

Management of severely ill children in Africa: pragmatics and pitfalls

Kathryn Maitland
Kilifi, Kenya



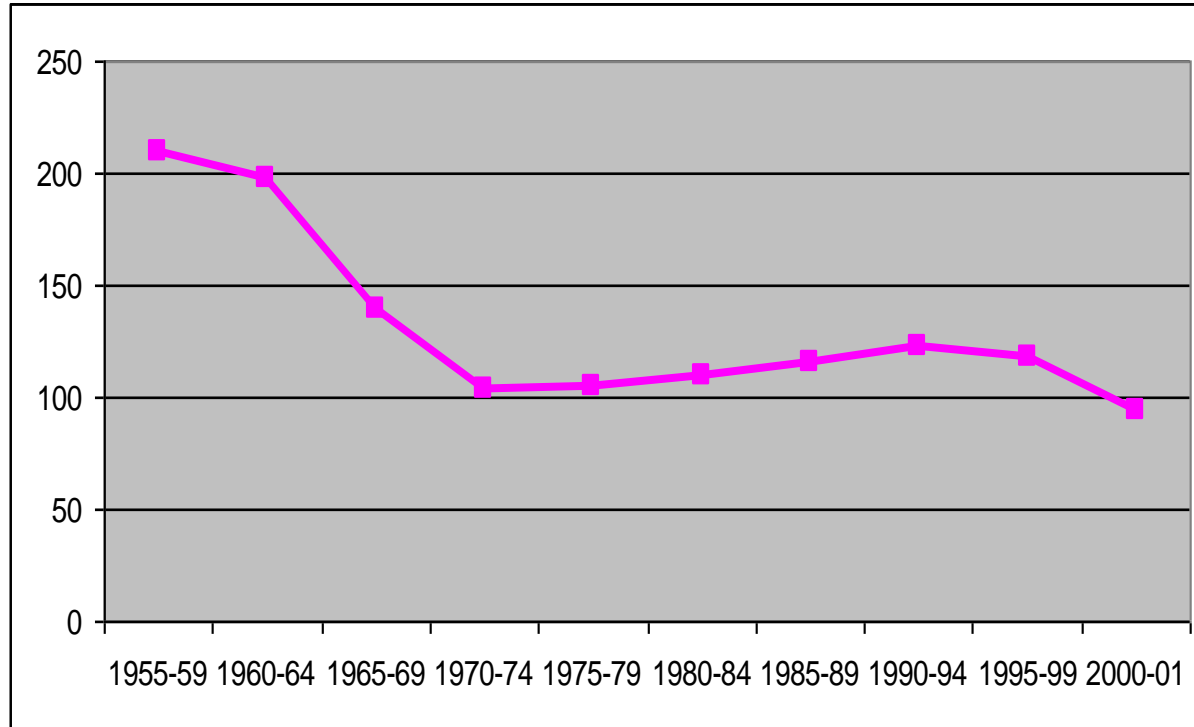
welcome trust

Child health in the new Millennium

- Annually >10.5 million children die each year
- Perinatal mortality ~ 4 million
- 48% of these deaths occur in Africa alone, 35% in SE Asia
- < 5 yrs (childhood) mortality falling from 1960's to 1990's by 3% per annum globally
- In many areas – arrested or even worsened in part of Africa

'The Silent Emergency'

Deaths in children <5 per 1000 live births



Papua New Guinea
Duke et al

- Many parts of Africa; decline stopped early/mid 90's – some getting worse
- Current projections: achieving MDG4 will take 'till 2035 (not 2015)

Millennium Developmental Goal 4: improving child survival

Aim

- To reduce child mortality rate of 1990 to two-thirds by 2015

Focus

- Improved nutrition, water and sanitation, prevention and early access to primary treatment (IMCI)

Improvements in acute care?

- Final illness ~ 1/4 access health care/ hospital for treatment
- Hospital based management important and highly cost effective means of improving survival
- Evidence based guidelines for treatmentrelatively neglected.....

Integrated Management of Childhood Illness: community based programme

Aims

- To improve first level of care for all conditions, identification and referral of sick to hospital in developing countries

Why?

- most deaths occur in the community (includes neonates)
- many referred children die before reaching hospital
- concern that promoting hospitals might detract from primary care

however.....

- little attention paid to issue of quality of care in hospital
- no international priority given to developing evidence base for management

Quality of hospital care : developing countries

- most seriously ill children present to district hospitals
- funding and resources largely allocated to tertiary institutions
- Most critically ill children are cared for where
 - resources are inadequate,
 - support from central agencies is lacking,
 - little ongoing professional development or staff training
 - staff morale is invariably low
- All impact adversely upon the quality of care

Themes for this talk:

Pragmatics and pitfalls for hospital management

- Reality of management of the sick child
- Evidence base for current guidelines
- Short coming of vertical programmes of management – independent guidelines
- Common misconceptions – reinforced through guidelines
- Implications for the WFPICCS Global Sepsis Initiative

What are the resources necessary to effectively manage a sick child?

- ✓ IMCI – priority signs: referred to local DGH

Reality –optimal care affected by

- Access to health facility: compounded by poor road access
- Rapid identification: limited use of triage
- Laboratory : often not reinforced through quality control
- Treatment
- Evidence based guidelines

**Delays in referral
compounded:
child presents at a
later stage of
illness**

Delivery of health care to children in Kenya reality check

14 hospitals across Kenya prospectively audited
(researchers and ministry of health)

- Absence of management protocols/ not followed
- Failure to provide basic health care
- Most treatment decisions unsupported diagnostic information
- Limited drug list/ 'stock outs' common

Theme 2 :
what is the evidence base for
management?

Efforts to improve hospital care

International Child Health Research Committee:

- International team of clinical scientists/ health professionals actively involved in patient care/policy
- Annual summaries of evidence in clinical trials- update guidelines

Direct input into WHO guidelines:

- ‘Management of the Child with a Serious Infection or Severe Malnutrition’
- ‘Guidelines for Management at a District Hospital’
- ‘New Pocket Book of Hospital Care for Children’

‘IMCI for hospitals’

POCKET BOOK
OF
**Hospital care
for children**

GUIDELINES FOR THE MANAGEMENT
OF COMMON ILLNESSES WITH
LIMITED RESOURCES



Shortcomings of current recommendations

- 'Vertical programmes of management' maintained – & non integrated approach to care of certain aspects
- Sepsis or SIRS +/- septic shock : not even considered as an entity
- Common physiological misconceptions – reinforced through these guidelines

Considerations for management of severely ill
child presenting in Africa?

Case history

how do the WHO guidelines perform?

- Pragmatics
- Pitfalls

Major considerations?

Initial management : which WHO guideline?

? Who

? Which solution

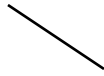
? How much

? What rate



Initial management : which WHO guideline?

Severe malaria



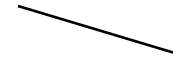
Sepsis/shock



Severe malnutrition



Diarrhoeal
disease



International recommendations: paediatric protocols

Special Article

Clinical practice parameters for hemodynamic support of pediatric and neonatal patients in septic shock*

Joseph A. Carcillo, MD; Alan I. Fields, MD; Task Force Committee Members

Background: The Institute of Medicine has called for the development of clinical guidelines and practice parameters to develop "best practice" and potentially improve patient outcome.

Objective: To provide American College of Critical Care Medicine clinical guidelines for hemodynamic support of neonates and children with septic shock.

Setting: Individual members of the Society of Critical Care Medicine with special interest in neonatal and pediatric septic shock were identified from literature review and general solicitation at Society of Critical Care Medicine Educational and Scientific Symposia (1998–2001).

Methods: The MEDLINE literature database was searched with the following age-specific keywords: sepsis, septicemia, septic shock, endotoxemia, persistent pulmonary hypertension, nitric oxide, and extracorporeal membrane oxygenation. More than 30 experts guard literature and drafted specific recommendations by using a modified Delphi method. More than 30 more experts then reviewed the compiled recommendations. The task-force chairman modified the document until <10% of experts disagreed with the recommendations.

Results: Only four randomized controlled trials in children with septic shock could be identified. None of these randomized trials led to a change in practice. Clinical practice has been based, for

the most part, on physiologic experiments, case series, and cohort studies. Despite relatively low American college of Critical Care Medicine-graded evidence in the pediatric literature, outcomes in children have improved from 97% mortality in the 1960s to 60% in the 1990s and 9% mortality in 1999. U.S. hospital survival was three-fold better in children compared with adults (9% vs. 27% mortality) in 1999. Shock pathophysiology and response to therapies is age-specific. For example, cardiac failure is a predominant cause of death in neonates and children, but vascular failure is a predominant cause of death in adults. Inotropes, vasodilators (children), inhaled nitric oxide (neonates), and extracorporeal membrane oxygenation can be more important contributors to survival in the pediatric populations, whereas vasopressors can be more important contributors to adult survival.

Conclusion: American College of Critical Care Medicine adult guidelines for hemodynamic support of septic shock have little application to the management of pediatric or neonatal septic shock. Studies are required to determine whether American College of Critical Care Medicine guidelines for hemodynamic support of pediatric and neonatal septic shock will be implemented and associated with improved outcome. (*Crit Care Med* 2002; 30:1365–1378)

Outcomes in neonatal and pediatric sepsis have improved with the advent of neonatal and pediatric intensive care (reduction in mortality from 97% to 9%) (1–3) and are markedly better than in adults (9% compared with 29% mortality) (3). The clinical practice parameters presented in this document are an attempt to provide a consensus statement on state-of-the-art hemodynamic support for neonates, infants, and children with septic shock. This document is designed to be an addendum to the previously published practice

parameters for hemodynamic support of adult sepsis (4). The reader who is in search of more detailed discussion of general principles in sepsis and cardiovascular support, or a more extensive reference list that concentrates on adult animal and human literature, is directed to this comprehensive document (4).

More than 30 clinical investigators and clinicians who were affiliated with the Society of Critical Care Medicine and who had special interest in hemodynamic support of pediatric patients with sepsis, were contacted and volunteered to be

members of the task force. Three invites declined to participate. Subcommittees were formed to review and grade the literature by using the evidence-based scoring system of the American College of Critical Care Medicine. The literature was accessed by using MEDLINE and indexing the following age-limited keywords: sepsis, septicemia, septic shock, endotoxemia, persistent pulmonary hypertension, nitric oxide, and extracorporeal membrane oxygenation (ECMO). The clinical parameters and guidelines were drafted by using a modification of the Delphi method. Briefly, the initial step included review of the literature and grading of the evidence by topic-based subcommittees during a 1-yr period. Of interest, the committee found only four randomized controlled trials in children that examined the effect of a hemodynamic support therapy on outcome from septic shock (5–8). Because of the pau-

guilines and clinical practice parameters for the critical care practitioner. New guidelines are practice parameters are continually developed and current ones are systematically reviewed and revised.

Address requests for reprints to: Joseph A. Carcillo, MD, Children's Hospital of Pittsburgh, Division of Critical Care Medicine, 2705 Fifth Avenue, Sixth Floor, Pittsburgh, PA 15261. E-mail: carcillo@upmc.edu
Copyright © 2002 by Lippincott Williams & Wilkins

*See also p. 1480.
From the American College of Critical Care Medicine.

The American College of Critical Care Medicine, which honors individuals for their achievements and contributions to multidisciplinary critical care medicine, is the consultative body of the Society of Critical Care Medicine that possesses recognized expertise in the practice of critical care. The College has developed administrative

Special Article

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

Brahm Goldstein, MD; Brett Giroir, MD; Adrienne Randolph, MD; and the Members of the International Consensus Conference on Pediatric Sepsis

Objective: Although general definitions of the sepsis continuum have been published for adults, no such work has been done for the pediatric population. Physiologic and laboratory variables used to define the systemic inflammatory response syndrome (SIRS) and organ dysfunction require modification for the developmental stages of children. An international panel of 20 experts in sepsis and clinical research from five countries (Canada, France, Netherlands, United Kingdom, and United States) was convened to modify the published adult consensus definitions of infection, sepsis, severe sepsis, septic shock, and organ dysfunction for children.

Design: Consensus conference.

Methods: This document describes the issues surrounding consensus on four major questions addressed at the meeting: a) How should the pediatric age groups affected by sepsis be delineated? b) What are the specific definitions of pediatric SIRS, infection, sepsis, severe sepsis, and septic shock? c) What are the specific definitions of pediatric organ failure and the validity of pediatric organ failure scores? d) What are the appropriate study populations and study and points required to successfully conduct clinical trials in pediatric sepsis? Five subgroups first met separately and then together to evaluate the following areas: signs and symptoms of sepsis, cell markers, cytokines, microbiological data, and coagulation vari-

ables. All conference participants approved the final draft of the proceedings of the meeting.

Results: Conference attendees modified the current criteria used to define SIRS and sepsis in adults to incorporate pediatric physiologic variables appropriate for the following subcategories of children: newborn, neonate, infant, child, and adolescent. In addition, the SIRS definition was modified so that either criteria for fever or white blood count had to be met. We also defined various organ dysfunction categories, severe sepsis, and septic shock specifically for children. Although no firm conclusion was made regarding a single appropriate study end point, a novel nonmortality end point, organ failure-free days, was considered optimal for pediatric clinical trials given the relatively low incidence of mortality in pediatric sepsis compared with adult populations.

Conclusion: We modified the adult SIRS criteria for children. In addition, we revised definitions of severe sepsis and septic shock for the pediatric population. Our goal is for these first-generation pediatric definitions and criteria to facilitate the performance of successful clinical studies in children with sepsis. (*Pediatr Crit Care Med* 2005; 6:2–8)

Key Words: sepsis; pediatric; consensus; child; critical care; intensive care; organ dysfunction; systemic inflammatory response syndrome

Based on the 1992 Consensus Conference on definitions for sepsis and organ failure, severe sepsis was defined in adult patients as sepsis associated with at least one acute organ dysfunction (1). This definition was upheld in the recent 2001 Consensus Conference (2). With the exception of certain pediatric-specific diagnostic criteria for sepsis introduced in the 2001 Consensus Conference report, little guidance or consensus exists in the

literature for the definition of pediatric systemic inflammatory response (SIRS) with infection, more generally termed pediatric sepsis.

Sepsis remains a major cause of morbidity and mortality among children (3–6). Sepsis-associated mortality in children decreased from 97% in 1969 (7) to 9% among infants in the early 1990s (8). A recent population-based study including SIRS, infection, sepsis, severe sepsis, septic shock, and multiple organ dysfunction syndrome (MODS) to aid in standardization of observational studies and evaluation of therapeutic interventions in clinical trials.

In an effort to address this need, a group of international experts in the field of adult and pediatric severe sepsis and clinical research gathered in 2002. A panel was chosen that consisted of published pediatric critical care physicians and physicians and scientists with clinical

Both the United States Food and Drug Administration and the U.S. Congress have recently emphasized the importance of testing biomedical therapeutics in children (10). As novel sepsis therapies continue to be developed, they will be increasingly evaluated in children. Thus, there is a need for a consensus definition of the pediatric sepsis continuum including SIRS, infection, sepsis, severe sepsis, septic shock, and multiple organ dysfunction syndrome (MODS) to aid in standardization of observational studies and evaluation of therapeutic interventions in clinical trials.

In an effort to address this need, a group of international experts in the field of adult and pediatric severe sepsis and clinical research gathered in 2002. A panel was chosen that consisted of published pediatric critical care physicians and physicians and scientists with clinical

literature for the definition of pediatric systemic inflammatory response (SIRS) with infection, more generally termed pediatric sepsis.

Although this represents a significant improvement over the past few decades, severe sepsis remains one of the leading causes of death in children, with >4,300 deaths annually (7% of all deaths among children) and estimated annual total costs of \$1.57 billion (9).

*See also p. 62.
PCCM, Oregon Health & Science University (OSU), Portland, OR; Children's Medical Center of Dallas (CMD), Dallas, TX; and Children's Hospital (CH), Boston, MA.
Sponsored, in part, by an unrestricted educational grant from GE Life and Composites.
Copyright © 2005 by the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies
DOI: 10.1097/01.PCC.000149131.7248.6B

Volume expansion

What is the evidence base?

Literature search to identify Randomised Trials in children with sepsis, diarrhoea, malaria, dengue haemorrhagic fever

The MEDLINE database was searched with the following MeSH terms:

- "Infant"[MeSH] OR "Child"[MeSH] OR "Child, Preschool"[MeSH] OR
- "Pediatrics"[MeSH]) AND "Fluid Therapy"[MeSH:NoExp]

These terms were combined with one of the following:

- "Shock, Septic"[MeSH:NoExp]
- "Sepsis"[MeSH]
- "Dengue Hemorrhagic Fever"[MeSH]
- "Malaria"[MeSH] OR "Malaria, Cerebral"[MeSH] OR "Malaria, Falciparum"[MeSH])
- "Hypovolemia"[MeSH]
- "Dehydration/therapy"[MAJR:No Exp] OR "Diarrhea/therapy"[MAJR:No Exp])

	Author, year	Setting/Disease	Sample size	Results
1	Akech, 2006	Kilifi District Hospital, Kilifi, Kenya Malaria and shock	88 (44=4.5% HAS; 44=Gelofusine)	No significant difference in mortality. Mortality not primary outcome
2	Juen, 2005	ED of Hospital Infantil Albert Sabin, Fortaleza, Ceara, Brazil Acute diarrhoea	36 (21=0.9% saline; 15=Polyelectrolyte Solution)	No difference in Volumes required or time to rehydration
3	Wills, 2005	PICU Hospital of Tropical Diseases, Ho Chi Minh City, Vietnam Dengue Haemorrhagic Fever & shock	512 Moderate: 126 (Dextran) 129 (Starch) 128 (Ringers) 129 Severe: 67 (Dextran) 62 (Starch)	No difference in either severity group
4	Upadhyay, 2005	PICU and ED in a tertiary care and teaching hospital, India Septic Shock	60 (31=N saline; 29= Gelatin polymer)	No difference between groups
5	Maitland, 2005	PHDU KEMRI-KDH, Kilifi, Kenya Malaria and shock	150 49 Severe (23=albumin; 26=saline;) Moderate (33=albumin; 35=saline; 33=control)	Mortality lower with albumin than with saline (3.6% v 18%, p=0.13)
6	Maitland, 2005	PHDU KEMRI-KDH, Kilifi, Kenya Malarial anaemia and shock	61 (20=saline; 23=albumin; 18=control)	Similar reduction in base excess in all three groups
7	Ngo, 2001	ICU of Dong Nai Paediatric Hospital, Vietnam- Dengue Haemorrhagic Fever & shock	230 (222 III, 8 IV); 55 (Ringer's lactate) 55 (dextran) 56 (N saline) 56 (gelatin)	No clear advantage to using any one of the four fluids
8	Dung, 1999	PICU Hospital of Tropical Diseases, Ho Chi Minh City, Vietnam Dengue Haemorrhagic Fever & shock	50 (12=saline; 12=dextran 70; 13=Ringer's;13=gelafundin)	Dextran 70 preferred solution for acute resuscitation in DSS

Initial management : which WHO guideline?

Severe malaria

- Treat dehydration only
- Shock?? : Only give fluid to ensure **CVP 0-5cm!**
- No fluid specified but rehydration linked to quinine infusion (4 hrs)

Picture of child

Severe malnutrition

Septic shock: As above + Imp. consciousness

Treat: 0.45% saline/ ½ strength Darrow's 15 mls/kg in 1 hr

No improvement: whole blood Tx (10mls/kg in 4hrs)

'Shock'

Only consider if cold hands and feet,
plus CRT>3 AND weak fast pulse

20mls/kg Ringers L or 0.9% saline
Repeat if not improving
(caution++ about fluid overload)

Diarrhoeal disease

Severe dehydration: 100mls/kg
30mls/kg Ringers L or 0.9% saline
Repeat if pulse volume weak
Rehydrate with 70ml/kg over 2.5 hr*

(*or 5hr if <1yr)

Clinical distinction: Severe malaria and sepsis

- Malaria often over diagnosed
- Sepsis/other conditions underdiagnosed / under treated
- Overlap in clinical presentation
- Co-morbidity – both may coexist
- Supportive laboratory confirmation – too late as early mortality substantial

High early mortality: Kilifi data 2002/2005 (unpublished)

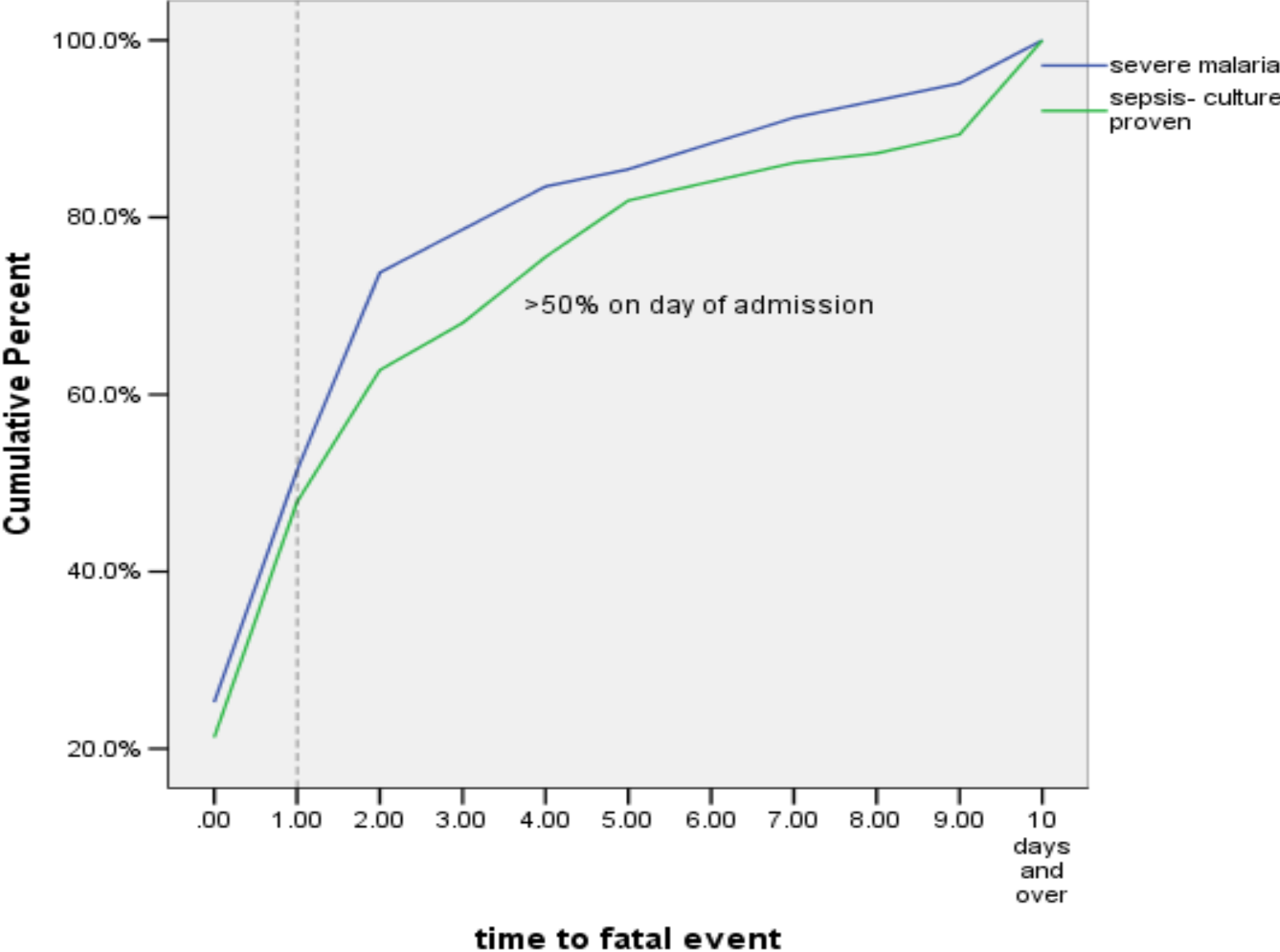


CHART 2. Triage of all sick children

ment(s), call for help, draw blood for
ations (glucose, malaria smear, Hb)

ASSESS

Airway and breathing

- Obstructed breathing,
or
- Central cyanosis,
or
- Severe respiratory distress

ANY SIGN
POSITIVE

Circulation

- Cold hands with:
- Capillary refill longer than 3 seconds,
and
 - Weak and fast pulse

ANY SIGN
POSITIVE

Check for
severe
malnutrition

TREAT

Do not move neck if cervical spine injury possible

If foreign body aspiration

- Manage airway in choking child (Chart 3)

If no foreign body aspiration

- Manage airway (Chart 4)
- Give oxygen (Chart 5)
- Make sure child is warm

- Stop any bleeding
- Give oxygen (Chart 5)
- Make sure child is warm

If no severe malnutrition:

- Insert IV and begin giving fluids rapidly (Chart 7)
- If not able to insert peripheral IV, insert an intraosseous or external jugular line (see pages 310, 312)

If severe malnutrition:

- If lethargic or unconscious:*
- Give IV glucose (Chart 10)
 - Insert IV line and give fluids (Chart 8)

If not lethargic or unconscious:

- Give glucose orally or by NG tube
- Proceed immediately to full assessment and treatment

Who should receive volume expansion?

WHO Shock defined as.....

Cold hands PLUS
Weak pulse AND
Capillary refill time > 3

Too little, too late

Bacterial sepsis :
Prevalence 15/228 (7%);
Case fatality mortality = 78%

Assessment of circulation status



Common misconceptions

- '.....examine frequently for signs of fluid overload. The most reliable sign is an enlarged liver'.

	Enlarged liver	Enlarged spleen
Severe malaria	28%	33%
Sepsis	22%	28%

- 'Additional signs are gallop rhythm, fine crackles at lung bases and/or fullness of neck veins when upright'.

Misconception 2: Hypovolaemia is not synonymous
with dehydration

What are the implications for the sepsis initiative?

Early Reversal of Pediatric-Neonatal Septic Shock by Community Physicians Is Associated With Improved Outcome

Yong Y. Han, MD*§; Joseph A. Carcillo, MD*‡§; Michelle A. Dragotta, RN§; Debra M. Bills, RN§; R. Scott Watson, MD, MPH*‡§; Mark E. Westerman, RT§; and Richard A. Orr, MD*‡§

ABSTRACT. *Objective.* Experimental and clinical studies of septic shock support the concept that early resuscitation with fluid and inotropic therapies improves survival in a time-dependent manner. The new *American College of Critical Care Medicine-Pediatric Advanced Life Support (ACCM-PALS) Guidelines* for hemodynamic support of newborns and children in septic shock recommend this therapeutic approach. The objective of this study was to determine whether early septic shock reversal and use of resuscitation practice consistent with the new ACCM-PALS Guidelines by community physicians is associated with improved outcome.

Methods. A 9-year (January 1993–December 2001) retrospective cohort study was conducted of 91 infants and children who presented to local community hospitals with septic shock and required transport to Children's Hospital of Pittsburgh. Shock reversal (defined by return of normal systolic blood pressure and capillary refill time), resuscitation practice concurrence with ACCM-PALS Guidelines, and hospital mortality were measured.

Results. Overall, 26 (29%) patients died. Community physicians successfully achieved shock reversal in 24 (26%) patients at a median time of 75 minutes (when the transport team arrived at the patient's bedside), which was associated with 96% survival and >9-fold increased odds of survival (9.49 [1.07–83.89]). Each additional hour of persistent shock was associated with >2-fold increased odds of mortality (2.29 [1.19–4.44]). Nonsurvivors, compared with survivors, were treated with more inotropic therapies (dopamine/dobutamine [42% vs 20%] and epinephrine/norepinephrine [42% vs 6%]) but not

mote ACCM-PALS recommended rapid, stepwise escalations in fluid as well as inotropic therapies may have value in improving outcomes in these children. *Pediatrics* 2003;112:793–799; *fluid resuscitation, inotropes, interfacility transport, hydrocortisone.*

ABBREVIATIONS. ACCM, American College of Critical Care Medicine; AHA, American Heart Association; PALS, Pediatric Advanced Life Support; CHP, Children's Hospital of Pittsburgh; SBP, systolic blood pressure; PRISM, Pediatric Risk of Mortality; PICU, pediatric intensive care unit.

Experimental and clinical studies of septic shock support the concept that persistent shock has an adverse impact on survival in a time-dependent manner.^{1–4} Recently, a randomized, controlled study of adult septic shock showed that early aggressive goal-directed resuscitation in the emergency department improves outcome.⁵ Although comparable randomized studies in children are lacking, the reported pediatric literature has been consistent with both experimental studies and the adult experience. We previously reported a role for early, aggressive fluid resuscitation in pediatric septic shock.⁶ Nadel et al⁷ (at St. Mary's Hospital in London, England) attributed poor outcome from severe meningococcal disease to delayed recognition and treatment. Booy et al⁸ extended their findings at St. Mary's Hospital by reporting decreased mortality from meningococ-

Phase III: Pragmatic trial

Application of Critical care approach works.....

- Sepsis/malaria trial run in parallel
- Enrolment- bedside criteria alone
- Results relevant to clinical practice entry criteria wont include sophisticated point of care analysis
- 3 arm trial albumin saline and control

If benefits of volume expansion confirmed

- Demonstration that improved outcome can come through effective delivery of emergency care
- Management of the sick child: protocol implemented by bedside assessments
- Rationale for generic approach to management
- Dispel common misconceptions
- Major changes in policy and rationalise fluid management

Finally.....Scope of programme (+/-advocacy)?

- Revolution in management of critically sick child barely affected children in developing countries
 - High early mortality on appropriate chemotherapy
 - Common physiological misconceptions – reinforced through these guidelines
- Demonstrate that improved outcome can come through effective delivery of emergency care- simple targets
- Equitable roll-out of new programmes or new interventions impossible unless functioning hospital sector

Thank you