

Making Sure that Kids Survive Sepsis: What's New, What's Old, and What's Different About Pediatric Sepsis

Halden Scott, MD, MSCS

Associate Professor of Pediatrics and Emergency Medicine



 halden.scott@cuanschutz.edu

 @halden_scott



University of Colorado
Boulder | Colorado Springs | Denver | Anschutz Medical Campus

1

Disclosures / Funding

No commercial conflicts of interest.

Professional panels: IPSO Steering Committee, SCCM Surviving Sepsis Guidelines, SCCM Pediatric Sepsis Definitions taskforce

Current funding:

- AHRQ K08 HS025696 (Scott)
Enhancing Quality in Pediatric Sepsis with Shock Prediction and Early Electronic Decision Support (EQUIP with SPEED)
- NICHD R01 HD087363 (Alpern)
PED Screen: Pediatric Sepsis EHR Registry, Clinical Outcomes, and Prediction Model



2

Objectives

The attendee will be able to:

1. Diagnose pediatric septic shock and assess hemodynamics
2. Develop an approach to the use of intravenous fluids and vasoactive agents in pediatric septic shock
3. Understand the 2020 pediatric Surviving Sepsis diagnosis and treatment algorithm, and apply it to their clinical setting



3

Surviving Sepsis Campaign International Guidelines for the Management of Shock and Sepsis-Associated Dysfunction in Children

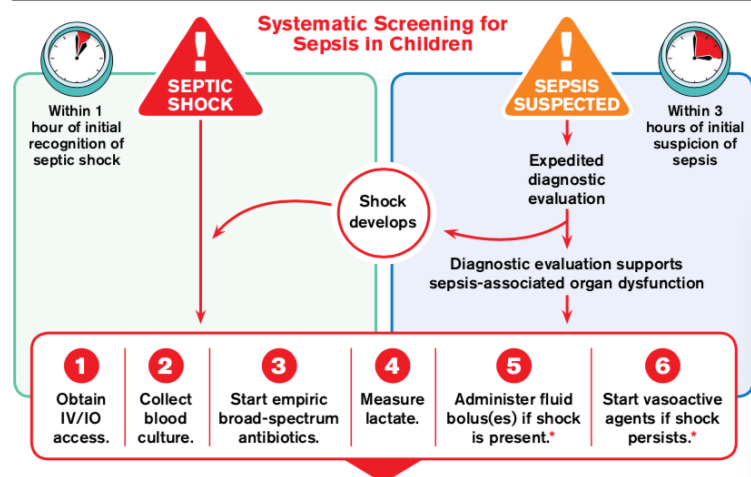
Scott L. Weiss, MD, MSCE, FCCM (Co-Vice Chair)*; Mar Waleed Alhazzani, MD, MSc, FRCP (Methodology Chair); Heidi R. Flori, MD, FAAP[†]; David P. Inwald, MB, BChir, FRCR; Simon Nadel, MBBS, MRCP, FRCP[‡]; Luregn J. Schlappbach, FCICM, FMH-ICU, FMH-Paed, FRCPC; Robert C. Tasker, MB BS, MA, AM, MD, FRCPHC, FRCP; Andrew C. Argent, MB BCh, MMed, MD (Paediatrics)*; J. Joseph Carcillo, MD[§]; Enitan D. Carroll, MB ChB, MD, FRCR; Christopher L. Carroll, MD, MS, FCCM, FAAP[‡]; Ira M. Cohen, MD, PhD, FRCP (C) (methodologist)*; Jeffrey J. Cies, PharmD, MPH, BCPS-AQ ID, BCPPS, FCCP; Andrea T. Cruz, MD, MPH, FAAP[‡]; Daniele De Luca, MD, I Saul N. Faust, MA, MB BS, FRCPCH, PhD, FHEA[§]; Clau Mark W. Hall, MD, FCCM, FAAP[‡]; Paul Ishimine, MD, FA; Koen F. M. Joosten, MD, PhD[‡]; Poonam Joshi, PhD[‡]; Oli Martin C. J. Kneyber, MD, PhD, FCCM[‡]; Joris Lemson, MD, Nitesh M. Mehta, MD[‡]; Morten Hylander Møller, MD, PhD; Christopher J. L. Newth, MD, ChB, FRCP, FRCP[‡]; Tris Akira Nishisaki, MD, MSCE, FAAP[‡]; Mark E. Nunnally, Margaret M. Parker, MD, MSc, FCCM, FAAP[‡]; Raima M. Paul Adrienne G. Randolph, MD, MS, FCCM, FAAP[‡]; Suchitra Halden F. Scott, MD, MSc, FAAP, FACEP[‡]; Lyvonne N. Judy T. Verger, RN, PhD, CPNP-AC, FCCM, FAAN[‡]; Eric Joshua Wolf, MBBS, PhD, FRCP[‡]; Hector R. Wong, MD, Niranjan Kissoon, MB BS, MSc, FRCP (C), FAAP, FAC Pierre Tissieres, MD, DSc (Co-Chair)^{§,¶}

These guidelines are simultaneously being published in Pediatric Critical Care Medicine (DOI: 10.1097/PCC.0000000000000198) and Intensive Care Medicine (DOI: 10.1007/s00134-019-05878-6). Copyright © 2020 by the Society of Critical Care Medicine, the European Society of Intensive Care Medicine, and the World Federation of Pediatric Intensive and Critical Care Societies. DOI: 10.1097/PCC.0000000000000198

www.pccjournal.org

Initial Resuscitation Algorithm for Children

Surviving Sepsis Campaign



4

Case: Primary Care Presentation

- 7-year-old unimmunized boy
- 6 days increasing fatigue, 'not acting right'
- No fever. No rhinorrhea, no cough, no sore throat.
- 1-day L leg pain, L shoulder pain
- On further history... Cut L finger while cooking 1 week prior, treated with triple antibiotic ointment



5

Case: Primary Care Presentation

7-year-old unimmunized boy, 6 days increasing fatigue, 'not acting right'

- Physical exam: T= 36.8 HR = 136 RR = 22 BP = 92/64
- Crusted lesions around mouth
- Dry mucus membranes
- L upper extremity erythematous, tender, cut on hand well-healed
- UA negative, rapid strep +, referred to local ED
- Concern for osteomyelitis



6

Case Presentation

Potential risk factor

7-year-old unimmunized boy, 6 days increasing fatigue, 'not acting right'

Physical exam: T= 36.8 HR = 136 RR = 22 BP = 92/6

Crusted lesions around mouth

Dry mucus membranes

L upper extremity erythematous, tender, cut on hand well-healed

UA negative, rapid strep +, referred to local ED

Concern for osteomyelitis

Worrisome overall health,
potential systemic process

Potential bacterial
infection, multiple sites



7

Case: Critical Access Emergency Department

7-year-old unimmunized boy with history of cut, L arm pain

- T: 38.2 HR: 162 RR: 20 Pulse ox: 91%
- Alert, interactive
- Dry MM
- Erythema to L arm and leg, tender, limited ROM at shoulder
- CBC: 4.6>13.7<181
- Blood culture pending
- 20 mL / kg NS
- Plan for transfer to tertiary hospital for osteomyelitis evaluation



8

Case: Critical Access Emergency Department

7-year-old unimmunized boy with history of cut, L arm pain

- T: 38.2 HR: 162 RR: 20 Pulse ox: 91%
- CBC: 4.6>13.7<181
- Blood culture pending
- 20 mL / kg NS
- Plan for transfer to tertiary hospital for osteomyelitis evaluation

What else do you want prior to transfer?



Case: Critical Access Emergency Department

7-year-old unimmunized boy with history of cut, L arm pain

- T: 38.2 HR: 162 RR: 20 Pulse ox: 91%
- CBC: 4.6>13.7<181
- Blood culture pending
- 20 mL / kg NS
- Plan for transfer to tertiary hospital for osteomyelitis evaluation

Does this patient have sepsis?



Pediatric Definitions

Infection

- Suspected or proven infection caused by any pathogen OR a clinical syndrome w/ probability of infection

Sepsis

- SIRS in the presence of infection

Severe Sepsis

- Sepsis + CV dysfunction OR ARDS OR ≥ 2 other organ dysfunction

Septic Shock

- Sepsis and CV organ dysfunction (hypotension, pressors or elevated lactate)



Goldstein PCCM 2005



11

Pediatric

Infection

- Suspected or proven infection caused by any pathogen OR a clinical syndrome w/ probability of infection

Sepsis

- SIRS in the presence of infection

Severe Sepsis

- Sepsis + CV dysfunction OR ARDS OR ≥ 2 other organ dysfunction

Septic Shock

- Sepsis and CV organ dysfunction (hypotension, pressors or elevated lactate)

The authors reply:

We would like to thank Nakagawa and Shime (1) for their thoughtful letter regarding our 2005 article

tant issues. First, the consensus conference article was meant as "a consensus definition of the pediatric sepsis continuum including systematic inflammatory response syndrome (SIRS), infection, sepsis, severe sepsis, septic shock, and multiple organ dysfunction syndrome to aid in standardization of observational studies and evaluation of therapeutic interventions in clinical trials" (2) and not as diagnostic criteria to guide clinical management. This is an important distinction

that the 2005 consensus definitions are due for revision and updating. Although it was not our original intent, the criteria have been used in guidelines and protocols for clinical diagnosis and management. The appropriateness of this requires further investigation with high-quality clinical studies adding further to the work of Nakagawa and Shime (1). Dr. Goldstein received grant support (grants for pediatric

The letter by Nakagawa and Shime (1) is timely and suggests that the 2005 consensus definitions are due for revision and updating. Although it was not our original intent, the criteria have been used in guidelines and protocols for clinical diagnosis and management. The appropriateness of this requires



pediatrics. *Pediatr Crit Care Med* 2005; 6:2-8
DOI: 10.1097/PCC.0000000000000025
Pediatric Critical Care Medicine

Goldstein PCCM 2014



12

"Sepsis 3.0"

Life-threatening organ dysfunction caused by a dysregulated host response to infection

Seymour JAMA 2016

Defining Pediatric Sepsis

VIEWPOINT

Lungu I, Schlapbach, MD, FRCPC
Faculty of Medicine,
The University of
Queensland, Brisbane,
Queensland, Australia,
and Pediatric Critical
Care Research Group,
Mater Research
Institute, University of
Queensland, Brisbane,
Queensland, Australia
Niraj K. Kishore, MD
University of British
Columbia, Vancouver,
British Columbia,
Canada, and British
Columbia Children's
Hospital, Vancouver,
British Columbia,
Canada

The resolution on sepsis by the United Nations World Health Assembly in May 2017 recognizes sepsis as a global threat in adults and children and a priority for the World Health Organization to address during the next decade.¹ This resolution on sepsis acknowledges that sepsis represents a major contributor to childhood morbidity and mortality and the associated economic burden. The United Nations Sustainable Development Goal 3 (https://sustainabledevelopment.un.org/sdgs) defined specific targets for infections and pandemics.² Despite the huge burden that sepsis imposes on the health of children,³⁻⁴ current definitions of pediatric sepsis are of limited value to bedside clinicians to identify cases of sepsis. Moreover, these definitions have poor predictive value and have not been validated, thus lessening their utility in benchmarking, performance monitoring, and patient stratification. These shortcomings have been increasingly recognized since the definitions were crafted by

sepsis of a criterion standard, the Adult Sepsis Definition Taskforce has operationalized sepsis definitions that were developed and validated in large cohorts using a data-driven approach rather than expert consensus alone.⁵ The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) definition⁶ emphasizes that sepsis is differentiated from uncomplicated infection by the presence of life-threatening organ dysfunction as a result of a dysregulated host response to infection. Septic shock is a subset of sepsis in which profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone. Using the Sequential Organ Failure Assessment (SOFA) score, patients with new organ dysfunction are identified. The paradigm change in content and methods applied to develop Sepsis-3 has stimulated a fruitful discussion among clinicians, researchers, and stakeholders in health, and the consensus article⁶ rep-

In conclusion, there is thus an urgent need to translate Sepsis-3 into definitions adapted for the specific disease characteristics, susceptibilities, and patterns of pediatric sepsis. Failure to re-

define sepsis as severe sepsis and cardiovascular dysfunction as septic shock. However, SIRS is very commonly manifested in otherwise well-ill children, and even in children without infections, leading to low specificity and thus limited use to clinicians.⁷ During the winter months, more than half the population of children in emergency department present with urinary tract infection, which would satisfy the present criteria for sepsis. Apart from the stress on resources even in high-income countries, many health care facilities in low- and middle-income countries do not have the resources to perform white blood cell counts (a requirement for diagnosing SIRS); hence, the present definitions of limited benefits in many parts of Asia and sub-Saharan Africa, where the burden of sepsis is highest and the most mortality from sepsis occurs. The difficulties in applying the definitions of sepsis have led to considerable variability in sepsis reporting. Accordingly, studies have identified considerable discrepancies in applying definitions of pediatric sepsis, leading to a large variation in incidence estimates when comparing clinical, administrative, and research data. Too often, sepsis was used interchangeably with severe sepsis, despite clear criteria for organ dysfunction, which is the final common pathway to adverse patient outcomes.

Recognizing the limitations of SIRS, and in view of difficulties in defining a diagnosis of sepsis in the ab-

sence of similar updated definitions for pediatric populations.^{8-10,11} Although the SOFA score was not designed for pediatric age groups, several recent studies have demonstrated, in principle, the feasibility of applying Sepsis-3-based criteria to pediatric age groups.¹²⁻¹⁴ Translating Sepsis-3 criteria into pediatrics will require taking age-related differences in pathophysiology and clinical manifestations into account. For example, arterial hypotension, which is of 3 essential criteria for septic shock in adults, represents an generally late sign of septic shock in children. Furthermore, the failure rate often seen in community-acquired pediatric sepsis will require careful evaluation of predictive vs descriptive performance of severity scoring systems. Finally, SOFA, and its pediatric counterpart Pediatric Logistic Organ Dysfunction, have been validated in primarily intensive care settings. However, both assessment tools remain strongly laboratory based; hence, the feasibility, and performance if applied outside the intensive care setting, in particular in low- and middle-income countries where laboratory resources are limited, remain to be investigated.

Definitions of pediatric sepsis have important implications on clinical care, accurate estimates of the burden of disease, quality improvement initiatives and benchmarking, and the design of research protocols. The present definitions are inadequate to serve these goals

JAMA Pediatrics | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Adaptation and Validation of a Pediatric Sequential Organ Failure Assessment Score and Evaluation of the Sepsis-3 Definitions in Critically Ill Children

Travis J. Matrics, DO; L. Nelson Sanchez-Pinto, MD, MBI



Queensland, Mount
Brisbane, Queensland
4005, Australia
l.n.sanchez@uq.edu.au

jama-pediatrics.com

JAMA Pediatrics Published online February 19, 2018



13

What is Organ Dysfunction and Why Should I Care?

CV: Hypotension, lactate, vasopressor use
Resp: New positive-pressure ventilation
Neuro: Altered mental status
Renal: Acute kidney injury
Hepatic: Elevated LFTs
Heme: DIC, low platelets

*precise cutpoints vary and subject to change!



Goldstein PCCM 2005, Matrics JAMA Pediatrics, Weiss PCCM 2020



14

PEDIATRIC CRITICAL CARE

Acute Kidney Injury in Pediatric Severe Sepsis: An Independent Risk Factor for Death and New Disability

Fitzgerald, Julie C. MD, PhD^{1,2}; Basu, Rajit K. MD, MMI³; Akcan-Arikan, Ayse MD⁴; Izquierdo, Ledys M. MD⁵; Piñeres Olave, Byron E. MD⁶; Harsinger Amanda R. MD, MS⁷; Szczepanska, Maria MD, PhD⁸; Deep Akash FRCPCH⁹; Williams, Duane MD, MS^{1,2}; Thomas, Neal J. MD, MSc^{1,3}; Wei, Y. MD, PhD^{1,2}

PREvalence, OUtcomes, and Therapies Investigators Network **Author Info**

Critical Care Medicine: December 2017
doi: 10.1097/CCM.0000000000002007

The JOURNAL of PEDIATRICS

Log in Register

ORIGINAL ARTICLES | ARTICLES IN PRESS

Purchase Subscribe

Disseminated Intravascular Coagulation Is an Independent Predictor of Adverse Outcomes in Children in the Emergency Department with Suspected Sepsis

Leonora R. Slatnick, MD • Dianne Thornhill, PhD • Sara J. Deakyne Davies, MPH • ...
Halden F. Scott, MD, MSCS • Marilyn J. Manco-Johnson, MD • Beth Boulden Warren, MD, MS, MSCS

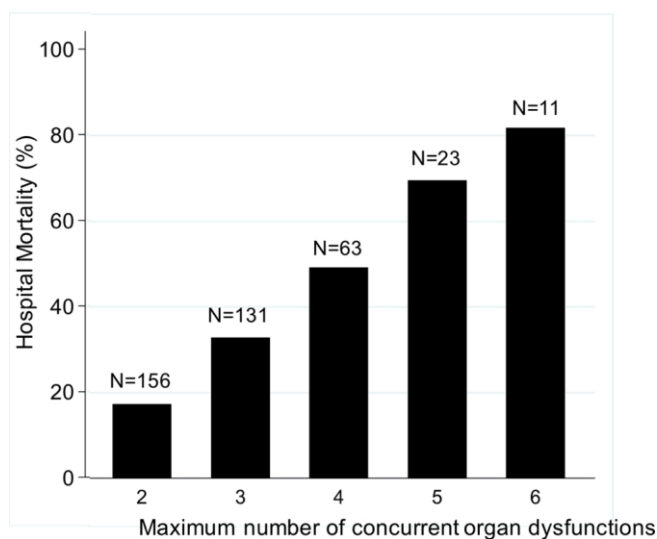
Validation of the Vasoactive-Inotropic Score in Pediatric Sepsis

Amanda M. McIntosh, MD¹; Suhong Tong, MS²; Sara J. Deakyne, MPH³; Jesse A. Davidson, MD, MPH⁴; Halden F. Scott, MD⁵

Pediatric Critical Care Medicine

15

Why is organ dysfunction important?



Lin PCCM 2017

16

Sepsis ≠ Serious Bacterial Infection



~~“Rule Out Sepsis”~~

An informal term for a diagnostic workup to identify serious bacterial infection, often in neonatal fever

Sepsis

Life-threatening organ dysfunction caused by infection



<https://www.methodsman.com/blog/a-blood-test-to-avoid-a-spinal-tap-in-an-infant-yes-please>



17

Suspected Infection + Organ Dysfunction

Hypotensive 8-year-old, ALL, central line; blood culture + gram negative rods

2-year-old **intubated, ventilated** with pneumonia

Lethargic 4-year-old, fever, and leukocytes & nitrites in her urine

16-year-old, **right lower quadrant pain** and fever, heart rate 140 bpm, **capillary refill of 5 seconds** and **lactate 4.1 mmol/L**



18

Sepsis = Infection + Organ Dysfunction

- Start treatment for suspicion of infection
- Diagnosis does not require microbiological confirmation
- Consider de-escalation if clinical picture/labs do not support infection

CV: Hypotension, lactate, vasopressor use

Resp: New positive-pressure ventilation

Neuro: Altered mental status

Renal: Acute kidney injury

Hepatic: Elevated LFTs

Heme: DIC, low platelets



Goldstein PCCM 2005, Matics JAMA Pediatrics, Weiss PCCM 2020



19

Case: Critical Access Emergency Department

T: 38.2 HR: 162 RR: 20
Pulse ox: 91%

CBC: 4.6 > 13.7 < 181

Blood culture pending
20 mL / kg NS

Does this patient have sepsis?

Organ Dysfunction

CV: Hypotension, lactate

Resp: New ventilation

Neuro: Altered mental status

Renal: AKI

Hepatic: Elevated LFTs

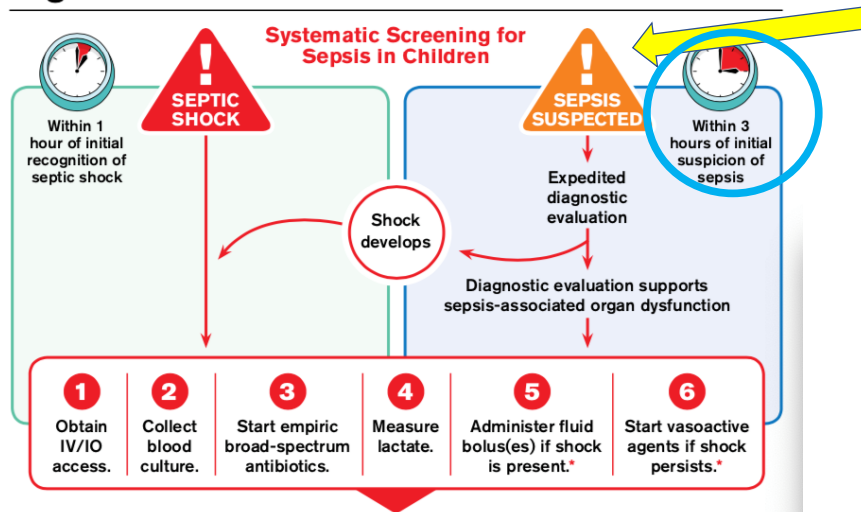
Heme: DIC, low platelets



20

Initial Resuscitation Algorithm for Children

Surviving Sepsis Campaign



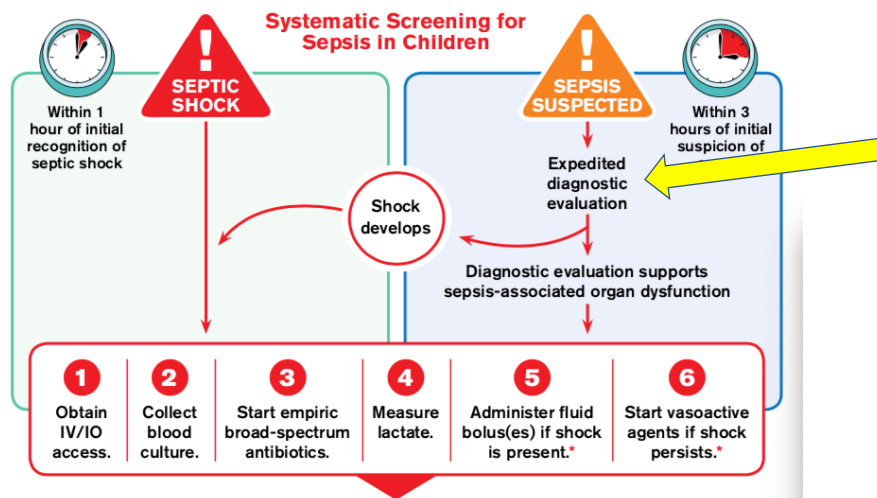
www.sccm.org/SurvivingSepsisCampaign/Guidelines/Pediatric-Patients



21

Initial Resuscitation Algorithm for Children

Surviving Sepsis Campaign



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



22

Case: Critical Access Emergency Department

7-year-old with arm pain

T: 38.2 HR: 162 RR: 20
Pulse ox: 91%

CBC: 4.6>13.7<181

Blood culture pending
20 mL / kg NS

More Information

BP: 73/37

Na 123, Cl 90, Cr 0.81

Lactate 2.6



23

▼ Critical Red Alert (Advisory: 1)

!!

Blood Pressure: (!) 60/30 (06/02/16 1508 : Zztest, Nurse Ed D)

HYPOTENSION!

This patient has low systolic blood pressure

- This is shock! Consider and treat sepsis, hypovolemia/ hemorrhage, anaphylaxis, cardiogenic or obstructive shock.
- Notify attending immediately.

The following actions have been applied: _____

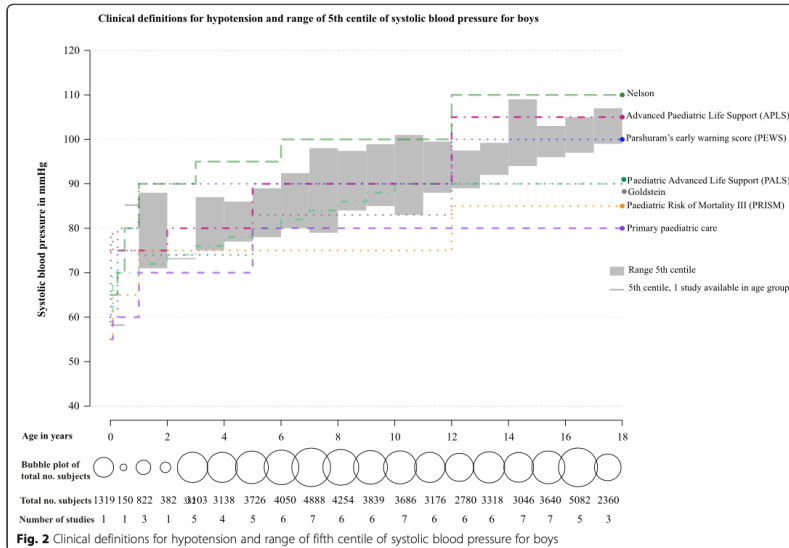
✓ Completed: Chco ed trigger hypotension event from bpa

! Acknowledge Reason _____



24

Pediatric Hypotension



PALS Systolic Hypotension

$70 + \text{Age} \times 2$

Adult 90 mmHg



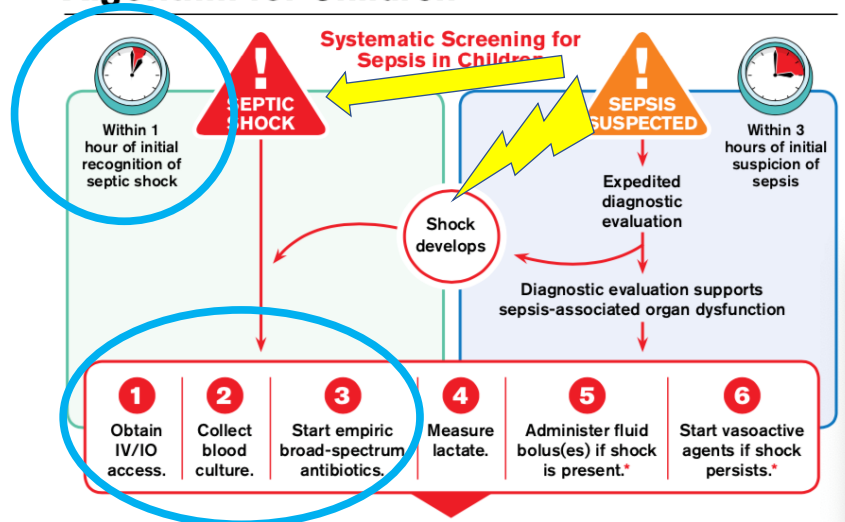
Hagedoorn et al. Critical Care (2019) 23:380



25

Initial Resuscitation Algorithm for Children

Surviving Sepsis Campaign



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



26

Case – Critical Access ED - waiting for transport

- HR: 160s
- BP: 73/37
- Na:123, Cl:90, Cr: 0.81
- Lactate 2.6
- Ceftriaxone and Vancomycin ordered and given



27

Antimicrobial Therapy

1. In children with **septic shock**, we recommend starting antimicrobial therapy *as soon as possible*, within 1 hr. of recognition (strong recommendation, very low quality of evidence).
2. In children with **sepsis-associated organ dysfunction** but without shock, we suggest starting antimicrobial therapy *as soon as possible* after appropriate evaluation, within 3 hrs. of recognition (weak recommendation, very low quality of evidence).
3. Additional recommendations: start broad/narrow coverage, stop asap, source control, specific pharmacodynamic/double coverage recommendations

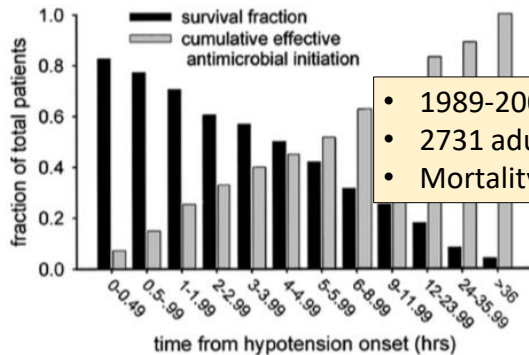


Weiss PCCM 2020

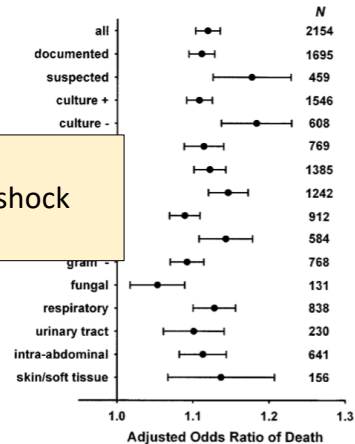
28

Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock*

Anand Kumar, MD; Daniel Roberts, MD; Kenneth E. Wood, DO; Bruce Light, MD; Joseph E. Parrillo, MD; Satendra Sharma, MD; Robert Suppes, BSc; Daniel Feinstein, MD; Sergio Zanotti, MD; Leo Taiberg, MD; David Gurka, MD; Aseem Kumar, PhD; Mary Cheang, MSc



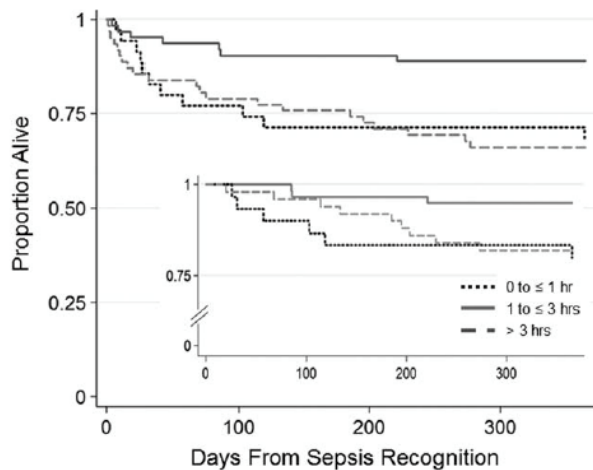
- 1989-2004
- 2731 adult patients septic shock
- Mortality 56.2%



Crit Care Med 2006 Vol. 34, No. 6



29



- Unexpected post-hoc finding
- Hypothesis-generating
- Possible explanations:
 - More severely ill patients
 - Early delivery may represent delayed recognition
 - Biologic plausibility for harm from very early antibiotics?



Han Shock 2017



30

Hospital Pediatrics

AN OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Research Article

Antibiotic Timing in Pediatric Septic Shock

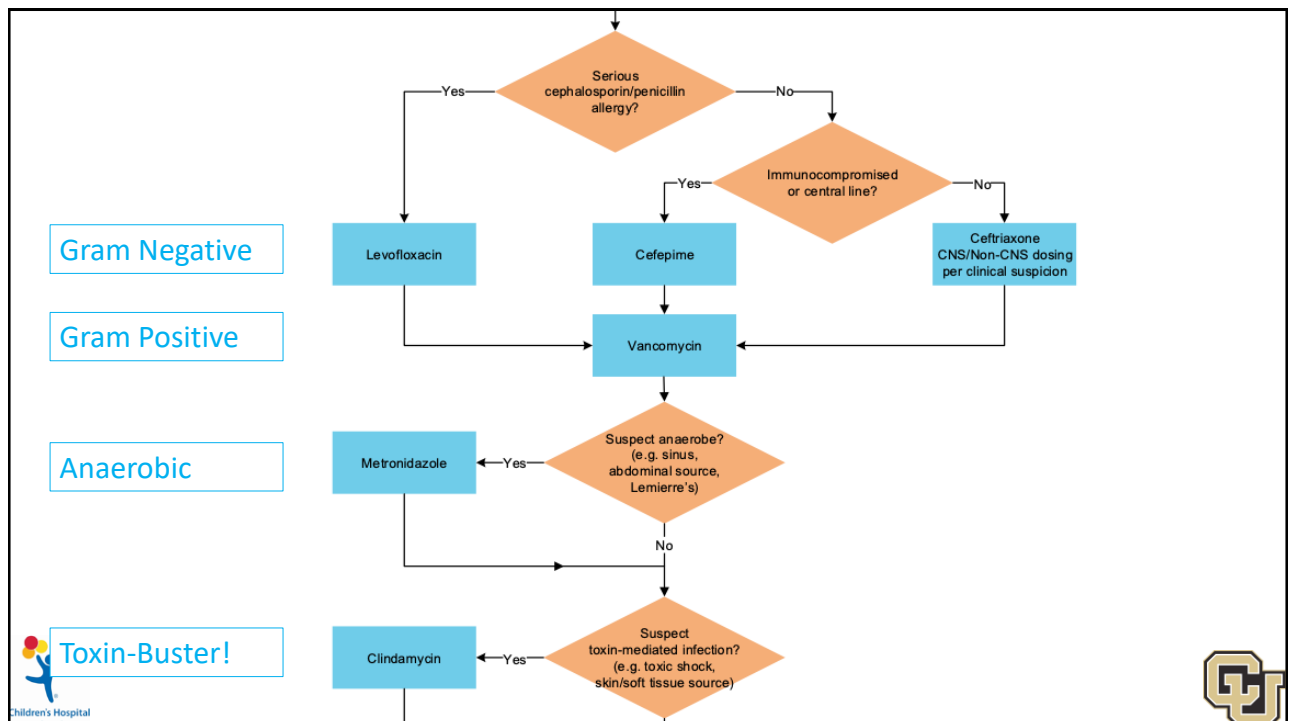
Roni D. Lane, Jared Olson, Ron Reeder, Benjamin Miller, Jennifer K. Workman, Emily A. Thorell and Gitte Y. Larsen

Hospital Pediatrics March 2020, hpeds.2019-0250; DOI: <https://doi.org/10.1542/hpeds.2019-0250>

- 1377 Patients
- 2007-2015
- 71% Antibiotics \leq 2 hours
- No association time to antibiotic and outcome



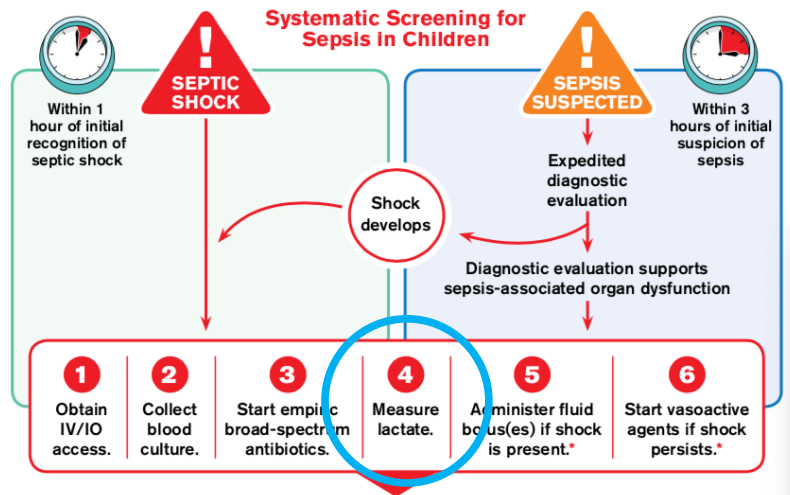
31



32

Initial Resuscitation Algorithm for Children

Surviving Sepsis Campaign



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

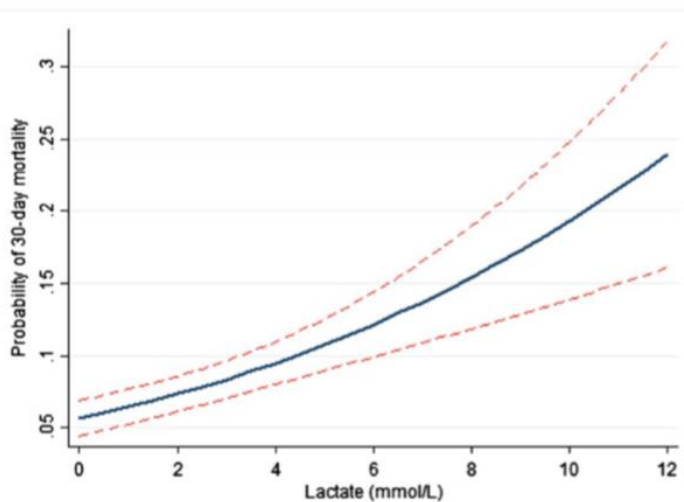


33

PEDIATRIC ORIGINAL

Prediction of pediatric sepsis mortality within 1 h of intensive care admission

Luregn J, Schlapbach^{1,2,3*}, Graeme MacLaren^{4,5}, Marino Festa⁶, Janet Alexander^{7,8}, Simon Erickson⁹, John Powell¹⁰, Andrew Clark², Andrew Caldwell^{1,2}, David Potho^{1,2,3,12}, John Kellie^{1,3}, John Powell^{1,3} and G.

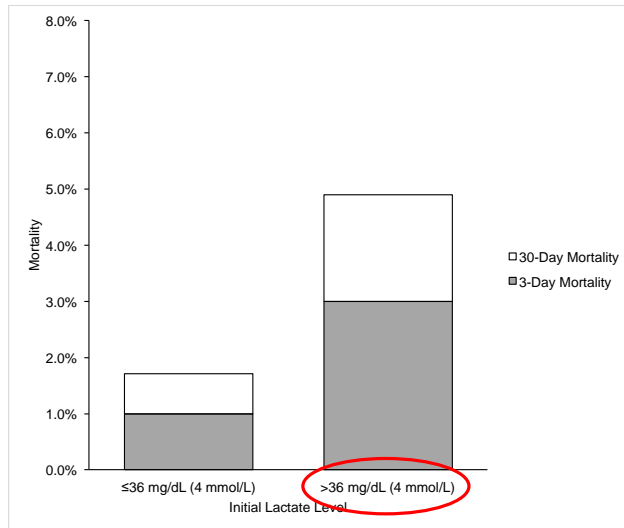


Schlapbach ICM 2017



34

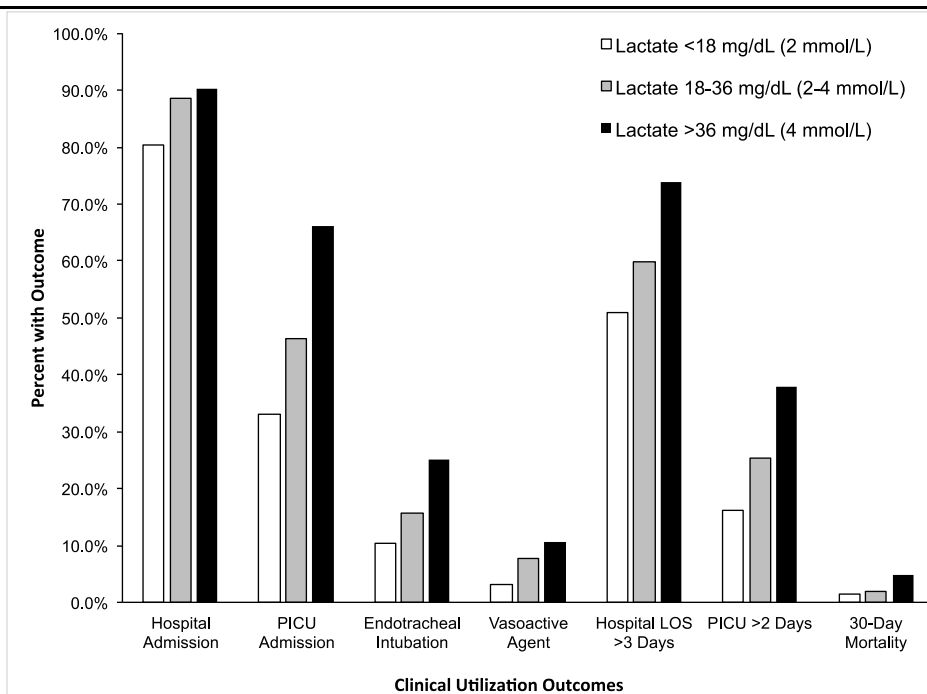
Lactate ≥ 4 mmol/L 30-Day Mortality RR= 2.90 [1.11-7.57]



Scott JAMA Peds 2017



35



Scott JAMA Peds 2017



36

Case – Critical Access ED - waiting for transport

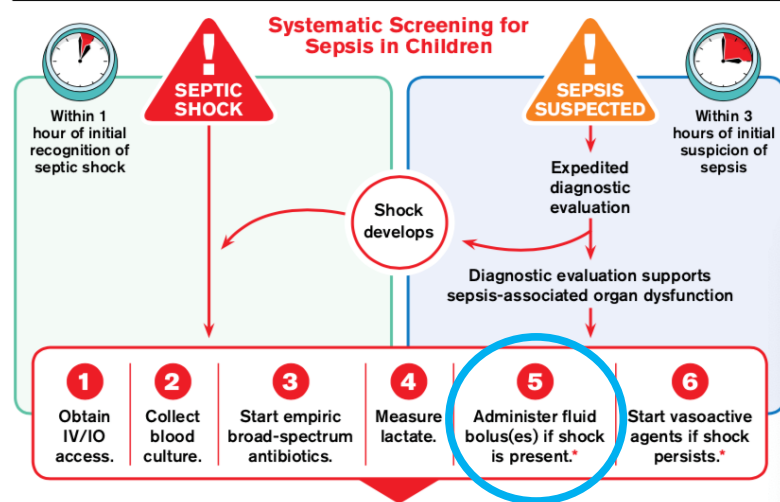
- HR: 160s BP: 73/37
- Na: 123, Cl: 90, Cr: 0.81
- Lactate 2.6
- Ceftriaxone and Vancomycin ordered and given
- Now 40 mL/kg crystalloid total given
- HR:158 BP: 80/40 RR: 22 Pulse Ox 91% RA
- Alert, oriented, moaning about pain in arm
- Capillary refill 3 seconds



37

Initial Resuscitation Algorithm for Children

Surviving Sepsis Campaign



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

38

Fluid Therapy

1. In health care systems with availability of intensive care, we suggest administering up to 40–60 mL/kg in bolus fluid (10–20 mL/kg per bolus) over the first hour, titrated to clinical markers of cardiac output and discontinued if signs of fluid overload develop, for the initial resuscitation of children with septic shock or other sepsis-associated organ dysfunction (weak recommendation, low quality of evidence).

Remarks: Clinical markers of cardiac output may include heart rate, blood pressure, capillary refill time, level of consciousness, and urine output. In all settings, the need for fluid administration should be guided by frequent reassessment of clinical markers of cardiac output, serial blood lactate measurement, and advanced monitoring, when available. Signs of fluid overload that should limit further fluid bolus therapy may include clinical signs of pulmonary edema or new or worsening hepatomegaly.



Weiss PCCM 2020

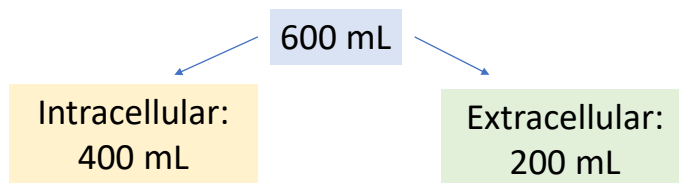


39

Physiologically, 60 mL/kg (sort of) makes sense

60% of human mass is water (70% in infants)

Per kg: 600-700 mL is water

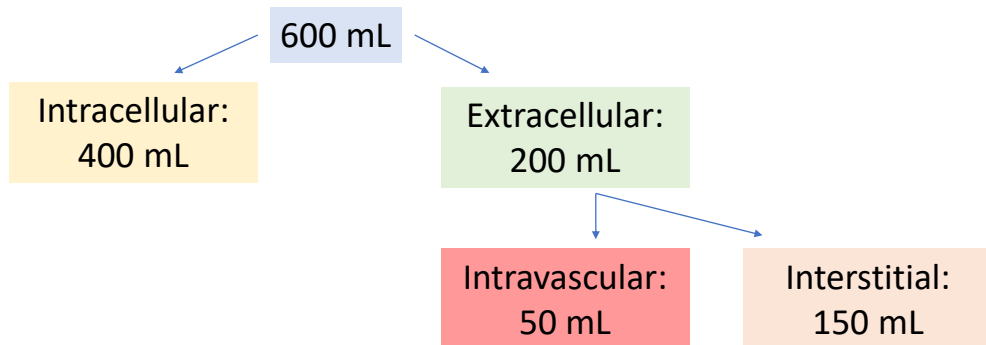


40

Physiologically, it makes sense

60% of human mass is water (70% in infants)

Per kg: 600-700 mL is water

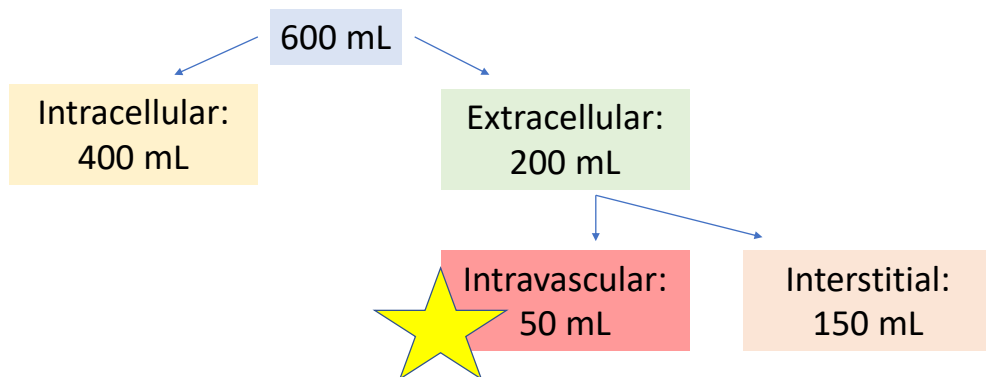


41

Physiologically, it makes sense

60% of human mass is water (70% in infants)

Per kg: 600-700 mL is water

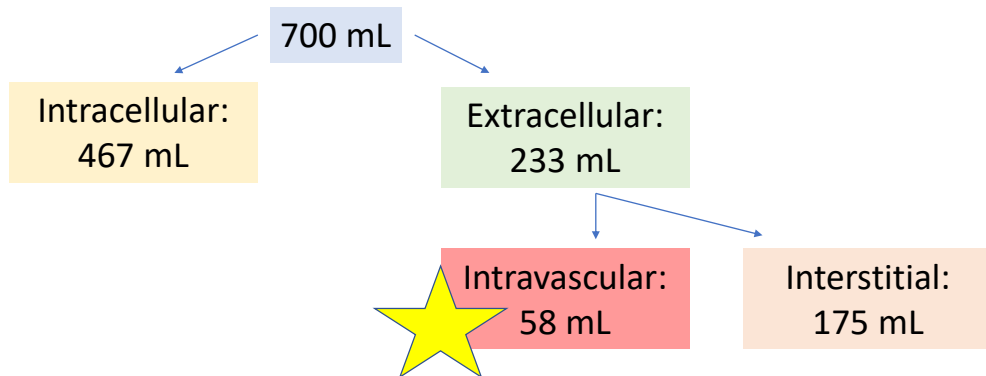


42

Physiologically, it makes sense

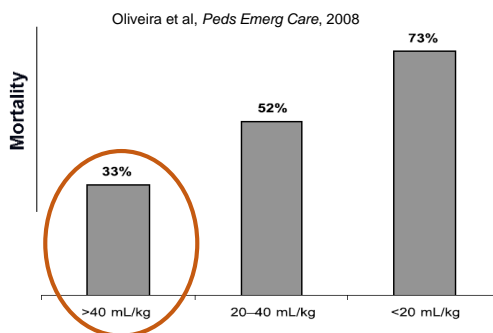
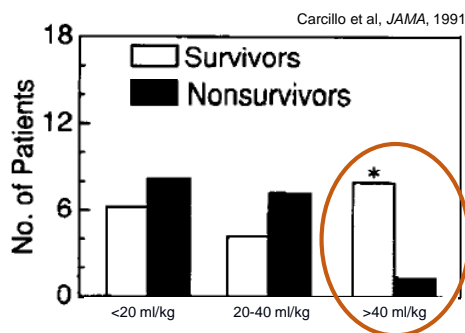
60% of human mass is water (70% in infants)

Per kg: 600-700 mL is water



43

Improved outcomes with higher volumes



44

Physiologically, it DOES NOT make sense



45

Cardiogenic

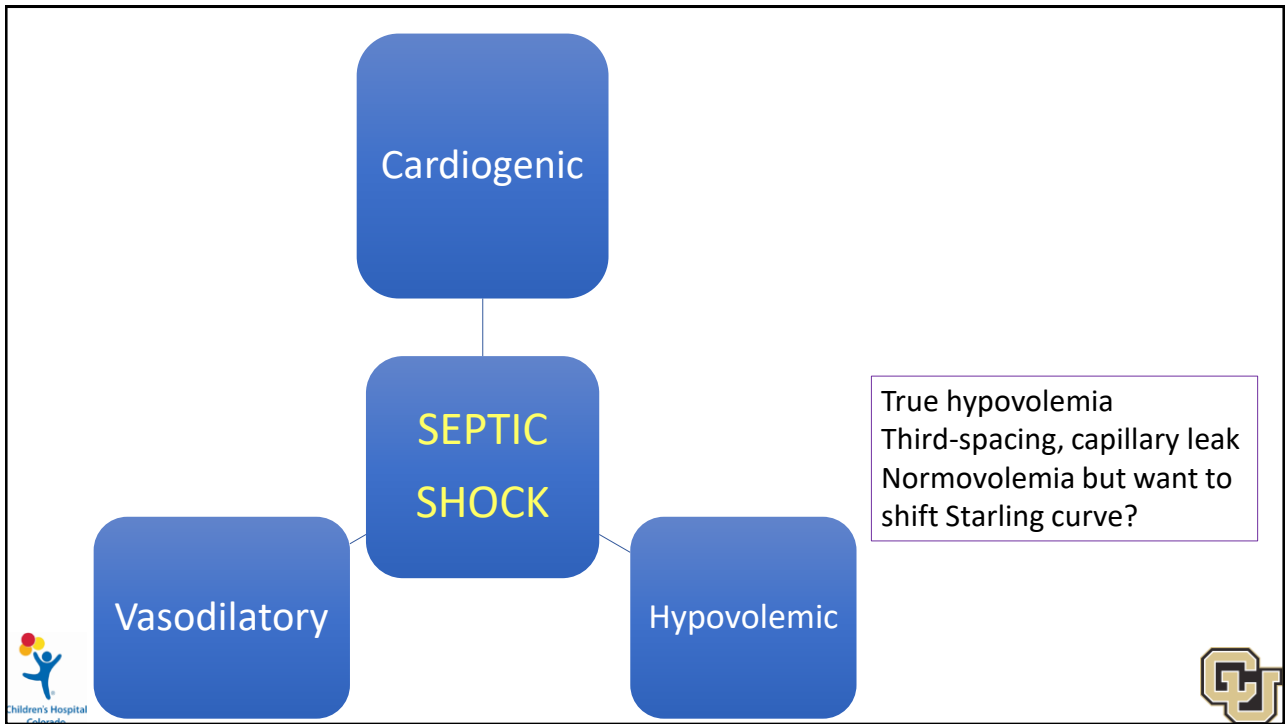
SEPTIC
SHOCK

Vasodilatory

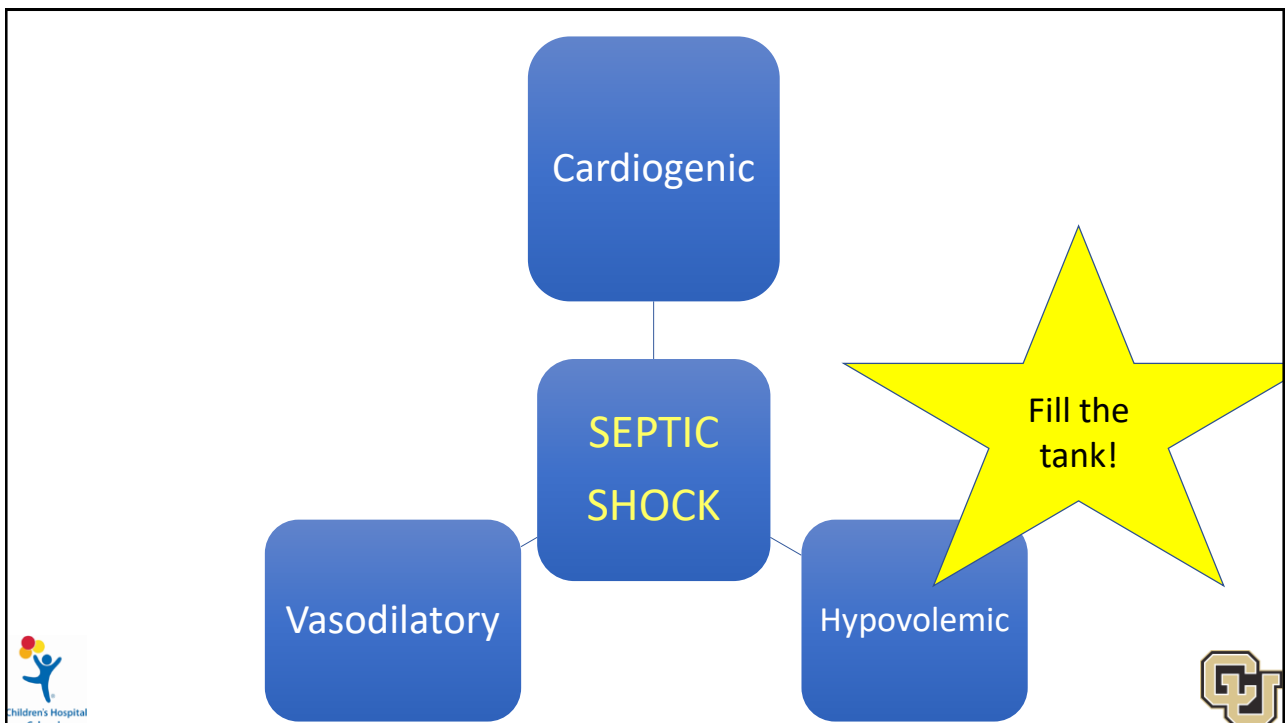
Hypovolemic



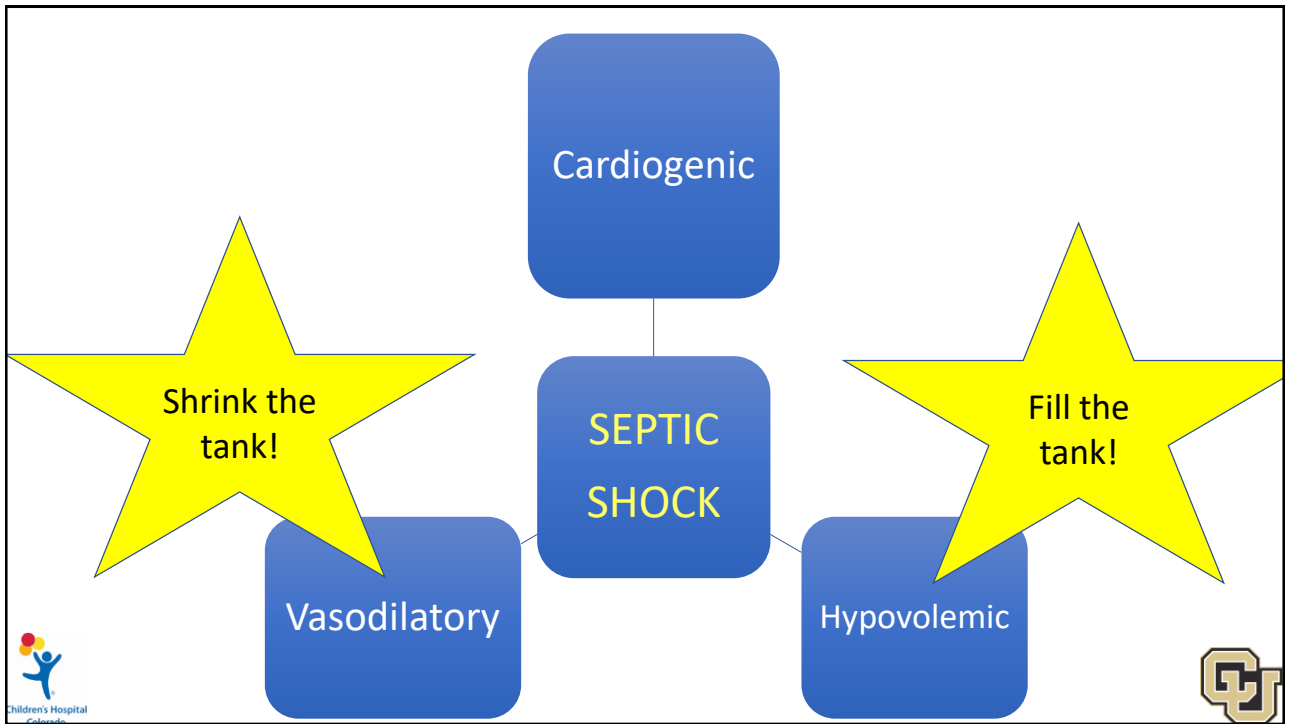
46



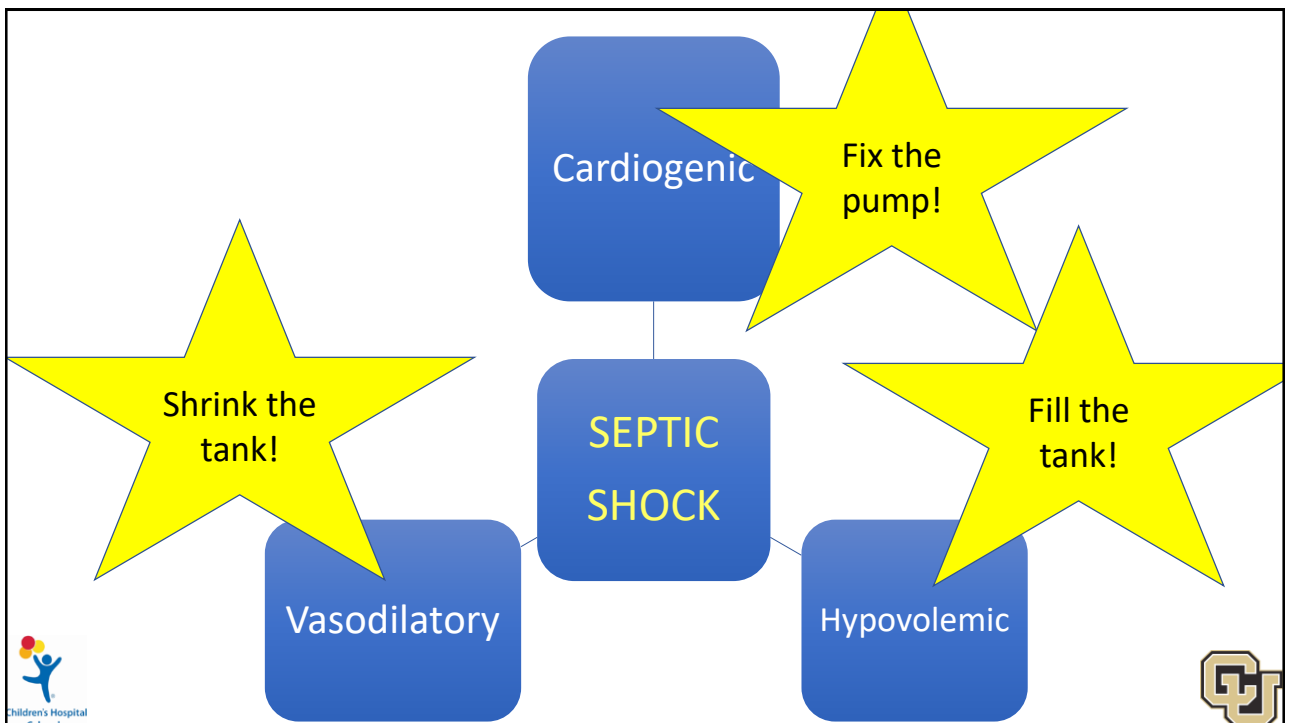
47



48



49



50



[Home](#) [Locations](#) [Public study information](#) [Bibliography](#) [Contact](#)

[Clinicians & Research](#)

A Trial to Determine Whether Septic Shock Reversal is Quicker in Pediatric Patients Randomized to an EGD Fluid-Sparing Strategy vs. Usual Care

Melissa Parker, McMaster University

Usual care (no vasoactives until after 60 mL/kg)

Vs. Vasopressor with 5-10 mL boluses

(After 1-3 L) Vasopressors first vs. fluid first in adult hypotensive septic shock

N: 2320 planned

3/7/2018 – projected 6/2021



52

So what am I supposed to give my patient?



53

PALS Fluid Recommendations

Administration of an initial fluid bolus... in shock is reasonable (Class IIa, LOE C-LD)

When caring for children with severe febrile illness in settings with limited access to critical care resources... administration of bolus intravenous fluids should be undertaken with extreme caution (Class IIb, LOE B-R)

Fluid not safe for all patients in all settings

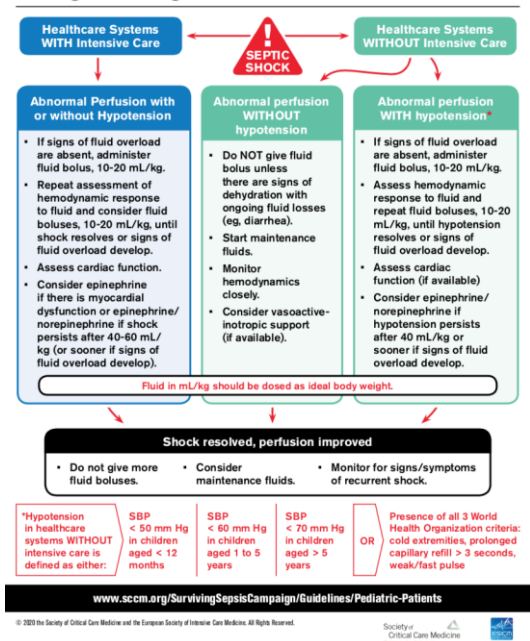
- e.g. shouldn't have 'standing orders'

Increased emphasis on

- Individual patient assessment and reassessment
- Consideration of vulnerabilities to fluid
 - Nutrition status
 - Diseases (i.e. anemia, malaria)
 - Critical care resources

Fluid and Vasoactive-Inotrope Management Algorithm For Children

Surviving Sepsis Campaign



de Caen *Circulation* 2015

54

Case – waiting for transport

Ceftriaxone and Vancomycin ordered and given

Now 40 mL/kg crystalloid given

HR:158

BP: 80/40

RR: 22

Pulse Ox 91% RA

Alert, oriented, moaning about pain in arm

Capillary refill 3 seconds

An additional 20 mL/kg crystalloid given (60 mL/kg total)

HR 150

BP: 82/37

Repeat lactate: 1.8 mmol/L

Transport arrives



55

Case - Transport

HR 154 BP: 78/37 Pox=89% RA → 95% with 2L NC

Alert, capillary refill 3 seconds

Started on norepinephrine via antecubital PIV

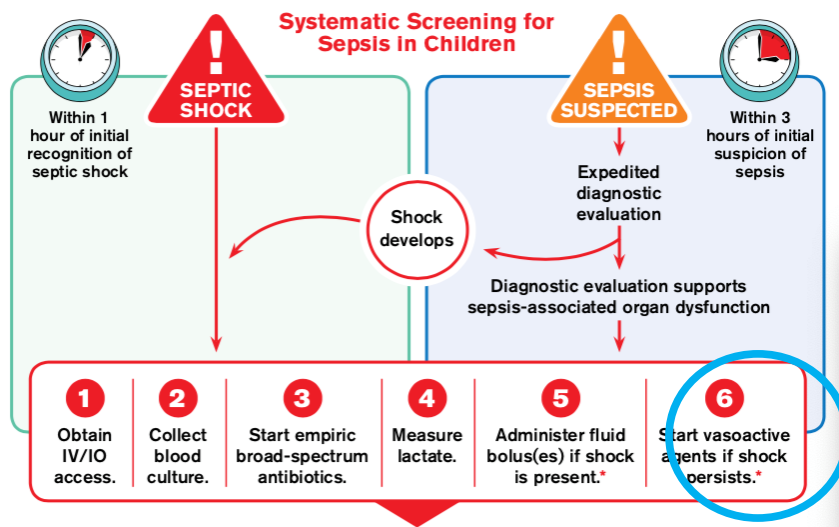
HR: 150 BP: 90/45



56

Initial Resuscitation Algorithm for Children

Surviving Sepsis Campaign



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

57

Hemodynamic Monitoring

25. We suggest not using bedside clinical signs in isolation to categorize septic shock in children as “warm” or “cold” (weak recommendation, very low quality of evidence)
26. We suggest using advanced hemodynamic variables, when available, in addition to bedside clinical variables to guide the resuscitation of children with septic shock or other sepsis-associated organ dysfunction (weak recommendation, low quality of evidence)
Remarks: Advanced hemodynamic monitoring may include cardiac output/cardiac index, systemic vascular resistance, or central venous oxygen saturation.
27. We suggest using trends in blood lactate levels, in addition to clinical assessment, to guide resuscitation of children with septic shock and other sepsis-associated organ dysfunction (weak recommendation, very low quality of evidence)



Weiss PCCM 2020



58

Warm Shock, Cold Shock: Assessing the Hemodynamics of Sepsis



Cold shock
Vasoconstricted
Low Cardiac Output

Warm shock
Vasodilated
High Cardiac Output



59

Hemodynamics of Pediatric Shock

Ceneviva, 1998: 50 PICU septic shock with PA catheters

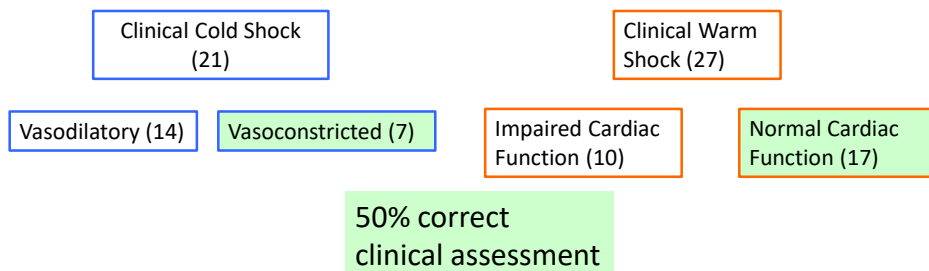
	Percent	CI	SVR	Mortality
Cold	58%	Low	High	28%
Warm	20%	High	Low	10%
Mixed	22%	Low	Low	9%

Brierley, 2008: 30 PICU fluid-refractory septic shock, USCOM device

- Central line patients “warm shock”
- Community-acquired “cold shock”



60



Ranjit PCCM 2014

61

Serial Lactate Measurement

Lactate Clearance:

Decrease by $\geq 10\%$, or < 2 mmol/L if initial level < 2 mmol/L

Lactate Normalization:

Lactate < 2 mmol/L

Is Lactate Normalization/Clearance associated with decreased rates of prolonged acute organ dysfunction (> 48 hours)?

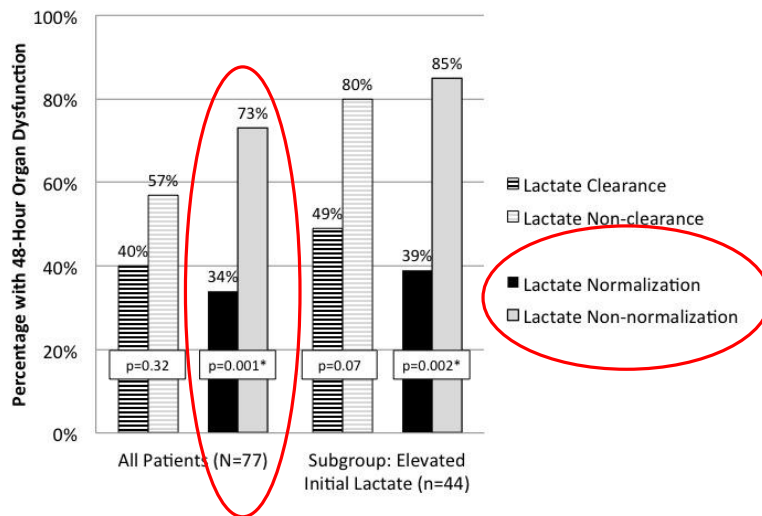
77 children with acute organ dysfunction and infection in the ED with lactate measured



Scott JPeds 2015



62



Scott JPeds 2015



63

Vasoactive Medications

28. We suggest using epinephrine, rather than dopamine, in children with septic shock (weak recommendation, low quality of evidence)
29. We suggest using norepinephrine, rather than dopamine, in children with septic shock (weak recommendation, very low quality of evidence)
30. We were unable to issue a recommendation for a specific first-line vasoactive infusion for children with septic shock
31. We were unable to issue a recommendation about initiating vasoactive agents through peripheral access in children with septic shock.

Remarks: It is reasonable to begin vasoactive infusions after 40–60 mL/kg of fluid resuscitation if the patient continues to have evidence of abnormal perfusion. Either epinephrine or norepinephrine may be administered through a peripheral vein (or intraosseous, if in place) if central venous access is not readily accessible. Dopamine may be substituted as the first-line vasoactive infusion, administered either peripherally or centrally, if epinephrine or norepinephrine is not readily available.



64

First-Line Vasoactive Agents (an ER guide)

	Inotropy	Systemic Vascular Resistance	BP	Use in Sepsis?
Norepinephrine (alpha > beta)	+	+++	↑	Most patients Premixed at all CHCO sites, more familiar in general ED's
Epinephrine (beta > alpha)	+++	+	↑	Younger Community-acquired gram positive Significant cardiogenic component
Dopamine (5-10 mcg/kg/min) Beta>alpha, dopa	++	++	↑	If desperate Problems: 'dirty drug' (variable effects at different doses), arrhythmogenic, HPA/immune effects (decreases GH, prolactin)
Vasopressin, milrinone, dobutamine... potentially useful, most sepsis should be in ICU by then...				



65

First-Line Vasoactive Agents (an ER guide)

	Inotropy	Systemic Vascular Resistance	BP	Use in Sepsis?
Norepinephrine (alpha)				
Epinephrine (beta)				
Dopamine (beta)				
Beta>alpha, dopa				different doses), arrhythmogenic, HPA/immune effects (decreases GH, prolactin)
Vasopressin, milrinone, dobutamine... potentially useful, most sepsis should be in ICU by then...				

Fix hypotension

Don't make a dosing error



66

Case – Arrival at Tertiary Hospital

HR 150 BP: 90/45 Pox= 95% with 2L NC

On norepinephrine via antecubital PIV

Alert, crying.

L shoulder decreased ROM, edema, redness. No crepitus. L third digit with crusted skin over PIP. Foot erythematous, red. L hand erythematous.



67

Case – Hospital Course

To ICU:

Clinda given, IVIG x 2 (suspected toxin-mediated illness)

To OR for I&D - grew Group A Strep from murky synovial fluid, frank pus subdeltoid: pyomyositis, septic joint osteomyelitis

Multiple organ dysfunction

- Transaminases elevated, AKI – both resolved
- Norepi x 3 days
- Intubated x 2 days post op
- DIC/thrombocytopenia, transfused x 1

Rehab, discharged home



68

Pediatric Sepsis

- Mortality: 7.5-25%
- Among survivors, 35% had not returned to baseline QOL by 1 year
- 5/1000 pediatric hospitalizations
- 8% prevalence in PICUs worldwide
- >75,000 pediatric US cases yearly



Hartman I2013; Balamuth PCCM 2014; Weiss AJRCCM 2015;
Weiss CCM 2020; Zimmerman CCM 2020



69

Standardized, Expedited Processes Save Lives in Pediatric Sepsis

Protocolized Treatment Is Associated With Decreased Organ Dysfunction in Pediatric Severe Sepsis*

Fran Balamuth, MD, PhD, MSCE^{1,2}; Scott L. Weiss, MD, MSCE^{3,4}; Julie C. Fitzgerald, MD, PhD^{3,4};

Katie Hayes, BSc

Jane Lavelle, MSc

Resuscitation Bundle in Pediatric Shock Decreases Acute Kidney Injury and Improves Outcomes

Ayşe Akcan Arikan, MD^{1,2}; Eric A. Williams, MD, MS¹; Jeanine M. Graf, MD¹; Curtis E. Kennedy, MD, PhD¹; Binita Patel, MD³; and Andrea T. Cruz, MD, MPH^{3,4}

Managing Diagnostic Uncertainty in Pediatric Sepsis Quality Improvement with a Two-Tiered Approach

Halden F. Scott, MD, MSCS^{*†}; Allison Kempe, MD, MPH^{*‡}; Sara J. Deakyne Davies, MPH[§]; Paige Krack, MBA, MS[¶]; Jan Leonard, MSPH^{*†}; Elise Rolison, RRT-NPS[¶]; Joan Mackenzie, MS, CPNP[†]; Beth Wathen, MSN, PNP^{||}; Lalit Bajaj, MD^{*†¶}

High Reliability Pediatric Septic Shock Quality Improvement Initiative and Decreasing Mortality

Roni D. Lane, MD,^a Tomohiko Funai, MS,^b Ron Reeder, PhD,^b Gitte Y. Larsen, MD, MPH^b



71

The Bundle is Greater than the Sum of its Parts

JAMA | Original Investigation

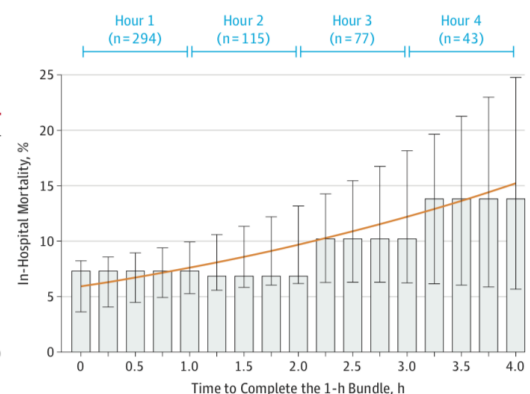
Association Between the New York Sepsis Care Mandate and In-Hospital Mortality for Pediatric Sepsis

Idris V. R. Evans, MD, MSc; Gary S. Phillips, MAS; Elizabeth R. Alpern, MD, MSCE; Derek C. Angus, MD, MPH; Marcus E. Friedrich, MD; Niranjana Kisson, MD; Stanley Lemeshow, PhD; Mitchell M. Levy, MD; Margaret M. Parker, MD; Kathleen M. Terry, PhD; R. Scott Watson, MD, MPH; Scott L. Weiss, MD, MSCE; Jerry Zimmerman, MD, PhD; Christopher W. Seymour, MD, MSc

Figure 2. Risk-Adjusted Odds Ratios of In-Hospital Death in the Primary Models

Model	Total Deaths/Total No. (%)		Risk-Adjusted In-Hospital Mortality, % (95% CI)		Risk Difference From Adjusted Model, % (95% CI)	Adjusted Odds Ratio for In-Hospital Mortality (95% CI)	In-Hospital Death Less Likely	In-Hospital Death More Likely
	Completed Within 1 h	Not Completed Within 1 h	Completed Within 1 h	Not Completed Within 1 h				
Completion of the entire 1-h bundle within 1 h	22/294 (7.5)	17/885 (1.9)	8.7 (5.4-12.0)	12.7 (10.5-14.7)	4.0 (0.9 to 7.0)	0.59 (0.38-0.93)	■	■
Antibiotics administered within 1 h	89/798 (11.2)	50/381 (13.1)	11.1 (9.1-13.1)	13.2 (9.7-16.6)	2.1 (-1.1 to 5.2)	0.78 (0.55-1.12)	■	■
Blood cultures prior to antibiotics completed within 1 h	71/740 (9.6)	68/439 (15.5)	10.7 (8.3-13.0)	13.3 (10.5-16.0)	2.6 (-0.5 to 5.7)	0.73 (0.51-1.06)	■	■
Intravenous fluid bolus completed within 1 h	59/548 (10.8)	80/631 (12.7)	11.2 (8.3-14.1)	12.3 (9.6-15.0)	1.1 (-2.6 to 4.8)	0.88 (0.56-1.37)	■	■

Figure 3. Crude In-Hospital Mortality and Predicted Risk of In-Hospital Death After the Time of Sepsis Protocol Initiation



72



Managing Diagnostic Uncertainty in Pediatric Sepsis Quality Improvement with a Two-Tiered Approach

Halden F. Scott, MD, MSCS*†; Allison Kempe, MD, MPH*‡; Sara J. Deakynne Davies, MPH§; Paige Krack, MBA, MS¶; Jan Leonard, MSPH*†; Elise Rolison, RRT-NPS¶; Joan Mackenzie, MS, CPNP†; Beth Wathen, MSN, PNP||; Lalit Bajaj, MD*†¶

1. High-quality, timely critical care to severe sepsis

Sepsis STAT Criteria: Fever/suspected infection and any of the following:

- Hypotension
- Altered mentation
- New need for positive pressure ventilation
- Lactate greater or equal to 4 mmol/L
- Acute kidney injury
- New coagulopathy
- New liver dysfunction
- Acute need for resuscitation room

In indeterminate patients

1. Expedite early evaluation and necessary treatment

2. Allow flexibility, promote stewardship

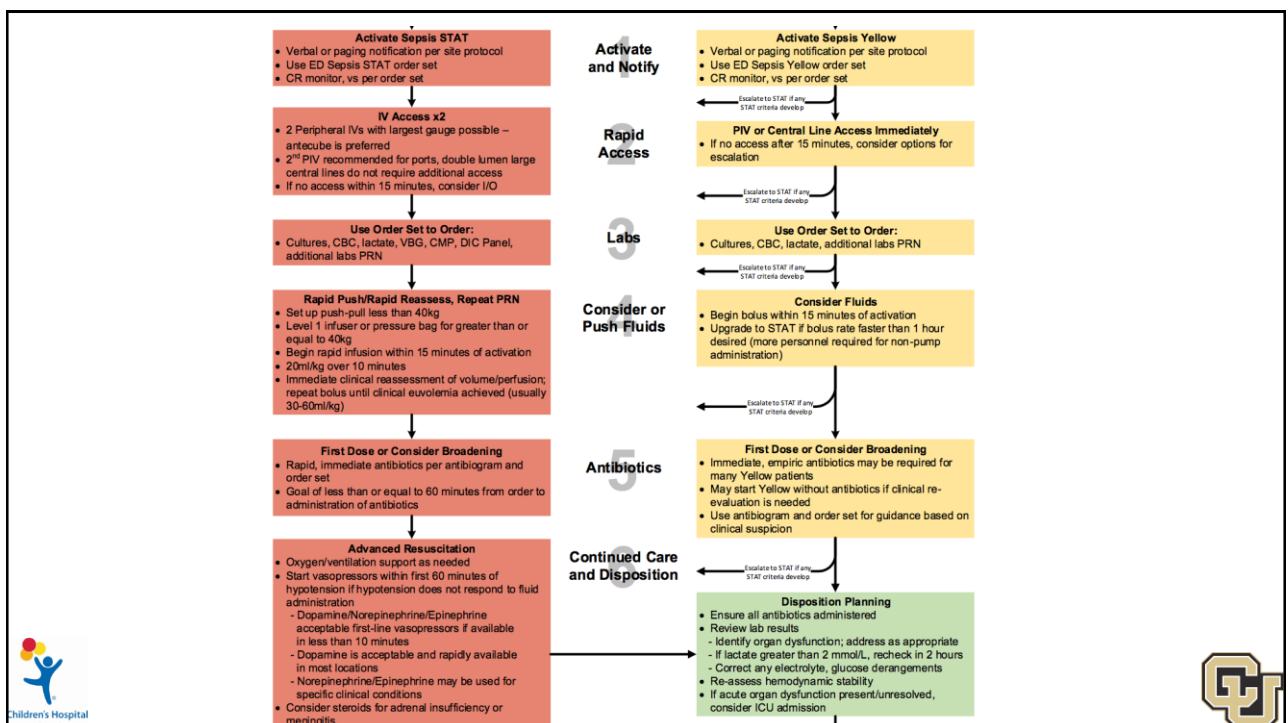
Sepsis Yellow Criteria: Fever/suspected infection and any of the following:

- Immunosuppression/immunocompromise (e.g. oncology patients, organ transplant patients, patients on immunomodulators)
- Central venous catheter
- Clinically concerning symptoms: changes to capillary refill, peripheral pulse quality, concerning rashes, orthostasis

Children's Hospital
Colorado



73



Children's Hospital
Colorado



74

IS THIS SEPSIS? WEIGHT: _____ kg

ACTIVATION/ START TIME:

SAY SEPSIS

GOAL: 10 MIN.

RAPID ACCESS TIME:

GOAL: 15 MIN.

USE ORDER SET

IVP TIME:

GOAL: 30 MIN.

ANTIBIOTIC TIME:

GOAL: 60 MIN.

HYPOTENSION START TIME:

DO NOT TOLERATE HYPOTENSION

HYPOTENSION END TIME:

DETERMINE AS EARLY AS POSSIBLE

Recognition/Suspicion

☐ Ask, "Is this sepsis?"

☐ Say sepsis

Shared mental model is key

Activate and Notify

☐ ED sepsis yellow page ☐ ED sepsis yellow order set

☐ ED sepsis STAT page ☐ ED sepsis STAT order set

☐ Update to STAT if organ dysfunction, AMS, hypotension

NOG: ☐ Early disposition/transport

Urgent Access

Use ED/ICU urgent access algorithm

☐ PIV ☐ Access central line

☐ Ultrasound guided ☐ IO

☐ External jugular ☐ Call for additional resources

☐ Page sepsis STAT for resource RN help

Labs/Imaging

☐ CBC w/ ☐ DIC Panel w/

☐ CMP w/ ☐ Cultures (blood, urine, CSF, etc.)

☐ Lactate w/ ☐ CXR

☐ VBG/STAT

Fluids As Clinically-Indicated

Bolus volume = _____ mL

Type: ☐ Lactated ringers bolus ☐ Normal saline bolus

Mode of delivery: ☐ Push/pull/L, U/L flow ☐ Pressure bag ☐ Pump ☐ Bagged infusion

Reassess hemodynamics after each bolus to determine if more fluid or vasopressors are needed

Antibiotics (Give as soon as available)

<input type="checkbox"/> Gram Negative	<input type="checkbox"/> Gram Positive	<input type="checkbox"/> Anaerobes	<input type="checkbox"/> Debridement
<input type="checkbox"/> Ceftriaxone	<input type="checkbox"/> Vancomycin	<input type="checkbox"/> Metronidazole	<input type="checkbox"/> IM Ceftriaxone
<input type="checkbox"/> Cefepime	<input type="checkbox"/> Linezolid	<input type="checkbox"/> Teicoplanin	<input type="checkbox"/> IM Cefepime
<input type="checkbox"/> Levofloxacin	<input type="checkbox"/> Clindamycin		

Do not use ceftriaxone with Lactate-ringers in the same line at the same time

Vasopressors

☐ Norepinephrine

☐ Epinephrine

☐ Dopamine

Start pressors within 60 minutes if hypotension still present

Disposition/Follow-Up

☐ Review lab results

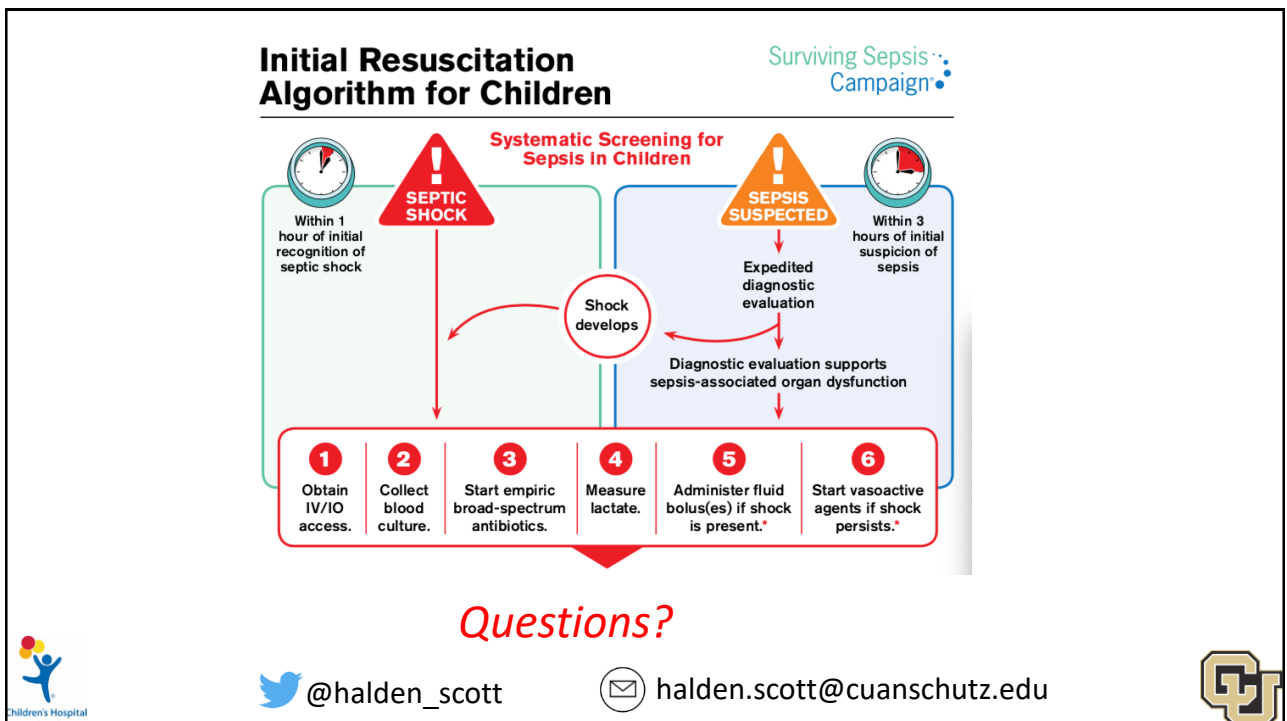
☐ Repeat lactate if > 2 mmol/L

☐ Hydration/urine output necessary?

☐ Call receiving provider with sepsis care summary

☐ Team feedback

75



76