Critical Decisions
in Emergency Medicine™

In This Issue

Hypothermia as a result of exposure to cold is relatively common, even in temperate climates. Emergency physicians must be ready to use the most appropriate methods of rewarming and be able to manage the cardiac arrest and ventricular arrhythmias that commonly result from profound hypothermia.

Children with sickle cell disease most often present with vasoocclusive crisis; however, their unique anatomic and physiologic characteristics also make them more prone to potentially life-threatening pulmonary, central nervous system, gastrointestinal, and infectious complications. This lesson reviews the pathophysiology, presentation, and management of these complications in pediatric patients.

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■ Also in This Issue

■ Next Month

- Rapid Sequence Intubation
- HIV Emergencies

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Lesson 9

Hypothermia

Alvin C. James, II, MD, and Jonathan Glauser, MD, MBA, FACEP

■ Objectives

On completion of this lesson, you should be able to:

1. Describe the clinical manifestations of hypothermia.

2. Describe the pathophysiology and organ dysfunction seen at different degrees of hypothermia.

3. Identify patient populations at increased risk for hypothermia.

4. Review techniques for rewarming.

5. Describe the methods for temperature monitoring in hypothermic patients.

6. Discuss modifications of advanced cardiac life support protocols necessary in the setting of hypothermia.

■ From the EM Model

6.0 Environmental Disorders

    6.6 Temperature-related Illness

Hypothermia is a relatively common condition that can result in significant morbidity and mortality. Published mortality rates in patients with severe hypothermia vary between 12% and 80%.[1] Between 1995 and 2004, hypothermia and other cold-related injuries accounted for 15,574 emergency department visits[2] and more than 650 deaths per year.[3] Hypothermia can result from a variety of disease states (secondary hypothermia) and exposures (primary hypothermia). This article will focus on primary or accidental hypothermia. Although more common in cold climates, it occurs even in temperate climates, and the diagnosis is more likely to be missed in these regions. In fact, elderly patients and those with impaired compensatory responses can suffer fatal hypothermia at ambient temperatures in the low 60°s (Fahrenheit). Mild to moderate hypothermia can often go undetected, especially early in care. A high degree of suspicion must be maintained, particularly in intoxicated patients and in those with altered mental status.

The management of hypothermia poses a variety of challenges to emergency physicians and requires a thorough knowledge of its pathophysiology and treatment. In addition, emergency physicians must be skilled in a variety of rewarming techniques and should be able to choose the most appropriate method on a case-by-case basis. Most patients who suffer fatal hypothermia die as a

result of cardiac arrest. Of particular importance is the management of cardiac arrest and ventricular arrhythmias that commonly result from profound hypothermia.

There are several patient populations at increased risk for developing hypothermia. Patients at extremes of age are at particular risk for hypothermia. The elderly have a higher incidence of comorbid central nervous system and cardiovascular disease as well as medications that can interfere with the body's ability to respond to changes in ambient temperature. Children have a high body-surface-area to body-mass ratio, which results in more rapid heat loss. In the United States, most hypothermic patients are intoxicated on ethanol or other drugs.[4] Patients who are intoxicated or have an altered sensorium have an increased risk of exposing themselves to cold environments and a decreased ability to respond. The homeless population is obviously at increased risk due to environmental exposure.

Patients with endocrine, central nervous system, and infectious conditions can also present with hypothermia. Although these topics will not be discussed in any detail, one point deserves mentioning—patients who are ill appearing and hypothermic without history of environmental exposure should be presumed septic until proved otherwise. There is ample evidence that patients with sepsis and hypothermia have increased mortality rates.[4] Empiric broad-

Critical Decisions

- What steps should be taken in prehospital and initial emergency department management of the hypothermic patient?
- How should core temperature be measured?
- When should a patient be warmed using noninvasive rewarming techniques?
- What group of patients benefits from active internal rewarming?

- How should cardiac arrhythmias be managed in a hypothermic patient?
- How does a history of cold water immersion affect the management of hypothermic patients?
- When should cessation of resuscitative efforts be considered?

spectrum antibiotics should be started on hypothermic patients in whom a noninfectious cause cannot be identified.[5]

Victims of trauma frequently present with or develop hypothermia; there have been numerous studies that have shown a high incidence of hypothermia in victims of trauma. These patients often have injuries that demand urgent definitive management; it is quite easy to allow the measurement of an accurate temperature to be significantly delayed. Up to 50% of trauma patients are hypothermic at some point during their care; this is associated with increased mortality.[3] The presence of hypothermia can worsen the degree of shock, limb ischemia, and coagulopathies. Managing hypothermic trauma patients presents a unique challenge as they are often less able to respond to even mild hypothermia because of decreased cardiac output. Hypothermia can be precipitated or worsened by the infusion of large volumes of nonwarmed crystalloid as well as by paralysis for intubation. For these reasons the management of this group of patients is complex and their care should be coordinated with a skilled trauma surgeon. This article will not focus heavily on the management of hypothermia in the setting of trauma.

A booming area of interest and ongoing research is in the use of therapeutic hypothermia in a variety of clinical settings, most notably cardiac arrest. For a discussion of therapeutic hypothermia, see *Critical Decisions in Emergency Medicine,* Volume 24, Number 5 (January 2010).

Case Presentations

■ Case One

A 30-year-old man is brought in by paramedics after being found unresponsive in a nearby park. When EMS arrived, the patient had no spontaneous movement, pupils were fixed and dilated, some agonal respirations were noted, and he had a weakly palpable femoral pulse at a rate of 30. Paramedics were unable to measure a blood pressure. On arrival in the emergency department, the patient is receiving bag-valve-mask ventilation and has a weakly palpable femoral pulse of 20. He has a rectal temperature of 25°C (77°F). He is wearing damp jeans and a thin sweatshirt.

■ Case Two

An 8-year-old girl arrives via EMS in asystole with cardiopulmonary resuscitation (CPR) in progress. She was sledding with her family when she skidded onto a nearby pond and fell through the ice. It took approximately 30 minutes to rescue her from the waters, which were estimated to be 35°F to 40°F. When she was pulled from the water she had no signs of life and CPR was initiated. Transport time to the emergency department was approximately 25 minutes. She was placed in warm blankets en route. On arrival in the emergency department, she is in full cardiopulmonary arrest, pupils are fixed and dilated, and the monitor shows asystole. A temperature-sensing Foley catheter is placed and confirms a temperature of 20°C (68°F).

■ Case Three

A 68-year-old man is brought in by local firefighters after being found extremely confused in his home by his son. It was noted at the scene that he was moaning and withdrawing to painful stimuli. He was not following any commands, breathing 7 times per minute, with a heart rate of 47, and a blood pressure of 90/50. They report that the inside of the house was extremely cold; the son suspects that the patient's furnace went out. The patient has a history of severe emphysema and some "heart trouble." He has an initial rectal temperature of 29°C (84.2°F). While being transferred onto the emergency department bed, he becomes extremely pale and loses pulses; the monitor indicates ventricular fibrillation.

Pathophysiology

The classic definition of hypothermia is a core body temperature lower than 35°C (95°F), but the condition can be best described as the temperature at which the body loses the ability to adequately generate enough heat to maintain its natural functions.[6] Hypothermia is typically classified in the following manner: mild hypothermia, 32°C to 35°C (90°F to 95°F); moderate hypothermia, 28°C to 32°C (82°F to 90°F); and severe hypothermia, below 28°C (82°F). It is important to note that the American Heart Association (AHA) defines a core temperature less than 30°C (86°F) as severe hypothermia.[7] For practical purposes, the distinction between moderate

and severe hypothermia for patients with temperatures between 28°C to 30°C can in part be determined by hemodynamic and cardiac stability. Patients with non–fluid-responsive hypotension, severe bradycardia, or ventricular arrhythmias should be considered to have severe hypothermia and treated aggressively.

Mild hypothermia can be thought of as the stage where the body is making physiologic adjustments to respond to heat loss. The primary response is shivering, which results in a three- to five-fold increase in metabolic demands. The temperature range below 30°C to 32°C is a critical range, because below these temperatures shivering ceases while bodily functions and metabolism slow down. At 28°C the metabolic rate is 50% of normal, and it drops to 20% of normal at 20°C. This is part of the reason that some hypothermic patients are able to survive prolonged cardiac arrest with relatively good neurologic outcomes.

Hypothermia has a profound effect on all organ systems; its effects on the myocardium are critically important. The initial response to hypothermia is an increase in heart rate, peripheral vascular resistance, and cardiac output. At between 30°C to 32°C, the heart rate starts to decline in a linear relationship as temperature decreases. Because the bradycardia associated with hypothermia is secondary to decreased spontaneous depolarization of pacemaker cells, it is resistant to atropine and pacing. Once core temperature falls below 30°C, myocardial irritability begins to develop, increasing the risk of ventricular arrhythmias. The classic progression of cardiac dysfunction is sinus bradycardia followed by atrial fibrillation, slow ventricular response, ventricular fibrillation, and finally asystole. It should be noted that this progression is variable, but asystole is universal at core temperatures below 15°C.

There are a multitude of ECG changes that can be seen in the setting of hypothermia. Some of the more commonly cited changes are prolonged PR, QRS, and QT intervals, Osborn J waves, and T-wave inversions. As mentioned earlier, heart rate starts to decrease as core temperatures reach 30°C to 32°C, and as hypothermia worsens, the P wave decreases in amplitude and can be lost altogether. This is typically followed by prolongation of the PR, QRS, and QT intervals, in that order.[8] By far the most famous ECG manifestation of hypothermia is the Osborn J wave (Figure 1). The Osborn J wave is most commonly seen in leads II and V_6, but in severely hypothermic patients it can be seen throughout the precordial leads. It is important to note that the Osborn J wave is characteristic but not pathognomonic of hypothermia and can be seen in a variety of other conditions, including central nervous system lesions, cardiac ischemia, Brugada syndrome, sepsis, and in young healthy persons. It is also important to note that its presence or absence has no prognostic value.[8]

Hypothermia has several effects on the respiratory system that deserve mention. Starting at around 32°C, the respiratory rate starts to decrease, and, at temperatures below 24°C, complete respiratory arrest is common. As temperature decreases, secretions increase, the so called "cold bronchorrhea." This can complicate airway management in the acute setting and lead to fatal pneumonias in the postresuscitation period. In obtunded patients or those with inadequate respirations, a definitive airway should be established early.

The renal manifestations of hypothermia are also significant and must be addressed early in resuscitation. Peripheral vasoconstriction occurs early in the course of hypothermia and persists throughout its course. This vasoconstriction results in a relative hypervolemia, which leads to an increase in urinary output termed "cold diuresis." As hypothermia worsens and cardiac output decreases, renal perfusion falls and acute renal failure develops.

Much is now known about the neuroprotective effects of hypothermia. These benefits seem to

Figure 1.
Osborn J wave: a positive deflection (blip) right at the end of the QRS complex (arrow). This pattern resolves as the patient is rewarmed.

	Admission	One hour	One day
Temperature (in degrees celsius)	24.1	29.4	36.6
Heart rate (beats per minute)	50	70	98
QRS interval (msec)	184	119	71
QTc interval (msec)	516	502	403
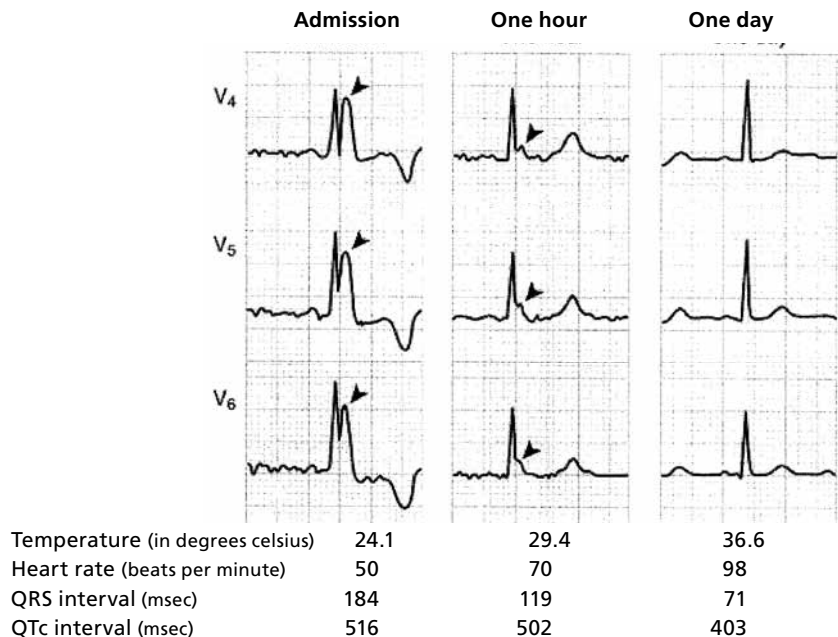
be most pronounced when the rate of cooling is rapid. Cerebral blood flow starts to decrease with the onset of hypothermia, up to 6% for every 1°C drop in core temperature. An early indicator of hypothermia that can be easily overlooked is a change in mental status or personality. At around 30°C the pupils dilate and may not react at all, and at core temperatures below 20°C the electroencephalogram is flat.

CRITICAL DECISION

What steps should be taken in prehospital and initial emergency department management of a hypothermic patient?

Initial treatment should focus on preventing further heat loss by removing the patient from the environment, removing cold or wet clothing, and insulating the patient. The AHA recommends that indicated procedures such as intubation and placement of vascular catheters not be withheld but should be done gently in order to reduce the risk of precipitating arrhythmias.[9] Intubation serves to prevent aspiration and also allows the effective delivery of warm humidified oxygen by endotracheal tube. The delivery of warm humidified oxygen results in only a small heat gain but minimizes heat loss from the lungs, which can account for up to 30% of the body's total metabolic heat production.[4] In patients who do not require intubation, warm humidified oxygen can be delivered via face mask. Concerns have been raised about endotracheal intubation precipitating ventricular arrhythmias; however, a multicenter review has found the complication rate to be extremely low.[10] Intubation is clearly indicated in the apneic or obtunded patient and should not be delayed. If intubation is indicated, it should be done by the most experienced and skilled physician available. Although to the authors' knowledge this has not been studied, it is possible that newer, widely available, fiberoptic laryngoscopes such as the Glide

scope that require less direct traction on the posterior oropharynx may further reduce the risk of precipitating ventricular arrhythmias during intubation. If possible, avoid paralysis and deep sedation to prevent loss of the shivering response, although this is less important in severe hypothermia when the body has already lost the shivering response. As a rule, severely hypothermic patients are hypocapnic, and hyperventilation should be avoided.

As mentioned earlier, the severely hypothermic myocardium is extremely irritable and ventricular fibrillation can be triggered by a variety of things such as CPR, rough handling of the patient, or even rapid rewarming.[11] A recent porcine model of hypothermia demonstrated an association with mechanical stimulation and ventricular arrhythmias at temperatures below 25°C.[12] If there is any heart beat, regardless of how slow, CPR should be withheld, because it can induce ventricular fibrillation.[6] This is an important point to remember because it differs from standard ACLS protocols, which specify that chest compressions should be initiated for a heart rate of less than 30. It is recommended that at least 45 seconds be spent attempting to palpate central pulses before initiating CPR. If no central pulse is detected, standard CPR should be initiated. If central lines are placed, careful attention to the depth of the guidewire is needed so as not to advance it into the heart, triggering preventricular contractions; that preventricular contraction may be the last organized electrical activity you see. For this reason, unless otherwise contraindicated, femoral lines may provide the best option for central venous access. In addition to eliminating the risk of the guidewire irritating the myocardium, femoral site are easily compressible. There are no clear indications as to what type of line is best, although they should be large bore, because small-bore triple-lumen central lines are inadequate for rapid resuscitation and not compatible

with any methods of active internal rewarming. Introducers or dialysis catheters are likely the best choice. Placement of these lines in the jugular or subclavian vein may be difficult while CPR is ongoing. Subclavian lines have the added problem of not being compressible, a consideration of critical importance given impairment of patients' coagulation cascade secondary to hypothermia.

CRITICAL DECISION

How should core temperature be measured?

Accurate temperature measurement is critical. The gold standard for measuring core temperature is a pulmonary artery catheter, but this is a time-intensive and invasive procedure that carries significant risks. Oral thermometers are not accurate enough in many situations, and many do not measure below 34°C (94°F). Axillary temperatures are dependent on peripheral blood flow and should be avoided. In most emergency department situations a rectal temperature provides the best balance between speed and accuracy but still has limitations and can be influenced by the temperature of the intestinal contents. Esophageal probes have been shown to have high accuracy but are often not readily available.

Many hospitals now have temperature-sensing Foley catheters. These devices are placed just like standard bladder catheters and do not add any increased time or difficulty in catheter placement. Their accuracy has been well validated in the ICU literature in normothermic patients.[13] Concerns have been raised about the accuracy of this method of core temperature measurement in severely hypothermic patients; however, a study in deep hypothermia for neurosurgical procedures with mean temperatures of 21.3°C found that bladder temperature correlated with brain temperature better than pulmonary artery catheter temperature did.[14] Given that the main concern in hypothermia

is ventricular fibrillation, the temperature of the myocardium may be of greater importance than the brain temperature. Even so, the difference between pulmonary artery temperature and bladder temperature in this study was within 1°C to 2°C through a wide range of temperatures, a difference that is unlikely to change management. A study directly comparing bladder and pulmonary artery temperatures in adults following cardiopulmonary bypass found bladder temperatures were 0.1°C to 0.2°C higher than pulmonary artery temperature with correlation coefficients of 0.94 to 0.99.[15] In a similar study 2 years earlier, urinary bladder temperature was found to correlate well with pulmonary artery temperatures, with correlation coefficients ranging from 0.78 to 0.94.[16] In all of these studies, rectal temperature correlated poorly with pulmonary artery temperature.[14-16] Based on the available literature, it is reasonable to conclude that temperature-sensing Foley catheters provide a fairly accurate temperature measurement and also a reliable way to follow the temperature. If available, they should be strongly considered for use in any hypothermic patient who requires bladder catheterization.

CRITICAL DECISION

When should a patient be warmed using noninvasive rewarming techniques?

It is important to mention that there are no prospective controlled trials comparing rewarming methods.[4] Current recommendations are generated from retrospective studies, case reports, theory, and animal models. Rewarming can generally be broken down into passive rewarming, active external rewarming, and active internal rewarming. Passive rewarming involves removing the patient from a cold environment, including clothing, and then insulating them. This allows the body's compensatory mechanisms, primarily shivering, to generate heat and rewarm the patient.

Passive rewarming typically results in an increase in core temperature of about 0.5°C to 4°C per hour.[17] Mild hypothermia can typically be treated with passive rewarming in young otherwise healthy patients. However, passive rewarming is not effective if the patient is paralyzed or has any impairment of innate thermoregulatory mechanisms and is likely inadequate for patients at extremes of age or with any underlying comorbid disease or injuries.

External active rewarming involves applying a heat source to the patient's exterior. This is most easily accomplished in the modern emergency department with commercially available heating blankets that use forced, heated air.[18] Their use has been shown to result in an increase in core body temperature of 1.7°C per hour.[19] There is some theoretical and anecdotal evidence that this method of rewarming could precipitate shock by producing a relative hypovolemia, worsened metabolic acidosis, continued decline in core temperature, and tissue ischemia. This is a phenomenon known as "afterdrop." Theoretically, this occurs secondary to the colder exterior now being perfused as a result of vasodilation, leading to a return of cold acidotic blood to the core. Some of the evidence for this comes from cases of hypothermia developing in cold water swimmers who were initially normothermic.[20] Despite this concern, several recent studies have shown this method to be effective in patients with moderate hypothermia, as well as in some with severe hypothermia without signs of cardiovascular compromise.[21] In addition, at least one study has demonstrated its effective use without any observed afterdrop effect.[19] In general, patients with moderate hypothermia may be rewarmed with this method as long as they are hemodynamically stable and have no cardiac arrhythmias.

When and how to initiate active internal rewarming are questions that are not always easily answered. In patients with temperatures above 30°C, the rate of ventricular fibrillation is relatively low and aggressive internal rewarming techniques are usually not indicated. For patients with severe hypothermia, the optimal rate of rewarming is unclear, but it is generally agreed that it should be done as rapidly as possible. Several case series have shown an association between the rate of warming and prognosis.[1,10] In-hospital rewarming times longer than 12 hours have been associated with increased mortality.[22]

The situation is different in the setting of cardiac arrest or ventricular fibrillation. If these are present, the AHA recommends that internal warming be initiated in addition to other ACLS measures even in patients with return of spontaneous circulation.[7] For patients with core temperatures slightly below 30°C (ie, 28°C to 29°C), the clinician will have to look at the individual situation. If internal warming is initiated in an otherwise stable patient, it seems prudent to use less invasive methods such as gastric, bowel, or bladder lavage rather than thoracic and peritoneal lavage. Clearly, hemodynamically stable patients with no ventricular arrhythmia should not be considered for extracorporeal warming. In addition, regardless of the method of warming, all of these patients should be placed on warm, humidified oxygen by face mask or endotracheal tube. They should also receive warmed intravenous fluids, typically normal saline at 40°C to 42°C. The administration of warmed fluids not only aids in rewarming but helps to support blood pressure. Hypothermic patients who are being rewarmed often have a relative hypovolemia related to vasodilation, especially in those being treated with active external rewarming. This can be worsened by a true hypovolemia related to lack of oral intake (depending on the duration of the exposure) and cold diuresis.[7]

CRITICAL DECISION

What group of patients benefits from active internal rewarming?

In general, active internal rewarming should be reserved for patients with severe hypothermia. There are multiple methods of active internal rewarming that have been successfully implemented. The most common involve the lavage of warmed fluids in an internal compartment such as peritoneal, thoracic, mediastinal, bladder, gastric, and large bowel lavage. The most invasive of these techniques, mediastinal lavage via open thoracotomy, has been used successfully in a small number of patients.[23] There are obviously many potential complications with this procedure, and it should only be considered in arrested patients. There is no "one size fits all" answer; it really depends on the clinical situation. Thoracic lavage can be extremely effective in raising core temperature. A study of hypothermia in canines comparing thoracic lavage to gastric lavage found thoracic lavage to be markedly superior. Mean time required to rewarm the animals 10°C was 210.9 +/- 18.6 minutes for the gastric group and 99.3 +/- 23.0 minutes for the thoracic group.[24] Although effective, this method of rewarming is not appropriate for all patients. A patient with underlying lung disease and decreased reserve may not tolerate the decrease in functional capacity associated with thoracic lavage. Patients with abdominal trauma or ascites are poor candidates for peritoneal lavage. Gastric lavage via nasogastric tube is less effective than more invasive methods, but it is quick and easy to implement. It should generally be avoided in nonintubated patients because of the increased risk of aspiration.

In addition to the methods listed above, extracorporeal blood rewarming may be useful in some situations of severe hypothermia. Hemodialysis is likely to be the most readily available of these techniques and has been reported to raise core temperature 2°C to 3°C per hour.[17] It should be strongly considered in patients with coexisting drug overdoses or severe electrolyte disturbances. There have been multiple case reports showing the successful use of hemodialysis to rewarm patients with presenting core temperatures as low as 24°C without cardiovascular collapse.[25,26] Veno-venous rewarming circuits that use roller pumps have been successfully used in animal models and proposed as an alternative when hemodialysis is not available.[27] This technique requires a large central line and a large peripheral line or second central venous catheter for the return of warmed blood. Continuous arteriovenous rewarming can also be effective but requires a systolic blood pressure of more than 60 mm Hg. Cardiopulmonary bypass is the most aggressive of these techniques and has been reported to raise core temperature 7°C to 10°C per hour.[17] It also has the added benefits of providing circulatory support and oxygenation and because of this should be strongly considered in the severely hypothermic patient in full cardiopulmonary arrest.

Cardiopulmonary bypass is a labor- and cost-intensive endeavor but in select patient populations has been shown to be effective. A retrospective analysis of cardiopulmonary bypass rewarming in severe hypothermia published in the *New England Journal of Medicine* in 1997 showed that of 32 patients who received the therapy, 15 (47%) survived, and all of those reportedly had full neurologic recovery. The survivors as a group were young and otherwise healthy and none suffered any asphyxia.[28] In 2001, a retrospective analysis of the use of extracorporeal warming for severe hypothermia found the survival rate to be 63% in the non-asphyxia group and 5% (1 patient who survived with significant neurologic impairment) in the asphyxia group.[29] The authors concluded that circulatory-arrested hypothermic patients with no hypoxic event preceding the exposure and those with vital signs at the time of rescue have a reasonable prognosis and should be considered for extracorporeal rewarming. Patients who suffer near-drowning/drowning and present to the emergency department in a comatose state with cardiorespiratory arrest have a dismal prognosis and are not likely to benefit from aggressive rewarming. They also recommend that patients with an indisputable history of asphyxia prior to cooling should not be rewarmed by cardiopulmonary bypass.[29] One potential reason physicians may be reluctant to initiate active internal rewarming is the amount of time needed to get it started. In the above cited study, the average CPR time until start of bypass was 150 minutes. Despite this, good outcomes were achieved, and it is recommended that CPR be continued without interruption until bypass rewarming can be initiated.

Endovascular rewarming is an emerging and promising method for internal rewarming. Endovascular rewarming entails placement of a catheter through a sheath introduced into the femoral vein. The catheter is then advanced into the inferior vena cava, and acts as an indwelling radiator. It has been reported to raise core body temperature by approximately 3°C per hour.[30] This is the same device used to cool comatose survivors of cardiac arrest, and may be familiar to emergency physicians already performing therapeutic hypothermia. In theory, it could be implemented fairly rapidly. Obviously, this technique provides no circulation, oxygenation, or metabolic function and is inappropriate as the sole rewarming technique in the arrested patient. In a patient being considered for cardiopulmonary bypass it is reasonable to use this technique, if available, along with other methods of internal rewarming while waiting for more definitive treatment.

Pearls

- If available, temperature-sensing Foley catheters should be used, because they are accurate and do not add any difficulty or additional time in patient care.

- Femoral access is the best option for central venous access, because it eliminates the risk of the guidewire irritating the myocardium and the site is easily compressible.

- Start empiric broad-spectrum antibiotics on patients in whom a noninfectious cause cannot be identified; patients with sepsis and hypothermia are at increased risk of mortality.

- Patients with hemodynamic instability and/or ventricular arrhythmias must be treated aggressively with active internal rewarming.

- Several different rewarming techniques can be used simultaneously to increase the rate of rewarming.

- In arrested patients with no history of asphyxia, strong consideration should be given to cardiopulmonary bypass, if it is available.

Pitfalls

- Failure to withhold CPR if there is any heart beat, regardless of how slow, because this could induce ventricular fibrillation.

- Failure to spend 45 to 60 seconds attempting to find a pulse before concluding that there is no pulse and beginning CPR.

- Failure to check serum glucose.

- Reliance on active external rewarming in patients who are not adequately perfusing.

- Failure to use warm humidified oxygen either via face mask or endotracheal tube.

- Failure to use warmed (40°C) fluids for resuscitation.

- Reliance on typical signs of death as indications to stop resuscitation.

CRITICAL DECISION

How should cardiac arrhythmias be managed in the hypothermic patient?

The management of cardiac arrhythmias in the setting of hypothermia varies significantly from traditional ACLS. If the patient is not breathing, begin bag-mask ventilation and prepare for intubation. If there is any heart beat, regardless of how slow, CPR should be withheld as it could induce ventricular fibrillation.[6] It has been recommended that at least 45 to 60 seconds be spent trying to find a pulse before beginning CPR. If no pulse is detected, begin compressions. There is very little good scientific data about the temperature at which defibrillation should be attempted, but the current AHA guidelines suggest attempting defibrillation for ventricular fibrillation or ventricular tachycardia at any temperature with one shock.[7] If this attempt is unsuccessful, further attempts should not be made until the core temperature reaches 30°C to 32°C.[7] In the setting of cardiac arrest, the primary therapy is rewarming. The hypothermic myocardium is generally unresponsive to pressors and for these reasons the AHA guidelines recommend withholding these medications until core temperatures are above 30°C. If they are given prior to this and the patient fails to respond, further doses should be withheld until the core temperature is above 30°C. Even at temperatures above 30°C, it is recommended that longer intervals between dosing be used because of decreased rate of drug metabolism and concern about the peripheral accumulation after repeated doses.[7] There are no clear recommendations as to what these longer intervals should be. The use of vasopressors is an area of ongoing debate and research, as there is a lack of evidence regarding what role, if any, they have in resuscitating severely hypothermic patients. At least one animal model has demonstrated increased coronary perfusion pressures and transient returns in spontaneous circulation with use of epinephrine and vasopressin compared to placebo.[31] A review of seven controlled studies of induced ventricular fibrillation in animal models found that cumulatively, among all studies administering vasopressors, the rate of return of spontaneous circulation was 62% in treatment groups contrasted to 17% in control groups (p <0.0001, n=77).[32] This led the authors to conclude that the recommendation to withhold vasopressors should be reevaluated. Whether data from canine and porcine models can be applied to the management of human hypothermic cardiac arrest remains to be established.

The use of antiarrhythmic drugs is also controversial. Historically, bretylium has been recommended as possibly being effective in the management of hypothermic ventricular fibrillation. A small canine model showed some decreased incidence of ventricular fibrillation when bretylium was given prophylactically.[33] It was not mentioned in the AHA guidelines published in 2000.[7] In fact, those guidelines suggested withholding all antiarrhythmic medications and vasopressors when body core temperatures are below 30°C. The use of amiodarone is controversial, and it is generally agreed that procainamide should not be used in hypothermic patients because of an increased risk of ventricular fibrillation.

CRITICAL DECISION

How does a history of cold water immersion affect the management of hypothermic patients?

Under dry temperate conditions, radiation accounts for most (55%-65%) heat loss; conduction and convection account for approximately 15%, and the rest occurs by evaporation and respiration. In windy environments, convection becomes increasingly important. Conduction is the primary mode of heat loss in immersion, because the thermal conductivity of water is approximately

25 to 30 times that of air. As a result, massive amounts of heat can be lost very quickly even when the temperature gradient is relatively small. There have been cases of hypothermia documented even in water as warm as 71°F to 77°F.[20] As with any other hypothermic patient, the first step is to remove the patient from the environment and insulate the patient. It is important to note that core temperature can continue to fall even after the person is removed from a cold environment. As mentioned earlier, afterdrop is the lowering of the body core temperature after the exposure has ended. It can be due to the return of cold blood from the periphery, or from conduction of heat from a warm core to a cold periphery.[34] This phenomenon may be more relevant in immersion injury than in other exposures because of the rapid temperature change and heat loss that occurs.

Patients who are hypothermic secondary to cold water immersion but have not suffered drowning/near-drowning have a good prognosis. This may be due in small part to the "diving reflex," which preferentially shunts the blood supply to vital organs such as the brain and heart. This response, which starts immediately on submersion, prevents aspiration of water, redistributes oxygen stores to heart and brain, slows cardiac oxygen use, and initiates a hypometabolic state. It is unclear how large a role this plays; one study found that a significant diving response was exhibited in only 15% of healthy volunteers.[35] In patients who have suffered asphyxia the prognosis is extremely poor.[29] Despite this, there are several case reports of pediatric patients surviving prolonged submersion, even longer than 1 hour, in the setting of hypothermia.[36,37] When a person is discovered in cold water, even if in full arrest with no signs of life, resuscitative efforts should generally be started. A recent analysis of cold water immersion/drowning victims in Scotland found that

patients were often declared dead at the scene or after only brief attempts at resuscitation. They concluded that members of the emergency services are failing to both initiate prehospital resuscitation and to continue this to hospital for victims of near drowning.[38] A recent survey supported this by finding that most laypersons and first responders underestimated the time available for survival during ice water immersion.[39] Obviously, good judgment is needed; patients who are known to have been submerged for long periods (ie, > 2 hours) are unlikely to benefit from any attempts at resuscitation. If the history is unclear, it is generally best to initiate resuscitation and transport the patient to the emergency department, where laboratory testing and further history can help guide the continuation of resuscitation attempts.

CRITICAL DECISION
When should cessation of resuscitative efforts be considered?

The typical signs for cessation of efforts on a patient in the field are not reliable in hypothermic patients. Cardiopulmonary arrest and even rigor mortis and fixed, dilated pupils are not reliable signs. There are many case reports of survival from profoundly hypothermic temperatures, even as low as 14.2°C (57.6°C).[40,41] It can take hours to rewarm patients from profound hypothermia, and survival has occurred after episodes of prolonged cardiac arrest. One patient treated with cardiopulmonary bypass survived after 6.5 hours of cardiac arrest.[41] Most of these cases have been in the pediatric population and very young adults, but cases of successful resuscitation have occurred in older patients as well. In 2002, a case report was published of a 37-year-old man who was found in his garden, cold, with no signs of life, pupils fixed and dilated, and a core temperature of 17°C. This patient underwent 3 hours of CPR before being rewarmed by cardiopulmonary bypass. He eventually regained spontaneous cardiac output and made a full neurologic recovery.[42] This

emphasizes the point that typical signs of life cannot be relied on in hypothermic patients and, as a rule, patients should be warm before being declared dead.

There are some patients who are clearly dead and will not benefit from attempts at resuscitation. For example, CPR is contraindicated in patients with a noncompressible chest, if there is ice formation in the airway, or if there are other traumatic injuries incompatible with life. Multiple studies have attempted to determine laboratory markers based on retrospective analysis that reliably predict mortality that can help guide resuscitative efforts. In general, victims of non-immersion hypothermic cardiac arrest with serum potassium greater than 9 mmol/L or pH less than 6.5 are not expected to survive.[43] Despite worsening prognosis with lower pH, it may not be completely reliable as a predictor of mortality. A European study on extracorporeal warming in severe hypothermia had a survivor who presented with an initial pH of 6.47.[29] A multicenter review of hypothermic patients in the 1980s found serum potassium greater than 10 mmol/L alone was a predictor of death.[10] This finding has been supported in several other analyses.[44,45] As mentioned earlier, patients whose primary event was drowning have an extremely grim prognosis. In patients with known prolonged periods of asphyxia or submersion or where the primary event was drowning, the clinician must use his or her judgment as to what efforts, if any, should be made.

Case Resolutions

■ Case One
The 30-year-old man who had been found in a park was gently transferred from the cot to the emergency department bed. His clothes were immediately cut off, and he was covered with warm blankets while equipment was being prepared for intubation. He was then carefully intubated by the most experienced and skilled practitioner available and ventilated

with warm humidified oxygen at a rate of 8 breaths per minute. Large-bore intravenous lines were placed, and warmed normal saline infusion was started. A temperature-sensing Foley catheter was placed. Two left-sided chest tubes were placed, and thoracic lavage was initiated. The patient was transferred to the medical ICU. Over the next 6 hours, his core temperature normalized and his heart rate gradually increased to 70 beats per minute. He never required vasopressors, and he was extubated the following day.

■ Case Two

In the case of the child who fell through the ice, no pulse was appreciated after 45 seconds, and the monitor showed asystole. CPR was resumed. A forced-air warming blanket was placed over the patient, and she was intubated without difficulty and placed on a ventilator with warm humidified oxygen. While CPR was continued, the cardiothoracic surgery team was contacted and plans were made to initiate cardiopulmonary bypass. While waiting for the team to arrive, an introducer was placed in the patient's right femoral vein, and the opposite groin was prepared for arterial catheter placement. CPR was continued for 2 hours while the patient was being warmed by cardiopulmonary bypass. She regained spontaneous perfusion, and after 2 days in a pediatric ICU she was discharged home with minor neurologic deficits.

■ Case Three

The older man who was in ventricular fibrillation was immediately cardioverted at 200 J with return to a narrow complex bradycardia at a rate of 40. He continued to be obtunded and was successfully intubated using etomidate and no paralytics. Thoracic lavage was considered but, given his history of severe emphysema, he instead received simultaneous peritoneal lavage and gastric lavage along with warmed intravenous normal saline. He was admitted to the medical ICU, where his

temperature increased to 35°C over the next 4 hours. He had no further cardiac arrhythmias. His course was complicated by pneumonia and difficulty weaning from the ventilator. After 1 week he had made a full recovery and was discharged from the hospital.

Summary

Hypothermia can present as a manifestation of other underlying medical disorders or as a primary result of cold exposure. The science behind optimal rewarming methods is evolving. What is clear is that survival with good neurologic outcomes can be attained despite prolonged resuscitative efforts in patients with no vital signs for extended periods of time. Aggressive management can prove lifesaving.

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The LLSA Literature Review

"The LLSA Literature Review" summarizes articles from ABEM's "2011 Lifelong Learning and Self-Assessment Reading List." These articles are available online in the ACEP LLSA Resource Center (www.acep.org/llsa) and on the ABEM Web site.

Article 9

Rhabdomyolysis and Acute Kidney Injury

Reviewed by J. Stephen Bohan, MS, MD, FACEP; Harvard Affiliated Emergency Medicine Residency; Brigham and Women's Hospital

Rhabdomyolysis is characterized by leakage of muscle cell contents into the circulation. Both trauma and toxic causes are common, and the end result of either is the same—limb weakness, myalgia, swelling, and pigmenturia without hematuria. Congenital myopathies can also be causative.

The incidence of acute kidney injury in rhabdomyolysis has been reported to be as high as 47% in some series and is highest in those who used illicit drugs or abused alcohol. The outcome is usually good as long as there is no renal failure, although when renal failure is present the mortality rate can exceed 3%.

Myoglobin is the offending agent causing kidney injury. It causes intrarenal vasoconstriction and tubular blockage and apparently is active only when the urine is acidic, in which setting free radicals cause renal cell injury. Renal injury is uncommon at creatine kinase levels of less than 20,000 units.

The diagnosis of myoglobinuria can be made when the urine dipstick is positive in the absence of red cells in microscopic examination of the urine.

Hyperkalemia is the most common and serious manifestation of the renal injury in rhabdomyolysis, although hypocalcemia occurs as well. The former requires specific aggressive treatment to reverse the volume depletion that is usually present and, although empirical evidence for the benefit of alkalinization of the urine is lacking, alkalinization is generally recommended given that it is inexpensive and nontoxic. Mannitol may also be useful.

Dialysis can correct the renal and electrolyte abnormalities in severely ill patients, but myoglobin is not dialyzable.

Highlights

- Renal injury is common in rhabdomyolysis and should be searched for. Its presence contributes to mortality and may result from the combination of myoglobin toxicity and volume depletion.
- Renal injury is uncommon in nonserious cases but can be assumed when the urine dipstick is positive in the absence of microscopic hematuria.
- Hyperkalemia is the most common serious electrolyte abnormality in rhabdomyolysis-associated renal injury.
- Volume repletion is the mainstay of treatment, and administration of agents to make the urine alkaline is recommended.

Lesson 10

Pediatric Sickle Cell Disease

Bernard L. Lopez, MD, MS, FACEP, and Cynthia Obi, MD

■ Objectives

On completion of this lesson, you should be able to:

1. Identify the common and life-threatening presentations of sickle cell disease (SCD) in children in the emergency department.

2. Describe the diagnosis and management of acute chest syndrome.

3. Explain the rationale for specific diagnostic studies and treatments.

4. List the indications for blood transfusion in a patient with SCD.

5. Describe the indications for hospital admission.

■ From the EM Model

8.0 Hematologic Disorders
    8.5 Red Blood Cell Disorders

Sickle cell disease (SCD) is a hereditary hemoglobinopathy that is characterized by anemia and a wide array of pathology secondary to intermittent small blood vessel occlusion. It is estimated that 1 in 600 African Americans in the United States has the disease; in addition, SCD can also be seen in people of Indian, Mediterranean, and Middle Eastern descent. Given its prevalence, the practicing emergency physician has a high likelihood of encountering a patient with SCD. In most cases, that encounter will be with an adult. In the adult, acute sickle cell vasoocclusive crisis (VOC) represents, by far, the most common chief complaint in the emergency department. It is due to tissue ischemia secondary to vascular occlusion from sickled red blood cells (RBCs). While other serious complications must be considered, the vast majority of these encounters will center on pain control.

Children with SCD presenting to the emergency department, on the other hand, represent a unique challenge to the emergency physician. Even though VOC represents (as in adults) the most common presentation, there is a much higher incidence of potentially life-threatening pulmonary, central nervous system, gastrointestinal, and infectious complications in children because of the unique anatomic and physiologic characteristics of children. This, along with the challenges in obtaining an accurate history and physical examination, makes it important that emergency physicians understand the complexities of SCD in children. Emergency physicians must maintain a high suspicion for these complications, as they may not be apparent on the initial evaluation. This article will focus on the pathophysiology, unique presentations, and management of the complications of SCD in pediatric patients.

Case Presentations

■ Case One

A 15-year-old girl with a history of SCD is brought to the emergency department by her mother because the girl is having severe pain in her legs, arms, and anterior chest. The pain in her arms and legs began 1 day prior to arrival, but the chest pain began today and has been very intense. The patient had only minimal relief of her symptoms with her outpatient pain control regimen. The patient reports that her legs and arms are the usual sites for her pain crises, but the chest pain is new. The chest pain is worse when she tries to take a deep breath. She denies any cough or wheezing but reports having a fever. She denies having a headache, visual changes, or abdominal pain.

Vital signs are blood pressure 110/60, pulse rate 100, respiratory rate 20, temperature 38°C (100.4°F), and pulse oximetry 93% on room air. On physical examination, the patient is lying on the gurney and appears uncomfortable. On examination, there is nasal flaring, lungs are clear to auscultation, the heart examination

Critical Decisions

- What are the findings associated with clinically significant complications of SCD in children?
- Is it pneumonia, pulmonary infarction, or acute chest syndrome?
- What diagnostic tests should be ordered?
- Does the patient require analgesics and/or antibiotics?
- Which patients require blood transfusions?
- Who requires admission to the hospital?

shows a regular rhythm with tachycardia, the chest wall is diffusely tender to palpation, and the abdomen is soft and nontender. The arms and legs are warm to the touch and diffusely tender to palpation. There is no swelling.

■ Case Two

A 7-year-old boy is brought to the emergency department by his parents because of a seizure at home about 1 hour prior to arrival. The seizure was described as generalized, uncontrolled shaking that lasted about 5 minutes. The patient had been complaining of a headache for several hours that was not relieved by over-the-counter analgesics. There is no fever, history of recent illness, nausea, or vomiting. The patient does not have a history of seizure disorder; his only significant medical history is SCD, although he has not had any problems in the previous year.

His vital signs are blood pressure 95/50, pulse rate 90, respiratory rate 20, temperature 36.7°C (98°F), and pulse oximetry 98% on room air. On physical examination, the child appears tired and is lying quietly on the gurney. He is able to answer questions appropriately. His pupils are equal and reactive to light, and extra-ocular movements are intact. There is no facial asymmetry. There is no nuchal rigidity. His lungs are clear to auscultation; his heart has a regular rate and rhythm, and there are no murmurs. His abdomen is nondistended, has normal bowel sounds, and is soft and nontender to palpation. Strength testing reveals mild weakness in the left upper and lower extremities.

Pediatric Sickle Cell Anemia

SCD is one of the most prevalent genetic diseases worldwide and is the most frequently inherited hemoglobinopathy in the United States. Approximately 2,000 infants with SCD are born each year, and it is estimated that 1 in 600 African Americans has some form of the disease.[1,2] Up to 10% of patients with sickling disorders are not of African descent but rather are of Mediterranean or Indian heritage.

Normal hemoglobin has two pairs of identical polypeptide chains. Two of these chains are always α, and the remainder may be β (hemoglobin A), δ (hemoglobin A2), or γ (hemoglobin F [fetal hemoglobin]) chains. Most (96%) of hemoglobin in nondiseased individuals is hemoglobin A. In patients with SCD, a point mutation results in the substitution of valine for glutamic acid at position 6 of the β chain and causes the formation of hemoglobin S. Patients who inherit the abnormal gene from both parents are said to have HbSS disease and have a predominance of hemoglobin S.[3] HbSS disease is associated with the most severe manifestations of SCD. Patients who inherit only one abnormal gene are said to have "sickle cell trait" and are usually asymptomatic because they produce more than 80% hemoglobin A. Another clinically significant type of abnormal hemoglobin is hemoglobin C. In this subset, lysine is substituted for glutamic acid at position 6 of the β chain. Patients who inherit one hemoglobin S and one hemoglobin C gene have HbSC disease. These patients can have the same complications as those with HbSS disease, but their clinical course tends to be less severe and with less

frequent complications than those with HbSS disease. Thalassemia is a related genetic hemoglobinopathy that affects globin chain production and can occur together with SCD. There are two major types: in α-thalassemia, there is a deficiency in the production of α-globin; in β-thalassemia, a genetic defect impairs globin mRNA production or translation and results in either inadequate supply of β globin or an imbalance of individual globin chain production.[4] These can occur in combination with hemoglobin S and can result in a clinical presentation ranging from mild to severe. Thus, when a parent offers a past history of thalassemia, one must consider the possible association of sickle cell anemia and its clinical presentations.

In SCD, under conditions of low oxygen tension, deoxygenated hemoglobin S molecules aggregate and polymerize intracellularly to form a gelatinous network of polymers. This causes the red cell to take on an abnormal sickle shape and renders the erythrocyte less deformable and more fragile. These RBCs are more prone to intravascular hemolysis leading to hemolytic anemia. Additionally, these red cells are more adherent to the endothelium and to other RBCs because of damage from repeated sickling and unsickling. Together, these processes result in sludging in the end arterioles and cause microvascular occlusion. This leads to decreased blood flow, reducing delivery of oxygen and other nutrients to tissues, and results in ischemia and acidosis.[5] A vicious cycle ensues – further tissue hypoxia leads to further RBC sickling and further tissue ischemia. The various complications seen in SCD are dependent on

the organ systems affected by ischemia. Fetal hemoglobin prevents the polymerization of sickle hemoglobin. Because of this, the initial presentation of sickle cell vasoocclusive complications usually coincides with the normal decline in hemoglobin F, with symptoms appearing as early as 6 months of age.[6]

Nitric oxide is an endothelium-produced molecule that causes vasodilation and modulates RBC adherence. It has been shown to play a significant role in protection against ischemic injury,[7] largely by enhancing blood flow to ischemic tissue.[8] In the presence of free hemoglobin (as is seen in the hemolysis found in sickle cell anemia), nitric oxide is significantly neutralized, thus removing many of the beneficial and protective effects. This lowered level of nitric oxide causes vasoconstriction, platelet aggregation, and red cell adhesion and results in further ischemia[9] and is associated with greater pain.[10] L-arginine, the substrate for nitric oxide, is deficient in SCD[11] and correlates with low nitric oxide during the complications of VOC.[12] Taken together, it would seem that enhancing the presence of nitric oxide, through administration of nitric oxide or L-arginine, would be beneficial in the treatment of the acute presentation of sickle cell anemia. Unfortunately, the studies to date examining the administration of inhaled nitric oxide and oral or intravenous L-arginine have not shown improvement in sickle cell pain in the emergency department.

Acute Vasoocclusive Crisis

VOC is considered to be the hallmark of SCD and is the most common emergency department presentation for pediatric patients, representing over 90% of all visits.[13] VOC is due to the ischemia or infarction of tissue that results from the sludging of sickled and nonsickled RBCs within the microvasculature and results in the mild to severe pain seen in this crisis.

Although a number of biologic (infection, dehydration, menstruation, physical exertion, hypoxia), environmental (change in ambient temperature), and emotional (anxiety, depression) precipitants for VOC exist, most VOC occurs spontaneously, and the cause is often not identified.

CRITICAL DECISION
What are the findings associated with clinically significant complications of SCD in children?

Preverbal children may present with fussiness, inconsolable crying, altered sleep patterns, or diminished feeding. Verbal children typically describe pain in almost any part of their body. It is most commonly seen in the chest, abdomen, low back, and extremities. In typical acute VOC, the pain in the spine, long bones, and chest is thought to occur from bone marrow ischemia as well as bone marrow hyperplasia (secondary to enhanced RBC production). The patient and/or caregiver may note similar patterns of pain in terms of location and severity from crisis to crisis and may thus be able to describe whether the current episode is "typical." The pattern, in some cases, can actually mimic other emergent conditions (acute abdomen, pulmonary embolus, renal colic) and can thus make the diagnosis more of a challenge. The duration of a painful crisis is variable but is typically 4 to 6 days. Some patients, however, can experience pain for weeks and could return to the emergency department for multiple visits during this time. Although most patients with SCD are able to manage their pain as outpatients, 10% to 20% have pain severe enough to require emergency department treatment and possible inpatient care.[4]

Anemia

Anemia can result from increased hemolysis due to the fragility of sickled RBCs. Hyperhemolytic crisis is characterized by an increased destruction of RBCs and can be seen in VOC or with associated infection.

Decreased hemoglobin, increased reticulocyte count, increased bilirubin, and increased lactic dehydrogenase are typical laboratory findings. Aplastic crisis occurs when RBC production is suppressed. There is variability in the decrease in hemoglobin, and the reticulocyte count is typically less than 2%. Infection is the most common etiology, with parvovirus B-19 as the most common agent. Aplastic crisis can also serve as the trigger for a VOC episode.[14]

Dactylitis

Dactylitis (or hand-foot syndrome) is the earliest clinical manifestation of SCD. It occurs most commonly in children between the ages of 6 months to 2 years. Dactylitis often presents with acute symmetric painful swelling of the dorsal part of the hands and feet and is caused by ischemia and infarction of the bone marrow. The edema is nonpitting and involves the soft tissue over the metacarpals and metatarsals and the proximal phalanges of the hands and feet. It occurs in these areas in this age group because hematopoiesis occurs in these peripheral areas. As children age, hematopoiesis shifts to more central locations such as the arms or legs. The patients can be febrile, and the physical examination will show erythema, warmth, and tenderness. If obtained, radiographs typically do not demonstrate bony abnormalities. Interestingly, patients who develop dactylitis before 12 months of age are 2.6 times more likely to develop severe SCD during their life.[15]

Infection

Children with SCD can develop splenic dysfunction as early as 3 months of age. The spleen, as part of the reticuloendothelial system, acts as a filter for abnormal RBCs. Uptake of sickled RBCs can lead to tissue ischemia and infarct, thus rendering the spleen less effective over time. Loss of the spleen's ability to clear encapsulated bacteria renders patients with SCD at higher risk for infection.

SCD patients are particularly at risk for infection by organisms such as *Pneumococcus, Staphylococcus* species, *Haemophilus influenzae,* and *Salmonella.* Children can present with signs of pneumonia, urinary tract infection, or meningitis. Children with SCD have a several hundred-fold higher risk for sepsis compared to healthy children. The risk for overwhelming sepsis is highest before age 3.[16]

Stroke

Children with SCD are at increased risk for stroke, with a 400-fold increase in cerebral infarction when compared to patients without the disease.[17] Stroke incidence peaks between 4 and 6 years of age, and it is estimated that 10% of all SCD patients will suffer a stroke by age 20.[18] In children, stroke is almost always due to large vessel occlusion. Although a variety of neurologic deficits can be found (based on the area of insult), hemiplegia is the most common physical examination finding, followed by focal seizures. Additional findings include any focal neurologic deficit, headache, seizure, and change in mental status.

Splenic Sequestration

The abdomen is the second most common site of pain in SCD after the musculoskeletal system. The spleen serves as a filter for abnormal RBCs and is one of the first organs to suffer from the effects of intravascular sickling. Children between 5 months and 2 years are the most vulnerable to acute splenic sequestration crisis, a condition in which the spleen acutely sequesters large numbers of RBCs. This results in obstruction of venous outflow from the spleen leading to pooling of red cells and platelets within the spleen. Diminished flow leads to an acidotic environment, further sickling, increased blood viscosity, and further obstruction.

Acute splenic sequestration is characterized by the following: (1) rapid fall in hemoglobin, (2) rise in reticulocyte count, (3) fall in platelet count, (4) acute pain and tenderness in the left upper quadrant with sudden increase in the size of the spleen, and (5) signs and symptoms of hypovolemia.[18] Splenic sequestration varies in severity from mild to life threatening.

Gallbladder Disease

Cholelithiasis is a relatively common occurrence in HbSS SCD patients and is due to repeated episodes of hemolysis with resultant bilirubin gallstone formation. The onset of cholelithiasis begins by age 4 and increases in prevalence with age. Gallstones develop in approximately 30% of patients with SCD by age 18.[18] Emergency physicians should look for evidence of cholecystitis in SCD patients with abdominal pain and should also consider the possibility of choledocholithiasis in patients with signs and symptoms of cholangitis or pancreatitis.

Intrahepatic cholestasis describes the reduction or complete prevention of bile excretion from the liver. In the SCD patient, this can result from erythrocyte sickling within the liver sinusoids, which leads to hepatic ischemia.[19] Two types of intrahepatic cholestasis can be seen in the patient with SCD. Most common is benign cholestasis (benign hyperbilirubinemia), in which the patient's only symptoms are jaundice and possibly pruritus. It is a self-limited process that resolves without any particular therapy. Progressive cholestasis, on the other hand, although quite rare, has an extremely high mortality rate. These patients will present with right upper quadrant abdominal pain, fever, nausea, vomiting, and jaundice. They can go on to develop a bleeding diathesis, encephalopathy, and renal failure. Abdominal examination reveals hepatomegaly with a tender right upper quadrant. Patients can become coagulopathic because of reduced synthesis of coagulation factors with resulting elevation of prothrombin and partial thromboplastin time. In progressive cholestasis, hepatic ischemia affects all aspects of liver function, which helps to explain its extremely high mortality rate and many symptoms.

Priapism

Priapism is a prolonged (4 hours or longer), painful erection caused by failure of timely penile detumescence. In SCD, the most common cause of priapism is sickled RBCs sludging in the venous outflow vessels of the corpora cavernosum, resulting in a low-flow, ischemic state. The mean age at which it occurs is 12 years, and it has been estimated that up to 90% of all male patients with SCD will experience at least one episode of priapism by age 20.[18] Untreated priapism can lead to cellular damage, fibrosis, and impotence.[20]

CRITICAL DECISION

Is it pneumonia, pulmonary infarction, or acute chest syndrome?

Acute chest syndrome is the most common cause of death, the leading cause of admission to an ICU, and the second most common cause (after VOC) of hospitalization in children with SCD.[21,22] The four classic findings in acute chest syndrome are chest pain, hypoxia, fever, and a chest radiograph with new pulmonary infiltrates. Other findings include cough, dyspnea, and wheezing. Because of the overlap of signs and symptoms with those of a respiratory infection, acute chest syndrome can be easily confused with pneumonia, pulmonary infarction, and pulmonary embolism. With severe presentations, it can even be confused with acute respiratory distress syndrome (ARDS). Acute chest syndrome tends to present 2 to 3 days after an episode of VOC. However, it can also present simultaneously with an acute infection. It can be difficult, if not impossible, for an emergency physician to distinguish between pneumonia, pulmonary infarction, and acute chest syndrome. The etiology of acute chest syndrome is multifactorial and includes both infectious and noninfectious causes, and it has been postulated that pneumonia and lung infarction

are precipitants of acute chest syndrome.[23] Infectious agents include *Streptococcus pneumoniae, H. influenzae,* and *Klebsiella pneumoniae.* Noninfectious causes include pulmonary microvascular sludging, in situ pulmonary vascular thrombus formation, pulmonary parenchymal infarction, and bone marrow fat embolization.

CRITICAL DECISION

What diagnostic tests should be ordered?

As with most disease processes, the use of laboratory and radiographic testing is guided by the history and physical examination. However, given the unique nature of the disease in children, emergency physicians should have a low threshold for ordering certain tests.

The CBC and the reticulocyte count are the two most important tests that should be considered when treating an SCD patient with complications. Anemia is of primary concern given the propensity for hemolysis and reticuloendothelial system sequestration. The hemoglobin and hematocrit offer information as to the level of anemia present; absolute levels can assist in determining disease severity. Most patients with HbSS disease have a baseline hemoglobin level of 6 to 9 g/dL and tolerate this level of anemia well because of physiologic adaptations. Levels below this suggest the need for transfusion. The WBC count can be elevated if an acute infection is present and could be the first clue to an early infection. However, because the WBC count could be elevated for reasons other than infection (increased hematopoiesis caused by bone marrow hyperactivity in response to anemia, stress-related increase in WBC demargination), it is not a particularly sensitive nor specific indicator for infection. Nonetheless, it remains as an important piece in the overall evaluation. The reticulocyte count is an indicator of bone marrow activity. A sickle cell patient, because of a chronic anemic state, normally has increased RBC production, thus resulting in a normally elevated reticulocyte count (>5%). Levels lower than 5% are a serious cause for concern in any sickle cell patient as it signifies bone marrow hypoactivity. A level from 2% to 5% suggests hypoplastic anemia; a level less than 2% suggests an aplastic crisis.

Although it seems intuitive, the requirement for the measurement of a CBC and reticulocyte count is unclear. There are no studies indicating the need for routine measurement for pediatric patients presenting to the emergency department. In a study done at a National Institute of Health-designated regional sickle cell center, the CBC and reticulocyte count were not found to be useful in the treatment and disposition of adult patients with uncomplicated VOC.[24] There was no difference in hemoglobin levels between those admitted and those discharged from the emergency department. No studies have been done in children to determine the need for these tests. Nevertheless, the emergency physician should have a very low threshold for routinely obtaining a CBC and a reticulocyte count for any emergency department presentation.

When a pediatric SCD patient with pulmonary complaints presents, the emergency physician should obtain a chest radiograph. The presence of cough, fever, wheezing, or shortness of breath should prompt a search for pneumonia, pulmonary infarct, and acute chest syndrome. For children without thoracic complaints, however, there is no clear evidence to support the use of routine chest radiographs. Pollack et al obtained routine chest radiographs in 134 uncomplicated VOC patients. Eight of the radiographs resulted in the diagnosis of acute pneumonia, yet none of the 8 had findings on history and physical examination suggestive of a pulmonary infectious process.[25] Ander and Vallee, in a retrospective study of 94 VOC patients, found 6 with a chest radiograph suggestive of pneumonia. All had signs and symptoms consistent with a respiratory infection.[26]

Other studies should be ordered based upon the clinical presentation. Given the susceptibility to encapsulated bacteria, emergency physicians should have a low threshold for ordering a urinalysis, blood cultures, and a lumbar puncture. CT scanning should be obtained in the SCD child presenting with a headache or a neurologic deficit.

CRITICAL DECISION

Does the patient require analgesics and/or antibiotics?

Immediate and aggressive analgesia (typically in the form of parenteral narcotics) is the mainstay of treatment for SCD patients presenting to the emergency department and is the required intervention in the patient suspected of experiencing a painful crisis. Many of the patients presenting to the emergency department have failed oral, outpatient analgesic therapy. Emergency physicians should assume that the child has severe pain and treat it appropriately. During the course of the emergency department visit, the patient's pain level should be regularly assessed to ensure adequacy of analgesia. A number of pain assessment tools for children exist (visual analog scale, numeric rating scale, Wong-Baker face scale). The choice of tool depends on factors such as age, cognitive ability, and emotional state.[6]

Acetaminophen and nonsteroidal anti-inflammatory drugs can be used for the management of mild to moderate pain. Opioids are considered to be the drugs of choice for more severe episodes of VOC pain. There are no studies that demonstrate superiority of one drug over another. Oral agents such as codeine (0.5-1 mg/kg), oxycodone (0.05-0.15 mg/kg), and hydromorphone (0.03-0.08 mg/kg) may be attempted. For severe pain, parenteral narcotics are indicated. Morphine is one of

the most frequently used parenteral narcotics in this setting. The starting dose is 0.1 to 0.15 mg/kg; it may be given intravenously, intramuscularly, subcutaneously, and rectally. The patient should be reassessed frequently; repeated doses can be administered until adequate pain control is achieved or until sedation or respiratory depression approaches an unacceptable level. Additional adverse effects include rash, pruritus, hypotension, and nausea and vomiting.

Meperidine has been (and in some institutions continues to be) one of the most commonly used narcotics for the treatment of VOC pain.[27] However, of all of the opioids, it likely has the most unfavorable pharmacologic profile. With repetitive dosing (as is commonly done in the treatment of VOC), accumulation of normeperidine (a toxic metabolite with a long half-life) can occur and increases the risk for seizures. Given the availability of other equally effective narcotics, emergency physicians should avoid meperidine.

In addition to analgesics, other adjunctive therapies such as fluids and oxygen have been traditionally used in the treatment of painful crisis. The use of fluids stems from the belief that hydration will increase the intravascular volume and thus improve the flow of sickled RBCs through the vasculature. However, there are no studies showing that fluid administration improves pain relief or outcome. Overly aggressive administration of intravenous fluids, in this setting, could trigger pulmonary edema and result in the development of acute chest syndrome.[28] Fluid therapy is therefore recommended only for those patients with evidence of volume depletion. The use of oxygen stems from the fact that deoxygenation causes sickling in vitro. Robieux et al, in the only randomized controlled study examining the use of oxygen in VOC, found no improvement in pain relief or outcome with the use of oxygen.[29] Additionally, oxygen

therapy can induce erythroid hypoplasia and decreased red cell production.[3] Oxygen therapy, thus, should be reserved for SCD patients with evidence of hypoxia or cardiopulmonary compromise.

CRITICAL DECISION
Which patients require blood transfusions?

Transfusion in the acute setting is used to treat significant and symptomatic anemia and to reduce or prevent complications.[30] Severe anemia usually occurs in the setting of aplastic crisis and hyperhemolytic syndrome. In general, SCD patients exhibiting signs (severe tachycardia, hypotension) or symptoms (dyspnea, syncope, severe pain) along with a significant drop in hemoglobin or an absolute hemoglobin below 6 g/dL will benefit from simple red cell transfusion. Exchange transfusion (in which the patient's abnormal RBCs are removed and replaced with normal RBCs) is generally accepted for the treatment for acute chest syndrome, stroke, intrahepatic cholestasis, acute splenic sequestration, and multiorgan failure.[30] Although not well studied, it is also used for the treatment of priapism that is unresponsive to pharmacologic therapy. All transfusions should be done in consultation with a hematologist.

CRITICAL DECISION
Who requires admission to the hospital?

In general, children who present to the emergency department with complications of SCD should be admitted to the hospital. This is because of the high risk for associated sepsis/infection, anemia, and acute chest syndrome. Additionally, the difficulties inherent in obtaining an accurate history and a reliable physical examination in children make it important that the emergency physician have a low threshold for admitting these patients. The patient with typical, uncomplicated VOC with adequate pain control in a timely fashion in the emergency department

(typically an older child with the ability to communicate effectively) can be discharged. Those discharged from the emergency department must have a supportive home environment along with close followup care.

Case Resolutions

■ Case One

The 15-year-old girl with leg, arm, and chest pain was placed on a cardiac monitor and 4 L of supplemental oxygen by nasal cannula. Her oxygenation status was monitored with continuous pulse oximetry. An ECG showed sinus tachycardia but was otherwise normal. A chest radiograph demonstrated a new infiltrate in the right lung base. The laboratory results showed an elevated WBC count of 18,200 and hemoglobin and hematocrit of 9 g/dL and 27%. The patient was treated with intravenous morphine for her pain and was given ceftriaxone for presumed pneumonia. She was admitted to the pediatric ICU and was subsequently diagnosed with acute chest syndrome. Her hospital course was uncomplicated.

■ Case Two

In the case of the 7-year-old boy who had a seizure, an emergent CT of the head showed an area of hypodensity in the right parietal lobe. There was no evidence of hemorrhage. Both a pediatric hematologist and a pediatric neurologist were consulted. Because of the patient's neurologic symptoms, arrangements were made for an exchange blood transfusion, and he was admitted to the pediatric ICU. During his hospital stay, the patient gradually regained strength in his left extremities and was eventually discharged from the hospital with minimal motor deficits. He was also seizure free throughout his hospital stay.

Summary

Understanding SCD is crucial for any emergency physician who treats patients of African or Mediterranean descent. Children with SCD represent

a unique challenge given the potential for life-threatening pulmonary, central nervous system, gastrointestinal, and infectious complications associated with the unique anatomic and physiologic characteristics of children. The additional challenge posed by the difficulties in obtaining an accurate history and physical examination makes it important that emergency physicians understand the complexities of SCD in children. Emergency physicians must maintain a high suspicion for complications, as they may not be apparent on the initial evaluation. Pain control, in the form of parenteral narcotics, is the mainstay of treatment for SCD patients presenting to the emergency department. Through vigilant care, the emergency physician can help provide improved outcomes for these patients.

Pearls

- Dactylitis (hand-foot syndrome) can be the first presentation of SCD in a child (typically under the age of 2).
- Pain from vasoocclusive sickle cell crisis is the most common presentation of SCD.
- Acute chest syndrome is the most common cause of death in pediatric sickle cell patients and can masquerade as pneumonia.
- Exchange transfusion is typically indicated for acute chest syndrome, stroke, and acute splenic sequestration.

Pitfalls

- Failing to provide adequate analgesia for pain control.
- Failing to consider sepsis in children with SCD presenting to an emergency department.
- Failing to consider acute splenic sequestration crisis as a cause for hypotension.
- Failing to obtain a CBC and reticulocyte count.

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The Critical ECG

A 61-year-old man with fever, productive cough, and dyspnea.
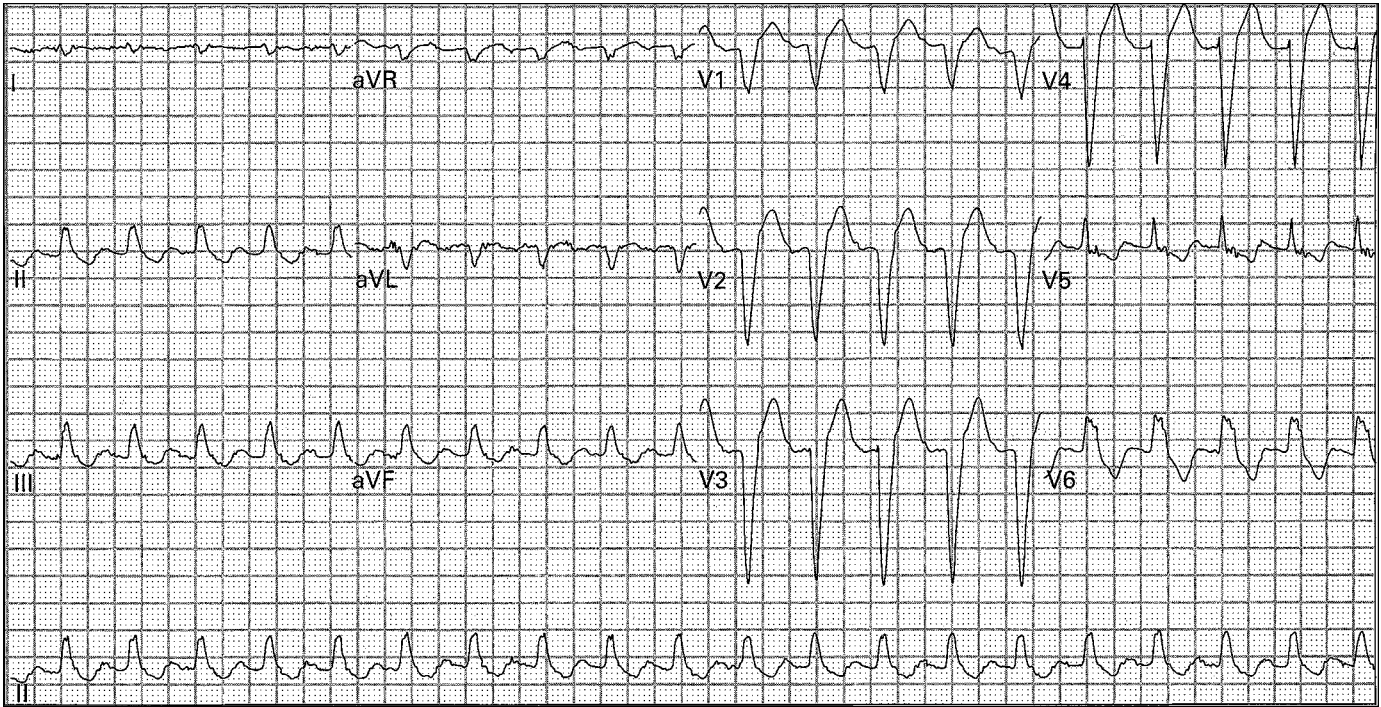
Probable sinus tachycardia (ST), rate 121, left bundle-branch block. The differential diagnosis for a wide-complex regular rhythm includes ventricular tachycardia, ST with aberrant conduction, supraventricular tachycardia with aberrant conduction, and atrial flutter with aberrant conduction. Close inspection of all 12 leads reveals the presence of subtle P-waves in lead V_1 that have a 1:1 relationship with the QRS complexes; therefore, an atrial tachycardia is diagnosed. In order to be certain that this is *sinus* tachycardia (as opposed to an ectopic atrial tachycardia), upright P-waves would be identified in lead I and in the inferior leads.

Feature Editor: Amal Mattu, MD, FACEP

From: Mattu A, Brady W. *ECGs for the Emergency Physician.* London: BMJ Publishing; 2003:109,143. Available at www.acep.org/bookstore. Reprinted with permission.

The Critical Image

A 76-year-old woman presenting with right hemiparesis and urinary incontinence. She was last seen in her normal state of health 4 hours prior to emergency department presentation; her husband found her in her current state on the floor by her bed. No seizure activity was witnessed, but she has a remote history of seizure. Her glucose is normal, and her blood pressure is 200/90. Head CT showed no hemorrhage.

Normal middle cerebral artery

Dense middle cerebral artery

This patient presents with findings consistent with middle cerebral artery (MCA) territory stroke, but also consistent with a seizure with postictal paralysis, given her history and new urinary incontinence. Critical decisions regarding treatment with tissue plasminogen activator (tPA) rest on resolving this differential diagnosis.

The dense MCA sign is a bright appearance seen with acute thrombosis of the middle cerebral artery. It can be an early sign of ischemic stroke on noncontrast brain CT and is associated with worse neurological outcomes.[1] A density threshold of 43 Hounsfield units (the standard unit of density with CT) helps to avoid false-positive results.[2]

Importantly, the dense MCA sign indicates a stroke involving the proximal MCA and possibly affecting the entire MCA territory. Strokes involving more than one-third of the MCA territory are associated with increased risk of subsequent intracranial hemorrhage. Such strokes were excluded from the ECASS III trial, which proponents of tPA therapy argue demonstrates the safety of intravenous tPA within a 4.5-hour window.[3]

Observational data suggest that intraarterial thrombolysis may lead to more favorable outcomes than intravenous thrombolysis in ischemic strokes with hyperdense MCA sign, although randomized controlled trials are needed to confirm this.[4,5]

In some nonrandomized studies, mechanical recanalization of proximal MCA occlusions has been achieved up to 8 hours after the incident using intraarterial devices, although outcomes are poor, with mortality in one-third of patients and poor neurological outcomes in two-thirds.[6]

In this patient, intraarterial therapy could not be administered before 8 hours had elapsed, and the patient was admitted to an ICU without invasive therapy.

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Feature Editor: Joshua S. Broder, MD, FACEP

CME Questions

Qualified, paid subscribers to *Critical Decisions in Emergency Medicine* may receive CME certificates for up to 5 ACEP Category I credits, 5 *AMA PRA Category I Credits™*, and 5 AOA Category 2-B credits for answering the following questions. To receive your certificate, go to www.acep.org/criticaldecisionstesting and submit your answers online. You will immediately receive your score and printable CME certificate. You may submit the answers to these questions at any time within 3 years of the publication date. You will be given appropriate credit for all tests you complete and submit within this time. Answers to this month's questions will be published in next month's issue.

1. According to the AHA guidelines, a patient who presents with a core temperature of 26°C in ventricular fibrillation who is successfully defibrillated to sinus bradycardia should be given which of the following?
   A. amiodarone
   B. bretylium
   C. high-dose epinephrine
   D. no medications
   E. procainamide

2. Which of the following is true regarding the Osborn J wave?
   A. can be seen in variety of other disease states and is not specific to hypothermia
   B. indicates severe hypothermia and is an indication for aggressive internal rewarming
   C. is associated with a poor prognosis
   D. is typically seen in lead aVL
   E. is only seen at temperatures below 23°C

3. A severely hypothermic patient is unresponsive on presentation, with no spontaneous respirations and a heart rate of 20. Which of the following interventions is appropriate?
   A. atropine
   B. chest compressions
   C. endotracheal intubation
   D. sitting the patient up
   E. transcutaneous pacing

4. In a patient with severe hypothermia, at what heart rate should CPR be initiated?
   A. <30 beats/min
   B. <20 beats/min
   C. <15 beats/min
   D. <10 beats/min
   E. CPR is not indicated if there is any detectable pulse

5. Which of the following lists the correct sequence of cardiac dysfunction as temperature is decreased?
   A. PR prolongation, P wave decreases in amplitude, QT prolongation, QRS prolongation
   B. P wave decreases in amplitude, PR prolongation, QRS prolongation, QT prolongation
   C. QRS prolongation, QT prolongation, PR shortening
   D. QT prolongation, PR prolongation, T-wave inversions, QRS prolongation
   E. T-wave inversions, PR prolongation, QT prolongation, QRS prolongation

6. All of the following patients are at increased risk for hypothermia except:
   A. elderly patients
   B. female patients
   C. intoxicated patients
   D. those with congestive heart failure
   E. young patients

7. For which of the following patients is passive rewarming an appropriate intervention?
   A. awake, alert, diabetic 60-year-old man presenting in septic shock with a temperature of 34°C
   B. an intoxicated patient with stable vital signs and temperature of 29°C
   C. an obtunded 70-year-old woman with a core temperature of 34°C found outside her home
   D. a previously healthy trauma patient with a temperature of 35°C, intubated for altered mental status using etomidate and rocuronium
   E. a previously healthy woman brought in from the scene of a motor vehicle accident with stable vitals and no obvious injuries and a temperature of 33°C

8. Which of the following is the primary mechanism for heat loss in cold water submersion?
   A. conduction
   B. convection
   C. evaporation
   D. radiation
   E. respiration

9. Which of the following findings in a severely hypothermic patient found with no signs of life would suggest that resuscitative efforts would be futile?
   A. cardiac monitor showing asystole
   B. core temperature <18°C
   C. fixed dilated pupils
   D. serum pH <6.8
   E. serum potassium >10 mmol/L

10. Which of the following portends a poor prognosis?
    A. bradycardia less than 40 beats/min
    B. elevated serum amylase
    C. history of drowning/near drowning
    D. presence of Osborn J wave on ECG
    E. urine output greater than 100 mL/hour

11. How long does the typical vasoocclusive crisis (VOC) last?
    A. 1 day
    B. 2 days
    C. 1 to 3 days
    D. 4 to 6 days
    E. more than 7 days

12. What is the cause of dactylitis?
    A. dependent edema
    B. idiopathic
    C. increased hematopoiesis
    D. infection
    E. trauma

13. A rapid fall in hemoglobin, abdominal pain, and hypotension are characteristic of:
    A. acute chest syndrome
    B. acute splenic sequestration crisis
    C. biliary colic
    D. pneumonia
    E. VOC

14. Which of the following combinations represents the classic presentation of acute chest syndrome?
    A. chest pain and fever
    B. fever, chest pain, hypoxia, cough, normal chest radiograph
    C. fever, chest pain, hypoxia, new infiltrate on chest radiograph
    D. fever, cough, hypoxia, abdominal pain
    E. hypoxia, shortness of breath, normal chest radiograph

15. Which of the following organisms is a likely cause of acute chest syndrome?
    A. *Escherichia coli*
    B. *Mycobacterium avium-intracellulare*
    C. *Mycoplasma pneumoniae*
    D. *Salmonella*
    E. *Streptococcus pneumoniae*

16. Which of the following is the most important test in the evaluation of an afebrile sickle cell patient in the emergency department?
    A. ALT
    B. AST
    C. blood cultures
    D. CBC
    E. prothrombin time

17. What reticulocyte count represents aplastic crisis in a sickle cell patient?
    A. <2%
    B. 2% to 5%
    C. 5%
    D. 5% to 10%
    E. >10%

18. Which of the following is the recommended analgesic for the treatment of severe VOC?
    A. acetaminophen
    B. nonsteroidal anti-inflammatory drugs
    C. oral narcotics
    D. parenteral narcotics
    E. phenothiazines

19. Which of the following is a potentially serious complication of aggressive fluid therapy in the emergency department for VOC?
    A. ascites
    B. overhydration
    C. peripheral edema
    D. pulmonary edema
    E. urinary frequency

20. Which of the following patients presenting with VOC can be safely discharged home from the emergency department?
    A. patient with hemoglobin of 6.1 g/dL, reticulocyte count of 1%, minimal relief of VOC pain
    B. patient with left arm and leg weakness with a headache
    C. patient with pulse oximetry 91% on room air, respiratory rate of 24, scattered rales on lung examination
    D. patient with relief of pain with analgesics, normal physical examination, good home situation
    E. patient with temperature 38°C (100.4°F), cough, right lower-lobe infiltrate

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Answer key for December 2010, Volume 25, Number 4

1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
C	C	C	E	C	C	D	A	C	D	D	A	D	B	E	A	B	C	E	C

The Drug Box

Hydromorphone

Gage Dixon DO; Summa Health System Emergency Medicine Residency

Hydromorphone is a potent centrally acting opioid that is very effective in managing acute pain. When properly dosed, hydromorphone is a safe and useful pharmacologic agent in the treatment of vasoocclusive crisis as well as other causes of moderate to severe pain. Hydromorphone is available in oral and intravenous forms, and the dosing is both age- and weight-based. Hydromorphone is estimated to be seven times more potent than morphine, so care must be taken to ensure the patient does not develop side effects (ie, respiratory depression).

Hydromorphone	
Mechanism of Action	Binds to opiate receptors in the CNS, producing altered perception to pain, analgesia, and sedation
Indications	Treatment and management of moderate to severe pain

Dosing	Infants >6 months and >10 kg:
	  Oral: 0.03 mg/kg/dose every 3-4 hours
	  IV: 0.01 mg/kg/dose every 3-4 hours
	Children <50 kg
	  Oral: 0.03-0.08 mg/kg/dose every 3-4 hours
	  IV: 0.015 mg/kg/dose every 3-4 hours
	Children >50 kg and adults
	  Oral: 1-2 mg/dose every 3-4 hours
	  IV: 0.2-0.6 mg/dose every 3-4 hours

Side Effects	Respiratory depression, bradycardia, hypotension, CNS depression, pruritus, rash
Estimated Cost to Hospital and Patient	Hospital cost: 1-mg IV = $0.90 - $1.00; patient cost varies by institution; Oral therapy: 2-mg tablet = $1.20
Contraindication/ Precautions	Hypersensitivity to opiates Severe respiratory depression Acute asthma Pregnancy class: C

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