Hypothermia and localized cold injuries

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Accidental hypothermia and localized cold injuries remain a significant public health problem. The deleterious effect of cold exposure on human performance and health has been documented for centuries. Some of the earliest descriptions came from Baron de Larrey, Napoleon's chief surgeon. During the disastrous invasion of Russia in 1812 he depicted the mental and physical hardships endured by the French soldiers as a result of exposure to severe cold. Of note, de Larrey observed that the cold victims placed closest to the fire often died [1]. Frostbite was also a major cause of severe morbidity and tissue loss among French soldiers during the invasion. The danger of repetitive freeze–thaw cycles became evident as the soldiers warmed their feet next to the fire at night only to refreeze again the following day. The resultant increase in tissue loss was erroneously attributed to the excessive speed of recovery next to the fire and massage of the exposed extremity with snow therefore became in vogue as a method of gradual rewarming. The practice was finally abandoned as a therapeutic intervention in 1956 after a report of the successful recovery of a severely hypothermic patient who had frostbite following rapid rewarming [2].

George Washington's troops suffered heavy casualties during the brutal winter of 1777 to 1778 and some 10% of his men were "left to perish by winter's cold" [3]. Nearly 200,000 allied and German troops suffered cold related injuries or deaths during World War II. Cold-related fatalities accounted for 10% of all deaths among American forces during the Korean War [4]. Today the majority of victims are in one of three categories: the urban poor, wilderness enthusiasts, and winter sports participants. From 1970 to 1979 the Public Health Service recorded 4826 deaths in the United States that were attributed directly to hypothermia [5]. In this group the major contributing factors were alcohol, malnutrition, and inadequate living conditions in addition to a median age of 50 years. Clearly, urban poverty,

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socioeconomic conditions, and age play major roles in the occurrence of accidental hypothermic deaths in major urban areas. It is important to note that numerous accidental hypothermia cases are reported every year in areas that are typically considered to be warm weather locales such as Florida, Texas, California, and Alabama [6,7].

The emerging popularity of wilderness activities such as mountaineering, backpacking, and extreme skiing has led to an increasing number of individuals at risk for hypothermia and, subsequently, a growing number of associated fatalities. Although classically a condition seen in colder climates, the continued poverty and poor socioeconomic conditions seen in many urban centers in conjunction with an aging population mandates that emergency physicians have a working knowledge of the pathophysiology and management options for patients suffering from these conditions. The majority of the reported literature is limited in applicability to clinical situations because it involves animal models or uses human volunteers who are exposed to mildly hypothermic conditions or frostbite. A number of anecdotal case series describe the therapeutic modalities used in treating severe accidental hypothermia and localized cold injury.

Hypothermia

Hypothermia is classically defined as a core body temperature of less than 35°C; however, it is best described as a decrease in body temperature that renders the body unable to adequately generate sufficient heat to continue its natural functions. Humans, as warm-blooded animals, are only able to adapt to their environment and maintain their core temperature within a relatively narrow temperature range. Hypothermia develops when this adaptive mechanism is overwhelmed.

Hypothermia has been classified by the degree to which the core temperature has decreased from baseline, which has important implications regarding the anticipated physiologic changes and, subsequently, the use of appropriate therapeutic modalities. Patients who have core body temperatures between 32°C and 35°C are considered to suffer from mild hypothermia. Moderate hypothermia exists in the setting of core temperatures between 28°C and 32°C. Severe hypothermia is defined as a measured core body temperature of less than 28°C. This classification system is shown in Table 1. The lowest recorded temperature for a survivor of accidental hypothermia is 15.2°C (59.2°F) in a 23-day-old infant. The lowest temperature recorded in an adult survivor is 16°C (60.8°F) [8].

Heat regulation

The human body regulates temperature and the physiologic response to cold by way of the hypothalamus. On initial cold exposure, increasing the

Table 1
Classification of hypothermia

Severity	Core temperature	Physiologic response
Mild	32°C–35°C	Tachypnea, tachycardia, dysarthria, shivering
Moderate	28°C–32°C	Loss of shivering, diminished level of consciousness
Severe	<28°C	Loss of reflexes, coma, ventricular fibrillation

Data from Jolly BT, Ghezzi KT. Accidental hypothermia. Emerg Med Clin N Am 1992; 10:311–27.

preshivering muscle tone can double basal heat production. Shivering can subsequently increase basal metabolism up to five times the baseline [9,10]. This compensatory mechanism is finite, often subsiding after hours and terminating when the core temperature drops below 30°C [11]. Because of humans' limited capacity to produce heat, any situation that promotes heat loss can hasten the onset of hypothermia. The human body loses heat through four mechanisms. Under normal conditions, approximately 60% of heat is lost by radiation. Conduction and convection account for 10% to 15% of heat loss, although this can increase dramatically in cold, wet, and windy environments. Evaporation from the skin and respiratory tract accounts for the remaining 25% to 30% of heat loss. This avenue of heat loss will increase in cool, dry, and windy conditions [6].

Predisposing factors

A large number of preexisting and concomitant factors have significant influence on a patient's ability to tolerate heat loss and prevent hypothermia. Extremes of age are considered to be risk factors because both groups are often unable to remove themselves from cold environments. In addition, young children have an increased surface area to body mass ratio, which increases the rate of heat loss. The elderly often have a decreased ability to sense cold as a result of autonomic neuropathy and a resultant poor vasoconstrictor response. In addition, the elderly are often unable to mount a heat response, leading to hypothermia in ambient environments that are well tolerated by younger patients. Major trauma is another entity that places the patient at risk. Injury inherently predisposes to hypothermia from a variety of intrinsic and iatrogenic causes. Hypothermia and associated coagulopathy often mandate an alternative treatment modality for severely traumatized patients [12]. Extended exposure time and resuscitation with large volumes of unwarmed fluids and oxygen increase the likelihood of developing hypothermia. Derangement of normal central metabolic control has a profound effect on the patient's ability to respond to cold environments. Hypothyroidism results in lower basal core temperatures and an ineffective metabolic response. Hypoglycemic conditions predispose patients to hypothermia secondary to a decreased glucose supply in the central nervous system. Adrenal insufficiency and hypopituitarism have also

been shown to have deleterious effects on the body's response to cold exposure [13]. Numerous recreational and therapeutic drugs are well known to promote hypothermia. Ethanol is the most common drug associated with hypothermia. [14,15]. Ethanol acts as a peripheral vasodilator because of its central nervous system depressant effect, which results in increased heat loss through radiation. Barbiturates and other depressants can result in extended periods of cold exposure. Phenothiazines have a direct suppressant effect on the shivering mechanism, which limits the body's ability to generate heat [13].

Pathophysiology

The effects of significant hypothermia are distributed across multiple organ systems. The most clinically important deleterious effects relate to the renal, cardiac, and central nervous systems as described below.

Renal system

Peripheral vasoconstriction develops as the external body cools with a resulting increase in blood flow to the kidneys. In conjunction with cold-induced diuresis, this "shunting" phenomenon results in a significant decrease in intravascular volume. Eventually, cardiac output declines and vascular tone increases, which act to decrease renal blood flow, which, in turn, decreases glomerular filtration rates and ultimately results in acute renal failure. Renal blood flow is depressed by 50% at temperatures between 27°C and 30°C [16]. Hypothermia can also result in significant hypokalemia, which is easily reversible during rewarming [17].

Cardiovascular system

The victim's heart rate, blood pressure, and cardiac output increase initially as a result of peripheral vasoconstriction and increased catecholamine production. After a plateau phase, progressive and often rapid decline develops in these physiological parameters. Bradycardia occurs in 50% of patients who have temperatures below 28°C [18]. Bradycardia associated with hypothermia is a direct result of decreased spontaneous depolarization of pacemaker cells and slowed propagation through the normal conduction system. As a result, atropine is often ineffective in this setting. In addition, the myocardium becomes irritable, leading to arrhythmias. Atrial fibrillation often precedes ventricular fibrillation, followed by asystole at temperatures of less than 25°C [5,19]. Approximately one third of hypothermic patients develop the distinctive Osborn or J wave on electrocardiogram. Originally described by Tomaszewski in 1938, the J wave is described as a "hump" seen at the QRS-ST junction, especially in leads aVL, aVF, and lateral chest leads [18]. The presence of J waves is suggestive of, but not pathognomonic for, hypothermia [20]. They can appear at any temperature below 32°C.

Central nervous system

Hypothermia results in decreasing cerebral blood flow in the setting of declining neuronal metabolism. This protective response explains why the brain is relatively protected from ischemic injury as a result of hypothermia. The clinical presentation manifests as a progressive decline in level of consciousness. Initially, there is a loss of fine motor skills, presenting as clumsiness or lack of coordination [21]. Eventually dysarthria, ataxia, and loss of gross motor skills occur. The subtle clinical signs and symptoms of mild hypothermia can mimic cognitive decline, cerebrovascular accident, hypothyroidism, and myxedema coma, especially in elderly patients. As the process intensifies, the patient has difficulty with thought processes and decision-making skills (eg, the phenomenon known as "paradoxical undressing," in which the hypothermic individual attempts to remove protective clothing). This phenomenon is felt to represent a preterminal response to impending thermoregulatory collapse.

Prehospital care

The patient's history and environmental situation frequently suggest the presence of hypothermia. Extended exposure in severe weather conditions makes the diagnosis obvious and straightforward; however, patients might present with history and physical examination that are subtle with regard to the development of hypothermia. Hypothermia can occur in any setting in which the ambient temperature is below the core body temperature. Patients might present with vague, mild complaints of nausea, vomiting, fatigue, and dizziness. It is imperative that assessment and treatment occur simultaneously in critically ill and injured patients.

The evaluation should begin at the initial patient contact, often at the scene of injury or recovery whenever possible. Scene safety is a major concern for rescuers in severe conditions. It is imperative that prehospital personnel prioritize their own safety and protection from cold conditions. Prehospital life support for hypothermic patients differs in many aspects from the management of normothermic individuals. The initial primary survey is conducted as in other situations. Airway, breathing, circulation, and neurologic deficits should be assessed closely and recorded. Attention to airway and respiratory status is critical in hypothermic patients. Hypothermia initially causes tachypnea, which leads to respiratory alkalosis. Severe hypothermia leads to stupor, coma, and impaired airway protection. Intubation is not only safe but often necessary in these patients. Ventilation is often compromised by associated chest rigidity and decreased diaphragmatic movement. Blind nasal intubation might be required to overcome severe jaw rigidity in prehospital settings in which rapid sequence induction is not available. Patients often require frequent tracheal suctioning in the setting of cold-induced bronchorrhea. Enhanced oxygenation is important as decreased temperature shifts the oxyhemoglobin

dissociation curve to the left, resulting in decreased oxygen delivery to tissues.

Initial treatment

Circulatory status is often difficult to assess in hypothermic patients secondary to significant peripheral vasoconstriction. Volume resuscitation with intravenous fluids should be monitored closely because fluid shifts and third spacing can reverse rapidly with rewarming. Early in the process, cellular metabolism is increased with a resultant osmotic gradient of fluid shifts to the extracellular space. Sustained hypothermic conditions will lead to extreme fluid and electrolyte abnormalities. Nasogastric drainage might help reduce vomiting and aspiration caused by decreased gastric motility. Cardiac responses to hypothermia have been well studied in human and animal models [14,15,22,23]. Tachycardia progresses rapidly to bradycardia because the conduction system is sensitive to cold temperatures. Early ECG changes include prolongation of the PR, QRS, and QT intervals. Repolarization abnormalities are seen as variable changes in the ST segments and T waves. Eventually, hemodynamic deterioration occurs secondary to hypovolemia, decreased cardiac filling pressures, and subsequent decreased cardiac output. Dysrhythmias are heralded by atrial fibrillation caused by atrial irritation. As core temperature drops, ventricular irritability increases, leading to premature ventricular contractions and ventricular tachycardia. The hypothermic heart is sensitive to excessive movement and jostling. Care should be taken to move patients in a slow and gentle manner to avoid precipitating ventricular arrhythmias. At 28°C, ventricular fibrillation becomes a more frequent development. The prophylactic use of antiarrhythmia medications has fallen out of favor. The effectiveness of these medications is limited in hypothermic conditions, and most arrhythmias resolve spontaneously as core temperatures rise. The Osborn or J wave is described as the ''classic'' electrocardiographic finding in severe hypothermia. This abnormality is a secondary wave following the S wave and is seen most prominently in aVL, aVF, and across the left chest leads (Fig. 1). The Osborn deflection increases and decreases in magnitude as core temperatures change [24,25].

Central nervous system symptoms are present to some degree in most hypothermic patients. The level of consciousness will decrease and eventually culminate in coma as core body temperatures fall. Changes in deep tendon reflexes occur; initial hyperreflexia progresses to hyporeflexia as temperatures drop below 32°C. All reflexes are absent below 26°C. The most important measure of the patient's condition is core body temperature, which is most accurately measured with rectal thermometers. Axillary temperature is the best alternative indicator of true core temperature. Every hypothermic patient requires an extensive and thorough secondary survey to determine the presence of conditions that led to or resulted from the hypothermia.
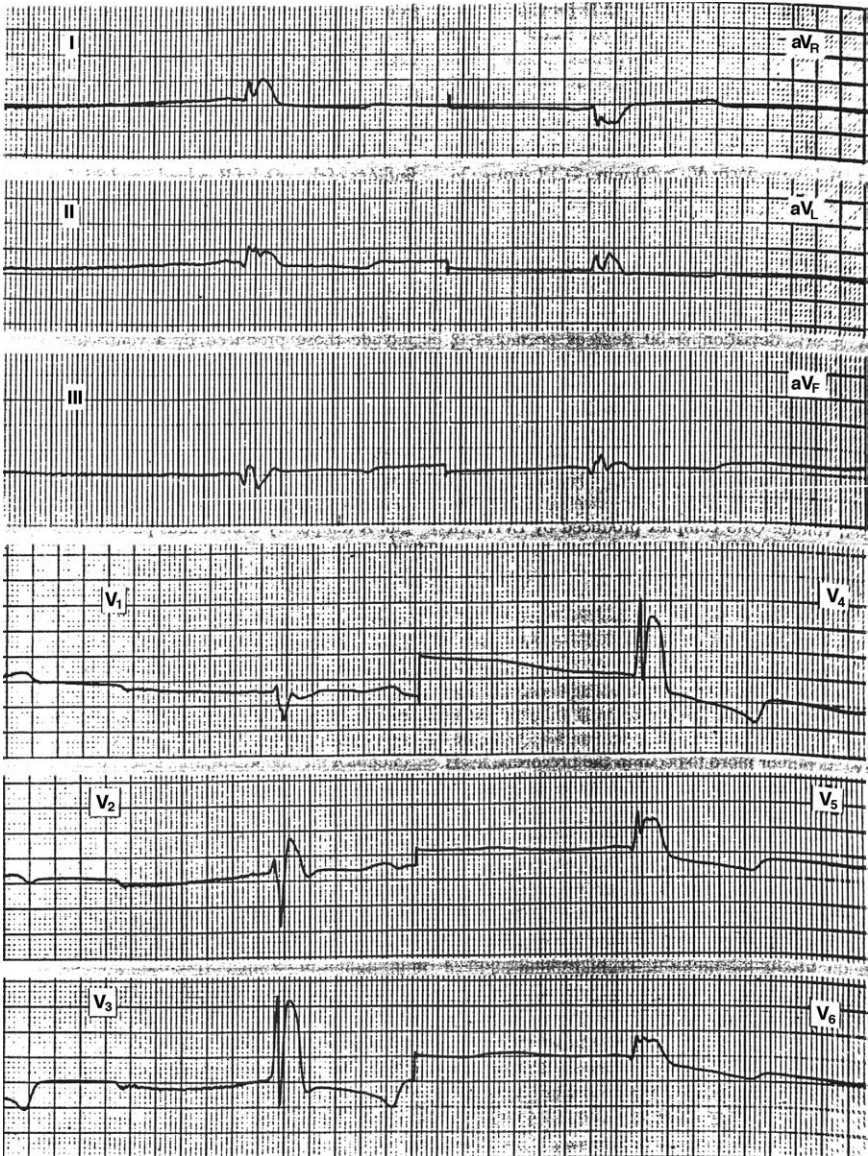
Fig. 1. ECG with J waves.

Laboratory evaluation

Laboratory evaluation of hypothermic patients might demonstrate numerous abnormalities that must be considered in the context of current acute and chronic conditions. Arterial blood gas analysis will commonly reveal evidence of acidemia. Metabolic acidosis develops secondary to

decreased tissue perfusion and subsequent accumulation of lactic acid. Respiratory acidosis is often present as decreased respiratory effort occurs because of central nervous system depression and frequently associated ingestions and intoxications. Previously it was believed that temperature correction was necessary for analysis of arterial blood samples [26], but numerous studies have indicated that the uncorrected values might have greater value in the assessment of actual acid–base status [27]. The patient's hematocrit might be elevated as a result of decreased plasma volume. As an accepted rule of thumb, the hematocrit should increase 2% for each degree C decrease in core temperature. In the setting of moderate to severe hypothermia, a normal hematocrit should raise concerns for acute blood loss or preexisting anemia. Serum electrolyte levels are important when monitoring hypothermic patients, although the patient's preexisting physiologic status, the severity and duration of hypothermic exposure, and the method of rewarming also have significant influence on measured levels. Therefore, previous studies have been unable to describe any consistent trend in electrolyte levels during rewarming [28]. Hypokalemia is the most frequent electrolyte abnormality associated with persistent hypothermia. The decreased potassium level results from an increase influx of potassium into muscle cells rather than from an increase in renal secretion [4]. Blood urea nitrogen and creatinine are poor indicators of the patient's true renal status because hypothermic fluid shifts and decreased renal perfusion often occur. Blood sugar levels might increase in acute hypothermia as a result of catecholamine-induced glycogenolysis and decreased insulin release. Hypoglycemia occurs in the setting of subacute or chronic hypothermia. Hypothermic coagulopathies commonly occur, particularly in association with major trauma [29]. The cause of coagulopathy appears to be multifaceted. Catecholamine surges, circulatory collapse, and release of tissue thromboplastin have deleterious effects on clotting. The clinical presentation is similar to disseminated intravascular coagulation. Hypothermia-induced thrombocytopenia, which is more common in very young and very old patients, is thought to be secondary to bone marrow suppression and or splenic and hepatic sequestration.

Rewarming techniques

The choice of rewarming techniques depends on the severity of hypothermia, the hemodynamic status of the patient, and the availability of specialized personnel and equipment.

Passive external rewarming

Passive external rewarming consists of placing the patient in a warm, dry environment after removal of wet clothing. The patient is covered with blankets. This method is sufficient for hemodynamically stable patients who have mild hypothermia (ie, a core temperature $> 32°C$) and can be expected to raise the core temperature approximately 0.5°C to 2°C per hour.

Active external rewarming

A combination of heating blankets and radiant heat from a light source or a forced heated air system is employed for moderate hypothermia (28–32°C). This technique can encumber access to the patient and should not be used for patients who have potential compromise of their airway and hemodynamic status. The trunk is warmed preferentially to the extremities to avoid the risk of a paradoxical core temperature decrease, which theoretically is caused by the return of cold, acidemic blood to the core circulation from the periphery. This ostensible phenomenon appears to be of minimal clinical importance and is based on descriptions of individual case reports. Heating blankets have been demonstrated to raise the core temperature at a rate of 0.8°C per hour.

Active core rewarming

Active internal rewarming techniques are the most effective and rapid methods of raising the core temperature. In the case of extracorporeal rewarming with cardiopulmonary bypass, the temperature can rise at a rate of 1°C to 2°C every 5 minutes. This is the modality of choice for patients in cardiopulmonary arrest because circulation is supported by a pump. Cardiopulmonary bypass is indicated in the following situations: (1) cardiac arrest or hemodynamic instability with a temperature of less than 32°C, (2) no response to less invasive techniques, (3) completely frozen extremities, and (4) rhabdomyloysis with severe hyperkalemia. A 47% long-term survival rate was obtained in a Swiss study of 32 young, otherwise healthy individuals including mountain climbers, hikers, and victims of suicide attempts [30]. Cardiopulmonary bypass is unlikely to confer similar benefit in an older, poorly conditioned population with underlying chronic disease. Similar rewarming rates have been obtained with hemodialysis, which is ideal for treating accompanying hyperkalemia and renal failure. Arteriovenous or venovenous catheters can be placed for this purpose with the creation of an artificial fistula. Other less aggressive (but also less effective) methods of active internal rewarming include infusion of warmed intravenous fluids, warmed supplemental oxygen, irrigation of the mediastinum by way of thoracostomy tubes, peritoneal lavage, and irrigation of the stomach and bladder.

Localized cold injury

Current scientific knowledge suggests that localized cold injury represents a continuous spectrum ranging from minimal to severe tissue destruction and loss. Frostbite is the primary subject of this discussion because it represents the most serious, limb-threatening extreme along this spectrum. Localized cold injuries are largely preventable if proper care and preparation is exercised in managing environmental factors. Proper preparation for outdoor winter activity in terms of clothing, nutrition,

and shelter are important preventive measures. The most susceptible body parts are located farthest from the body's core and include the hands, feet, earlobes, nose, and male genitalia. These apical structures are rich in arteriovenous anastomoses that shunt blood away from peripheral tissue when necessary. There is no predilection for cold injury based on gender; however, alcohol intoxication, homelessness, and major psychiatric disorders remain important predisposing factors. Localized cold injury now occurs most commonly in participants in winter outdoor recreational and sports activities [31]. Direct exposure of skin and wearing constricting clothing such as tight-fitting footwear predispose to frostbite. Assuming a cramped position for a prolonged period of time, trauma resulting in inability to move extremities, and prolonged vibration injury (eg, tightly gripping the handles of a snowmobile) lead to soft tissue swelling, impaired circulation, and a higher incidence of cold injury.

Types of injuries

Specific terminology has been applied to nonfreezing localized cold injuries depending on whether the ambient environment during exposure was wet (trench or immersion foot) or dry (pernio or chilblains). Trench or immersion foot follows exposure to wet cold for 1 to 2 days with ambient temperatures above freezing. This injury was common among soldiers in the first and second World Wars and during the Vietnam conflict [32]. The skin remains inflamed and painful to touch upon rewarming. Pain with ambulation, cold sensitivity, and hyperhidrosis might persist for an extended period of time after the initial injury. Pernio or chilblain follows prolonged exposure of an extremity to dry, cold temperatures and is most commonly seen in mountain climbers. Frostnip is a precursor to frostbite, and produces reversible skin changes including blanching and numbness. Tissue injury does not occur, but it is important to treat frostnip early to avoid progression to full-blown frostbite.

Pathophysiology

During cold exposure, the core temperature is protected at the expense of peripheral structures to maintain the viability of critical organs. Peripheral vasoconstriction and capillary shunting maintain core homeostasis, and peripheral tissues can potentially reach subzero temperatures and freeze as a consequence. Nerve and muscle tissues are more sensitive to cold injury than connective tissue (eg, ligaments and tendons) [33]. The basic pathophysiologic mechanism of cold injury is direct cellular toxicity and progressive microvascular thrombosis.

Exposure to 15°C results in maximal vasoconstriction and interruption of blood flow. Accompanying dehydration reduces blood flow to the skin and limbs. Progressive cooling to 10°C produces intermittent paradoxical vasodilatation, which is also known as the "hunting response." These

periods of vasodilatation last between 5 and 10 minutes and serve to protect exposed tissue against uninterrupted ischemia. It has been noted that individuals of Nordic origin (eg, Lapps and Eskimos) demonstrate a more pronounced "hunting response" than inhabitants of the tropics [34]. With further cooling below 10°C, the paradoxical vasodilatation stops and formation of extracellular ice crystals causes vasoconstriction of venules and subsequently of arterioles. Capillary circulation slows secondary to vasospasm and increased blood viscosity, which eventually leads to shunting of peripheral blood to the core. Water exits cells into the extracellular space to promote the progressive formation of ice crystals. Freezing disrupts endothelial cell integrity in particular because of the extreme susceptibility of these cells to cold injury. The intracellular fluid eventually becomes markedly hypertonic, which contributes to loss of cellular integrity, exposure of the endothelial cell basement membrane, and circulatory stasis. Progressive microvascular thrombosis and embolization eventually result in tissue hypoxia and advancing dermal injury in otherwise viable cells. Robson studied the blister fluid from frostbitten hands and found markedly elevated levels of prostaglandin F2a and thromboxane, which are known to cause vasoconstriction, platelet aggregation, and leukocyte adhesion [35]. The importance of these mediators of tissue inflammation and tissue destruction in frostbite has not been established.

Evidence suggests that while the direct cold injury is usually reversible, permanent tissue damage actually occurs during rewarming. Despite vigorous thawing, viable vasculature can develop progressive microvascular thrombosis and will remain distorted and susceptible to platelet and erythrocyte aggregation. The interface between normal and injured tissue remains prone to severe vasoconstriction and arteriovenous shunting after thawing. Tissue edema develops during the first 2 to 3 days after initial thawing, followed by the development of thrombosis, infiltration of leukocytes, and early signs of gangrene and necrosis. Partial thawing and refreezing is responsible for the most recalcitrant injuries because repetitive freeze–thaw cycles result in progressively severe thrombosis and vessel damage. Proliferation of the vascular intima and degeneration of the tunica media eventually cause localized vasculitis of involved tissue.

Physical examination

Initially, skin involvement appears deceptively benign until blanching develops and a "stinging" or "burning" sensation is noted by the patient. The coloration can range from white or pale yellow to a mottled, purplish hue. With progressive cooling, the exposed tissue becomes insensate and the patient may lose coordination when limbs are involved. The severity of anesthesia is an early indication of the severity of injury and is caused by ischemia and neuropraxia. Severely affected skin feels waxy and is immobile over joints and bony protuberances.

A functional classification scheme that is based primarily on the probability of eventual tissue loss has gained acceptance in recent years. Superficial frostbite is confined to the skin and subcutaneous tissues and does not result in tissue loss. Exposed skin exhibits pallor and edema, and clear blisters typically develop in the first 24 to 48 hours. Deep frostbite also involves muscle, bones, and joints and causes tissues to feel "stony" or "woody." Hemorrhagic blisters may develop 1 to 3 weeks after deep exposure (Fig. 2). On thawing, edema and severe pain develop, which eventually can progress to gangrene and ulceration. In contrast to other forms of gangrene, frostbite causes a superficial partial-thickness eschar that does not fully demarcate for at least 3 to 4 weeks [36] followed by autoamputation of nonviable tissue. When this process is complete, injured tissue will eventually be replaced by normal-appearing skin that is often hypersensitive.

Fig. 2. Progression of deep frostbite in 47-year-old man who had deep frostbite of the hands after falling asleep outdoors on a cold, wintry night. (*A*) Clear blisters developed 36 hours after initial exposure. (*B*) Blisters have broken and desquamation has occurred 2 weeks later. (*C*) Gangrene developed 4 weeks later. The patient eventually lost the distal aspects of all fingers down to the proximal interphalangeal (PIP) joints.

Fig. 2 (*continued*)

Prehospital care

As an initial step the patient must be removed from the cold environment and protected with proper shelter. Wet clothing should be removed and the involved area must be insulated from the cold. Multiple victims can potentially help each other by warming involved areas against the unaffected body parts of a partner. Exposed skin should be covered, and the hands can be protected by placement in the patient's axillae or on the abdomen under dry garments. Exercising the exposed body part may have the beneficial effect of causing vasodilatation. Vigorous rubbing and massage are to be avoided, however, because they can potentially exacerbate the impairment. Injured tissue should not be exposed to dry heat during transport because of the potential for partial thawing followed by refreezing, which merely exacerbates the initial damage [37]. Rewarming should be attempted in the field only if it can be ensured that refreezing will not occur en route to definitive care or if evacuation is expected to be delayed significantly.

Treatment

The optimal definitive treatment is rapid rewarming by immersion of the involved area in 40°C to 42°C (104–108°F) circulating water for 15 to 30 minutes [38]. This approach was initially proposed by Mills based on extensive experience from Alaska [2,36]. Rewarming is now universally accepted as initial treatment of choice, and the process should continue until capillary refill returns and the tissue is supple. Normal sensation will not return for several weeks, until tissue healing is complete. The sensory examination should not, therefore, be used as a gauge for terminating rewarming. Use of dry or excessive heat is potentially harmful because it predisposes tissues to liquefaction necrosis and subsequent bacterial infection. The benefits of other therapeutic interventions have not been demonstrated in experimental studies. Intact, clear, hemorrhagic blisters should not be disrupted unless they interfere with the patient's functional

status. Surgical debridement or needle aspiration of the blisters does not appear to confer a therapeutic benefit over conservative management. The presence of hemorrhagic fluid reflects damage to the underlying subdermal vascular plexus. It is therefore particularly important to leave them intact to avoid further damage and dessication of the microvascular network and surrounding viable tissue. Aggressive analgesia is indicated during rewarming because it can be an intensely painful process [39]. Patients who have a combination of frostbite and hypothermia are typically dehydrated because of decreased oral intake and cold-induced diuresis. Intravenous hydration with crystalloid will theoretically reduce blood viscosity and capillary sludging [40]. Topical antibiotics and tetanus prophylaxis should be instituted as indicated for a potentially contaminated skin wound [41].

In the post-thaw phase, injured tissue should be handled gently and covered with dry, sterile dressings, which must be loose, noncompressive, and nonadherent. Hands and feet should be splinted and elevated to reduce edema, and the digits must be separated by protective sterile cotton gauze. Compartment pressures should be monitored frequently to facilitate early diagnosis and intervention for impending compartment syndrome. Loss of sensation is not a discriminating measure of compartment pressure. Fasciotomy is rarely indicated in the acute management of the patient. Whirlpool therapy should be instituted on a daily basis and continued until the eschar begins to slough. This practice, combined with physical therapy, will help patients recover full mobility and coordination of the involved extremities.

Early experimental evidence suggested that thromboxane and prostaglandins played an important role in the etiology of cold injury. Inhibitors of these agents were therefore advocated for use in severe frostbite patients with preservation of the dermal microcirculation as the ultimate goal. Topical and systemic antiprostanoid and antithromboxane agents with specific inhibitory effects on the biosynthetic pathway for prostanoic acid were combined in one experimental study [42]. Topical aloe vera or methylprednisolone were combined with oral ibuprofen (systemic antiprostaglandin agent), methimazole, or acetylsalicylic acid. Administration of these topical and systemic agents was associated with significant improvement in tissue viability in an animal model, but these favorable results have not been duplicated in human trials. In one experimental series thromboxane inhibition with methimazole did not improve tissue survival [43]. Topical aloe vera has also not been proven to improve tissue viability [44]. Steroids and nonsteroidal anti-inflammatory agents have not been conclusively demonstrated to offer therapeutic benefit.

Adjunctive agents such as thrombolytic agents, low molecular weight dextran, and anticoagulants have been used with the goal of restoring blood flow and increasing tissue survival [45,46]. Phenoxybenzamine provides long-acting α blockade and decreases vasospasm, which is of theoretical benefit in frostbite [47]. These agents have been used to prevent progressive thrombosis, but their clinical effectiveness remains questionable. Early

surgical intervention is not indicated because differentiation between viable and nonviable tissue does not begin until a minimum of 2 to 5 days after the exposure. Ultimate tissue loss will eventually be demarcated after 3 to 4 weeks, after which time surgical intervention may be indicated. Regional sympathectomy has not been proven to be beneficial in the acute setting, but it may be indicated for the relief of intolerable chronic sequelae.

Prognosis

Early intervention is critical in terms of ultimate outcome. Delay in seeking medical care for more than 24 hours is associated with an 85% likelihood that surgical intervention will be required. Patients who present within the first 24 hours require surgery in less than 30% of cases. The predictive value of the initial physical examination is limited; however, the presence of nonblanching cyanosis, hemorrhagic blisters, and impaired sensation appear to indicate a poor prognosis [48].

Attempts have been made to predict eventual tissue viability based on radiographic imaging techniques, but the results do not typically affect management decisions. Technetium pertechnetate bone scanning does not consistently correlate with eventual demarcation because absence of radionuclide uptake does not necessarily indicate infarction or the need for amputation, even when performed 10 days after injury [49]. Hyperemia indicates mild ischemia, whereas absent blood flow is diagnostic for severe circular compromise. Angiography, duplex ultrasound, and plethysmography have been employed with varying degrees of success. Magnetic resonance angiography can distinguish viable from nonviable tissue before it becomes clinically apparent [50].

Late sequelae of superficial frostbite include cold hypersensitivity (53%), numbness (40%), decreased sensation (33%), and impaired ability to work (13%) [51]. Deep frostbite is additionally accompanied by cold sensitivity (80%), skin color changes (75%), hyperhidrosis (60%), pain on use (40%), hyperkeratosis and ulcerations (35%), hyperesthesia (25%), and pain at rest (15%). A chronic syndrome resembling reflex sympathetic dystrophy develops in some cases. Frostbite arthritis is a well described, but fortunately rare, consequence of severe exposure.

Summary

Hypothermia and localized cold injuries are largely preventable with proper preparation for activities in cold environments. Proficient field management is crucial to the final outcome in terms of function and viability because proper care is vital to preventing exacerbation of the initial exposure and injury. Rapid rewarming is optimal when further cold exposure can be avoided reliably. Repetitive freeze–thaw cycles are associated with increased morbidity and tissue loss caused by progressive

microvascular injury and thrombosis. The subsequent care is largely supportive and consists of wound care and physical and hydrotherapy to promote optimal functional recovery.

References

[1] Larrey DJ. Memoirs of military surgery, Vol. II. Baltimore: Joseph Cushing; 1814. p. 156–64.
[2] Mills WJ. Frostbite: a discussion of the problem and a review of an Alaskan experience. Alaska Med 1973;15:27–47.
[3] Danzl DF, Pozos RS, Hamlet MP. Accidental hypothermia. In: Auerbach PS, editor. Wilderness medicine. Management of wilderness and environmental emergencies. 3rd edition. St. Louis (MO): Mosby; 1995.
[4] Francis TJR. Non-freezing cold injury: a historical review. J R Nav Med Serv 1984;70:134.
[5] Rango N. Exposure-related hypothermia in the United States, 1970–79. Am J Public Health 1984;74:1159–60.
[6] Jolly BT, Ghezzi KT. Accidental hypothermia. Emerg Med Clin N Am 1992;10:311–27.
[7] Taylor AJ, McGwin G, Davis GG, Brissie RM, Holley TD, Rue LW. Hypothermia deaths in Jefferson County, Alabama. Inj Prev 2001;7:141–5.
[8] Nozaki R, Ishibashi K, Adachi N, et al. Accidental profound hypothermia [letter]. N Engl J Med 1986;315:1680.
[9] Myers RAM, Britten JS, Cowley RA. Hypothermia: quantitative aspects of therapy. JACEP 1979;8:523–7.
[10] Blum FC, Veach J. Hypothermia and frostbite. In: Howell JM, editor. Emergency medicine. 1st edition. Philadelphia: WB Saunders; 1998. p. 1574–84.
[11] Tikuisis P, Eyolfson DA, Xu X, et al. Shivering endurance and fatigue during cold water immersion in humans. Eur J Appl Physiol 2002;87:50–8.
[12] Kirkpatrick AW, Chun R, Brown R, Simons RK. Hypothermia and the trauma patient. Can J Surg 1999;42:333–43.
[13] Reuler JB. Hypothermia: pathophysiology, clinical setting, and management. Ann Intern Med 1978;89:519–27.
[14] White JD. Hypothermia: the Bellevue experience. Ann Emerg Med 1982;11:417–23.
[15] Shields CP, Sixsmith DM. Treatment of moderate-to-severe hypothermia in an urban setting. Ann Emerg Med 1990;19:1093–7.
[16] Segar WE. Effect of hypothermia on tubular transport mechanism. Am J Physiol 1956;185: 528.
[17] Rose BD. Clinical physiology of acid–base and electrolyte disorders. 2nd edition. New York: McGraw-Hill; 1984.
[18] Danzl DF. Accidental hypothermia. In: Rosen P, Barkin R, editors. Emergency medicine: concepts and clinical practice. 4th edition. St Louis (MO): Mosby; 1998. p. 963–86.
[19] Elenbass RM, Mattson K, Cole H, et al. Bretylium in hypothermia-induced ventricular fibrillation in dogs. Ann Emerg Med 1984;13:994–9.
[20] Graham CA, McNaughton GW, Wyatt JP. The electrocardiogram in hypothermia. Wilderness Environ Med 2001;12:232–5.
[21] Ozaki H, Nagai Y, Tochihara Y. Physiologic responses and manual performance in humans following repeated exposure to cold at night. Eur J Appl Physiol 2001;84:343–9.
[22] Mathew CB, Bastille AM, Gonzalez PR, et al. Heart rate variability and electrocardiogram waveforms as predictors of morbidity during hypothermia and rewarming in rats. Can J Physiol Pharmacol 2002;80:925–33.
[23] Mattu A, Brady WJ, Perron AD. Electrocardiographic manifestations of hypothermia. Am J Emerg Med 2002;20:314–26.

[24] Vassallo SU, Delaney KA, Hoffman RS, et al. A prospective evaluation of the electrocardiographic manifestations of hypothermia. Acad Emerg Med 1999;6:1121–6.

[25] Yan G-X, Antzelevitch C. Cellular basis for electrocardiographic J wave. Circulation 1996; 93:373–9.

[26] Kelman GR, Nunn JF. Nomograms for correction of blood pO_2, pCO_2, pH and base excess for time and temperature. J Appl Physiol 1966;21:1484–90.

[27] Cohen DJ, Cline JR, Lepinski SM, et al. Resuscitation of the hypothermic patient. Am J Emerg Med 1988;6:475–8.

[28] Ferguson J, Epstein F, Van de Leuv J. Accidental hypothermia. Emerg Med Clin North Am 1983;1:619.

[29] Patt A, McCoskey BL, Moore EE. Hypothermia-induced coagulopathies in trauma. Surg Clin N Am 1988;68:775.

[30] Walpoth BH, Walpoth-Aslan BN, Mattle HP, et al. Outcome of survivors of accidental deep hypothermia and circulatory arrest treated with extracorporeal blood warming. N Engl J Med 1997;337:1500–5.

[31] Hauty MG, Esrig BC, Hill JE, et al. Prognostic factors in severe accidental hypothermia: experience from the Mt. Hood tragedy. J Trauma 1987;27:1107–12.

[32] Hamlet MP. An overview of medically related problems in the cold environment. Mil Med 1987;152:393–6.

[33] Kennett RP, Gilliatt RW. Nerve conduction studies in experimental non-freezing cold injury: I. Local nerve cooling. Muscle Nerve 1991;14:553–62.

[34] McCauley RL, Smith DJ, Robson MC, et al. Frostbite and other cold-induced injuries. In: Auerbach PS, editor. Wilderness medicine. Management of wilderness and environmental emergencies. 3rd edition. St Louis (MO): Mosby; 1995. p. 129–45.

[35] Robson MC, Heggers JP. Evaluation of hand frostbite blister fluid as a clue to pathogenesis. J Hand Surg 1981;6:43–7.

[36] Mills WJ, Whaley R, Fish W. Frostbite: experience with rapid rewarming and ultrasonic therapy. Part III. Alaska Med 1993;35:19–27.

[37] Kyosola K. Clinical experiences in the management of cold injuries: a study of 110 cases. J Trauma 1974;14:32–6.

[38] Malhotra MS, Mathew L. Effect of rewarming at various water temperatures in experimental frostbite. Aviat Space Environ Med 1978;49:874–6.

[39] Punja K, Graham M, Cartotto R. Continuous infusion of epidural morphine in frostbite. J Burn Care Rehab 1998;19:142–5.

[40] Purdue GF, Hunt JL. Cold injury: a collective review. J Burn Care Rehab 1986;7: 331–42.

[41] Didlake RH, Kokokra JS. Tetanus following frostbite injury. Contemp Orthop 1985;4:784.

[42] Heggers JP, Robson MC, Manavalen K, et al. Experimental and clinical observations on frostbite. Ann Emerg Med 1987;16:1056–62.

[43] Goldberg BD, Robinson WA, Watson WA. Impact of delayed presentation on the efficacy of thromboxane inhibition in the treatment of frostbite. J Wilderness Med 1994; 5:325.

[44] Heggers JP, et al. Frostbite: experimental and clinical evaluations of treatment. J Wilderness Med 1990;1:27.

[45] Zdeblick TA, Field GA, Shaffer JW. Treatment of experimental frostbite with urokinase. J Hand Surg 1988;13:948–53.

[46] Skolnick AA. Early data suggest clot dissolving drug may help save frostbitten limbs from amputation. JAMA 1992;267:2008–10.

[47] Lazarus HM, Hutto W. Electric burns and frostbite: patterns of vascular injury. J Trauma 1982;22:581–5.

[48] Biem J, Koehncke N, Classen D, et al. Out of the cold: management of hypothermia and frostbite. CMAJ 2003;168:305–11.

[49] Bhatnagar A. Diagnosis, characterisation and evaluation of treatment response of frostbite using pertechnetate scintigraphy: a prospective study. Eur J Nucl Med Mol Imaging 2002; 29:170–5.

[50] Barker JR, et al. Magnetic resonance imaging of severe frostbite injuries. Ann Plast Surg 1997;38:275.

[51] Ervasti O. Sequelae of moderate finger frostbite as assessed by subjective sensations, clinical signs and thermophysiological responses. Int J Circumpolar Health 2000;59: 137–45.