis Campaign

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Antibiotics

Early Antibiotic Administration:

In children with septic shock, start antibiotics within 1 hour of recognition (strong recommendation, very low quality of evidence). In children with sepsis-associated organ dysfunction, start antibiotics within 3 hours of recommendation (weak recommendation, very low quality of evidence)

Broad Spectrum Therapy:

Start empiric broad-spectrum therapy with one or more antimicrobial agents to cover all likely pathogens until sensitivities are available (*Based on Best Practice Statement from SCCM Surviving Sepsis Campaign*)

Patient Category	Medication Dosing			
Neonates 0-28 days	Ampicillin 0-7 days: 100 mg/kg/dose 8-28 days: 75 mg/kg/dose	Cefotaxime 50 mg/kg/dose	Vancomycin 20 mg/kg/dose	+/- Acyclovir 20 mg/kg/dose
Neonates 29-60 days	Ampicillin 75 mg/kg/dose	Ceftriaxone 50 mg/kg/dose	Vancomycin 20 mg/kg/dose	+/- Acyclovir 20 mg/kg/dose
Infants and children > 60 days	Ceftriaxone Bacteremia/Pyelonephritis: 50 mg/kg/dose (max 2000 mg/dose) Pneumonia: 75 mg/kg/dose (max 2000 mg/dose) Meningitis: 100 mg/kg/day (max 4000 mg/day)		Vancomycin <i>Per institution guidelines</i>	+/- Metronidazole 10 mg/kg (max 500 mg)
High risk patients*	Cefepime 50 mg/kg/dose (max 2000 mg/dose)	Tobramycin <i>Per institution guidelines</i>	Vancomycin <i>Per institution guidelines</i>	+/- Metronidazole 10 mg/kg (max 500 mg)
Febrile Neutropenia	Cefepime 50 mg/kg/dose (max 2000 mg/dose)		+/- Vancomycin <i>Per institution guidelines</i>	
Sickle cell fever	Ceftriaxone 75 mg/kg/dose (max 2000 mg/dose)		+/- Vancomycin <i>Per institution guidelines</i>	

*Patients at high risk for drug resistant pathogens or nosocomial infections:

- Hospitalization > 48 hours
- Recent antibiotics (either currently on antibiotics or on greater than 7 days within the past 6 weeks)
- Chronic lung disease, including chronic mechanical ventilation
- Immunosuppression, immunodeficiency, immunosuppressive drug therapy (recent chemo, recent (acute) steroids for greater than 5 days within the past 6 weeks, chronic daily steroids (greater than 5 mg/day prednisone equivalent))
- Malignancy or organ transplant
- Resident of a chronic care facility
- Recent hospitalization (within the past 1 month)
- History of resistant organisms

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Intravenous Fluid Resuscitation

Fluid Volume:

In children with septic shock or sepsis-associated organ dysfunction, initial resuscitation with 40-60mL/kg in fluid boluses (10-20mL/kg per bolus) over the first hour is recommended. Titrate to markers of cardiac output (heart rate, blood pressure, capillary refill time, urine output) and discontinue if signs of fluid overload develop.

Weak recommendation, low quality of evidence

Signs of fluid overload

include but are not limited to :

- Pulmonary crackles
- Development of hepatomegaly
- Worsening unexplained hypoxia

Fluid Type:

Crystalloids, rather than albumin, are the preferred fluid type for initial resuscitation in children with septic shock or sepsis-associated organ dysfunction.

Weak recommendation, moderate quality of evidence

Both 0.9% normal saline and Lactated Ringers solution are acceptable crystalloids in children, but the use of balanced/buffered crystalloids such as Lactated Ringers' are suggested.

Weak recommendation, very low quality of evidence

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Deterioration & Escalation of Care

Identification of Deterioration:

- Worsening cardiac output (tachycardia, hypotension, delayed capillary refill)
- Worsening end-organ perfusion (altered mental status, decreased urine output, renal dysfunction, liver dysfunction)
- Fluid overload (hepatomegaly, pulmonary edema)

Escalation of Care Protocol:

Patient should be re-evaluated, and further management should be guided by clinical assessment

Consider the following interventions:

- IV fluid resuscitation
- Vasopressors
- Non-invasive mechanical ventilation
- Intubation
- Invasive blood pressure monitoring
- Central line placement
- Admit to the PICU

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Respiratory Support

Noninvasive Mechanical Ventilation:

A trial of noninvasive mechanical ventilation in children with sepsis-induced ARDS who are responding to initial resuscitation is warranted (weak recommendation, very low quality of evidence). It is recommended to use a high PEEP in children with sepsis-induced ARDS (weak recommendation, very low quality of evidence).

Intubation:

Consider intubation in children with fluid-refractory, catecholamine-resistant septic shock without respiratory failure (*Based on Best Practice Statement from SCCM Surviving Sepsis Campaign*).

RSI medication:

Ketamine is recommended when intubating children with septic shock or sepsis-associated organ dysfunction (weak recommendation, low quality of evidence).

Based on Best Practice Statement from SCCM Surviving Sepsis Campaign

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Vasopressors

Vasopressors:

- Epinephrine and norepinephrine are preferred first-line vasoactive medications in children with septic shock.
 - There are no recommendations for a specific first line vasoactive medication for children with septic shock. This decision should be determined by clinical preference and patient physiology.
- Vasopressin is preferred for second-line vasoactive in children with septic shock who require high-dose catecholamines (*weak recommendation, low quality of evidence*).

Administration of dilute vasoactive medications can be administered through a peripheral vein if central venous access is not readily accessible

Based on Best Practice Statement from SCCM Surviving Sepsis Campaign

Vasopressor	Initial Dose	Max Dose
Epinephrine	0.05 mcg/kg/min	2 mcg/kg/min
Norepinephrine	0.05 mcg/kg/min	2 mcg/kg/min
Vasopressin	0.6 milli-units/kg/min	2 milli-units/kg/min

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Corticosteroids

Corticosteroids:

Consider IV hydrocortisone (2mg/kg, max 100mg) in children with septic shock who have persistent hemodynamic instability who have received adequate fluid resuscitation and vasopressor therapy.

Weak recommendation, low quality of evidence

Based on Best Practice Statement from SCCM Surviving Sepsis Campaign

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Treatments Not Recommended

Albumin:

There is no difference in outcomes when compared to crystalloids, but albumin is not recommended when taking into consideration the cost and other barriers of administering albumin.

Dopamine:

When compared to epinephrine, children receiving epinephrine had a lower risk of mortality and more organ failure-free days among survivors. When compared to norepinephrine in adults, norepinephrine had a lower mortality rate and lower incidence of arrhythmia.

Based on Best Practice Statement from SCCM Surviving Sepsis Campaign

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Admission Criteria

Floor Criteria

- No further hypotension noted for 1-2 hours after resuscitation is complete
- Improvement of tachycardia, abnormal mental status, respiratory status, cap refill, and/or peripheral pulses after 40-60 mL/kg of fluids

If 60 mL/kg IVF given, consider discussion with PICU & Safety Officer

For subspecialty patients, specifically Complex Care, discussion with the attending on call can be helpful for determining the optimal admission location.

PICU Criteria

- ≥ 3 IVF fluid boluses with persistent hemodynamic instability
- Need for positive pressure ventilation
- Altered mental status
- Requires pressors

Consider discussion with PICU regarding patients at high risk of further decompensation who may require more intensive monitoring.

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Clinical Pathway Development

This clinical pathway was developed using the process described in the NCH Clinical Pathway Development Manual Version 6, 2022. Clinical Pathways at Nationwide Children's Hospital (NCH) are standards which provide general guidance to clinicians. Patient choice, clinician judgment, and other relevant factors in diagnosing and treating patients remain central to the selection of diagnostic tests and therapy. The ordering provider assumes all risks associated with care decisions. NCH assumes no responsibility for any adverse consequences, errors, or omissions that may arise from the use or reliance on these guidelines. NCH's clinical pathways are reviewed periodically for consistency with new evidence; however, new developments may not be represented, and NCH makes no guarantees, representations, or warranties with respect to the information provided in this clinical pathway.

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Quality Measures

Outcome Metrics:

- 3-day and 30-day mortality in Emergency Department Sepsis Alert patients
- Hospital and ICU length of stay in Emergency Department Sepsis Alert patients

Process Metrics:

- Primary: Percent of Sepsis Alert patients receiving both IVF and antibiotics within 60 minutes of the Sepsis Alert
Defined as Sepsis Alert patient having ANY fluid and ANY antibiotic initiated (but not necessarily completed)
- Secondary: Average time to administration of antibiotics on patients made a Sepsis Alert
- Utilization rate of Emergency Department Sepsis Alert order set of those made a Sepsis Alert

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