

## Capillary refill time is a *very* useful clinical sign in early recognition and treatment of very sick children\*

In this issue of *Pediatric Critical Care Medicine*, Lobos et al (1) report that when they evaluated a series of children who were not sick but were undergoing cardiac catheterization, they did not find a correlation between cardiac index and capillary refill time (CRT) but instead found a correlation between CRT and hematocrit. The authors embarked on this study because their staff believed before this study that CRT was a marker of cardiac output, which they wanted to disprove. The strength of the population sample is that the patients were not receiving inotropes; the weakness is that the children did not have low cardiac output. Tibby and colleagues (2) evaluated this same question in 1999 using a sample of sick patients in the pediatric intensive care unit who were being treated with inotropes and/or fluids. They found an inverse correlation between CRT and stroke volume and a direct correlation with lactate levels in general patients but not in cardiac surgery patients. In a series of classic studies, Parr, Kirklin, Pacifico, and others (3, 4) evaluated risk factors for sudden cardiac death after cardiac surgery in infants. They noted that blood pressure and heart rate did not predict death but low cardiac output and low mixed venous oxygen tension did. Interestingly, for any given cardiac output, high, normal, or low, the mortality risk was higher if mixed venous oxygen tension was low. They further evaluated the peripheral circulation and defined it as cool, tepid, and warm and found that for any given cardiac index cool was associated with worse mortality and warm was associated with better survival. They suggested that although normal blood pressure and heart rates are very important, reduction in death from cardiac events would be best served by

also maintaining the cardiac index at  $>3.0$  L/min/m<sup>2</sup>, the mixed venous oxygen tension at  $>35$  mm Hg, and the skin temperature warm or at a CRT of  $<2$  secs. These could be attained with adequate filling and use of inotropes and vasodilator therapies. Most recently, Raimer and colleagues (5) have reported that a CRT of  $<2$  secs is associated with a superior vena cava oxygen saturation of  $>70\%$  in children in the pediatric intensive care unit. Thus, the warm toe or CRT of  $<2$  secs provides excellent negative predictive value for a cardiac index of  $<3$  or a superior vena cava oxygen saturation of  $>70\%$  and presumably a mixed venous oxygen tension of  $>35$  mm Hg.

The best physical exam measure of cardiac output comes with palpation of the central and peripheral arterial pulses. An experienced practitioner will be able to recognize the qualitative differences in a small pulse volume (low cardiac output), a full volume, and a hammer pulse volume (high cardiac output, low vascular resistance) and most importantly equal or unequal (low cardiac output and or high peripheral resistance) volumes between central and peripheral pulses. In this regard, machine-derived quantitative intravascular pulse volume contour analyses are presently used in pediatric intensive care units to calculate the stroke volume and then multiplied by the heart rate to provide continuous cardiac output. In contrast, CRT is an inexpensive bedside clinical sign of peripheral microvascular perfusion, not cardiac output or even peripheral arterial blood flow *per se*. This has been ably demonstrated in two pediatric investigations measuring Doppler arterial blood flow and CRT in isolated upper and lower extremities (6, 7). An increase in the pressure generated by a cuff to the point of reducing arterial blood flow by 90% was related to only a 0.86-sec further prolongation in healthy children, much less than the prolongation seen under pathologic conditions. When blood is ejected from the heart, it does not go directly to the capillaries; it first travels to the arterioles, which are the body's major resistance vessels. When one applies an external pressure to the capillary bed, the capil-

lary empties its blood and the skin color changes from pink to white. When the pressure is released, the skin will become pink again. The time of this color change back to pink is called the CRT. The determinants of this refill time are many, including arteriolar resistance, venular resistance, viscosity, microvessel thrombosis, polycythemia, hyperleukocytosis, obliterative arteriosclerosis (8), external temperatures (but not fever [9]), and dehydration. Flash capillary refill is seen with vasodilated states and prolonged capillary refill in hypertensive states (10). CRT is age dependent with a 2-sec time found to be normal in children (11). Delayed CRT can be seen in well children under healthy circumstances. For example, in infants placed in a bath by mom or dad and then removed to ambient temperature, CRTs are prolonged and the extremities are cold and blue. However, the parent knows the child is not sick; the child is cold coming out of the bath. Delayed CRT should *never* be assumed benign when it occurs in an infant or child whom the caretaker has brought to you for a sick visit. Prolonged CRT in a sick child tells you that you should do something rather than proceed to the next patient after conferring reassurance.

In two studies of 5,000 sick children presenting to community hospitals in the United States and subsequently transferred to five referral centers, Orr and colleagues (12, 13) noted that hemodynamic signs at presentation were related to outcome. Mortality rates were 1.9% without hemodynamic abnormalities, 3.1% with tachycardia alone, 4.4% with hypotension alone, 7.6% with prolonged CRT, and 26.9% with prolonged CRT and hypotension. Treatment with Pediatric Advanced Life Support (PALS)/Advanced Paediatric Life Support-recommended guidelines of fluid resuscitation followed by inotropic support when needed to restore CRT to  $<2$  secs was associated with a 50% reduction in mortality and abrogation of new onset functional morbidity. Leonard and Beattie (14) and Thompson and colleagues (15) both demonstrated that the recognition of prolonged CRT can improve early diagnosis and treat-

\*See also p. 136.

Key Words: capillary refill time; sick child; triage  
The author has not disclosed any potential conflicts of interest.

Copyright © 2012 by the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies

DOI: 10.1097/PCC.0b013e3182231667

ment of serious infections, including meningococemia in children seen by U.K. general practitioners and subsequently referred to emergency care. Kumar and colleagues (16) developed a triage score in an Indian hospital and similar to Orr demonstrated that prolonged CRT along with high temperature, low oxygen saturation, low systolic blood pressure, and poor sensorium predicted mortalities of 2.2% with one, 6.1% with two, 15.3% with three, 19.4% with four, and 29.4% with all five abnormalities. Evans et al (17) reported that children in Ghana with severe malaria who had a CRT of  $>2$  secs had a two-fold higher risk of death. Pamba and colleagues (18) reported in Kenya that 8% of 4,160 sick children admitted had prolonged CRT, being present in 23% of nonsurvivors compared to 7.5% of survivors. Han et al (12) demonstrated in U.S. community hospitals that each hour that went by without restoring blood pressure and a CRT of  $<3$  secs was associated with a seven-fold increased mortality from multiple-organ failure. Use of PALS/Advanced Paediatric Life Support resuscitation guidelines reduced this mortality risk in a time-dependent fashion. Lima and colleagues (19) tested this association in critically ill adults and similarly noted that prolonged CRT and cool extremities in the first day after resuscitation predicted worsening organ failure and higher lactate levels. Steiner and colleagues (20) reviewed 26 studies and concluded that the most useful clinical sign for predicting severe dehydration in children is a prolonged CRT. Combinations of prolonged CRT, abnormal skin turgor, and abnormal respiratory pattern further improved diagnosis (21). Saavedra and colleagues (22) demonstrated that CRT directly correlated to the degree of dehydration, with a CRT of  $>3$  secs indicating a fluid deficit of more than 100 mL/kg. Jucá and colleagues (23) demonstrated a reduction of CRT from  $>10$  to  $<3$  secs with improved pulses and mental status in children with severe dehydration and shock after 50 mL/kg of fluid infusion in the first hour. Shavit and colleagues (24) reported that accuracy in diagnosing severe dehydration could be further improved by using a digital measure of CRT rather than clinical assessment.

The American Heart Association's Subcommittee on Pediatric Resuscitation (Dallas, TX), through its Pediatric Advanced Life Support curricula, advocates use of CRT to assess peripheral perfusion and response to time-sensitive treatments in children to prevent death as well as secondary functional morbidity

(13, 25, 26). It teaches that a prolonged CRT of  $>2$  secs is an early indicator of compensated shock, an effort to shunt blood from nonvital organs (e.g., skin) to vital organs. Vascular resistance is increased in peripheral beds, resulting in prolonged capillary refill. Treatment during this compensatory phase will be more effective in reducing morbidity and mortality than treatment in the uncompensated shock phase when hypotension occurs despite vasoconstriction (13). The World Health Organization (Geneva, Switzerland) has incorporated CRT in the Emergency Triage and Assessment Guidelines using the presence of prolonged CRT in the sick child to support progression to treatments, as well as triage to facilities where these treatments can be delivered (27). The Global Sepsis Initiative (28) and PALS/American College of Critical Care Medicine guidelines for hemodynamic support of septic shock recommend reversal of prolonged CRT in a time-sensitive manner (29). Use of CRT among other clinical signs is a very useful tool in the quest to reduce global child mortality in resource-poor and -rich settings alike. When resources are not available, the parent or health worker can recognize illness in the child by lack of playing or smiling (abnormal mental status). Medical attention should be afforded. Palpable or measured fever supports infection as the cause, and administration of antibiotics and temperature control can be considered. If accompanied by tachycardia ( $>10\%/^{\circ}\text{C}$  increase in temperature) and tachypnea, then the child is severely ill and should be afforded access to antibiotics and oxygen with triage to a referral medical facility. If accompanied by a prolonged CRT of 2 secs, this child is even sicker and intravenous fluids will be needed if hypovolemia/dehydration is present. In resource-rich settings, a CRT of  $<2$  secs has an excellent negative predictive value for both low cardiac index and low superior vena cava oxygen saturation (assuming normal hematocrit). When the CRT is  $>2$  secs, PALS recommends early goal-directed resuscitation to normal blood pressure and a capillary refill of  $<2$  secs, and this should be possible in the community hospital setting. Once in the pediatric intensive care setting, children who remain in shock despite these earlier efforts can have therapies further directed to the goals of superior vena cava oxygen saturations of  $>70\%$  and a confidence interval of 3.3–6.0 L/min/m<sup>2</sup> in

addition to normal blood pressure and a CRT of  $<2$  secs (30).

Joseph A. Carcillo, MD  
Anesthesiology  
Children's Hospital of  
Pittsburgh  
Pittsburgh, PA

## REFERENCES

1. Lobos A-T, Lee S, Menon K: Capillary refill time and cardiac output in children undergoing cardiac catheterization. *Pediatr Crit Care Med* 2012; 13:136–140
2. Tibby SM, Hatherill M, Murdoch IA: Capillary refill and core-peripheral temperature gap as indicators of haemodynamic status in pediatric intensive care patients. *Arch Dis Child* 1999; 80:163–166
3. Parr GV, Blackstone EH, Kirklin JW: Cardiac performance and mortality early after intracardiac surgery in infants and young children. *Circulation* 1975; 51:867–874
4. Kirklin JK, Blackstone EH, Kirklin JW, et al: Intracardiac surgery in infants under age 3 months: Predictors of postoperative in-hospital cardiac death. *Am J Cardiol* 1981; 48:507–512
5. Raimer PL, Han YY, Weber MS, et al: A normal capillary refill time of 2 seconds is associated with superior vena cava oxygen saturation of  $\geq 70\%$ . *J Pediatr* 2011; 158: 968–972
6. Gray K, Briseno MR, Otsuka NY: The association between capillary refill time and arterial flow in the pediatric upper extremity. *J Pediatr Orthop B* 2008; 17:257–260
7. Karpitskaya Y, Miller J, Otsuka NY: The influence of arterial flow on capillary refill in pediatric lower extremity. *J Surg Orthop Adv* 2008; 17:74–76
8. Sosa T, Lončarić L, Boljević S: Capillary refill test—A possible auxiliary diagnostic method in obliterative arteriosclerosis. *Cor Vasa* 1991; 33:404–413
9. Gorelick MH, Shaw KN, Murphy KO, et al: Effect of fever on capillary refill time. *Pediatr Emerg Care* 1997; 13:305–307
10. LeFlore JL, Engle WD: Capillary refill time is an unreliable indicator of cardiovascular status in term neonates. *Adv Neonatal Care* 2005; 5:147–154
11. Schriger DL, Baraff L: Defining normal capillary refill: variation with age, sex, and temperature. *Ann Emerg Med* 1988; 17:932–935
12. Han YY, Carcillo JA, Dragotta MA, et al: Early reversal of pediatric-neonatal septic shock by community physicians is associated with improved outcome. *Pediatrics* 2003; 112:793–799
13. Carcillo JA, Kuch BA, Han YY, et al: Mortality and functional morbidity after use of PALS/APLS by community physicians. *Pediatrics* 2009; 124:500–508
14. Leonard PA, Beattie TF: presenting features of paediatric meningococcal disease—a five year experience from a paediatric accident

- and emergency department. *Health Bull (Ed-inb)* 2000; 58:148–151
15. Thompson M, Coad N, Harnden A, et al: How well do vital signs identify children with serious infections in paediatric emergency care? *Arch Dis Child* 2009; 94:888–893
  16. Kumar N, Thomas N, Singhal D, et al: Triage score for severity of illness. *Indian Pediatr* 2003; 40:204–210
  17. Evans JA, May J, Ansong D, et al: Capillary refill time as an independent prognostic indicator in severe and complicated malaria. *J Pediatr* 2006; 149:676–681
  18. Pamba A, Maitland K: Capillary refill: Prognostic value in Kenyan children. *Arch Dis Child* 2004; 89:950–955
  19. Lima A, Jansen TC, van Bommel J, et al: The prognostic value of the subjective assessment of peripheral perfusion in critically ill patients. *Crit Care Med* 2009; 37:934–938
  20. Steiner MJ, DeWalt DA, Byerley JS: Is this child dehydrated? *JAMA* 2004; 291:2746–2754
  21. Steiner MJ, DeWalt DA, Byerley JS: Review: Capillary refill time, abnormal skin turgor, and abnormal respiratory pattern are useful signs for detecting dehydration in children. *Evid Based Nurs* 2005; 8:57
  22. Saavedra JM, Harris GD, Li S, et al: Capillary refilling (skin turgor) in the assessment of dehydration. *Am J Dis Child* 1991; 145:296–298
  23. Jucá CA, Rey LC, Martins CV: Comparison between normal saline and a polyelectrolyte solution for fluid resuscitation in severely dehydrated infants with acute diarrhea. *Ann Trop Paediatr* 2005; 25:253–260
  24. Shavit I, Brant R, Nijssen-Jordan C, et al: A novel imaging technique to measure capillary refill time: Improving diagnostic accuracy for dehydration in young children with gastroenteritis. *Pediatrics* 2006; 118:2402–2408
  25. Ralston M, Hazinski MF, Zaritsky A, et al (Eds): Pediatric Advanced Life Support Provider Manual. Dallas, TX, American Heart Association, 2006
  26. Carrillo Alvarez A, Martinez Gutierrez A, Salvat German F: Recognition of the child at risk of cardiopulmonary arrest. *An Pediatr (Barc)* 2006; 65:147–153
  27. Gove S, Tamburlini G, Molyneux E, et al: Development and technical basis of simplified guidelines for emergency triage assessment and treatment in developing countries. WHO Integrated Management of Childhood Illness (IMCI) Referral Care Project. *Arch Dis Child* 1999; 81:473–477
  28. Global Sepsis Initiative. Available at: <http://www.pediatricsepsis.org> or <http://www.wfpiccs.org>. Accessed June 7, 2011
  29. Brierley J, Carcillo JA, Choong K, et al: Clinical practice parameters for hemodynamic support of pediatric and neonatal septic shock: 2007 update from the American College of Critical Care Medicine. *Crit Care Med* 2009; 37:666–688
  30. De Oliveira CF, de Oliveirs DS, Gottschald AF, et al: ACCM/PALS hemodynamic support guidelines for paediatric septic shock: An outcomes comparison with and without monitoring central venous oxygen saturation. *Intensive Care Med* 2008; 34:112:793–799

## Exhaled breath condensate: A breathalyzer for lung inflammation\*

“Every breath you take ... I’ll be watching you.”—Sting, Summers A, The Police, Synchronicity, 1983

Various pulmonary diseases represent the most common reasons for admission to pediatric intensive care units (1). Accordingly, children with asthma, bronchiolitis, pneumonia, aspiration pneumonitis, acute lung injury/acute respiratory distress syndrome, and ventilator-associated lung injury are commonly cared for in pediatric intensive care units. Unlike adult critical care where bronchoalveolar lavage is frequently used to obtain samples for theranostic biomarkers (2), logistic challenges frequently prevent use of this technology to guide diagnostic treatment and disease trajectory questions associated with pulmonary failure in the pediatric intensive care unit. Children present with critical pulmonary illness typically with inability to produce spu-

tum samples when tracheally extubated and with smaller proximal conducting airways and hence smaller endotracheal tubes while intubated.

Accordingly, the report submitted by Hasan and colleagues from Mercy Children’s Hospital, Toledo, OH, describing of the use of exhaled breath condensate (EBC) monitoring among children hospitalized for status asthmaticus should be of great interest to pediatric critical care practitioners (3). These investigators assessed two lipid biomarkers in EBC and compared these findings with other clinical indicators of asthma severity, specifically the Woods Score and the Pulmonary Index, the latter a surrogate for forced expiratory volume at 1 sec. It is of interest that although these children were initially too distressed to provide measurements of forced expiratory volume at 1 sec or forced vital capacity, they were able to breathe through the EBC apparatus to collect an EBC sample, essentially droplets of airway-lining fluid into which water soluble analytes are absorbed, without any change in their work of breathing. Accordingly, the EBC methodology does not perturb the biological system being monitored. More specifi-

cally, no adverse events or changes in patient status were observed during collection of EBC.

For this investigation, the authors chose to follow two lipid biomarkers. 8-isoprostane is a derivative of arachidonic acid that reflects lipid peroxidation oxygen toxicity (4). Isoprostanes do not require cyclooxygenase for their production and are derived *in situ* within phospholipids and subsequently released through phospholipases. This marker reflects production of parent-free radical species by various mechanisms, including activated xanthine oxidase in ischemia–reperfusion settings; increased electron bleed from the mitochondrial electron transport chain in settings of inflammation and high oxygen concentration; activation of polymorphonuclear leukocyte and eosinophil NADPH oxidoreductase; and enhanced catecholamine metabolism such as occurs in stress to generate the family of isoprostane isomers. Lipoxins represent a specific enzymatic product of 15-lipoxygenase known to modulate inflammation (5). This lipid metabolite has been extensively studied in asthma and is known to be involved in inflammatory cell trafficking

\*See also p. 141.

Key Words: 8-isoprostane; exhaled breath condensate; lipoxin A<sub>4</sub>; lipid peroxidation; status asthmaticus  
The author has not disclosed any potential conflicts of interest.

Copyright © 2012 by the Society of Critical Care Medicine and the World Federation of Pediatric Intensive and Critical Care Societies

DOI: 10.1097/PCC.0b013e31823db213