



Assessing Patients During Septic Shock Resuscitation

How to integrate capillary refill time and skin mottling score into the six-hour bundle.

ABSTRACT: In 2015, the Surviving Sepsis Campaign six-hour bundle was updated. The revised version now recommends documenting the reassessment of volume status and tissue perfusion after initial fluid resuscitation through a repeated focused examination. This article addresses the practice and interpretation of two components of this examination in adults: capillary refill time and skin mottling score. It further discusses how to best integrate these noninvasive parameters into the care of patients undergoing resuscitation for septic shock.

Keywords: capillary refill time, peripheral perfusion, peripheral perfusion indicators, septic shock resuscitation, skin mottling score, Surviving Sepsis Campaign

Between May 2014 and April 2015, the *New England Journal of Medicine* published three investigations into the guided resuscitation of patients with septic shock.¹⁻³ As a result of these trials, the Surviving Sepsis Campaign (SSC) has revised its six-hour bundle (see *Surviving Sepsis Campaign: Updated Bundles in Response to New Evidence*, at www.survivingsepsis.org/SiteCollectionDocuments/SSC_Bundle.pdf).⁴ The revisions have profound implications for nursing practice. Severe sepsis strikes an estimated 19.4 million people worldwide annually,⁵ with between 894,000 and 3.1 million cases occurring in the United States.⁶ In 2014, 182,242 of these U.S. cases resulted in death.⁷ In fact, an analysis of two inpatient cohorts from Kaiser Permanente Northern California and the Healthcare Cost and Utilization Project Nationwide Inpatient Sample found that sepsis was a factor in one-third to one-half

of all hospital deaths.⁸ The Centers for Disease Control and Prevention has identified the early recognition and treatment of sepsis as a national priority.

One revision to the SSC bundle is the recommendation to document reassessment of volume status and tissue perfusion after initial fluid resuscitation—either through a repeated examination focused on vital signs, cardiopulmonary function, capillary refill time (CRT), pulse, and skin mottling score (SMS) or through two of the following methods⁴:

- central venous pressure (CVP) measurement
- central venous oxygen saturation (ScvO₂) measurement
- bedside cardiovascular ultrasound
- dynamic assessment of fluid responsiveness through passive leg raising or a fluid challenge

This article discusses two of these components—CRT and SMS—for which practice and interpretation

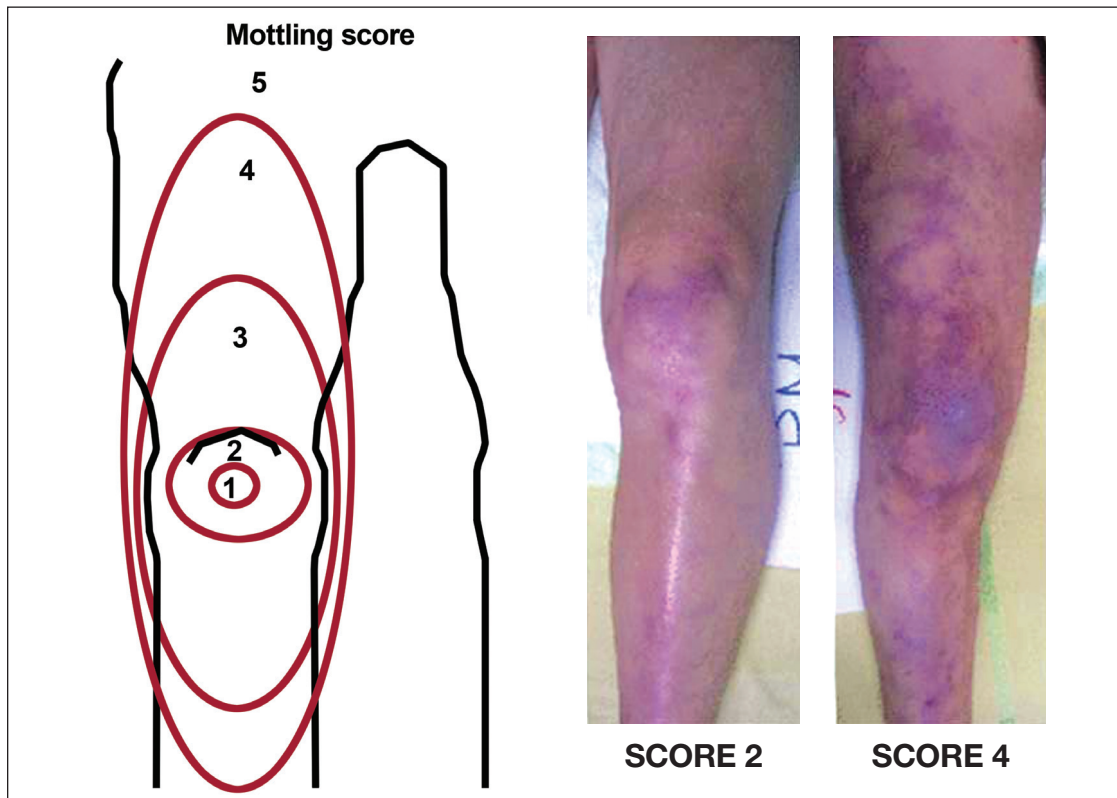


Figure 1. The skin mottling score is based on the extension of the mottling on the leg. Score 0 indicates no mottling; score 1, modest mottling area (coin size) localized to the center of the knee; score 2, moderate mottling area that does not exceed the superior edge of the kneecap; score 3, mild mottling area that does not exceed the middle thigh; score 4, severe mottling area that does not exceed the fold of the groin; score 5, extremely severe mottling area that exceeds the fold of the groin. Reprinted with permission from Ait-Oufella H, et al. *Intensive Care Med* 2011;37(5):801-7.

vary widely. The discussion is informed by articles related to the use of these noninvasive assessments both in patients with septic shock and in normal control groups. The articles were identified through a literature search using PubMed, CINAHL, Web of Science, and the Cochrane databases; spanning 1985 through 2016; and including the following search terms: *septic shock*, *capillary refill time*, *skin mottling*, *microcirculation physiology*, and *microcirculation monitoring*, as well as links to additional citations, major conference abstracts, and references cited in the relevant research and review articles.

CRT PRACTICE AND INTERPRETATION

CRT refers to the time required for blood flow—and thus color—to return to the distal capillaries after the release of compression sufficient to cause blanching of the fingertip or knee. CRT is believed to indicate

peripheral perfusion, with a longer CRT denoting reduced capillary perfusion.⁹ Although CRT is often measured as a part of patient assessment, there are no standard recommendations for the practice or interpretation of this measurement (see *Variations in CRT Practice*¹⁰⁻¹⁷).

Threshold value. There is no agreement on what constitutes normal or threshold values for CRT. In 1988, Schriger and colleagues conducted a seminal study that included 304 healthy volunteers (ages two weeks to 95 years) and found that the median fingertip CRT differed by age and sex.¹⁷ For young men and women (ages 20 to 49 years), the median CRT was one second and 1.2 seconds, respectively, but in older men and women (ages 62 to 95 years), it was 1.8 and 1.5 seconds, respectively, though the men were, on average, five years older than the women. Based on these findings, the upper limits of normal (CRT values that

include 95% of Schriger's healthy volunteers) were two seconds for adult men, 2.9 seconds for adult women, and 4.5 seconds for the older adult population (men and women combined).¹⁷ A more recent study by Anderson and colleagues, which included 1,000 healthy adults ages 29 to 89, compared Schriger's age- and sex-specific limits for fingertip CRT with a two-second upper limit, which is commonly regarded as an indication of normal peripheral perfusion.¹¹ The investigators found they could more accurately identify normal versus abnormal peripheral perfusion using Schriger's limits, though the approach was not flawless. They found that CRT increased with age at a rate of 3.3% per decade and was, on average, slightly less in men than in women, with the upper limit of normal being 3.5 seconds. Applying a two-second upper limit of normal would have misclassified 45% of the Anderson sample, but using Schriger's age- and sex-specific values would have misclassified only 19% of the younger adults and 5% of the older adults in that sample.¹¹ While Anderson and colleagues found that age, sex, and both ambient and patient temperature affect CRT, these factors accounted for only 8% of CRT variance in their study. As is true for healthy patients, there is no standardized threshold by which to classify CRT as normal or abnormal in patients with septic shock.

Since the publication of those studies, some investigators have used Schriger's age- and sex-specific values for CRT,¹⁶ while others have used CRT fingertip thresholds of four or 4.5 seconds.¹²⁻¹⁵

Sites of measurement. In studies of CRT, only two sites—fingertip and knee—have been used, with most studies using the fingertip. In one study of patients with septic shock, knee CRT was assessed and found to be longer than fingertip CRT both in survivors and nonsurvivors.¹⁰

CRT and skin tone. CRT has not been studied widely in patients with dark skin. One study in which 10% of participants were nonwhite, however, found no CRT differences due to ethnicity.¹¹

Compression time varies, but ranges from five^{11,16-19} to 15 seconds.^{10,13,14} The time required for color to return to the tissues is generally measured by a chronometer or a stopwatch. No studies have been conducted in adults to determine the effect of the differences in compression time on CRT.

Compression firmness. A majority of the research on CRT describes the pressure applied as moderate or firm.^{11,17-20} Ait-Oufella and colleagues attempted to standardize compression firmness with a protocol specifying that clinicians should apply sufficient pressure to cause blanching at the tip of their own fingernail, as indicated by the "appearance of a thin white distal crescent" beneath the nail.¹⁰

Repeated CRT measurements. For adult patients, there are no recommendations regarding whether to repeat CRT measurements, the time between CRT measurements, or whether to average two CRT measurements. However, in their 2008 study of 1,000 healthy adults, Anderson and colleagues measured CRT twice, with the measurements one minute apart, and averaged the two.¹¹ They found the mean difference between the repeated measurements was only -0.1 second, suggesting that repeated CRT measurements taken one minute apart are reproducible.

Interobserver agreement. Because so many aspects of CRT measurement are not standardized, it can be challenging to achieve agreement between those performing the assessment. The following factors, however, may improve CRT interobserver agreement:

- standardization of practice
- measurement using a stopwatch or chronometer
- averaging two measurements
- using thresholds to indicate values that are abnormal in healthy people and values that are associated with poorer outcomes in patients with septic shock

Two studies of critically ill patients demonstrate how these factors may be integrated into the practice of measuring and interpreting CRT. In a study of 48 critically ill patients, in which CRT measurement was standardized (15 seconds of firm pressure was applied to the distal phalanx, with the time to

Variations in CRT Practice^{10-17, a}

The practice of capillary refill time (CRT) measurement varies widely among clinicians. Although there are no standard recommendations for performance or interpretation, the following practices have been adopted in several studies of CRT's use and efficacy as an indicator of peripheral perfusion in septic shock.

- **Threshold value.** Commonly used fingertip thresholds include four seconds, 4.5 seconds, or Schriger's age- and sex-specific values (two seconds for young adult men, 2.9 seconds for young adult women, and 4.5 seconds for older adults).
- **Sites of measurement.** One of two sites is commonly used for measurement: the index fingertip (distal phalanx) or the center of the knee, with the extremity at heart level. There appears to be no clinically significant difference in the measurements obtained from other fingers, but subsequent measurements should be taken from the same site. Knee CRT is longer than fingertip CRT.
- **Compression time** ranges from five to 15 seconds. It's recommended that practitioners use one compression time for all measurements.
- **Compression firmness.** The pressure applied should be firm enough to cause blanching (the appearance of a thin white crescent) at the tip of the clinician's own fingernail.
- **Repeated measurement.** Measure CRT twice, waiting one minute between measurements, and average the two values.

^aCRT has not been widely studied in patients with dark skin.

return of normal color recorded by chronometer) and a five-second threshold was used, the observers demonstrated significant agreement regarding normal versus abnormal CRT.²⁰ In a pilot study conducted to assess CRT reproducibility in patients with septic shock, firm pressure was applied for 15 seconds to either the distal phalanx of the index finger or the center of the knee, and a chronometer was used to measure the time to return of normal color.¹⁰ Two intensivists separately completed two CRT measurements on each of 59 patients with septic shock and averaged the two successive values they obtained. Interrater concordance was 80% (73% to 86%) for the finger CRT and 95% (93% to 98%) for the knee.

Another study of interobserver agreement provides an example of how CRT education and performance evaluation can be provided to a large number of individuals.²¹ In this study, investigators videotaped CRT measurements performed on six medical patients and showed them to 37 nurses and nine nurse assistants. Each participant viewed the videos (on which a counter displayed elapsed time in seconds), recorded a CRT measurement, and classified the response as normal or abnormal without being given predefined levels of normalcy. When comparing participants' measurements of CRT, investigators found acceptable agreement, but when comparing participants' assessment of CRT normalcy, they found only moderate agreement. Agreement as to whether measurements were normal or abnormal was better when Schriger's age- and sex-specific thresholds were used than when a two-second threshold was used.

CRT interpretation. CRT has been associated with other perfusion indicators—such as lactate levels, organ function, urinary output, forearm–finger temperature gradient, and central–toe temperature gradient—but is not generally associated with systemic hemodynamic indicators such as cardiac index, CVP, ScvO₂, mean arterial pressure (MAP), and heart rate.^{10, 12–14, 19, 22} In 41 patients with septic shock, Hernandez and colleagues found that both CRT and lactate levels decreased over the six-hour resuscitation period.¹³ Patients who had a normal CRT of less than four seconds and a central–toe temperature gradient below 7°C at six hours attained a normal lactate level at 24 hours. In a subsequent study, investigators observed similar results for CRT in 84 patients who survived septic shock.¹² Although the median cardiac index, CVP, and MAP were all within normal ranges at the start of resuscitation, the lactate level was abnormal in all 84 patients, and CRT was abnormal (greater than four seconds) in 39. Notably, these patients demonstrated a progressive decrease in lactate level and CRT over the first six hours of resuscitation. These studies demonstrate the relationship between CRT and other perfusion indicators, as well as the variable period during which hemodynamic and perfusion indicators normalize during resuscitation.

In addition, they underscore the fact that no single value can be used to assess the adequacy of perfusion or resuscitation.

Lima and colleagues evaluated the relationship between abnormal perfusion and subsequent development of end-organ dysfunction.¹⁴ Investigators defined abnormal perfusion as a CRT greater than 4.5 seconds, based on the upper limit of normal identified by Schriger and colleagues, or an abnormally low skin temperature, as indicated by extremities that were cool to the touch or a forearm–fingertip skin temperature gradient greater than 4°C. After initial resuscitation, patients with abnormal perfusion were 7.4 times more likely than patients with normal perfusion to have severe organ or metabolic dysfunction and 4.6 times more likely to have hyperlactatemia (lactate levels greater than 2 mmol/L). These findings were independent of systemic hemodynamics and vasopressor dose.¹⁴

CRT provides insight into perfusion status, independent of changes in systemic hemodynamics.

The CRT at the end of resuscitation is a strong predictive factor of short-term mortality in patients with severe sepsis.^{10, 16} In one prospective observational study that included 59 patients with septic shock, at the end of the initial six-hour resuscitation, CRT for both the index finger and the knee was significantly shorter ($P < 0.0001$) in patients who were alive at day 14 than in nonsurvivors (2.3 ± 1.8 seconds versus 5.6 ± 3.5 seconds for the index finger; 2.9 ± 1.7 seconds versus 7.6 ± 4.6 seconds for the knee), with an index finger CRT greater than 2.4 seconds and a knee CRT greater than 4.9 seconds predicting 14-day mortality.¹⁰ The investigators found that changes in CRT during resuscitation were also associated with prognosis. A 20% decrease in CRT from the start of resuscitation to hour 6 was considered an improvement. In 18 of the 22 patients who died, CRT did not improve and remained elevated during resuscitation, independent of changes in cardiac index.

These studies demonstrate the association of CRT with other indicators of peripheral perfusion and the importance of ongoing CRT assessment throughout the resuscitation period. CRT provides insight into perfusion status, independent of changes in systemic hemodynamics. If CRT remains abnormal or has not improved by the six-hour reassessment point, resuscitation may be incomplete and reassessment and treatment may be warranted.

SKIN MOTTLING

One aspect of a perfusion skin assessment is skin mottling (patchy discoloration), which is often observed on the knee and anterior leg. Skin mottling, in the absence of microvascular clotting, is an indicator of hypoperfusion.²² Changes in mottling and skin perfusion often occur independent of changes in systemic hemodynamics.²³ This assessment has been limited, however, by the fact that there is no standardized method for quantifying mottling severity.

To address this limitation, Ait-Oufella and colleagues created a scoring system with which to quantify the extent of mottling on the leg (when positioned at heart level).^{23,24} The SMS incorporates a six-point scale, ranging from 0, no mottling, to 5, severe mottling extending to the groin (see Figure 1). The SMS is limited, however, in that it cannot be used on patients with dark skin.^{23,25}

Interpreting the SMS. The SMS is associated with other perfusion indicators, such as lactate level and urine output,²⁶ and an increased SMS at six hours is associated with low tissue oxygenation at the knee.²⁷ In patients with septic shock, skin perfusion as measured by laser Doppler was significantly correlated with the SMS and with changes in the SMS during resuscitation.²⁴

The SMS at six hours of resuscitation is a strong predictor of mortality. At hour 6 of resuscitation, Ait-Oufella and colleagues found that among 60 vasopressor-dependent patients with septic shock, 31 (52%) had no or modest mottling (SMS 0–1), 17 (28%) had mild or moderate mottling (SMS 2–3), and 12 (20%) had severe mottling (SMS 4–5).²³ The 14-day mortality rate increased from 13% for those with an SMS of 0–1 to 70% for those with an SMS of 2–3 and 92% for those with an SMS of 4–5. Most patients with severe mottling at hour 6 died on day 1 of admission. After excluding the 22 patients with an admission SMS of 0–1, 10 (77%) of the 13 patients whose SMS improved (decreased) between hours 0 and 6 of resuscitation survived. By contrast, of the 25 patients whose SMS either did not change or worsened despite normalization of systemic hemodynamics,

only three (12%) survived. A higher SMS in patients with moderate or extensive mottling on admission was associated with an increase in lactate level. Among patients receiving high-dose vasopressors at hour 6, those with an SMS of 0–1 had a survival rate of 72%, whereas none with higher scores survived.²³

Similar results were observed in a study of 42 patients with cirrhosis and septic shock: six-hour SMS was the strongest predictor of 14-day mortality, and all 19 patients with a six-hour SMS greater than 1 died.²⁷ Changes in SMS between initiation and hour 6 of resuscitation were also associated with mortality: all 10 of the patients whose SMS increased during that period died, while four of the five patients (80%) whose SMS decreased survived.

A high SMS after volume expansion was also found to be associated with increased 28-day mortality in adult patients with septic shock²⁸ and with increased mortality—independent of vasopressors, mechanical ventilation, or hyperlactatemia—in a general population of 791 ICU patients (65 of whom had septic shock).²⁹

THE RELATIONSHIP BETWEEN LACTATE, CRT, AND SMS

Repeated assessments, including lactate monitoring, are central to sepsis resuscitation. The CRT and SMS measurements are not meant to replace lactate monitoring, but to augment the ongoing perfusion assessment. While there are no studies that associate absolute values for CRT or SMS with any specific lactate levels, research has demonstrated a relationship between all three perfusion indicators. For example, in a study in which 39 patients had circulatory shock on admission, including 21 with septic shock, the proportion of patients with hyperlactatemia (lactate levels greater than 2 mmol/L) was significantly greater among patients with a CRT greater than 4.5 seconds than among those with a normal CRT (67% versus 33%).¹⁴ Similar results were observed in patients with severe sepsis and septic shock.³⁰ Six hours following resuscitation, median fingertip and knee CRT measurements were significantly greater in patients with septic shock than in those with severe sepsis (fingertip: 2.5 versus 1.6 seconds, $P = 0.002$; knee: 4.2 versus 2.2 seconds, $P < 0.001$), though there were no significant differences in MAP or cardiac index.³⁰

There is also a relationship between changes in CRT, SMS, and lactate levels during resuscitation, though no studies have directly compared CRT and SMS. In a study of 84 hospital survivors of septic shock, both the lactate levels and CRT measurements decreased during the ICU phase of resuscitation.¹² (See Table 1.¹²) Of note, the perfusion indicators were abnormal despite normalization of the MAP and cardiac index. During resuscitation, CRT has also been found to resolve more rapidly than lactate, and a CRT of less than two seconds at hour 6

Table 1. Changes in Perfusion and Hemodynamic Indicators During Resuscitation^{12, a}

Parameter	Baseline	2 Hours	6 Hours
Lactate, mmol/L	4 (3–4.9)	3.4 (2.4–4.2)	2.8 (2–3.8)
CRT, seconds	6 (5–8)	4 (3–5)	3 (2–6)
Cardiac index, L/min/m ²	3.1 (2.5–3.9)	3.5 (2.9–4.6)	3.2 (2.6–3.8)
MAP, mmHg	73 (67–79)	71 (68–74)	71 (68–74)

CRT = capillary refill time; MAP = mean arterial pressure.

^a All values are reported as median (interquartile range).

is associated with successful resuscitation (a lactate level below 2 mmol/L) at 24 hours.¹³ In patients with septic shock and moderate or severe mottling (an SMS greater than 1) on admission, worsening of the SMS between hours 0 and 6 of resuscitation is associated with an increase in lactate and a decrease in urine output.²³

INTEGRATING PERIPHERAL PERFUSION MEASUREMENTS AND CARE

Although the SSC six-hour bundle recommends that patient reassessment include peripheral perfusion measurements, it provides no guidance on integrating such findings into the plan of care.⁴ A randomized controlled trial compared peripheral perfusion–targeted fluid management with early goal-directed resuscitation in 30 patients with septic shock.³¹ The peripheral perfusion indicators were CRT, peripheral perfusion index (from a pulse oximeter), forearm–finger skin temperature gradient, and tissue oxygenation. If at least three of four peripheral perfusion indicators were abnormal, the patient would receive up to two 250-mL colloid boluses to increase peripheral perfusion. If the boluses did not improve the perfusion indicators, no additional fluid was administered and alternate therapies were considered. In the early goal-directed therapy group, if the patient did not achieve target values for MAP, CVP, cardiac index, urinary output, heart rate, and arterial oxygen saturation, fluid boluses were administered until target values were achieved or the patient became a fluid nonresponder (as indicated by a stroke volume increase of 10% or less). The treatment groups did not differ in systemic hemodynamics, lactate levels, or ScvO₂ over time; however, the peripheral perfusion–targeted fluid management group received 1.8 L less fluid during the initial six-hour resuscitation and 2.5 L less fluid between hours 7 and 72. There were no differences in ventilator-free days, ICU mortality, or ICU length of stay between the groups. The early goal-directed therapy group, however, had a significantly longer hospital stay and higher organ failure scores. An important aspect of this study was that the four perfusion indicators were used, not as targets, but rather to signal when fluid resuscitation was no longer appropriate (that is, when the indicators no longer improved with fluid resuscitation).

NURSING IMPLICATIONS

These studies identify several implications for nursing practice (see *CRT and SMS Fundamentals*). Most notably, the practice and assessment of these skin perfusion measurements should be standardized, with all providers taught how to correctly perform and interpret findings. It should be emphasized that the normalization of CRT and SMS are not resuscitation end points, but rather indirect indicators of perfusion and components of the ongoing assessment of resuscitation

CRT and SMS Fundamentals

When integrating capillary refill time (CRT) and skin mottling score (SMS) into septic shock reassessment, keep the following in mind:

- CRT and SMS are associated with other indicators of peripheral perfusion, but may remain abnormal despite normalization of systemic indicators such as mean arterial pressure, heart rate, central venous pressure, cardiac index, and central venous oxygen saturation.
- An abnormal CRT and SMS at hour 6 of resuscitation, and failure of the CRT or SMS to improve during resuscitation, indicate increased risk of morbidity and mortality.
- CRT and SMS are not end points of resuscitation, but may be included in the assessment that guides initial resuscitation.
- CRT and SMS are dynamic indicators and should be monitored repeatedly over the resuscitation period.
- CMS and SMS should be used in conjunction with other indicators of peripheral perfusion.

adequacy. Serial monitoring and documentation of these parameters is recommended, and as outlined in the SSC six-hour bundle, resuscitation should continue toward an established end point, such as the normalization of lactate levels. CRT and SMS should not be used as the sole indicators of perfusion. However, poor outcomes are associated with the failure of CRT or SMS to improve and with continued abnormal peripheral perfusion following the normalization of systemic hemodynamic indicators. Either situation suggests the need for a more in-depth assessment and continued resuscitation.

CASE STUDY

Test your understanding of peripheral perfusion indicators by considering the case of Julia Smith, an otherwise healthy 65-year-old who is admitted to an acute care unit with a diagnosis of community-acquired pneumonia. (This case is a composite based on my experience.) On admission, her vital signs are as follows:

- blood pressure—112/72 mmHg
- MAP—85 mmHg
- heart rate—90 beats per minute
- respiratory rate—22 breaths per minute
- temperature—100.5°F
- peripheral capillary oxygen saturation (SpO₂)—90% on room air

Antibiotics and oxygen (2 L/min by nasal cannula) are initiated. Over the next several hours, Ms. Smith's condition deteriorates (blood pressure, 94/52 mmHg; MAP, 66 mmHg; heart rate, 98 beats per minute; respiratory rate, 26 breaths per minute), and she has become mildly confused, with a Glasgow Coma Scale score of 14. A rapid response team is called. Additional assessment findings include CRT,

six seconds; SMS, 4; lactate level, 4 mmol/L. Fluid resuscitation is initiated for sepsis, and Ms. Smith is transferred to the ICU. Upon completion of the initial fluid resuscitation (after two hours), reassessment is completed. Her vital signs have improved (blood pressure, 102/64 mmHg; MAP, 77 mmHg; heart rate, 86 beats per minute; respiratory rate, 24 breaths per minute; SpO₂, 93% on oxygen 3 L/min by nasal cannula). Her CRT is 4.5 seconds and her SMS is 3.

Clinical question: Is resuscitation complete?

Discussion: Although Ms. Smith's vital signs have improved, she still has indications of altered peripheral perfusion (prolonged CRT and moderately increased skin mottling). A repeat lactate level should be obtained, with the understanding that lactate may have a slower resolution than CRT or SMS. In this case, the lactate level was 3.5 mmol/L. Combined, these perfusion indicators suggest a need for continued resuscitation, despite normalization of vital signs. ▼

For five additional continuing nursing education activities on the topic of sepsis, go to www.nursingcenter.com/ce.

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