

# Additional File 4: SQUEEZE Study Algorithm as Illustrated in ACCM Guideline Format

0 min  
 5 min  
 15 min  
 60 min  
 Emergency Department  
 Pediatric Intensive Care Unit

Recognize decreased mental status and perfusion. Begin high flow O<sub>2</sub>. Establish IV/IO access.

**Initial Resuscitation**  
 Push boluses of 20 mL/kg isotonic normal saline or colloid up until perfusion improves or unless rales or hepatomegaly develop.  
 Correct hypoglycemia & hypocalcemia.  
 Begin antibiotics.

## ELIGIBLE IF FLUID REFRACTORY SEPTIC SHOCK

1. AGE 29 days to <18 years of age
- 2a. **PERSISTENT SIGNS OF SHOCK**, defined as one or more of:
  - i) Vasoactive medication dependent, ii) Hypotension
  - iii) Abnormal perfusion (≥ 2 of: abnormal cap refill, tachycardia, decreased urine output, decreased level of consciousness)
- 2b. **SUSPECTED OR CONFIRMED SEPTIC SHOCK**
- 2c. **FLUID RESUSCITATION THRESHOLD MET**
  - Ongoing shock despite 40 mL/kg of isotonic crystalloid or colloid (or 2L for children ≥ 50 kg) as IV/IO boluses within previous 6 hrs

## \*GOAL DIRECTED TARGETS PER ACCM GUIDELINES IN BOTH STUDY ARMS

- Emergency Dept./Pre-Intensive Care Unit**
- Threshold heart rate
  - Normal blood pressure
  - Capillary refill <3 seconds
- Intensive Care Unit**
- ScvO<sub>2</sub> > 70%
  - Hemoglobin > 10 g/dL
  - Cardiac Index > 3.3 and <6.0 L/min/m<sup>2</sup>

# RANDOMIZATION

## \*USUAL CARE (FLUID LIBERAL)

**Ongoing Fluid Refractory Shock**  
 Continue to push FLUID up to and over 60 mL/kg as deemed clinically necessary by MD. Begin inotrope at MD discretion, but not before 60 mL/kg (3L for ≥ 50 kg) IV fluid. Reverse *cold shock* by titrating central dopamine or if resistant, titrate central epinephrine  
 Reverse *warm shock* by titrating central norepinephrine

dose range:  
 dopamine up to 10 mcg/kg/min,  
 epinephrine 0.05 to 0.3 mcg/kg/min

*shock not reversed?*

**Catecholamine resistant shock:**  
 Begin hydrocortisone if at risk for absolute adrenal insufficiency

Monitor CVP in PICU, attain normal MAP - CVP & ScvO<sub>2</sub>

### Cold Shock with Normal Blood Pressure

1. Titrate FLUID & Epinephrine ScvO<sub>2</sub>>70%, Hgb>10g/dL
2. If ScvO<sub>2</sub> still <70% Add vasodilator with volume loading (nitrosovasodilators, milrinone, imrinone, & others) Consider levosimendan

### Cold Shock with Low Blood Pressure

1. Titrate FLUID & Epinephrine ScvO<sub>2</sub>>70%, Hgb>10g/dL
2. If still hypotensive consider norepinephrine
3. If ScvO<sub>2</sub> still <70% consider dobutamine, milrinone, enoximone or levosimendan

### Warm shock with Low Blood Pressure

1. Titrate FLUID & Norepinephrine. ScvO<sub>2</sub>>70%, Hgb>10g/dL
2. If still hypotensive consider vasopressin, terlipressin or angiotensin
3. If ScvO<sub>2</sub> still <70% consider low dose epi.

*shock not reversed?*

### Persistent catecholamine resistant shock

Rule out and correct pericardial effusion, pneumothorax, & intra-abdominal pressure >12 mm/Hg  
 Consider pulmonary artery, PICCO or FATO catheter, &/or doppler ultrasound e.g. USCOM to guide FLUID, inotrope, vasopressor, vasodilator and hormonal therapies.  
 Goal Cardiac Index >3.3 and <6.0 L/min/m<sup>2</sup>

*shock not reversed?*

**Refractory Shock: ECMO**

## \*INTERVENTION: FLUID SPARING

**Ongoing Fluid Refractory Shock**  
 Begin INOTROPE IV/IO. Escalate INOTROPE to SPARE FLUID. Administer further fluid as 5-10 mL/kg (250-500 mL for ≥ 50 kg) aliquots to maintain intravascular euvolesmia. Reverse *cold shock* by titrating central dopamine or if resistant, titrate central epinephrine  
 Reverse *warm shock* by titrating central norepinephrine

dose range:  
 dopamine up to 10 mcg/kg/min,  
 epinephrine 0.05 to 0.3 mcg/kg/min

*shock not reversed?*

**Catecholamine resistant shock:**  
 Begin hydrocortisone if at risk for absolute adrenal insufficiency

Monitor CVP in PICU, attain normal MAP - CVP & ScvO<sub>2</sub>

### Cold Shock with Normal Blood Pressure

1. Titrate EPINEPHRINE to SPARE FLUID administration ScvO<sub>2</sub>>70%, Hgb>10g/dL
2. If ScvO<sub>2</sub> still <70% Add vasodilator with volume loading (nitrosovasodilators, milrinone, imrinone, & others) Consider levosimendan

### Cold Shock with Low Blood Pressure

1. Titrate EPINEPHRINE to SPARE FLUID administration ScvO<sub>2</sub>>70%, Hgb>10g/dL
2. If still hypotensive consider norepinephrine
3. If ScvO<sub>2</sub> still <70% consider dobutamine, milrinone, enoximone or levosimendan

### Warm shock with Low Blood Pressure

1. Titrate NOREPINEPHRINE to SPARE FLUID admin. ScvO<sub>2</sub>>70%, Hgb>10g/dL
2. If still hypotensive consider vasopressin, terlipressin or angiotensin
3. If ScvO<sub>2</sub> still <70% consider low dose epi.

*shock not reversed?*

### Persistent catecholamine resistant shock

Rule out and correct pericardial effusion, pneumothorax, & intra-abdominal pressure >12 mm/Hg  
 Consider pulmonary artery, PICCO or FATO catheter, &/or doppler ultrasound e.g. USCOM to guide fluid, inotrope, vasopressor, vasodilator and hormonal therapies.  
 Goal Cardiac Index >3.3 and <6.0 L/min/m<sup>2</sup>

*shock not reversed?*

**Refractory Shock: ECMO**