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325--Addressing Challenges in the Recognition and Management of Pediatric Sepsis in the Emergency Department, Critical Care, and Post-Sepsis Care

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Speaker Disclosure

- I have no conflicts of interest to disclose.

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Learning Objectives

- Define key terms related to sepsis and septic shock
- Identify children presenting with sepsis and/or septic shock
- Differentiate between common septic shock presentations
- Describe initial management and treatment goals of children with septic shock
- Define post-sepsis care
- Discuss the importance of post-sepsis care management
- Examine current use of sepsis and septic shock algorithms
- Compare past and present pediatric sepsis and septic shock guidelines developed by SCCM
- Discuss how to incorporate sepsis and septic shock guidelines into practice

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Meet Ana

- 9-month-old girl with 4-day history of profuse diarrhea and poor PO intake admitted to the floor with concerns for dehydration
- Initial vitals: BP 80/50, HR 170, RR 70
- Physical exam:
  - Irritable
  - Cool, mottled extremities
  - Sluggish capillary refill
  - Weak peripheral pulses

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Some Say…

SEPSIS IS A
JOURNEY

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- Identifying pediatric patients with sepsis can be difficult
- Many pediatric patients have fever and tachycardia
- Most of them are not septic

…But some are

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Epidemiology

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Is Sepsis Really A Big Deal?

- Sepsis remains a leading cause of childhood mortality, also significant morbidity
- Over ½ of the globe reported incidence of sepsis related to the neonatal and pediatric population
- Morbidity is too high
  - Up to 1/3 of children develop ongoing, life-long sequelae

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Sepsis: **Epidemiology**

- Estimated 25 million children worldwide experienced sepsis in 2017
  - Resulting in more than 3 million deaths
  - Most disproportionate effect is found among children in the early years and in lower-resource settings

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What Do We Know About Sepsis?

- We know…
  - Sepsis is **PREVENTABLE**
  - Sepsis Timeline…
    - **2001** SCCM developed adult sepsis criteria
    - **2005** **Pediatric-specific** criteria first published for sepsis (IPSCC expert task force)
    - **2016** Third International Consensus Definition for Sepsis and Septic Shock (Sepsis-3)
    - **2020** SCCM – Executive Summary: Surviving Sepsis Campaign International Guidelines for the Management of Septic Shock and Sepsis-Associated Organ Dysfunction in Children
    - **2024** SCCM - Phoenix Sepsis Scoring

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Definitions

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Definitions: What is Currently Needed?

- Clear need for standard definitions, but why….?
  1) More accurately characterize the epidemiologic features and how this relates to pediatrics
  2) Accurately identify patients early in septic shock
  3) Development of sepsis recognition and management algorithms
  4) Standard definitions are crucial

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…So, Let's Take a Look at the Definitions?

- What is SIRS?
  - Presence of **≥ 2 of the following**…1 of which **MUST** be abnormal temperature **OR** abnormal leukocyte count
    - Core temperature **≥ 38.5 C or < 36 C**
    - Elevated or depressed **leukocyte count** or >10% immature neutrophils
    - **Tachycardia** or, in infants, bradycardia or unexplained persistent depression over 30 minutes
    - **Tachypnea**

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What SIRS is **Not**…

- SIRS is **not** a diagnosis
- SIRS represents a state of inflammation and/or immune activation
- Patients with diverse clinical diagnoses may meet the SIRS criteria

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So What is **SEPSIS**?

- Life threatening organ dysfunction caused by a dysregulated host response to infection (CDC)
- **Pediatric Definitions:**
  - **SIRS in the presence of or as a result of suspected or proven infection**
  - **SIRS secondary to an infection, documented by microbiology cultures or in the presence of other clinical evidence markers of infection**

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Sepsis: More Definition Building

- Body's extreme response to an infection and is a life-threatening emergency
- Life-threatening organ dysfunction caused by a dysregulated host response to infection (Phoenix)

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How is **Severe Sepsis** Defined?

- Sepsis plus at least **one** of the following:
  - Cardiovascular-organ dysfunction
  - Pediatric acute respiratory distress syndrome (P-ARDS)
  - Two or more other body systems revealing organ dysfunction

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And What About **Septic Shock?**

- Severe infection leading to cardiovascular dysfunction (Scott)
  - Hypotension
  - Need for vasoactive medications
  - Impaired perfusion
- "Sepsis-associated organ dysfunction"
  - Cardiovascular organ dysfunction
  - Non-cardiovascular dysfunction
  - Septic Shock: Subset of sepsis in which underlying circulatory and cellular metabolism abnormalities are profound enough to substantially increase mortality (Alder)

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Recognition

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Difficult to define sepsis and terms related to sepsis

- Most cases of sepsis start before a patient or caregiver decides to seek treatment
  - **BEFORE PATIENTS AND FAMILIES SEEK MEDICAL CARE**
- Most commonly found in…
  - Lung
  - Urinary tract
  - Skin
  - GI tract

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Sepsis: Clinical Manifestations

- Can happen as the result of any infection
- There is no **ONE** symptom that magically defines sepsis
  - Hyper/hypothermia
  - Tachycardia/bradycardia
  - Tachypnea
  - Hypotension
  - Fatigue, low energy
  - Mental status changes-confuson and/or agitation, lethargy, somnolence
  - Rash (purpura)
  - Decrease in urine output/wet diapers

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From Sepsis/Severe Sepsis to Septic Shock

- Progression of Shock:
  - Compensated
  - Uncompensated
  - Irreversible
- Pediatric patients often present in **compensated shock without hypotension**

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Association of Clinical Signs and Progression of Septic Shock

Compensated	Uncompensated	Irreversible
Order function is maintained	End-organ dysfunction and microvascular failure	End-organ cellular death
Tachycardia	Tachycardia ➤ Bradycardia	Bradycardia
Normotensive for age	Hypotension	Hypotension
Increased WOB	Cap refill ≥ 4 secs	Cap refill > 10 secs
Cap refill ≥ 3 secs	Tachypnea	Tachypnea/Apnea
Agitation/Anxiety	Altered mental status	Altered mental status/Coma
Oliguria	Anuria	Anuria

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Age	Heart Rate (bpm)	Resp Rate (breaths/min)	Systolic BP (mm Hg)	Temp (°C)
0-3 months	< 80 or >205	>60	< 60	<36 or >38
3-12 months	< 70 or >190	>60	< 70	<36 or >38.5
1-3 years	>140	>40	< 70 + (2 × age in years)	<36 or >38.5
3-6 years	>140	>34	< 70 + (2 × age in years)	<36 or >38.5
6-10 years	>140	>30	< 70 + (2 × age in years)	<36 or >38.5
10-12 years	>110	>30	< 90	<36 or >38.5
>12 years	>100	>20	< 90	<36 or >38.5

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Sepsis or Not?

- 3-year-old unimmunized male with hisotry of GBS meningitis with resultant encephalopathy, seizures, Lennox Gastaut syndrome, hydrocephalus w/p VP shunt, abnormal temperature regulation, g-tube dependence.
- Patient screaming in pain, passed gas, went pale and passed out per Mom's report. Taken to ED.
  - Vital Signs: Temp 34.5, HR 55-155, RR 50, BP 39/23, O2 sat 72% RA
  - Labs: Glu 59, Na 158, WBC 15.4, Plt 55, VBG – 6.92/77/32/-17, blood, urine cultures sent
  - PE: Pale, lethargic, increased WOB, cap refill 4-5 secs

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Yes. Sepsis.

- IO placed, Epinephrine initiated 0.05 mcg/kg/min
- Transferred to PICU
  - Intubated immediately for respiratory failure-resp culture sent
  - Fluid resuscitation
  - Antimicrobials initiated
  - Epinephrine increased, added Norepinephrine, and Vasopressin
- Positive cultures—Blood, urine, and respiratory +Serratia marcescens

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Sepsis or Not?

- 4-month-old with history of prematurity (34 2/7) admitted with +rhino/entero and +Covid tests. Other history-complete balanced AV canal, Trisomy 21. On the peds floor overnight became tachycardia in the setting of new fever and increase in stool output. Hemodynamically stable. Etiology of new fever unclear, possibly secondary to new viral illness. Gave 15 mL/kg NS boluses.
  - Vital Signs at 1400: Temp 39.4, RR 49, HR 187-212, BP 62/32 (41)
  - Labs: WBC 19.3, CRP 1.2, BUN 68, Crt 1.1, increase from 0.3 yesterday, enteric panel sent, + hemoccult stool
  - PE: Lethargic, subcostal retractions, dry, cracked skin and lips, cool

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Yes. Sepsis.

- Admitted to PICU
  - Placed on RAM cannula of 8
  - Labs: Sent blood and urine cultures, lactate 5.4, K 5.8, VBG 7.24/61/45/-8; fluid resuscitation continued~25 mL/kg NS boluses and $NaHCO_3$ given
  - RAM increased to 10, repeat labs 30" later and abdominal xrays obtained
  - Repeat labs: Lactate 7.9, K 4.8, VBG 7.18/77/40/-17
  - Abdominal imaging: Pneumatosis intestinalis found, Pediatric Surgery consulted
  - Enteric panel: Rotavirus +, cultures pending

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Management

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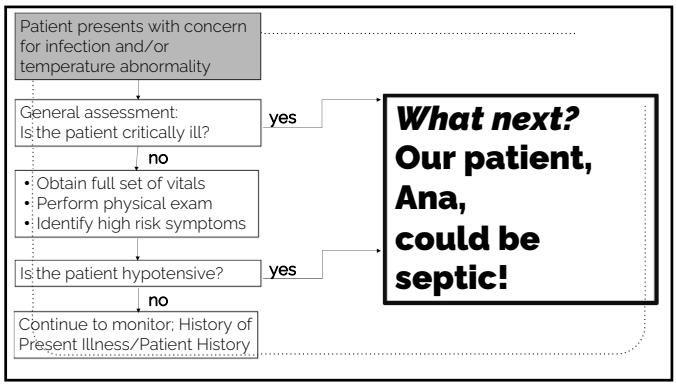

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OK, so maybe it's sepsis...

...Now what?

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Start with this.

- Provide supplemental oxygen
- Begin resuscitation with 10-20 cc/kg NS, albumin, plasmalyte bolus; Don't forget to reassess
- Order antibiotics and administer within the golden hour
- Send labs including lactate, obtain cultures

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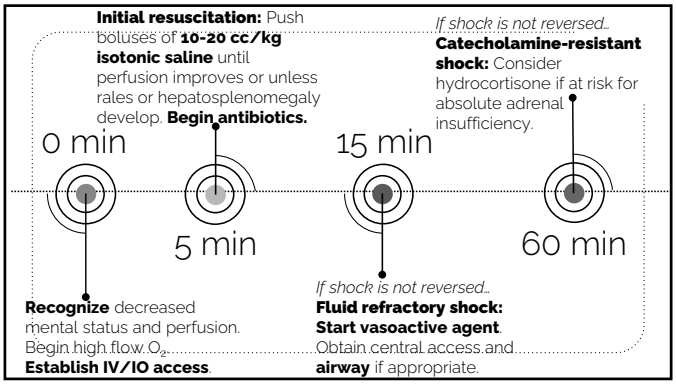

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Initial Resuscitation Targets...

- Normal BP for age
- Normal pulses for age
- Capillary refill 1-2 seconds
- Warm extremities
- Urine output > 1 cc/kg/hr
- Normal mentation

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Important Sepsis Management Take Homes

- Septic shock can be identified from vitals and physical exam
- Early resuscitation improves outcomes
- Antibiotics should be given within the golden hour of presentation
  - THERE WILL BE MORE ON MANAGEMENT!!!

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Post-Sepsis Care

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Post-Sepsis Care: What Is It?

- Long-term sequelae from sepsis/septic shock is becoming more common
- Research is shifting
- Sequelae Burden Post-Sepsis
  - Physical
  - Psychological
  - Developmental

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Post-Sepsis Care: How Can We Help?

- Recognize the value of patient-centered-care for sepsis survivors and families
- Families are at high risk of isolation
- Investigate support structures and provide holistic patient care

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Post-Sepsis Care: Where Are The Gaps?

- Practice
- Research
- Education
- ***Streamlined, unified approach is needed to standardize and align care

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Post-Sepsis Care: Initiatives

- Expansion of community awareness initiatives
- Embedded into school curriculums
- Embedded into nursing curricula
- Integration of the community, health care, and university sectors

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Sepsis Pathways…Why They Matter

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Sepsis Pathways: They Do Matter!

- To date…
  - No reliable early diagnostic test to identify sepsis
  - No standardized assessment or management of sepsis in adults/children
- Comprehensive approach is warranted
- Key themes identified

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Sepsis Pathways

- Aim:
  - Guide clinicians in recognizing and managing sepsis
  - Provide standardization of approaches
  - Assist in data collection for benchmarking and evaluation
  - ***Urgent need to ensure EMS is able to recognize and manage sepsis

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Sepsis Care Bundle

- Includes initial resuscitation and treatment actions
- Lower mortality rates noted with use of sepsis bundles
- Additional pediatric studies are needed

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Sepsis Care Bundle Components

- When to huddle—Who needs to be there—Who is the decision-maker?
- Blood culture collection
- Administration of antimicrobials
- Fluid boluses (increased scrutiny)
  - FEAST study

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2020 SCCM Executive Summary: Surviving Sepsis Campaign

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SCCM: Surviving Sepsis Campaign - **Inclusion**

- 37-week gestation at birth to 18 years of age
- Diagnosis of septic shock or other sepsis-associated acute organ dysfunction
- Did not address neonates with perinatal infection or an association with neonatal sepsis

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SCCM: Surviving Sepsis Campaign

- Expert panel:
  - Issued 77 statements of management and resuscitation of children
    - Strong recommendations – **6**
    - Weak recommendations – **49**
    - No recommendations – **13**
    - Best Practices – **9**
  - Knowledge gaps and research opportunities - **52**

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SCCM Surviving Sepsis Campaign Conclusions

- Most recommendations had low quality of supporting evidence
- Many weak recommendations
- Executive summary provides a foundation for consistent care to improve outcomes and guide future research

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SCCM: Surviving Sepsis Campaign – **Best Practices**

- Screening, Diagnosis, and Systematic Management of Sepsis
  - Implementation of a protocol/guideline for management of children with septic shock or **other sepsis-associated organ dysfunction**
  - Obtaining blood cultures before initiating antimicrobial therapy

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SCCM: Surviving Sepsis Campaign – **Best Practices**

- Antimicrobial Therapy
  - Empiric broad spectrum therapy with one or more antimicrobials
  - Narrowing empiric antimicrobial therapy
  - No pathogen identified, narrowing or discontinuing empiric antimicrobial therapy is appropriate if symptoms have improved or resolved

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SCCM: Surviving Sepsis Campaign – **Best Practices**

- Antimicrobial Therapy
  - Utilization of optimal antimicrobial dosing strategies based on published evidence
  - Daily assessment for de-escalation
  - Determine duration according to site infection, microbial etiology, treatment response, and achievement of source control

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SCCM: Surviving Sepsis Campaign – **Best Practices**

- Source Control
  - Emergent source control intervention implemented ASAP after diagnosis of infection amenable to a source control procedure

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SCCM: Surviving Sepsis Campaign – **Best Practices**

- Fluid Therapy
  - None
- Hemodynamic Monitoring
  - None
- Vasoactive Medications
  - None

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SCCM: Surviving Sepsis Campaign – **Best Practices**

- Endocrine and Metabolic
  - None
- Nutrition
  - None
- Blood Products
  - None

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SCCM: Surviving Sepsis Campaign – **Best Practices**

- Plasma Exchange, Renal Replacement, and Extracorporeal Support
  - None
- Immunoglobulins
  - None
- Prophylaxis
  - None

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SCCM: Surviving Sepsis Campaign - **Ventilation**

Recommendation #34	Strength & Quality of Evidence
We were ***unable to issue a recommendation*** about whether to intubate children with fluid-refractory, catecholamine-resistant septic shock. However, in our practice, we commonly intubate children with fluid-refractory, catecholamine-resistant septic shock without respiratory failure.	Insufficient

Recommendation #35	Strength & Quality of Evidence
We ***suggest not to use*** etomidate when intubating children with septic shock or other sepsis-associated organ dysfunction.	• Weak • Low-Quality of Evidence

Recommendation #36	Strength & Quality of Evidence
We ***suggest*** a trial of noninvasive mechanical ventilation (over invasive mechanical ventilation) in children with sepsis-induced pediatric ARDS (PARDS) without a clear indication for intubation and who are responding to initial resuscitation.	• Weak • Very Low-Quality of Evidence

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SCCM: Surviving Sepsis Campaign – **Adrenal Insufficiency**

SURVIVING SEPSIS CAMPAIGN INTERNATIONAL GUIDELINES FOR THE MANAGEMENT OF SEPTIC SHOCK AND SEPSIS-ASSOCIATED ORGAN DYSFUNCTION IN CHILDREN

CORTICOSTEROIDS RECOMMENDATIONS TABLE

RECOMMENDATION #44	STRENGTH & QUALITY OF EVIDENCE
We ***suggest against*** using IV hydrocortisone to treat children with septic shock if fluid resuscitation and vasopressor therapy are able to restore hemodynamic stability.	• Weak • Low-Quality of Evidence

RECOMMENDATION #45	STRENGTH & QUALITY OF EVIDENCE
We **suggest** that either IV hydrocortisone or no hydrocortisone may be used if adequate fluid resuscitation and vasopressor therapy are not able to restore hemodynamic stability.	• Weak • Low-Quality of Evidence

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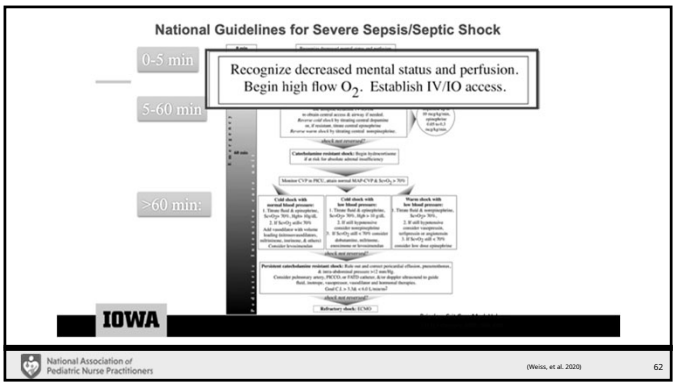

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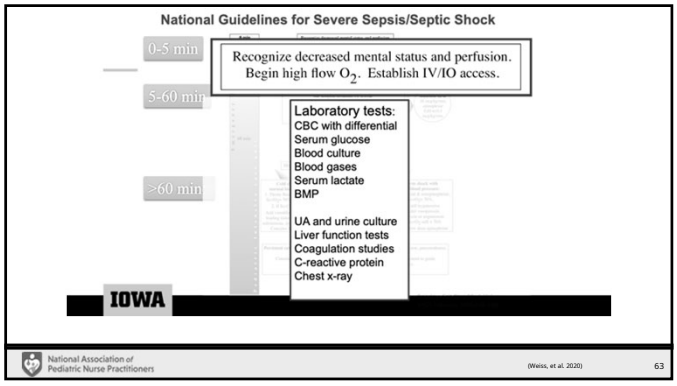

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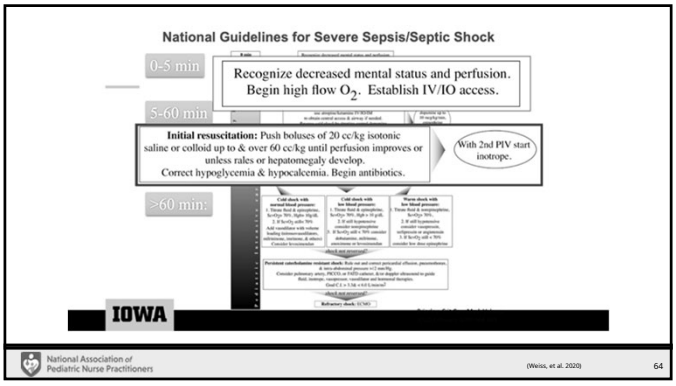

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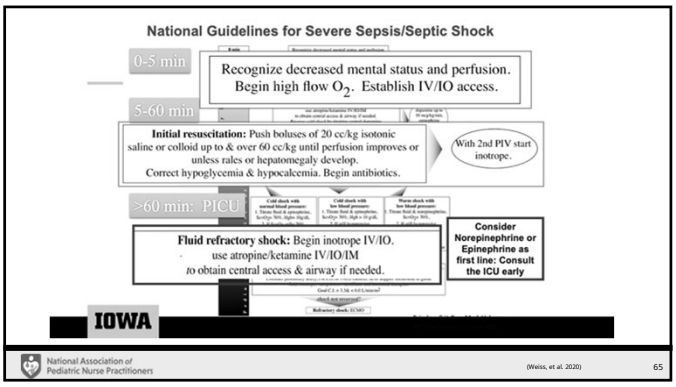

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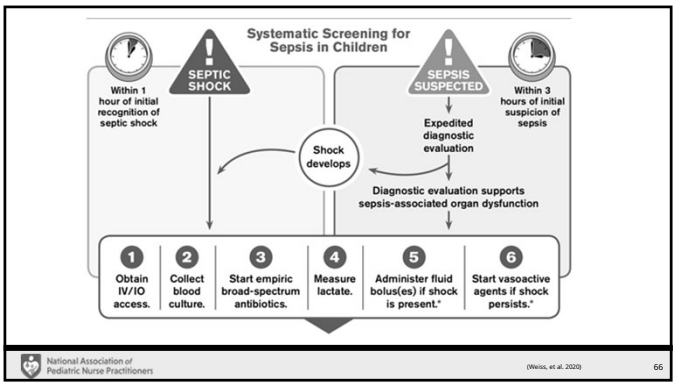

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Limitations of Current Criteria for Sepsis in Children

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Sepsis Criteria: **Limitations**

- Includes mild illness severity
- SIRS criteria – Not reliable
- Discrepancies in how the criteria are applied clinically
- Poor evaluation of lower-resource settings

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Process Development and Validation for New Sepsis Criteria

- New criteria should be based on robust data from diverse settings
- Prior use of SOFA scores
- Current criteria based on intensive care settings
  - 80% of sepsis diagnoses begin in emergency departments or general inpatient care settings

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International Consensus Criteria for Pediatric Sepsis and Septic Shock: Introducing The Phoenix Sepsis Score

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Phoenix Criteria for Pediatric Sepsis and Septic Shock

- Objective: To update and evaluate criteria for sepsis and septic shock in children
- Comprised of 35 pediatric experts
  - Critical care
  - Neonatology
  - Emergency medicine
  - Public health
  - Infectious disease
  - General pediatrics
  - Nursing

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Sepsis – Septic Shock Guidelines from SCCM Task Force

- Evidence from international survey
- Systematic review
- Meta-analysis
- New organ-dysfunction score
- Based on more than 3 million EHR encounters
- Modified Delphi consensus process employed

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Limitations of Current Criteria for Sepsis in Children

- IPSCC criteria
  - Mild illness severity
  - SIRS criteria is not a reliable identifier of children with infection at risk of poor outcomes
- Discrepancies in application of criteria in the clinical setting
- Populations of lower resource settings have not been properly evaluated

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Limitations of Current Criteria for Sepsis in Children

- Sepsis-3 criteria does provide guidance from the adult populations and validated the revising of new pediatric sepsis criteria
- Pre-existing SOFA score utilization is unclear
- 80% of pediatric sepsis patients present to the ED
  - Majority of sepsis research focuses on intensive care units
  - Data across the entire hospital continuum should be addressed

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Process of Developing and Validating New Criteria

- Consensus process
  - Data presented to task force for review
  - Voting per REDCap surveys
  - ≥80% agreement of ≥80% of task force members for any given question
- Exclusion criteria
  - Preterm neonates (<37 weeks gestation)
  - Newborns who remained in the hospital after birth

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Survey Highlights

- Concerns
  - Inconsistent availability of diagnostic tests and therapeutic tools
  - Identified need for new criteria
    - Clinical care
    - Benchmarking
    - Quality improvement
    - Epidemiology
    - Research

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Survey Highlights

- Confirmation by Survey
  - Preferred use of the term sepsis
    - Children with infection-associated organ dysfunction (no SIRS, widespread adaptation of the Sepsis-3)
  - Septic shock
    - Sepsis leading to cardiovascular dysfunction
    - Utilized as starting points by the task force

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Organ-Specific Sub-Scores

- 8-existing pediatric organ dysfunction scores
  - Calculated from data within first 24 hours of presentation to the hospital
- Compared in-hospital mortality among children with suspected infection
  - Receiving systemic antimicrobials
  - Undergoing microbiological testing
- After data analyzed, task force decided on inclusion

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Final Model

- Levels of dysfunction
  - Cardiovascular
  - Respiratory
  - Neurological
  - Coagulation
- Comparable performance from an 8-organ system, also including renal, hepatic, endocrine, and immunological dysfunction (Phoenix-8 Score)

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Results

- Criteria to identify children with sepsis
- Criteria to identify children in septic shock
- Organ dysfunction remote from the primary site of infection

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Discussion

- Intention:
  - Be globally applicable
  - Named in reference to the meaning of the mythological phoenix
  - Location criteria were presented, 2024

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Phoenix Sepsis Score

- Use of the Phoenix Pediatric Sepsis Criteria
  - SOFA-based calculation via EHR, generally adults
  - Considerations: Phoenix scoring could do same

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Phoenix Sepsis Score

- Organ Dysfunction Not Included in the Phoenix Sepsis Score
  - Inclusion of 4-organ systems
  - Scoring system sensitive with good positive predictive value in comparison to the Phoenix-8-score
  - Task force prioritization
  - Not meant to diminish other assessment and management strategies

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Table. Comparison of Phoenix Pediatric Sepsis Criteria With International Pediatric Sepsis Consensus Conference Criteria

	International Pediatric Sepsis Consensus Conference criteria	Phoenix pediatric sepsis criteria
Sepsis		
Definition	SIRS in the setting of a suspected or confirmed infection: ≥2 SIRS criteria, of which 1 must be temperature or white blood cell count	Life-threatening organ dysfunction in the setting of suspected or confirmed infection, defined as ≥2 points on the Phoenix Sepsis Score
Criteria	Pediatric SIRS Criteria • Core temperature • White blood cell count • Heart rate • Respiratory rate	Organ dysfunction may include • Respiratory (Pa_{O_2}, F_{IO_2}, or Sp_{O_2}, F_{IO_2}) • Cardiovascular (vasoactive medications, lactate, age-specific MAP • Coagulation (platelets, INR, D-dimer, fibrinogen) • Neurologic systems (Glasgow Coma Scale)
Severe sepsis		
Definition	Sepsis with at least 1 of the following: cardiovascular organ dysfunction, acute respiratory distress syndrome, or ≥2 other organ dysfunctions.	Term no longer used now that sepsis definition requires organ dysfunction
Criteria	Organ dysfunctions include • Respiratory (Pa_{O_2}, F_{IO_2}, ratio, Pa_{CO_2}, F_{IO_2}, mechanical ventilation) • Neurological (Glasgow Coma Scale) • Hematologic (platelet count, INR) • Kidney (serum creatinine) • Hepatic (bilirubin, alanine aminotransferase)	
Septic shock		
Definition	Sepsis and cardiovascular organ dysfunction[a]	Sepsis with ≥1 point in the cardiovascular system[b]

Abbreviations: F_{IO_2}, fraction of inspired oxygen; INR, international normalized ratio; MAP, mean arterial pressure; Pa_{CO_2}, atrial partial pressure of carbon dioxide; Pa_{O_2}, atrial partial pressure of oxygen; SIRS, Systemic Inflammatory Response Syndrome; Sp_{O_2}, oxygen saturation as measured by pulse oximetry.

[a] The International Pediatric Sepsis Consensus Conference Criteria definition of cardiovascular organ dysfunction is despite 40 mL/kg or more isotonic fluid in 1 hour, hypotension (<5% percentile for age or systolic blood pressure <2 SD for age) or need for vasoactive or at least 2 of the following: unexplained metabolic acidosis, arterial lactate >2 times the upper limit of normal, oliguria, prolonged capillary refill, or core to peripheral temperature gap.

[b] The Phoenix definition of cardiovascular organ dysfunction includes severe hypotension for age, venous or arterial blood lactate value of more than 5 mmol/L (>45.05 mg/dL), or need for vasoactive medication.

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Phoenix Sepsis Score

- Lower Resource Settings
  - Accurately identified sepsis in data sets
    - Facilitates dissemination and data collection for future studies
    - 4-organ system
      - Reduction in laboratory testing and data collection
      - Use of lactates
      - Other laboratory testing
      - Coagulation parameters-Redundancy

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Phoenix Sepsis Score

- Identification of Children at Risk for Sepsis
  - Not designed for screening
  - Not designed for early identification
  - Continue developing screening and early warning tools
  - Future goals of the SCCM Pediatric Sepsis Definition Task Force

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Phoenix Sepsis Score

- Quality Improvement and Antimicrobial Stewardship
  - Not all patients that meet criteria have bacterial infections
  - Antimicrobial stewardship
    - Timely administration
    - Antimicrobial appropriateness

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Phoenix Sepsis Score

- Development Toward Phenotype-Based Sepsis Criteria
  - Definition of sepsis
  - Differences in…
    - Organ dysfunction
    - Tissue damage
    - Site of infection

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Phoenix Sepsis Score

Limitations

1. Too simplistic
2. Resource availability and local practice
3. Characterization of specific markers and findings not validated
4. Poor representation of higher resource settings
5. End points in mortality and morbidity

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Phoenix Sepsis Score

Limitations

6. 24-hour presentation windows exclude certain populations
7. Measures for deteriorating patients
8. Interventions exclude pertinent therapies
9. Exclusion of patient populations

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Conclusions

- Phoenix sepsis score of at least 2 identified potentially life-threatening organ dysfunction in children younger than 18 years of age with infection, and its use has the potential for many improvements
  - Clinical care
  - Epidemiological assessment
  - Pediatric sepsis and septic shock global research

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RECAP~In Summary…

- Too many children are affected by sepsis worldwide
- Many survivors experience ongoing physical, cognitive, emotional. and psychological sequelae
  - The struggle is **REAL**
- More studies, research, validated assessment tools and management guidelines, more research and educational support to EDs, PCPs, EMS, and parents/caregivers…**MORE of EVERYTHING PLEASE! Sepsis is PREVENTABLE!**

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References

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Questions?

Thank you!

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