The “reanimations” of profoundly cold victims in prolonged cardiac arrest and the emergence of therapeutic hypothermia after cardiac arrest help explain the contemporary allure of hypothermia. A 29-year-old Norwegian physician was successfully resuscitated from accidental hypothermia at 13.7°C after a 9-hour resuscitation. This included cardiopulmonary resuscitation initiated at the scene and 179 minutes of cardiopulmonary bypass.

Medical uses of cold were not scientifically evaluated until the 18th century, although it has been used for medical purposes for millennia. The hemostatic, analgesic, and therapeutic effects of cold were well known. Accidental hypothermia was also common and its treatment controversial. Biblical references cite truncal rewarming of King David by a damsel, and various remedies, including rubbing of the extremities with hot oil, were mentioned by Hippocrates, Aristotle, and Galen.

Cold weather has had a major impact on military history. Hannibal lost nearly half of his army of 46,000 while traversing the Alps in 218 BCE. The winter of 1777 took its toll on Washington's troops at Valley Forge. Napoleon's chief surgeon, Baron Larrey, reported that only 350 of the 12,000 men in the 12th division survived the cold during their retreat from Russia in 1812. Those soldiers who were rapidly rewarmed closest to the campfire died. The French subsequently suffered heavy losses in the Crimean War (1845-1855). These lessons were relearned during both world wars. Many pilots and U-boat crews perished from the cold water during the 20th century, although it has been used for medical purposes for millennia. The hemostatic, analgesic, and therapeutic effects of cold were well known. Accidental hypothermia was also common and its treatment controversial. Biblical references cite truncal rewarming of King David by a damsel, and various remedies, including rubbing of the extremities with hot oil, were mentioned by Hippocrates, Aristotle, and Galen.

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Innumerable cold-related tragedies affect both military personnel and civilians, in particular hunters, sailors, skiers, climbers, boaters, swimmers, and survivors of some natural disasters. Widespread participation in outdoor winter sports increases the number of patients who have hypothermia. Hypothermia is geographically and seasonally pervasive. Most cases occur in urban settings. “Primary” hypothermia fatalities are classified as accidental, homicidal, or suicidal. Death certificate data, however, underreport secondary hypothermia deaths, in which cold complicates many systemic diseases. The effect of cold on mortality from cardiovascular and neurologic disorders is greatly underestimated.

Hypothermia is defined as a core temperature below 35°C. Many variables contribute to the development of accidental hypothermia. Exposure, age, health, nutrition, medication, and intoxicants can decrease heat production, increase heat loss, or interfere with thermostability. The healthy individual's compensatory responses to heat loss through conduction, convection, radiation, and evaporation are often overwhelmed by exposure. Medications can also interfere with thermoregulation. Central nervous system (CNS) problems commonly decrease the efficiency of thermoregulation.

PRINCIPLES OF DISEASE

Physiology of Temperature Regulation

Human basal heat production increases with food ingestion, muscle activity, fever, and acute cold exposure. Cold stress increases preshivering muscle tone, potentially doubling heat production. Maximal heat production lasts only a few hours because of fatigue and glycogen depletion.

Shivering thermogenesis increases the basal metabolic rate two to five times. Shivering, which markedly increases oxygen consumption, is modulated by the posterior hypothalamus and the spinal cord.

The preoptic anterior hypothalamus orchestrates nonshivering heat conservation and dissipation. Serotonergic and dopaminergic neurons are pivotal. They exert immediate control through the autonomic nervous system and delayed control through the endocrine system. Thermal suppression or activation of the sympathetic nervous system with cold-induced release of norepinephrine also occurs. Cold stimulates the hypothalamus to release thyrotropin-releasing hormone. This activates the anterior pituitary gland, which releases thyroid-stimulating hormone and results in the release of thyroxine from the thyroid gland.

Heat loss occurs through five mechanisms: radiation, conduction, convection, respiration, and evaporation. Assuming an average basal metabolic rate in a normally clothed person at room temperature, 55 to 65% of this loss is through radiation. Heat loss by radiation is greatest when one is spread out nude and least when one is curled up and insulated. Radiative heat loss depends on the temperature gradient between the environment and the exposed body surface area. Conduction normally accounts for only approximately 2 to 3% of the heat loss, but this may increase up to five times in wet clothing. Convection in cold water can increase heat loss by a factor of 25.

Close correlation exists between subcutaneous fat thickness and cooling rates. Individuals with greater insulation lose heat more slowly. Conduction and convection normally account for about 15% of the body’s heat loss, but convective losses increase with shivering. Respiration and evaporation account for the remainder of the loss, with 2 to 9% lost in heating of inspired air and 20 to 27% lost to insensible evaporation from the skin and lungs.

Cutaneous and respiratory heat loss is markedly influenced by the ambient temperature, air motion, and relative humidity. Greater losses occur in a cool, dry, windy environment (windchill index). When the body is not perspiring, most heat loss is through...
radiation and convection. Convective losses become significant in immersion-induced hypothermia. Children cool faster than adults do because of the elevated ratios of surface area to mass. Chronic cold exposure may result in gradual evolutionary adaptations and thermal acclimation (Fig. 140-1).

When core temperature is between 37 and 32°C, vasoconstriction, shivering, and nonshivering basal and endocrinologic thermogenesis generate heat. From 30 to 24°C, a progressive depression of the basal metabolic rate occurs without shivering thermogenesis. At temperatures below 24°C, autonomic and endocrinologic mechanisms for heat conservation become inactive.

**Pathophysiology**

The physiologic characteristics of hypothermia are described in Table 140-1.

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**Cardiovascular**

After initial tachycardia, progressive bradycardia develops. The pulse usually decreases by 50% at 28°C. If an observed tachycardia is inconsistent with a patient’s temperature, associated conditions such as hypoglycemia, drug ingestion, and hypovolemia should be considered.

The bradycardia of hypothermia results from decreased spontaneous depolarization of the pacemaker cells. As a result, the bradycardia is refractory to atropine. The electrocardiographic features of hypothermia are unique. Initially described by Tomaszewski in 1938, the Osborn (J) wave is seen at the junction of the QRS complex and ST segment (Fig. 140-2). J waves are potentially diagnostic but not prognostic. They may appear at any temperature below 32°C. The size of the J wave is not related to arterial pH but does increase with temperature depression.

J waves are normally upright in the aVL, aVF, and left precordial leads. The J deflection may be a result of hypothermic ion flux alterations, with delayed depolarization or early repolarization of the left ventricular wall. It can also be seen during local cardiac ischemia and with sepsis or CNS lesions, hypercalcemia, and the Brugada syndrome.

Some J waveform abnormalities simulate a myocardial injury current. Hypothermic electrocardiographic changes are not easily recognized by computer programs. Reliance on computer interpretations can result in mistaken thrombolysis, which would be expected to exacerbate preexistent coagulopathies.

All atrial and ventricular dysrhythmias are common in moderate or severe hypothermia. Reentrant dysrhythmias result from decreased conduction velocity with increased myocardial conductive time and a decreased absolute refractory period. Because the conduction system is more sensitive to the cold than the myocardium, cardiac cycle prolongation occurs. Fluctuations of available oxygen, pH, electrolytes, and nutrients also alter conduction. As hypothermia worsens, the PR interval, then the QRS interval, and finally (and most characteristically) the QTc interval become prolonged. In the absence of obvious shivering, thermal muscle tone may obscure P waves or produce artifacts.

Atrial fibrillation is common when the core temperature is below 32°C. Other rhythms are sinus, atrial, or junctional. Atrial

---

### Table 140-1 Physiologic Characteristics of the Four Zones of Hypothermia

<table>
<thead>
<tr>
<th>STATE</th>
<th>CORE TEMPERATURE ° C (° F)</th>
<th>CHARACTERISTICS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>35 (95)</td>
<td>Urine temperature 34.8°C; increased shivering thermogenesis; increase in metabolic rate</td>
</tr>
<tr>
<td></td>
<td>34 (93.2)</td>
<td>Amnesia and dysarthria develop; normal blood pressure; maximum respiratory stimulation</td>
</tr>
<tr>
<td></td>
<td>33 (91.4)</td>
<td>Ataxia and apathy develop</td>
</tr>
<tr>
<td>Moderate</td>
<td>32 (89.6)</td>
<td>Stupor; 25% decrease in oxygen consumption</td>
</tr>
<tr>
<td></td>
<td>31 (87.8)</td>
<td>Decreased shivering thermogenesis</td>
</tr>
<tr>
<td></td>
<td>30 (86)</td>
<td>Atrial fibrillation and other dysrhythmias; poikilothermia; pulse and cardiac output two-thirds normal; insulin ineffective</td>
</tr>
<tr>
<td></td>
<td>29 (85.2)</td>
<td>Progressive decrease in level of consciousness, pulse, and respiration; pupils dilated</td>
</tr>
<tr>
<td>Severe</td>
<td>28 (82.4)</td>
<td>Ventricular fibrillation susceptibility; 50% decrease in oxygen consumption and pulse</td>
</tr>
<tr>
<td></td>
<td>27 (80.6)</td>
<td>Losing reflexes and voluntary motion</td>
</tr>
<tr>
<td></td>
<td>26 (78.8)</td>
<td>Major acid-base disturbances; no reflexes or response to pain</td>
</tr>
<tr>
<td></td>
<td>25 (77)</td>
<td>Cerebral blood flow one-third normal; cardiac output 45% normal; pulmonary edema may develop</td>
</tr>
<tr>
<td></td>
<td>24 (75.2)</td>
<td>Significant hypotension</td>
</tr>
<tr>
<td></td>
<td>23 (73.4)</td>
<td>No corneal or oculocephalic reflexes</td>
</tr>
<tr>
<td></td>
<td>22 (71.6)</td>
<td>Maximum risk of ventricular fibrillation; 75% decrease in oxygen consumption</td>
</tr>
<tr>
<td>Profound</td>
<td>20 (68)</td>
<td>Lowest resumption of cardiac electromechanical activity; pulse 20% of normal</td>
</tr>
<tr>
<td></td>
<td>19 (66.2)</td>
<td>Flat electroencephalogram</td>
</tr>
<tr>
<td></td>
<td>18 (64.4)</td>
<td>Asystole develops</td>
</tr>
<tr>
<td></td>
<td>14.2 (57.6)</td>
<td>Lowest accidental hypothermia survival in an infant¹¹²</td>
</tr>
<tr>
<td></td>
<td>13.7 (56.7)</td>
<td>Lowest accidental hypothermia survival in an adult¹¹¹</td>
</tr>
<tr>
<td></td>
<td>9 (48.2)</td>
<td>Lowest therapeutic hypothermia survival¹¹¹</td>
</tr>
</tbody>
</table>
Central Nervous System

Hypothermia progressively depresses the CNS. Significant alteration of the brain’s electrical activity begins below 33.5° C. The electroencephalogram silences at 19 to 20° C.

Cerebral autoregulation is maintained with an increase in vascular resistance until 25° C. In cases of severe hypothermia, there is a disproportionately higher redistribution of blood flow to the brain. Like the heart, the brain has a critical period of tolerance to hypothermia. There are temperature-dependent neural enzyme systems that are unable to function at temperatures that are well tolerated by the kidney.

Renal System

Simple exposure to cold induces a diuresis regardless of an individual’s state of hydration. Hypothermia depresses renal blood flow, reducing it by 50% at 27 to 30° C. The kidneys then excrete a large amount of dilute urine, termed cold diuresis. Cold diuresis is essentially glomerular filtrate, which does not clear nitrogenous waste products. Severe hypothermia causes an initial relative central hypervolemia as a consequence of peripheral vasoconstriction. Cold diuresis may act as a volume regulator to diminish the vasoconstriction-induced capacitance vessel overload. Cold-water immersion can further increase urinary output by 3.5 times. Ethanol doubles that increase.

Respiratory System

Hypothermia initially stimulates respiration. This is followed by a progressive decrease in the respiratory minute volume. Carbon dioxide production decreases 50% with an 8° C fall in temperature. The normal stimuli for respiratory control are altered in severe hypothermia, and carbon dioxide retention with
respiratory acidosis can occur. Hypercapnia increases core temperature cooling during snow burial.\textsuperscript{21}

Numerous other pathophysiologic factors adversely affect the respiratory system. These include viscous bronchorrhea, decreased ciliary motility, and noncardiogenic pulmonary edema.

**Predisposing Factors**

Predisposing factors that contribute to the pathophysiologic changes accompanying core temperature depression can be categorized as those that decrease heat production, increase heat loss, or impair thermoregulation (Box 140-1).

**Decreased Heat Production**

Decreased thermogenesis is often secondary to an endocrinologic failure, such as hypopituitarism, hypoadrenalism, or myxedema. Myxedema coma is several times more common in women; up to 80% of these persons are hypothermic. Hypothyroidism is often occult in this setting. There is usually no available history of lassitude, dry skin, arthralgias, or cold intolerance.

Hypoglycemia with central neuroglycopenia also predisposes to hypothermia. Another cause of decreased heat production is malnutrition, which causes a decrease in subcutaneous fat. Severe malnutrition, as with marasmus, contributes to heat loss. Kwashiorkor is less commonly associated with hypothermia because of the insulating effect of the hypoproteinemic edema.\textsuperscript{15}

The young and the old are commonly at risk. The neonate has a large surface area–to–mass ratio, a relatively deficient subcutaneous tissue layer, and an inefficient shivering mechanism. Neonates lack behavioral defense mechanisms.

Acute neonatal hypothermia is common after emergency deliveries or resuscitations. Many neonates are lethargic, fail to thrive, and have a weak cry. Half have deceptively rosy cheeks. Late-onset hypothermia, which occurs after 72 hours of life, is commonly a result of septicemia. Hypothermia can occur in the shaken baby syndrome and may be a factor in some cases of apparent sudden infant death syndrome.

Homeostatic capability progressively decreases with aging. Thermal perception is altered and elderly people manipulate the indoor ambient temperature less precisely. Most elderly patients are capable of normal thermoregulation but are prone to conditions, including immobility and systemic diseases, that interfere with heat production and conservation. Inability to sense cold, abnormal adaptive behavioral responses, and decreased peripheral blood flow reflect geriatric autonomic dysfunction.\textsuperscript{22}

**Increased Heat Loss**

Patients with erythrodermas, including psoriasis, exfoliative dermatitis, ichthyosis, eczema, and burns, can have increased peripheral blood flow. Iatrogenic causes of heat loss include exposure during resuscitations, massive cold or room temperature infusions, overcooling of patients with heat stroke, and overzealous burn treatment.

Ethanol is metabolized at a slower rate in hypothermic individuals and interacts with every putative thermoregulatory neurotransmitter. It may directly suppress the activity of the posterior hypothalamus and the mammillary bodies. Cutaneous heat loss increases through vasodilation, and shivering thermogenesis is decreased.\textsuperscript{23}

Ethanol is the most common cause of excessive heat loss in urban settings.\textsuperscript{7,16} Intoxicated persons often lack protective adaptive behavior to avoid the cold. “Paradoxical undressing,” which is the removal of clothing in response to a cold stress, is common.\textsuperscript{24} Aging is associated with an increased sensitivity to the hypothemic actions of ethanol. Hypothermic alcoholic ketoacidosis also occurs. Hypothermia is common in patients with Wernicke’s encephalopathy. Hypothermia can mask the usual clinical triad of ophthalmoplegia, confusion, and truncal ataxia. Intravenous thiamine can be both diagnostic and therapeutic.

**Impaired Thermoregulation**

Thermoregulation can be impaired centrally, peripherally, or metabolically. Skull fractures, particularly basilar fractures, and chronic subdural hematomas are implicated in central impairment. Other causes include cerebrovascular accidents, neoplasms, anorexia nervosa, and Hodgkin’s and Parkinson’s diseases. The final common pathway in these disorders may be centrally mediated vasodilation. Cerebellar lesions produce choreiform, less efficient shivering.

In therapeutic or toxic doses, antidepressants, antimanic agents, antipsychotics, anxiolytics, and general anesthetics interfere with thermoregulation by impairing centrally mediated vasoconstriction. Overdosage of these medications and others (e.g., the organophosphates, heroin, glutethimide, and carbon monoxide) predisposes to hypothermia.\textsuperscript{25}

Peripheral thermoregulatory failure classically occurs in neurogenic shock after acute spinal cord transection. The interruption of the autonomic nervous system eliminates vasoconstrictive

### Box 140-1 Factors Predisposing to Hypothermia

<table>
<thead>
<tr>
<th>Decreased Heat Production</th>
<th>Acute spinal cord transection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endocrinologic failure</td>
<td>Diabetes</td>
</tr>
<tr>
<td>Hypopituitarism</td>
<td>Central failure, neurologic</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>Central nervous system trauma</td>
</tr>
<tr>
<td>Diabetes</td>
<td>Cerebrovascular accident</td>
</tr>
<tr>
<td>Insufficient fuel</td>
<td>Toxicologic</td>
</tr>
<tr>
<td>Hypoglycemia</td>
<td>Metabolic</td>
</tr>
<tr>
<td>Malnutrition</td>
<td>Subarachnoid hemorrhage</td>
</tr>
<tr>
<td>Marasmus</td>
<td>Pharmacologic</td>
</tr>
<tr>
<td>Kwashiorkor</td>
<td>Hypothalamic dysfunction</td>
</tr>
<tr>
<td>Extreme exertion</td>
<td>Parkinson’s disease</td>
</tr>
<tr>
<td>Neuromuscular inefficiency</td>
<td>Anorexia nervosa</td>
</tr>
<tr>
<td>Age extremes</td>
<td>Cerebellar lesion</td>
</tr>
<tr>
<td>Impaired shivering</td>
<td>Neoplasm</td>
</tr>
<tr>
<td>Inactivity</td>
<td>Congenital intracranial</td>
</tr>
<tr>
<td>Lack of adaptation</td>
<td>anomalies</td>
</tr>
<tr>
<td>Increased Heat Loss</td>
<td>Multiple sclerosis</td>
</tr>
<tr>
<td>Environmental</td>
<td>Miscellaneous</td>
</tr>
<tr>
<td>Immersion</td>
<td>Associated</td>
</tr>
<tr>
<td>Nonimmersion</td>
<td>Clinical States</td>
</tr>
<tr>
<td>Induced vasodilation</td>
<td>Recurrent hypothermia</td>
</tr>
<tr>
<td>Pharmacologic</td>
<td>Episodic hypothermia</td>
</tr>
<tr>
<td>Toxicologic</td>
<td>Sepsis</td>
</tr>
<tr>
<td>Erythrodermas</td>
<td>Pancreatitis</td>
</tr>
<tr>
<td>Burns</td>
<td>Carcinomatosis</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>Cardiopulmonary disease</td>
</tr>
<tr>
<td>Ichthyosis</td>
<td>Vascular insufficiency</td>
</tr>
<tr>
<td>Exfoliative dermatitis</td>
<td>Uremia</td>
</tr>
<tr>
<td>Iatrogenic</td>
<td>Paget’s disease</td>
</tr>
<tr>
<td>Emergency deliveries</td>
<td>Giant cell arteritis</td>
</tr>
<tr>
<td>Cold infusions</td>
<td>Sarcoidosis</td>
</tr>
<tr>
<td>Heatstroke treatment</td>
<td>Shaken baby syndrome</td>
</tr>
<tr>
<td>Impaired Thermoregulation</td>
<td>Multisystem trauma</td>
</tr>
<tr>
<td>Peripheral failure</td>
<td>Shapiro’s syndrome</td>
</tr>
<tr>
<td>Neuropathies</td>
<td>Wernicke-Korsakoff syndrome</td>
</tr>
<tr>
<td>Hodgkin’s disease</td>
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</tbody>
</table>

*Environment and Toxicology / Section One • Environment*
control. The patient effectively becomes poikilothermic and can rapidly become hypothermic. Neuropathies and diabetes are additional peripheral causes of heat loss. An abnormal plasma osmolality may explain hypothalamic interference in uremia, lactic acidosis, diabetic ketoacidosis, and hypoglycemia.26

Miscellaneous Causes

Hypothermia occurs in conjunction with several infections, most commonly overwhelming gram-negative sepsis, pneumonia, meningitis, and encephalitis. Other associated infections include bacterial endocarditis, brucellosis, malaria, syphilis, typhoid, miliary tuberculosis, and trypanosomiasis.

Medical conditions associated with hypothermia include carcinoma, pancreatitis without secondary infection, peritonitis, and severe cerebrovascular disease. Low cardiac output resulting from a myocardial infarction can induce hypothermia. Fetal and maternal bradycardia and hypothermia may result from magnesium sulfate infusion during preterm labor. Delayed recovery from neuromuscular blockade may also result from unrecognized hypothermia.

Traumatic Factors

After trauma, hypotension and hypovolemia jeopardize thermoregulation.27 In patients with major injuries, a fall in core and skin temperature with no compensatory shivering thermogenesis occurs. Thermoregulation is impaired, and heat production decreases.

Hypothermia may exacerbate blood loss by inducing a coagulopathy through three mechanisms: the coagulation cascade of enzymatic reactions is impaired, plasma fibrinolytic activity is enhanced, and platelets are sequestered and poorly functional.28 Traumatic injuries may be overlooked if hypotension or neurologic findings such as areflexia or paralysis are misattributed to hypothermia. Major risk factors for hypothermia in trauma patients include age, type of injury, level of intoxicants, transfusion requirements, and elapsed time spent in the field, emergency department, and operating room.

Hypothermia can protect the brain from ischemia only when it is induced before shock develops. This reduces adenosine triphosphate (ATP) use while the ATP stores are nearly normal. In traumatized patients, the ATP stores are already depleted.29

CLINICAL FEATURES

Appreciation of subtle presentations helps facilitate the early diagnosis of mild to moderate hypothermia. Vague symptoms include hunger, nausea, confusion, dizziness, chills, pruritus, and dyspnea (Box 140-2). During outdoor activities, individuals may simply become uncooperative, uncoordinated, moody, or apathetic. Indoors, elderly patients may exhibit confusion or simply become less communicative and display lassitude or a peculiar “flat” affect. Subtle progression of mental deterioration or motor skill impairment may mimic dementia. Symptoms such as slurred speech and ataxia may resemble symptoms of a cerebrovascular accident or intoxication.26

Some elderly people have a decreased ability to sense cold and thus fail to take appropriate adaptive action. The maladaptive phenomenon of paradoxical undressing is not uncommon.27 This last preterminal effort of the victim may be related to the peripheral vasoconstrictive changes of profound hypothermia. The patient can be mistaken for a victim of sexual assault.

In urban settings, hypothermia is most commonly associated with ethanol ingestion or underlying illness. Other common causes include strokes, overdoses, psychiatric emergencies, and coexistent major trauma.26

<table>
<thead>
<tr>
<th>Presenting Signs of Hypothermia</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Head, Eye, Ear, Nose, Throat</strong></td>
</tr>
<tr>
<td>Mydriasis</td>
</tr>
<tr>
<td>Decreased corneal reflexes</td>
</tr>
<tr>
<td>Extraocular muscle abnormalities</td>
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<tr>
<td>Erythropsia</td>
</tr>
<tr>
<td>Flushing</td>
</tr>
<tr>
<td>Facial edema</td>
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<tr>
<td>Epistaxis</td>
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<tr>
<td>Rhinorrhea</td>
</tr>
<tr>
<td>Strabismus</td>
</tr>
<tr>
<td><strong>Cardiovascular</strong></td>
</tr>
<tr>
<td>Initial tachycardia</td>
</tr>
<tr>
<td>Subsequent bradycardia</td>
</tr>
<tr>
<td>Dysrhythmias</td>
</tr>
<tr>
<td>Decreased heart tones</td>
</tr>
<tr>
<td>Hepatojugular reflux</td>
</tr>
<tr>
<td>Jugular venous distention</td>
</tr>
<tr>
<td>Hypotension</td>
</tr>
<tr>
<td><strong>Gastrointestinal</strong></td>
</tr>
<tr>
<td>Ileus</td>
</tr>
<tr>
<td>Constipation</td>
</tr>
<tr>
<td>Abdominal distention or rigidity</td>
</tr>
<tr>
<td>Poor rectal tone</td>
</tr>
<tr>
<td>Gastric dilation in neonates or in adults with myxedema</td>
</tr>
<tr>
<td><strong>Genitourinary</strong></td>
</tr>
<tr>
<td>Anuria</td>
</tr>
<tr>
<td>Oliguria</td>
</tr>
<tr>
<td>Polyuria</td>
</tr>
<tr>
<td>Testicular torsion</td>
</tr>
<tr>
<td><strong>Neurologic</strong></td>
</tr>
<tr>
<td>Depressed level of consciousness</td>
</tr>
<tr>
<td>Ataxia</td>
</tr>
</tbody>
</table>

Neurologic manifestations vary widely. A progressive decrease in the level of consciousness is usually proportional to the degree of hypothermia. Some patients, however, continue to be verbally responsive and display intact reflexes at 27 to 25°C C.

Eye movement abnormalities and extensor plantar responses do not correlate directly with the degree of hypothermia. Cranial nerve signs may be seen with bulbar damage from central pontine myelinolysis. Above 22°C C, it should be assumed that nonreactive dilated pupils reflect inadequate tissue perfusion and not hypothermia.

The rest of the neuromuscular examination may suggest the diagnosis. The patient’s posture ranges from stiff to pseudo–rigor mortis to opisthotonos. Reflexes are usually hyperactive down to 32°C, then become hypoactive until they disappear around 26°C C. Cremasteric reflexes are absent because the testicles are already retracted. The plantar response usually remains flexor until 26°C C. The knee jerk is the last reflex to disappear and the first to reappear with rewarming. The diagnosis of an antecedent CNS disorder, including spinal cord lesions, may be obscured by hypothermia.
Between 30 and 26°C, both contraction and relaxation phases of the reflexes are equally prolonged. If it is intact, the ankle jerk is helpful in diagnosis of hypothermic myxedema. Myxedema prolongs the relaxation phase more than the contraction phase. No psychiatric disorder improves when the patient is cold. Mental status alterations include anxiety, perseveration, neurosis, and psychosis. Many individuals who are functional in temperate climates decompensate in colder weather. Hypothermia-induced psychiatric presentations and suicide attempts are commonly misdiagnosed.31

**DIAGNOSTIC STRATEGIES**

**Laboratory Evaluations**

**Acid-Base Balance**

Blood gas analyzers warm blood to 37°C, which increases the partial pressure of dissolved gases. This results in an arterial blood gas report showing higher oxygen and carbon dioxide levels and a lower pH than the patient’s in vivo values.30-32 In fact, attempting to maintain a corrected pH at 7.4 and arterial partial pressure of carbon dioxide (PaCO₂) at 40 mm Hg during hypothermia depresses cerebral and coronary blood flow and cardiac output and increases the incidence of VF.33 The ideal acid-base strategy is the ectothermic alpha-stat approach.10 Simply put, the goal is an uncorrected pH at 7.4 and PacO₂ at 40 mm Hg.

Cold blood buffers poorly. In normothermia, when the PaCO₂ increases 10 mm Hg, the pH decreases 0.08 unit. At 28°C, the decrease in pH doubles. Because the neutral point of water at 37°C is a pH of 6.8, the normal 0.6-unit pH offset between blood and intracellular water should be maintained at all temperatures (Fig. 140-3).

Intracellular electrochemical neutrality ensures optimal enzymatic function at all temperatures.31 Relative alkalinity affords myocardial protection and improves the heart’s electrical stability.33 Carbogen could prove valuable in the treatment of accidental hypothermia because it flattens and shifts the oxyhemoglobin dissociation curve to the right.

**Hematologic Evaluation**

A patient’s hematocrit can be deceptively high as the result of the decreased plasma volume. The hematocrit level increases 2% for every 1°C fall in temperature. A low-normal hematocrit level in a moderately to severely hypothermic patient should suggest acute or chronic blood loss.

A normal white blood cell count never excludes infection, especially if the patient is debilitated, alcoholic, myxedematous, or at either age extreme. Splenic, hepatic, and splanchnic sequestration in hypothermia decreases leukocyte and platelet counts.

Frequent evaluation of serum electrolytes during rewarming is essential. There are no safe predictors of their values or trends.16 Changes occur in membrane permeability and in the sodium-potassium pump. The patient’s preexisting physiologic status, the severity and chronicity of hypothermia, and the method of rewarming alter the serum electrolyte values.

The plasma potassium level is independent of the primary hypothermic process. Hyperkalemia is often associated with metabolic acidosis, rhabdomyolysis, or renal failure. An important caveat is that hypothermia enhances the cardiac toxicity of hyperkalemia and obscures the premonitory electrocardiographic changes associated with it.

Hypokalemia is most common with chronic hypothermia. It results from potassium’s entering muscle, not a kaliuresis. A discrepant decline in serum potassium level despite a decreasing serum pH is caused by intracellular pH fluxes greater than extracellular pH fluxes.

Conditions associated with hypokalemia include preexisting diabetic ketoacidosis, hypopituitarism, inappropriate secretion of antidiuretic hormone, previous diuretic therapy, and alcoholism. If the potassium level is less than 3 mEq/L, supplementation may be necessary during rewarming.

The blood urea nitrogen and creatinine levels are elevated with preexisting renal disease or decreased clearance. Because of hypothermic fluid shifts, the hematocrit and blood urea nitrogen levels are poor indicators of a patient’s actual fluid status.

The blood glucose level may also provide a subtle clue to the type of hypothermia. Acute hypothermia initially elevates blood glucose levels through catecholamine-induced glycolysis, diminished insulin release, and inhibition of cellular membrane glucose carrier systems. On the other hand, subacute and chronic hypothermia produce glycogen depletion, leading to hypoglycemia. Symptoms of hypoglycemia can be masked by hypothermia. A cold-induced renal glycosuria does not imply hyperglycemia or guarantee normoglycemia.26

When hyperglycemia persists during rewarming, one should suspect hemorrhagic pancreatitis or diabetic ketoacidosis. Patients with diabetic ketoacidosis should be actively rewarmed past 30°C because insulin is ineffective below that temperature. Correction of hypoglycemia corrects the level of consciousness only to that of the corresponding level of hypothermia.

Severe hypothermia also causes serum enzyme elevation because of the ultrastructural cellular damage. Rhabdomyolysis is commonly associated with cold exposure.

Ischemic pancreatitis may result from the microcirculatory shock of hypothermia. The decreased pancreatic blood flow then activates proteolytic enzymes.7

**Hypothermic Coagulation**

A physiologic increase in coagulation occurs with hypothermia, and a disseminated intravascular coagulation type of syndrome occurs. The cause may be catecholamine or steroid release, simple circulatory collapse, or release of tissue thromboplastin from cold, ischemic tissue.25,34
Hypothermic patients also have coagulopathies because the enzymatic nature of the activated clotting factors is depressed by the cold. The clotting prolongation is proportional to the number of steps in the cascade. Because the kinetic tests of coagulation are performed in the laboratory at 37°C, the physician will see a disparity between the in vivo, clinically evident coagulopathy and the deceptively “normal” prothrombin time, partial thromboplastin time, or international normalized ratio reported by the laboratory. The only effective treatment is rewarming, not administration of clotting factors. In vitro, desmopressin partially reverses hypothermia-induced coagulopathy.

The leukopenia and thrombocytopenia usually reverse with rewarming. Clinically significant coagulopathies occur, particularly in association with trauma. Cold-induced thrombocytopenia may be from either direct bone marrow suppression or splenic and hepatic sequestration. Platelet thromboxane B2 production is also temperature dependent. Thrombocytopenia is more common at both age extremes.

The elevated viscosity seen with hypothermia may be exacerbated in patients with cryoglobulinemia or cryofibrinogenemia, especially in elderly patients. Cryofibrinogen, which is a cold-precipitated fibrinogen, is associated with the collagen vascular diseases, carcinomas, and coliform sepsis. The pathophysiologic changes of cold hemagglutination result from cold agglutinins that produce either hemolysis or agglutination with thrombosis. This could explain the increase in coronary and cerebral thromboses in winter.

In summary, except in mild cases, the immediate laboratory evaluations should include the following: glucose concentration; arterial blood gas values uncorrected for temperature; complete blood cell count; comprehensive metabolic panel, including serum calcium, serum magnesium, and serum amylase or lipase levels; and coagulation studies. Baseline serum blood urea nitrogen and creatinine tests are indicated because renal failure may occur after rewarming in patients with chronic hypothermia.

A toxicologic screen may be helpful by history or when the depression of the level of consciousness is inconsistent with the degree of hypothermia. Thyroid function studies, cardiac markers, and serum cortisol levels have selective utility.

The indications for radiography should be liberalized from normothermia. If the patient is not alert, spinal radiographs should be obtained if there is any possibility of trauma. Bedside ultrasonography or computed tomography may show pancreatic calcifications, unsuspected pneumoperitoneum, small bowel dilation from hypothermia-induced mesenteric vascular occlusion, or colonic dilation associated with myxedema coma.

**MANAGEMENT**

Patients who are cold, stiff, and cyanotic, with fixed pupils and inaudible heart tones, without visible thoracic excursions, conduce to be successfully resuscitated. Embarrassingly, some patients still recover completely in the morgue.

An adequate history includes available pertinent information about preexisting cardiac, pulmonary, neurologic, or endocrinologic disease. The duration of exposure, circumstances of discovery, associated injuries, and predisposing conditions should be documented. Initial management should emphasize the prevention of further heat loss. The goals of prehospital care are to rescue, to examine, to insulate, and to gently transport in a horizontal position.

If the patient is unresponsive and not shivering, presume that the hypothermia is severe. At temperatures below 32°C, one should expect an irritable myocardium, a temperature gradient between the core and periphery, and relative hypovolemia.

In the emergency department, hypothermia should be confirmed and monitored with continuous core temperature evaluation. Clinically, the rectal temperature is the most widely used; however, it can lag behind core changes and is influenced by lower extremity temperatures and probe placement. The probe should be inserted to 15 cm and not placed in cold feces.

The epitympanic temperature equilibrates most rapidly with the core temperature and is closest to the hypothalamic temperature but is not widely available. Infrared thermography (tympanic temperature) should not be used alone in the setting of suspected hypothermia because the reliability of commercially available devices remains uncertain. If the patient is tracheally intubated, an esophageal probe is the ideal method for continuous core temperature monitoring, although it can read falsely high with heated inhalation.

A Doppler measuring device may be necessary to establish the presence of a spontaneous pulse or blood pressure. Focused ultrasound evaluation of the hypothermic heart should precede chest compressions. The accuracy of pulse oximetry during conditions of poor perfusion and hypothermia is uncertain, and it is often impossible to obtain an adequate plethysmograph. Similarly, end-tidal carbon dioxide measurements accurately assess tissue perfusion and tracheal tube placement only at normal temperatures. Commercially available devices do not function with humidified air used for airway rewarming.

Endotracheal intubation may be necessary unless the patient is alert or has intact protective airway reflexes. Cold depression of ciliary activity allows secretory accumulation, with the production of frothy sputum and chest congestion. Failure to differentiate between this bronchorrhea and pulmonary edema may explain the conflicting reports of the association of hypothermia with pulmonary edema. Nasotracheal intubation is a noninvasive option when cold-induced trismus is present, unless there is a significant coagulopathy.

In a multicenter survey, endotracheal intubation was performed on 117 patients by multiple operators in various settings. No induced dysrhythmias were recognized. Factors commonly precipitating dysrhythmias include failure to preoxygenate, mechanical jetting, acid-base changes, and electrolyte fluctuations.

A nasogastric tube is indicated in patients with moderate and severe hypothermia after endotracheal intubation. Decreased gastric motility and gastric dilation occur commonly. Physical examination of the abdomen is unreliable because the cold can induce rectus muscle rigidity. A large percentage of moderately and severely hypothermic patients have decreased or absent bowel sounds. It is important to evaluate the patient carefully for an associated ileus, pancreatitis, or occult trauma.

In cases of moderate and severe hypothermia, indwelling bladder catheters with urine meter bags are essential to monitor urinary output and to help determine the severity of vascular fluid shifts.

Cardiac monitoring should be continued. Insertion of a central venous pressure catheter tip into the heart can precipitate dysrhythmias and should be avoided. Arterial catheters for continuous monitoring of intra-arterial blood pressure may rarely be necessary in selected profoundly hypothermic patients. The clinician should avoid placement of pulmonary artery catheters that risk perforation of the cold, stiff pulmonary artery.

**Volume Resuscitation**

Patients with moderate or severe hypothermia are usually volume depleted, and they are also prone to thromboembolism resulting from the increased viscosity. During rewarming, a relatively high total plasma volume and low circulatory plasma volume are often present. As hypothermia develops, other effects include increased peripheral vascular resistance with a decreased circulatory volume.

Rapid volume expansion is critical. In hypothermic neonates, the mortality risk is dramatically lessened. Adult patients with
moderate or severe hypothermia should initially receive a 500-mL fluid challenge of heated 5% dextrose in normal saline solution pending laboratory analyses. Lactated Ringer’s solution should be avoided because the cold liver inefficiently metabolizes lactate.

Fluids administered intravenously should be heated to 40 to 42°C. There are many commercially available fluid and blood warmers. If these are not available, another option is to microwave intravenous fluids in plastic containers. A 1-L bag of crystalloid requires an average of 2 minutes on high power. The fluid should be shaken before administration to avoid hot spots. Rapid central venous administration, which may produce myocardial thermal gradients, should also be avoided. Another option in vasoconstricted patients is the intraosseous route.

Countercurrent heat exchangers effectively heat crystalloids and blood from 10 to 35°C. There can be significant conductive heat loss through intravenous tubing. Long lengths of tubing increase heat loss, especially at slow flow rates.

Normally, hypothermia induces an increased natriuresis. Preexisting gastrointestinal losses or previous diuretic treatment can also contribute to sodium loss. Patients with normal sodium and osmolality values may have preexisting sodium overload as a result of cirrhosis, nephrosis, or congestive heart failure; however, most patients will be free water depleted, which elevates their sodium and osmolality values.

Hemoconcentration resulting from decreased plasma volume, fluid shifts, and increased vascular permeability usually is present. Hemodilution can occur from parenteral crystalloid administration, but a low hematocrit can also result from acute hemorrhage or preexisting anemia.

Advanced Life Support

Blood flow during cardiopulmonary resuscitation (CPR) in patients with hypothermia differs from that during normothermia, in which some flow results from phasic alterations in the intrathoracic pressure and not necessarily from direct cardiac compression.

In hypothermia, the heart is a passive conduit. The “thoracic pump” concept notes that the phasic alterations in the intrathoracic pressure are exerted equally on all cardiac chambers. The mitral valve remains patent during systole, and blood continues to circulate through the left side of the heart. This explains the observation of Althaus and associates, who noted that in one of three survivors at thoracotomy, “the heart was found to be hard as stone and it is hardly conceivable how effective external cardiac massage could have been.” There are innumerable neurologically intact survivors after prolonged closed chest compressions.

Chest wall elasticity and pulmonary compliance are decreased with cold. Therefore, more force is needed to depress the chest wall sufficiently to generate intrathoracic pressure gradients. Pneumatic-powered thoracic compression devices are useful during prolonged resuscitations pending decisions about extracorporeal rewarming. Apparent rigor mortis, dependent lividity, and fixed, dilated pupils are not always reliable criteria for withholding of CPR in the hypothermic patient. Because intermittent flow may provide adequate support during evacuation, CPR should not be withheld just because continuous compressions cannot be ensured.

In a multicenter survey of 428 cases, 9 of the 27 patients receiving CPR initiated in the field survived, as did 6 of 14 patients with CPR initiated in the emergency department. Rescuers should initiate CPR in cases of accidental hypothermia unless do-not-resuscitate status is documented and verified, obviously lethal injuries are present, chest wall depression is impossible, signs of life are present, or rescuers are endangered by evacuation delays or altered triage conditions. If possible, verify with Doppler ultrasound examination that there is no spontaneous mechanical cardiac activity before chest compressions are initiated.

PHARMACOLOGY

The efficacy of most medications is temperature dependent. Protein binding increases during hypothermia, and liver metabolism is decreased. Overmedication could be required to achieve a therapeutic response, and subsequent toxic levels would develop with rewarming. In severe hypothermia, consider withholding of medications until the patient is warmer or longer intervals between doses. No medication should be given orally because of decreased gastrointestinal motility; none should be given intramuscularly because of poor absorption from vasoconstricted sites.

Cardiovascular

The effects of hypothermia on the autonomic nervous system vary. In primate studies, the sympathetic nervous system responds rapidly to cooling from 37 to 31°C. It then switches off around 29°C, which suggests that modest catecholamine support might be useful below that temperature.

In general, pharmacologic manipulation of the pulse and blood pressure should be avoided. Vasoconstrictors may be dysrhythmogenic while having a minimal effect on the maximally constricted peripheral vasculature. Epinephrine and other vasoconstrictors should generally be avoided. The indications for vasopressors are unclear. Of note, in controlled animal models, the return of spontaneous circulation after induced VF below 30°C is higher after administration of vasopressor medications.

Inotropes usually are not necessary to support the blood pressure. Low-dose (2-5 µg/min) dopamine infusions should be considered in disproportionately hypotensive patients who do not maintain a mean arterial pressure of 60 mm Hg in response to crystalloids, colloids, and rewarming. To facilitate perfusion of a vasoconstricted cardiovascular system while the patient is receiving dopamine, some investigators add an infusion of low-dose nitroglycerin.

Dysrhythmia Treatment

Preexisting chronic premature ventricular contractions can be suppressed during hypothermia and recur during rewarming. Most hypothermia-induced dysrhythmias convert spontaneously during rewarming. Asystole that develops during rewarming is not a more ominous rhythm than VF. Biphasic defibrillation should be attempted at 2 Wsec/kg up to 200 Wsec. A successful reestablishment of electromechanical activity has been reported at 20°C. If the defibrillation attempt is unsuccessful, active rewarming should be initiated with available equipment while CPR is continued. Defibrillation attempts are usually unsuccessful until the core temperature is well above 28 to 30°C. If the defibrillation attempt is unsuccessful, the core temperature should be raised above 30°C before further reattempts.

Virtually all atrial dysrhythmias are common below 32°C and are associated with a slow ventricular response. Atrial fibrillation is common and considered innocent. It usually converts spontaneously during rewarming. Digitalization and calcium channel blockade are not warranted.

The ideal approach to ventricular dysrhythmias is unresolved. Lidocaine and propranolol have minimal hemodynamic effects during hypothermia. Their efficacy in treatment of ventricular dysrhythmias appears limited.
Bretylium tosylate is not available in the United States but was extremely effective in several animal studies when it was given before invasive maneuvers performed after induction of hypothermia. Several clinical chemical defibrillations with bretylium in cases of severe hypothermia are reported. In a canine model of severe hypothermic VF, neither amiodarone nor bretylium was effective. Amiodarone can cause torsades de pointes through QT prolongation, and its safety during both accidental and induced hypothermia is unknown.

In cases of normothermia, group I ventricular antidysrhythmics directly decrease conduction velocity and possess indirect antiadrenergic activity. In cases of hypothermia, at least one agent in this group, procainamide, increases the incidence of VF. Another drug in the group, quinidine, can prevent VF during induced profound hypothermia and during cardiac manipulation at 25 to 30° C.

Transvenous intracardiac pacing is hazardous for hypothermia-induced bradydysrhythmias. External noninvasive pacing by means of large low-resistance electrodes may be a successful alternative to emergency transvenous pacing in the rare setting of a profoundly disproportionate bradycardia. Transcutaneous pacing in two perfusing patients with blood pressure below 60 mm Hg facilitated continuous arteriovenous rewarming. Other active rewarming techniques, however, do not require specific pressure gradients.

**Failure to Rewarm**

Cold exposure normally induces adrenal unresponsiveness to adrenocorticotropic hormone. A false diagnosis of decreased adrenal reserve is possible. The increase in adrenocorticotropic hormone level seen in hypothermic individuals may be a neurogenic or emotional response to the cold. Acute cold stress initially stimulates cortisol secretion. The patient may already have a very high level as a result of an underlying stress. In clinical series, serum cortisol levels are commonly elevated. The percentage of cortisol bound to protein is increased with hypothermia, and therefore the active free fraction is decreased.

If a patient fails to rewarm, the historian should search for evidence of adrenocortical insufficiency or steroid dependence. At that juncture, administration of 100 mg intravenous hydrocortisone should be considered. Empirical treatment with thyroxine should be reserved for patients thought to be myxedematous. Thyroid hormone replacement is recommended if a history of hypothyroidism is present, a suggestive neck scar is present, or a failure to rewarm occurs. After thyroid function study samples are drawn, 250 to 500 µg of levothyroxine should be administered cautiously intravenously during several minutes. Daily injections of 50 to 100 µg are necessary for 5 to 7 days. Hydrocortisone (100-200 mg) should be added to the first several liters of crystalloid fluid. The absorption of levothyroxine is variable when it is administered orally or intramuscularly. Administration intravenously results in a smooth effect after the onset of action at 6 to 12 hours. This is evidenced by improvement in the vital signs and the rewarming rate. Half the dose is converted by the peripheral tissues into l-triiodothyronine (T₃). An underlying infection also compromises thermogenesis. In an urban setting, infection is the leading cause of failure to rewarm and of mortality.

**Septicemia**

Hypothermia compromises host defenses and predisposes to infection. The usual signs of infection, including fever, are absent. Shaking chills from sepsis may be mistaken for shivering. If a patient’s mental status remains altered despite rewarming, CNS injury or infection should be suspected.

Diminished bone marrow release and circulation of neutrophils, along with impaired neutrophil migration and bacterial phagocytosis, is a factor contributing to infection. In children younger than 3 months, empirical antibiotics after culture are indicated. No reliable clinical or laboratory indicators of infection exist, but bradycardia, anemia, uremia, and serum glucose levels as well as leukocyte abnormalities are common clues.

The role of empirical antibiotics in adults is less clear. Although gram-negative septicemia may be the cause of hypothermia, coexistent infections from gram-positive cocci, Enterobacteriaceae, and oral anaerobes are common.

Elderly patients with thermoregulatory failure have a high risk of mortality and should be considered septic until proven otherwise. Routine empirical antibiotics in hypothermic adults, unlike in elderly patients and in children, does not appear warranted. Antibiotics should be administered if the clinical picture is consistent with septic shock, if there is failure to rewarm, or if aspiration has occurred. Cellulitis, myositis, bacteriuria, or infiltrates present on chest radiographs warrant immediate antimicrobial therapy.

**REWARMING**

Because no controlled studies comparing rewarming methods in hypothermia exist, rigid treatment protocols would not be evidence based. As a result, the clinician should consider the advantages, disadvantages, indications, contraindications, and specific guidelines for the various reported techniques of rewarming that follow.

**Passive External Rewarming**

Spontaneous passive external rewarming is noninvasive and is the treatment of choice for most patients with mild hypothermia. The patient should be able to generate sufficient heat metabolically to maintain an acceptable rate of spontaneous rewarming. Elderly patients are commonly glycogen depleted, centrally hypovolemic, and not capable of normal cardiovascular or metabolic homeostasis.

The normal processes of heat dissipation are minimized by passive external rewarming. Cessation of evaporation and convective coupling is possible with insulation against further radiation of heat. This technique simply involves covering the patient with an insulating material in a favorable atmospheric condition. The ambient temperature should exceed 21° C. When the air is stationary, less heat is lost to conduction, convection, and radiation.

Below 30° C, humans are functionally poikilothermic. No shivering thermogenesis occurs. Shivering is the thermoregulatory neuromuscular response to cold that increases heat production from 250 to 1000 kcal/hr. Without shivering, endogenously generated metabolic heat is insufficient to raise the core temperature. When the core temperature exceeds 32° C, the major source of heat production is shivering thermogenesis, unless complete glycogen depletion occurs.

Recommended rewarming rates vary between 0.5 and 2.0° C/hr. The rewarming rate should be rapid enough to avoid prolonged exposure to dysrhythmias.

**Active Rewarming**

Active rewarming is the direct transfer of exogenous heat to the patient. It can be accomplished by either external or internal techniques.

Cardiovascular instability and decompensation require rapid elevation of the core temperature (Box 140-3). Defibrillation is rarely successful at temperatures below 28 to 30° C. Active
rewarming is indicated with cerebrovascular accidents and other conditions that impair CNS control of thermoregulation. Active rewarming is also indicated in patients when endogenous thermogenesis is insufficient or when glycogen depletion is present. These diseases are usually endocrine and include hypopituitarism, adrenal insufficiency, hypothyroidism, and Wernicke’s encephalopathy. Active rewarming is also indicated if diabetic ketoacidosis is present because the core temperature must be elevated well above 30°C before insulin becomes effective.65

Pharmacologically induced peripheral vasodilation or acute spinal cord transaction renders a patient incapable of sufficient thermogenesis. Such patients should be actively rewarmed. Active rewarming in patients with moderate or severe hypothermia is also indicated because of the potential for cardiovascular decompensation or ventricular irritability. Patients with severe hypothermia and a sustained perfusing rhythm do not necessarily require invasive extracorporeal rewarming techniques.66

Aggressive treatment of hypothermia in infants is also indicated. Rapid rewarming may be advantageous because it minimizes energy expenditures.67 Vigorous monitoring for infectious, respiratory, hematologic, and metabolic complications is needed.

Active External Rewarming

Early concern with active external rewarming (AER) was voiced by Duguid and colleagues in 1961,68 when 20 of their 23 patients died. Retrospective analysis of numerous clinical series notes widely varying mortality rates with AER.6,16,65

Various methods are available to conduct heat directly to the skin. Rewarming options include plumped garments that recirculate warm fluids, hot-water bottles, heating pads, forced-air warming systems, and radiant sources. Thermal injury to vasoconstricted hypoperfused skin is a common hazard with local heat application.69

Forced air warming systems efficiently transfer heat.70 The Bair Hugger circulates hot air through a “blanket.” The air exits apertures on the patient’s side of the cover, which allows a convective transfer of heat. In one study in which accidental hypothermia victims were rewarmed in the emergency department, rewarming shock and core temperature afterdrop were not noted.71 Both groups of patients were also treated with heated inhalation and warmed intravenous fluids. The use of forced-air warming systems is most practical in the emergency department.72 Although these devices decrease shivering thermogenesis, afterdrop is minimized and heat transfer can be significant. Another option is the use of a temperature regulation device traditionally used for therapeutic hypothermia in patients after cardiac arrest.73 In addition, a thermoregulatory system that circulates warm water through energy transfer pads is available.74

Arteriovenous anastomosis (AVA) rewarming is another noninvasive AER technique.75 Exogenous heat is provided by immersion of the lower parts of the extremities (hands, forearms, feet, calves) in 44 to 45°C water. The heat opens the AVAs. These organs are 1 mm below the epidermal surface in the digits.76 As a result, there is an increased flow of warmed venous subcutaneous blood returning directly to the heart. The forearms and calves must be included for this technique to be effective. A permutation of AVA rewarming is negative-pressure rewarming. In combination with localized heat application, the application of subatmospheric pressure distends the venous rete and increases flow through the AVAs. The clinical practicality and efficacy of AVA rewarming is unclear; with vasoconstricted extremities, burns are a real hazard.

Optimal candidates for AER are previously healthy patients with acute hypothermia. In these patients, minimal dehydration and pathophysiologic circulatory changes have occurred. If AER is chosen and the extremities are vasoconstricted, the heat source should preferentially be applied to the thorax and not to the extremities. Application of heat to the extremities increases the cardiovascular load by increasing the metabolic requirements of the peripheral musculature. The depressed cardiovascular system may not be able to meet the demands, and cardiovascular collapse can occur.

Combining of truncal AER with core rewarming can also be successful. The provision of heated humidified oxygen and warmed intravenous fluids in addition to AER may anticipate and avert hypoxia, metabolic acidosis, core temperature afterdrop, and hypotension. If AER is chosen as the method of treatment for moderate or severe hypothermia, it should be combined with one of the active core rewarming techniques.

Active Core Rewarming

Numerous alternatives achieve active rewarming of the core. These techniques minimize rewarming collapse in patients with temperatures below 32°C.

Airway Rewarming. Airway rewarming as an adjunctive active core rewarming technique has been explored since it was first suggested by Lloyd.20 This simple technique is indicated in all cases of moderate or severe hypothermia.16,77

Advantages of heated humidified oxygen include noninvasiveness, cost, simplicity, assurance of adequate oxygenation, and avoidance of afterdrop. Additional benefits are the stimulation of pulmonary cilia, a decrease in pulmonary secretion viscosity, and a reduction of cold-induced bronchорrhea. Pulmonary absorption occurs without adverse effects on surfactant or increased pulmonary congestion.

The respiratory tract is a limited site for heat exchange. Nevertheless, both the oxygen content and the temperature in the pulmonary vasculature rise. The myocardium is perfused by warmer oxygenated blood, stabilizing against intermittent temperature gradients.

A sufficient respiratory minute volume and complete humidification are necessary for maximal heat delivery. Because of the low thermal conductivity of dry air, ventilation with warm dry air provides negligible heat. Depending on the technique used, one should expect a rewarming rate between 1 and 2.5°C/hr.6,16 The higher rates are with endotracheal intubation; the lower rates are with the use of a mask. Heated mask ventilation is also of interest. A thermal countercurrent heat exchanger exists in the cerebrovascular bed of humans. This system, known as the rete mirabile, could preferentially rewarm the brainstem. Another option is heated inhalation through face mask with continuous positive airway pressure.

Maintenance of sufficient oxygenation is also critical in moderate and severe cases. Fisher21 considered the effects of hypothermia, pH, PaCO2, and level of 2,3-diphosphoglycerate on the left shift of the oxyhemoglobin dissociation curve. In patients on cardiopulmonary bypass cooled to 28 to 30°C, the capacity of hemoglobin to unload oxygen to the tissue is less than half that found in normothermic patients. Despite lower metabolic requirements, this decrease in “functional” hemoglobin combined with a

**Box 140-3 Indications for Active Rewarming**

- Cardiovascular instability
- Moderate or severe hypothermia (≤32.2°C)
- Inadequate rate of rewarming or failure to rewarm
- Endocrinologic insufficiency
- Traumatic or toxicologic peripheral vasodilation
- Secondary hypothermia impairing thermoregulation
depressed respiratory minute volume results in minimal oxygen reserves.

Some patients maintain a level of spontaneous respiration appropriate to the depressed carbon dioxide production. This is not the case in patients with coexisting toxicologic, traumatic, or metabolic depression of their respiratory centers. During spontaneous or assisted ventilation with heated ventilation, there is the flexibility to alter the fraction of inspired oxygen ($FiO_2$), to monitor airway pressure, and to deliver continuous positive airway pressure or positive end-expiratory pressure.

The technique for patients with spontaneous respirations requires a heated cascade nebulizer. An immersion heater can be connected to a hose with a warming wire. Because patients with a depressed level of consciousness do not complain of pain, it is essential to check the temperature of the inspired air frequently with an in-line temperature probe. The gas temperature should be maintained at 42 to 45°C. Most heater modules require modification to allow the temperature to reach 42 to 45°C and should be so labeled to avoid routine use.

Most humidifiers are manufactured in accordance with the International Standards regulations. The humidifier will not exceed 41°C close to the patient outlet with a 6-foot tubing length. Strategies to circumvent the 41°C ceiling include reduction of tubing length, addition of more heat sources, disabling of the humidifier safety system, and placement of the temperature probe outside the patient circuit. Because of the modest clinical benefit in stable patients, it is probably not worth the effort to circumvent the 41°C ceiling. The only report of thermal airway injury is in a patient ventilated by endotracheal tube for 11 hours with 80°C inhalant. Complete airway protection decreases the risk of aspiration. Hypothermia is associated with ileus, bronchorrhea, and depressed protective airway reflexes. Although the airway rewarming technique provides less heat than other forms of active core rewarming do, it is safe, noninvasive, and practical.

**Peritoneal Dialysis.** This technique delivers dialysate at 40 to 45°C to the peritoneal cavity. Heat is conducted directly to the intraperitoneal structures, through the posterior parietal peritoneum to the solid viscera and through the hemidiaphragms to the heart and lungs.

A double-catheter system can increase the rate of rewarming with suction at the outflow. The usual clinically attainable rate is 6 L/hr. Two liters are infused, retained for 20 minutes, and then aspirated. Rewarming rates average 1 to 3°C/hr, depending on gradients and flow rates and dwell times.

An additional benefit of this invasive technique is hepatic rewarming, which reactivates depressed detoxification and conversion enzymes. Peritoneal dialysis can exacerbate preexistent hypokalemia; therefore, serum electrolyte levels should be carefully monitored. Peritoneal lavage rewarming should not be selected routinely for stable patients. It should be considered in severe cases and in combination with all available rewarming techniques for patients without spontaneous perfusion.

**Heated Irrigation.** Heat transfer from irrigation fluids is usually limited because the surface area available for heat exchange is minimal. Gastric or colonic irrigation can cause fluid and electrolyte fluxes. These techniques are rarely indicated.

Closed thoracic lavage in accidental hypothermia is another option. Two large-bore thoracostomy tubes are inserted into one or both hemithoraces. One is inserted anteriorly in the second or third intercostal space at the midclavicular line. The other is inserted between the fifth and sixth intercostal space in the posterior axillary line. Normal saline solution is heated to 40 to 42°C and steriley infused into either tube and drained. The dwell time for thermal transfer will be longest if the fluid is infused into the inferior tube. One should leave the inferior tube for drainage after rewarming. Left-sided tube insertion in perfusing patients risks causing VF.

The efficiency of heat transfer varies with the flow rate and dwell times. Pleural adhesions prevent adequate infusion rates and can result in a tension hydrothorax. Adequate drainage should be ensured to prevent intrathoracic hypertension.

Thoracic lavage should be reserved for the severely hypothermic patient who does not respond to standard techniques or the patient with another indication for a chest tube. It should be combined with all other available rewarming modalities in potentially salvageable cardiac arrest patients. The rate of rewarming averages 3°C/hr.

Mediastinal irrigation and direct myocardial lavage should be considered only in patients without spontaneous perfusion. The procedure requires a standard left lateral thoracotomy incision. The pericardium is not incised unless an effusion or tamponade is present. The heart is bathed in 1 to 2 L of an isotonic solution heated to 40°C for several minutes. The fluid is then removed and the lavage repeated. Internal defibrillation is attempted at intervals of 2°C after the myocardial temperature exceeds 26 to 28°C. When a perfusing rhythm is achieved, lavage is continued until the myocardial temperature exceeds 32°C. A median sternotomy approach allows ventricular decompression in addition to direct defibrillation. Open cardiac massage of a cold, rigid, and contracted heart may not generate flow.

**Endovascular Rewarming.** Another active core rewarming option uses endovascular warming devices that are used for therapeutic cooling and subsequent rewarming of comatose resuscitated cardiac arrest patients. These systems involve femoral vein catheterization with a closed-loop catheter that has a temperature control element at the tip. If the core temperature is below 30°C, the fail-safe feature on the console must be circumvented to allow rewarming.

**Diathermy.** Truncal diathermy involves the conversion of energy waves into heat. Large amounts of heat can be delivered to deep tissues with ultrasonic and low-frequency microwave irradiation. Frostbite, burns, significant edema, and the presence of all types of metallic implants and pacemakers contraindicate diathermy.

Regional heating of hypothermic dogs after immersion does not damage tissue at 4 to 6 W/kg and rapidly elevates the core temperature. Zhong warmed 16 piglets with microwave irradiation “until they squealed and sucked.” In a subsequent experiment, 20 of 28 human infants were successfully rewarmed with microwave irradiation at 90 to 100 W. Diathermy is still experimental.

**Extracorporeal Blood Rewarming.** The four common techniques to rewarmin blood are venovenous rewarming, hemodialysis, continuous arteriovenous rewarming, and cardiopulmonary bypass (Chapter 140-2).

Extracorporeal venovenous rewarming is an option for warming and recirculation of the blood. With this technique, blood is removed (usually by a central venous catheter), heated to 40°C, and returned through a second central or large peripheral venous catheter. Flow rates are 150 to 400 mL/min. The circuit is not complex and is more efficient than many other nonbypass modalities. There is no oxygenator, and because the method does not provide full circulatory support, volume infusion is the only option to augment inadequate cardiac output.

Standard hemodialysis is a widely available and practical rewarming technique. It is portable and efficient and should be considered in patients with electrolyte abnormalities, renal failure, or intoxication with a dialyzable substance. Two-way flow catheters allow cannulation of a single vessel. A Drake Willock single-needle dialysis catheter can be used with a portable hemodialysis machine and external warmer. After central venous cannulation, exchange cycle volumes of 200 to 250 mL/min are possible. Although heat exchange is less than with standard two-vessel hemodialysis, the ease of percutaneous subclavian vein placement is a major advantage. Hemodialysis by two separate single-lumen
catheters placed in the femoral vein can achieve continuous blood flow at 450 to 500 mL/min.

Continuous arteriovenous rewarming is another option if the blood pressure is at least 60 mm Hg. Continuous arteriovenous rewarming involves the use of percutaneously inserted femoral arterial and contralateral femoral venous catheters. The Seldinger technique is used to insert the 8.5F catheters. Heparin-bonded tubing circuits obviate the need for systemic anticoagulation. The blood pressure of spontaneously perfusing traumatized hypothermic patients creates a functional arteriovenous fistula by diverting part of the cardiac output out the femoral artery through a commercially available countercurrent heat exchanger. The heated blood is then returned with admixed heated crystalloids through the femoral vein. Continuous arteriovenous rewarming does not require the specialized equipment and perfusionist necessary for cardiopulmonary bypass. The average flow rates are 225 to 375 mL/min, resulting in a rate of rewarming of 3 to 4°C/hr. Because the catheters are 8.5F, the patient should weigh at least 40 kg.

Cardiopulmonary bypass uses the standard femoral-femoral circuit and includes arterial and venous catheters, a mechanical pump, a membrane or bubble oxygenator, and a heat exchanger. A 16F to 30F venous cannula is inserted through the femoral vein to the right atrium–inferior vena cava junction. The tip of the shorter 16F to 20F arterial cannula is inserted 5 cm or just proximal to the aortic bifurcation. Transesophageal echocardiography can help evaluate ventricular load and valve function. There are techniques to decrease the need for intravenous anticoagulation that previously limited clinical applicability. Heparin-coated perfusion equipment and the use of nonthrombogenic pumps can be coupled with the enhanced physiological fibrinolysis seen in the first hour of cardiopulmonary bypass. Heated, oxygenated blood is returned through the femoral artery. Femoral flow rates of 2 to 3 L/min can elevate the core temperature 1 to 2°C every 3 to 5 minutes. In one review, the mean temperature increase was 9.5°C/hr. Most pumps can generate full flow rates up to 7 L/min. The optimal temperature gradient and bypass rewarming rates are unknown. An excessive temperature gradient between brain tissue and circulate can adversely affect electroencephalographic regeneration. The electroencephalogram is a surrogate marker of brain recovery. The other concern is the possibility of increased bubbling if high perfusate temperature gradients are used. Most investigators use 5 to 10°C gradients. Extracorporeal rewarming by extracorporeal membrane oxygenation appears to reduce the risk of intractable cardiorespiratory failure after rewarming.

The major advantage of cardiopulmonary bypass in perfusing patients is the preservation of flow if mechanical cardiac activity is lost during rewarming. Other candidates for cardiopulmonary bypass are patients who do not respond to less invasive rewarming techniques, those with completely frozen extremities, and those with rhabdomyolysis accompanied by major electrolyte disturbances. One proposed algorithm suggests direct transfer of the patient to the operating suite to shorten door-to-reperfusion time with hypothermic cardiac arrest without obvious major trauma.

Of note, rapid acceleration of the rate of rewarming does not necessarily improve survival rates. Complications of rapid rewarming in severe hypothermia include disseminated intravascular coagulation, pulmonary edema, hemolysis, and acute tubular necrosis. Percutaneous cardiopulmonary bypass can provide cardiovascular support in perfusing but hemodynamically unstable patients.

Extracorporeal blood rewarming should be considered in hypothermic cardiac arrest patients when no contraindications to CPR exist. A realistic assessment of the risk-benefit ratio for debilitated patients with secondary hypothermia should be made. The lowest temperature in a survivor of induced hypothermia was 9°C. Extracorporeal blood rewarming is unlikely to succeed below 5 to 10°C. Resuscitation should be discontinued if frozen or clotted intravascular contents are identified.

**DISPOSITION**

Otherwise healthy patients who have mild primary accidental hypothermia (35-32.2°C) usually warm easily. They can be safely discharged if a warm environment is available.

Patients with more severe hypothermia (<32.2°C) generally require admission. These patients should be evaluated for the presence of underlying medical disorders (see Box 140-1). Cardiac monitoring should be considered in patients with persistent toxicologic or metabolic abnormalities. This is essential for those patients displaying cardiovascular instability or an inadequate rate of rewarming. Transfer of patients to tertiary care centers is generally not necessary; however, some severely hypothermic patients are best managed in facilities with cardiopulmonary bypass capabilities.

**OUTCOME**

In the past, the treatment dictum was that “no one is dead until they are warm and dead.” Some patients are cold and dead, and it would be useful and humane if they could be safely identified. Because of the variability of human physiologic responses, outcome is difficult to predict. The type and severity of the underlying or precipitating disease process are the major determinants. Age of the patient is not an independent predictor of mortality.

Trauma, infection, and toxin ingestions also affect survival unpredictably. Outcome prediction based on the Glasgow Coma Scale score is unreliable. Significant predictors of outcome include asphyxia, prehospital cardiac arrest, low or absent blood pressure, elevated blood urea nitrogen level, and need for either endotracheal or nasogastric intubation in the emergency department.
The search for a valid triage marker of death continues. Grave prognostic indicators include evidence of intravascular thrombosis (fibrinogen < 50 mg/dL), cell lysis (hyperkalemia > 10-12 mEq/L), and ammonia levels greater than 250 mmol/L.

**KEY CONCEPTS**

- Indications for active rather than passive rewarming include cardiovascular instability, temperature below 32° C, poor rate of rewarming, endocrinologic insufficiency, and vasodilation.
- One should consider hypoglycemia, hypovolemia, or an overdose if there is a tachycardia disproportionate to the temperature.
- The efficacy of most medications is temperature dependent. Overmedication to achieve an effect when the patient is cold could cause toxicity during rewarming.
- Kinetic laboratory tests of coagulation are performed at 37° C. Despite a clinically obvious coagulopathy, the values will be deceptively "normal."
- There are no safe predictors of serum electrolytes. Hypothermia enhances the cardiac toxicity of hyperkalemia and obscures premonitory electrocardiographic changes.
- Failure to rewarm despite good technique should suggest infection, endocrinologic insufficiency, or a futile resuscitation.

The references for this chapter can be found online by accessing the accompanying Expert Consult website.
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