What’s Happening Now?

**AAP Supports World Sepsis Day - September 13**  
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Sepsis is the leading killer of children worldwide, but this is not reflected in estimates of global mortality. For instance, the Global Burden of Disease study, a systematic analysis of global and regional mortality, reports “sepsis and infectious disorders of the newborn” representing 17% of neonatal deaths; however another 15% of neonatal deaths due to infections are not identified as death due to sepsis although sepsis is the final common pathway to death. The term “sepsis” is also excluded in the under-5 childhood deaths although 61% of deaths are due to infectious causes of which malaria (20.8%), diarrheal diseases (11.9%) and lower respiratory infections (12.4%) are the most common.

From the clinician’s standpoint, the three most common causes of death (pneumonia, malaria and diarrheal diseases) in children often co-exist and any or all, when severe, lead to sepsis and septic shock. While it is important to classify deaths according to specific causes, we contend that it is a mistake to ignore the unifying feature of all of these deaths – that they are due to sepsis.

The issue of highlighting sepsis as the end result of severe infections is not merely cosmetic but is important for a provision of care especially in resource limited environments where skilled healthcare workers are in short supply and care is being delivered by teams with limited training and clinical skills. The failure to highlight the syndrome of sepsis, regardless of the infecting organism(s), as a major killer and public health issue is an oversight with serious implications for the clinician because the most important interventions to reduce sepsis morbidity and mortality must be made generically and before a definitive diagnosis is available. Thus, calling attention to the need for time-sensitive treatment in severe infections is unlikely to happen if severe infections are compartmentalized in separate silos such as malaria, pneumonia and diarrheal diseases.
Sepsis has clinical, social, economic and political origins and implications as highlighted by the ongoing Ebola outbreak in West Africa. Care for sepsis especially in the developing world is plagued by delays in recognition and in many cases basic care and personal protective procedures are not followed. Sepsis is also a social and economic problem in the developing world where lack of education and money, faith and supernatural causes and home remedies complicates care. Long distances and non-availability of transport as well as many stops and long waiting time leads to lack of faith in the healthcare system. In addition, lack of empowerment of women in many parts of the world results in poor health seeking care behavior for their children. In many parts of the developing world, there are also low emphasis on preventative services, staff shortages, inequity of health care, and poorly regulated managed healthcare sectors.

Thus, the adoption of a broader concept to highlight the burden and far reaching implications of sepsis is paramount for advocacy for resources to support innovative programs. This was the impetus for the creation of the World Sepsis Declaration and subsequently World Sepsis Day. The intent of World Sepsis Day was two-fold: First, to raise awareness of sepsis among all stakeholders, including members of the public and policymakers, and second, to encourage capacity building and quality improvement initiatives for sepsis recognition and management by hospitals and healthcare providers toward delivering the goals set out in the World Sepsis Declaration.

These goals are:
1. Reducing sepsis incidence through prevention by at least 20%
2. Improving survival for children and adults in all countries
3. Raising public and professional awareness and understanding of sepsis
4. Ensuring improved access to adequate rehabilitation services
5. Creating and maintaining sepsis incidence and outcomes databases.

You can take action and help to increase the awareness and participate in education about sepsis. You can support the World Sepsis Declaration by registering on the World Sepsis Day website and by speaking out about sepsis and supporting our request to get sepsis on the agenda of the United Nations. You can also help by educating the public about sepsis prevention measures and long-term outcomes, educating administrators about the issues of sepsis in your own organization, participating in many events and seminars about sepsis that are gaining ground for medical professions in many parts of the world. Engage government agencies to enable them to recognize sepsis as a national health topic and join in the global movie event which will focus on
collecting video material to create a compelling informative movie about World Sepsis Day 2014. You can also stay connected on Twitter and Facebook. Finally, inform others of your activities on the World Sepsis Day website and help make World Sepsis Day a success.

Who’s Advocating How?

AAP & CDC Coordinate Pediatric Influenza Webinar - September 18

September is National Preparedness Month (NPM)! This year’s theme is “Be Disaster Aware, Take Action to Prepare”. The AAP has collaborated with the Centers for Disease Control and Prevention (CDC) to coordinate a 1-hour Clinician Outreach and Communication Activity (COCA) call/webinar during NPM, titled “Management and Prevention of Pediatric Influenza in Healthcare Settings”, that will be taking place on Thursday, September 18, 2014, at 2:00pm ET/1:00pm CT.

During this COCA call, subject matter experts from CDC and the AAP will discuss pediatric recommendations, strategies to improve influenza prevention and control in children, and ways to leverage seasonal influenza planning in pediatric offices and hospitals to improve pandemic preparedness. For more information about the COCA call/webinar, please see: http://emergency.cdc.gov/coca/calls/2014/callinfo_091814.asp

CDC Provides Guidance for Emergency Medical Services regarding Ebola Virus Disease

On September 5, 2014, the Centers for Disease Control and Prevention (CDC) changed the “Interim Guidance for Emergency Medical Services (EMS) Systems and 9-1-1 Public Safety Answering Points (PSAPs) for Management of Patients with Known or Suspected Ebola Virus Disease in the United States” to reflect harmony with all other CDC guidance on cleaning solutions. The updated guidance is still posted online at the same URL: http://www.cdc.gov/vhf/ebola/hcp/interim-guidance-emergency-medical-services-systems-911-public-safety-answering-points-management-patients-known-suspected-united-states.html

What Opportunities Exist?

Register for Fun in the Sun with Pediatric Critical Care Simulation! - October 12

Please join us on October 12 and 13 in beautiful San Diego for the Section on Critical Care’s (SOCC) educational program to be held as part of the AAP National Conference. We will celebrate the 30th anniversary of the SOCC’s founding with history and trivia throughout the session.
A highlight of this year’s program will be held on the afternoon of Sunday, October 12 where the SOCC, in conjunction with the AAP Division of Life Support Programs, will provide a variety of simulation stations including patient scenarios, advanced airway techniques, and cardiac dysrhythmias. This promises to be an exciting educational experience and a great way to interact with colleagues from across the country.

Space is limited for optimal hands-on learning:
- Catered Event # M18 - $50 for members
- Catered Event #M19 - $25 for trainees

To register for Fun with Pediatric Critical Care Simulation (includes box lunch), there are 3 options:
1. Online: http://s15.a2zinc.net/clients/AAP/NCE2014/Public/Content.aspx?ID=145
3. Call 800/433-9016, option 3 for help registering.

**AAP SOCC Scientific & Educational Program at 2014 AAP NCE! - October 12 & 13**

On the morning of October 12, the SOCC will conduct a half day of scientific presentations (oral and poster format) that focus on clinical and laboratory research topics that impact the clinical care of critically ill and injured infants, children and adolescents.

If all that wasn’t enough, the SOCC will hold a joint session with the Section on Hospital Medicine on Monday, October 13. This session is designed to update attendees on the Post-Intensive Care Syndrome and current efforts to define its epidemiology, treatment, and outcomes.

The full SOCC program is online: http://www.aap.org/en-us/Documents/socc_nce_program.pdf

**AAP Section on Transport Medicine Program at 2014 AAP NCE! - October 12-14**

The Section on Transport Medicine’s (SOTM) is sponsoring the 2014 Course on Neonatal and Pediatric Critical Care Transport Medicine, October 12-14, 2014 in San Diego. The theme of the 2014 Transport Course is “Grooming the Next Generation of Transport Leaders.” In addition to the clinical care updates, there will be a leadership/management track. Director, medical director or committee chair, there is something for everyone: dysfunctional team management, high stakes negotiation, “budgets for dummies,” performance management amongst peers, and legal issues.

Download program information at: http://www2.aap.org/sections/transmed

Register for the 2014 Course on Neonatal and Pediatric Critical Care Transport Medicine – held as part of the AAP’s National Conference & Exhibition - at www.aapexperience.org
Save the Dates: Upcoming AAP Advocacy Training Opportunities

2015 AAP Legislative Conference - April 12-14, 2015 in Washington, DC

The AAP Legislative Conference will be held April 12-14, 2015, in Washington, DC. Participants will have the opportunity to develop their federal advocacy skills through interactive workshops, learn about timely child health policy topics, hear from several guest speakers from Congress and the Administration and visit with their legislators on Capitol Hill. If you are interested in attending and would like to be notified when registration opens, please email LegislativeConference@aap.org. For more information, please visit aap.org/legcon.

Advocacy Day Trainings - October 27, 2014 & February 9, 2015 in Washington, DC

The AAP will also be hosting two Advocacy Day trainings in Washington, DC, on Monday, October 27, 2014, and Monday, February 9, 2015. Beginning with an in-depth training session on how to advocate to members of Congress led by pediatrician federal policy experts and AAP staff, the day will culminate with in-person visits to federal legislators on Capitol Hill. If you are interested in attending either of the trainings, please email kids1st@aap.org.

PREP ICU Q&A

To subscribe to the PREP® ICU Self-Assessment programs, visit http://prepicu.aap.org.

Question

You are treating a 15-month-old girl for sepsis. She has mild purpura fulminans and is supported with dopamine at 8 mcg/kg per minute and epinephrine at 0.07 mcg/kg per minute. She is receiving mechanical ventilation with a tidal volume of 6 mL/kg, a rate of 25, a positive end-expiratory pressure of 7 cmH2O, and an FiO2 of 0.6. Her most recent arterial blood gas shows a pH of 7.25, PCO2 of 50 mmHg, PaO2 of 63 mmHg, and base excess of -6 mEq/L. Other laboratory studies demonstrate:

- Sodium, 135 mEq/L (135 mmol/L)
- Potassium, 2.9 mEq/L (2.9 mmol/L)
- Chloride, 98 mEq/L (98 mmol/L)
- Bicarbonate, 18 mEq/L (18 mmol/L)
- Blood urea nitrogen, 28 mg/dL (10.0 mmol/L)
- Creatinine, 1.1 mg/dL (97.2 mcmol/L)
- Glucose, 123 mg/dL (6.8 mmol/L)
- White blood cell count, 17.3x103/mcL (17.3x109/L)
- Hemoglobin, 8.1 g/dL (81 g/L)
- Hematocrit, 24% (0.24)
- Platelet count, 97x103/mcL (97x109/L)
On physical examination, the girl's temperature is 37.8°C, heart rate is 153 beats/min, respiratory rate is 27 breaths/min, and blood pressure is 88/61 mmHg. Her distal extremities are cool and capillary refill is delayed. Echocardiography suggests mildly decreased contractility globally but good intraventricular volumes.

Of the following, the intervention MOST likely to increase microvascular blood flow to the tissues for this girl is to:

A. begin a milrinone infusion
B. change epinephrine to norepinephrine
C. cool the child to 36.0 degrees Celsius
D. normalize the pH
E. transfuse 20 mL/kg packed red blood cells

Answer

The patient described in the vignette has evidence of satisfactory intracardiac volumes, but skin signs of impaired perfusion, depressed contractility by echocardiography, and metabolic acidosis, suggesting inadequate nutrient delivery at the tissue level. Milrinone is a type III phosphodiesterase inhibitor that can increase cyclic adenosine monophosphate concentrations, which can lead to improved myocardial contractility, improved diastolic relaxation, and vasodilation. The combination of actions results in increased cardiac output and oxygen delivery through improved contractility, stroke volume, and tissue blood flow. In addition, in some situations, phosphodiesterase inhibitors have been shown to reduce platelet and white blood cell interactions that may lead to more sluggish flow through capillaries. The clinician should assure good intravascular volume before administering milrinone because vessel dilation could lead to hypotension unless volume is addressed adequately. Many patients who have catecholamine-resistant shock demonstrate improved cardiac output with milrinone. Milrinone is considered appropriate therapy for the treatment of shock in the presence of low cardiac index, normal blood pressure, and high systemic vascular resistance, as described for the girl in the vignette.

Many factors interact to determine microvascular blood flow to tissues. The clinician treating a patient who has any form of shock ultimately must consider how to deliver oxygen and other nutrients to the capillaries perfusing vital organs. Increasing oxygen delivery at the macrocirculation level, as measured by pulmonary artery catheters, can be beneficial, but augmenting nutrient delivery at the microvascular level is believed to be a better target for resuscitation. Abnormalities of microvascular flow are a hallmark of sepsis, and the clinician must consider all factors that increase or decrease microvascular flow through a given capillary and an entire capillary bed. In shock states, and particularly in sepsis, capillaries within tissues may have
no or reduced flow due to microthromboses, arteriole-venule shunts, and leukocyte aggregation, even in the presence of normal vital signs.

The first priority in resuscitation from shock is improving cardiac output and blood pressure. Cardiac output is dependent on four variables: preload, afterload, contractility, and heart rate. In most forms of pediatric shock, intravascular volume is depleted, preload is reduced, and aggressive volume administration improves outcome by increasing myocardial stretch and intraventricular volume that enhances stroke volume and, subsequently, blood pressure. Increasing blood pressure leads to augmented flow through the microcirculation. Normally, increased flow enhances oxygen and nutrient delivery, which reduces local release of hydrogen ion, adenosine, and other factors, leading to vasoconstriction. Increased flow also leads to a reflexive "myogenic" constriction and endothelial cell shear stress. Such stress prompts release of nitric oxide, resulting in local arteriolar dilatation and a decrease in blood pressure and systemic vascular resistance.

When microvascular blood flow, hypoxemia, or other micronutrient (glucose, vitamin B complex) deficiency do not meet the metabolic needs of tissues, anaerobic metabolism produces hydrogen ions and releases adenosine from the breakdown of adenosine triphosphate, causing local vasodilation that enhances local blood flow. In addition, inadequate nutrient substrate does not provide adequate energy for smooth muscle contraction, prompting the blood vessels to dilate.

Because norepinephrine has more potent alpha-agonist effects than epinephrine, it is a drug of choice for warm shock with hypotension and brisk capillary refill. It may increase blood pressure, which could increase flow, but the concomitant vasoconstriction likely would impair flow to many vascular beds. Once blood pressure is adequate, as in the vignette, the clinician’s goal should be to improve overall clinical perfusion by using vasodilators and inodilators in conjunction with ongoing attention to the provision of adequate intravascular volume.

Attempts to decrease metabolic requirements are appropriate when struggling to deliver adequate nutrients to cells. Early intubation to reduce the work of breathing has become part of clinical practice parameters for pediatric shock. Changing the body temperature by 1.0°C changes oxygen consumption, carbon dioxide production, and related metabolic parameters by approximately 10% to 12%. However, a patient usually is cooled with cooling blankets or garments that can lead to vasoconstriction of the skin, patient discomfort, and endogenous release of alpha-agonist catecholamines. Also, in areas where vascular reactivity is normal, blood flow is autoregulated to meet the metabolic needs of those tissues, so a reduction in metabolism by decreasing temperature could lead to decreased microvascular blood flow.
A common goal of intensive care is to correct acid-base disturbances to a normal pH of 7.4. However, acidosis (increased hydrogen ion concentration or elevated PCO2) is a stimulus for vasodilation. Correction of the acidosis for this girl by administering exogenous alkali or increasing minute ventilation could lead to vasoconstriction and reduced microvascular blood flow. Optimizing microvascular blood flow should improve nutrient delivery and allow spontaneous improvement in metabolic acidosis. Although myocardial contractility may be optimized at normal pH, a pH of 7.25 generally is well tolerated, and increasing the pH is unlikely to improve flow related to improved cardiac output significantly. Similarly, catecholamine responsiveness is minimally depressed by modest acidosis.

Global oxygen delivery is determined by oxygen content of the blood and cardiac output:

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\text{Oxygen delivery} = ([\text{PaO}_2](0.003) + (\text{hemoglobin})(1.34)(\% \text{ oxygen saturation})) \times \text{cardiac output}
\]

Packed red blood cell transfusion can increase hemoglobin and increase oxygen delivery, but increasing hemoglobin increases blood viscosity, thereby reducing microvascular flow. Transfused red blood cells are relatively depleted in 2,3 diphosphoglycerate and, therefore, are less deformable, leading to more sluggish flow through capillaries and reduced ability to unload the oxygen at the tissue level. Paradoxically, some studies have shown decreased microvascular blood flow after transfusion, as measured by gastrointestinal tonometry and orthogonal polarization spectral imaging. This finding may explain, in part, the increased mortality seen among adult patients who receive transfusions to maintain hemoglobin greater than 10 g/dL (100 g/L) compared with patients transfused to maintain hemoglobin greater than 7 g/dL (70 g/L).

Suggested Readings


American Board of Pediatrics Content Specifications

- Understand how pH alters myocardial function
- Understand the relationship between intravascular volume and pressure and organ blood flow
- Understand the concept of blood flow autoregulation
- Understand the contribution of autoregulation to cardiac output
- Know which humoral factors influence tissue blood flow
- Understand the effects of hypoxemia on systemic vascular resistance
- Understand how acidosis affects tissue perfusion
- Understand how alkalosis affects tissue perfusion