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Pediatric Shock and Sepsis

Review and Update on Definitions and Therapies

Dr. Glenn Stryjewski
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Cardiac Variables in Shock

- Cardiac Output (CO)
- Systemic Vascular Resistance (SVR)
- Mean Arterial Pressure (MAP)
- Central Venous Pressure (CVP)
- DO2
- VO2
- CaO2
- SaO2
- PaO2
- SV

Introduction

- Shock is a syndrome that results from inadequate oxygen delivery to meet metabolic demands
- Oxygen delivery (DO_2) is less than Oxygen Consumption (< VO_2)
- Untreated this leads to metabolic acidosis, organ dysfunction and death

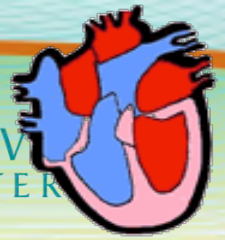
Oxygen Delivery

- Oxygen delivery = Cardiac Output x Arterial Oxygen Content

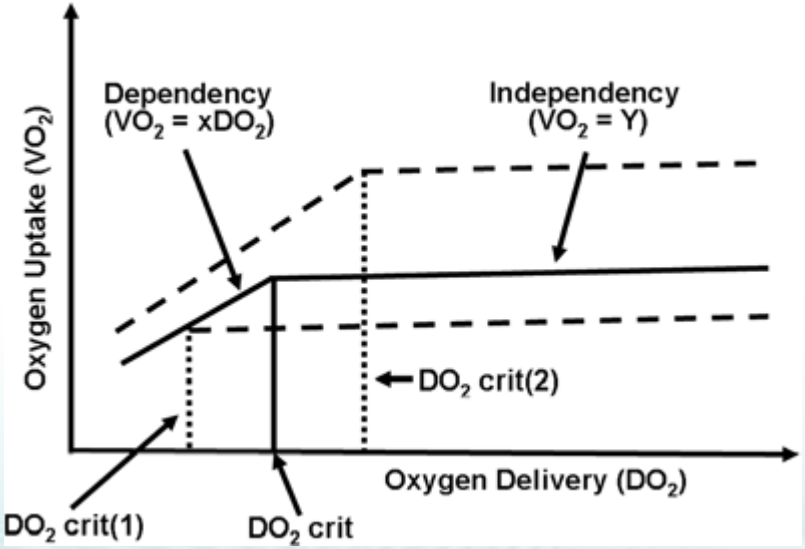
  ($DO_2 = CO \times CaO_2$)
- Cardiac Output = Heart Rate x Stroke Volume

  (CO = HR x SV)
  - SV determined by preload, afterload and contractility
- Art Oxygen Content = Oxygen content of the RBC + the oxygen dissolved in plasma

  ($CaO_2 = Hb \times SaO_2 \times 1.34 + (.003 \times PaO_2)$)

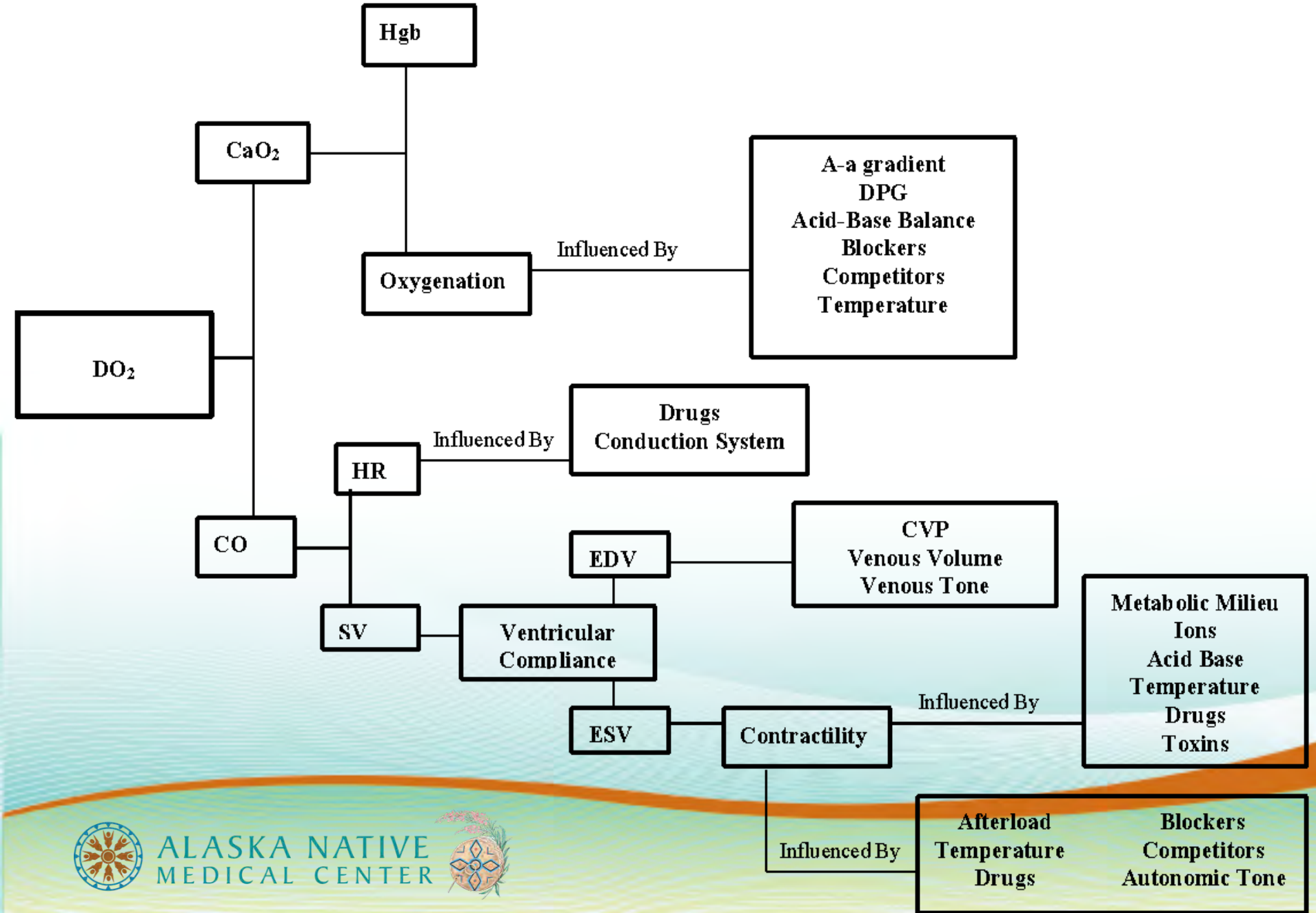


Imbalance Between Delivery (DO2) and Consumption (VO2)



- DO2 crit: Critical DO2 below which VO2 becomes dependent on DO2
- DO2 crit (1): Decreased critical DO2 in low VO2 states (hypothermia, sedation)
- DO2 crit (2): Increased critical DO2 in high VO2 states (fever, sepsis)
- Flat part of the curve is the range of autoregulation or delivery- independent consumption

Figure 1. **FACTORS AFFECTING OXYGEN DELIVERY**



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Types of Shock

- Hypovolemic
- Distributive
- Cardiogenic
- Obstructive
- Neurogenic
- Septic

Cardiac Variables in Shock

	CO	SVR	MAP	Wedge	CVP
Hypovolemic	↑	↑	↔ Or ↓	↓↓↓	↓↓↓
Cardiogenic	↓↓	↑↑↑	↔ Or ↓	↑↑	↑↑
Obstructive	↓	↑	↔ Or ↓	↑↑	↑↑
Distributive	↑↑	↓↓↓	↔ Or ↓	↔ Or ↓	↔ Or ↓
Septic: Early	↑↑↑	↓↓↓	↔ Or ↓	↓	↓
Septic: Late	↓↓	↑↑	↓↓	↑	↑ or ↔

Sepsis

Old Definitions

Box 29–7 Definitions for Sepsis and Septic Shock

Bacteremia	**Presence of Viable Bacteria in Blood**
Infection	Proven infection (culture, stain, PCR) or clinical syndrome with high probability of infection (e.g., lobar pneumonia with negative culture, purpura fulminans in meningococcemia)
Systemic inflammatory response syndrome	At least 2 of 4 of the following criteria (one must be abnormality of temperature or WBC count) 1. Core temperature >38.5° C or <36° C 2. Tachycardia (HR >2 SD for age) or bradycardia (HR <10th percentile for age) if <1 year old 3. Tachypnea (RR >2 SD for age) 4. WBC count elevated or depressed, or >10% band forms
Sepsis	SIRS + infection
Severe sepsis	Sepsis + ≥1 of the following organ dysfunctions: 1. Cardiovascular dysfunction or 2. Respiratory dysfunction or 3. Two other organ dysfunctions
Septic shock	Sepsis + cardiovascular dysfunction

PCR, Polymerase chain reaction; *WBC,* white blood cell; *HR,* heart rate; *SD,* standard deviation; *RR,* respiratory rate.
Modified from Goldstein B, Giroir B, Randolph A, et al: International pediatric sepsis consensus conference: definitions for sepsis and organ dysfunction in pediatrics, *Pediatr Crit Care Med* 6:2-8, 2005.

New Definitions

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

JAMA. 2016;315(8):801-810. doi:10.1001/jama.2016.0287

- Adult have been defined (not pediatrics)
- No longer use the term “severe sepsis”
- SOFA score

Table 2. Terminology and *International Classification of Diseases* Coding

Current Guidelines and Terminology	Sepsis	Septic Shock
1991 and 2001 consensus terminology[9,10]	Severe sepsis Sepsis-induced hypoperfusion	Septic shock[13]
2015 Definition	Sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection	Septic shock is a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality
2015 Clinical criteria	Suspected or documented infection and an acute increase of ≥2 SOFA points (a proxy for organ dysfunction)	Sepsis[a] and vasopressor therapy needed to elevate MAP ≥65 mm Hg and lactate >2 mmol/L (18 mg/dL) despite adequate fluid resuscitation[13]
Recommended primary *ICD* codes[a]		
ICD-9	995.92	785.52
ICD-10[a]	R65.20	R65.21
Framework for implementation for coding and research	Identify suspected infection by using concomitant orders for blood cultures and antibiotics (oral or parenteral) in a specified period[b] Within specified period around suspected infection[c]: 1. Identify sepsis by using a clinical criterion for life-threatening organ dysfunction 2. Assess for shock criteria, using administration of vasopressors, MAP <65 mm Hg, and lactate >2 mmol/L (18 mg/dL)[d]	

SOFA Score

Table 1. Sequential [Sepsis-Related] Organ Failure Assessment Score[a]

	Score				
System	0	1	2	3	4
Respiration					
Pao_2/Fio_2, mm Hg (kPa)	≥400 (53.3)	<400 (53.3)	<300 (40)	<200 (26.7) with respiratory support	<100 (13.3) with respiratory support
Coagulation					
Platelets, $\times 10^3/\mu L$	≥150	<150	<100	<50	<20
Liver					
Bilirubin, mg/dL (μmol/L)	<1.2 (20)	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	>12.0 (204)
Cardiovascular	MAP ≥70 mm Hg	MAP <70 mm Hg	Dopamine <5 or dobutamine (any dose)[b]	Dopamine 5.1-15 or epinephrine ≤0.1 or norepinephrine ≤0.1[b]	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1[b]
Central nervous system					
Glasgow Coma Scale score[c]	15	13-14	10-12	6-9	<6
Renal					
Creatinine, mg/dL (μmol/L)	<1.2 (110)	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440)	>5.0 (440)
Urine output, mL/d				<500	<200

Abbreviations: Fio_2, fraction of inspired oxygen; MAP, mean arterial pressure; Pao_2, partial pressure of oxygen.

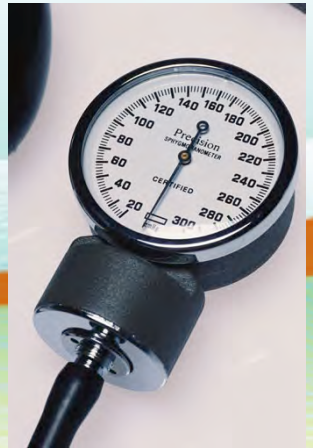
[a] Adapted from Vincent et al.[27]

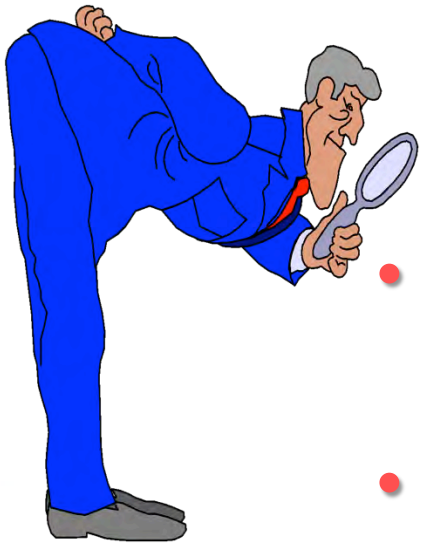
[b] Catecholamine doses are given as μg/kg/min for at least 1 hour.

[c] Glasgow Coma Scale scores range from 3-15; higher score indicates better neurological function.

Clinical Presentation

- Early diagnosis requires a high index of suspicion
- Diagnosis is made through the physical examination focused on tissue perfusion
- Hypotension is a late and premorbid sign





Initial Evaluation: Physical Exam Findings of Sepsis

- **Neurological:** Fluctuating mental status, sunken fontanel
- **Skin and extremities:** Cool, pallor, mottling, cyanosis, poor cap refill, weak pulses, poor muscle tone.
- **Cardio-pulmonary:** Hyperpnea, tachycardia.
- **Renal:** Scant, concentrated urine

Sepsis Therapy

Early Goal Directed Therapy

- Rivers et al. *NEJM* 2001;345:1368-1377
- Does rapid therapy targeting specific hemodynamic outcome variable improve mortality from septic shock
- Adult study over 3 years

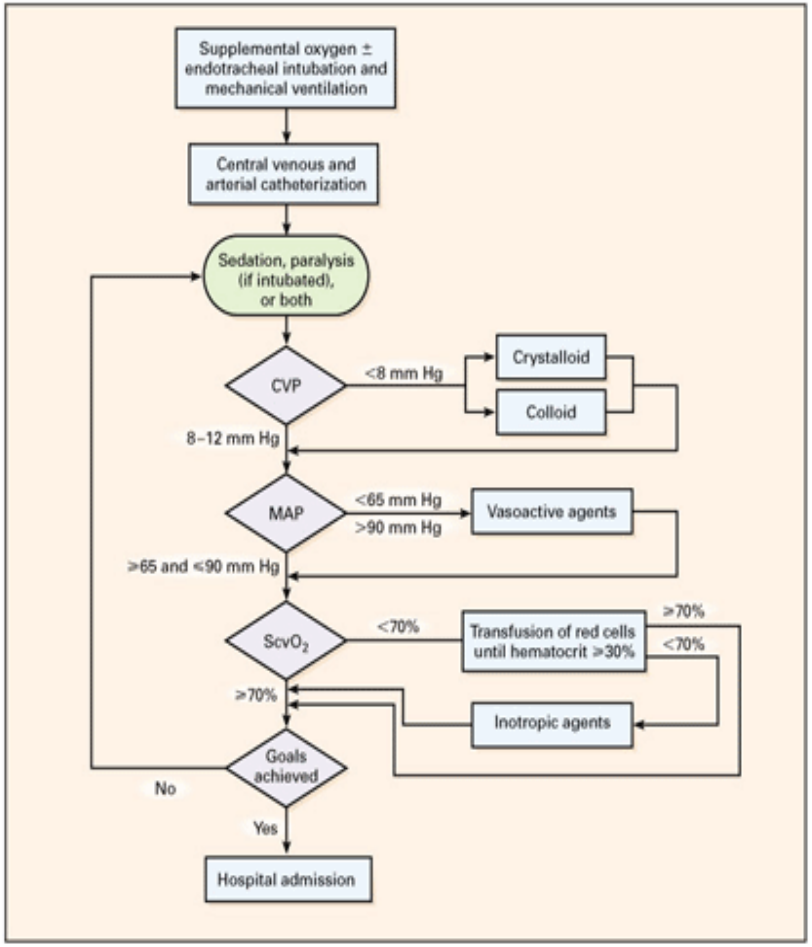
Early Goal Directed Therapy

- Eligible were all adults presenting to the ED of a tertiary medical center
- Inclusion: 2 of 4 SIRS criteria and a SBP < 90 mmHg after 20cc/kg of fluid bolus (or lactate > 4)
- Exclusion
  - Age < 18
  - CVA
  - ACS
  - Asthma
  - GI hemorrhage
  - Trauma
  - Immunosuppression
  - DNR status

Early Goal Directed Therapy

- Subjects treated by ED team during the normal ED workflow
- Patients randomized to receive standard therapy or early goal directed therapy groups
- Appropriate informed consent and randomization performed
- Standard care
  - CVP 8 -12
  - MAP ≥ 65 mmHg
  - Urine Output ≥ 0.5 c/kg/hr

- 500 ml q 30 min until CVP 8 -12
- Vasopressors if MAP < 65 mmHg
- Vasodilators if MAP > 90 mmHg
- pRBC's to maintain HCT>30 if $ScvO_2$ < 70%
- Addition of dobutamine if all above met and $ScvO_2$ < 70%



Outcomes

- 263 enrolled
- 130 early goal directed therapy
- 133 standard therapy
- No significant between the two groups in terms of baseline characteristics or baseline APACHE II scores

Outcomes

- During the study interval of 7 – 72 hours the patients assigned to early goal directed therapy had significantly:
  - Higher mean $ScvO_2$
  - Lower lactate
  - Lower base deficit
  - Higher pH
  - Lower APACHE II scores

Mortality

- **In – hospital mortality (p=0.009)**
  - **30.5 % early goal directed tx**
  - **46.5% standard tx**
  - **ARR 16.5%**
  - **NNT = 6**
- These findings were also paralleled by 28 and 60 day mortality

Therapy

- Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012
  - Crit Care Med 2013; 41(2): 580 – 620
  - Update from 2008

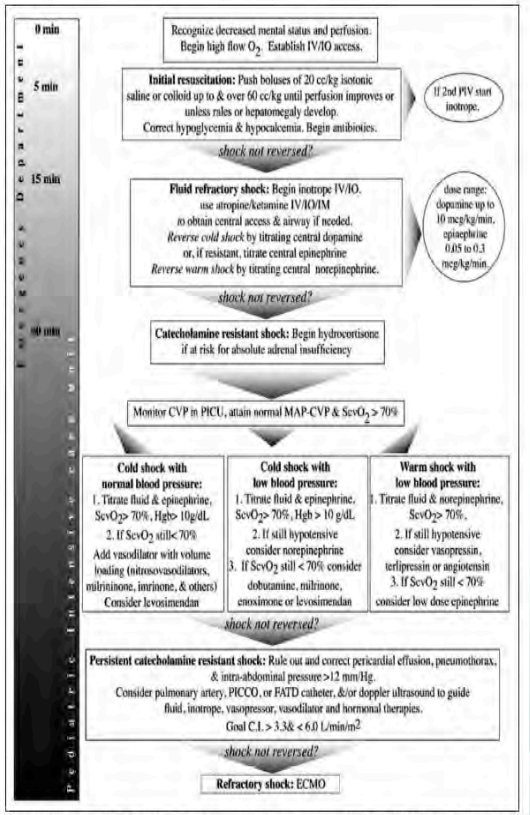


Figure 2. Algorithm for time sensitive, goal-directed stepwise management of hemodynamic support in infants and children. Reproduced from Elterlay J, Carcillo J, Choong K, et al: Clinical practice parameters for hemodynamic support of pediatric and neonatal septic shock: 2007 update from the American College of Critical Care Medicine. *Crit Care Med* 2009; 37:666–688.

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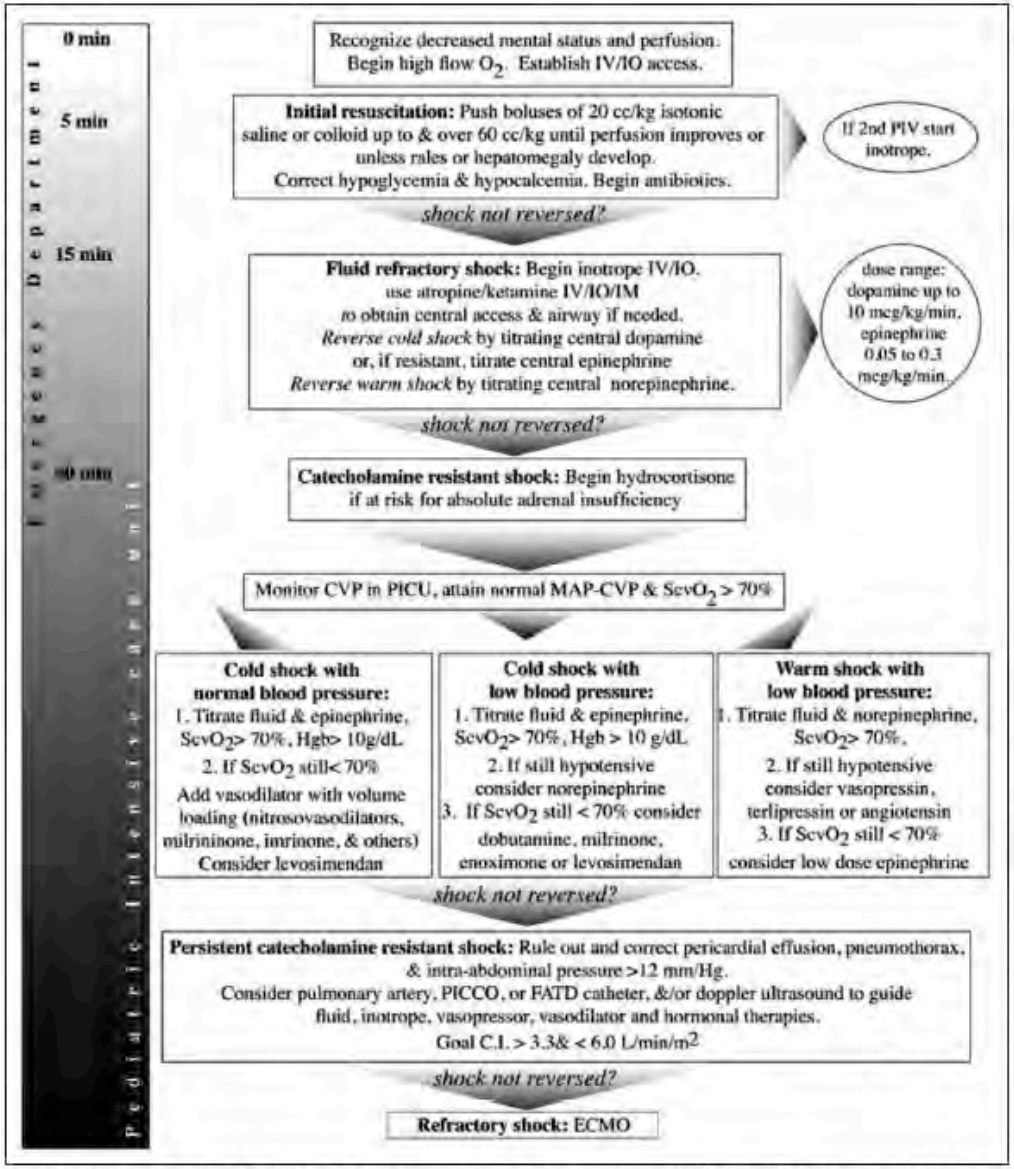
Grading System

- Quality of Evidence
  - (A) high
  - (D) very low
- Strength of Recommendation
  - (1) Strong
  - (2) Weak



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Fluid Resuscitation (Grade 2C)

- Initial resuscitation of hypovolemic shock with 20 cc/kg isotonic crystalloid or albumin (5%) over 5 – 10 minutes
- Target reverse hypotension, increase urine output, normal cap refill and peripheral pulses, and level of consciousness
- Without inducing hepatomegaly or rales. If these present, then inotropic support
- In non hypotensive children with severe hemolytic anemia, then blood transfusion superior to crystalloid.

Initial Resuscitation

- Follow American College of Critical Care Medicine – Pediatric Life Support (ACCM – PALS) guidelines **(Grade 1C)**

- Evaluate for and reverse pneumothorax, pericardial tamponade, or endocrine emergencies **(Grade 1C)**

Initial Resuscitation

- Oxygen, non-invasive positive pressure ventilation, or intubation. *If mechanical ventilation required, then cardiovascular instability during intubation less likely after appropriate cardiovascular resuscitation* **(Grade 2C)**

- Initial therapeutic endpoints of resuscitation
  - Cap refill $\leq$ 2 sec
  - Normal BP for age
  - Normal pulses
  - Warm extremities
  - Urine output > 1 cc/kg/hr
  - Normal mental status

- Once resuscitated, targeted endpoints should be:
  - ScvO2 $\geq$ 70%
  - CI between 3.3 and 6.0 cc/min/m^2
  - **(Grade 2C)**

What's an ScvO2?

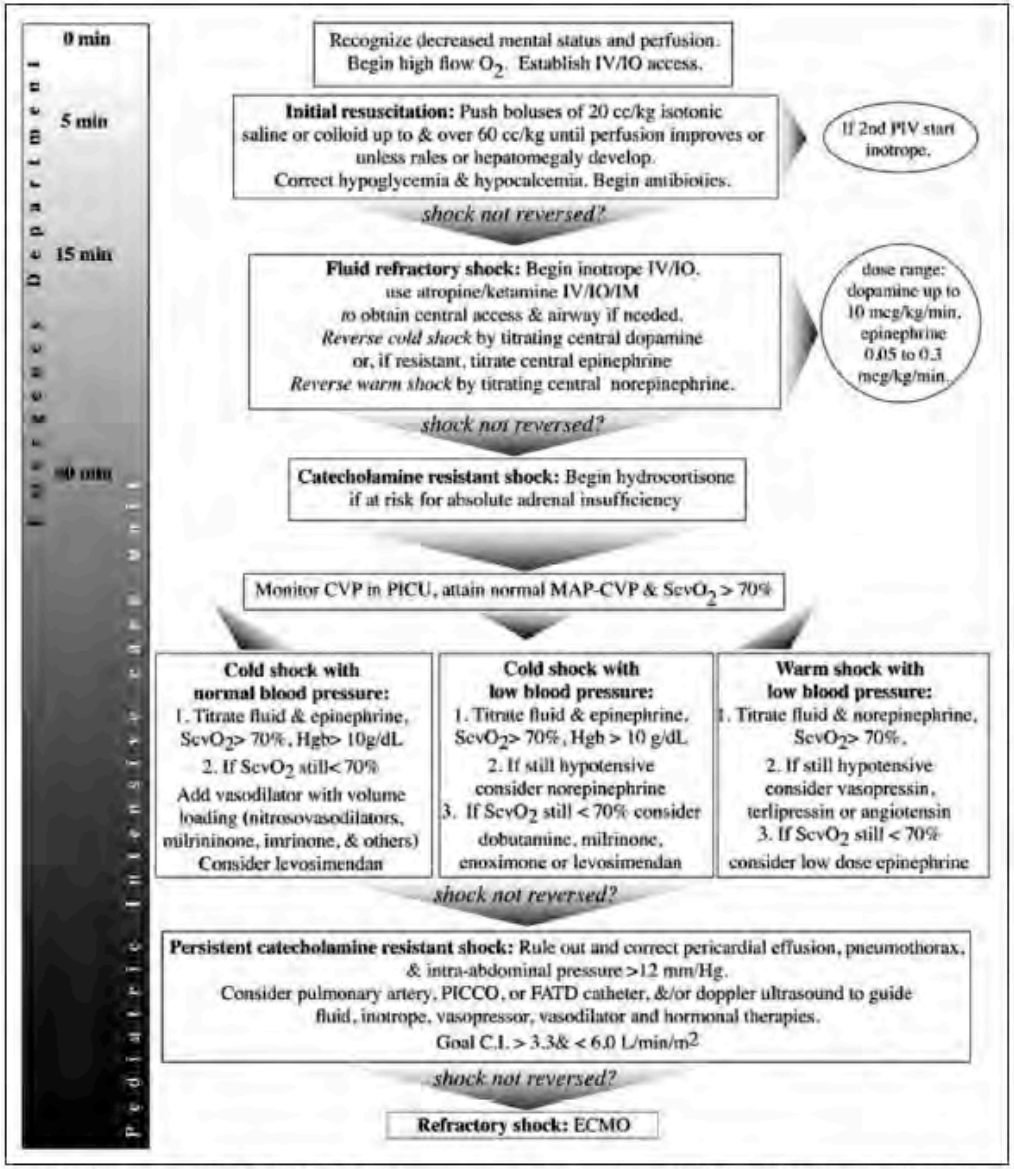
Early Goal-Directed Therapy in Pediatric Septic Shock: Comparison of Outcomes "With" and "Without" Intermittent Superior Venacaval Oxygen Saturation Monitoring: A Prospective Cohort Study*

Jhuma Sankar, MD1; M. Jeeva Sankar, DM2; C. P. Suresh, MD1; Nandkishore K. Dubey, MD1;

Archana Singh, MD1

Blood Products and Plasma Therapies

- **If ScvO2 low (< 70%) the target hemoglobin should be > 10 g/dL. If ScvO2 normal then target > 7 g/dL (Grade 1B)**
- Platelet target > 20K unless active bleeding **(Grade 2C)**
- Plasma therapy to correct sepsis induced thrombotic purpura disorders **(Grade 2C)**



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Inotropes/Vasopressors/Vasodilators

- Begin peripheral administration of inotropes until central access can be established **(Grade 2C)**
- **Low cardiac output with elevated SVR and normal blood pressure should be given vasodilators (Grade 2C)**

Vasoactive Infusions (generalizations)

- Choice depends upon pathophysiology
- Catecholamines common
  - Dopamine, Dobutamine, Epinephrine, Norepinephrine, Phenylephrine
- Vasopressin (Terlipressin) rare but increasing in use
- Phosphodiesterase inhibitors rare early on except in cardiac failure
  - milrinone
- Vasodilators – may be a good choice for heart failure early on since very short acting
  - Nipride
  - Nicardipine

Inotropes/Vasopressors/Vasodilators

- Isoproterenol
- Dobutamine
- Dopamine
- Epinephrine
- Norepinephrine
- Phenylephrine
- Milrinone
- Nipride

Alpha and Beta Agonism

- Alpha
  - Vasoconstriction
  - Increase SVR
- Beta 1
  - Increase heart rate
  - Increase contractility
- Beta 2
  - Vasodilation
  - Decrease SVR

Infusions

Table 27–2 Vasoactive Medications

	α_1	β_1	β_2	D_1	V_1
Dopamine*	Vasoconstriction	Inotropy, chronotropy	Vasodilation	Renal vasodilation	
Norepinephrine	Vasoconstriction	Inotropy			
Epinephrine†	Vasoconstriction	Inotropy, chronotropy	Vasodilation		
Dobutamine		Inotropy	Vasodilation		
Vasopressin	Potentiates	Potentiates			Vasoconstriction
Inamrinone, milrinone		Non–receptor-mediated inotropy, lusitropy, and vasodilation			

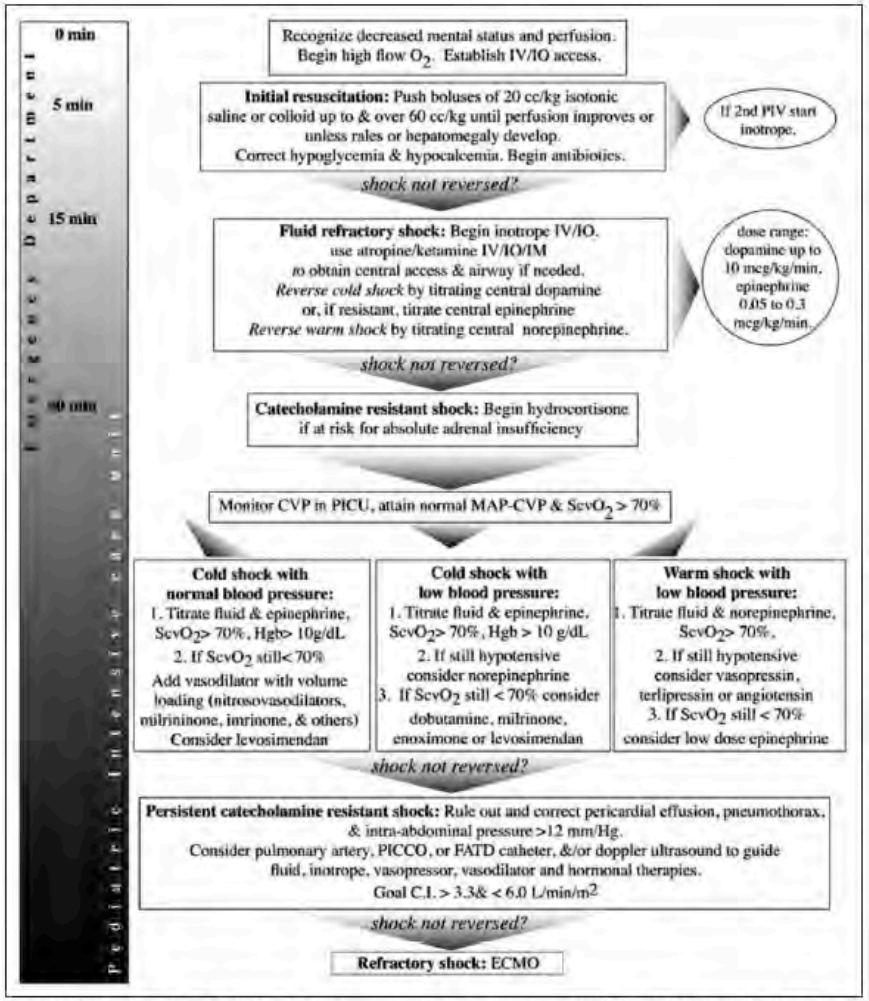
*Dose related: at low infusion rates, D_1 receptor effects predominate; at intermediate rates, β_1 and β_2 receptor effects predominate; at high rates, α_1 effects predominate on peripheral vasculature.
†Dose related: at low infusion rates, β receptor effects predominate; at high rates, α effects predominate on peripheral vasculature.

Infusions

Table 29–1 Therapies for Hemodynamic Patterns in Shock States

Hemodynamic Pattern	Blood Pressure or Systemic Vascular Resistance: Normal	Decreased	Elevated
Septic shock			
Stroke index ↑↔	None	α_1, V_1	None
Stroke index ↓	β_1	α_1 and β_1	$\beta_1 + \beta_2$, or PDE
Cardiogenic shock	β_1	α_1 and β_1	$\beta_1 + \beta_2$, or PDE
Myocardial dysfunction (complicating critical illness)*	β_1 and/or β_2	α_1 and β_1	$\beta_1 + \beta_2$, or PDE
Congestive heart failure	β_1 and/or β_2	β_1	$\beta_1 + \beta_2$, or PDE
Bradycardia	None	β_1	None

*For example, acute respiratory distress syndrome or anthracycline therapy.
PDE, Phosphodiesterase inhibitor.



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Infusion Dosing Guidelines

Dopamine	3 – 20 mcg/kg/min
Dobutamine	3 – 20 mcg/kg/min
Epinephrine	0.1 – 1 mcg/kg/min
Norepinephrine	0.1 – 1 mcg/kg/min
Vasopressin	0.5 – 2 milliunits/kg/minute
Milrinone	0.25 – 1 mcg/kg/min
Nicardipine	0.5 – 5 mcg/kg/min
Nipride (Thiocyanate)	0.5 – 5 mcg/kg/min

Should we EVER use dopamine?

Double-Blind Prospective Randomized Controlled Trial of Dopamine Versus Epinephrine as First-Line Vasoactive Drugs in Pediatric Septic Shock

Andréa M. C. Ventura, MD1; Huei Hsin Shieh, MD1; Albert Bousso, MD1; Patrícia F. Góes, MD1;Iracema de Cássia F. O. Fernandes, MD1; Daniela C. de Souza, MD1; Rodrigo Locatelli Pedro Paulo, MD2;Fabiana Chagas, RN1; Alfredo E. Gilio, MD1

Low cardiac output with elevated SVR and normal blood pressure should be given vasodilators (Grade 2C)

Amrinone in pediatric refractory septic shock: An open-label pharmacodynamic study

Jose E. Irazuzta, MD; Robert K. Pretzlaff, MD; Mark E. Rowin, MD

Pediatr Crit Care Med 2001 Vol. 2, No. 1

- **Objective: To investigate the short-term hemodynamic effects of amrinone in pediatric patients with refractory septic shock.**
- **9 patients in a Pediatric Intensive Care Unit with septic shock on stable doses of vasopressors and inotropes**

Corticosteroids

- **Give hydrocortisone (2 mg/kg) in children with *"fluid refractory, catecholamine resistant shock and suspected or proven absolute (classic) adrenal insufficiency"* (Grade 1A)**

ECMO

- **Consider ECMO for refractory pediatric septic shock and respiratory failure (Grade 2C)**

Antibiotics and Source Control

- Empiric antibiotics should be started within 1 hour of identification of sepsis. Blood and other cultures should be obtained before antibiotics, but not delay administration. Antibiotic choices should be changed as epidemic and endemic ecologies dictates. **(Grade 1D)**
- Clindamycin and anti-toxin therapies for toxic shock syndrome with refractory hypotension. **(Grade 2D)**
- **Early and aggressive source control (Grade 1D)**
- **Clostridium difficile colitis should be treated with enteral antibiotics if tolerated (Grade 1A)**

Aggressive Source Control (Grade 1D)

- A local insult such as infection or tissue injury triggers innate host defense mechanisms that result in local vasodilatation increases in microvascular permeability, activation of coagulation, and the influx of large numbers of activated neutrophils
- The evolving “mélange” of microorganisms, debris, and fluid becomes enclosed within a fibrin capsule (abscess)
- This structure prevents dissemination of microorganisms but also protects them from systemic host defenses

Basis of source control

- Drainage of infected fluid collections
- Debridement of infected solid tissue
- Removal of devices or foreign bodies

Source control in the management of severe sepsis and septic shock: An evidence-based review

John C. Marshall, MD; Ronald V. Maier, MD, FACS; Maria Jimenez, MD; E. Patchen Dellinger, MD
(Crit Care Med 2004; 32[Suppl.]:S513–S526)

What is the optimal approach to abscess drainage in the patient with severe sepsis or septic shock?

Recommendation: As a general principle, the optimal method of drainage is that which accomplishes full drainage of the collection with the least degree of anatomic and physical trauma to the patient; not only does such an approach minimize the immediate morbidity associated with drainage, it also ensures the broadest range of options for subsequent reconstructive surgery.

Grade E

Source control in the management of severe sepsis and septic shock: An evidence-based review

John C. Marshall, MD; Ronald V. Maier, MD, FACS; Maria Jimenez, MD; E. Patchen Dellinger, MD
(Crit Care Med 2004; 32[Suppl.]:S513–S526)

Can an infected vascular catheter
be safely exchanged over a guidewire?

Recommendation: An infected intravascular
catheter can be safely exchanged over a guidewire, provided there is no significant evidence of soft-tissue infection at the exit site.

Grade B

Source control in the management of severe sepsis and septic shock: An evidence-based review

John C. Marshall, MD; Ronald V. Maier, MD, FACS; Maria Jimenez, MD; E. Patchen Dellinger, MD
(Crit Care Med 2004; 32[Suppl.]:S513–S526)

What is the optimal approach to source control when sepsis results from a perforation of the gastrointestinal tract?

Recommendation: The therapeutic objective in managing a perforation at any level of the gastrointestinal tract is to eliminate ongoing leakage of luminal contents through removal of the perforation or through the creation of a controlled sinus or fistula. How this objective is best accomplished depends on the anatomic site and extent of the perforation, the degree of localization, and the physiologic stability of the patient. **Grade E; except Grade C** for gastrointestinal perforations secondary to diverticulitis

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John C. Marshall, MD; Ronald V. Maier, MD, FACS; Maria Jimenez, MD; E. Patchen Dellinger, MD
(Crit Care Med 2004; 32[Suppl.]:S513–S526)

What is the optimal mode of source control when sepsis results from intestinal ischemia or infarction?

Recommendation: Intestinal infarction is a surgical emergency because gangrenous intestine produces rapid physiologic decompensation, and in the absence of surgical resection, is almost invariably lethal. On the other hand, intestinal ischemia in the absence of infarction is potentially reversible with hemodynamic support and correction of the circumstances that produced the ischemia. Thus, early diagnosis and timely surgical intervention are critical to a successful outcome for patients with severe sepsis secondary to intestinal ischemia.

Grade E

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(Crit Care Med 2004; 32[Suppl.]:S513–S526)

Is there a role for diagnostic laparotomy or abdominal washout in the patient with a possible intraabdominal focus but negative radiographic investigations?

Recommendation: Advances in diagnostic imaging techniques have essentially eliminated the radiographically occult but clinically important focus on intraabdominal infection. Provided the clinician has access to resources for CT, it is very unlikely that surgical exploration will reveal treatable foci of infection that cannot be detected radiologically, and there is no evidence that blind laparotomy results in improved clinical outcomes.

No, Grade E

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(Crit Care Med 2004; 32[Suppl.]:S513–S526)

What is the role of diagnostic sampling in the diagnosis of intrathoracic or sinus infection?

Recommendation: Access to fluid collections for diagnosis and potential therapeutic drainage is a priority. Sampling of intraparenchymal, intrapleural, mediastinal, or sinus collections, either blindly or by ultrasound or CT-guided needle aspiration, is usually diagnostic. Patients receiving antibiotics may have sterile aspirates.

Grade E

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What is the role of fibrinolytics in treatment of empyema?

Recommendation: The use of fibrinolytics via tube thoracostomy for retained infected loculations, when administered early before the fibrotic phase of disease, decreases length of stay, time to resolution, and necessity for surgical intervention.

Grade C

Clostridium difficile colitis treat with enteral antibiotics (Grade 1A)

Clinical Review of the Management of Fulminant *Clostridium difficile Infection*

M. Raffat Jaber, M.D., Snorri Olafsson, M.D., Ph.D., M.P.H., Wesley L. Fung, M.D., and Mark E. Reeves, M.D., Ph.D.

American Journal of Gastroenterology 2008

- *Clostridium difficile infection (CDI) is one of the most common* nosocomial infections and a frequent cause of morbidity and mortality among elderly hospitalized patients
- Both the frequency and severity of CDI are increasing
- C. diff drug resistance being reported

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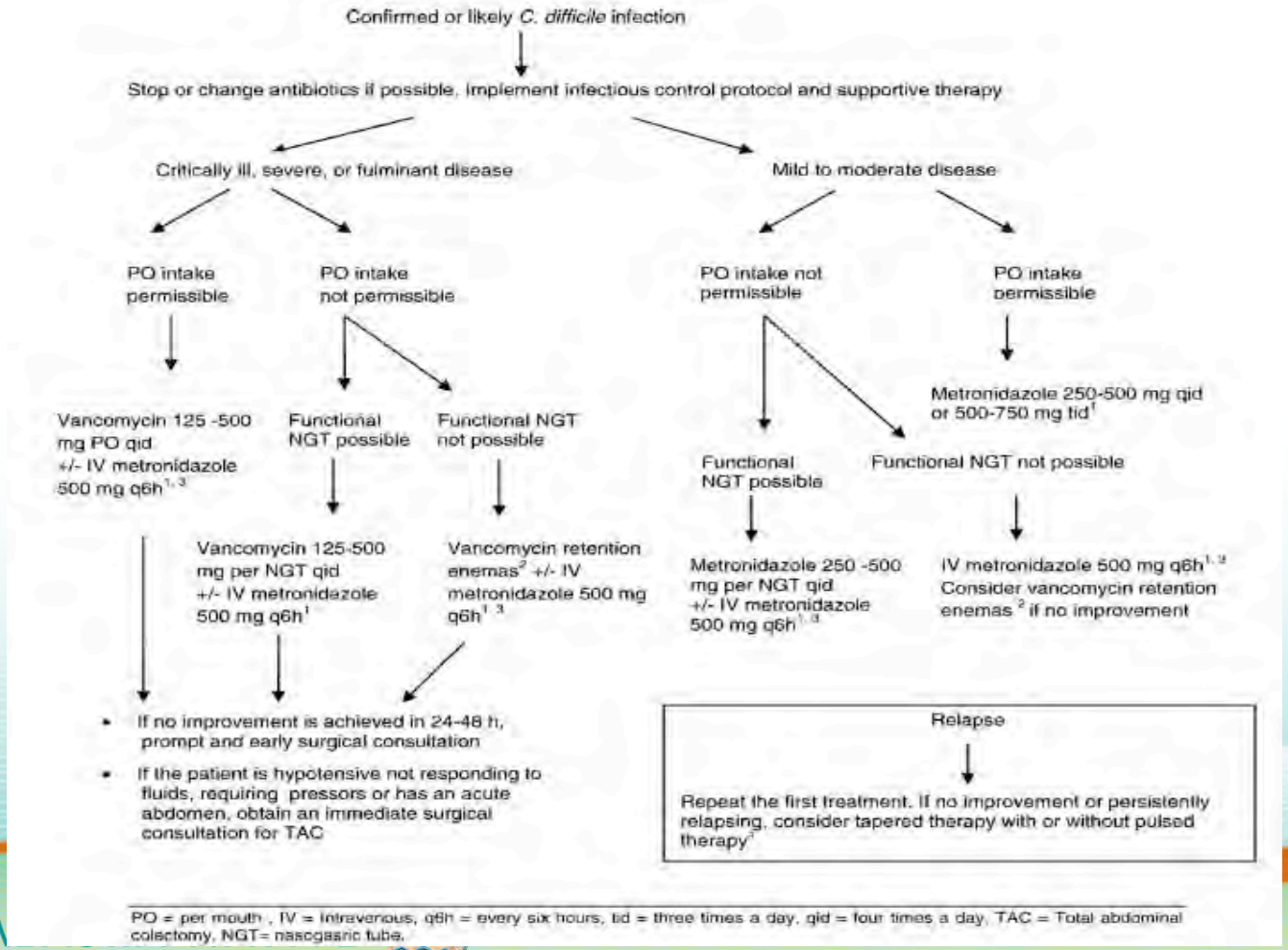

Clinical Review of the Management of Fulminant *Clostridium difficile Infection*

M. Raffat Jaber, M.D., Snorri Olafsson, M.D., Ph.D., M.P.H., Wesley L. Fung, M.D., and Mark E. Reeves, M.D., Ph.D.

American Journal of Gastroenterology 2008

- Oral vancomycin preferred treatment in severe disease
- Oral vancomycin poorly absorbed so stool concentrations high, systemic effects minimal
- Less than 15% of IV metronidazole excreted by fecal route, so may not be effective, especially with ileus

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- Zar et al. (Clin Infect Dis 2007;45:302–7.)
- 69 patients with severe disease, rate of cure
  - 29 of 38 patients with IV metronidazole (76%)
  - 30 of 31 patients with enteral vancomycin (97%)

Avoiding Colectomy during Surgical Management of Fulminant Clostridium difficile Colitis

Andrea D. Olivas, Konstantin Umanskiy, Brian Zuckerbraun, and John C. Alverdy

SURGICAL INFECTIONS Volume 11, Number 3, 2010

- Studies in the 1980s showed no difference in efficacy between oral metronidazole and oral vancomycin [33,34]
- Metronidazole became the preferred initial treatment mainly because of its low cost and the risk that vancomycin may induce colonization by vancomycin-resistant enterococci.
- However, the failure rate of metronidazole therapy has increased from 2.5% to approximately 18.2% [35]

33. Cherry R, Portnoy D, Jabbari M, et al. Metronidazole: An alternate therapy for antibiotic-associated colitis. Gastroenterology 1982;82:849–851.

34. Teasley D, Gerding D, Olson M. Prospective randomized trial of metronidazole versus vancomycin for Clostridium difficile-associated diarrhea and colitis. Lancet 1983;2:1043–1046.

35. Musher D, Aslam S, Logan N. Relatively poor outcome after treatment of Clostridium difficile colitis with metronidazole. Clin Infect Dis 2005;40:1586–1590.

Other Therapies

Mechanical Ventilation

- Lung protective strategies (6 cc/kg tidal volume, moderate to high PEEP if needed) **(Grade 2C)**
  - Is chest moving?
  - 6 cc/kg tidal volume delivered (air leak?)
  - Tube in good position
  - Cuffed tube
  - Get FiO2 below 60% if you can

Glycemic Control

- Control hyperglycemia with target ≤ 180 mg/dL **(Grade 2C)**
  - Start insulin infusion 0.1 units/kg/hour
  - Simultaneously, have maintenance IVF with dextrose going
  - Accuchecks every hour

Deep Vein Thrombosis Prophylaxis

- No recommendation on the use of DVT prophylaxis in prepubertal children with sepsis

Stress Ulcer Prophylaxis

- No recommendation on the use of SU prophylaxis on prepubertal children with severe sepsis

Nutrition

- Early enteral nutrition to those who can be fed enterally **(Grade 2C)**
  - We use ND tubes in all intubated children
  - Obviously not if the source of sepsis is intra-abdominal
  - We also hold enteral feeds if on alpha agents such as norepinephrine
- Patients who get early parenteral nutrition (< hospital day 7) may have worse clinical outcomes

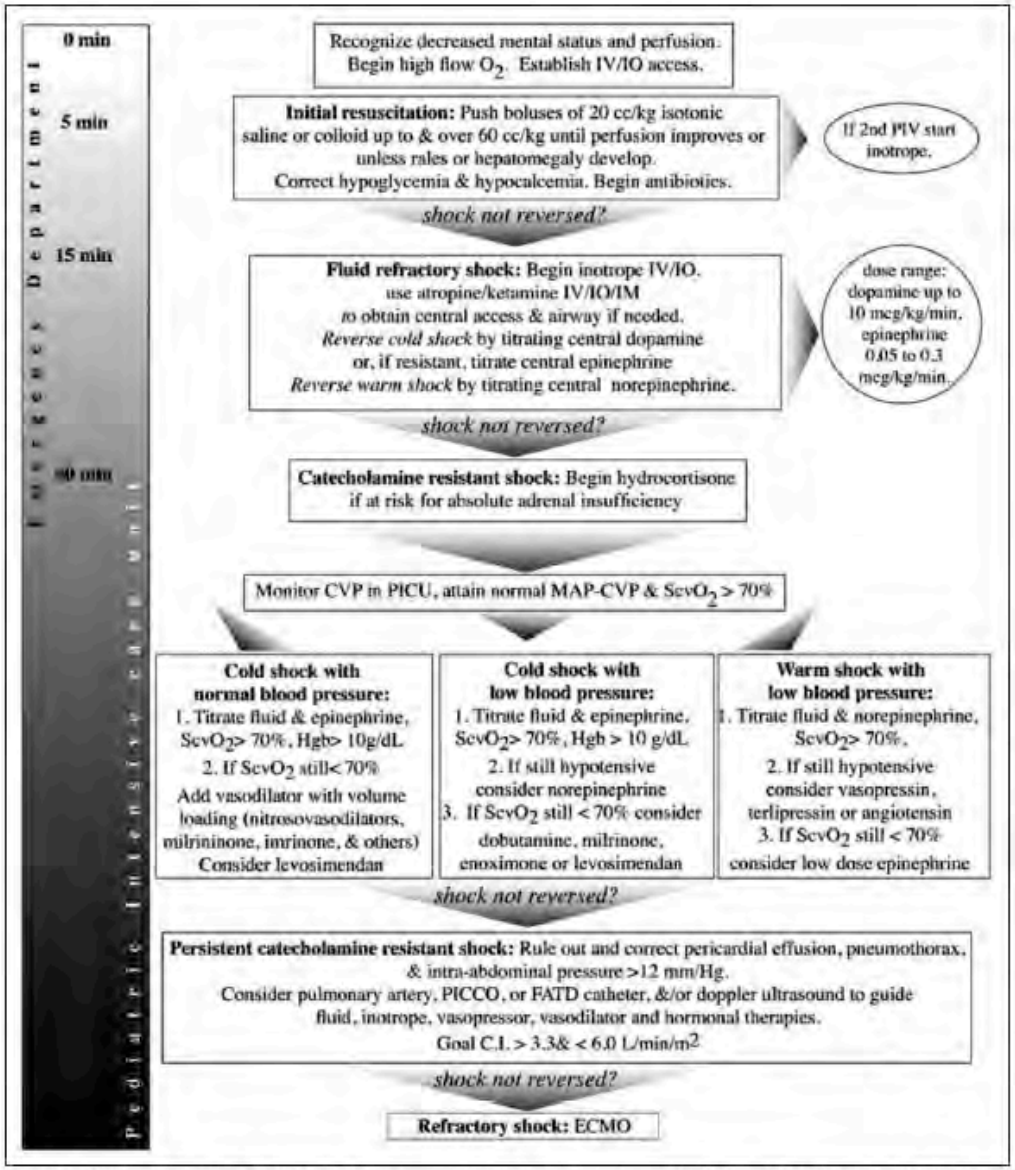

Figure 2. Algorithm for time sensitive, goal-directed stepwise management of hemodynamic support in infants and children. Reproduced from Brierley J, Carcillo J, Choong K, et al: Clinical practice parameters for hemodynamic support of pediatric and neonatal septic shock: 2007 update from the American College of Critical Care Medicine. *Crit Care Med* 2009; 37:666–688.