CONNECTICUT CHILDREN'S MEDICAL CENTER
282 Washington Street, Hartford, CT 06106

Clinical Pathway: Pediatric Septic Shock: **Initial Management**

Pathway	Initial Evaluation	Ongoing Evaluation
Diagnostics	**Recognize Sepsis** **Temperature** AND: **Heart Rate** A: <1 y/o; 1-2 y/o; 2- 10 y/o; ≥ 11 y/o >38°C OR <36°C N D: ≥180; ≥160; ≥140; ≥110 **Accompanied by one or more signs of shock / poor organ perfusion as defined by ACCM guidelines:** **Vascular: capillary refill > 2 sec, decreased pulses, cool/mottled extremities (cold shock) OR flash capillary refill, bounding pulses (warm shock)** Hypotension for age (LATE finding; may be preceded by narrowed or widened pulse pressure or diastolic hypotension): • SBP <60 mm Hg in term neonates (0 to 28 days) • SBP <70 mm Hg in infants (1 month to 12 months) • SBP <70 mm Hg + (2 × age in years) in children 1 to 10 years • SBP <90 mm Hg in children ≥10 years of age **Renal: Urine output < 1mL/kg/hr** **Neuro: altered mental status, lethargy** **Patients with septic shock may have:** **ID: Abnormal WBC count (>12,000/µL or < 4,000/µL or >10% immature [band] forms)** **Metabolic acidosis (base deficit > -4 or lactate > 2)** **GI: nausea, vomiting, ileus, ↑LFTs** **Renal: Acute kidney injury (↑Cr)** **Heme: disseminated intravascular coagulation, purpura**	MD evaluates patient within 15 minutes, confirms diagnosis of septic shock and need to proceed with pathway. If MD not readily available, contact Medical Emergency Team (except in ED or PICU) Continue resuscitation until therapeutic endpoints achieved: • capillary refill ≤2 secs • normal pulses with no differential between the quality of peripheral and central pulses • warm extremities • urine output ≥1 mL/kg/h • normal mental status • normal blood pressure for age • normal glucose concentration • normal ionized calcium concentration • normal lactate

Nursing Care	Pulse oximeter, CR monitor, NIBP q 5 minutes	
	Establish IV access (goal: minimum 2 points of access)	Re-assess adequacy of access to achieve patient-specific therapy needs within the first hour • Completion of fluid resuscitation (up to 60-100 mL/kg) • Correction of electrolyte abnormalities • Start of all antibiotics • Start of pressors Add additional IOs, IVs, CVLs as needed
	Place Intraosseus line if IV access not established in 5 minutes	
	Provide supplemental oxygen if O2 saturations ≤ 97%	
	First doses of antibiotics to be obtained from Omnicell as available, mixed by nursing, and given within 1 hr of MD order; if access available, antibiotics should be given immediately and can run simultaneously; if access limited, please give Vancomycin 2nd due to long infusion time	Confirm first doses of appropriate antibiotics given
Labs:	Laboratory evaluation: iStat Blood Gas and Lactate* iStat Chem 8* Blood culture* CBC with differential Cortisol DIC panel *Priorities if limited blood sample available	Repeat laboratory evaluation as indicated by clinical status Further attempt at any labs not obtained on initial evaluation

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Pathway	Initial Evaluation	Ongoing Evaluation
Treatments Airway, Breathing	Assess need for intubation, mechanical ventilation 1. Etomidate should be used with caution due to reports of adrenal suppression and increased risk of mortality 2. Consider atropine and ketamine for RSI 3. Strongly consider volume loading and vasoactive initiation prior to RSI	Assess need for intubation, mechanical ventilation 1. Etomidate should be used with caution due to reports of adrenal suppression and increased risk of mortality 2. Consider atropine and ketamine for RSI 3. Strongly consider volume loading and vasoactive initiation prior to RSI
Fluids	0.9% normal saline (NS) or lactated ringers (LR) 20 ml/kg over 5 minutes by "pull- push" method or rapid infuser	0.9% normal saline (NS) or lactated ringers (LR) 20 ml/kg every 5 minutes or less until ≥ 60 ml/kg, signs of volume overload (pulmonary crackle, hepatomegaly) or perfusion normal
Antibiotics	**Select both Gram positive and Gram negative Coverage** **Start gram negative coverage first unless neonate ≤28 days** **Gram Positive – You Must Pick One** • Standard o Vancomycin IV: ≤44 weeks PMA‡/about ≤1 month old: 15 mg/kg x1; >44 weeks PMA‡/about >1 month old: 20 mg/kg x1 (max dose 2 g/dose); subsequent dosing per hospital pharmacy vancomycin protocol to avoid AKI ‡*PMA (Post-Menstrual Age) = gestational age + postnatal age* • Vancomycin allergy*/Renal insufficiency o Linezolid IV: <12 years: 30 mg/kg/day div q8hr (max 600 mg/dose); ≥12 years: 600 mg q12hr; if ≥12 yrs old but <45 kg: 20 mg/kg/day q12hr (max 600 mg/dose) • Neonate ≤28 days: o Ampicillin 300 mg/kg/day (q8hr for ≤7 day olds; q6hr for >7 day olds) o Consult ID if concern for MRSA or MSSA (e.g., SSTI, hx of CVL) **Gram Negative – You Must Pick One** *If there is a history of resistant organisms in the past 6 months, suspicion of salmonella or other less common pathogens, 3rd or higher generation cephalosporin allergy: consult ID for appropriate antibiotics.* • Standard o Ceftriaxone IV 100 mg/kg/day div q12hr (max 2000 mg/dose) • (continued on next page)	**Adjunctive Antibiotics** • Intra-abdominal infection/anaerobic coverage: o Metronidazole 30 mg/kg/day div q8hr (max 500 mg/dose) o Note: if patient is already receiving meropenem or piperacillin/tazobactam, no additional anaerobic coverage is needed with metronidazole. • Double Coverage of Gram Negatives is no longer routine practice. **Notes:** • For Vancomycin Flushing Syndrome (VFS), which can present with flushing, pruritis, chest pain, hypotension: give Vancomycin but slow infusion rate to 2 hours and consider diphenhydramine • *Vancomycin allergy is rare; hallmarks are angioedema, wheezing, respiratory distress.

	• Neonate ≤28 days:
	  ○ ≤21 day old: Gentamicin 4 mg/kg q24hr (for ≥35 weeks gestation only)
	  ○ 22-28 days: Ceftriaxone 100 mg/kg/day div q12hr (max 2000 mg/dose)
	• Fever and Neutropenia / Immunocompromised / Chronically Hospitalized:
	  ○ Ceftazidime IV 150 mg/kg/day div q8hr (max 2000 mg/dose)
	• If concern for toxic shock: Add clindamycin IV 40 mg/kg/day div q8hr (max 900 mg/dose)	

Electrolyte Correction	Correct Hypoglycemia (<60 mg/dl) D10W 5mL/kg or D25W 2mL/kg Correct Hypocalcemia(<1.1 mg/dl) Calcium gluconate 50-100 mg/kg IV (max 2000 mg)	Correct Hypoglycemia (< 60 mg/dl) D10W 5mL/kg or D25W 2 mL/kg Correct Hypocalcemia(< 1.1 mg/dl) Calcium gluconate 50-100 mg/kg IV (max 2000 mg)
Steroids	Consider Hydrocortisone (2 mg/kg, standard adult dose 100 mg), then 0.5 mg/kg q6hr for patients: • With fluid refractory, vasopressor refractory shock (defined as 2 or more pressors AND cortisol unknown or <18) • At presentation for any patient at risk for adrenal sufficiency (chronic steroid use, purpura fulminans, intubation with etomidate)	Consider Hydrocortisone (2 mg/kg, standard adult dose 100 mg), then 0.5 mg/kg q6hr for patients: • With fluid refractory, vasopressor refractory shock (defined as 2 or more pressors AND cortisol unknown or <18) • At presentation for any patient at risk for adrenal sufficiency (chronic steroid use, purpura fulminans, intubation with etomidate)

Clinical Pathway: Pediatric Septic Shock: **Initial Management**

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Fluid Refractory	If signs of hypoperfusion after 60 ml/kg of fluids: 1. Reassess ventilation status, mentation and work of breathing 2. Start vasoactive agent Rapidly deteriorating patients may benefit from concurrent start of fluids and vasopressors	
	Hypotensive and vasoconstricted: Epinephrine (start 0.05 mcg/kg/min) Hypotensive and vasodilated: Norepinephrine (start 0.05 mcg/kg/min)	Titrate to effect If not responding to vasopressors as anticipated, perform recheck of pump weight, medication concentration, calculated drip rate and integrity of access.
Nutrition	NPO	NPO
Activity	Bedrest	Bedrest
Consults	Discuss patient with PICU Consider ID consultation if: • Neonate ≤28 days, • History of resistant organisms in past 6 months, or suspicion of salmonella or other less common pathogens • 3rd or higher generation cephalosporin allergy • Positive blood culture • Diagnostic/therapeutic concerns	
Notify MD	The following conditions should immediately be reported to a physician. Significant change in vital signs or perfusion Worsening mental status Worsening respiratory distress	The following conditions should immediately be reported to a physician. Significant change in vital signs or perfusion Worsening mental status Worsening respiratory distress
Disposition	Identify admitting service	Facilitate transfer to inpatient unit

	Notify inpatient unit of pending admission PICU admission for: 1. Persistent signs of poor cardiac output unresponsive to initial rehydration 2. Required ≥ 60 ml/kg in ≤ 1 hour 3. Meets other established PICU admission criteria PICU admission should be considered for: 1. Required ≥ 60 ml/kg ≤ 2 hours	

Process Measures:

1. Use of General Sepsis or Septic Shock Order Set
2. Initiation of first fluid bolus within 10 minutes of IV/IO access
3. Initiation of Antibiotics within 60 minutes of MD order
4. Antibiotics prescribed per pathway
5. Mortality

Clinical Pathway: Pediatric Septic Shock: **ICU Management**

Pathway	ICU Admission	Ongoing management
Admission	Admit to Critical Care Medicine service	
Diagnostics	Draw initial management labs that have not been obtained	
	Blood, urine, tracheal cultures (if not already done)	Repeat blood cultures q 24 h if patient persistently febrile and/or clinically unstable
	istat Blood Gas q1h	Wean as clinically indicated
	istat Chem 8 q1h	Decrease Chem 8 to q6-12 h when no longer requiring electrolyte correction
	Consider istat lactate q1h	If lactate stable/decreasing, space lactate to q4-8 h If lactate normal x 2 and on single low dose vasopressor, decrease lactate to q12-24 h
	ScvO2 "Blood gas, venous, O2 group only" q1h (best drawn from SCV, IJ but femoral is acceptable)	If ScvO2 > 70 x 2, decrease to q12-24 h
Nursing Care	Prepare CVP monitoring set-up, if indicated	
	Prepare arterial pressure monitoring set-up, if indicated	
	Have 0.9 % NS or LR and push-pull set-up ready at bedside	
	Initial vasopressor drips will be made by PICU nursing staff (not pharmacy staff)	
	Highly consider placing urinary catheter	

Clinical Pathway: Pediatric Septic Shock: **ICU Management**

Pathway	ICU Admission	Ongoing Evaluation
Treatments Airway, Breathing	Assess need for intubation, mechanical ventilation 1. Etomidate should be used with caution due to reports of adrenal suppression and increased risk of mortality 2. Consider atropine and ketamine for RSI 3. Strongly consider volume loading and vasoactive initiation prior to RSI	Assess need for intubation, mechanical ventilation 1. Etomidate should be used with caution due to reports of adrenal suppression and increased risk of mortality 2. Consider atropine and ketamine for RSI 3. Strongly consider volume loading and vasoactive initiation prior to RSI
Access and monitoring	Consider placing central venous access Consider arterial line	Re-evaluate for removal of lines daily
Antibiotics	Order ongoing antibiotic therapy with consideration of renal function/estimated GFR, history of resistant organisms in past 6 months, and possible focus of infection Order drug monitoring levels Evaluate for focus of infection amenable to source control Consider removal of potentially infected intravascular access devices	• Re-evaluate antibiotic dosing daily for changes in renal function • In 36-48 hours, if all cultures are negative, consider de-escalating antibiotic regimen. • Typical duration of therapy is 7-10 days. Consult ID if longer duration is considered.
Fluids	Additional fluid therapy can be guided by CVP and/or other parameters to determine fluid responsiveness.	Additional fluid therapy can be guided by CVP and/or other parameters to determine fluid responsiveness.
Vasopressors	Hypotensive and vasoconstricted: Epinephrine (start 0.05 mcg/kg/min) Hypotensive and vasodilated: Norepinephrine (start 0.05 mcg/kg/min)	Titrate to effect If not responding to vasopressors as anticipated, perform recheck of pump weight, medication concentration, calculated drip rate and integrity of access. If hypotensive and vasodilated shock refractory to norepinephrine, consider adding vasopressin Consider echocardiogram for refractory shock to 1 pressor
Inotropes	For patients with fluid-refractory shock on vasopressors, consider milrinone 0.5 mcg/kg/min if: 1. Low cardiac output, high vascular resistance suspected 2. ScvO2 <70% and Hgb > 10 g/dL (*Caution should be used when interpreting ScvO2 drawn from femoral source)	Monitor for vasodilatory effects of milrinone, need for further volume loading

Clinical Pathway: Pediatric Septic Shock: **ICU Management**

Pathway	ICU Admission	Ongoing Evaluation
Treatments Blood Products	Transfuse PRBCs if Hgb < 7 g/dL (if tissue hypoperfusion resolved [normal lactate and ScvO2] and in absence of severe hypoxemia, cyanotic heart disease, acute hemorrhage) If ScvO2 < 70 %, transfuse PRBCs to Hgb 10 g/dL (*Caution should be used when interpreting ScvO2 drawn from femoral source) When transfusing blood, request PRBCs <14d of age	Transfuse PRBCs if Hgb < 7 g/dL (if tissue hypoperfusion resolved [normal lactate and ScvO2] and in absence of severe hypoxemia, cyanotic heart disease, acute hemorrhage) If ScvO2 < 70%, transfuse PRBCs to Hgb 10 g/dL (*Caution should be used when interpreting ScvO2 drawn from femoral source) When transfusing blood, request PRBCs <14 d of age
Steroids	Consider Hydrocortisone (2 mg/kg, standard adult dose 100 mg), then 0.5 mg/kg q6hr for patients: • With fluid refractory, vasopressor refractory shock (defined as 2 or more pressors AND cortisol unknown or <18) • At presentation for any patient at risk for adrenal sufficiency (chronic steroid use, purpura fulminans, intubation with etomidate)	Consider Hydrocortisone (2 mg/kg, standard adult dose 100 mg), then 0.5 mg/kg q6hr for patients: • With fluid refractory, vasopressor refractory shock (defined as 2 or more pressors AND cortisol unknown or <18) • At presentation for any patient at risk for adrenal sufficiency (chronic steroid use, purpura fulminans, intubation with etomidate)
Electrolyte Correction	Correct Hypoglycemia (< 60 mg/dl) D10W 5 mL/kg or D25W 2 mL/kg Correct Hypocalcemia(<1.1 mg/dl) Calcium gluconate 50-100 mg/kg IV (max 2000 mg)	Correct Hypoglycemia (< 60 mg/dl) D10W 5 mL/kg or D25W 2 mL/kg Correct Hypocalcemia(< 1.1 mg/dl) Calcium gluconate 50-100 mg/kg IV (max 2000 mg)
Glucose control	Benefits of tight glycemic control are equivocal. Insulin therapy is at provider discretion.	Consider use of the euglycemic protocol for patients with sustained hyperglycemia (> 200 mg/dL)
Bicarbonate therapy	Consider sodium bicarbonate 1-4 mEq/kg if pH < 7.15	Consider sodium bicarbonate 1-4 mEq/kg if pH < 7.15

Clinical Pathway: Pediatric Septic Shock: **ICU Management**

	ICU Admission	Ongoing management
Treatments DVT prophylaxis	Per **CT Children's VTE Prophylaxis Clinical Pathway**	Per **CT Children's VTE Prophylaxis Clinical Pathway**
RRT		**RENAL REPLACEMENT THERAPY** Consider RRT if patient > 10% total body fluid overloaded
Nutrition	NPO	TPN when electrolytes stabilized Enteral feeds when off vasopressors
Activity	Bedrest	Bedrest
Notify MD	The following conditions should immediately be reported to a physician. Significant change in vital signs or perfusion Worsening mental status Worsening respiratory distress	The following conditions should immediately be reported to a physician. Significant change in vital signs or perfusion Worsening mental status Worsening respiratory distress Urine output < 1mL/kg/hr CVP < 8 mmHg (< 12 mmHg mechanically ventilated patient)

Consults	• Surgery consult if infection source control needed or intra-abdominal catastrophe suspected
	• Consider ID consultation if:
	  • Neonate ≤28 days,
	  • History of resistant organisms in past 6 months, or suspicion of salmonella or other less common pathogens
	  • 3rd or higher generation cephalosporin allergy
	  • Positive blood culture
	  • Diagnostic/therapeutic concerns	

Disposition	When there is no longer evidence of hypoperfusion, there has been no need for volume resuscitation or inotropic support within the previous 24 hours, the source of infection appear to be adequately treated, and there are no other established indications for PICU care, discussions of transfer should be made with an accepting physician	Assess for possibility of transfer

Process Measures:

1. Use of General Sepsis or Septic Shock Order Set
2. Initiation of first fluid bolus within 10 minutes of IV/IO access
3. Initiation of Antibiotics within 60 minutes of MD order
4. Antibiotics prescribed per pathway
5. Mortality

Note: time zero will be identified from flowsheet documentation of diagnostic criteria

Clinical Pathway : Pediatric Septic Shock: **Algorithm**

Recognition Phase

Defined as:
- Fever
- Tachycardia

And one of the following
- Hypotension
  - Systolic
  - Diastolic
  - Widened Pulse Pressure
- Purpura
- Diminished or bounding pulses
- Cap refill time ≥ 3 sec or "Flash" cap refill
- Decreased mental status

MD evaluates patient within 15 minutes, confirms diagnosis of septic shock and need to proceed with pathway; if MD not readily available, contact Medical Emergency Team (except in ED or PICU)[1]

Management

Laboratory Evaluation:

iStat Blood Gas and lactate*, iStat chem. 8*, DIC panel, Blood culture*, CBC, cortisol
*Priorities if limited blood sample

1. **Correct hypoglycemia** (<60 mg/dl) with 5 mL/kg D10W or 2 mL/kg D25W
2. **Correct hypocalcemia** (<1.1 mg/dl) with 50-100mg/kg CaGluc IV (max 2000mg)
3. **Recognize** low Na, elevated K and low glucose as **adrenal insufficiency** and treat with hydrocortisone (2 mg/kg, adult dose 100 mg)

1. Pulse Oximetry, CR monitor,
2. Obtain IV access: Peripheral IV within 5 minutes or place Intraosseus line
3. Supplemental oxygen
4. Vital signs q5 minutes
5. 20 ml/kg of 0.9% NS or LR in 5 minutes pushed or via rapid infuser
6. Repeat until ≥ 60 ml/kg, signs of volume overload (pulmonary crackles or hepatomegaly) or perfusion is normal
7. MD/RN presence at bedside

Antibiotics started within 1 hour

Start gram negative first (unless neonate)

1. **Gram Positive: Must pick one**
   - Standard: Vancomycin IV (vancomycin allergy or renal insufficiency: linezolid IV)
   - Neonate ≤28 days: Ampicillin IV
2. **Gram Negative: Must pick one**
   - Standard: Ceftriaxone IV
   - Neonate ≤21 days old: Gentamicin IV (≥35 wks gestation only); Neonate 22-28 days old: Ceftriaxone
   - Fever & neutropenia / immunocompromised / chronically hospitalized: Ceftazidime IV
   - Concern for toxic shock: add clindamycin IV
   - Note: double coverage of gram negatives is no longer routine practice
3. **Adjunctive Antibiotics**
   - Intra-abdominal infection/anaerobic coverage: metronidazole if not already on meropenem or piperacillin/tazobactam
     ***Note**: if history of resistant organisms in past 6 months, suspicion of salmonella or less common pathogens, or 3rd or higher generation cephalosporin allergy: consult ID for antibiotics*

Clinical Pathway : Pediatric Septic Shock: **Algorithm**

Fluid Responsive

1. Observation in the PICU if ≥ 60 ml/kg fluid in ≤ 1 hour or meets other established PICU admission criteria
2. Consider PICU admission if ≥ 60 ml/kg in ≤ 2 hrs

Fluid Refractory Phase

1. Reassess ventilation status, mentation and work of breathing [2]
2. **Start Vasoactive**:
   Hypotensive vasoconstricted (Cold) shock: Epinephrine (start 0.05 mcg/kg/min)
   Hypotensive vasodilated (Warm) shock: Norepinephrine (start 0.05 mcg/kg/min)

PICU Management

Laboratory Evaluation

1. Draw DIC panel, cortisol and other initial management labs if not yet obtained
2. Blood, urine, tracheal and other appropriate cultures as clinically indicated
3. iStat blood gas, iStat Chem 8 q1hr, and consider iStat lactate q1hr (decrease frequency if stable/decreasing)
4. Consider ScvO2 q1 (best drawn from SCV or IJ but femoral is acceptable)

Antibiotic Therapy

1. Order ongoing antibiotics with consideration of renal function
2. If all cultures are negative in 36~~-48~~ hrs, consider de-escalating antibiotics
3. Order drug monitoring levels
4. Evaluate for focus of infection amenable to source control
5. Consider removal of potentially infected intravascular access device

Fluid Therapy

1. Additional fluid therapy can be guided by CVP and/or other parameters to determine fluid responsiveness.

Blood Products

1. Only transfuse PRBCs if Hgb < 7 g/dL [if tissue hypoperfusion resolved (normal lactate and ScvO2) and in the absence of severe hypoxemia, cyanotic heart disease, acute hemorrhage]
2. If ScvO2 < 70%, transfuse PRBCs to Hgb 10 g/dL
3. When transfusing blood, request PRBCs <14 d of age

Vasopressors

1. Hypotensive and vasoconstricted: Epinephrine (start 0.05 mcg/kg/min)
2. Hypotensive and vasodilated: Norepinephrine (start 0.05 mcg/kg/min)
3. For hypotensive and vasodilated shock refractory to norepinephrine, consider adding vasopressin
4. Consider Echo for refractory shock to 1 pressor
5. For patients with fluid-refractory shock on vasopressors, consider milrinone 0.5 mcg/kg/min if:
   a. Low cardiac output, high vascular resistance suspected
   b. ScvO2 < 70% and Hgb >10 g/dL

Steroids

1. Consider hydrocortisone loading dose 2 mg/kg (adult dose 100 mg) then 0.5 mg/kg q6hr, if on 2 or more pressors and if concern for adrenal insufficiency

Glucose control:

1. Insulin therapy at provider discretion

Bicarbonate therapy

1. Consider NAHCO3 1-4 mEq/kg if pH < 7.15

Consider ECMO

1. If Attending Physician or Medical Emergency Team decides not to proceed with pathway, reason should be documented
2. If intubation and mechanical ventilation is indicated, strong consideration should be given to starting vasoactives prior to initiation of RSI