The Evaluation and Management of Accidental Hypothermia

Robert R Kempainen MD and Douglas D Brunette MD

Accidental hypothermia is defined as an unintentional decrease in core body temperature to below 35°C. Hypothermia causes hundreds of deaths in the United States annually. Victims of accidental hypothermia present year-round and in all climates with a potentially confusing array of signs and symptoms, but increasing severity of hypothermia produces a predictable pattern of systemic organ dysfunction and associated clinical manifestations. The management of hypothermic patients differs in several important respects from that of euthermic patients, so advance knowledge about hypothermia is prerequisite to optimal management. The paucity of randomized clinical trials with hypothermic patients precludes creation of evidence-based treatment guidelines, but a clinically sound management strategy, tailored to individual patient characteristics and institutional expertise and resources, can nonetheless be gleaned from the literature. This article reviews the epidemiology, pathophysiology, clinical presentation, and treatment of accidental hypothermia. Initial evaluation and stabilization, selection of a rewarming strategy, and criteria for withholding or withdrawing support are discussed. *Key words: hypothermia, rewarming, thermoregulation.* [Respir Care 2004; 49(2):192192192–205. © 2004 Daedalus Enterprises]

Introduction

The human body functions optimally with a core temperature between 36.4 and 37.5°C, and core temperatures outside that narrow range are poorly tolerated. Accidental hypothermia is defined as an unintentional decrease in core body temperature to < 35°C (95° F) and is the reported cause of death in approximately 700 people per year in the United States.[1] Advance knowledge of the pathophysiology and management of hypothermia is a prerequisite to providing optimal care to hypothermic patients. The purpose of this article is to provide clinicians with an overview of the epidemiology, pathophysiology, clinical presentation, and treatment of accidental hypothermia.

Epidemiology

Media reports of victims of accidental hypothermia typically focus on young outdoor enthusiasts exposed to cold conditions in wilderness areas. Perhaps underappreciated is the frequency with which hypothermia occurs among elderly individuals living in urban areas. Approximately 50% of all United States deaths attributed to hypothermia occur in persons ≥ 65 years old (Fig. 1).[2] Others at high risk include homeless, chemically dependent, and mentally ill individuals.[3–7] Although the incidence of accidental hypothermia increases during the winter months, cases are diagnosed throughout the year.[5,6,8] A surprisingly large number of cases occur in mild climates or in individuals without a history of outdoor exposure.[3–6,8,9] The rate of hypothermia-related deaths in the United States has fallen over the past 20 years (see Fig. 1).[2] Whether this is due to changes in reporting, improved preventive measures and treatment, or changing weather patterns is unclear.

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Normal Thermoregulation

Maintenance of a normal core temperature is contingent upon balancing heat production with heat loss in light of ambient conditions and physical activity. Approximately 90% of heat escapes through the skin, with the remainder lost via the lungs.[10] Table 1 outlines mechanisms and modifying factors that contribute to heat loss. The preoptic nucleus of the anterior hypothalamus is responsible for thermoregulation and mediates physiologic and behavioral responses to cold exposure. Peripheral and cutaneous vasoconstriction reduce heat loss from radiation, and shivering increases heat production. These physiologic responses, however, are easily overwhelmed by environmental stressors, and the ability of humans to survive in temperate climates is based largely on behavioral adaptation. The alert individual with intact peripheral and central neurologic function experiences a feeling of being cold, which prompts exercise, seeking shelter, or putting on another layer of clothing.

The robustness of these physiologic and behavioral adaptations differs among individuals. Conditions associated with impaired heat production, increased heat loss, and impaired thermoregulation compromise the physiologic response to cold exposure. Endocrine disorders, hypoglycemia, malnutrition, impaired shivering, and extremes of age can limit heat production.[10,11] As outlined in Table 1, a number of conditions exacerbate heat loss, including skin disorders and inappropriate peripheral vasodilation. Impaired thermoregulation arises from both peripheral and central neurologic dysfunction. Individuals with peripheral neuropathies, spinal-cord injuries, and diabetes may be unaware of environmental conditions. Cerebrovascular accidents, trauma, neoplasms, neurodegenerative disorders, and drugs can act centrally to disrupt hypothalamic function.[10,11] In addition, sepsis, pancreatitis, carcinomatosis, uremia, vascular insufficiency, and multisystem trauma are all associated with hypothermia.[11] Table 2 summarizes conditions that impair behavioral responses to cold exposure. In our experience, impaired decision-making resulting from alcohol intoxication is the single most common reason for accidental hypothermia in young, otherwise healthy patients.

Clinical Manifestations

The severity of hypothermia is categorized as mild (core temperature 32–35°C), moderate (28–32°C), or severe (< 28°C). Increasing severity of hypothermia produces a predictable pattern of organ dysfunction and associated clinical manifestations (Table 3). It is important for the clinician to be familiar with the relationship between core temperature and altered physiology, as it provides a blueprint and rationale for management decisions that are often unique to the hypothermic state. Of note, the use of this classification system is not applicable to patients with multisystem trauma. Hypothermia in that population is associated with dismal outcomes, with a reported mortality

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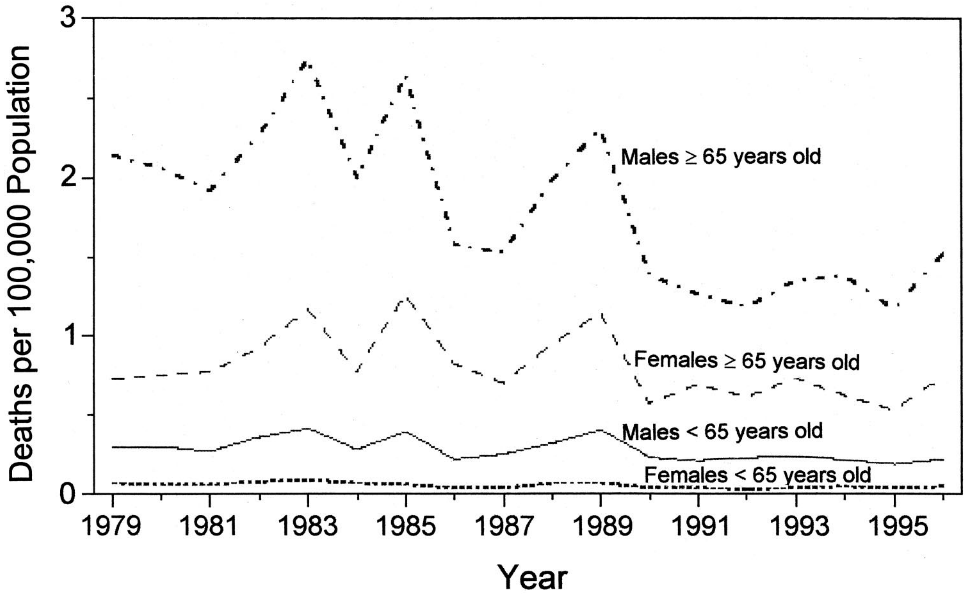

Fig. 1. Rate of hypothermia-related death, by age and sex, in the United States, 1979–1996. (Adapted from Reference 2.)

Table 1. Sources of Heat Loss and Exacerbating Factors

Mechanism	Normal Contribution (%)	Exacerbating Factors
Skin		
Radiation (nonparticulate emission of heat from body)	55	Vasodilation (eg, alcohol, spinal-cord injury)
Evaporation (cooling by conversion of fluid to vapor)	25	Skin disorders (eg, burns, psoriasis)
Conduction (transfer of heat by direct contact)	15	25-fold increase with water submersion
Convection (transmission of heat by movement of heated particles)	minor	Up to 5-fold increase in windy conditions
Respiratory		
Evaporation	5	Cold, dry air

Table 2. Causes of Impaired Behavioral Response to Cold Stress

Impaired cognition
Dementia
Drug-induced: alcohol, sedatives
Other encephalopathies: central nervous system, metabolic
Inadequate shelter and clothing
Homelessness, poverty
Wilderness exposure
Immobility
Neonates
Neuromuscular failure: stroke, hip fracture, spinal-cord injury

approaching 100% when core temperature falls below 32°C.[12] Some authors advocate the use of a separate scale for grading trauma-related hypothermia.[13]

The body's initial response to cold stress is to generate and conserve heat via activation of the sympathetic nervous system. Shivering increases the metabolic rate and is associated with tachypnea, tachycardia, and oxygen consumption up to 6 times the basal rate.[14] Blood pressure rises as a result of peripheral vasoconstriction and increased cardiac output. In contrast, with progression to moderate and severe hypothermia the initially elevated catecholamines return to baseline as the patient enters a state of globally depressed organ function.[15] It is unclear whether this marked shift from elevated to depressed oxygen consumption is protective or merely reflects limited physiologic response to the stress of cold.

Patients presenting with accidental hypothermia do not create a diagnostic conundrum when there is a clear history of sustained exposure to a cold environment, but the presence of comorbidities and absence of outdoor exposure can obscure the diagnosis. Manifestations of individual organ dysfunction viewed in isolation are a source of a broad, and misleading, differential diagnosis. Patients with moderate and severe hypothermia present with profound neurologic deficits that could

Table 3. Physiologic Changes and Clinical Manifestations Associated With Hypothermia

	Mild (32–35°C)	Moderate (28–32°C)	Severe (< 28°C)
Neurologic	Confusion, amnesia Dysarthria Ataxia ↓ cerebral metabolism	Progressive ↓ in level of consciousness Pupils dilate Hallucinations	Coma Global loss of reflexes ↓ in EEG activity EEG silent at < 26°C
Metabolic and Endocrine	↑ catecholamines ↑ $\dot{V}_{O_2}$ Shivering Hyperglycemia	↓ metabolic rate ↓ $\dot{V}_{O_2}$ Loss of shivering	Progressive ↓ to 20% of basal metabolic rate
Cardiovascular	↑ HR ↑ CO ↑ BP Prolonged PR and QT intervals Atrial fibrillation at < 33°C	Progressive ↓ HR and CO J waves on ECG ↑ risk of atrial and ventricular arrhythmia	↓ BP ↓ HR ↓ CO Ventricular arrhythmias Asystole at < 20°C
Respiratory	↑ RR ↑ $\dot{V}_E$ Bronchorrhea	Progressive ↓ RR and $\dot{V}_E$ Loss of airway protection	Apnea at < 24°C Pulmonary edema
	←Oxyhemoglobin-dissociation curve is shifted to the left→		
Renal	Cold diuresis	Cold diuresis	↓ renal perfusion Oliguria
	←Unpredictable changes in electrolytes→		
Hematologic	Hematocrit rises 2% per 1°C decline in core temperature (hemoconcentration) Coagulopathy 1. Decreased enzyme function in coagulation cascade 2. Thrombocytopenia (marrow suppression and splenic sequestration) 3. Decreased platelet function (decreased thromboxane B_2 production)		
Gastrointestinal	Ileus, pancreatitis, gastric stress ulcers, impaired hepatic function		

EEG = electroencephalogram, $\dot{V}_{O_2}$ = oxygen consumption, HR = heart rate, CO = cardiac output, BP = blood pressure, ECG = electrocardiogram, $\dot{V}_E$ = minute ventilation, RR = respiratory rate

be attributed to cerebrovascular accident, infection, or metabolic encephalopathy. J (Osborn) waves (Fig. 2), which appear on electrocardiograms at core temperatures below 33°C and become more pronounced with further temperature decline,[16] have precipitated the mistaken use of thrombolytics.[11] Hypothermia-associated arrhythmia and hypotension can likewise be misinterpreted as primarily cardiac or infectious conditions.

The hypotension associated with hypothermia is multifactorial. Dehydration, fluid shifts, and inappropriately increased urine output deplete the intravascular volume and cause hemoconcentration. The mechanism for this "cold diuresis" is probably depressed secretion of antidiuretic hormone. Initial peripheral vasoconstriction in response to cold exposure increases core intravascular volume and renal blood flow, thereby decreasing antidiuretic hormone release. A subsequent decrease in core temperature impairs hypothalamic function, thereby further decreasing antidiuretic hormone levels and promoting diuresis.[10,17] The decrease in heart rate and cardiac output in moderate hypothermia appropriately matches the decline in oxygen consumption that occurs with loss of shivering. In severe hypothermia, however, cardiac output becomes inadequate and contributes to hypotension and inadequate oxygen delivery.

Acid-Base Status

The changes in acid-base status that occur with hypothermia are particularly germane to providers with an interest in respiratory medicine. Patients with profound hypothermia have an uncompensated metabolic acidosis as a result of cardiopulmonary failure and hepatic insufficiency. Patients with milder degrees of hypothermia, however, typically present with metabolic alkalosis, when blood gases are corrected for the patient's temperature. Rosenthal discovered that blood pH in a closed system rises by 0.015 units for each 1°C drop in temperature (the Rosenthal formula).[18] This phenome-

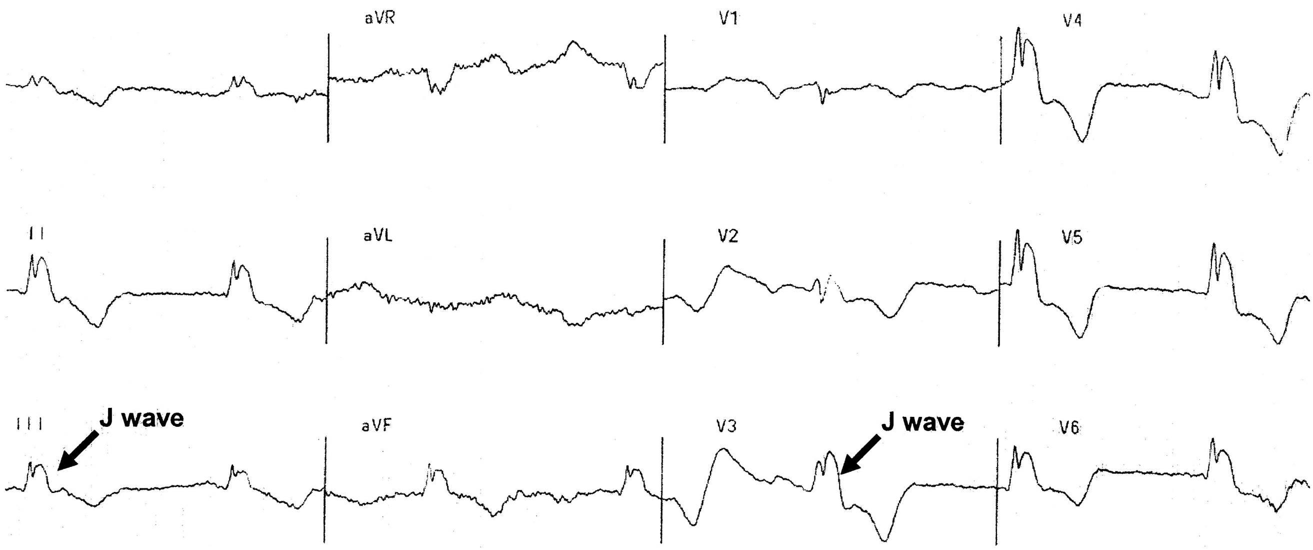

Fig. 2. Twelve-lead electrocardiogram from hypothermic patient, showing J (Osborn) waves, bradycardia, and prolonged QT interval.

non is termed *alpha-stat* regulation and is present in cold-blooded animals (ectotherms) and probably humans (homeotherms).[19,20] The rise in blood pH with cooling is due to buffering by the imidazole group of histidine residues present in hemoglobin.[21] As temperature decreases, more hydrogen ions bind to imidazole groups and the concentration of free hydrogen ion decreases. In order to maintain constant total-body carbon dioxide content, ectotherms hyperventilate relative to their total carbon dioxide production,[20] which elevates arterial pH, reduces P_{aCO_2}, and maintains a neutral pH. For example, the acid-base status of 37°C blood with a pH of 7.40 and P_{aCO_2} of 40 mm Hg is equivalent to that of 25°C blood with a pH of 7.60 and P_{aCO_2} of 22 mm Hg.[21] That is, the pH of neutrality rises as the temperature decreases. In contrast, hibernators develop respiratory acidosis in order to maintain a pH of 7.40, despite a decrease in core temperature. This is referred to as *pH-stat* regulation.[20]

In practice, arterial blood gas samples are routinely heated to 37°C prior to analysis. The blood gas values at 37°C are uncorrected for temperature, and corrected values based on the patient's core temperature are derived from the Rosenthal formula and similar corrections for P_{aCO_2} and P_{aO_2}. Whether hypothermic patients should be managed with a pH-stat strategy in which the corrected pH is maintained at 7.40, or with an alpha-stat approach in which ventilation is adjusted to maintain an uncorrected pH of 7.40, is a source of ongoing debate. Some animal models indicate that a pH-stat strategy during deep hypothermic circulatory arrest reduces ventricular irritability and improves postoperative neurologic outcomes,[22–25] but support for these findings in humans is inconsistent and limited to infants.[26,27] In contrast, comparisons of alpha-stat and pH-stat ventilation in adults undergoing coronary artery bypass graft with hypothermic cardiopulmonary bypass indicate that alpha-stat regulation improves neurologic outcomes.[28–30] A number of investigators have found that the alpha-stat approach improves cellular enzyme function, myocardial function, myocardial electrical stability, and cerebral blood flow.[19,21,31–33] However, there are few direct comparisons of alpha-stat and pH-stat management in the setting of sustained hypothermia,[34] and it is unclear whether studies from the surgery literature are applicable to the management of accidental hypothermia, in which the duration of hypothermia and rewarming is longer. At this juncture we recommend the use of uncorrected arterial blood gas values (ie, an alpha-stat approach) to assess the adequacy of ventilation in hypothermic patients.

Initial Stabilization

Because organ function recovers as core temperature rises, it is critical that clinicians focus primarily on supportive care and rewarming, and not put undue emphasis on the evaluation and treatment of individual signs and symptoms of hypothermia. Another tenet of early management is that manipulation of the patient should be kept to a minimum, as movement and invasive monitoring may precipitate arrhythmia.

Temperature Monitoring

Detecting a low core temperature clinches the diagnosis of accidental hypothermia and provides the clinician with a wealth of information about the patient's pathophysiologic state at any given temperature. Sublingual, rectal, esophageal, bladder, tympanic, and pulmonary artery sites are acceptable for monitoring; axillary temperatures are less reliable. With a patient suffering moderate or severe hypothermia, temperature should be monitored continuously from multiple sites. Rectal temperatures often lag behind other core sites during rewarming, independent of the falsely low values that occur with inadvertent insertion of the thermometer into cold stool. Furthermore, the site of rewarming interventions also may produce discrepancies in core temperature. For instance, peritoneal lavage may elevate bladder temperatures more rapidly than at other sites.

Endotracheal Intubation

Although there is concern that endotracheal intubation predisposes hypothermic patients to cardiac arrhythmia,[35] large case series indicate that in experienced hands the risk is small.[5,8,36] Hence, the threshold for intubating patients should be the same as in other patient populations. Oral intubation is preferable because hypothermic patients are coagulopathic, but the risk of epistaxis appears to be modest with the nasal intubation approach.[37,38] We avoid the use of neuromuscular blockers. They are largely ineffective at core temperatures below 30°C, and impaired renal, hepatic, and plasma enzyme function make metabolism and clearance unpredictable, thereby increasing the risk of providing inadequate sedation to paralyzed patients. Supplemental oxygen should be given empirically.

Cardiac Arrest

Standard protocols for managing bradycardic and ventricular arrhythmias are widely viewed as inapplicable in the setting of moderate and severe hypothermia. Cardioversion of ventricular arrhythmias is uncommon at core temperatures below 30°C, although a trial of electrical defibrillation is appropriate in pulseless patients, as there are case reports of successful cardioversion at substantially lower core temperatures.[39,40] Animal studies and case reports suggest that bretylium increases the threshold for ventricular fibrillation and allows cardioversion in severely hypothermic patients,[41–45] but there are insufficient data to support routine use of bretylium. Data from a porcine model of hypothermic cardiac arrest indicate that administration of epinephrine or vasopressin results in superior coronary perfusion pressures, greater rates of cardioversion, and improved short-term survival, compared to saline placebo,[46,47] but we are unaware of any clinical studies supporting the use of those medications. An animal model suggests that transcutaneous pacing for bradyarrhythmias may improve hemodynamics if there is evidence of inadequate cardiac output,[48] but efficacy in humans is unproven. Transvenous pacing is not recommended, as it may precipitate ventricular arrhythmias.[49] Because the majority of arrhythmias will resolve spontaneously during rewarming, it is imperative that attempts to manage cardiac arrest do not unduly delay interventions to correct the underlying hypothermia.

The literature supports both open- and closed-chest cardiac massage in arrested hypothermic patients. Compared to closed massage, open massage in normothermic patients produces superior coronary vessel perfusion,[50] and can be effectively combined with mediastinal irrigation and cardiopulmonary bypass in hypothermic patients.[51,52] Many institutions, however, lack the expertise and resources needed to safely and promptly perform the prerequisite left-lateral thoracotomy. Closed-chest massage is a viable, and not necessarily inferior, alternative; one hypothermia survivor received more than 6 hours of closed-chest compressions.[53] The term "cardiac massage" is probably a misnomer in this setting. External compressions create swings in intrathoracic pressure that produce forward blood flow independent of the flow generated by direct compression of the heart.[54]

Volume Resuscitation

Most patients with severe hypothermia are intravascularly depleted and will require intravenous fluids throughout the warming process. Fluids should be warmed to 40–42°C in a commercial fluid warmer to avoid exacerbating heat loss. However, hypothermic patients have concomitant impaired myocardial contractility, so clinicians must be vigilant for signs of volume overload. Arterial catheters provide continuous blood pressure monitoring and facilitate arterial blood gas monitoring, which is particularly important when peripheral vasoconstriction and hypotension interfere with pulse oximetry. Central venous pressure monitoring is helpful in patients with unclear volume status, but contact between the catheter and myocardium should be minimized because of the lowered threshold for arrhythmia. Catheterization of a femoral vein may be safer than internal jugular or subclavian sites, and pulmonary artery catheterization is best avoided altogether. Hypothermia may also elevate the risk of vascular perforation during right heart catheterization.[55] A trial of low-dose pressors is warranted in euvolemic patients who remain hypotensive despite rewarming.

Laboratory Evaluation

The broad spectrum of organ dysfunction associated with severe hypothermia requires close laboratory monitoring. Renal function is often impaired as a result of decreased perfusion, and electrolyte changes are unpredictable.[8] In the absence of disseminated intravascular coagulation, hypothermia-induced coagulopathy reverses with rewarming, and hence the severity of in vivo clotting dysfunction is not accurately reflected in routine coagulation studies, since they are performed at 37°C.[56–58] The presence of thrombocytopenia, elevation of clot degradation products, and depletion of fibrinogen suggest the presence of disseminated intravascular coagulation, regardless of core temperature. Patients with hypothermia are at risk of both depression and elevation of blood sugars.[8] Typical symptoms of hypoglycemia may be absent as a result of depressed nervous system function.

Other Measures

Hypothermia-induced ileus is common, and placement of an orogastric tube is routinely indicated. A Foley catheter is necessary for monitoring the adequacy of volume resuscitation and course of renal insufficiency. Wet clothes contribute to conductive heat loss and should be removed. The skin should be kept dry and covered with insulating material. Providers should defer warming the extremities until intravenous access is established and volume resuscitation is underway. Premature warming of the extremities may result in the return of cooler blood to the central circulation with consequent further decline in core temperature. This phenomenon, referred to as "afterdrop," entails a decrease of only 0.3–1.5°C in experimental models,[59,60] yet it can be clinically important in critically ill patients. Peripheral vasodilation with external warming may also exacerbate hypotension. Empirical antibiotics are appropriate for patients with suspected aspiration or sepsis.

During the transition from initial stabilization to embarking on a rewarming strategy, it is important to assess the patient for risk factors for thermal instability. The identification of predisposing intoxications, medications, and medical conditions such as hypothyroidism and adrenal insufficiency allows the clinician to tailor treatment to address specific causes of hypothermia. Furthermore, with recognition of these entities, clinicians are better able to anticipate the response to various rewarming interventions and adjust the aggressiveness of their approach accordingly.

Rewarming Options

Methods to correct hypothermia fall into one of 3 categories of rewarming: passive external, active external, and active internal. Table 4 summarizes minimally-invasive rewarming techniques, based on those categories. The reported efficacy of the various treatments differs. Differences in patient characteristics, severity of hypothermia, institutional expertise, and study design probably account for the discrepancies in the findings of the published research. Regardless, individual responses to minimally-invasive interventions are unpredictable, and it is unclear whether combining modalities has an additive effect.

Passive External Rewarming

The crux of passive external rewarming is to eliminate any sources of heat loss and to allow the core temperature to correct via endogenous heat production. A disproportionate amount of radiative and convective heat loss occurs at the head and neck, so it is particularly important they are covered.[10,13] With shivering, heat production can increase up to 5-fold above baseline,[61] allowing healthy, mildly hypothermic individuals to rewarm spontaneously in a timely fashion. In contrast, experimental models suggest that loss of shivering slows the rate of rewarming by up to 37%.[60] Since shivering is impaired at core temperatures less than 32°C, patients with moderate or severe hypothermia can be expected to warm slower initially. Individuals with concomitant decreased muscle mass, depleted glycogen stores, or endocrinopathies likewise have decreased capacity for endogenous heat production. Moreover, the 3–5-fold increase in oxygen consumption that accompanies vigorous shivering can be problematic for patients with limited cardiopulmonary reserve.[13] Greater reliance on active rewarming, coupled with meperidine, may be necessary in that population.

Table 4. Noninvasive Rewarming Interventions

Category	Options	Comments	Rewarming Rate (°C/h)
Passive External	Unwarmed blankets	Including head and neck reduces evaporative heat loss	0.5–4
	Humidified inspired air	Including head and neck reduces evaporative heat loss	Unknown
Active External	Forced heated air	After-drop risk low with adequate intravenous fluids	1–2.5
	Warm-water immersion	Difficult to monitor patient	2–4
	Heat cradles, diathermy	Limited experience, risk of burns	Unknown
Active Internal	42°C humidified air	Low heat transport capacity	0.5
	40–42°C intravenous fluids	Fluid temperature entering patient lower	Unknown

Active External Rewarming

Forced heated air units act by preventing heat loss while providing convective heat transfer. Such units are widely available and can be easily and rapidly instituted. Both an experimental human model and a randomized, controlled trial found warming rates with forced heated air superior to passive rewarming,[62,63] and a small case series suggests it is a viable treatment option even in the setting of severe hypothermia.[40] As previously noted, premature active rewarming can precipitate "afterdrop" and hypotension, but these risks appear to be modest with concomitant administration of warm intravenous fluids.

Patients with core temperatures as low as 23°C have been successfully managed with warm-water immersion.[64] However, that approach poses substantial barriers to monitoring and resuscitation, and safer techniques have largely supplanted warm-water immersion. There are limited data supporting the use of heat cradles, warm blankets, circulating warm-water blankets, and radio wave hyperthermia.[36,65,66] Peripheral vasoconstriction makes the skin of hypothermic patients especially vulnerable to burn injuries from externally applied heat sources.

Active Internal Rewarming: Minimally Invasive Methods

A number of interventions, ranging from airway rewarming with warm, humidified air to full cardiopulmonary bypass, fall into the category of active internal rewarming. In order to better understand the efficacy differences of these approaches, it is helpful to review the concept of specific heat. Specific heat is defined as the number of kilocalories (kcal) required to warm 1 kg of a substance by 1°C. The specific heat of water is 1 kcal/kg/°C, and thus 10 kcals are required to raise the temperature of 1 kg (1 L) of water by 10°C. The specific heat of the human body is 0.83 kcal/kg/°C. One can calculate the heat needed to raise the temperature of a 70-kg patient from 25°C to 35°C as follows:

$$70 \text{ kg} \times 0.83 \text{ kcal/kg/°C} \times 10\text{°C} = 581 \text{ kcals (or 58 kcal/°C in temperature gain).}$$

The response to administering warm intravenous fluids illustrates this concept. Crystalloids are typically warmed to 40–42°C in a warm water bath or microwave and then rapidly infused into the patient. If 1 L of 42°C saline is infused into a patient with a core temperature of 25°C, the heat transfer will be: $1 \text{ kcal/kg/°C} \times 1 \text{ kg} \times (42\text{°C} - 25\text{°C}) = 17$ kcals. This is sufficient heat to raise the temperature of the aforementioned 70 kg patient by $17 \div 58 = 0.29$°C. The actual heat transferred with infusion of 42°C fluids can be substantially less than that. The temperature of warmed saline decreases rapidly in room-temperature air, and further cooling is proportional to the length of tubing traversed prior to reaching the patient.[67–69] Rapid infusion using ≤ 25 cm of tubing maximizes heat delivery. A tympanic thermometer can also be used to directly measure the temperature of the fluid as it enters the patient.[70] Although their impact on the core temperature of a 25°C patient is relatively modest, warm intravenous fluids play an important role in the resuscitation of trauma victims, in whom temperature elevations of 1–2°C could be life-saving. Regardless, warming crystalloid and blood prior to infusion is indicated for all hypothermic patients, as administering room-temperature (21°C) fluids causes additional heat loss. Active internal rewarming with 65°C fluid improved recovery rates in animal studies, without precipitating hemolysis, but experience with humans is lacking.[71,72]

The use of heated inspired air is minimally invasive and has been examined in several studies. The small volume of water present in fully saturated air, however, limits the potential for heat transfer with inspired air to only about 10 kcal/h.[13] This is consistent with a reported rewarming rate of approximately 0.5°C/h attributable to the use of warm inspired air.[62,73–75] Most commercial ventilators will not heat air beyond 41°C. Because the use of higher temperatures is of modest clinical benefit and carries the risk of patient injury and ventilator damage, we do not recommend measures to circumvent that 41°C ceiling. Humidified air prevents evaporative heat loss and is readily available; humidity is arguably a more important factor than the temperature of the inspired air.

Active Internal Rewarming: Body Cavity Lavage

Lavage of body cavities with warm fluid is of variable efficacy. Easy access to the stomach, bladder, and colon make them attractive sites for irrigation, but there is a paucity of data supporting this approach.[11] The contribution to rewarming is probably nominal, as these cavities have a small mucosal surface area available for heat exchange. Given the modest benefit, gastric lavage in non-intubated patients arguably poses an unacceptable risk of aspiration. To avoid mucosal injury, care must be taken to heat isotonic fluids to no higher than 45°C. All variations of body cavity lavage require matching the volume of the instilled and recovered fluid.

Pleural cavity lavage entails infusing large volumes (10–120 L/h) of 40–45°C fluid through a thoracostomy tube placed in the 2nd or 3rd anterior intercostal space in the midclavicular line. The fluid is drained via a 2nd thoracostomy tube in the 4th, 5th, or 6th intercostal space in the posterior axillary line.[76,77] Alternatively, warm saline can be repeatedly infused and drained through a single chest tube, using 15–20 min dwell time. Pleural lavage offers rapid, albeit variable, rewarming. Experience with humans

Table 5. Extracorporeal Rewarming Interventions

Rewarming Method	Advantages	Disadvantages
Cardiopulmonary bypass	Very rapid rewarming (7–10°C/h)	Less available
	Provides full circulatory support	Requires trained perfusionist
	Allows oxygenation	Potential for delays in initiating
	Treatment of renal failure/electrolytes	Anticoagulation standard
Continuous arteriovenous rewarming	Rapid rewarming (3–4°C/h)	Requires adequate blood pressure
	Rapid initiation	Cannot oxygenate or dialyze blood
	Trained perfusionist not required	Less available
	Anticoagulation not required	Less experience with non-trauma patients
Hemodialysis and hemofiltration	Widely available	Modest rewarming rate (2–3°C/h)
	Rapid initiation; 1-catheter option	Requires adequate blood pressure
	Anticoagulation not required	
	Treatment of renal failure/electrolytes	

is limited to case reports and small case series.[74,76–79] The use of open mediastinal irrigation for rewarming dates back to the 1950s. More recently it has been combined successfully with open cardiac massage and cardiopulmonary bypass in hypothermic patients in cardiac arrest.[51,52] The preferential warming of the myocardium may allow for more rapid cardioversion in these patients. Many medical centers, however, lack the expertise and resources to safely employ this approach. Mediastinal lavage is not recommended for patients with perfusing rhythms.

Peritoneal lavage with warm saline or dialysate is widely available, relatively simple to initiate, and is a diagnostic test for occult abdominal trauma, which we have observed in a sizeable number of young, otherwise healthy hypothermic patients. Placement of 2 or more catheters in the intraperitoneal space improves rewarming rates by increasing net flow through the cavity. Direct irrigation of the liver is believed to accelerate the recovery of hepatic function and thereby facilitate the clearance of toxins and lactic acidosis. Instillation of warm dialysate, with 20–30 min dwell time, allows for removal of dialyzable toxins and treatment of concomitant renal failure or rhabdomyolysis.[80–84]

Active Internal Rewarming: Extracorporeal Methods

Table 5 compares extracorporeal rewarming methods. The use of cardiopulmonary bypass in the successful treatment of accidental hypothermia dates back to 2 case reports from the late 1960s.[85,86] Both patients had perfusing rhythms, but the majority of patients in subsequent published series received cardiopulmonary bypass in the setting of cardiac arrest.[87] Indeed, cardiopulmonary bypass is an attractive option in patients suffering cardiac arrest, as it provides rapid rewarming, circulatory support, oxygenation, and can be combined with hemodialysis.[84,88,89] Femoral-femoral bypass and medial sternotomy approaches appear to be equally effective.[87] As outlined in Table 5, the primary disadvantages of cardiopulmonary bypass are lack of availability, delay in initiating treatment, and need for anticoagulation. Data supporting the use of heparin-coated catheters in lieu of full anticoagulation in high-risk groups such as trauma victims are very limited.[90]

In continuous arteriovenous rewarming, the patient's blood pressure generates flow from the femoral artery through a countercurrent fluid rewarmer. Blood then reenters the patient through the contralateral femoral vein.[91] Aluminum tubing within the fluid rewarmer maximizes thermal conduction between a 40°C water bath and the circulating blood. The resultant rewarming rates are excellent, albeit slower than those obtained with cardiopulmonary bypass.[91,92] Compared to cardiopulmonary bypass, continuous arteriovenous rewarming can be more rapidly initiated and requires less specialized equipment and personnel to operate. Heparin-coated arterial and venous catheters are percutaneously placed at the bedside, and additional anticoagulation is unnecessary. A prospective, randomized study found that continuous arteriovenous rewarming reduced fluid requirements and improved short-term survival in trauma patients, compared to a multifaceted minimally invasive strategy.[92] The reported experience in other populations, however, is limited.[93,94]

Extracorporeal venovenous rewarming, continuous venovenous hemodialysis, arteriovenous hemodialysis, and hemofiltration are additional options for directly rewarming blood.[95–101] Extracorporeal venovenous rewarming entails catheterization of 2 central veins and use of a roller pump to maintain flow.[96] The flow and rewarming rate are slower than with cardiopulmonary bypass and continuous arteriovenous rewarming. Hemodialysis and hemofiltration are useful in the setting of renal insufficiency, electrolyte abnormalities, volume overload, or following ingestion of a dialyzable toxin.[95,97] Insertion of 2-way flow catheters allows for dialysis following cannulation of a single vessel, which may be important in patients with difficult vascular access. The reported clinical experience with these approaches is favorable but limited to case series that had only a modest number of patients.

Selecting a Rewarming Strategy

Deciding on a rewarming strategy is a complex but not insurmountable task. An evidence-based approach to management is severely hampered by the paucity of published randomized clinical trials on the subject. The heterogeneity of study populations, institutional expertise, and clinical presentation further undermine an algorithmic approach to hypothermia decision-making. Nonetheless, a number of useful general guidelines can be gleaned from the literature.

First, the aforementioned passive external rewarming measures are appropriate for all hypothermia victims, regardless of severity.

Second, passive external rewarming should be adequate for most patients with mild hypothermia. Published case series suggest that, in the absence of severe underlying disease, passively warmed patients with mild hypothermia have good outcomes.[5,8,38]

Third, although faster rewarming is not proven to reduce mortality, there is a strong physiologic rationale for using invasive methods to hasten rewarming in arrested patients. Cardioversion at core temperatures below 28°C is unlikely, and extracorporeal rewarming, preferably with cardiopulmonary bypass or continuous arteriovenous rewarming, is appropriate in that population. In our experience, extracorporeal rewarming may also reduce tissue loss in a patient with a deeply frozen limb. In centers that lack by-pass capability, combinations of active external rewarming, body cavity lavage, and other forms of extracorporeal rewarming are indicated.

The optimal approach is less clear for a patient with (1) adequate blood pressure (ie, mean arterial pressure > 60 mm Hg) but moderate or severe hypothermia or (2) mild hypothermia that has not responded to passive rewarming. Some authors advocate the use of temperature cutoffs to initiate invasive rewarming measures,[35,66,87] as rapid temperature correction may reduce the window of time the patient is vulnerable to developing arrhythmias. However, the presence of comorbid conditions appears to be a much more consistent predictor of mortality than initial core temperature.[4–6,8,38,102,103] A number of studies report good outcomes with minimally-invasive rewarming of hemodynamically stable patients suffering moderate or severe hypothermia.[3,4,6,63,84,104]

Studies of the relationship between rewarming rate and postoperative cognitive function in patients undergoing hypothermic coronary artery bypass graft are potentially relevant to the management of accidental hypothermia. One study following hypothermic coronary artery bypass graft found better 6-week postoperative cognitive function among patients rewarmed at slower rates,[105] although no difference in cognitive function was observed in a subsequent comparable study of diabetics undergoing bypass surgery.[106] Of note, patients in both studies were rewarmed by over 13°C/h, which is substantially faster than the rate reported with cardiopulmonary bypass in the setting of accidental hypothermia. At this juncture there is insufficient evidence to make firm recommendations on the management of hemodynamically stable patients with severe hypothermia.

The Decision to Defer Rewarming

The presentation of a dead and a profoundly hypothermic patient may be indistinguishable, particularly upon initial evaluation in the field. Hence, the adage "no one is dead until they are warm and dead" is not without merit. Hypothermia victims have survived prolonged periods of cardiopulmonary resuscitation,[53] presented with core temperatures as low as 13.7°C,[107] and recovered after 45 min of submersion in 4°C water.[108] Furthermore, the reported long-term outcome of survivors of severe accidental hypothermia is excellent. An extensive neurologic evaluation of survivors of severe hypothermia complicated by cardiac arrest found no evidence that hypothermia-induced injury affected quality of life.[109] Subjects were young and healthy at baseline and were able to resume their former lifestyles, despite requiring up to 30 days to regain consciousness. Whether older age and comorbid conditions result in less favorable outcomes in these circumstances is unclear.

The underlying cause of hypothermia, the reversibility of that process, and the presence of comorbid conditions are consistent predictors of outcome,[4–6,8,38,102] but a simple marker for irreversible injury remains elusive. Serum potassium > 10 mmol/L is believed to be a marker of extensive cell death and was associated with 100% mortality in 2 series of avalanche and climbing accident victims.[103,110] However, a subsequent case report of survival of a hypothermic patient with an initial serum potassium of 9.5 mmol/L calls into question the use of 10 mmol/L as an absolute cutoff for withholding resuscitation.[90] Renal failure, drug toxicities, rhabdomyolysis, and adrenal insufficiency are all reversible causes of hyperkalemia that should be considered prior to attributing elevated potassium levels to irreversible cell death. Other purported markers for worse outcome are advanced age, low presenting pH, renal insufficiency, ammonia $> 250\ \mu$mol/L, fibrinogen < 50 mg/dL, coagulopathy, cardiac arrest, need for mechanical ventilation, Glasgow coma scale ≤ 5, vasopressor requirement, absence of outdoor exposure, and greater duration of exposure. But none of these factors taken in isolation is sufficiently predictive to preclude resuscitation.[4,5,66,102,103,111,112]

Hypothermia victims who are diffusely frozen, who have clearly lethal injuries, or are critically ill and cannot be treated for a prolonged period need not be resuscitated. In the absence of clear-cut signs of irreversible injury, the decision to forego resuscitation is contingent upon the patient's comorbidities and advance medical directive, the reversibility of any underlying acute illness, and the need to triage other critically ill individuals. In clinically ambiguous situations we agree with the American Heart Association recommendation to rewarm patients to at least 35°C before declaring futility and withdrawing support.[113]

Summary

Victims of accidental hypothermia present year-round and in all climates, with a potentially confusing array of life-threatening systemic organ dysfunction. Advance knowledge of the pathophysiology and management of hypothermia allows clinicians to "see the forest through the trees," and thereby pursue a diagnostic and therapeutic course most advantageous to the patient. The optimal approach to rewarming in severe hypothermia is unknown, but studies of rewarming rates and associated neurocognitive outcomes ultimately may serve as an additional guide to making treatment decisions. For now, the choice of rewarming strategy is largely dictated by individual patient characteristics and institutional resources and expertise. Since even profound, global hypothermia is potentially reversible with rewarming, resuscitation should be withheld only in selected circumstances. Regardless of advances in treatment, accidental hypothermia will probably remain a resource-intensive illness with substantial mortality. Prevention of accidental hypothermia through patient education and provision of shelter to at-risk individuals remains an important public health priority.

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