SEPSIS: UPDATE ON TREATMENT GUIDELINE

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1st INTERNATIONAL CRITICAL CARE AND EMERGENCY MEDICINE CONGRESS
NOVEMBER 6-8, 2013
THE GREEN PARK PENDİK HOTEL- İSTANBUL

DEFINITIONS

stop sepsis save lives

SEPSIS The most common, but least recognized disease.

1991

American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis.

Crit Care Med. 1992 Jun;20(6):864-74

2001

2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference.

Crit Care Med. 2003 Apr;31(4):1250-6.

2004
2008
2012

Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012.

Crit Care Med. 2013 Feb;41(2):580-637

What is sepsis?

stop sepsis save lives

- **Lots of terms!!**
  - Sepsis
  - Septic Shock,
  - SIRS
  - SSI (signs and symptoms of infection),
  - Septicaemia, Bacteraemia,
  - Toxic Shock Syndrome,
  - Bloodstream infection etc, etc ….

TABLE 1. Diagnostic Criteria for Sepsis

Infection, documented or suspected, and some of the following:
General variables
Fever (> 38.3°C)
Hypothermia (core temperature < 36°C)
Heart rate > 90/min^{-1} or more than two SD above the normal value for age
Tachypnea
Altered mental status
Significant edema or positive fluid balance (> 20 mL/kg over 24 hr)
Hyperglycemia (plasma glucose > 140 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 greater than 10% immature forms
Plasma C-reactive protein more than two SD above the normal value
Plasma procalcitonin more than two SD above the normal value
Hemodynamic variables
Arterial hypotension (SBP < 90 mm Hg, MAP < 70 mm Hg, or an SBP decrease > 40 mm Hg in adults or less than two SD below normal for age)
Organ dysfunction variables
Arterial hypoxemia (Pao_2/Fio_2 < 300)
Acute oliguria (urine output < 0.5 mL/kg/hr for at least 2 hrs despite adequate fluid resuscitation)
Creatinine increase > 0.5 mg/dL or 44.2 μmol/L
Coagulation abnormalities (INR > 1.5 or aPTT > 60 s)
Ileus (absent bowel sounds)
Thrombocytopenia (platelet count < 100,000 μL^{-1})
Hyperbilirubinemia (plasma total bilirubin > 4 mg/dL or 70 μmol/L)
Tissue perfusion variables
Hyperlactatemia (> 1 mmol/L)
Decreased capillary refill or mottling

WBC = white blood cell; SBP = systolic blood pressure; MAP = mean arterial pressure; INR = international normalized ratio; aPTT = activated partial thromboplastin time.

Diagnostic criteria for sepsis in the pediatric population are signs and symptoms of inflammation plus infection with hyper- or hypothermia (rectal temperature > 38.5° or < 35°C), tachycardia (may be absent in hypothermic patients), and at least one of the following indications of altered organ function: altered mental status, hypoxemia, increased serum lactate level, or bounding pulses.

Adapted from Levy MM, Fink MP, Marshall JC, et al: 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. *Crit Care Med* 2003; 31: 1250–1256.

Crit Care Med. 2013;41(2):580.

stop sepsis save lives

TABLE 2. Severe Sepsis

Severe sepsis definition = sepsis-induced tissue hypoperfusion or organ dysfunction (any of the following thought to be due to the infection)
Sepsis-induced hypotension
Lactate above upper limits laboratory normal
Urine output < 0.5 mL/kg/hr for more than 2 hrs despite adequate fluid resuscitation
Acute lung injury with Pao_2/Fio_2 < 250 in the absence of pneumonia as infection source
Acute lung injury with Pao_2/Fio_2 < 200 in the presence of pneumonia as infection source
Creatinine > 2.0 mg/dL (176.8 μmol/L)
Bilirubin > 2 mg/dL (34.2 μmol/L)
Platelet count < 100,000 μL
Coagulopathy (international normalized ratio > 1.5)

Adapted from Levy MM, Fink MP, Marshall JC, et al: 2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference. *Crit Care Med* 2003; 31: 1250–1256.

Crit Care Med. 2013;41(2):580.

World Sepsis Day …

stop sepsis save lives

THE GLOBAL SEPSIS ALLIANCE

World wide: **1,930 supporter**
Hospitals and health care related organizations: **1,099**
Health care workers: **658**
Private individuals: **165**

www.world-sepsis-day.org/

September 13 2013 | World Sepsis Day

stop sepsis save lives

- **Globally 20 to 30 million patients are estimated to be afflicted every year**
- **Over 6 million cases of neonatal and early childhood death due to sepsis**
- **Over 100 000 cases of maternal death due to sepsis**
- **Hospital mortality rate 30-60%**
- **A person dies from sepsis every 3-4 seconds**

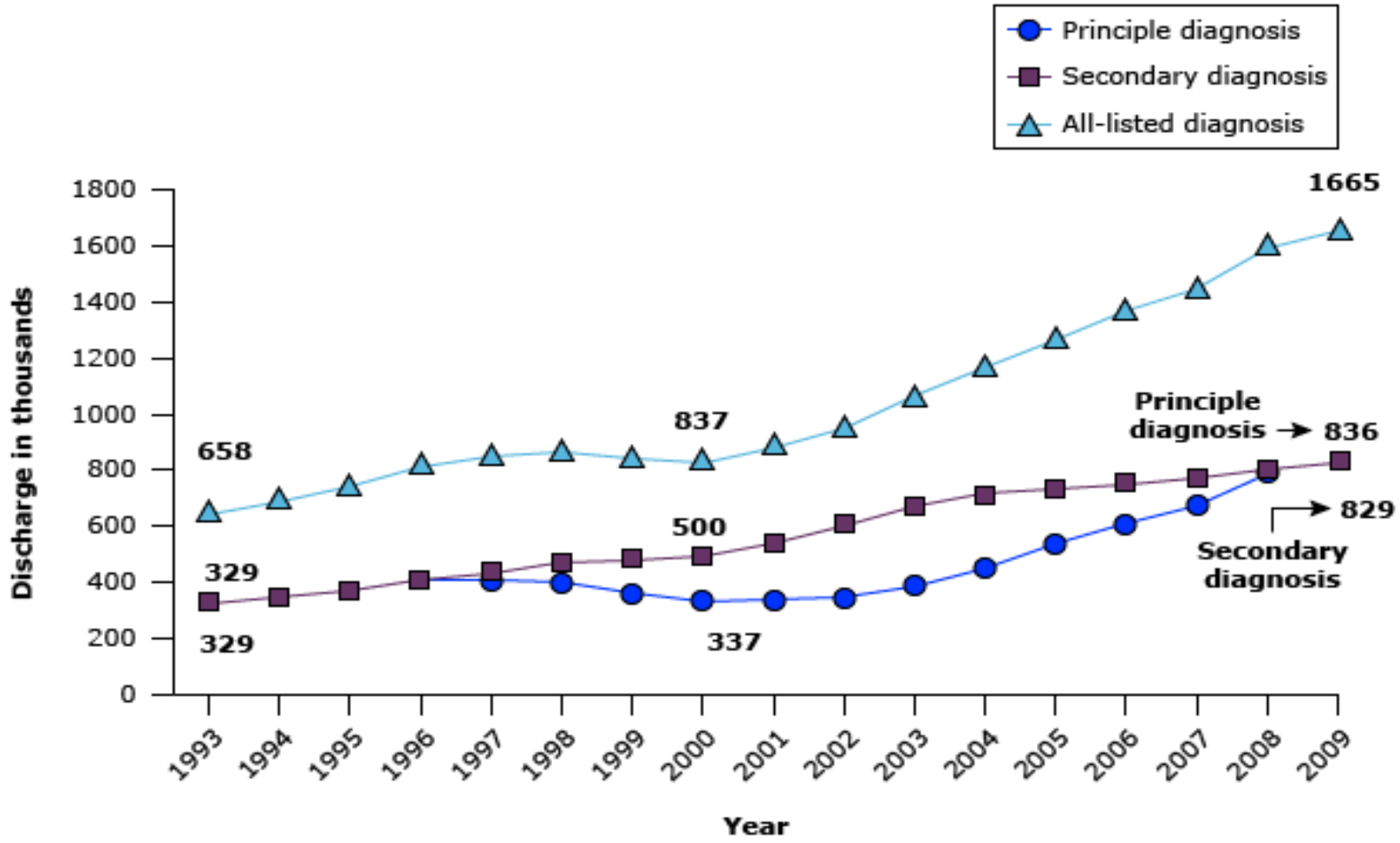
September 13 2013 | World Sepsis Day

Celebrities and Sepsis

Anyone can get Sepsis, even celebrities. These celebrities are Sepsis's victims.

The detailed list of famous people who died of Sepsis

10% annual increase in sepsis diagnosis: 1993-2009

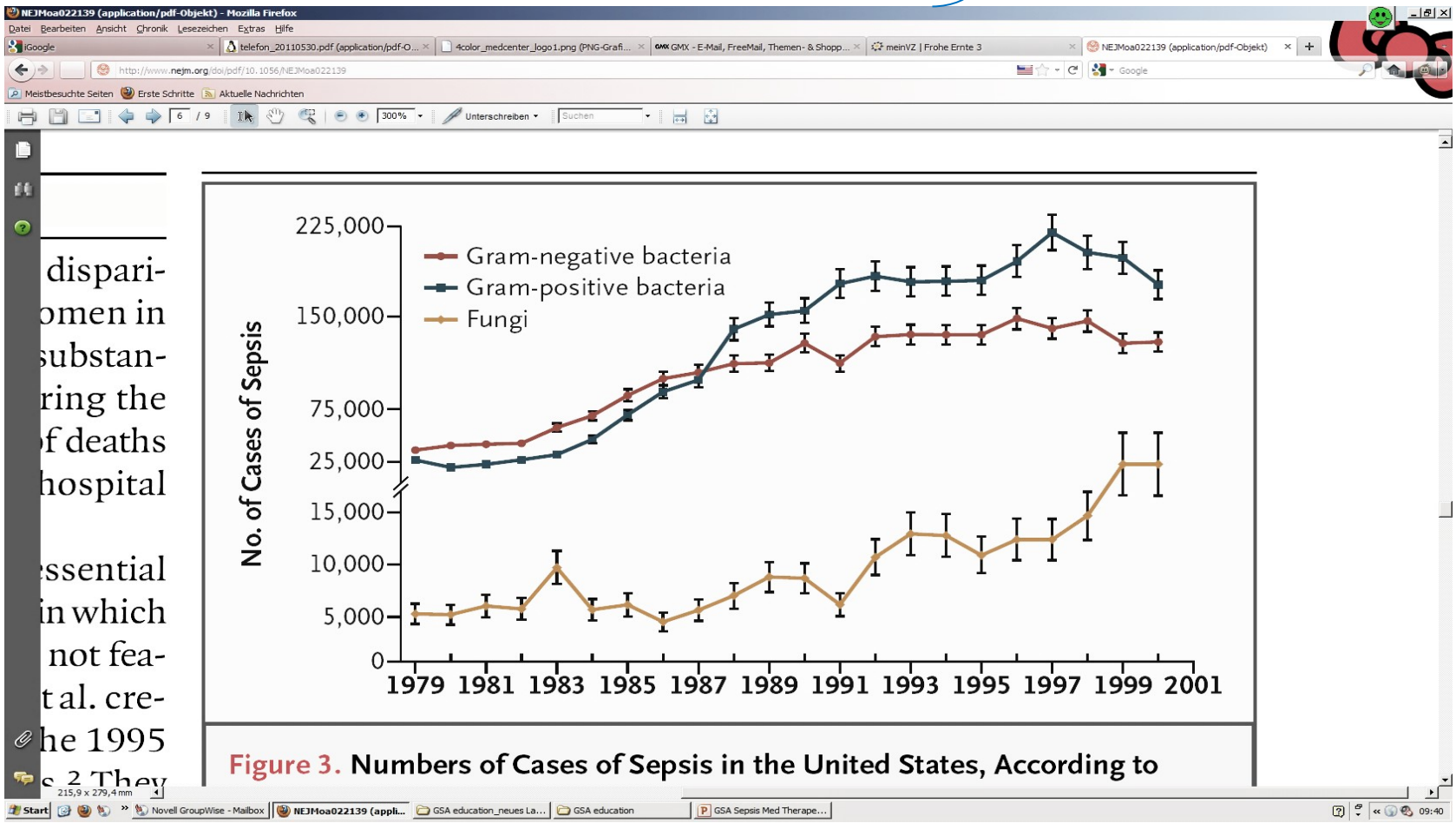


In the United States between 2000 and 2009, hospital stays with a principal diagnosis of septicemia increased 148 percent (10.6 percent annually), while those with secondary diagnoses of septicemia increased by only 66 percent (5.8 percent annually).

Reproduced from: Agency for Healthcare Research and Quality Center for Delivery, Organization, and Markets. Healthcare Cost and Utilization Project, Nationwide Inpatient Sample, 1993-2009

Organisms Found in Sepsis

- Community origin
- Nosocomial origin



Only about 30% have a positive blood culture

Martin et al, NEJM 2003:348;1546-54.

Clinical practice parameters for hemodynamic support of pediatric and neonatal septic shock: 2007 update from the American College of Critical Care Medicine*

Joe Brierley, MD; Joseph A. Carcillo, MD; Karen Choong, MD; Tim Cornell, MD; Allan DeCaen, MD; Andreas Deymann, MD; Allan Doctor, MD; Alan Davis, MD; John Duff, MD; Marc-Andre Dugas, MD; Alan Duncan, MD; Barry Evans, MD; Jonathan Feldman, MD; Kathryn Felmet, MD; Gene Fisher, MD; Lorry Frankel, MD; Howard Jeffries, MD; Bruce Greenwald, MD; Juan Gutierrez, MD; Mark Hall, MD; Yong Y. Han, MD; James Hanson, MD; Jan Hazelzet, MD; Lynn Hernan, MD; Jane Kiff, MD; Niranjan Kissoon, MD; Alexander Kon, MD; Jose Irazusta, MD; John Lin, MD; Angie Lorts, MD; Michelle Mariscalco, MD; Renuka Mehta, MD; Simon Nadel, MD; Trung Nguyen, MD; Carol Nicholson, MD; Mark Peters, MD; Regina Okhuysen-Cawley, MD; Tom Poulton, MD; Monica Relves, MD; Agustin Rodriguez, MD; Ranna Rozenfeld, MD; Eduardo Schnitzler, MD; Tom Shanley, MD; Sara Skache, MD; Peter Skippen, MD; Adalberto Torres, MD; Bettina von Dessauer, MD; Jacki Weingarten, MD; Timothy Yeh, MD; Arno Zaritsky, MD; Bonnie Stojadinovic, MD; Jerry Zimmerman, MD; Aaron Zuckerberg, MD

Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012

R. Phillip Dellinger, MD[1]; Mitchell M. Levy, MD[2]; Andrew Rhodes, MB BS[3]; Djillali Annane, MD[4]; Herwig Gerlach, MD, PhD[5]; Steven M. Opal, MD[6]; Jonathan E. Sevransky, MD[7]; Charles L. Sprung, MD[8]; Ivor S. Douglas, MD[9]; Roman Jaeschke, MD[10]; Tiffany M. Osborn, MD, MPH[11]; Mark E. Nunnally, MD[12]; Sean R. Townsend, MD[13]; Konrad Reinhart, MD[14]; Ruth M. Kleinpell, PhD, RN-CS[15]; Derek C. Angus, MD, MPH[16]; Clifford S. Deutschman, MD, MS[17]; Flavia R. Machado, MD, PhD[18]; Gordon D. Rubenfeld, MD[19]; Steven A. Webb, MB BS, PhD[20]; Richard J. Beale, MB BS[21]; Jean-Louis Vincent, MD, PhD[22]; Rui Moreno, MD, PhD[23]; and the Surviving Sepsis Campaign Guidelines Committee including the Pediatric Subgroup*

PEDIATRIC CONSIDERATIONS IN SEVERE SEPSIS (TABLE 9)

While sepsis in children is a major cause of death in industrialized countries with state-of-the-art ICUs, the overall mortality from severe sepsis is much lower than that in adults, estimated at about 2% to 10% (497–499). The hospital mortality rate for severe sepsis is 2% in previously healthy children and 8% in chronically ill children in the United States (497). Definitions of sepsis, severe sepsis, septic shock, and multiple organ dysfunction/failure syndromes are similar to adult definitions but depend on age-specific heart rate, respiratory rate, and white blood cell count cutoff values (500, 501). This document provides recommendations only for term newborns and children in the industrialized resource-rich setting with full access to mechanical ventilation ICUs.

Crit Care Med. 2013;41(2):580.

Intensive Care Med
DOI 10.1007/s00134-012-2468-5

SPECIAL ARTICLE

Recommendations for sepsis management in resource-limited settings

Martin W. Dünser
Emir Festic
Arjen Dondorp
Niranjan Kissoon
Tsenddorj Ganbat
Arthur Kwizera
Rashan Haniffa
Tim Baker
Marcus J. Schultz
Global Intensive Care Working Group of the European Society of Intensive Care Medicine

Published online: 14 February 2012

WHAT IS BENEFIT OF USAGE OF SEPSIS GUIDELINES?

*** 100% survival when fluid resustation was provided to children with denque shock**

**** Early Usage of 2002 guideline in the comunity hospital improved newborns and children mortality from 38% to 8%**

***** Usage of 2002 guideline with continous central venous O2 saturation monitoring, and directed to maintance of Scvo2 >70%, reduced mortality from 39% to 12%**

*N Engl J Med. 2005 Sep 1;353(9):877-89., **Pediatrics. 2003 Oct;112(4):793-9.
***Intensive Care Med. 2008 Jun;34(6):1065-75

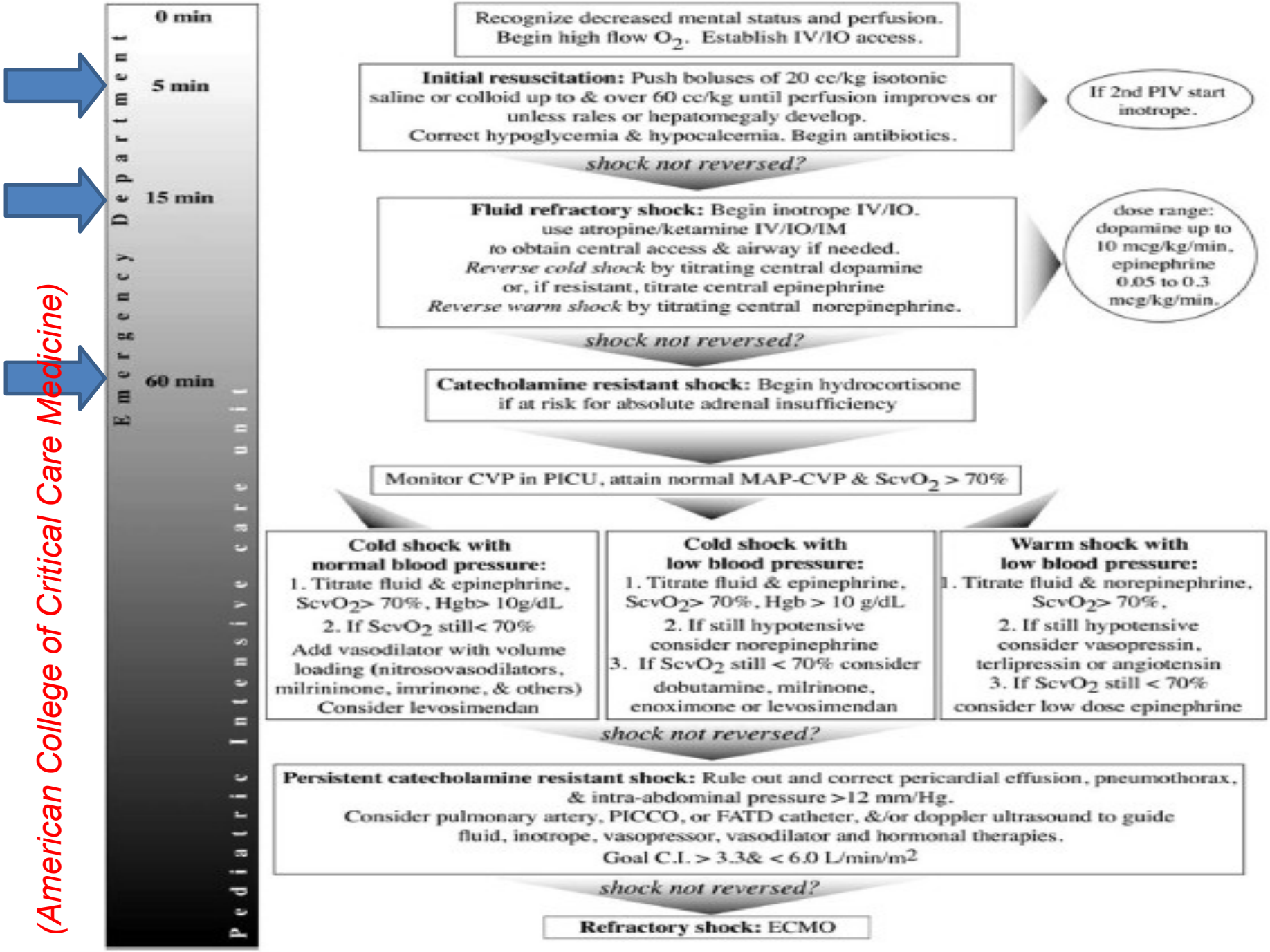
GOLDEN HOUR

- **Early regognation and treatmet is very important**
- **First 1 hour resuscitation is critical**

« Each hour delay in initiation of appropriate resuscitation significant increase risk of mortality; odds ratio > 2 »

Early reversal of pediatric-neonatal septic shock by community physicians is associated with improved outcome.

Pediatrics. 2003 Oct;112(4):793-9.


0 min
5 min
15 min
60 min
Emergency Department
Pediatric Intensive care unit
(American College of Critical Care Medicine)
Recognize decreased mental status and perfusion.
Begin high flow O_2. Establish IV/IO access.
Initial resuscitation: Push boluses of 20 cc/kg isotonic saline or colloid up to & over 60 cc/kg until perfusion improves or unless rales or hepatomegaly develop.
Correct hypoglycemia & hypocalcemia. Begin antibiotics.
If 2nd PIV start inotrope.
shock not reversed?
Fluid refractory shock: Begin inotrope IV/IO.
use atropine/ketamine IV/IO/IM
to obtain central access & airway if needed.
Reverse cold shock by titrating central dopamine
or, if resistant, titrate central epinephrine
Reverse warm shock by titrating central norepinephrine.
dose range:
dopamine up to 10 mcg/kg/min,
epinephrine 0.05 to 0.3 mcg/kg/min.
shock not reversed?
Catecholamine resistant shock: Begin hydrocortisone if at risk for absolute adrenal insufficiency
Monitor CVP in PICU, attain normal MAP-CVP & $ScvO_2$ > 70%
Cold shock with normal blood pressure:
1. Titrate fluid & epinephrine, $ScvO_2$> 70%, Hgb> 10g/dL
2. If $ScvO_2$ still< 70%
Add vasodilator with volume loading (nitrosovasodilators, milrininone, imrinone, & others)
Consider levosimendan
Cold shock with low blood pressure:
1. Titrate fluid & epinephrine, $ScvO_2$> 70%, Hgb > 10 g/dL
2. If still hypotensive consider norepinephrine
3. If $ScvO_2$ still < 70% consider dobutamine, milrinone, enoximone or levosimendan
Warm shock with low blood pressure:
1. Titrate fluid & norepinephrine, $ScvO_2$> 70%,
2. If still hypotensive consider vasopressin, terlipressin or angiotensin
3. If $ScvO_2$ still < 70%
consider low dose epinephrine
shock not reversed?
Persistent catecholamine resistant shock: Rule out and correct pericardial effusion, pneumothorax, & intra-abdominal pressure >12 mm/Hg.
Consider pulmonary artery, PICCO, or FATD catheter, &/or doppler ultrasound to guide fluid, inotrope, vasopressor, vasodilator and hormonal therapies.
Goal C.I. > 3.3& < 6.0 L/min/m^2
shock not reversed?
Refractory shock: ECMO

A. INITIAL RESUSCITATION in 5 Minutes

- **For respiratory distress and hypoxemia**

✓ Start with face mask oxygen or if needed and available, high flow nasal cannula oxygen or nasopharyngeal CPAP, if needed mechanical ventilation

- **For improved circulation, peripheral intravenous access or intraosseus access can be used when a central line is not available**

✓ İnitial therapeutic end points of resuscitation of septic shock:

- Capillary refil of ≤ 2 secs, normal blood pressure for age, normal pulses, warm extremities, urine output > 1 mL/kg/hr and normal mental status.
- Scvo2 saturation ≥ 70% and cardiac index between 3.3 and 6.0 L/min/m2 should be targeted.

- **Follow American College of Critical Care Medicine-Pediatric Life Suport quidelines**

- **Evaluate for and reverse pneumothorax, pericardial tamponade, or endocrine emergencies in patients with refractory shock**

Crit Care Med. 2013;41(2):580.

A. INITIAL RESUSCITATION in 5 Minutes

stop sepsis save lives

(American College of Critical Care Medicine)

PUSH BOLUSES OF 20 cc/kg ISOTONIC SALINE OR COLLOID UP TO OVER 60 cc/kg PERFUSION IMPROVES OR RALLES OR HEPATOMEGALY DEVELOP

↓

CORRECT HYPOGLEYCEMIA AND HYPERCALCEMIA, BEGIN ANTIBIOTICS

↓

Check?
SHOCK NOT REVERSED?

↓

FLUID REFRACTORY SHOCK

A. INITIAL RESUSCITATION

stop sepsis save lives

If needed ıntubation should be done with using rapid sequence intubation

- **For sedation ketamine is preferable**
- **Etomidate SHOULD NOT be used routinely**
- **Thiopental and propofol are associated with hypotension should be avoided in children**

B. ANTIBIOTICS AND SOURCE CONTROL-I

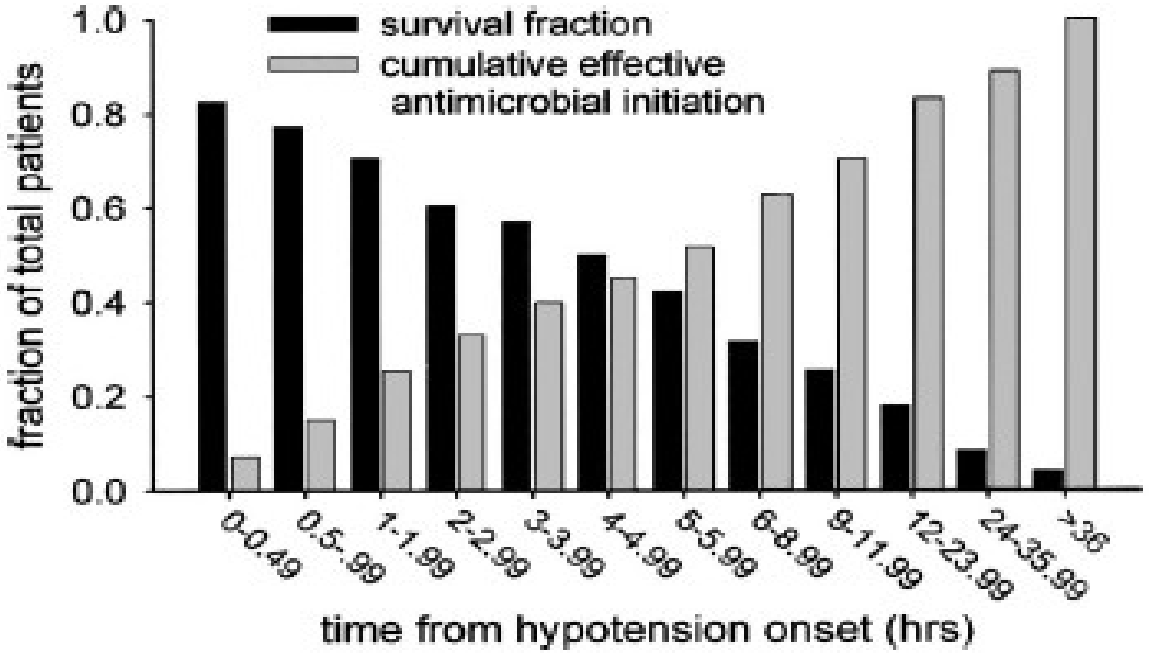
stop sepsis save lives

- Empiric antibiotics should be administered within 1 hr of the idendification of severe sepsis.
- Blood cultures should be obtained before antibx therapy but this should not delay initiation of antibiotics.
- Antibiotics choice should be targeted with respect to epidemic and endemic etiologies.
- Consider clindamycin and anti-toxin therapies for toxic shock syndromes with refractory hypotension
- Early and aggressive source control
- Clostridum difficile colitis should be treated with enteral antibiotics if tolerated. oral vancomycine is prefered for severe disease.

Crit Care Med. 2013;41(2):580.

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



GOLDEN HOUR **Each hour delay in antibiotics administration 8% increase in mortality**

B. ANTIBIOTICS AND SOURCE CONTROL-II

- **Children > 28 days of age who are normal host**

Vancomycin (15 mg/kg, max 1 to 2 g) PLUS cefotaxime (100 mg/kg, max 2 g) OR ceftriaxone

- **Cildren > 28 days who are immunosupressed or at risk for infection Pseudomonas spp**

Vancomycin (15 mg/kg, max 1 to 2 g) PLUS cefepime (50 mg/kg) OR ceftazidime

- **Children who have recently received broad-spectrum antibiotics**

Vancomycin (15 mg/kg, max 1 to 2 g) PLUS Meropenem

FLUID REFRACTORY SHOCK

(American College of Critical Care Medicine)

BEGIN INOTROPE IV/IO

Dopamine up to 10 mcg/kg/min, Epinephrine 0.05 -0 0.3 mcg/kg/min

USE ATROPHINE/KETAMINE IV-IO-IM
To obtain central acces & airway if needed

REVERSE COLD SHOCK
by titrating central dopamine or
If resistant titrate central epinephrine

REVERSE WARM SHOCK
by titrating central norepinephrine

Check?
SHOCK NOT REVERSED?

CATECHOLOMINE RESISTANT SHOCK

CATECHOLOMINE RESISTANT SHOCK

(American College of Critical Care Medicine)

BEGIN HYDROCORTISONE
If at risk for absolute adrenal insufficiency

MONITOR CVP in PICU, attain normal MAP-CVP & Scvo2 > 70%

COLD SHOCK WITH NORMAL BLOOD PRESSURE

1. Titrate fluid & Epinephrine
   Scvo2 > 70% , Hb> 10 g/dL

2. If Scvo2 still < 70%
   add vasodilator with volume loading
   (nitrovasodilators, milrininone,imrinone)
   Consider levosimendan

COLD SHOCK WITH LOW BLOOD PRESSURE

1. Titrate fluid & Epinephrine
   Scvo2 > 70% , Hb> 10 g/dL
2. If still hypotensive consider norepinephrine
3. If Scvo2 still < 70%
   consider dobutamine,milrininone,imrinone
   enoximone or levosimendan

WARM SHOCK WITH LOW BLOOD PRESSURE

1. Titrate fluid & norepinephrine
   Scvo2 > 70% ,
2. If still hypotensive consider vasopressin,
   terlipresin, or angiotensin
3. If Scvo2 still < 70%
   consider low dose epinephrine

SHOCK NOT REVERSED?

PERSISTENT CATECHOLOMINE RESISTANT SHOCK

PERSISTENT CATECHOLOMINE RESISTANT SHOCK

(American College of Critical Care Medicine)

RULE OUT AND CORRECT PERICARDIAL EFFUSION, PNEUMOTHORAX &/OR intra-abdominal pressure > 12 mmHG

CONSIDER PULMPNARY ARTERY, PICCO OR FATD cathater &/or doppler ultrasound to quide fluid, inotrope, vasopressor, vasodilator and hormonal therapies

GOAL CARDIAC INDEX > 3.3 < 6.0 L/min/m2

SHOCK NOT REVERSED?

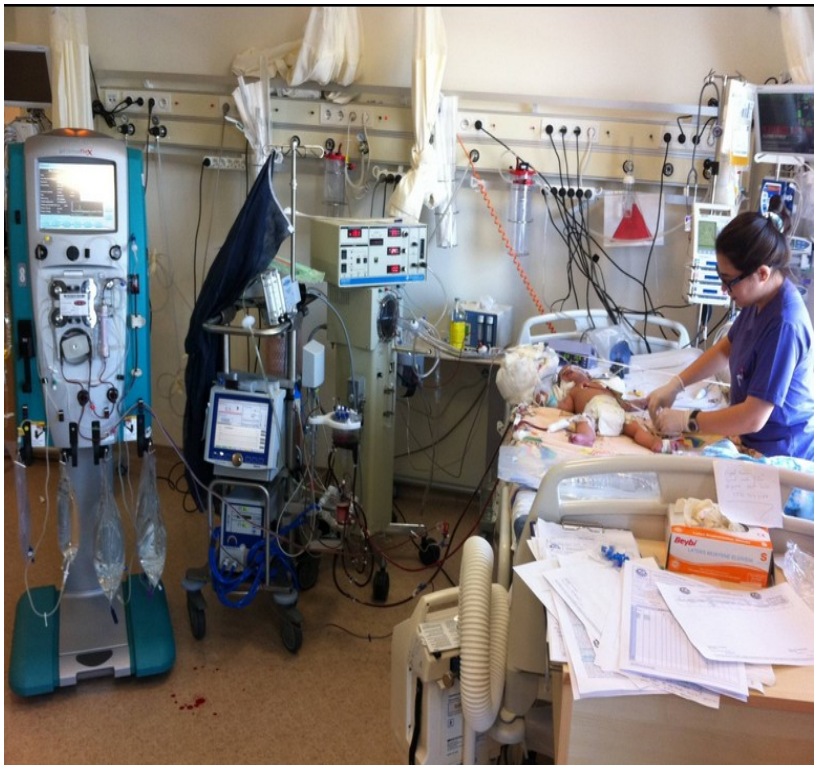
REFRACTORY SHOCK

REFRACTORY SHOCK

(American College of Critical Care Medicine)

EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO)

Consider ECMO for refractory pediatric septic shock and respiratory failure



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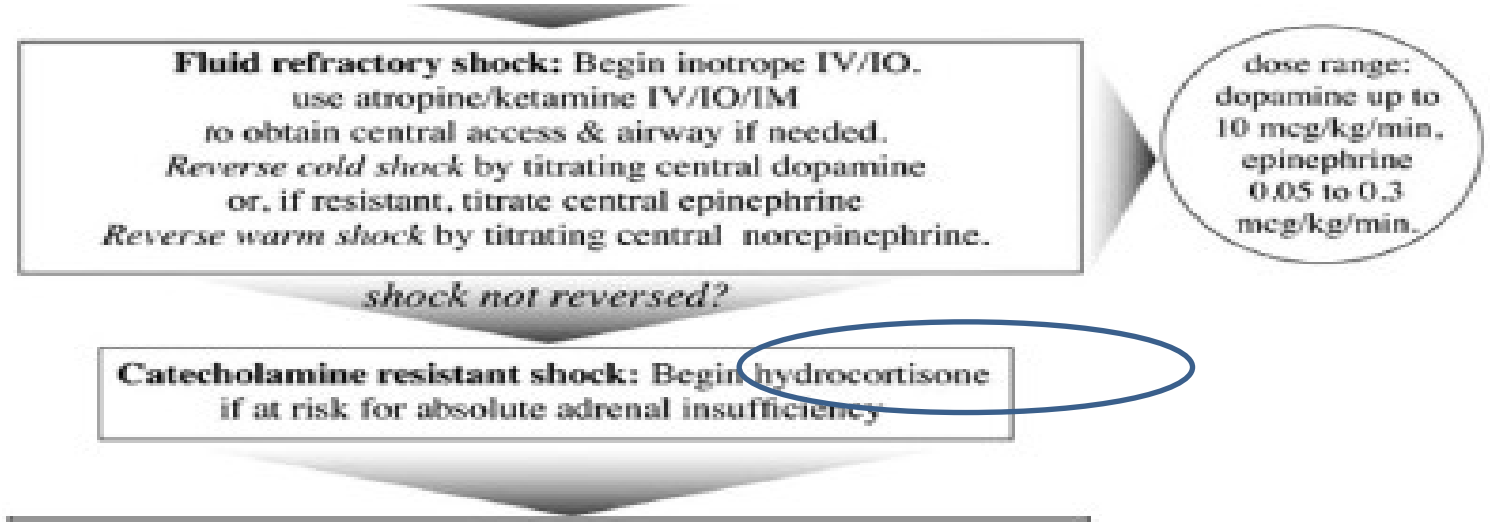
C. CORTICOSTEROIDS

- Consider hydrocortisone therapy in children with fluid refractory, catecholamine resistant shock and **suspected or proven absolute adrenal insufficiency.**

- No best method to identify adrenal insufficiency in children

(either baseline serum cortisol or adrenocorticotropin hormone stimulation testing)



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D. PROTEİN C AND ACTIVATED PROTEIN CONCENTRATE

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- **No reccommendation as no longer available**

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E. BLOOD PRODUCTS AND PLASMA THERAPIES

- **Similiar hemoglobin targets in children as in adults**
- **Low superior vena cava oxygen saturation shock < 70%**
  Hb levels of 10 g/dL are targeted.
- **After stabilization and recovery from shock and hypoxemia**
  Hb > 7g/dL be considered.

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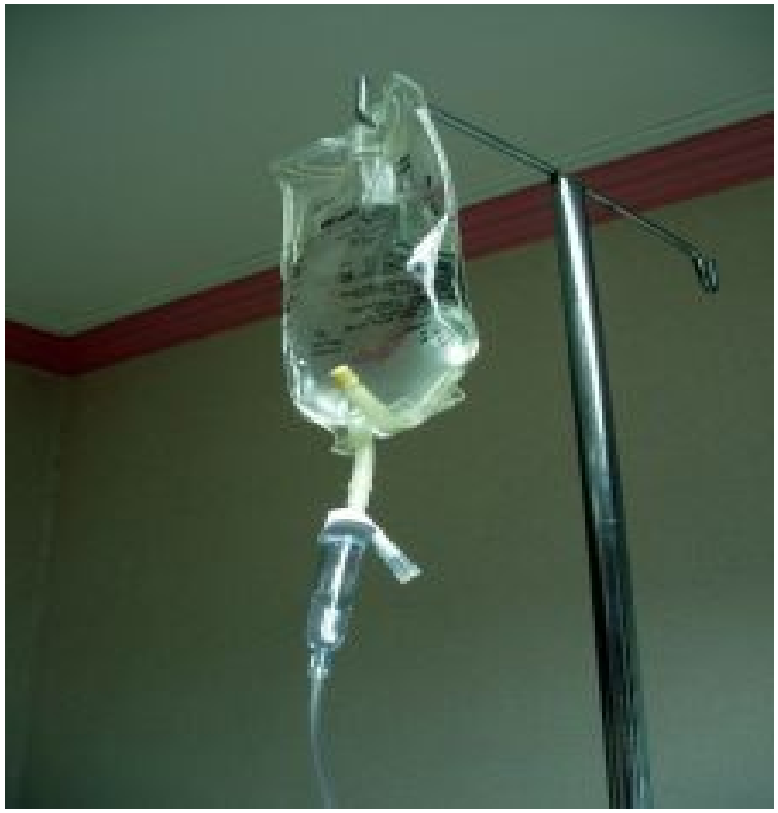
F. GLYCEMIC CONTROL

stop sepsis save lives

- **Control hyperglycemia using similar targets as in adults ≤ 180 mg/dL**
- **Glucose infusion should accopany inslulin therapy in newborns and children**



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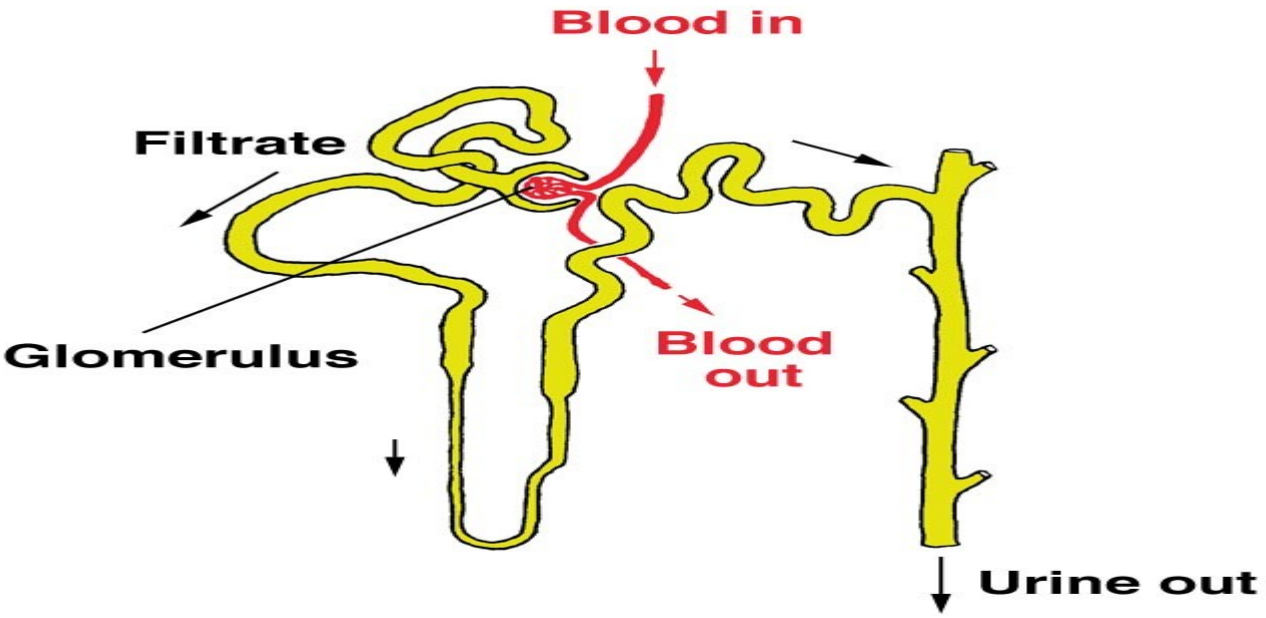
G. DIURETICS AND RENAL REPLACEMENT THERAPY

- **Use diuretics to reverse fluid overload when shock has reseolved.**

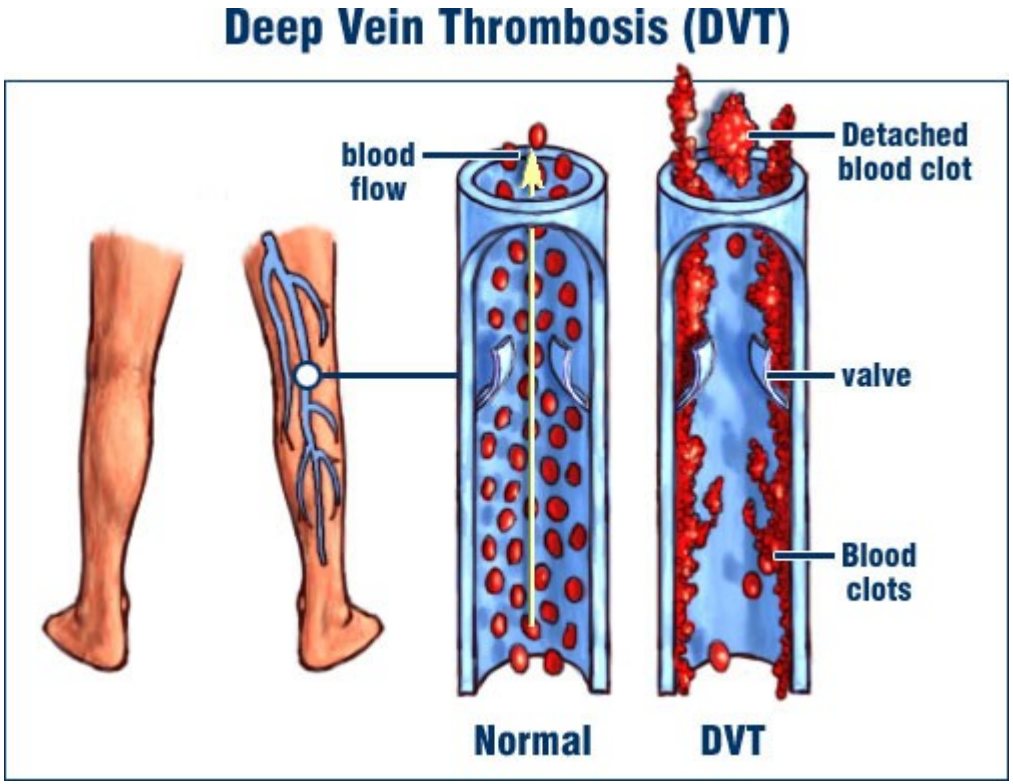
- **If unsuccessful, continous venovenous hemofiltration or intermittent dialysis to prevent greater than 10% total body weight fluid overload.**



Crit Care Med. 2013;41(2):580.

J. DEEP VEIN THROMBOSIS (DVT) PROPHYLAXIS

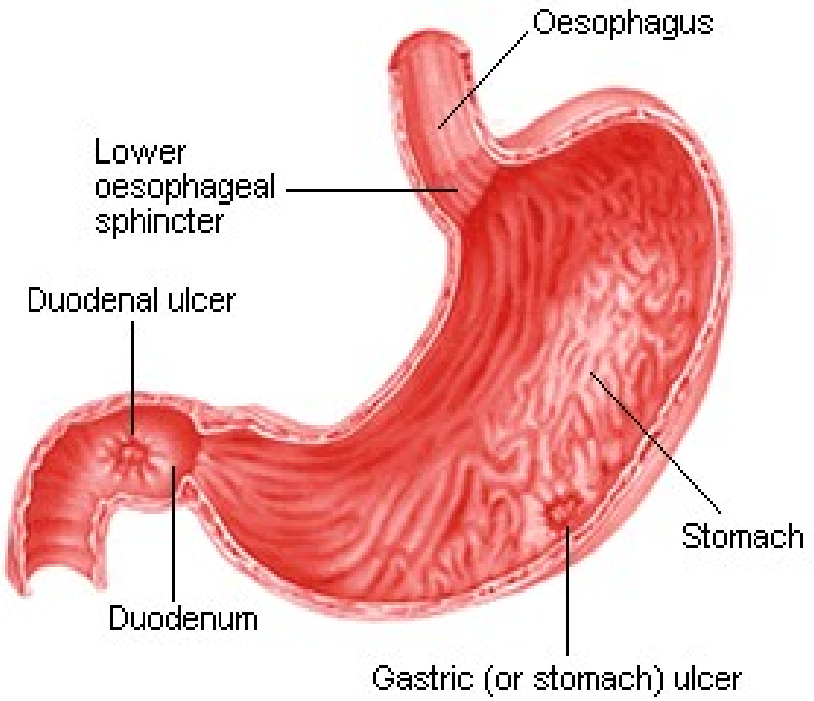
- **No recommendations on the use of DVT prophylaxıs ın prepubertal children with severe sepsis.**



Crit Care Med. 2013;41(2):580.

K. STRESS ULCER PROPHYLAXIS

- **No recommendations on the use of stress ulcer prophylaxis ın prepubertal children with severe sepsis.**



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L. NUTRITION

- **Enteral nutrition given to children who can be fed enterally, parenteral feeding in those who can not.**

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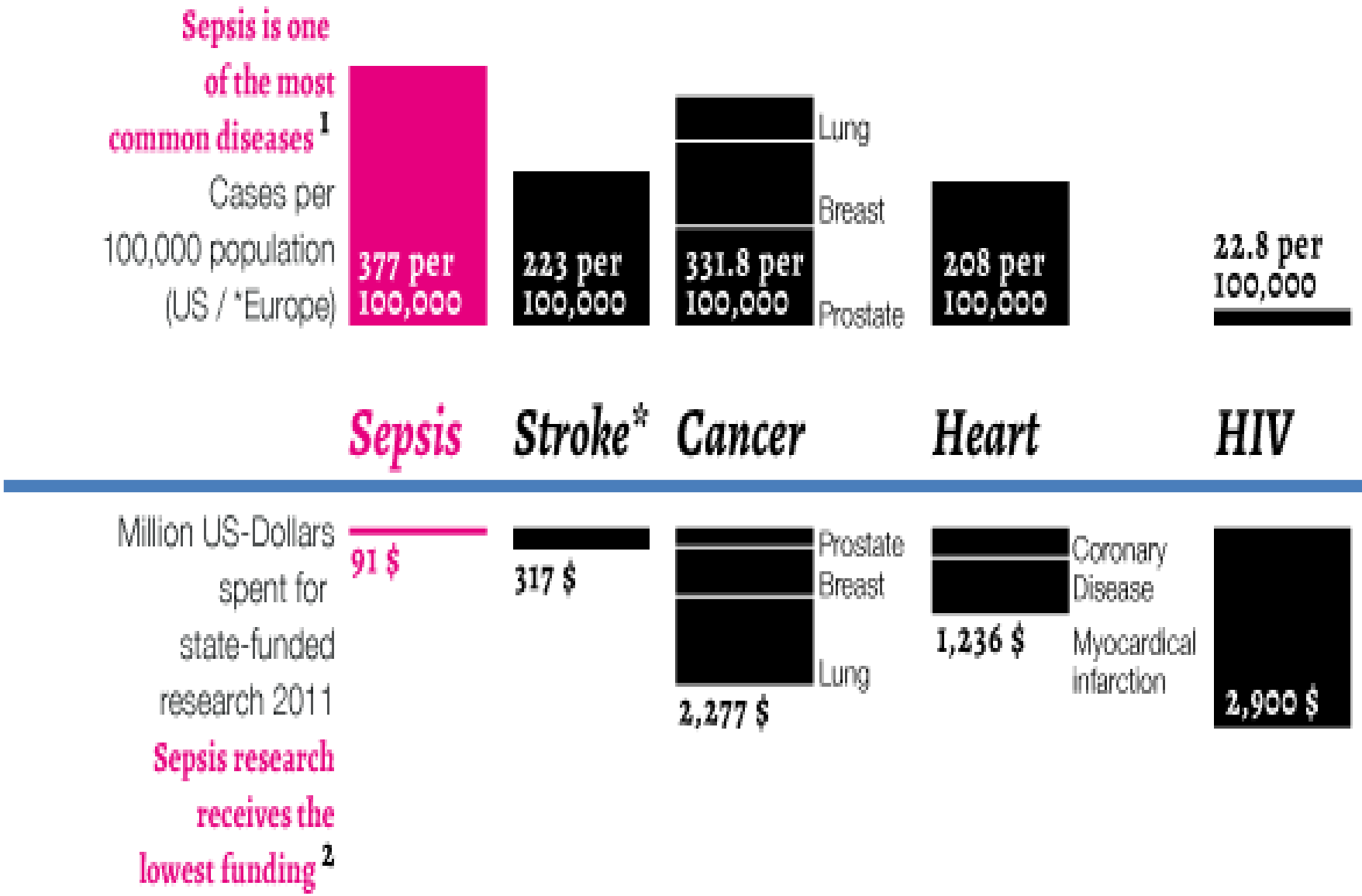
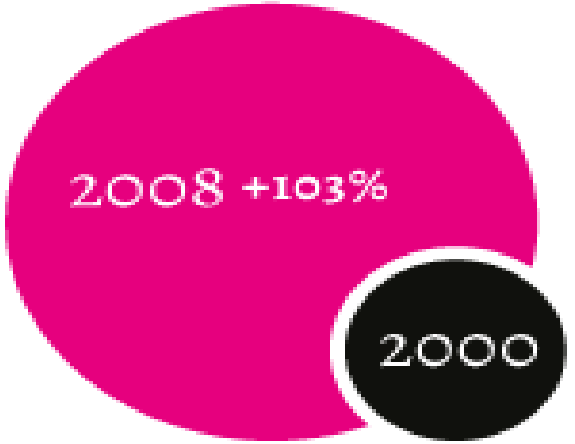

Sepsis is one of the most common diseases [1]
Cases per 100,000 population (US / *Europe)
377 per 100,000
223 per 100,000
331.8 per 100,000
Lung
Breast
Prostate
208 per 100,000
22.8 per 100,000
Sepsis
Stroke*
Cancer
Heart
HIV
Million US-Dollars spent for state-funded research 2011
Sepsis research receives the lowest funding [2]
91 $
317 $
Prostate
Breast
Lung
2,277 $
Coronary Disease
1,236 $
Myocardical Infarction
2,900 $

stop
sepsis
save
lives

- **Sepsis is dramatically increasing by an annual rates of between 8-10% over the last decade.**



Sepsis kills

>6,000,000

newborn and small children every year in the Developing world

September 13 2013

World Sepsis Day

NOT LOGGED IN
LOG IN

World Federation of Pediatric Intensive & Critical Care Societies

Pediatric Sepsis Initiative

Creating a global environment where all children have access to a high standard of care.

Sepsis Forum

Join the discussion and ask questions at the WFPICCS Forum.

» ENTER

Sepsis Guidelines

Find out how you can diagnose and manage sepsis and septic shock using our guidelines and videos.

» ENTER

Sepsis Bundle Registry

Enter your bundle details in the Sepsis Bundles Registry and help us eradicate sepsis.

» You are here

Help Us

Enter your bundle details in the Sepsis Bundles Registry and help us eradicate sepsis.

To begin, either LOG IN or CREATE AN ACCOUNT.

KEY TARGETS 2020

- Decrease incidence of sepsis by at least 20%
- Achive routine sepsis screen in at least 2/3 of acute health systems and primary care units
- İmprove survival rates of sepsis at least 10%
- İmprove public and professional awereness of sepsis
- Access to appropriate rehabilitation services for sepsis survivers

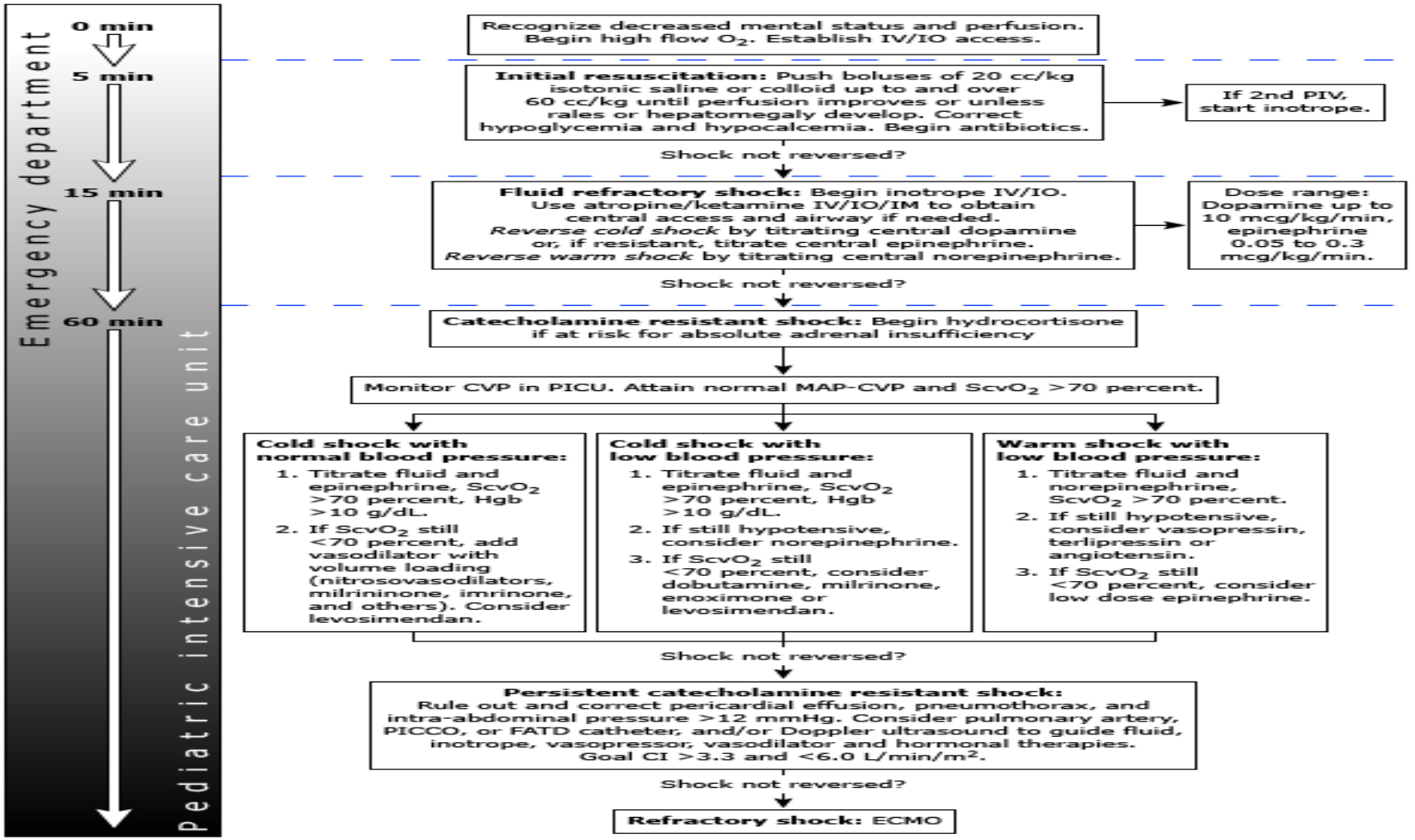
Evaluation of common sources of sepsis

Suspected site	Symptoms/signs	Microbiologic evaluation
Upper respiratory tract	Pharyngeal inflammation plus exudate ± swelling and lymphadenopathy	Throat swab for aerobic culture
Lower respiratory tract	Productive cough, pleuritic chest pain, consolidative auscultatory findings	Sputum of good quality, rapid influenza testing, urinary antigen testing (eg, pneumococcus, legionella), quantitative culture of protected brush or bronchoalveolar lavage
Urinary tract	Fever, urgency, dysuria, loin pain	Urine microscopy showing pyuria
Vascular catheters: arterial, central venous	Redness or drainage at insertion site	Culture of blood (from the catheter and a peripheral site), culture catheter tip (if removed)
Indwelling pleural catheter	Redness or drainage at insertion site	Culture of pleural fluid (through catheter), culture of catheter tip (if removed)
Wound or burn	Inflammation, edema, erythema, discharge of pus	Gram stain and culture of draining pus, wound culture not reliable
Skin/soft tissue	Erythema, edema, lymphangitis	Culture blister fluid or draining pus; role of tissue aspirates not proven
Central nervous system	Signs of meningeal irritation	CSF microscopy, protein, glucose, culture, bacterial antigen test
Gastrointestinal	Abdominal pain, distension, diarrhea, and vomiting	Stool culture for Salmonella, Shigella, and Campylobacter
Intraabdominal	Specific abdominal symptoms/signs	Aerobic and anaerobic culture of percutaneously or surgically drained abdominal fluid collections
Peritoneal dialysis (PD) catheter	Cloudy PD fluid, abdominal pain, fever	Cell count and culture of PD fluid
Genital tract	Women: Low abdominal pain, vaginal discharge Men: Dysuria, frequency, urgency, urge incontinence, cloudy urine, prostatic tenderness	Women: Endocervical and high vaginal swabs onto selective media Men: Urine Gram stain and culture
Joint	Pain, warmth, decreased range of motion	Arthrocentesis with cell counts, Gram stain, and culture

CSF: cerebrospinal fluid; PD: peritoneal dialysis.

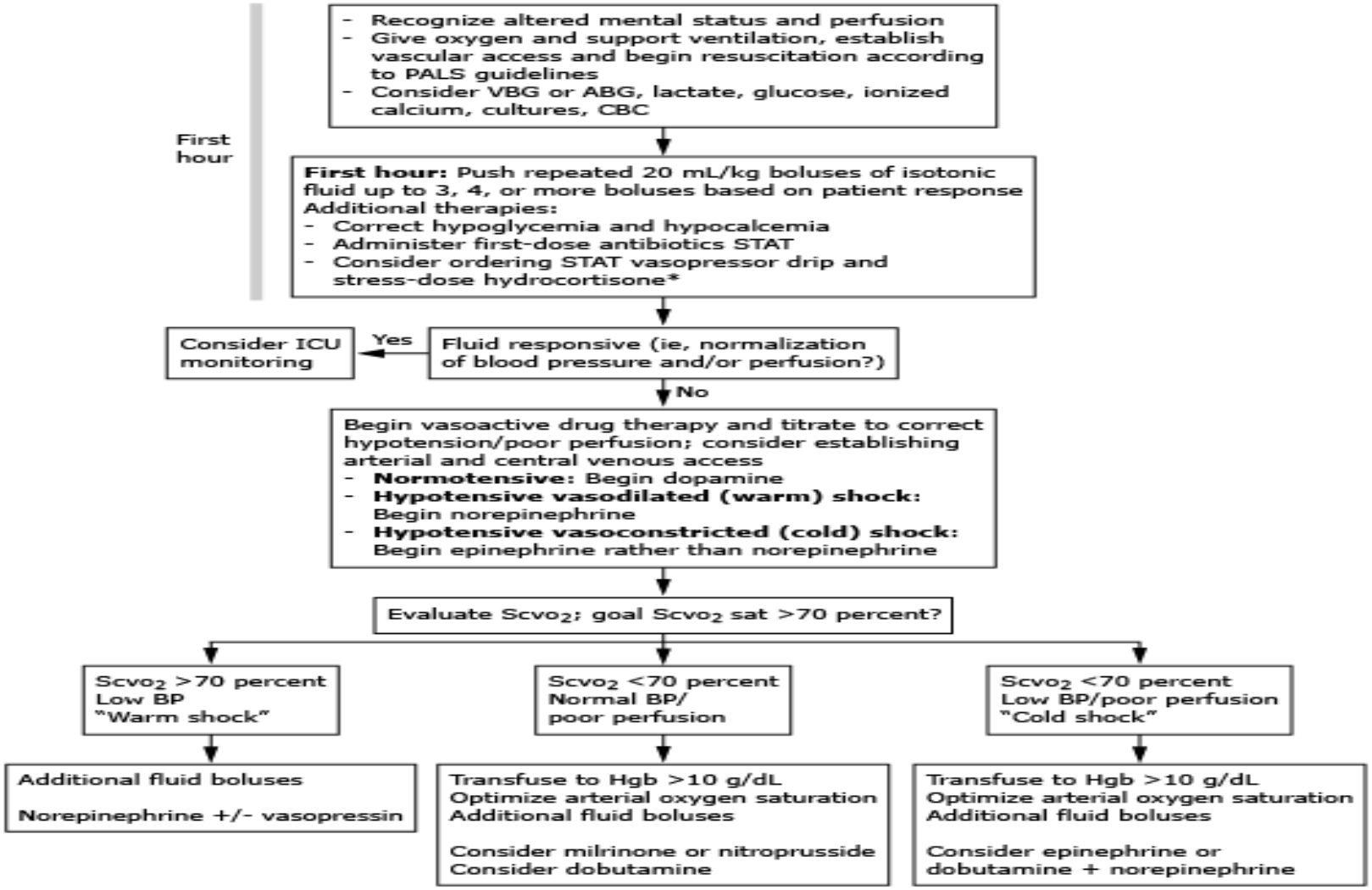
Adapted from: Cohen J, Microbiologic requirements for studies of sepsis. In: Sibbald WJ, Vincent JL (eds), Clinical Trials for the Treatment of Sepsis, Springer-Verlag, Berlin, 1995, p.73.

Recommendations for stepwise management of hemodynamic support in infants and children with sepsis



Algorithm for time sensitive, goal-directed stepwise management of hemodynamic support in infants and children. Proceed to next step if shock persists. (1) First hour goals—Restore and maintain heart rate thresholds, capillary refill ≤2 sec, and normal blood pressure in the first hour/emergency department. Support oxygenation and ventilation as appropriate. (2) Subsequent intensive care unit goals—If shock is not reversed, intervene to restore and maintain normal perfusion pressure (mean arterial pressure [MAP]-central venous pressure [CVP]) for age, central venous O_2 saturation >70 percent, and CI >3.3, <6.0 L/min/m^2 in pediatric intensive care unit (PICU).
Hgb: hemoglobin; PICCO: pulse contour cardiac output; FATD: femoral arterial thermodilution; ECMO: extracorporeal membrane oxygenation; CI: cardiac index; CRRT: continuous renal replacement therapy; IV: intravenous; IO: interosseous; IM: intramuscular.

Pediatric Advance Lifes Support septic shock algorithm



* **NOTE**: Fluid refractory and dopamine- or norepinephrine-dependent shock defines patient at risk for adrenal insufficiency. Draw baseline cortisol; consider ACTH stimulation test if unsure of need for steroids. If adrenal insufficiency is suspected give hydrocortisone ≅2 mg/kg bolus IV; maximum 100 mg.

Sepsis-induced hypotension is defined as a systolic blood pressure (SBP) <90 mmHg or mean arterial pressure (MAP) <70 mmHg or a SBP decrease >40 mmHg or less than two standard deviations below normal for age in the absence of other causes of hypotension

Septic shock — Septic shock is defined as sepsis-induced hypotension persisting despite adequate fluid resuscitation, which may be defined as infusion of 30 mL/kg of crystalloids (a portion of this may be albumin equivalent).

Multiple organ dysfunction syndrome — Multiple organ dysfunction syndrome (MODS) refers to progressive organ dysfunction in an acutely ill patient, such that homeostasis cannot be maintained without intervention. It is at the severe end of the severity of illness spectrum of both SIRS and sepsis. MODS can be classified as primary or secondary:

Primary MODS is the result of a well-defined insult in which organ dysfunction occurs early and can be directly attributable to the insult itself (eg, renal failure due to rhabdomyolysis)

Secondary MODS is organ failure that is not in direct response to the insult itself, but is a consequence of the host's response (eg, acute respiratory distress syndrome in patients with pancreatitis)

There are no universally accepted criteria for individual organ dysfunction in MODS. However, progressive abnormalities of the following organ-specific parameters are commonly used to diagnose MODS and scoring systems are used to predict ICU mortality [5]:

PaO2/FiO2 ratio

Platelet count

Serum bilirubin

Serum creatinine (or urine output)

Glasgow coma score

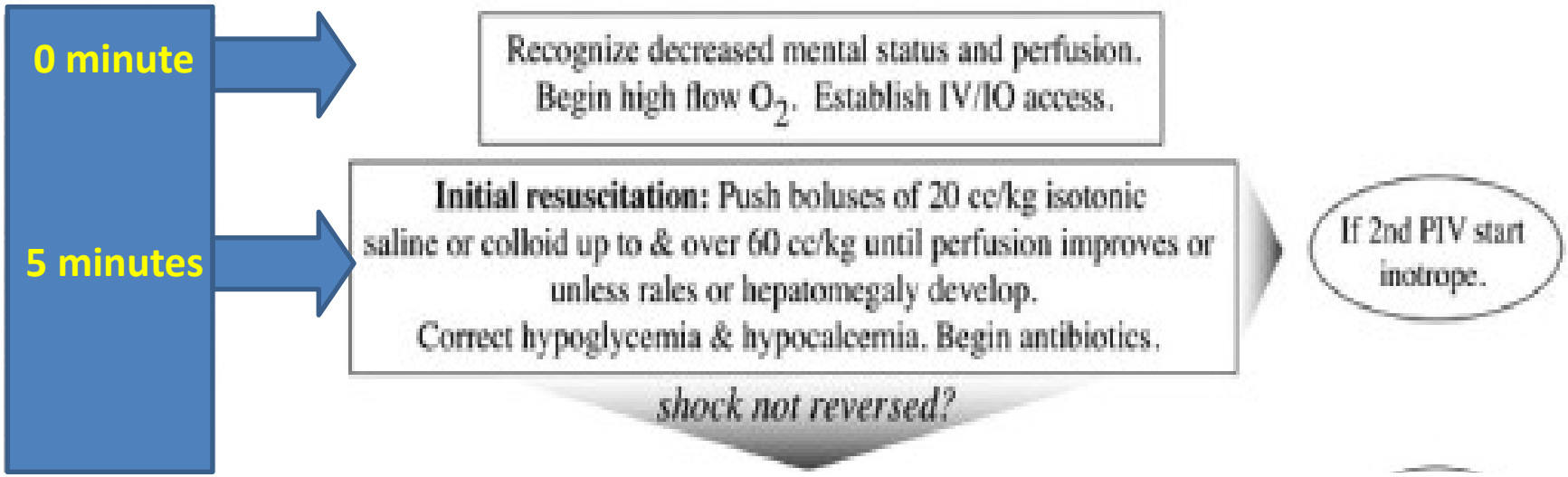
Hypotension

RISK FACTORS — Th

C. FLUID RESUSCITATION

- **Initial resuscitation of hypovolemic shock**

- Push boluses of 20 cc/kg isotonic saline or colloid up to over 60 cc/kg until perfusion improves or unless rales or hepatomegaly develop.



Crit Care Med. 2013;41(2):580.

Definitions

- **Infection**
  - Inflammatory response to microorganisms, or
  - Invasion of normally sterile tissues
- **Systemic Inflammatory Response Syndrome (SIRS)**
  - Systemic response to a variety of processes
- **Sepsis**
  - Infection plus
  - $^{24}_{12}2$ SIRS criteria
- **Severe Sepsis**
  - Sepsis
  - Organ dysfunction
- **Septic shock**
  - Sepsis
  - Hypotension despite fluid resuscitation

Bone RC et al. Chest. 1992;101:1644-55.

PATHOGENS: SEPSIS

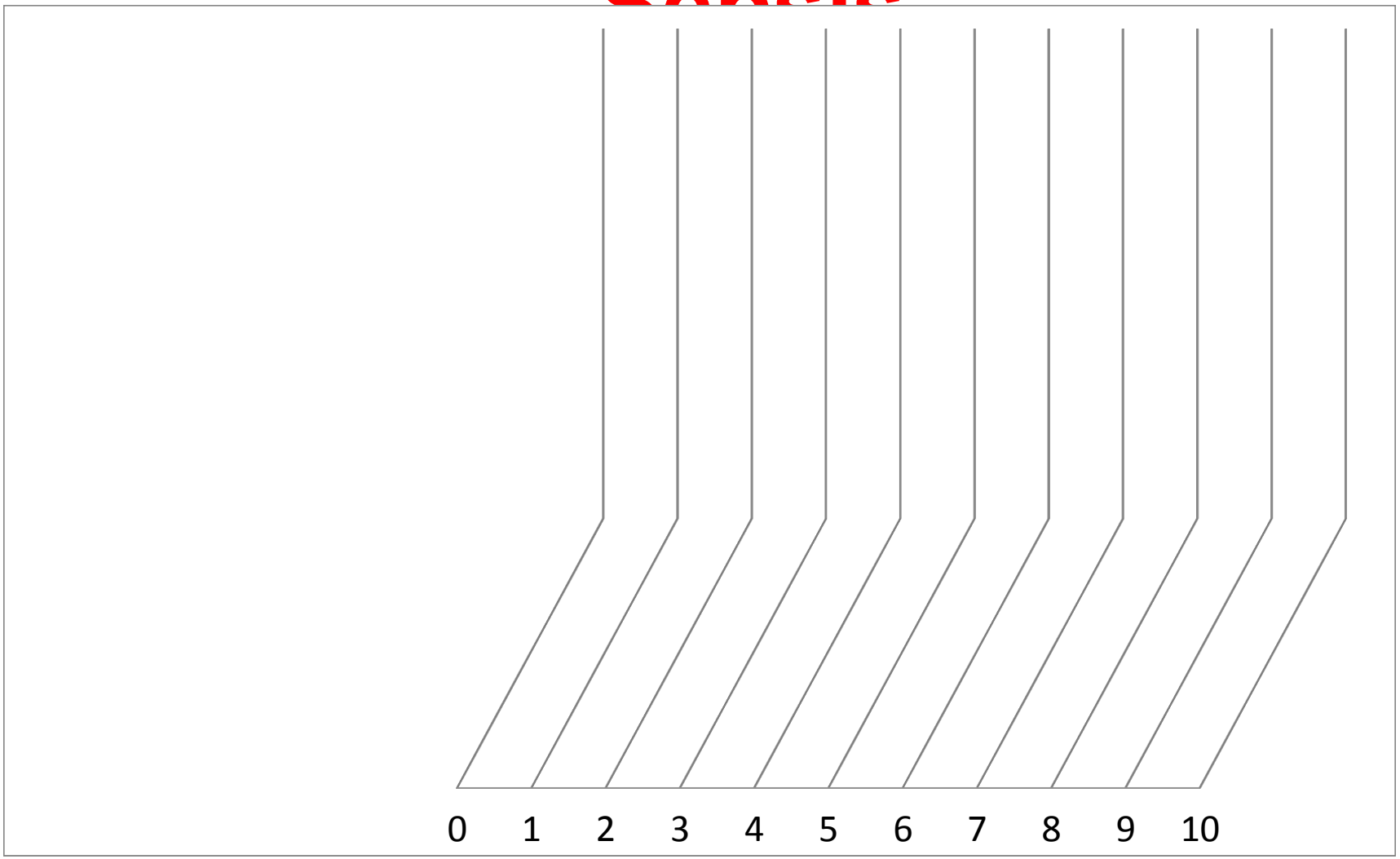
- Community aquired
- Nosocomial origin

	Estimated frequency*
Gram-positive bacteria	30–50%
Meticillin-susceptible *S aureus*	14–24%
Meticillin-resistant *S aureus*	5–11%
Other *Staphylococcus* spp	1–3%
Streptococcus pneumoniae	9–12%
Other *Streptococcus* spp	6–11%
Enterococcus spp	3–13%
Anaerobes	1–2%
Other gram-positive bacteria	1–5%
Gram-negative bacteria	25–30%
E coli	9–27%
Pseudomonas aeruginosa	8–15%
Klebsiella pneumoniae	2–7%
Other *Enterobacter* spp	6–16%
Haemophilus influenzae	2–10%
Anaerobes	3–7%
Other gram-negative bacteria	3–12%
Fungus	
Candida albicans	1–3%
Other *Candida* spp	1–2%
Yeast	1%
Parasites	1–3%
Viruses	2–4%

*From published clinical trials[349,350] and epidemiological studies.[3,6]

Table 1: Main pathogens in septic shock

Sites of Infection in Severe Sepsis



Angus et al, Crit Care Med 2001; 29: 1303-10

Category A: Nonindustrialized Setting With Child Mortality Rate >30 of 1,000 Children

Table 1. Administrative bundle

Clean water provided	Yes☐ No☐
Rural/urban health workers provided	Yes☐ No☐
Immunizations provided	Yes☐ No☐
Zinc/vitamin A supplementation provided	Yes☐ No☐

Clinical practice parameter bundle

Parent education provided on signs to call for health worker	Yes☐No☐
Tachypnea, poor feeding, diarrhea	Yes☐No☐
Five days of intramuscular gentamicin and oral cotrimoxazole (or trimethoprim-sulphamethoxizole)	Yes☐No☐NA☐
Oral World Health Organization hydration	Yes☐No☐NA☐
Oral antimalarials in malaria belts	Yes☐No☐NA☐

NA, not applicable.

Category B: Nonindustrialized Setting With Child Mortality Rate <30 of 1,000 Children

Table 2. Administrative bundle

Clean water provided	Yes☐ No☐
Rural/urban health workers provided	Yes☐ No☐
Immunizations provided	Yes☐ No☐
Zinc/vitamin A supplementation provided	Yes☐ No☐
Provide hospital emergency room/clinic stocked with IV fluids (D10, normal saline, lactated Ringers)	Yes☐ No☐ NA☐
Albumin (malaria belt)	Yes☐ No☐
IV catheters	Yes☐ No☐
IV antibiotics/antimalarials	Yes☐ No☐
Oxygen with high-flow capabilities (pneumonia)	Yes☐ No☐

Clinical parameter bundle

Parent education provided on signs to call for health worker	Yes☐No☐
Tachypnea, poor feeding, diarrhea	Yes☐No☐
Five days of intramuscular gentamicin and oral clotrimaxazole and oral World Health Organization hydration	Yes☐No☐NA☐
Oral antimalarials in malaria belts	Yes☐No☐NA☐
Capillary refill restored to <2 secs and blood pressure restored to normal in ED/first hour	Yes☐No☐
Administer IV fluids in ED/first half-hour for stage III/IV shock	Yes☐No☐NA☐
Administer IV antibiotics/antimalarials if appropriate in ED/first hour	Yes☐No☐NA☐
Administer high-flow oxygen/nasal continuous positive airway pressure in ED/first hour for tachypnea/pneumonia	Yes☐No☐NA☐
D10 with sodium administered at maintenance to prevent hypoglycemia	Yes☐No☐

IV, intravenous; ED, emergency department; NA, not applicable.

Category C: Industrialized Developing Nation

Table 3. Administrative bundle

ED/intensive care unit available for patients	Yes☐ No☐
High-flow oxygen/nasopharyngeal continuous positive airway pressure available to all patients	Yes☐ No☐
Ventilator available for all patients	Yes☐ No☐
Peripheral and central IV catheters available to all patients	Yes☐ No☐
Inotropes available for all patients	Yes☐ No☐
Intravascular pressure monitoring available for all patients	Yes☐ No☐
Superior vena cava or inferior vena cava/RA pressure, oxygen saturation monitoring available for all patients	Yes☐ No☐
Dialysis available for patients	Yes☐ No☐
Infusion pumps available	Yes☐ No☐

Clinical parameter bundle

Capillary refill restored to <2 secs in ED/first hour	Yes☐No☐
Blood pressure restored to normal in ED/first hour	Yes☐No☐
Administer IV fluids in ED/first half-hour for stage III/IV shock	Yes☐No☐NA☐
Administer IV antibiotics/antimalarials if appropriate in ED/first hour	Yes☐No☐NA☐
Administer high-flow oxygen/nasopharyngeal continuous positive airway pressure in ED/first hour for tachypnea/pneumonia	Yes☐No☐NA☐
D10 with sodium administered at maintenance to prevent hypoglycemia	Yes☐No☐
Fluid resuscitation >20 mL/kg up to 60 mL/kg administered in first hour if appropriate	Yes☐No☐NA☐
Peripheral epinephrine administered in first hour if appropriate	Yes☐No☐NA☐
Central epinephrine for cold shock/norepinephrine for warm shock in first hour if appropriate	Yes☐No☐NA☐
Normal mean arterial pressure–central venous pressure and superior vena cava or inferior vena cava/RA oxygen saturation >70% targeted in intensive care unit	Yes☐No☐NA☐
Absolute adrenal insufficiency treated with steroids	Yes☐No☐NA☐
Ketamine used as sedation agent for intubation/central line placement	Yes☐No☐NA☐
Ventilator provided for respiratory failure	Yes☐No☐NA☐
Tidal volume maintained at 6-8 mL/kg	Yes☐No☐NA☐
Appropriate (sensitive) antibiotic administered in first 2 hrs	Yes☐No☐NA☐
Immunosuppressants held if using immune suppressive therapy	Yes☐No☐NA☐
Hyperglycemia controlled by insulin	Yes☐No☐NA☐
Intravenous immunoglobulin/clindamycin administered for toxic shock (group A Streptococcus or Staphylococcus)	Yes☐No☐NA☐
Surgical nidus removed if appropriate	Yes☐No☐NA☐

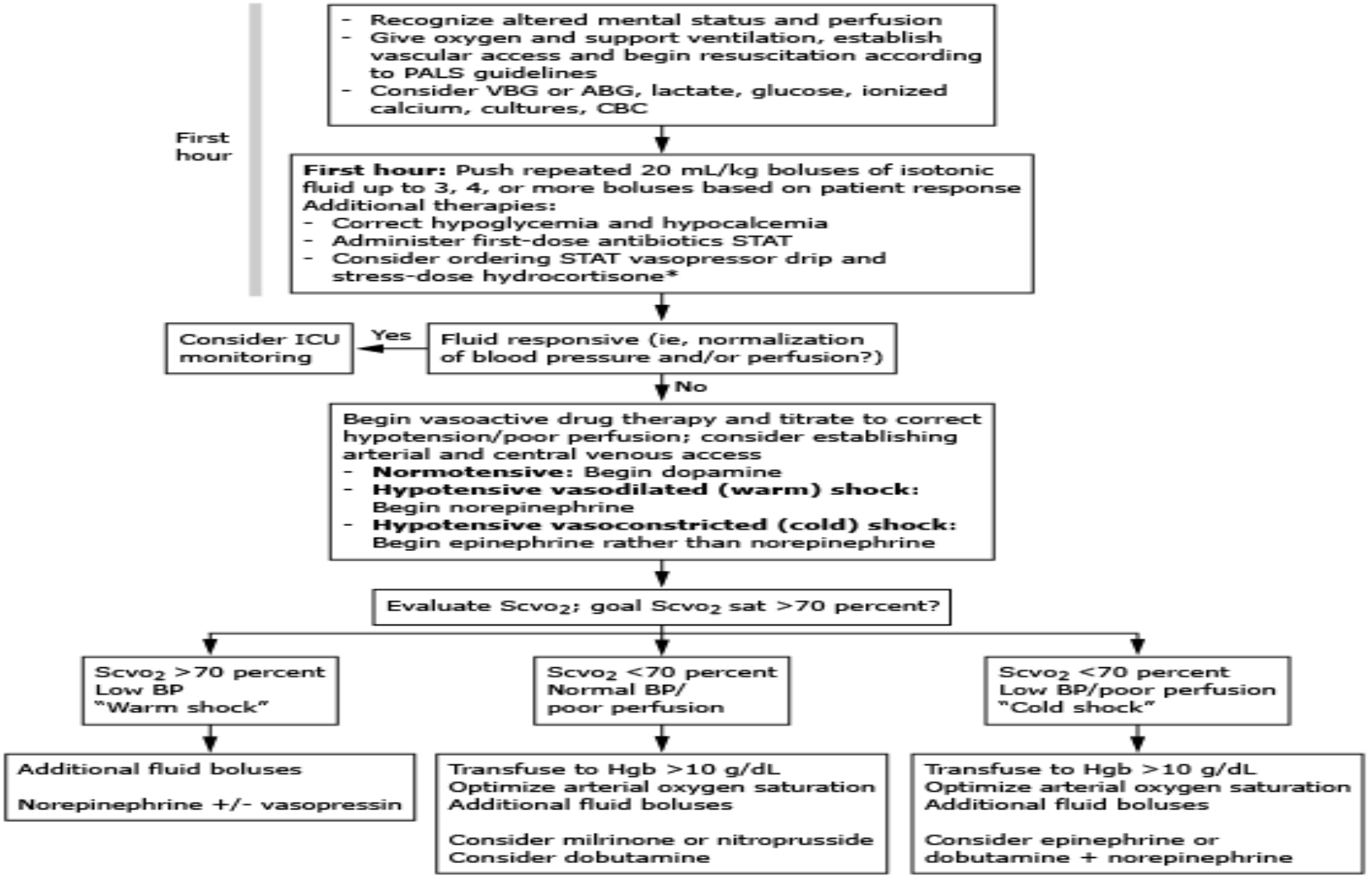
Category D: Industrialized Developed Nation

Table 4. Administrative bundle

ED/intensive care unit available for patients	Yes☐	No☐	
High-flow oxygen/nasopharyngeal continuous positive airway pressure available to all patients	Yes☐	No☐	
Ventilator available for all patients	Yes☐	No☐	
Peripheral and central IV catheters available to all patients	Yes☐	No☐	
Infusion pumps available	Yes☐	No☐	
Inotropes available for all patients	Yes☐	No☐	
Intravascular pressure monitoring available for all patients	Yes☐	No☐	
Superior vena cava or inferior vena cava/RA pressure/oxygen saturation monitoring available for all patients	Yes☐	No☐	
Cardiac output monitoring available for all patients	Yes☐	No☐	
Continuous renal replacement therapy available for all patients	Yes☐	No☐	
Plasma exchange available for all patients	Yes☐	No☐	
Extracorporeal membrane oxygenation available for all patients	Yes☐	No☐	
High-flow oxygen ventilation available for all patients	Yes☐	No☐	
Inhalable nitric oxide available for all patients for persistent pulmonary hypertension of the newborn	Yes☐	No☐	
Clinical parameter bundle			
Capillary refill restored to <2 secs in ED/first hour	Yes☐	No☐	
Blood pressure restored to normal in ED/first hour	Yes☐	No☐	
Administer IV fluids in ED/first half-hour for stage III/IV shock	Yes☐	No☐	NA☐
Administer IV antibiotics/antimalarials if appropriate in ED/first hour	Yes☐	No☐	NA☐
Administer high flow oxygen in ED/first hour for tachypnea or pneumonia	Yes☐	No☐	NA☐
D10 with sodium administered at maintenance to prevent hypoglycemia	Yes☐	No☐	
Fluid resuscitation >20 mL/kg up to 60 mL/kg administered in first hour if appropriate	Yes☐	No☐	NA☐
Peripheral epinephrine administered in first hour if appropriate	Yes☐	No☐	NA☐
Central epinephrine for cold shock/norepinephrine for warm shock in first hour if appropriate	Yes☐	No☐	NA☐
Normal mean arterial pressure–central venous pressure and superior vena cava or inferior vena cava/RA oxygen saturation >70% targeted in intensive care unit	Yes☐	No☐	NA☐
	Yes☐	No☐	NA☐
Absolute adrenal insufficiency treated with steroids	Yes☐	No☐	NA☐
Ketamine used as sedation agent for intubation/central line placement	Yes☐	No☐	NA☐
Ventilator provided for respiratory failure	Yes☐	No☐	NA☐
Effective tidal volume maintained at 6-8 mL/kg	Yes☐	No☐	NA☐
Appropriate (sensitive) antibiotic administered in first 2 hrs	Yes☐	No☐	NA☐
Immunosuppressants held if using immune suppressive therapy	Yes☐	No☐	NA☐
Hyperglycemia controlled by insulin	Yes☐	No☐	NA☐
Intravenous immunoglobulin/clindamycin administered for toxic shock (group A Streptococcus or Staphylococcus)	Yes☐	No☐	NA☐
Surgical nidus removed if appropriate	Yes☐	No☐	NA☐
Cardiac index maintained between 3.3 and 6.0 using American College of Critical Care Medicine guidelines	Yes☐	No☐	NA☐
Continuous renal replacement therapy used for fluid overload and multiorgan failure before 3 days if appropriate	Yes☐	No☐	NA☐
Plasma exchange used to treat thrombocytopenia-induced multiorgan failure until resolution of thrombocytopenia	Yes☐	No☐	NA☐
High-flow oxygen ventilation used if peak inspiratory pressure >35 cmH_2O	Yes☐	No☐	NA☐
Inhalable nitric oxide used for persistent pulmonary hypertension of the newborn	Yes☐	No☐	NA☐
Extracorporeal membrane oxygenation used for refractory cardiopulmonary failure	Yes☐	No☐	NA☐

ED, emergency department; IV, intravenous; NA, not applicable; RA, right atrium.

Pediatric Advance Lifes Support septic shock algorithm



* **NOTE**: Fluid refractory and dopamine- or norepinephrine-dependent shock defines patient at risk for adrenal insufficiency. Draw baseline cortisol; consider ACTH stimulation test if unsure of need for steroids. If adrenal insufficiency is suspected give hydrocortisone ≅2 mg/kg bolus IV; maximum 100 mg.

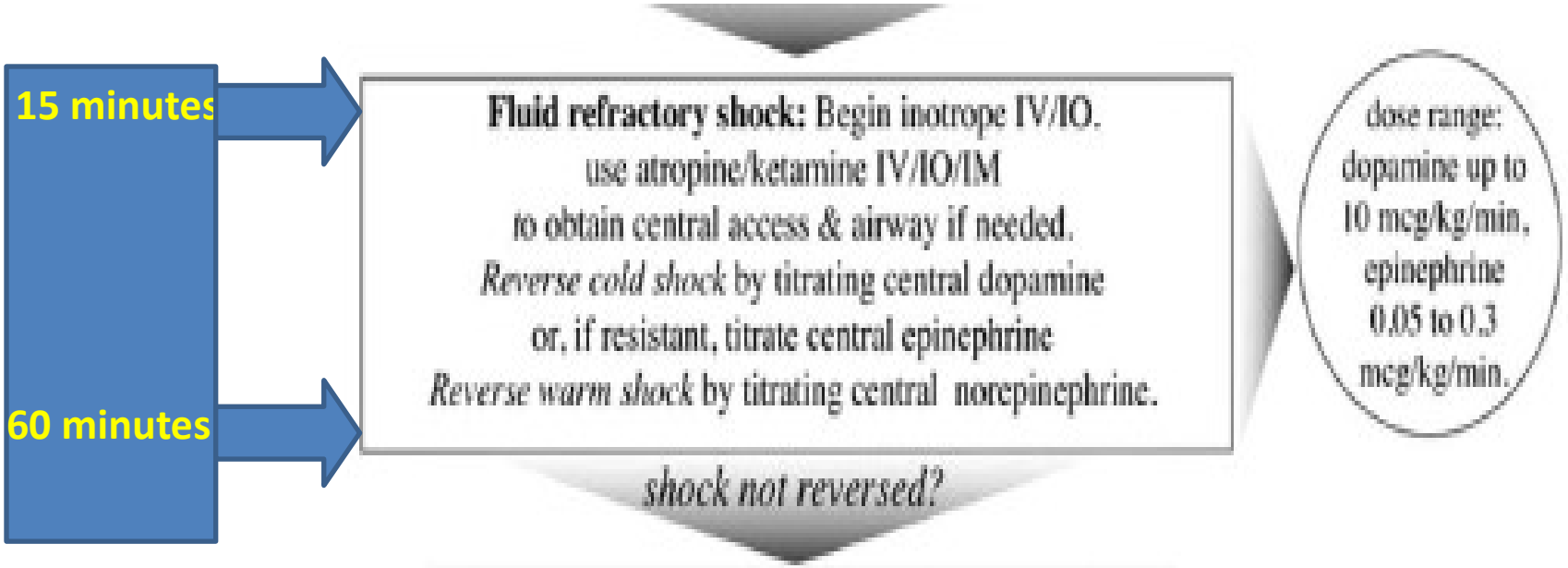
Rapid overview of rapid sequence intubation in children

Preoxygenation
Begin preoxygenation as soon as the decision to intubate is considered.
Administer oxygen at the highest concentration available.
Preparation
Identify conditions that will affect choice of medications.
Identify conditions that will predict difficult intubation or bag-mask ventilation.
Assemble equipment and check for function.
Develop contingency plan for failed intubation.
Pretreatment
Atropine: All children ≤1 year, children <5 years receiving succinycholine, and older children receiving a second dose of succinylcholine. Dose: 0.02 mg/kg IV (maximum single dose 0.5 mg, minimum 0.1 mg; if no IV access, can be given IM).
Lidocaine: Optional for increased intracranial pressure. Dose: 1.5 mg/kg IV (maximum dose 100 mg). Give 2 to 3 minutes before intubation.
Sedation
Etomidate: Safe with hemodynamic instability, neuroprotective, transient adrenal corticosuppression. Do **not** use routinely in patients with septic shock. Dose: 0.3 mg/kg IV.
Ketamine: Safe with hemodynamic instability if patient is not catecholamine depleted. Use in patients with bronchospasm and septic shock. Use with caution in patients with increased intracranial pressure. Dose: 1 to 2 mg/kg IV. (If no IV access, can be given IM dose: 3 to 7 mg/kg).
Midazolam: Time to clinical effect is longer, inconsistently induces unconsciousness. May cause hemodynamic instability at doses required for sedation. Dose: 0.2 to 0.3 mg/kg IV (maximum dose 2 mg, onset of effect requires 2 to 3 minutes).
Thiopental: Neuroprotective. Do not use with hemodynamic instability. Dose: 3 to 5 mg/kg IV.*
Paralytic
Succinycholine: Do not use with chronic myopathy or denervating neuromuscular disease; 48 to 72 hours after burn, crush, or denervating injury; malignant hyperthermia; or pre-exisiting hyperkalemia. Dose: infants and young children: 2 mg/kg IV, older children: 1 to 1.5 mg/kg IV. (If IV access unobtainable, can be given IM, dose: 3 to 5 mg/kg).
Rocuronium: Use for children with contraindication for succinylcholine. Suggested dose: 1 mg/kg IV (range 0.6 to 1.2 mg/kg).•
Protection and positioning
Maintain manual cervical spine immobilization during intubation in the trauma patient.
If cervical spine injury is not potentially present, put the patient in the "sniffing position" (ie, head forward so that the external auditory canal is anterior to the shoulder and the nose and mouth point to the ceiling). Apply cricoid pressure when the child is unconscious. Remove cricoid pressure if it causes airway obstruction or difficulty viewing the larynx.
If used, maintain cricoid pressure until tracheal tube position is verified.
Positioning, with placement
Confirm tracheal tube placement with end-tidal CO2 detection and auscultation.
Postintubation management
Chest radiograph for tracheal tube placement; provide ongoing sedation (eg, midazolam), analgesia (eg, fentanyl 1 mcg per kilogram), and, if indicated, paralysis.Δ

If IV access unobtainable, intraosseous administration of drugs listed is feasible (no data for ketamine).
* Not available in the United States and Canada.
• Vecuronium may be used in children with contraindications to succinylcholine and when rocuronium is not available. Suggested dose for RSI: 0.15 to 0.2 mg/kg. Patients may experience prolonged and unpredictable duration of paralysis at this dose.
Δ If decompensation after successful intubation use DOPE mnemonic to find cause:
- D: Dislodgement of the tube (right mainstem or esophageal)
- O: Obstruction of tube
- P: Pneumothorax
- E: Equipment failure (ventilator malfunction, oxygen disconnected or not on).

C. INOTROPES/VASOPRESSORS/VASODILATORS

- Begin peripheral inotropic support until cental venous access can be done in children who are not responsive to fluid resuscitation.



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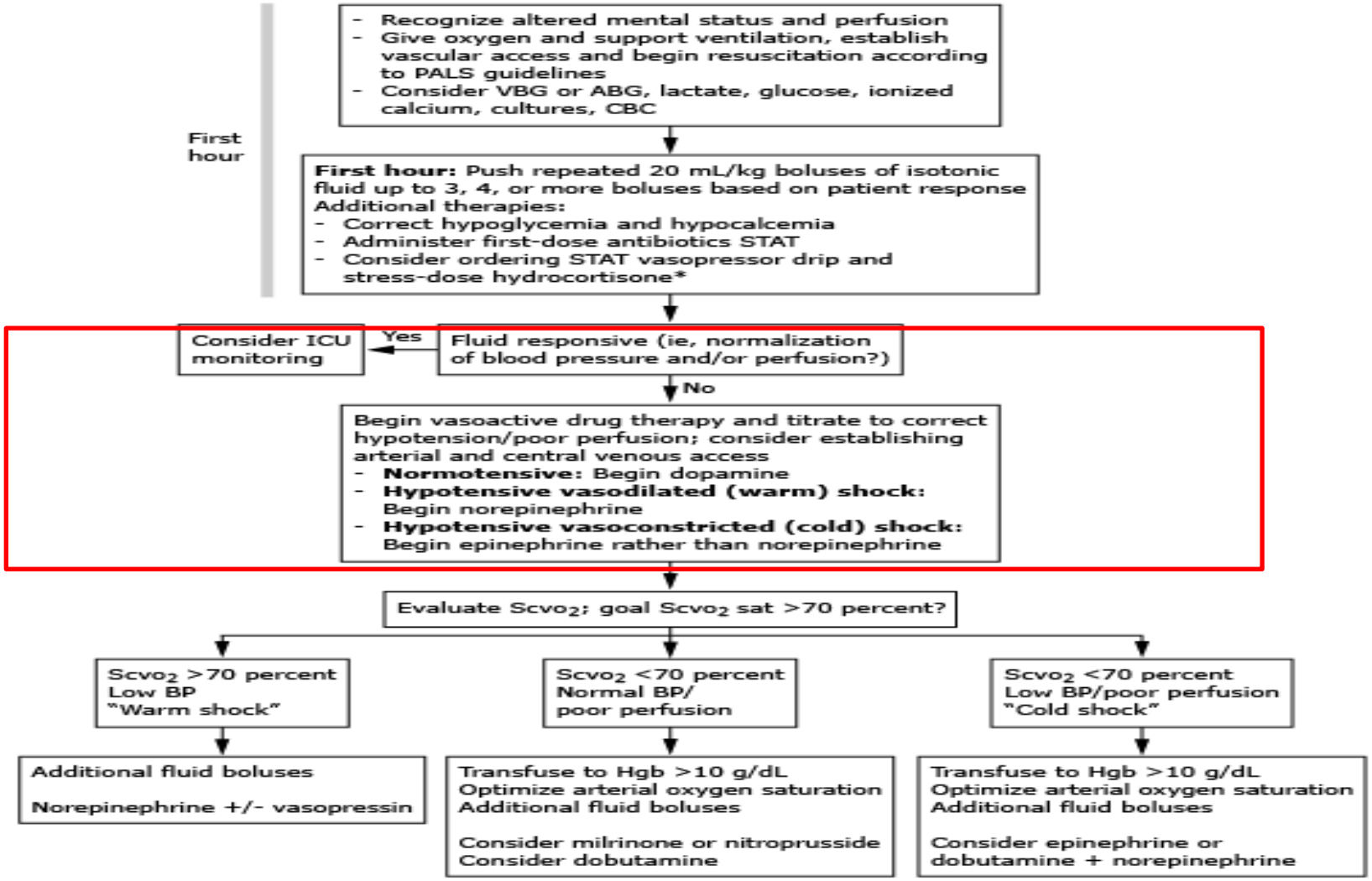
Pediatric Advance Lifes Support septic shock algorithm



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I. MECHANICAL VENTILATION

stop sepsis save lives

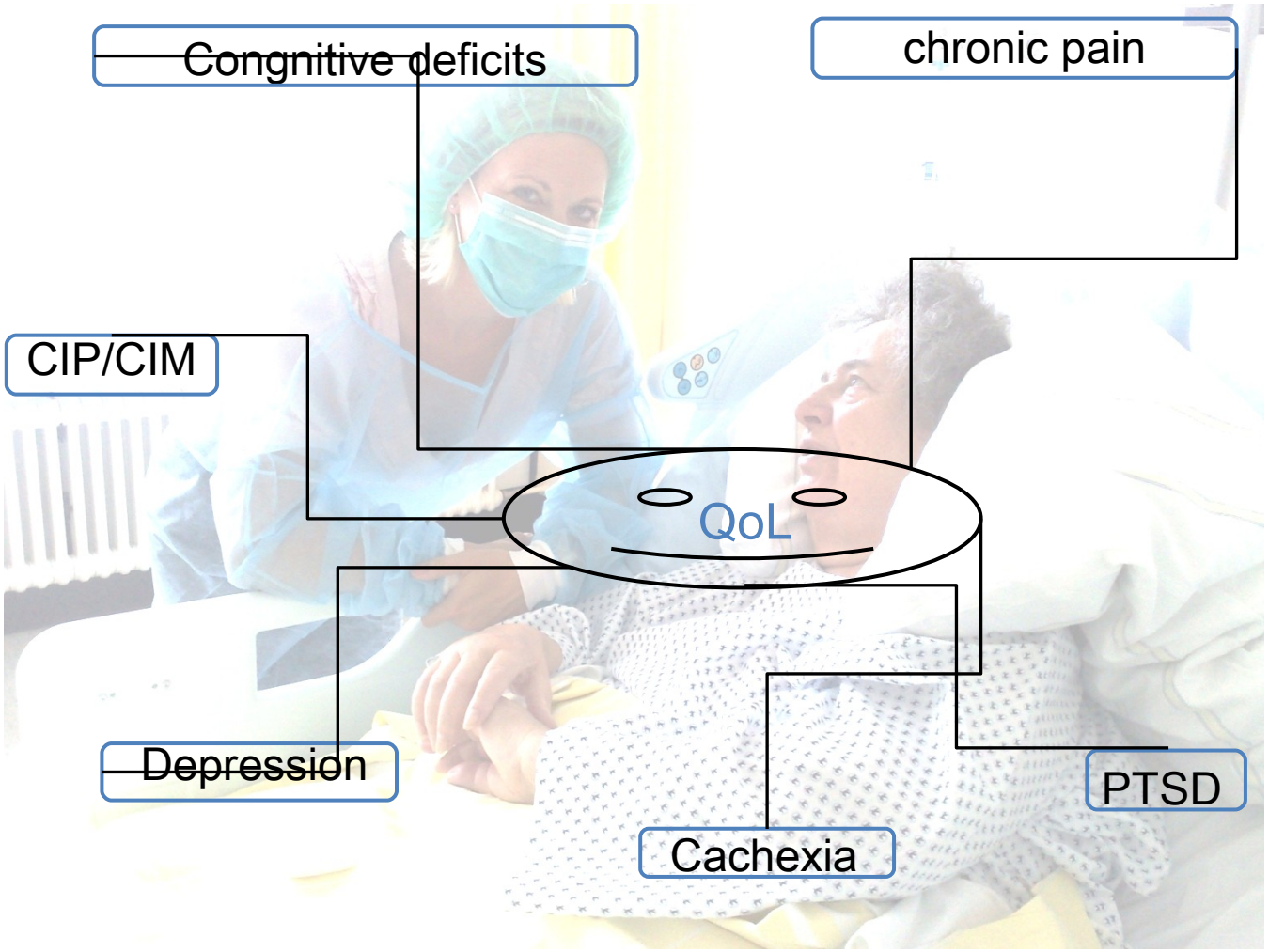
- Lung-protective strategies during mechanical ventilation

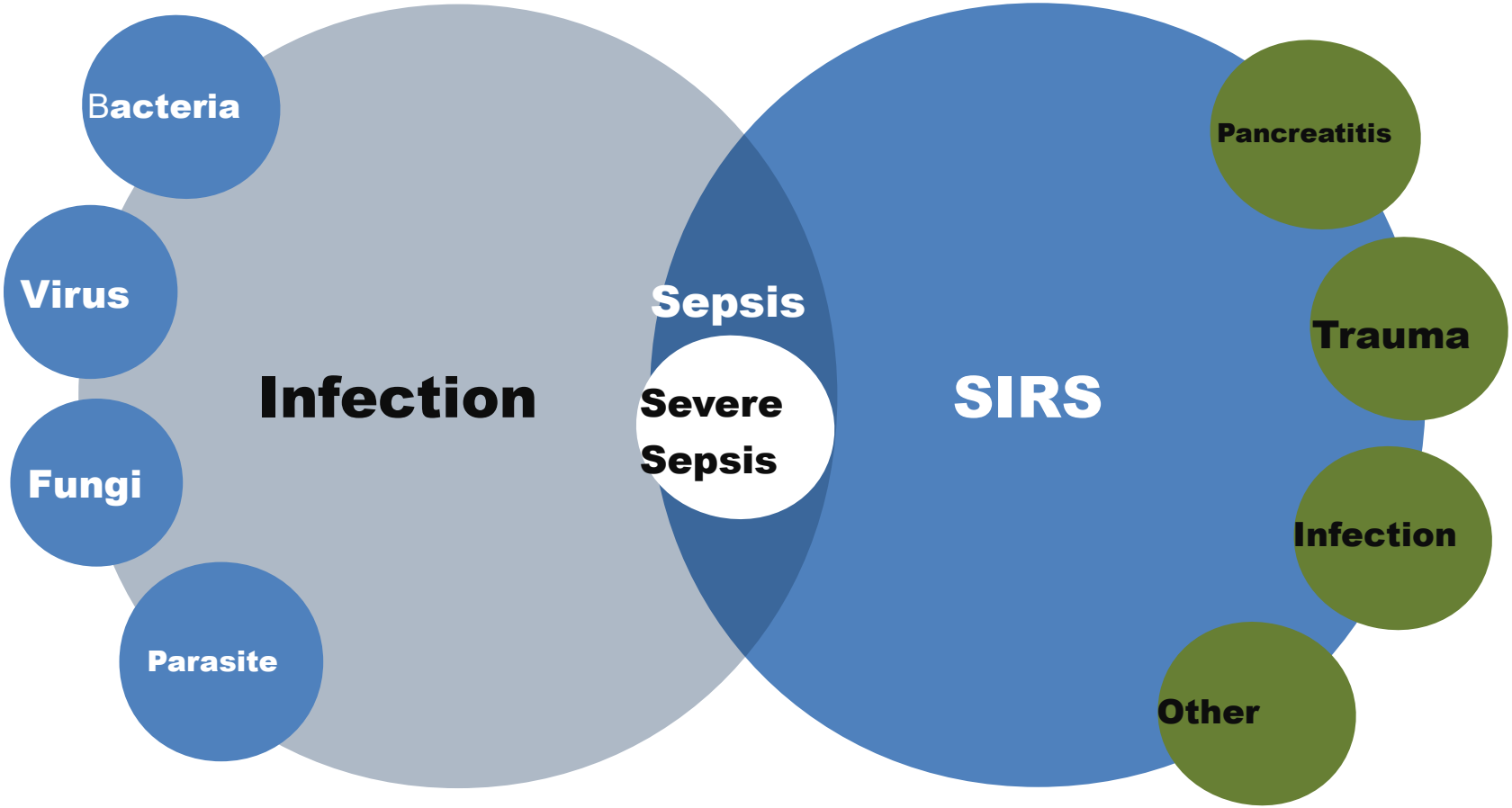
J. SEDATION/ANALGESIA/DRUG TOXICITIES

stop sepsis save lives

- Sedation usage recommended in critically ill mechanically ventilated ones
- Monitor drug toxicity because reduced drug metobolism in children with sepsis

„Post Sepsis Six“




Bacteria
Virus
Fungi
Parasite
Infection
Sepsis
Severe
Sepsis
SIRS
Pancreatitis
Trauma
Infection
Other

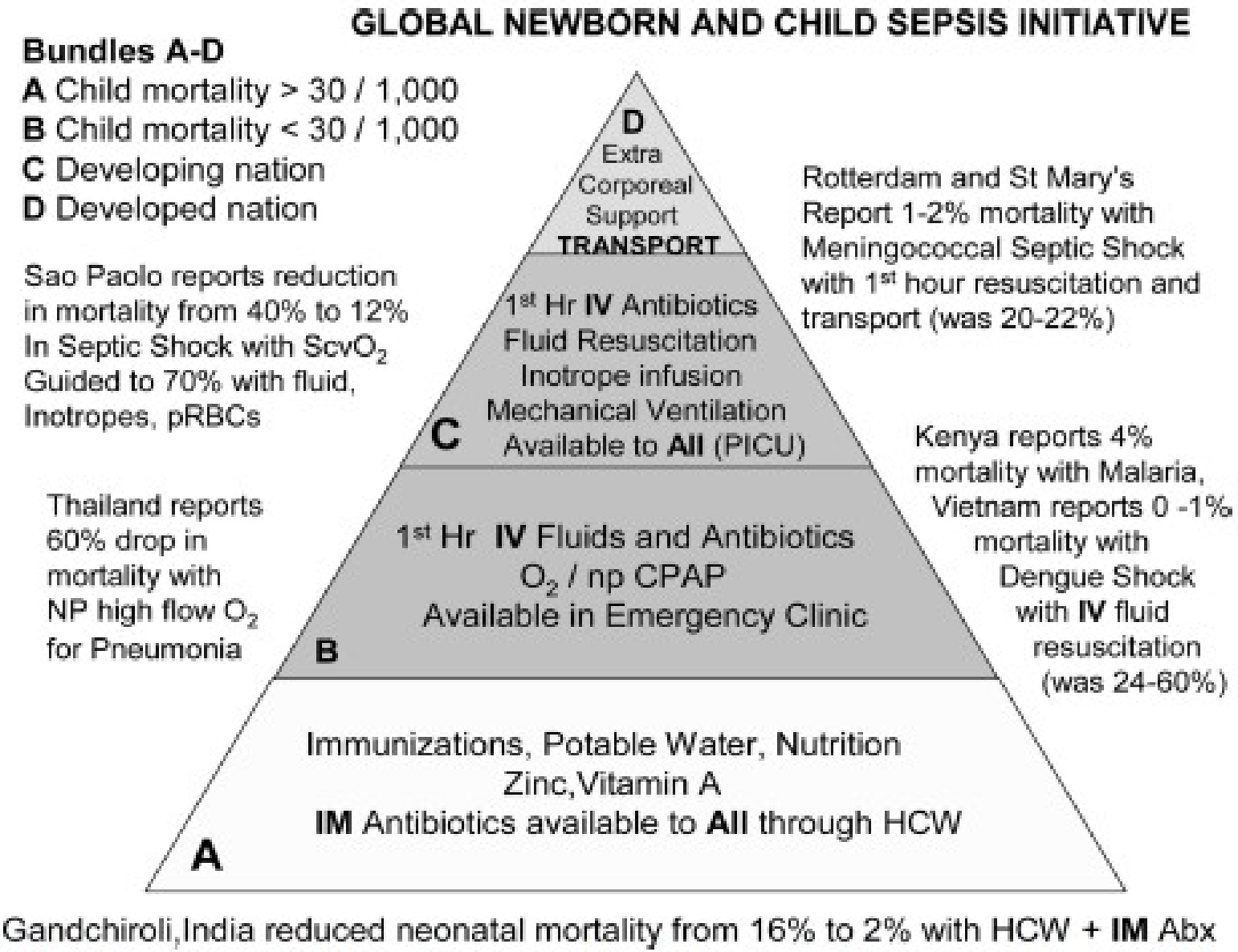


Figure 1. The sepsis initiative administrative bundles pyramid. This pyramid demonstrates the administrative recommendations according to levels of health resources from the health resource-scarce (level A) to health resource-abundant (level D). The foundation of care is level A. It is expected