

# Early Identification of Shock in Critically Ill Patients

Matthew C. Strehlow, MD<sup>a,b,\*</sup>

## KEYWORDS

• Shock • Hypotension • Lactate • Base deficit • Evaluation

In the eighteenth century the French surgeon Le Dran coined the term *choc* for soldiers suffering from severe traumatic injuries and heavy blood loss. Shock began appearing in the medical literature in the nineteenth century, and in 1872 the venerated trauma surgeon Samuel D. Gross defined shock as “the rude unhinging of the machinery of life.”<sup>1</sup> Over the centuries the term shock became synonymous with hypotension.

The misconception that hypotension is necessary to define shock persists, despite evidence and international consensus recommendations to the contrary. More appropriately, shock is defined as a life-threatening condition characterized by inadequate delivery of oxygen and nutrients to vital organs relative to their metabolic demand. Inadequate oxygen delivery typically results from poor tissue perfusion but occasionally, may also be caused by an increase in metabolic demand.<sup>2</sup>

In the setting of persistent inadequate oxygen delivery, cells are unable to produce adenosine triphosphate (ATP) to power vital functions. Cells transition to anaerobic metabolism to continue production of ATP, generating lactic acid, which accumulates in the cell and is transported into the blood. The accumulation of lactic acid in the cell is compounded by an increase in production of its precursor, pyruvate, via the stress response.<sup>3</sup> Increased production of lactate accounts for most elevation in blood levels, but a reduction in lactate metabolism also occurs.<sup>4,5</sup>

Systemically, the stress response is intended to release energy stores and augment perfusion to vital organs. Receptors in large arteries detect a decrease in wall tension, activating a hormonal response via the hypothalamus-pituitary-adrenal axis and a neurogenic response through sympathetic stimulation. The resultant increase in circulating levels of epinephrine, norepinephrine, corticosteroids, renin, and glucagon

---

The author has no financial interests to disclose.

<sup>a</sup> Division of Emergency Medicine, Department of Surgery, Stanford University School of Medicine, 701 Welch Road, Building C, Palo Alto, CA 94304, USA

<sup>b</sup> Emergency Department, Stanford University Hospital and Clinics, Stanford, 701 Welch Road, Building C, Palo Alto, CA 94304, USA

\* Department of Surgery, Division of Emergency Medicine, Stanford University School of Medicine, 701 Welch Road, Building C, Palo Alto, CA 94304.

E-mail address: [Strehlow@stanford.edu](mailto:Strehlow@stanford.edu)

Emerg Med Clin N Am 28 (2010) 57–66

doi:10.1016/j.emc.2009.09.006

[emed.theclinics.com](http://emed.theclinics.com)

0733-8627/09/\$ – see front matter © 2010 Elsevier Inc. All rights reserved.

elevates the heart rate and produces vasoconstriction of peripheral arteries. As a whole, cardiac output is augmented, blood pressure elevated, and increased glucose and fatty acids are available to cells as energy precursors.

Counteracting these effects is the build-up of toxic metabolites and inflammatory mediators. Endogenous toxic metabolites derived from damaged cells and exogenous toxins can cause cellular dysfunction, myocardial depression, and vasodilation. Inflammatory mediators are released from the up-regulated immune system, leading to further organ dysfunction and microischemia. The corresponding acidemia potentiates cellular and organ dysfunction.

If the imbalance between oxygen delivery and demand persists, compensatory mechanisms fail, blood pressure and cardiac output decrease, and multiple organ dysfunction syndrome (MODS) develops. Once MODS develops, mortality is high and it is challenging to reverse the cycle of cellular death and dysfunction.

Despite the high prevalence and morbidity of shock, the lack of a widely accepted definition and clear diagnostic criteria have limited the development of robust epidemiologic data. Estimates suggest that more than 1.2 million emergency department (ED) visits annually are for patients in shock.<sup>6,7</sup> Mortality for patients in shock varies depending on the cause, but common causes of shock including sepsis, trauma, and cardiac failure have mortality ranging from 20% to 50%.<sup>8-10</sup> ED patients with persistent hypotension incur the highest rate of death, but mortality is also substantial in those with cryptic shock, or shock without overt hypotension. In patients with presumed septic shock without hypotension, for example, mortality ranges from 18% to 27%.<sup>11,12</sup>

## EARLY DETECTION OF SHOCK

Early recognition and, correspondingly, early intervention before the onset of multiple organ dysfunction have been demonstrated to decrease morbidity and mortality in critically ill patients. The “golden hour” of trauma care has been a tenant for emergency practitioners for decades and more recently the “golden hour” for medical patients is being hailed as imperative to improving outcomes.<sup>13</sup> Goal-directed therapy, attempted for years in the intensive care unit (ICU) with variable results, when implemented within the first 6 hours of presentation to the ED improved absolute mortality by 16% in the original study by Rivers.<sup>14</sup> Evidence has continued to accumulate and more recently a meta-analysis reported that an early, quantitative resuscitation strategy in patients with severe sepsis and septic shock significantly reduced mortality. In contrast, the same investigators concluded that equivalent strategies initiated later in the patient’s course were not effective.<sup>15</sup>

Although most recent research has focused on septic shock, studies of alternate causes of shock have also shown that early intervention is a critical factor in determining outcomes. Sebat and colleagues<sup>16</sup> described a 5-year process of implementing an early recognition and rapid-response strategy for patients with all forms of shock. Mortality was reduced by a factor of 3 (40%–12%). Although results of this magnitude are difficult to replicate, they suggest that reducing time to recognition is a critical aspect of caring for patients in shock. In contrast to the mortality reductions seen with strategies that target early recognition and intervention, care decisions in later stages of shock, such as choice of vasopressor, administration of steroids, and implementation of tight glycemic control, have proven to have minimal if any effects.<sup>17-21</sup>

## HISTORY AND PHYSICAL EXAMINATION

Emergency providers are frequently presented with the undifferentiated patient and must be intimately familiar with the elements of history, physical examination, and

diagnostic testing that may suggest early shock, before the onset of significant organ dysfunction (**Box 1**).

Vital-sign abnormalities have long been the cornerstone of shock recognition. Traditionally, a patient was deemed to be in shock when tachycardic, tachypneic, and possessing a systolic blood pressure (SBP) less than 90 mm Hg. Current evidence suggests that traditional vital signs are insensitive markers of early hypoperfusion. Advanced trauma life support (ATLS) teaches that decreased blood pressure is a marker of hemorrhage that is already moderate to severe. Despite this, a SBP of less than 90 mm Hg is still used as a screening criterion for the activation of trauma patients. Recent evidence supports ATLS teaching that a SBP less than 90 mm Hg is a late and insensitive finding of hemorrhage and shock.<sup>22-27</sup> Parks and colleagues<sup>26</sup> performed a retrospective evaluation of the National Trauma Database. They evaluated a cohort of trauma patients with a median initial SBP of 90 mm Hg; mortality in these patients was 65% and the base deficit 20. Lipsky and colleagues<sup>28</sup> determined that patients who were hypotensive (<90 mm Hg) in the prehospital setting but normotensive in the ED had a 2-fold increase in mortality and a 3-fold increase in injuries requiring an emergency therapeutic operation when compared with patients normotensive in both settings. Although an SBP of less than 90 mm Hg is a marker of severe disease in trauma patients, higher cut-offs could improve sensitivity for life-threatening injury. Studies in the ED and prehospital setting show an increase in patients' mortality and injuries when blood pressure decreases to less than 110 mm Hg.<sup>22,24</sup> As a result of these studies many trauma experts now argue that blood pressures less than 110 mm Hg should be considered hypotension.

**Box. 1****Signs of shock***Early signs<sup>a</sup>*

- Tachypnea
- Tachycardia
- Weak or bounding peripheral pulses
- Delayed capillary refill (>2 seconds)
- Pale or cool skin
- Narrowed pulse pressure
- Oliguria
- Lactic acidosis
- Elevated base deficit

*Late signs*

- Decreased mental status
- Weak or absent central pulses
- Central cyanosis
- Hypotension
- Bradycardia

<sup>a</sup> Early signs of shock are frequently seen in later stages and late signs such as altered mental status may present early depending on the cause and the patient.

In nontrauma patients systemic hypotension is likewise a late finding of critical illness and mortality ranges from 20% to 60% for common causes of hypotensive shock.<sup>29,30</sup> A single episode of hypotension (<100 mm Hg) in the prehospital or ED setting portends an increased risk of death during hospital admission.<sup>31,32</sup> As the frequency or duration of hypotension increases, so does the patient's risk of death. Although concerning when identified, ED hypotension is an insensitive marker of critical illness and in-hospital mortality.<sup>33,34</sup>

Likewise, an elevated heart rate has limited predictive value in trauma and nontrauma patients.<sup>35</sup> Despite ATLS teaching that tachycardia is present after moderate acute blood loss, studies in healthy phlebotomized patients and trauma patients reveal supine heart rate to be an insensitive marker of injury severity and mortality.<sup>25,27,36</sup> Furthermore, tachycardia is frequently absent in patients with significant dehydration and hypovolemia.<sup>25</sup>

Calculation of the shock index—the heart rate divided by the SBP—can improve the detection of critically ill patients compared to HR and BP alone.<sup>34,37</sup> Values falling significantly outside normal (0.5–0.7), those greater than 0.9, indicate impaired cardiac function and correspondingly a reduced cardiac output. Although an elevated shock index heralds an increased risk of critical illness and mortality, its sensitivity remains low and it cannot be used in isolation to evaluate for occult shock.

In addition to vital signs, which focus on the cardiac and respiratory systems, other physical examination findings are helpful in the recognition of tissue hypoperfusion. Altered mental status, poor skin perfusion, and oliguria are markers of decreased end-organ perfusion and have been found to be independent predictors of 30-day mortality in patients with cardiogenic shock.<sup>38</sup>

Lima and colleagues<sup>39</sup> studied poor peripheral skin perfusion, defined as a delayed capillary refill time greater than 4.5 seconds or extremity coolness to the examiner's touch, in recently admitted, critically ill patients in the ICU after resolution of hypotension. Poor peripheral skin perfusion was identified as an independent predictor of worsening organ failure and persistent lactic acidosis. Other studies have determined signs of poor perfusion on extremity skin examination to correlate with global hemodynamic dysfunction, such as decreased cardiac output.<sup>40,41</sup> In children with meningococcal disease, cool extremities and abnormal skin signs have been shown to be an early indicator of disease before the onset of other, more classic findings.<sup>42</sup>

Urine output is a marker of kidney perfusion. In the setting of decreased blood flow, blood redistributes from the renal cortex to the renal medulla, lowering the glomerular filtration rate and urine production. Urine output should be monitored by Foley catheter placement early in the ED course, because an accurate estimation requires at least 30 minutes of collection. During resuscitation, urine production is considered normal if greater than 1 mL/kg/h, reduced if 0.5 to 1 mL/kg/h, or severely reduced if less than 0.5 mL/kg/h.

## LABORATORY MARKERS OF HYPOPERFUSION

### *Lactate*

---

Elevated lactate levels in the setting of critical illness are associated with a worse prognosis for medical and trauma patients. Multiple conditions resulting in inadequate oxygen delivery, disproportionate oxygen demand, and diminished oxygen use may lead to elevated lactate levels (**Box 2**), but most of these conditions are readily apparent or cause only modest, transient elevations in the blood lactate levels. An abnormal lactate level is generally considered greater than 2 mmol/L. A level greater

**Box. 2****Causes of an elevated lactate**

## Inadequate oxygen delivery

- Volume depletion or profound dehydration

- Significant blood loss

- Septic shock

- Profound anemia

- Severe hypoxemia

- Prolonged carbon monoxide exposure

- Trauma

## Disproportionate oxygen demands

- Hyperthermia

- Shivering

- Seizures

- Strenuous exercise

## Inadequate oxygen use

- Systemic inflammatory response syndrome

- Diabetes mellitus

- Total parenteral nutrition

- Human immunodeficiency virus infection

- Drugs such as metformin, salicylate, antiretroviral agents, isoniazid, propofol, cyanide.

than 4 mmol/L is significantly elevated and in most settings is a sign of tissue hypoperfusion.

Several trials have demonstrated the prognostic value of lactate levels.<sup>11,12,43–45</sup> Mikkelsen<sup>12</sup> studied initial ED lactate levels in patients with presumed sepsis and determined that elevations predicted an increased 28-day mortality independent of organ dysfunction and hypotension. A corresponding study by Howell<sup>11</sup> looked at patients with presumed sepsis but who did not qualify as having septic shock; patients with a lactate level greater than 4 mmol/L at the time of admission had a mortality of 26.5%.

Lactate clearance can be used to risk stratify patients and determine their response to therapy.<sup>33,46</sup> One ED study determined that a lactate reduction of greater than 10% at 6 hours was associated with a 3-fold lower mortality and reduced need for vasopressors. It has been recommended that patients with a decline in lactate of less than 50% at 1 hour require additional resuscitation measures.<sup>6</sup>

Lactate levels may be arterial, central venous, or peripherally obtained. Studies document good correlation between samples acquired from different locations.<sup>47,48</sup> Ideally, peripheral venous lactates should be drawn without the use of a tourniquet as prolonged tourniquet times may falsely elevate levels.

**Arterial Base Deficit**

Arterial base deficit is a calculation of the quantity of base required to raise the pH of blood to the expected level. It is calculated from the partial pressure of carbon dioxide ( $P_{aCO_2}$ ), pH, and serum bicarbonate. Base deficit is more sensitive to tissue

hypoperfusion than pH or serum bicarbonate levels alone. A normal value is  $-2$  to  $2$  and a significantly elevated base deficit is greater than  $6$ . Similar to lactate, it has been shown in trauma patients to predict the severity of injury and mortality during initial resuscitation.<sup>26,43,49,50</sup> Because many hospitals can perform bedside arterial blood gas analysis, determination of base deficit is a useful screening tool for trauma patients. Evidence as to its utility in nontrauma patients with shock or later in the course of patients with traumatic injuries is less robust, although base deficit can be used in these circumstances to identify occult hypoperfusion and guide resuscitation when lactate is unavailable.<sup>51-53</sup>

Various other biomarkers of shock and organ dysfunction have been proposed. A recent study by Shapiro and colleagues<sup>54</sup> identified 3 biomarkers (neutrophil gelatinase-associated lipocalin, protein C, interleukin 1) that, when used in conjunction, predicted severe sepsis, septic shock, and death in ED patients. This unique biomarker panel and other biomarkers hold promise but require further study before their widespread clinical implementation.

### ***Noninvasive Monitoring of Regional Tissue Perfusion***

---

Multiple noninvasive techniques to monitor regional tissue perfusion have been developed. The most established of these include sublingual capnometry ( $Slco_2$ ), near-infrared spectroscopy to monitor muscle tissue oxygen saturation ( $Sto_2$ ), and transcutaneous tissue oxygenation and capnometry ( $Ptco_2$ ,  $Ptcco_2$ ). These techniques are based on the concept that under physiologic stress the body will preferentially shunt blood away from the peripheral and splanchnic tissues to augment perfusion of vital organs, primarily the brain and heart. Therefore, unlike more global markers of tissue hypoperfusion such as lactate and base deficit, these regional markers will demonstrate abnormalities in perfusion and oxygenation earlier in the course of the patient's illness. Furthermore, most can be rapidly obtained and continuously monitored.

Sublingual capnometry is a measurement of the carbon dioxide ( $CO_2$ ) level in the vascular bed underlying the tongue. It is measured in a manner similar to an oral temperature.  $Slco_2$  has been demonstrated to be a sensitive marker of splanchnic perfusion and gut ischemia.<sup>55-57</sup> In the critical-care setting, splanchnic perfusion has long been identified as an early marker of hypoperfusion. Multiple studies in trauma and nontrauma patients have determined  $Slco_2$  to be a predictor of injury severity, organ dysfunction, and mortality.<sup>43,49,58,59</sup> Widespread adoption of sublingual capnometry monitoring in the ED has been limited by the requirement for new equipment, difficulties with obtaining accurate, reproducible measurements, and the need for further study.

Muscle  $Sto_2$  uses light absorption to determine the oxygen saturation in the microcirculation in muscle tissue. An external probe is commonly placed on the biceps or thenar eminence. Continuous monitoring can be performed similarly to pulse oximetry. Recently, Cohn and colleagues<sup>50</sup> demonstrated that an  $Sto_2$  less than  $75\%$  during the initial resuscitation of trauma patients performed equivalently to an arterial base deficit as a predictor of MODS. This cut-off was found to have a high sensitivity but low specificity for significant injury. Other studies of muscle  $Sto_2$  found similar results in trauma patients, but it has not performed so well in patients with sepsis.<sup>60-62</sup>

Transcutaneous tissue oxygenation and capnometry measurements most often use heated probes placed on the skin to determine peripheral tissue perfusion. Studies have shown  $Stco_2$  and  $Stcco_2$  to be markers of early hemodynamic compromise and increased mortality.<sup>23,63-65</sup> Tissue trauma resulting from the probes and a lack of established critical values have limited its widespread adoption.

### ***Bedside Ultrasonography***

---

Bedside ultrasonography has become an essential tool in the evaluation of shock patients in the ED. In addition to the focused abdominal sonography in trauma examination, bedside ultrasound can augment the assessment and management of critically ill patients. Although most ED-based ultrasound studies of critically ill have focused on the evaluation of hypotensive patients, a recent study evaluated trauma patients who were normotensive after initial resuscitation. The study found that patients with a smaller inferior vena cava diameter were at increased risk for recurrent hypotension.<sup>66</sup> Furthermore, determining the correct etiology of shock in ED patients is challenging, with providers able to accurately diagnose only 25% to 50% of cases.<sup>67,68</sup> Early, protocol-driven bedside ultrasound performed by emergency physicians can improve diagnostic accuracy to 80%.<sup>68</sup> Overall, the literature illustrates that bedside ultrasonography performed by ED providers plays a crucial role in the early recognition and evaluation of patients in shock. See also article by Perera and colleagues elsewhere in this issue.

### **SUMMARY**

Shock is a state of inadequate tissue perfusion and, although hypotension is often present, it is a late finding and not necessary for the diagnosis. Timely recognition and intervention are critical to reducing the morbidity and mortality of shock. Clinical suspicion, thorough physical examination, and laboratory screening using base deficit or lactate can improve early identification of patients suffering from shock.

### **REFERENCES**

1. Cairns CB. Rude unhinging of the machinery of life: metabolic approaches to hemorrhagic shock. *Curr Opin Crit Care* 2001;7:437.
2. Antonelli M, Levy M, Andrews PJ, et al. Hemodynamic monitoring in shock and implications for management. International Consensus Conference, Paris, France, 27–28 April 2006. *Intensive Care Med* 2007;33:575.
3. Gore DC, Jahoor F, Hibbert JM, et al. Lactic acidosis during sepsis is related to increased pyruvate production, not deficits in tissue oxygen availability. *Ann Surg* 1996;224:97.
4. Levraut J, Ciebiera JP, Chave S, et al. Mild hyperlactatemia in stable septic patients is due to impaired lactate clearance rather than overproduction. *Am J Respir Crit Care Med* 1998;157:1021.
5. Levraut J, Ichai C, Petit I, et al. Low exogenous lactate clearance as an early predictor of mortality in normolactatemic critically ill septic patients. *Crit Care Med* 2003;31:705.
6. Marx JA, editor. *Marx: Rosen's emergency medicine: concepts and clinical practice*, vol. 1. 6th edition. Philadelphia: Mosby Elsevier, 2006.
7. Pitts SR, Niska RW, Xu J, et al. National Hospital Ambulatory Medical Care Survey: 2006 emergency department summary. *Natl Health Stat Report* 2008;7:1–38.
8. Astiz ME, Rackow EC. Septic shock. *Lancet* 1998;351:1501.
9. Janssens U, Graf J. [Shock—what are the basics?] *Internist (Berl)* 2004;45:758–66 [in German].
10. Shoemaker WC, Peitzman AB, Bellamy R, et al. Resuscitation from severe hemorrhage. *Crit Care Med* 1996;24:S12.
11. Howell MD, Donnino M, Clardy P, et al. Occult hypoperfusion and mortality in patients with suspected infection. *Intensive Care Med* 2007;33:1892.

12. Mikkelsen ME, Miltiades AN, Gaijeski DF, et al. Serum lactate is associated with mortality in severe sepsis independent of organ failure and shock. *Crit Care Med* 2009;37:1670.
13. Shapiro NI, Howell MD, Talmor D, et al. Implementation and outcomes of the Multiple Urgent Sepsis Therapies (MUST) protocol. *Crit Care Med* 2006;34:1025.
14. Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med* 2001;345:1368.
15. Jones AE, Brown MD, Trzeciak S, et al. The effect of a quantitative resuscitation strategy on mortality in patients with sepsis: a meta-analysis. *Crit Care Med* 2008;36:2734.
16. Sebat F, Musthafa AA, Johnson D, et al. Effect of a rapid response system for patients in shock on time to treatment and mortality during 5 years. *Crit Care Med* 2007;35:2568.
17. Abraham WT, Adams KF, Fonarow GC, et al. In-hospital mortality in patients with acute decompensated heart failure requiring intravenous vasoactive medications: an analysis from the Acute Decompensated Heart Failure National Registry (ADHERE). *J Am Coll Cardiol* 2005;46:57.
18. Annane D, Vignon P, Renault A, et al. Norepinephrine plus dobutamine versus epinephrine alone for management of septic shock: a randomised trial. *Lancet* 2007;370:676.
19. Cuffe MS, Califf RM, Adams KF Jr, et al. Short-term intravenous milrinone for acute exacerbation of chronic heart failure: a randomized controlled trial. *JAMA* 2002;287:1541.
20. Finfer S, Chittock DR, Su SY, et al. Intensive versus conventional glucose control in critically ill patients. *N Engl J Med* 2009;360:1283.
21. Sprung CL, Annane D, Keh D, et al. Hydrocortisone therapy for patients with septic shock. *N Engl J Med* 2008;358:111.
22. Bruns B, Gentilello L, Elliott A, et al. Prehospital hypotension redefined. *J Trauma* 2008;65:1217.
23. Chien LC, Lu KJ, Wo CC, et al. Hemodynamic patterns preceding circulatory deterioration and death after trauma. *J Trauma* 2007;62:928.
24. Eastridge BJ, Salinas J, McManus JG, et al. Hypotension begins at 110 mm Hg: redefining "hypotension" with data. *J Trauma* 2007;63:291.
25. McGee S, Abernethy WB 3rd, Simel DL. The rational clinical examination. Is this patient hypovolemic? *JAMA* 1999;281:1022.
26. Parks JK, Elliott AC, Gentilello LM, et al. Systemic hypotension is a late marker of shock after trauma: a validation study of Advanced Trauma Life Support principles in a large national sample. *Am J Surg* 2006;192:727.
27. American College of Surgeons Committee on Trauma, editor. Advanced trauma life support for doctors. 7th edition. Chicago: American College of Surgeons; 2004.
28. Lipsky AM, Gausche-Hill M, Henneman PL, et al. Prehospital hypotension is a predictor of the need for an emergent, therapeutic operation in trauma patients with normal systolic blood pressure in the emergency department. *J Trauma* 2006;61:1228.
29. Menon V, White H, LeJemtel T, et al. The clinical profile of patients with suspected cardiogenic shock due to predominant left ventricular failure: a report from the SHOCK Trial Registry. SHould we emergently revascularize Occluded Coronaries in cardiogenic shock? *J Am Coll Cardiol* 2000;36:1071.
30. Rivers E. The outcome of patients presenting to the emergency department with severe sepsis or septic shock. *Crit Care* 2006;10:154.

31. Jones AE, Stiell IG, Nesbitt LP, et al. Nontraumatic out-of-hospital hypotension predicts in hospital mortality. *Ann Emerg Med* 2004;43:106.
32. Jones AE, Yiannibas V, Johnson C, et al. Emergency department hypotension predicts sudden unexpected in-hospital mortality: a prospective cohort study. *Chest* 2006;130:941.
33. Nguyen HB, Rivers EP, Knoblich BP, et al. Early lactate clearance is associated with improved outcome in severe sepsis and septic shock. *Crit Care Med* 2004;32:1637.
34. Rady MY, Smithline HA, Blake H, et al. A comparison of the shock index and conventional vital signs to identify acute, critical illness in the emergency department. *Ann Emerg Med* 1994;24:685.
35. Wo CC, Shoemaker WC, Appel PL, et al. Unreliability of blood pressure and heart rate to evaluate cardiac output in emergency resuscitation and critical illness. *Crit Care Med* 1993;21:218.
36. Brasel KJ, Guse C, Gentilello LM, et al. Heart rate: is it truly a vital sign? *J Trauma* 2007;62:812.
37. Toosi MS, Merlino JD, Leeper KV. Prognostic value of the shock index along with transthoracic echocardiography in risk stratification of patients with acute pulmonary embolism. *Am J Cardiol* 2008;101:700.
38. Hasdai D, Holmes DR Jr, Claff RM, et al. Cardiogenic shock complicating acute myocardial infarction: predictors of death. GUSTO Investigators. Global Utilization of Streptokinase and Tissue-Plasminogen Activator for Occluded Coronary Arteries. *Am Heart J* 1999;138:21.
39. 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.
40. Bailey JM, Levy JH, Kopel MA, et al. Relationship between clinical evaluation of peripheral perfusion and global hemodynamics in adults after cardiac surgery. *Crit Care Med* 1990;18:1353.
41. Kaplan LJ, McPartland K, Santora TA, et al. Start with a subjective assessment of skin temperature to identify hypoperfusion in intensive care unit patients. *J Trauma* 2001;50:620.
42. Thompson MJ, Ninis N, Perera R, et al. Clinical recognition of meningococcal disease in children and adolescents. *Lancet* 2006;367:397.
43. Baron BJ, Dutton RP, Zehtabchi S, et al. Sublingual capnometry for rapid determination of the severity of hemorrhagic shock. *J Trauma* 2007;62:120.
44. Schmiechen NJ, Han C, Milzman DP. ED use of rapid lactate to evaluate patients with acute chest pain. *Ann Emerg Med* 1997;30:571.
45. Shapiro NI, Howell MD, Talmor D, et al. Serum lactate as a predictor of mortality in emergency department patients with infection. *Ann Emerg Med* 2005;45:524.
46. Abramson D, Scalea TM, Hitchcock R, et al. Lactate clearance and survival following injury. *J Trauma* 1993;35:584.
47. Lavery RF, Livingston DH, Tortella BJ, et al. The utility of venous lactate to triage injured patients in the trauma center. *J Am Coll Surg* 2000;190:656.
48. Weil MH, Michaels S, Rackow EC. Comparison of blood lactate concentrations in central venous, pulmonary artery, and arterial blood. *Crit Care Med* 1987;15:489.
49. Baron BJ, Sinert R, Zehtabchi S, et al. Diagnostic utility of sublingual PCO<sub>2</sub> for detecting hemorrhage in penetrating trauma patients. *J Trauma* 2004;57:69.
50. Cohn SM, Nathens AB, Moore FA, et al. Tissue oxygen saturation predicts the development of organ dysfunction during traumatic shock resuscitation. *J Trauma* 2007;62:44.

51. Husain FA, Martin MJ, Mullenix PS, et al. Serum lactate and base deficit as predictors of mortality and morbidity. *Am J Surg* 2003;185:485.
52. Martin MJ, FitzSullivan E, Salim A, et al. Discordance between lactate and base deficit in the surgical intensive care unit: which one do you trust? *Am J Surg* 2006; 191:625.
53. Smith I, Kumar P, Molloy S, et al. Base excess and lactate as prognostic indicators for patients admitted to intensive care. *Intensive Care Med* 2001;27:74.
54. Shapiro NI, Trzeciak S, Hollander JE, et al. A prospective, multicenter derivation of a biomarker panel to assess risk of organ dysfunction, shock, and death in emergency department patients with suspected sepsis. *Crit Care Med* 2009; 37:96.
55. Pernet A, Weil MH, Tang W, et al. Effects of hyper- and hypoventilation on gastric and sublingual PCO<sub>2</sub>. *J Appl Phys* 1999;87:933.
56. Povoas HP, Weil MH, Tang W, et al. Comparisons between sublingual and gastric tonometry during hemorrhagic shock. *Chest* 2000;118:1127.
57. Weil MH, Nakagawa Y, Tang W, et al. Sublingual capnometry: a new noninvasive measurement for diagnosis and quantitation of severity of circulatory shock. *Crit Care Med* 1999;27:1225.
58. Marik PE. Sublingual capnography: a clinical validation study. *Chest* 2001;120: 923.
59. Marik PE, Bankov A. Sublingual capnometry versus traditional markers of tissue oxygenation in critically ill patients. *Crit Care Med* 2003;31:818.
60. Creteur J. Muscle StO<sub>2</sub> in critically ill patients. *Curr Opin Crit Care* 2008;14:361.
61. Ikossi DG, Knudson MM, Morabito DJ, et al. Continuous muscle tissue oxygenation in critically injured patients: a prospective observational study. *J Trauma* 2006;61:780.
62. Wan JJ, Cohen MJ, Rosenthal G, et al. Refining resuscitation strategies using tissue oxygen and perfusion monitoring in critical organ beds. *J Trauma* 2009; 66:353.
63. Shoemaker WC, Belzberg H, Wo CC, et al. Multicenter study of noninvasive monitoring systems as alternatives to invasive monitoring of acutely ill emergency patients. *Chest* 1998;114:1643.
64. Shoemaker WC, Wo CC, Chan L, et al. Outcome prediction of emergency patients by noninvasive hemodynamic monitoring. *Chest* 2001;120:528.
65. Tatevossian RG, Wo CC, Velmahos GC, et al. Transcutaneous oxygen and CO<sub>2</sub> as early warning of tissue hypoxia and hemodynamic shock in critically ill emergency patients. *Crit Care Med* 2000;28:2248.
66. Yanagawa Y, Sakamoto T, Okada Y. Hypovolemic shock evaluated by sonographic measurement of the inferior vena cava during resuscitation in trauma patients. *J Trauma* 2007;63:1245.
67. Jones AE, Tayal VS, Sullivan DM, et al. Randomized, controlled trial of immediate versus delayed goal-directed ultrasound to identify the cause of nontraumatic hypotension in emergency department patients. *Crit Care Med* 2004;32:1703.
68. Moore CL, Rose GA, Tayal VS, et al. Determination of left ventricular function by emergency physician echocardiography of hypotensive patients. *Acad Emerg Med* 2002;9:186.