Defining Pediatric Sepsis: Saving Lives With Early Recognition

A WEBINAR PRESENTED ON OCTOBER 4, 2023

acdis Association of Clinical Documentation Integrity Specialists

hcpro

Presented By

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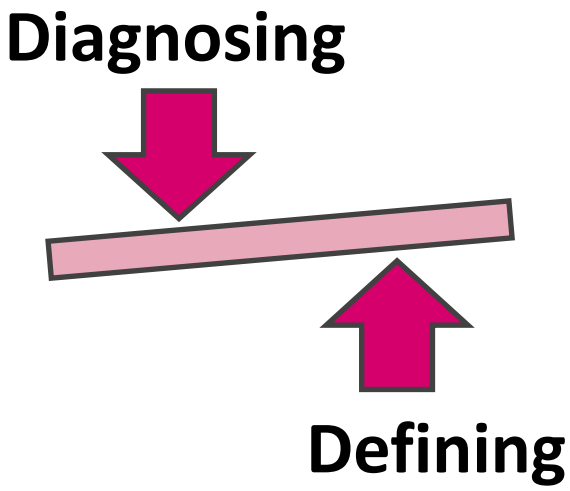
Amy Sanderson, MD, is a pediatric intensivist at Boston Children’s Hospital (BCH) and is an assistant professor in anaesthesia at Harvard Medical School. She was the physician advisor for the BCH CDI program for eight years. Sanderson has presented at several national conferences, has published scholarly articles on medical documentation, and contributed to the book *Pediatric CDI: Building Blocks for Success*. In addition, she is a founding member of the Pediatric Documentation Research Collaborative, a research group that focuses on documentation-related issues in pediatric hospitals.

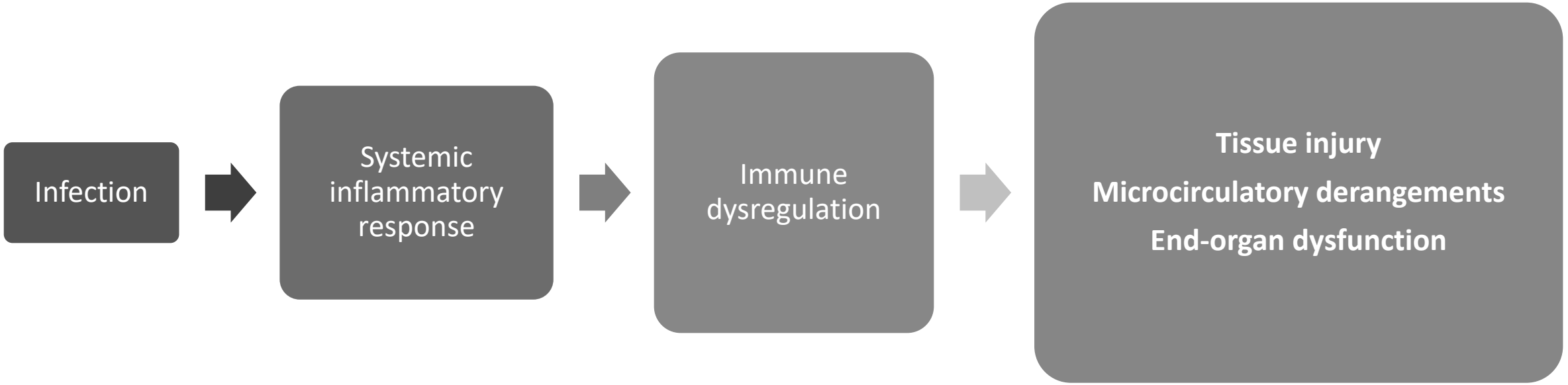
Learning Outcomes

- At the completion of this educational activity, the learner will be able to:
  - Describe the contemporary guidelines for pediatric sepsis
  - List the differences between pediatric sepsis and adult sepsis
  - Examine the impact of early recognition on outcomes
  - Identify common payer denials for pediatric sepsis



Defining and Diagnosing Pediatric Sepsis

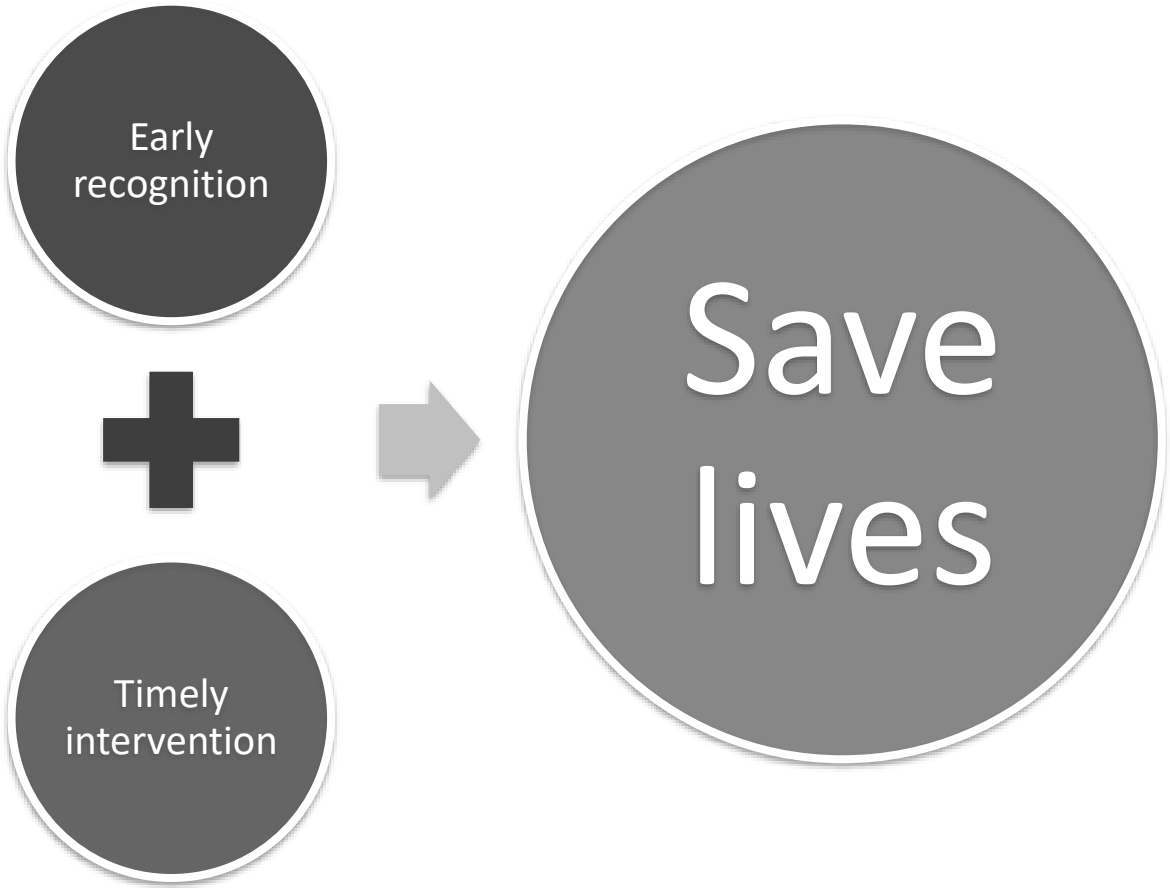
Continuum:
SIRS → Sepsis → Severe Sepsis / Septic Shock



Evolution of Definitions of Sepsis, Severe Sepsis, and Septic Shock			
	Sepsis-3 (2016)	**Sepsis-2 (2001)**	**Sepsis-1 (1991)**
Sepsis	Infection + Organ dysfunction (SOFA)	≥ 2 SIRS + infection	≥ 2 SIRS + infection
Severe Sepsis	----------	Sepsis + Organ dysfunction	Sepsis + Organ dysfunction
Septic Shock	Sepsis + Hypotension with vasopressors + Lactate ≥ 2	Severe sepsis + Refractory hypotension	Severe sepsis + Refractory hypotension

Diagnosing Sepsis in Children

- **Sick children are challenging**
  - Febrile illnesses happen ALL.THE.TIME.
  - Poor specificity of features – variable clinical signs
  - May have delayed development of clinical signs
  - Compensate until advanced stages of shock
- **Children get sick rapidly…but also tend to improve rapidly**



Defining Sepsis: Adults vs Children

ADULTS

- Sepsis-3: Adult sepsis definition corresponds to the pediatric definition of severe sepsis
- Organ dysfunction in adults is based upon the SOFA score
  - SIRS criteria no longer included in the definition
- Adult definition for septic shock includes vasopressors and hyperlactatemia

CHILDREN

- 2005 International Consensus: SIRS + infection
- Studies support using a stratified scoring system for organ dysfunction over SIRS criteria in children
  - Efforts to update the definition and clinical criteria for pediatric sepsis are underway
- No *modern* generalized consensus on scoring system to use for pediatric organ dysfunction

Pediatric Vital Signs

Table 3. Age-specific vital signs and laboratory variables (lower values for heart rate, leukocyte count, and systolic blood pressure are for the 5th and upper values for heart rate, respiration rate, or leukocyte count for the 95th percentile)

Age Group[a]	Heart Rate, Beats/Min[b,c]		Respiratory Rate, Breaths/Min[d]	Leukocyte Count, Leukocytes × 10^3/mm^3[b,c]	Systolic Blood Pressure, mm Hg[b,c,e,f]
	Tachycardia	Bradycardia			
0 days to 1 wk	>180	<100	>50	>34	<65
1 wk to 1 mo	>180	<100	>40	>19.5 or <5	<75
1 mo to 1 yr	>180	<90	>34	>17.5 or <5	<100
2–5 yrs	>140	NA	>22	>15.5 or <6	<94
6–12 yrs	>130	NA	>18	>13.5 or <4.5	<105
13 to <18 yrs	>110	NA	>14	>11 or <4.5	<117

NA, not applicable.
[a]Modified from Ref. 24; [b]modified from Ref. 25; [c]modified from Ref. 22; [d]modified from Ref. 55; [e]Ref. 26; [f]Ref. 56.

Goldstein, et al. International pediatric sepsis consensus conference: Definitions for sepsis and organ dysfunction in pediatrics. Pediatr Crit Care Med 2005 Vol. 6, No. 1

Defining Pediatric Sepsis: 2005 Consensus

Review > Pediatr Crit Care Med. 2005 Jan;6(1):2-8. doi: 10.1097/01.PCC.0000149131.72248.E6.

International pediatric sepsis consensus conference: definitions for sepsis and organ dysfunction in pediatrics

Brahm Goldstein [1], Brett Giroir, Adrienne Randolph; International Consensus Conference on Pediatric Sepsis

Affiliations + expand

PMID: 15636651 DOI: 10.1097/01.PCC.0000149131.72248.E6

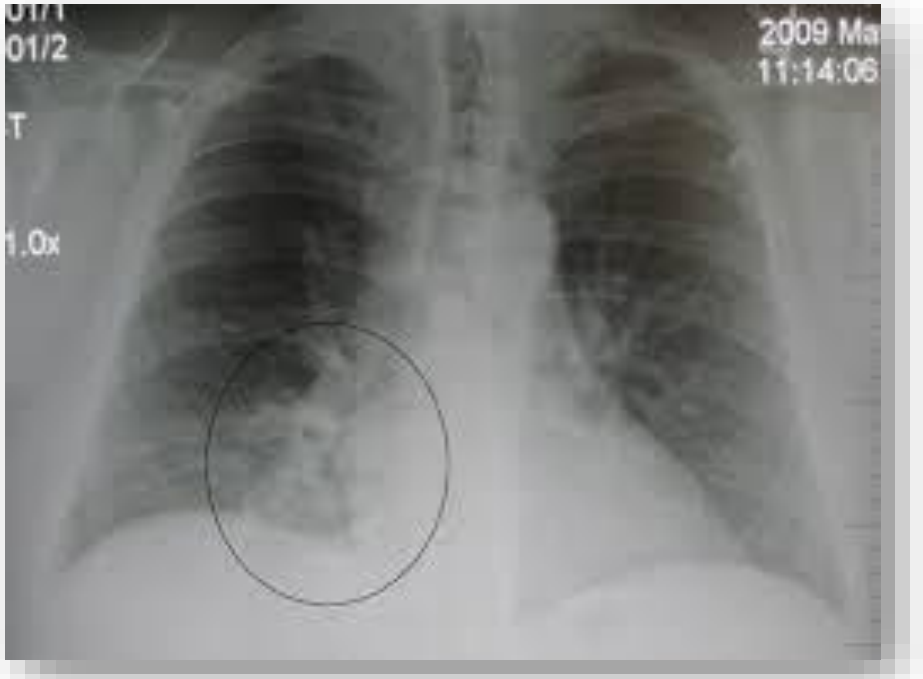
Pediatric Sepsis Consensus (2005)	
SIRS	See next slide!
Sepsis	SIRS + Infection
Severe Sepsis	Sepsis + Organ dysfunction
Septic Shock	Sepsis + Cardiovascular organ dysfunction

SIRS in Children

SIRS Criteria for Children	
Mandatory:	Core temperature of >38.5°C or <36°C **or** WBC ↑ or ↓ for age, or >10% immature neutrophils
Plus at least one of the following:	Tachycardia (HR > 2 SD above normal for age)
	For children < 1 y/o: bradycardia (HR <10th percentile for age)
	RR > 2 SD above normal for age
	Mechanical ventilation

Infection

- Proven infection caused by any pathogen
  - Positive culture
  - Tissue stain
  - Other diagnostic test
- Suspected infection
  - **“Clinical diagnosis”:** Clinical syndromes associated with high probability of infection



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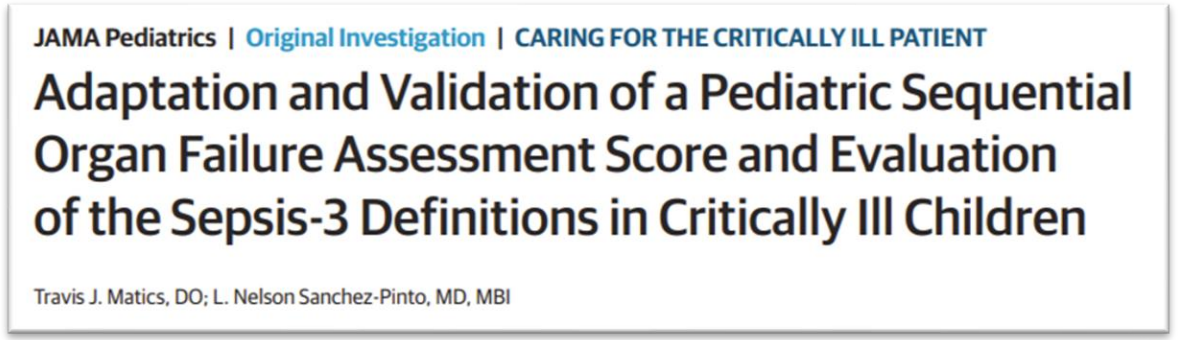
Pathogens

Culture-negative sepsis:

30-75% have no infectious etiology identified

Bacteria	Viruses	Fungi	Other
• Staph • Strep • Pseudomonas • E. Coli • Enterococcus • Klebsiella	• Respiratory • EBV • CMV • HSV • COVID	• Aspergillus • Candida • Cryptococcus • Pneumocystis • Mucormycetes	• Parasitic • Rickettsial

Organ Dysfunction in Sepsis



- Organ dysfunction scoring systems
  - MODS, LODS, and SOFA
- Scoring systems were originally created for research purposes and predicting mortality
- ***Not necessarily intended to be used as clinical criteria***
- Limitations of SOFA scoring in pediatric patients
  - Age-related variability in some measures [vital signs, creatinine]
  - ABGs are not used frequently
- Pediatric SOFA (pSOFA)
  - Validated in retrospective studies, not necessarily (yet) validated in prospective studies

Major Organ System Dysfunction in Sepsis

Hypotension
Hypoperfusion
Tachycardia
Abnormal echocardiography

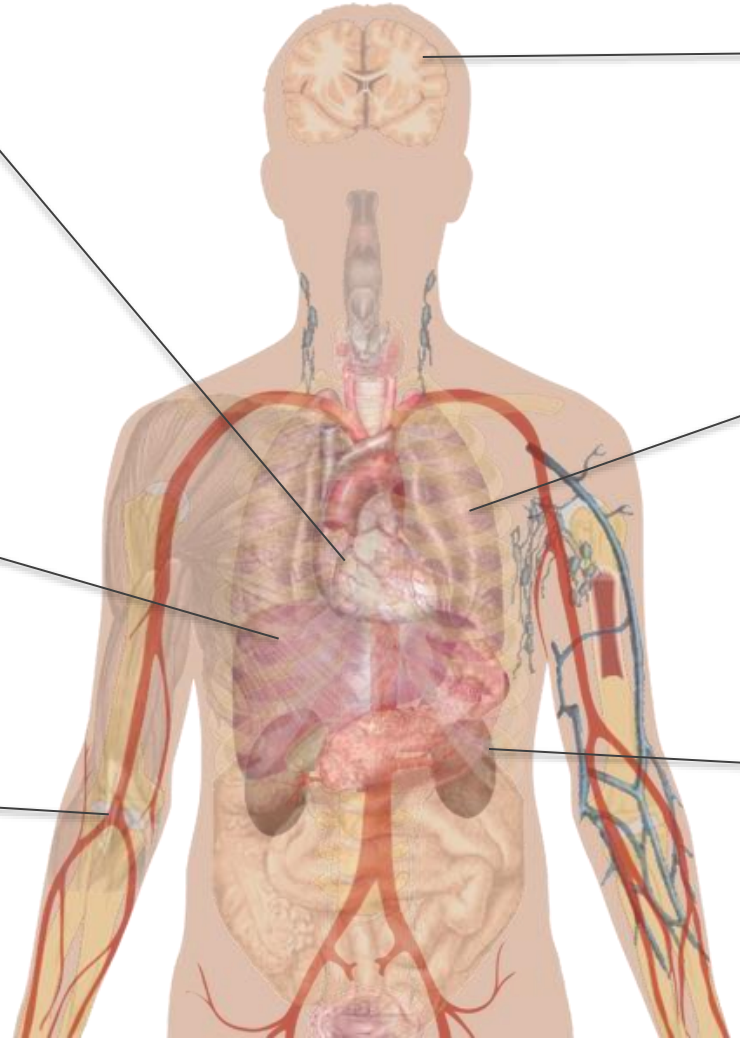
Encephalopathy
Altered consciousness
Decreased GCS
Hypotonia

Respiratory failure
Hypoxemia, hypercarbia
Decreased PaO2 (or SpO2) : FiO2

Elevated transaminases
Elevated bilirubin

DIC
Thrombocytopenia
Petechiae, purpura

Oliguria
Hypertension (renal)
Elevated creatinine
Elevated BUN



https://commons.wikimedia.org/wiki/File:Adult_male_with_organs.png

SOFA vs pSOFA

Pulse oximetry

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

System	Score 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.

Age-related variability

Table 1. Pediatric Sequential Organ Failure Assessment Score

Variables	Score[a] 0	1	2	3	4
Respiratory					
$Pao_2:Fio_2$[b] or $Spo_2:Fio_2$[c]	≥400 / ≥292	300-399 / 264-291	200-299 / 221-264	100-199 With respiratory support / 148-220 With respiratory support	<100 With respiratory support / <148 With respiratory support
Coagulation					
Platelet count, $\times 10^3/\mu L$	≥150	100-149	50-99	20-49	<20
Hepatic					
Bilirubin, mg/dL	<1.2	1.2-1.9	2.0-5.9	6.0-11.9	>12.0
Cardiovascular					
MAP by age group or vasoactive infusion, mm Hg or μg/kg/min[d]					
<1 mo	≥46	<46	Dopamine hydrochloride ≤5 or dobutamine hydrochloride (any)	Dopamine hydrochloride >5 or epinephrine ≤0.1 or norepinephrine bitartrate ≤0.1	Dopamine hydrochloride >15 or epinephrine >0.1 or norepinephrine bitartrate >0.1
1-11 mo	≥55	<55			
12-23 mo	≥60	<60			
24-59 mo	≥62	<62			
60-143 mo	≥65	<65			
144-216 mo	≥67	<67			
>216 mo[e]	≥70	<70			
Neurologic					
Glasgow Coma Score[f]	15	13-14	10-12	6-9	<6
Renal					
Creatinine by age group, mg/dL					
<1 mo	<0.8	0.8-0.9	1.0-1.1	1.2-1.5	≥1.6
1-11 mo	<0.3	0.3-0.4	0.5-0.7	0.8-1.1	≥1.2
12-23 mo	<0.4	0.4-0.5	0.6-1.0	1.1-1.4	≥1.5
24-59 mo	<0.6	0.6-0.8	0.9-1.5	1.6-2.2	≥2.3
60-143 mo	<0.7	0.7-1.0	1.1-1.7	1.8-2.5	≥2.6
144-216 mo	<1.0	1.0-1.6	1.7-2.8	2.9-4.1	≥4.2
>216 mo[e]	<1.2	1.2-1.9	2.0-3.4	3.5-4.9	≥5

Septic Shock

- Shock = inadequate tissue perfusion and oxygen delivery

- Sepsis 2 definition
  - Sepsis with hypotension (SBP <90, MAP <60, or decrease in SBP >40 from baseline)
- Sepsis 3 definition
  - Sepsis with hypotension *requiring vasopressors* (to maintain MAP >65) ***and*** *lactate* >2*
  - *Lactate criterion is controversial

- **Pediatrics**
  - Infants and children maintain a high vascular tone at baseline
  - **Shock state develops well before hypotension**
  - Rely upon physical exam signs

Diagnosis, not definition

Septic Shock in Pediatrics

Distributive ("warm") shock

- Hyperdynamic physiology
- Decreased SVR & increased cardiac output
- Flash cap refill
- Bounding pulses
- Warm extremities
- Wide pulse pressure

Cold shock

- Increased SVR
- Decreased cardiac output
- Delayed cap refill
- Diminished pulses
- Mottled or cool extremities
- Narrow pulse pressure

Managing Pediatric Sepsis

- Adult sepsis
  - ~~Sepsis-1~~
  - Sepsis-2
  - Sepsis-3
- Pediatric sepsis

Surviving Sepsis Campaign®

Online Special Article

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

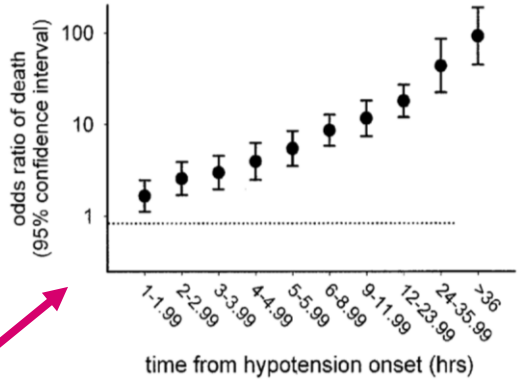
Scott L. Weiss, MD, MSCE, FCCM (Co-Vice Chair)[1]; Mark J. Peters, MD, PhD (Co-Vice Chair)[2]; Waleed Alhazzani, MD, MSc, FRCPC (Methodology Chair)[3]; Michael S. D. Agus, MD, FCCM, FAAP[4]; Heidi R. Flori, MD, FAAP[5]; David P. Inwald, MB, BChir, FRCPCH, FFICM, PhD[6];

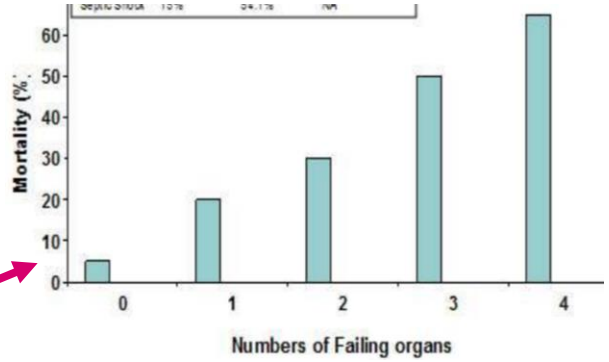
Surviving Sepsis Campaign

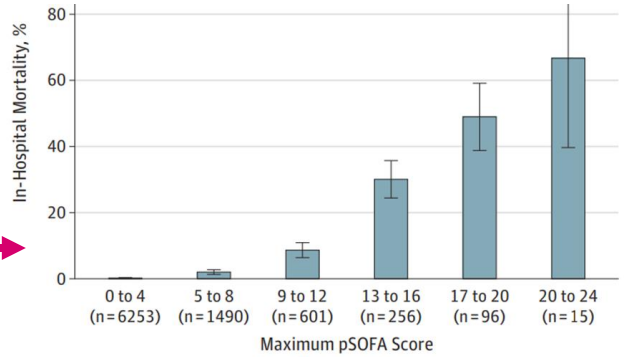
- https://www.sccm.org/SurvivingSepsisCampaign/Guidelines/Pediatric-Patients
- Executive Summary: Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children. Pediatric Critical Care Medicine: February 2020 - Volume 21 - Issue 2 - p 186-195 doi: 10.1097/PCC.0000000000002197
- Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children. Pediatric Critical Care Medicine: February 2020 - Volume 21 - Issue 2 - p e52-e106 doi: 10.1097/PCC.0000000000002198

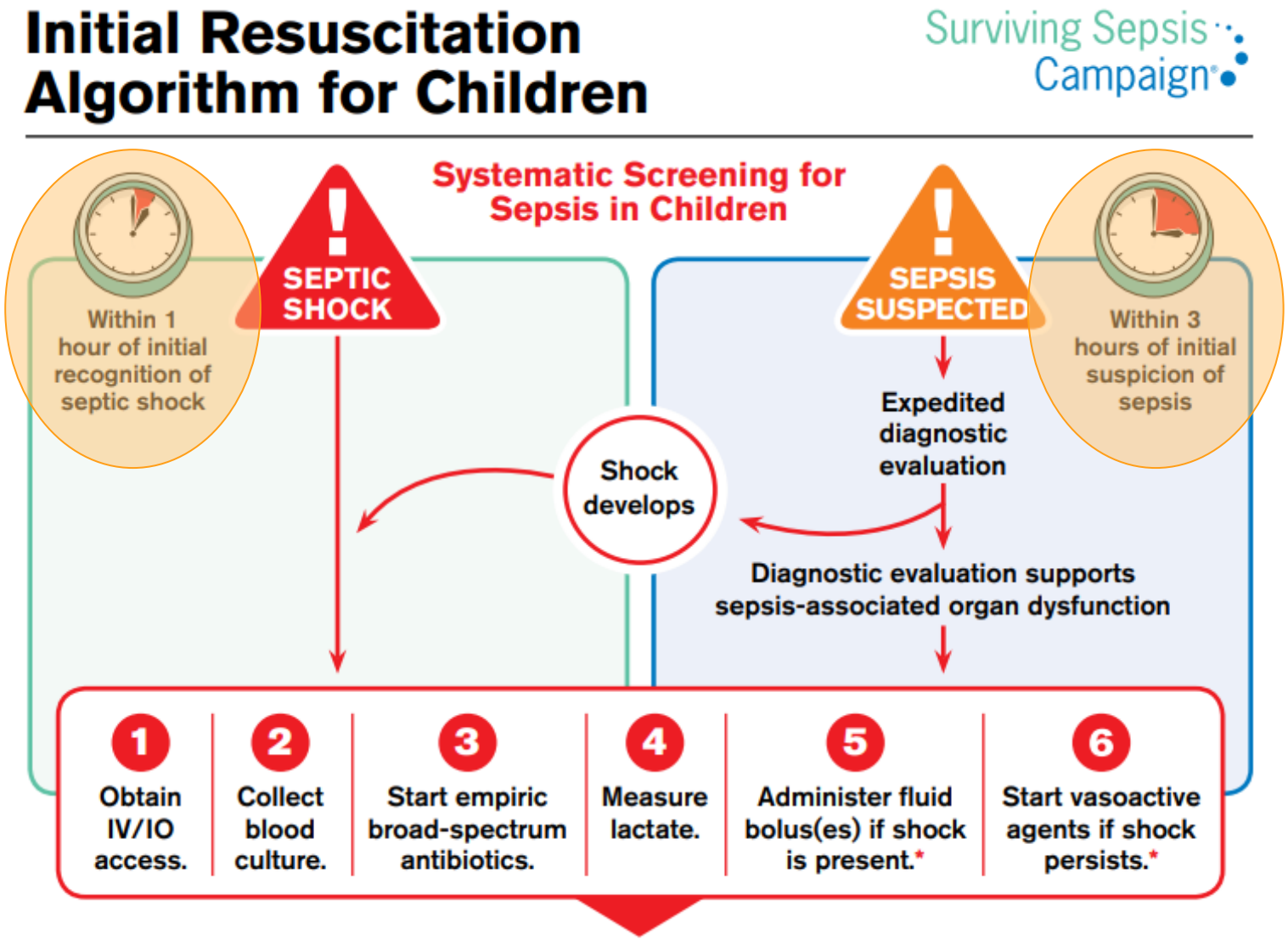
Treating Pediatric Sepsis:
Early recognition & Timely intervention

- **Risk of death increases significantly with:**
  - Increasing delays before initiation of antimicrobial therapy
    - Every 1-hour delay in antibiotics led to a 7.5% increase in mortality (Kumar et al CCM 2006)
    - In a pediatric study, ≥3-hour delay in antibiotics was associated with >20% mortality (Weiss et al CCM 2014)
  - Increasing number of failing organs (Quereshi. BMJP. 2008)
  - Increasing pSOFA score (Sanchez-Pinto JAMA Peds 2017)







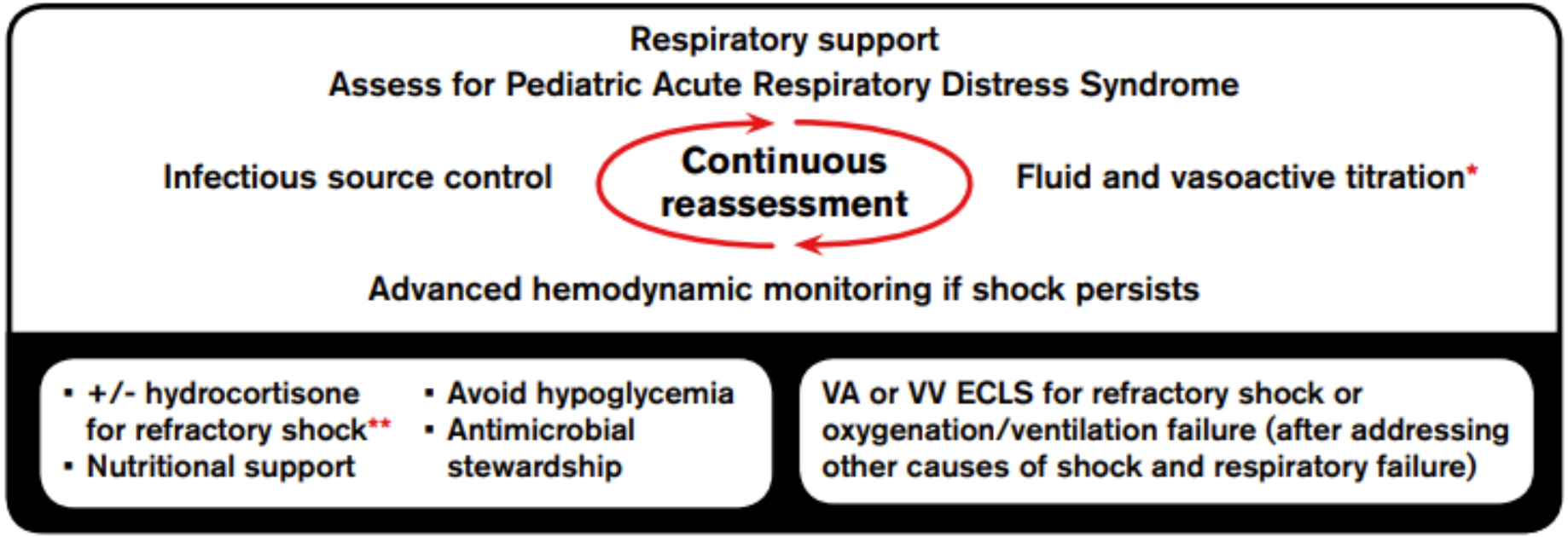


Early recognition

&

Timely intervention

https://www.sccm.org/getattachment/SurvivingSepsisCampaign/Guidelines/Pediatric-Patients/Initial-Resuscitation-Algorithm-for-Children.pdf.aspx?lang=en-US



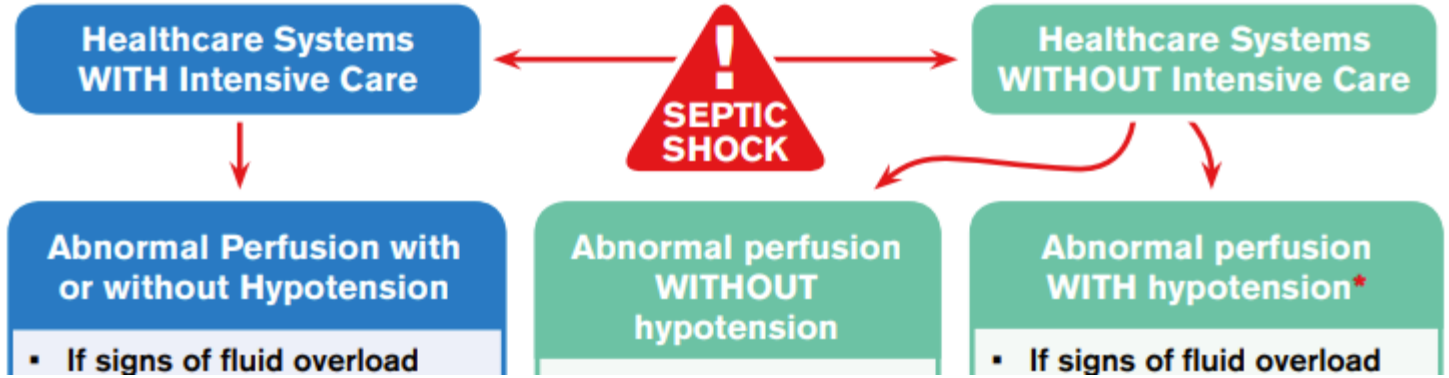
*See fluid and vasoactive algorithm. Note: Fluid bolus should be omitted from bundle if a) fluid overload is present or b) it is a low-resource setting without hypotension. Fluid in mL/kg should be dosed as ideal body weight.

**Hydrocortisone may produce benefit or harm.

https://www.sccm.org/getattachment/SurvivingSepsisCampaign/Guidelines/Pediatric-Patients/Initial-Resuscitation-Algorithm-for-Children.pdf.aspx?lang=en-US

Fluid and Vasoactive-Inotrope Management Algorithm For Children

Surviving Sepsis Campaign



*Hypotension in healthcare systems WITHOUT intensive care is defined as either:

- SBP < 50 mm Hg in children aged < 12 months
- SBP < 60 mm Hg in children aged 1 to 5 years
- SBP < 70 mm Hg in children aged > 5 years

OR

- Presence of all 3 World Health Organization criteria: cold extremities, prolonged capillary refill > 3 seconds, weak/fast pulse

https://www.sccm.org/getattachment/SurvivingSepsisCampaign/Guidelines/Pediatric-Patients/Initial-Resuscitation-Algorithm-for-Children.pdf.aspx?lang=en-US

Pediatric Sepsis Denials . . . and Appeals

Querying for Sepsis in Pediatrics

- Pediatric sepsis is different

- Sepsis is a clinical diagnosis
- Clinicians are diagnosing sepsis – not necessarily *defining* it
- Clinicians' goals:
  - Early recognition and diagnosis
  - Timely intervention to save lives

- Clinical documentation may not describe clinical criteria right away

- Health plan reviewers' goal is to find reasons that sepsis diagnosis does not meet (their) definitions
- Using decision-making tools that are:
  1. Not designed for pediatrics
  2. Not designed as *clinical* criteria – research & mortality predictions
- Sepsis diagnosis added by query will invite scrutiny

Clinical Example

- 21-year-old 26kg (57#) developmentally delayed patient with an inborn error of metabolism, has a PICC line for supplemental fluids as needed at home
- Presented to the ED with fever 101.4, HR 129, RR 43, MAP <70, elevated procalcitonin, decreased platelets
- Remained febrile and tachycardic for the first 24hrs of admission
- Multiple days of IV antibiotics
- PICC grew MSSA and developed thrombus
- PICC removal & replacement

- “Sepsis” documented consistently: ED note, admission H&P, ID notes x4, Hospitalist notes x4, Palliative care note, and DC summary

Health Plan's Initial Review

aureus) as a secondary diagnosis. It was noted that the physician documented sepsis in the discharge summary. However, according to the guideline cited below known as Sepsis 2, to clinically validate sepsis the medical record is examined for consistent documentation of the condition, and evidence of a systemic response to infection which is both progressive and injurious. Only findings that cannot be easily explained by other causes should be considered. Although useful in identifying infection, SIRS criteria by themselves are overly sensitive and inadequately specific for diagnosing sepsis. It is acknowledged a positive blood culture was obtained; however, bacteremia is not evidence of sepsis. There was insufficient clinical evidence and supportive

Sepsis-2

Infection
+
“some of the following”

Table 1. Diagnostic criteria for sepsis

Infection,[a] documented or suspected, and some of the following:[b]
General variables
Fever (core temperature >38.3°C)
Hypothermia (core temperature <36°C)
Heart rate >90 min^{-1} or >2 SD above the normal value for age
Tachypnea
Altered mental status
Significant edema or positive fluid balance (>20 mL/kg over 24 hrs)
Hyperglycemia (plasma glucose >120 mg/dL or 7.7 mmol/L) in the absence of diabetes
Inflammatory variables
Leukocytosis (WBC count >12,000 μL^{-1})
Leukopenia (WBC count <4000 μL^{-1})
Normal WBC count with >10% immature forms
Plasma C-reactive protein >2 SD above the normal value
Plasma procalcitonin >2 SD above the normal value
Hemodynamic variables
Arterial hypotension[b] (SBP <90 mm Hg, MAP <70, or an SBP decrease >40 mm Hg in adults or <2 SD below normal for age)
$S\bar{v}O_2$ >70%[b]
Cardiac index >3.5 $L \cdot min^{-1} \cdot M^{-23}$
Organ dysfunction variables
Arterial hypoxemia (PaO_2/FIO_2 <300)
Acute oliguria (urine output <0.5 $mL \cdot kg^{-1} \cdot hr^{-1}$ or 45 mmol/L for at least 2 hrs)
Creatinine increase >0.5 mg/dL
Coagulation abnormalities (INR >1.5 or aPTT >60 secs)
Ileus (absent bowel sounds)
Thrombocytopenia (platelet count <100,000 μL^{-1})
Hyperbilirubinemia (plasma total bilirubin >4 mg/dL or 70 mmol/L)
Tissue perfusion variables
Hyperlactatemia (>1 mmol/L)
Decreased capillary refill or mottling

Health Plan's Subsequent Review

criteria were published in 1992, extensive research occurred throughout the next two decades. By 2003 it was clear that simply detecting signs of inflammation (i.e. SIRS criteria) was insufficient in defining sepsis. To clinically validate sepsis, the medical record is examined for consistent documentation of the condition, and for evidence of a dysregulated systemic response to infection causing organ injury. Sepsis is a condition where the patient's immune system attacks body organs. These processes are distinct and separate from local organ dysfunction caused by an infection itself. Though the patient was noted to have tachycardia, tachypnea and reported fever, these findings are to be expected with an infection. While we acknowledge this patient had a positive blood culture, this alone would not validate the diagnosis of sepsis. While we further acknowledge the Procalcitonin in this patient with a diagnosis of bacteremia this clinical indicator is not criteria utilized in the routine assessment of sepsis as they are

Sepsis-3?

Sepsis-3

Infection
+
SOFA* >2

*pSOFA used for P/F ratio

SpO2:FiO2 = 323

Table 1. Sequential [Sepsis-Related] Organ Failure A

System	Score 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) respiratory su
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 >1 epinephrine > or norepinepl
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 indicate neurological function.

Pediatric Sepsis Denials and Appeals

- Clinicians have a high index of suspicion for early diagnosis of pediatric sepsis to ensure timely intervention
- No current (i.e. after 2005) consensus of definitions for pediatric sepsis and septic shock
- Sometimes early diagnosis does not quite meet the definition
- Denials for pediatric sepsis may reflect this confusion
- Appeals must include all relevant evidence

Take Home Points

- Sepsis in children presents differently than in adults . . . but available studies agree that early diagnosis and timely intervention decrease mortality
- No one knows what set of criteria to use to define pediatric sepsis (not even health plan reviewers)
  - 2005 consensus
  - SOFA/pSOFA (and all other scoring systems) scores are intended for research and mortality prediction, not clinical criteria
- Individual institutions develop own clinical pathways or criteria
  - Mostly for early detection/intervention to impact mortality risk
- Ongoing studies for a more contemporary set of definitions for pediatric sepsis

. . . TBD

Pediatrics is Easy

https://www.youtube.com/@DGlaucomflecken

"Is it easy when your patients have completely different physiology that changes rapidly as they age?"

References

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Questions & Answers

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