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REVIEW

Summary: International Consensus Criteria for Pediatric Sepsis and Septic Shock

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Sepsis is the leading cause of death in children worldwide. Almost twenty years after the publication of the International Pediatric Sepsis Consensus Conference in 2005—which defined sepsis as the presence of Systemic Inflammatory Response Syndrome (SIRS) associated with suspected or confirmed infection—a new consensus for the definition of pediatric sepsis was published in January 2024 [1].

The International Consensus Criteria for Pediatric Sepsis and Septic Shock was proposed by a task force of 35 pediatric medicine and nursing specialists working in intensive care, emergency care, and infectious diseases from 12 countries on six continents. The consensus document was developed in three stages: a global survey with 2835 healthcare professionals, a systematic review and meta-analysis, and a derivation and validation study based on 3,000,000 electronic medical records of inpatients under 18 (excluding preterm infants younger than 37 weeks and newborns hospitalized after birth) from ten locations on four continents (including low-, middle-, and high-income countries). A Delphi consensus was used in the development of the criteria.

Eight organ dysfunction scores were used as the basis for the study to determine which systems were stronger predictors of hospital mortality in children with infection. From there, two scores were created, one comprising four systems (cardiovascular, respiratory, neurological, and coagulation) and another with eight (the previous four plus the renal, hepatic, endocrine, and immune systems), demonstrating similar performance. Due to greater simplicity in application, greater dissemination capacity, and less dependence on laboratory tests, the score with four systems was used to define the Phoenix criteria (Table 1). The exclusion of other systems, such as the renal and hepatic systems, does not diminish their relevance in patient management.

In the Phoenix score, sepsis was defined as a suspected infection plus a score of two or more points. Septic shock was defined as sepsis plus a score of 1 or more points in the "cardiovascular system" category. The term "severe sepsis" should no longer be used since sepsis is itself a life-threatening condition and a severe health condition.

The Phoenix Sepsis score demonstrated greater sensitivity and positive predictive value when compared to the 2005 criteria.

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Table 1. Escore de sepse de Phoenix

Variables	0 points	1 point	2 points	3 points
Respiratory	PaO_2:FiO_2 ≥ 400	PaO_2:FiO_2 < 400 with respiratory support	PaO_2:FiO_2 100-200 and IMV	PaO_2:FiO_2 < 100 and IMV
(0 - 3 points)	OR	OR	OR	OR
	SaO_2:FiO_2 ≥ 292[b]	SaO_2:FiO_2 < 292 with respiratory support[b,c]	SaO_2:FiO_2 148-220 and IMV[b]	SaO_2:FiO_2 < 148 and IMV[b]
Cardiovascular		1 point each (up to 3)	2 points each (up to 6)	
(0 - 6 points)				
	No VAD [d]	1 VAD [d]	≥ 2 VAD [d]	
	Lactate < 5mmol/L	Lactate 5 – 10.9 mmol/L	Lactate ≥ 11mmol/L	
	(< 45mg/dL)[e]	(45 to 98mg/dL)[e]	(≥ 99mg/dL)[e]	
Age [f]	MAP (mmHg) [g]			
< 1 month	> 30	17 - 30	< 17	
1 to 11 months	> 38	25 - 38	< 25	
1 to < 2 years	> 43	31 - 43	< 31	
2 to < 5 years	> 44	32 - 44	< 32	
5 to < 12 years	> 48	36 - 48	< 36	
12 to < 17 years	> 51	38 - 51	< 38	
Coagulation [h]		1 point each		
(0 to 2 points)		(maximum of 2 points)		
	Platelets ≥ 100 x 10^3	Platelets ≤ 100x10^3		
	INR ≤ 1.3	INR > 1.3		
	D-dimer ≤ 2mg/L	D-dimer > 2mg/L		
	Fibrinogen ≥ 100mg/dL	Fibrinogen < 100mg/dL		
Neurological [i]	Glasgow > 10	Glasgow ≤ 10 [j]	Fixed pupils bilaterally	
(0 a 2 pontos)	Pupils reactive			

Abbreviations: FEU, fibrinogen equivalent units; IMV, invasive mechanical ventilation; INR, international normalized ratio of prothrombin time; MAP, mean arterial pressure; PaO2:FIO2, partial pressure of oxygen: fraction of inspired oxygen; SpO2, oxygen saturation measured by pulse oximetry (97% SpO2 only); VAD, vasoactive drug.

* The Phoenix Sepsis Criteria are not intended for early screening or recognition of possible cases of sepsis.

[a] The score can be calculated without some variables (e.g., when lactate levels were not measured and vasoactive drugs were not used, a cardiovascular score can still be calculated based on blood pressure). Laboratory tests and other measurements should be obtained at the discretion of the medical team based on clinical judgment. Unmeasured variables do not contribute points. Ages are not adjusted for prematurity, and the criteria do not apply to postnatal admissions, neonates with postconceptional age of less than 37 weeks, or individuals aged 18 years and older.

[b] The SpO2:FIO2 ratio is calculated only if SpO2 is 97% or less.

[c] Respiratory dysfunctions assigned 1 point can be assessed in patients on oxygen therapy, high-flow nasal cannula, noninvasive positive pressure ventilation, or IMV, and includes a PaO2:FIO2 ratio of less than 200 and a SpO2:FIO2 ratio of less than 220 in children not receiving IMV. For children on IMV with a PaO2:FIO2 of less than 200 and SpO2:FIO2 of less than 220, see criteria for 2 and 3 points.

[d] Vasoactive medications include epinephrine, norepinephrine, dopamine, dobutamine, milrinone, and/or vasopressin (for shock).

[e] The reference range for lactate is 4.5 to 18 mg/dL. Lactate may be arterial or venous.

[f] Age is not adjusted for prematurity, and the criteria do not apply to newborns hospitalized at birth, children with a postconceptional age of less than 37 weeks, or individuals aged 18 years and older.

[g] Measured MAP (invasive measurement, if available, or noninvasive oscillometric measurement) is preferred, and if measured MAP is not available, a calculated MAP (1/3 × systolic + 2/3 × diastolic) may be used as an alternative.

[h] Variable coagulation reference ranges, platelets 150 to 450 × 103/μL; D-dimer.

[i] The neurologic dysfunction subscore has been pragmatically validated in sedated and unsedated patients and individuals on and off IMV.

[j] The Glasgow Coma Scale measures consciousness based on verbal, ocular, and motor responses (range 3–15, with a higher score indicating better neurological function).

The new criteria for sepsis and septic shock aim to identify life-threatening organ dysfunctions secondary to infections in children. They were not developed to screen at-risk children or to identify early sepsis and septic shock.

The new consensus has rekindled discussions on the topic. Particular attention has been devoted to the creation of screening instruments to identify cases of sepsis early on and patients at risk so that early interventions are introduced to decrease morbidity and mortality associated with pediatric sepsis.

The Phoenix criteria can potentially enhance pediatric septic patients' care significantly. Their adoption could lead to better clinical outcomes and the inclusion of more patients in clinical studies, potentially paving the way for new therapeutic advances.

The authors conclude the article by citing the limitations of the consensus, which include the simplification of a complex and heterogeneous biological process; the use of microbiological markers, which may be affected by the availability of resources and local practices; the use of the primary outcome of death in children with infections, which, although more objective, cannot be considered in the assessment of morbidity associated with infection and does not include long-term effects for patients and their families; the criteria were not developed for patients with nosocomial infections, preterm infants younger than 37 weeks of gestational age, or full-term newborns hospitalized shortly after birth.

By adopting the Phoenix criteria, we can potentially revolutionize the clinical care of sepsis, its epidemiological assessment, and clinical research. This shift may ultimately lead to improved outcomes and reduced mortality related to pediatric sepsis.

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