Chapter 14

CLINICAL ASPECTS OF FREEZING COLD INJURY

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INTRODUCTION

Military medical officers need to be aware of the various modes of freezing cold injury (FCI), or frostbite, because it has been a persistent problem over the ages, usually associated with mountain warfare; winter military campaigns; or the civilian catastrophe of deprivation of shelter, food stocks, and warm clothing in the wake of military conquest (Exhibit 14-1). In addition, natural calamities (such as famine, earthquake, pestilence, flood, and fire) have left many communities exposed to harsh winters, resulting in FCI. FCI due to altitude exposure has occurred worldwide; the injury is often associated with freeze-thaw-refreeze injury, or with hypothermia, mountain sickness, and cerebral or pulmonary edema.

To the various cold-weather activities on Earth we now have added space exploration. In spring 1993 this author had occasion to consult with and share the treatment of an astronaut who froze his fingers at –143°F in a simulated space chamber and space walk. Even lower temperatures may be anticipated in that environment. With the advent of men and machines into space, further exposure to extremes of temperatures, greater than those on Earth, are expected. As the explorations of man continue into the wilderness throughout the world,

EXHIBIT 14-1

MILITARILY RELEVANT MODES OF FREEZING INJURY

1. True freezing cold injury (FCI, also called frostbite), superficial or deep.
2. A mixed injury: immersion (cold–wet) injury (as in trench foot) followed by FCI. The result is often disastrous, with great tissue loss.
3. Freeze–thaw–refreeze injury, wherein freezing is followed by thawing at any temperature or by any method, followed by subsequent refreezing. This is also a disastrous event with total tissue destruction and early mummification of distal tissues, often within 5 to 7 days, even earlier.
4. High altitude environmental freezing; this injury is associated often with hypoxia, accompanied by hypovolemia, dehydration, and extremity freezing. The prognosis is poor if associated with other trauma. An interesting aspect of altitude injury occurs in mountain climbers wearing neoprene stockings with tightly laced boots. At high altitudes (eg, 3 15,000 ft on Mount McKinley) the atmospheric pressure is halved. This allows expansion of gases in cellular foot covering so that in a tight boot, often double-layered, expansion outward is blocked and the pressure is then directed downward against the foot, cutting off circulation and permitting a freezing injury. The ambient temperature at altitude decreases approximately two Centigrade degrees (3.5°F) for every 1,000 ft of increase in altitude. The temperature becomes stable at about –55°C (–67°F) at an altitude of 35,000 ft or higher, and exposure to these very low temperatures may instantaneously result in severe injury to exposed body parts.
5. Extremity compartment compression from any cause, followed by freezing. Very poor results follow if the compartment pressures are not relieved by medical or surgical means.
6. Extremity fractures or dislocations followed by freezing. The final result is poor if the fracture dislocation is left unreduced. The best results follow rapid rewarming.
7. Hypothermia, associated with superimposed FCI of the extremities. Paramount importance is given to restoration of heat in the victim, under total physiological control and monitoring. Best results for FCI appear to be associated with tub rewarming of hypothermia and simultaneous thawing in warm water of the frozen extremity. The danger here is a sudden release of metabolites and the release of excessive amounts of potassium from muscle degradation and injury, which may cause cardioplegia. The immediate balance of electrolytes and the restoration of normal pH levels is imperative. The excellent method of rewarming with peritoneal dialysis may require almost simultaneous warming of the frozen extremity by other means.
8. FCI with superimposed burn injury, or burn injury with superimposed FCI. In addition to military casualties, medical officers may also see civilians whose cold injuries are perhaps confounded by their age or previously existing conditions:
9. Freezing injury in children often results in epiphyseal necrosis. So fragile is the epiphyseal plate of small children that very little exposure time or lowered temperature is required to cause epiphyseal damage.
10. Freezing superimposed on small vessel disease, as found in diabetes or peripheral vascular disease.
11. Congenital deformity of hands or feet associated with neurovascular deficit and superimposed freezing.

searching for oil, minerals, and the bounty of the oceans, it is more appreciated that hypothermia, immersion injury (now called nonfreezing cold injury [NFCI]), and FCI are injury risks of those who work and live in the arctic and subarctic areas, including the circumpolar sea of the Arctic and Antarctic oceans and the cold northern seas of the Atlantic and Pacific oceans.

The Experience of Larrey

There probably is no better introduction to a chapter on FCI than excerpts from the *Surgical Memoirs of the Occupation of Russia, Germany and France*, by Baron Dominique Jean Larrey. The writings of Baron Larrey, Chief Surgeon of Napoleon's Grande Armée, indicate his distrust of warming by heat, and his opinion held sway in Europe and America for well over 100 years. One of the pillars of the "modern" thawing technique of the frozen extremity has been and is rapid rewarming in warm water (37.7°C–41°C; 100°F–106°F). It was not always so.

In his memoirs regarding the French army's advance and retreat during the Russian winter campaign (1812/13), Larrey writes:

> Persons were seen to fall dead at the fires of the bivouacs—those who approached the fires sufficiently near to warm frozen feet and hands, were attacked by gangrene, in all points, where the vital powers had been reduced. These fatal occurrences mutilating the majority of our soldiers, threw them into the power of the enemy—unfortunate was the fate of him, who, with his animal functions nearly annihilated and his external sensibility destroyed by the cold, should suddenly enter too warm a room, or approach too near a large bivouac fire. The projecting parts of the body, grown insensible or being frozen and remote from the center of circulation, were attacked with gangrene which manifested itself at the same moment, and was developed with such rapidity, that its progress was susceptible to the eye—or else the individual was suffocated by a sort of turgescence, that apparently invaded the pulmonary and cerebral systems. The individual perished in a state of asphyxia.[1(p83)]

Larrey continues:

> It will easily be conceived, after what I have just said, why, in mortification of some external part of the body, caused by cold, instead of submitting it to heat, which provokes gangrene, it is necessary to rub the affected part with substances containing very little caloric, but which may absorb a good deal at the moment of their melting, and transmit it to the frozen part by rubbing. For it is well known that the effect of caloric on an organized part, which is almost deprived of life, is marked by an acceleration of fermentation and putrefaction. Before pointing out the means to be employed, let us succinctly describe the symptoms which characterize congelation [freezing]. The part laboring under this affection is whiter than other parts of the surface of the body; all its sensibility is extinct and the individual has no longer any sensation in it. [Even today, an excellent description of the frozen part.—W.J.M.][1(p84)]
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> Snow and ice are the substances, to which recourse should be had, for the first application. Dry frictions also, are very serviceable, and should always be made with substances which possess but little heat. I employed no other means for defending myself from gangrene affections, which would at least have taken place in my toes and fingers, for they were frequently deprived of all sensibility. In this state, I took care to rub the affected parts with snow, and continued, as much as possible, the use of these or dry frictions.
>
> Should these remedies fail, the part ought to be plunged in cold water, in which it should be bathed, until bubbles of air are seen to disengage themselves from the congealed part. This is the process, adopted by the Russians, for thawing a fish. If they soak it in warm water, they know from experience, that it will become putrid in a few minutes; whereas, after immersion in cold water, it is as fresh as if it had just been caught.[1(pp84–85)]

Larrey further comments that

> [n]ot even the overwhelming Russian forces, nor the distances traveled in the retreat, caused so much problem as the weather. The most cruel sufferings experienced in our retreat (from Moscow) were undoubtedly cold and hunger.[1(p76)]

In addition, he gives notice to the fact that

> not far from the situation in which we endured

Fig. 14-1. *The Crossing of the Berezina River, 26 November 1812.* Watercolor by an anonymous artist; attributed elsewhere to General Fournier-Sarloveze, a participant in the action. Harassed by the enemy, overwhelmed by cold, the remnants of the summer campaign of Napoleon's Grande Armée retreated from Moscow in the fall of 1812; many attempted to swim the Berezina River, falling victim to hypothermia as well as extremity freezing. Thousands of French soldiers perished from starvation, dehydration, hypothermia, and freezing; and from unrelenting Cossack attacks on their flanks. The Grand Armée lost more than 80% of its remaining troops, one of winter's greatest triumphs over a military force. Reproduced with permission from Musée de L'Armée, Paris, France.

> so many hardships, Charles the XII of Sweden, a hundred years before the French debacle of 1812–13, lost an entire division of his army, in consequence of those two united causes, hunger and cold.[1(pp79–80)]

In retrospective evaluation, Larrey's comments concern men who were constantly harassed by the enemy, overwhelmed by freezing weather, hungry, emaciated, and without shelter or adequate clothing—and who certainly were hypovolemic, dehydrated, and in various states of hypothermia, often with severe peripheral extremity freezing. Regardless of current thought, Larrey's graphic, descriptive passages on the plight of soldiers at bivouac fires, written almost 2 centuries ago, state resoundingly that no more disastrous event occurs to the frozen extremity than thawing with excessive heat, with perhaps one exception. The catastrophe following thawing with excessive heat is matched only by a further event common in retreating or disorganized, beaten armies: that of freezing, then thawing by any means, followed by refreezing.[2–7] For a military surgeon, or anyone in a leadership position, no better instructional course on the tragic freezing disasters of winter warfare exist than the memoirs of Larrey, in his description of the invasion of Russia with a French army of more than 400,000 men and its subsequent destruction during the famed retreat from Russia, the French losing nearly 80% of the 100,000 men who survived to retreat from Moscow (Figure 14-1).

Implications for the Future

It comes as no surprise then, that in the same Russian area, more than 130 years after the destruction of Napoleon's Grande Armée and more than 200 years after the winter loss of the army of Sweden's Charles XII in the nearby forests of Lithuania (see Chapter 10, Cold, Casualties, and Conquests: The Effects of Cold on Warfare), that in

World War II, a modern, massive German army was roundly defeated in the winter of 1941/42. Failing, as had other armies, to overcome Russian troops and the civilian patriots, the German army's mechanized forces and infantry sustained a major loss of equipment and men to the cold, the Russian winter, and the Russian forces.

An introduction to a chapter on militarily relevant aspects of FCI would seem to permit a viewpoint that troops may fail to avoid cold injury of epidemic proportions due to the destructive forces of nature, encompassing severe lowered temperatures, high winds, deep snow, and extreme cold, all combined with a relentless enemy force. Constant leadership even at the lowest squad level is required to avoid disaster. A major field-rescue problem faces military leaders at every level and all field medical personnel, if the weather; the pursuing enemy; and the lack of food, clothing, and shelter combine to give trouble to an army in retreat.

Avoidance of overwhelming cold disaster obviously favors the winning troops, not those in retreat. Prevention of cold injury is enhanced by forces' being able to stop; establish shelter; provide heat; and dispense food, warm clothing, and proper foot and hand gear. Naturally, a warm army requires leadership and knowledge of cold weather's effects on machines, equipment, and personnel at all levels. Prevention requires outstanding demonstrations of morale, fortitude, and courage for beleaguered troops of all ranks, to prepare for and overcome the lethal developments of cold weather and enemy forces.

Winter weather and its associated freezing temperatures are likely to always be a threat to military forces. Failing their ability to prevent cold injury, it behooves medical and nonmedical personnel alike to understand, under the worst as well as the best circumstances, how to diagnose, treat, and transport the casualty with cold injuries. This is no mean task, as the casualty often has FCI, or immersion injury, or hypothermia with accompanying battle injuries, penetrating or open wounds, or the myriad nonbattle diseases of the local area.

The study and evaluation of hardship and catastrophe, the result of winter wars, may prevent future military disasters and medical complications. Certainly, as in Napoleon's retreat from Russia in the fall of 1812, the destruction of the Grande Armée should be explained so that such a debacle would not be repeated in the future, and the numerous losses to cold by other armies over the centuries be similarly evaluated. For example, Larrey, describing clearly the clinical signs and symptoms of freezing (and what was obviously hypothermia with associated freezing) noted that "men warming near bivouac fires developed early gangrene and those entering warm rooms suddenly died."[1(pp82–83)] We can only hazard a guess that as a frozen extremity usually does not in itself cause "sudden death," it is likely that the casualty was also hypothermic, probably with an electrolyte imbalance and with destruction of muscle as a result of FCI. Any warming then, in an uncontrolled situation without physiological control of electrolytes and acid–base balance, may cause a influx of released potassium into the vasculature from injured muscle cells or cooled tissues, and with the resultant hyperkalemia, the cold-injured soldier would die a victim of cardioplegia.[7,8] In wartime conditions, it will be impossible to carry out the current recommendation: to rewarm cold soldiers in warm water or in tubs or whirlpools. Possibly, if we can restore circulation by spontaneous thawing so as to (1) control the endothelial injury, (2) avoid damage caused by ice-crystal intercellular growth and the subsequent cellular dehydration, and (3) avoid the development of overwhelming thrombosis, we may produce an adequate protocol, particularly for field use. This would obviously require a new form of rapid thawing of the frozen area so that heat can be provided to tissues without tissue destruction.

THE EVOLUTION OF UNDERSTANDING FREEZING COLD INJURY

Advances in General Knowledge From Wartime Experiences

Paton,[9] in an excellent summary of the pathophysiology of frostbite, noted that "frostbite is as old as history itself."[9(p329)] And indeed, as an extensive bibliography demonstrates, particularly during periods of war, cold injury has played a paramount role in the outcome of military operations throughout history. A review of the world's literature on cold injury would indicate the casualties to be literally in the millions, resulting in destruction of tissue, loss of function, neurocirculatory loss, amputation (minor and major), and death.

Wartime experience with cold has advanced our knowledge of cold injury in at least two directions. First, from the varied cold injuries, especially FCI, incurred by massive numbers of troops, much clinical experience resulted, allowing for new, innovative, and comparative treatment regimens. Second, military medical personnel in the field, and clinical and laboratory investigators in research laborato-

ries and hospitals, were given impetus, encouragement, and funding (especially by the Department of Defense and the Office of Naval Research) to provide insight into the etiology, pathophysiology, and treatment of cold problems.

Before World War II and the Korean War, little information regarding the basic physiological response to cold was available to the physiologist or clinician. One reason was the unfortunate fact that in the United States, little clinical or scientific data from Europe, Russia, or Japan were available in translated form. Further, clinicians and physiologists did not as a rule read each others' journals to the extent seen today. Consequently, particularly in the United States, the massive clinical and investigative material from Europe and Asia was little known. For example, until the translated World War II works of Killian (German),[10] Ariev (Russian),[11] and Yoshimura (Japanese)[12] were published in this country, we did not realize that the medical departments of these armies and navies had utilized rapid rewarming for initial thawing for frozen extremities.

The period following World War II and the Korean War found an exciting and rewarding liaison between the clinician in the field and the hospital on the one hand, and the physiologist, biochemist, biophysicist, and cryobiologist on the other. This interchange allowed the clinician to evaluate the results of drug, surgical, and manipulative procedures first performed on laboratory animals, and permitted the physiologist to perform on laboratory animals previously untested surgical or medical procedures that appeared to have promise.[3,13-16]

Highly recommended to the student of cold injury are the texts or monographs summarized below, which form a nucleus of military and civilian research activities. Each explores, reports, and summarizes a concept of pathophysiology and treatment, and a pattern of injury sequelae.

One of history's earliest accounts of an army decimated by cold was that of Xenophon,[17] who in 400 BC led 10,000 Greek soldiers from Sardis to Babylon and back, through the mountains of Armenia, battling the hazards that a retreating and disorganized army faces when pursued by the combined unrelenting foes of severe cold weather and harassing enemy forces. Warmth was obtained by campfire heat; friction massage of the body with greases, oils, and unguents; and preservation of heat by covering up in snow. Amputation and death from exposure was common.

An even more detailed, factual, and vivid description of the effects of cold on a retreating army was related by Larrey,[1] whose memoirs (previously quoted) precisely described FCI and its etiology, including data on general body cooling. Larrey recommended slow rewarming, or delayed warming with ice and snow techniques, and friction massage, all out of favor now although accepted for well over 150 years after his reports. His monograph is replete with the problems of prevention and care involving massive numbers of troops—in an army in which more than 80% of its force perished from cold and cold-related problems. Much can still be gained by a study of this classic. Larrey disapproved of rapid rewarming, and his words discouraged the use of rapid thawing for more than 150 years. He did note the disastrous effect of excessive heat (as has also been documented in 20th-century reports[18]), apparently recognizing that frozen extremities, warmed in close proximity to bivouac fires, sustained a second thermal injury—a burn—with disastrous effect. For the student of FCI, Larrey's monograph is highly recommended.

Monographs of the experience of the military surgeons of modern armies soon appeared following World War II. Whayne and DeBakey,[19] In their official history of the US Army experience in that war,

- pointed out that the lessons of previous wars were poorly understood and often forgotten by military surgeons in World War II;
- reported and discussed the 71,000 cold casualties in the European theater;
- recorded the new syndrome of high-altitude freezing in air crewman (freezing and hypoxia); and
- stated that cold injuries were due to the intensity of combat, wet cold, inadequate clothing, and lack of troop education.

Injuries were to be considered a calculated risk. It was the stated hope of the authors "that if their volume was read well, there would be no need for problems in future wars."[19(pviii)] But as was later found in Korea (1951/52), in the Yom Kippur War in Israel (1973) on the Golan Heights of Syria, and in the Falkland War (1982), weather, enemy action, military demands, and unforeseen events determine the effects of wet and cold.

Killian[10] related the cold problems of the axis forces in World War II with a discussion, still of concern today, of slow as compared to rapid rewarming, the latter being preferred by many German military physicians despite slow-thawing methods being the European dictum. He reminded his readers of van't Hoff's law, which implies

> that under conditions of hypothermia, local or general, metabolic processes are slowed down

> so that oxygen demand of the tissues is reduced, thus prolonged survival of ischemic tissue."[10(p81)]

Much later, Mills described this condition as "being in a metabolic icebox."[7(p58),20(p134),21(p410),22(p10)] He characterized the victim in this condition as in a midlethal state, so that further exposure would result in death, as cooling of vital organs continued without intervention and warming. Warming in this state, however, if not controlled physiologically, would often result in death because of uncorrected acid–base imbalance and electrolyte imbalance, usually acidosis, with hypovolemia and dehydration. Warming of the hypothermic victim, when FCI is also present, may release potassium from increased cell permeability or cell destruction. The often-sudden, high-level hyperkalemia may result in cardioplegia and death. From Russia, Ariev,[11] in a little-known but true classic on cold, reviewed the current European pathophysiology concept, listing the nomenclature for describing cold injury and classification of frostbite, as well as recommending that rapid rewarming be the method of choice in the thawing of FCI. This report was followed by a report from Japan, in which Yoshimura[12] proposed thawing methods similar to those of Killian and Ariev.

A further report of low-temperature investigation, encouraged because of the needs of military surgeons, was Burton and Edholm's classic monograph, *Man in a Cold Environment*.[23] This monograph, sponsored by the Defense Research Board of Canada, originally proposed to review experiences in cold in World War II but was later changed to include all aspects of cold, and is included here as a "must" reference in the field of cold. Viereck[24] edited the proceedings of a US Air Force-sponsored symposium on frostbite in 1964, which brought together clinicians, laboratory investigators, pathologists, and others experienced in cold-related problems. An outstanding textbook edited by Meryman[25] soon followed, which gathered together the works of 18 prominent physiologists, biophysicists, and cryobiologists delving into the theoretical basis of FCI. It is a definitive review and a framework text on the comprehensive background of biological freezing, and it includes studies of the physical and chemical bases of injury in single-cell microorganisms.

In 1975, LeBlanc[26] published another landmark monograph, *Man in the Cold*, unique in that his observations were made primarily on humans rather than laboratory animals. In his section on frostbite, LeBlanc graphically describes the cooling, freezing, and postfreeze states, and reviews data regarding the pathophysiological stages of vascular disturbance, membrane permeability, and postthaw edema formation.

Chronology of Important Investigative Reports and Results

As much of this section consists of a review of our understanding of FCI, it is perhaps pertinent to preface what follows with Meryman's concept of freezing:

> The single most important and fundamental concept in biological freezing is that regardless of the mysterious complexity of the biological matrix, freezing represents nothing more than the removal of pure water from solution and its isolation into biologically inert foreign bodies, the ice crystals.[27(p515)]

With slow freezing, ice-crystal formation is generally confined to the extracellular spaces. Frozen tissue cells may, upon thawing and refreezing, demonstrate uniform intracellular crystallization, with formation of large, destructive crystals of ice. The formation of these large crystals may account for the disastrous freeze-thaw-refreeze injury seen clinically, in which after initial extraction of cellular water, with increased permeability and trauma to cell membranes or endothelial lining of small vessels, a second freeze will affect intracellular supercooled water, resulting in the destruction of the cells.[18] Meryman's concept needs to be borne in mind as the chronology of FCI research is set forth.

The 1930s and 1940s: Supercooling and Tissue Freezing

Love,[28] in his description of freezing phenomena, points out that Koonz and Ramsbottom,[29] working with poultry, proposed in 1939 that tissue initially froze extracellularly. This was so because the freezing point of lymph (equated with extracellular fluid) is higher than that of the cellular fluid. Love concludes that ice first forms outside the cells and is then augmented by intracellular water that diffuses through the cell wall and condenses on the ice surface because of the high osmotic pressure of the extracellular solution, which has been concentrated by freezing. The temperature of the intracellular fluid never falls below its freezing point, because intracellular water is continuously being lost with a corresponding continuous reduction of freezing point.

Karow and Webb[30] further note that pure water cooled below 0°C does not crystallize until a tem-

perature is reached that will permit substances within the water to act as a nucleus for ice formation. The nuclear material may consist of relatively large inclusion bodies, such as colloids; dissolved substances; or it may simply be water molecules clumped together by hydrogen bonds, called microcrystals. Karow and Webb acknowledged Mazur's[18] work, which reported that in slow freezing there is a tendency for water in cells to supercool, as there is a low probability that such a minute volume would contain a nucleation center. At relatively high temperatures (–10°C), extracellular water freezes. As water freezes in the external medium, its vapor pressure drops below that of the still-supercooled intracellular water and thus draws free water from the cells.

Supercooling is defined as the cooling of a substance below the temperature at which a change of state would ordinarily take place, without such a change occurring (eg, the cooling of a liquid below its freezing point without freezing taking place). This results in a *metastable* state, defined as an excited stationary energy state whose lifetime is unusually long. A further example of the state of supercooling is provided by Burton and Edholm reporting on the observations of Sir Thomas Lewis,[31] who states that the freezing point of skin is about –1°C to –2°C, but that supercooling often occurs, during which freezing is not demonstrated until the surface temperature falls to –5°C to –10°C. Lewis further notes that the fat content of the skin affects supercooling. These concepts permit us, then, to define FCI as true tissue freezing that occurs when there is sufficient heat lost in the cooling area to allow ice crystals to form in the extracellular spaces in slow freezing (the usual human freezing event) and the extracellular water.

Blackwood[32] in 1943 and Denny-Brown[33] in 1945 demonstrated microscopic degenerative histologic changes in nerve and muscle in immersion injury as a direct action of cooling. In 1962, Sayen[34] similarly reported the histological changes found after immersion injury and noted that in extending cooling, tissue destruction was more severe and recovery more prolonged, with vacuolization and fragmentation of nerve axons.

Utilizing rabbit ear chambers, Lange[35,36] in 1945, Quintanella[37] in 1947, and Crismon and Fuhrman[38] in 1947 demonstrated that after immediate thawing, ear tissue appears normal, the circulation returns, followed by hyperemia, then massive edema, circulatory slowing, and red cell clumping in the capillaries. Shumacher and colleagues[39–44] investigated the pattern of vascular change and injury following cold insult, and investigated varied drug therapy in an attempt to improve circulation and thawing.

In 1949, Kreyberg[45] entered the controversy as to whether actual freezing of tissue is the lethal event. He considered that low temperatures, whether freezing or not, damage cells and tissues, but that freezing is not as lethal as heat coagulation. He postulated that after the freeze, further tissue damage ensues during the period of thawing, as demonstrated by hyperemia and stasis.

Also in 1949, Scow[46] reviewed the direct effect of cold on tissues of newborn rats, demonstrating remarkable distortion and retardation of growth in limbs and tails. He found cartilage cells to be susceptible to even brief refrigeration and concluded that changes occur as the result of necrosis of cartilage cells that are normally active in skeletal growth. He considered his findings to support the hypothesis that the lethal effects of cold act directly on these cells by altering protein in the cytoplasm and nucleus. In support of these observations, Bigelow[47] in 1963 and Hakstian[48] in 1972 reported that cold can destroy the cartilage of the epiphyseal plate, which may result in digital shortening or angulation deformity of the digits, or joint dysfunction. Lytic destruction of periarticular cartilage and bone have been reported in adults and children.[8]

The 1950s: Extracellular Ice Crystals and Vascular Stasis

In 1951, Lewis[49] similarly demonstrated that degenerative changes in muscle occur almost immediately after exposure to freezing. Later, in 1953, Lewis and Moe[50] studied the effects of rutin, a flavonol glucoside, and Hydergine (ergoloid mesylates; manufactured by Sandoz Pharmaceuticals, East Hanover, NJ), a dehydrogenated ergot vasodilator, to determine their effects on experimental cold injury. Shumacher[42] had also studied the effects of rutin in 1951, demonstrating more beneficial effects in reducing gangrene than had Lewis. Of interest is that both rutin and Hydergine are now considered efficacious in overcoming the effect of free radical injury, which is a likely cause of cell damage after thawing and reperfusion of the vascular system.[51]

In keeping with the military interest in cold injury, Orr[52] reported in 1953 on findings of his cold injury research teams in Japan and Korea during the Korean War. One member of that team, H. T. Meryman (Figure 14-2), a US Navy medical officer, was to go on to become one of the world's leading investigators in cold-related science and cryobiol-

Fig. 14-2. H. T. Meryman, MD, an early proponent of rapid rewarming in warm water for frozen extremities.

ogy. His contributions include the description of the role of extracellular ice formation and cell damage, the effect of extracellular solute concentration, and the methods of ice-crystal nucleation. During the years 1955 through 1957, he presented a lucid explanation of the effect of the rate of freezing (slow or rapid) on cellular biological systems.[25,27,53] His work includes the development of injury classification, the postulation of a time–temperature relation in clinical cold injury, and the presentation of a pattern of ice-crystal formation with the resulting biochemical effects. Meryman summarized the knowledge to that date on the mechanism of slow freezing injury in tissue, namely, extracellular ice crystals, which displace and partially dehydrate soft-tissue cells. While some tissues may be injured or destroyed by this process alone, most tissues passively collapse without significant mechanical injury. However, the removal of water results in high concentrations of electrolytes and other cell constituents, which produce a cumulative injury to the cell. As the temperature falls from the freezing point to between –10°C and –15°C, more water is frozen out, increasing the solute concentration and the potential for injury.

Bellman and Adams-Ray[54] in 1956 and Sullivan and Towle[55] in 1957 investigated vascular response to cold, finding that cold trauma involving rapid freezing, then rapid thawing, injured the tissue less than slow thawing. Other studies[46,56–58] indicated that an increase in the rate of blood flow occurred during the postthaw stage, accompanied by the emergence of many platelet emboli from the area of injury. Stasis was found to begin in the venules, spreading throughout the vascular bed. Hemoconcentration was considered the cause of stasis following local cold injury.

The 1960s: Intracellular Ice and Freeze-Thaw-Refreeze Injury

In 1960, Mills, Whaley, and Fish[3] proposed a total-care system approach, including the avoidance of trauma to the frozen extremity, rapid rewarming in warm water (preferably in a whirlpool bath) at 42°C to 48°C (later changed to 38°C to 42°C). Postthaw whirlpool at 32°C to 37°C was utilized to massage tissue, promote circulation, and dilute the superficial accumulation of bacteria and thus discourage infection. Isotope and enzyme studies were utilized to determine circulatory status, and for early diagnosis of extent of injury. Recognition of the freeze-thaw-refreeze injury was noted, the latter quite possibly a result of intracellular ice formation as a result of the second freeze, and therefore, usually lethal to the affected tissue. The authors also suggested that the time-honored description of first-, second-, third-, and fourth-degree frostbite be changed to a more descriptive clinical diagnosis of *superficial* and *deep* (discussed later).

In 1964, one of cryobiology's pioneers, Luyet,[59,60] published, with his colleagues, observations on the invasion of living tissue by ice, listing three stages of invasion: (1) superficial freezing, (2) intercellular freezing (extracellular spaces), and (3) intracellular freezing. He demonstrated shrinkage of erythrocytes by osmotic differential in extracellular freezing. Also in 1964, Mundth[56] demonstrated platelet clumping soon after thawing, arising from injured endothelium of vessel walls followed by corpuscular aggregation that eventually became occlusive. Mundth recognized that local tissue injury from freezing was associated with local vascular damage after thawing, involving increased endothelial permeability, intravascular cellular aggregation, capillary stasis, occlusion of small vessels by cellular aggregates, and thrombosis. He demonstrated that low molecular weight dextran (MW 41,000), given intravenously prior to freezing, improved tissue survival after freezing by improving capillary

flow and inhibiting corpuscular aggregation.[57] This work was corroborated in 1965 by Anderson and Hardenbergh,[61] but only when test animals were rapidly thawed after freezing.

In 1965, Karow and Webb presented their "Theory for Injury and Survival."[30] They assumed that bound water, in the form of lattices, was essential to cell integrity, especially protein structure and function. Tissue death in freezing seemed to occur primarily as a result of the extraction of bound water from vital cellular structures. This extracted water, incorporated into growing ice crystals, left proteins dehydrated and denatured. Their explanation of why extracellular freezing initially began was that water cooled below 0°C does not crystallize until a temperature is reached that will permit the utilization of substances within the water to act as a center or nucleus for ice formation. That nuclear material may be relatively large inclusion bodies, such as colloids, it may be dissolved substances, or it may be simply water molecules clumped together by hydrogen bonds, the microcrystals.

In 1969, Hanson and Goldman[62] reviewed the etiology of cold injury, with particular reference to injuries of World War I, World War II, and the Korean War, deciding that after review of all data, prediction of the incidence of cold injury was almost impossible. In 1969, Hardenbergh and Ramsbottom[15] confirmed the findings of Mills and colleagues[3–5] that "double freeze" injury (ie, freeze–thaw–refreeze) was indeed more clinically significant, causing much more harm than a single freeze.

In 1969, Knize and colleagues[63] proposed a system for clinical prognosis for tissue loss after frostbite, based on duration and condition of exposure and the lowest temperature reached. In similar fashion, in 1970 Sumner and colleagues[64] developed a prognostic sign based on experiments with dogs that indicated that blood flow in the involved extremity 24 hours after freezing had prognostic significance. Also in 1970, Sumner and a different group of colleagues[65] used xenon 133 to predict the extent of tissue loss in frostbite as early as 10 minutes postthaw. Mills[3-5] and Salini and colleagues[66] in 1986 reported similar prognostic use of technetium 99m pyrophosphate.

The 1970s: Hyperosmolality and Membrane Damage

In 1971, Meryman[16] proposed that hypertonic alteration of cell membranes is preceded by a stress that increases as osmolality is increased. His contention is that reduction in cell volume leads to membrane injury.

Meryman considered salt concentration as a cause of injury when salt denaturation of membrane components occurs. In 1974, he reported[67] that the primary site of cell freezing injury is the cell plasma membrane, which includes membrane permeability alterations, along with the effect of elevated extracellular osmolality, which results in loss of cell water and cell volume reduction.

In 1970, Mazur[18] reviewed the responses of living cells to ice formation and considered that although the freezing point of cytoplasm is usually above –10°C, cells generally remain unfrozen and therefore supercooled to –10°C or –15°C even when ice is present in the external medium. This indicated that the cell membrane can prevent the growth of external ice in the supercooled interior and further suggested that cells neither are, nor contain, effective nucleators of supercooled water. Mazur believed that to understand the solution effect as a mechanism of cell damage, one needs to consider that four discrete events occur during freezing: (1) water is removed as ice, (2) solutes of high and low molecular weight concentrate, (3) cell volume decreases, and (4) solutes precipitate. Contrary to the theories of Lovelock and Meryman,[68] Mazur considered the cause of injury from extracellular ice to be that the ice exerts sufficient force to rupture not only the plasma membranes but also the membranes of organelles such as mitochondria. His rationale for this suggestion is that recrystallizing ice crystals can disrupt protein gels, and that cells killed by intracellular freezing have suffered membrane damage and become leaky.

In 1971, Carpenter and colleagues[69] demonstrated the beneficial effects of rapid rewarming at 42°C, reporting that endothelial cells remain attached to the arterial intima, with the internal elastic lamina remaining intact and the surrounding media appearing less distorted. During slow thawing, the endothelial cells are almost completely shed into the vascular lumen, the internal elastic membrane is disrupted, and the cells of the media are distorted and necrotic.

In 1972, Molnar and colleagues[70] attempted an analysis of the events leading to freezing, using finger temperatures. They concluded that the incidence of either freezing or cold-induced vasodilation could not be correlated with the relative cooling rate because of indeterminate supercooling. These authors concluded that the factors that induced both crystallization and vasodilation remain to be discovered.

In 1973, Bowers and colleagues,[71] investigating in vivo freezing, viewed ultrastructural changes occurring in capillary endothelium by electron microscopy.

He discovered no precipitous changes in muscle cell mitochondria or capillary endothelium as a result of hypoxia after cooling tissues to 2°C or supercooling to –13°C. However, reducing the temperature by one Centigrade degree per minute until freezing occurred, and continuing to cool for 10 minutes, followed by rapid rewarming, resulted in consistent mitochondrial damage in muscle cells. There was also marked degeneration of associated capillaries.

The 1980s: Vasoactive Metabolites and Microvascular Dysfunction

In 1980, Vanore and colleagues,[72] followed by Purdue and Hunt[73] in 1986 and Britt and colleagues[74] in 1991, published well-detailed summaries of the events leading to the tissue effects of cold injury. The events following cold insult were categorized using the direct effect of the cooling and cold period, the freezing period, and the immediate and delayed postthaw periods. Their reviews are comprehensive and rich in the pertinent bibliography of cold injury; their method of event analysis is utilized in the Pictorial Atlas of Freezing Cold Injuries at the end of this textbook.

Beginning in 1981, Robson and Heggers[75] published observations on metabolites of arachidonic acid (the eicosanoids dinoprost [$PGF_{2\alpha}$] and thromboxane [TXB_2]) in frostbite blister fluid. These authors suggested these two vasoactive metabolites as a cause of dermal ischemia and a possible cause of the progressive vascular changes that are seen in cold injury. Based on these data, the authors developed a "rational approach" to treatment of frostbite based on the pathophysiology of freezing injury. Having demonstrated the breakdown products of arachidonic acid, they used antiprostaglandin agents and thromboxane inhibitors to preserve the dermal microcirculation.

In 1989, utilizing light and electron microscopy, Marzella and colleagues[58] studied morphologic changes in the vascular endothelium of the skin. They concluded that the endothelial cell is the initial target of the injury induced by freezing, and further, that the injury is mediated by a non–free radical mechanism. They stated that "by now it is generally agreed that direct thermal injury alone is not sufficient to cause cell death,"[58(p67)] and also suggested that the initial freezing impairs microvascular function, leading to edema, stasis, thrombosis, and finally, to ischemic necrosis. This may be followed by the production of arachidonic acid metabolites after thawing. These physiologically active substances result in inflammatory responses that modulate vascular contraction and permeability, platelet aggregation and recruitment, and activation of leukocytes. Marzella and colleagues introduced a "new player" into the game, indicating the participation of free radicals in the induction of tissue damage. They pointed out that the consideration of free radical injury has been suggested by evidence showing that there are at least three approaches for preventing free radical injury if given at the time of thawing: (1) use of the enzyme superoxide dismutase, which destroys the superoxide anion radical; (2) use of a radical scavenger, which reacts with free radicals and converts them into less-destructive moieties; and (3) use of substances such as chelators of free iron, which prevent the generation of free radicals in the first place.

In their studies with experimental rabbits, however, Marzella and colleagues[58] found that freezing caused an immediate separation of endothelial cells from the internal elastic lamina. They believed that the separation was present even in samples removed immediately after freezing and before skin thawing, so that reperfusion could not be considered responsible for that lesion. Separation of endothelial cell junctions was seen in venules and capillaries soon after freezing. They also suggested that other inflammatory mediators released after injury, such as leukotrienes, may have contributed to separation of cell junctions.

The 1990s: Oxygen-Derived Free Radicals and Reperfusion Injury

During the 1980s and 1990s, research interest focused on the formation of oxygen-derived free radicals as a cause of tissue injury in both freezing and nonfreezing conditions. This reaction has been noted in postoperative organ warming, as after cardiac surgery, suggesting that free radical formation may follow rewarming and reperfusion of cooling or cold or frozen parts.[76,77] Investigation of irreversible tissue damage in cold injury was considered to be related to oxidation of protein sulfhydryl groups, and that the oxidation process probably involved hydroxyl radicals (OH•). Miller and Cornwell[78] suggested that removal of the hydroxyl radical by a scavenger would add cryoprotection to cell membranes. In this regard it is noted further that the classic cryoprotective agents, dimethyl sulfoxide (DMSO) and glycerol, are hydroxyl radical scavengers.

Studies have investigated reperfusion injury and involvement of the oxygen-derived free radicals (and also activated neutrophils), which are incrimi-

nated in endothelial injury during reperfusion.[79] Because various methods of warming are accepted treatment of hypothermia and of both nonfreezing and freezing peripheral cold injury, this form of reperfusion must be examined for free radical formation. Laboratory and clinical studies[7,58,71,80–82] regarding cold problems have brought our attention to a somewhat overlooked area of organ anatomy subject to cold insult–and one that may assume an area of great importance. The new investigations have demonstrated the impact of cold on the vascular intima, specifically the endothelial cell.

The importance of the endothelial cell structure is realized when we recall that the entire circulatory system is lined with a single layer of endothelium. The normal endothelial cell wall forms a tight, smooth surface on the luminal side of the vessel and serves as a semipermeable membrane for the interchange of material between blood and tissues. The intact wall prevents the larger elements of the circulating medium from leaving the lumen of the vessels. Any alteration of the endothelium affects flow patterns; changes adsorption capability; and causes release of substances that influence platelet and fibrin deposition, and therefore enhance clot formation and capillary blockage–the latter factor causing the vascular ischemia and occlusion that may cause severe, often irreversible, tissue damage after freezing.

Important to the endothelial cell response to cooling are the surface cell receptors that respond, for example, to interleukin 1 and other factors that are said to constitute the prime starting signals for the inflammatory response. Endothelial cells contribute to the manufacture of plasminogen activator and inhibitor, prostaglandins, reactive oxidant, and cytotoxic proteases. Cooke and Theilmeier[82] in 1996 reviewed the importance of this fragile lining in the formation of vasodilating mediators such as prostacyclin and nitric oxide (NO; the substance was originally called endothelium-derived relaxing factor [EDRF] but is now recognized to be NO). The most potent endogenous vasodilator known, NO is released when circulating thrombin is present or when serotonin is released by aggregating platelets. Such triggered NO induces vasodilation and inhibits further growth of platelet thrombi. There are also receptors in the endothelial wall for agonists, so that when their effect is to cause NO to be released, potent vasoconstriction may occur. As a result, normal endothelium tends to maintain vascular potency by inhibiting platelet adherence and aggregation, attenuating the response to vasoconstrictors. When the endothelium is injured (as in cold insult) or vascular trauma occurs, this protective influence of endothelium is lost, and as a result, vasoconstriction and platelet aggregation occur, allowing hemostasis. Further, NO inhibits platelet adherence and aggregation. NO and endothelial-produced protocyclin confer resistance to platelet–vessel wall interaction, and NO also inhibits the adherence of leukocytes to endothelium. Cooke and Theilmeier further reviewed the evidence that when reperfusion is associated with further injury to the myocardium, in part due to adherence and infiltration of neutrophils and concomitant release of oxygen-derived free radicals, this phenomenon may be inhibited using perfusion with sodium nitrate or other exogenous NO donors.

The endothelial cell plays an important role in vascular wall defense by hemostasis and the removal of thrombin and vasoactive substances from circulating blood. Thus the cell's importance as an organ that is especially susceptible to cooling and freezing cannot be neglected. Freezing causes immediate alteration of the vascular intima, especially the endothelial cell, as well as causing separation of the endothelial cell layer from the basement membrane.[83] This separation may result in overwhelming platelet aggregation (further contributing to vascular injury), luminal occlusion, ischemia, and eventually gangrene. If the target cell of severe cooling and freezing insult is the endothelial cell, then its early protection, preservation, and early reendothelialization is a matter of the highest priority for future laboratory and clinical research.

In 1990, Vedder and colleagues,[84] studying reperfusion injury using the rabbit ear, determined that tissue injury from ischemia and reperfusion formed the basis of several important disorders, including circulatory shock. Using the rabbit model, and monoclonal antibody (MAb) 60.3 directed to cluster of differentiation 18 (CD18, the human leukocyte in adherence glycoprotein), Vedder noted that intravascular neutrophil aggregation and neutrophil adherence to endothelium were blocked in his rabbit model of forehead tissue ischemia and reperfusion. Antibody treatment–before and after ischemia but prior to reperfusion–resulted in the same degree of significant protection against endothelial, microvascular, and tissue injury. From this finding, Vedder and colleagues concluded that under these circumstances, injury is primarily a result of reperfusion. This eventually may be important to us, as the frostbite injury, warmed after freezing insult, is primarily a problem of reperfusion.

In 1993, Mileski and colleagues[85] tested the hypothesis that blocking neutrophil adherence or aggregation or both reduced the tissue injury that re-

sults when tissue is frozen and rewarmed. Using the rabbit model, the extremities were frozen and then rewarmed. The test rabbits were then treated with MAb 60.3, thereby blocking adherence and aggregation. Tissue edema and tissue loss were less in the MAb-treated rabbits, supporting the view that a substantial component of severe cold injury is neutrophil mediated and occurs after rewarming.

In 1994, Buckey, Vedder, and colleagues,[86] working on another thermal injury, burns, recognized that monoclonal antibodies directed to the β_2-integrin adherence receptor family on leukocytes have shown significant tissue preservation in myocardial, intestine, rabbit ear, and hypovolemic shock models of ischemia of reperfusion injury. They noted that neutrophils can exert their damaging effect via several mechanisms. After being exposed to inflammatory mediators, neutrophils become activated and adhere to endothelium. This adherence allows the establishment of a microenvironment that is protected from regular plasma inhibitors. The adherent neutrophils then release cytotoxic phospholipase products, granule constituents, and toxic oxygen metabolites, resulting in endothelial injury and leading to increased neutrophil infiltration, microvascular occlusion, and tissue destruction. They state further, of interest in cold trauma, that oxygen-derived free radicals are known to be involved in neutrophil attraction and activation. Neutrophils are not only attracted by products of oxygen-derived free radicals but are themselves an important source of the oxygen-derived radical species that cause direct tissue destruction and may further amplify tissue damage. As in the foregoing studies, the use of MAb 60.3 in rabbits demonstrated less tissue edema and thinner eschar, and the researchers believed that in burns (as in cold thermal injury), the moderate burn injury may be significantly attenuated by blocking neutrophil adherence functions with CD18 and MAb.

Summary of the Pathogenesis of Freezing Cold Injury

The pathophysiological changes in FCI occur in two phases: (1) those occurring in and induced by the cooling, supercooling, and freezing stage, and (2) those occurring during the thawing (rewarming) and postthaw stage (Exhibit 14-2).

EXHIBIT 14-2

PATHOPHYSIOLOGICAL CHANGES DURING FREEZING, THAW, AND POSTTHAW

First, the following changes occur in and are induced by the freezing state:

- structural damage by ice crystal growth;
- protein denaturation;
- pH changes (intracellular and extracellular);
- dehydration within the cells as a result of extracellular ice formation and extraction of cellular water;
- endothelial cell disruption;
- loss of protein-bound water;
- rupture of cell membranes;
- abnormal cell-wall permeability;
- destruction of essential enzymes;
- ultrastructural damage to the capillaries; and
- consistent mitochondrial damage in muscle cells.

Second, the following changes occur during the thaw and postthaw stages:

- circulatory stasis;
- corpuscular aggregation;
- piling of red cells back to the capillary bed;
- development of hyaline plugs in the vascular tree;
- marked tissue edema;
- anoxia–ischemia of tissues;
- increase of compartment space pressure;
- capillary and peripheral vessel collapse, with endothelial cell disruption; and
- eventually, thrombosis of vessels, ischemia, regional necrosis, and tissue death if the process is not reversed.

The Cooling, Supercooling, and Freezing Stage

With exposure to cold, there is an early tissue response to cooling. This is described as a cold-induced vasoconstriction and is followed by a cold-induced vasodilation, also called the "hunting response."[87] Another hypothesis states that at the same time, or as cooling continues, arteriovenous anastomoses open, with shunting of blood away from the periphery of the vascular bed.[88] Soon, after sufficient heat loss occurs to allow freezing, ice crystals form in the extracellular fluid spaces, with extracellular freezing.[53] This event is precipitated by inclusion bodies and microcrystals. It is possible that some structural damage may result from continued ice-crystal growth.[30] Extracellular osmotic pressure increases,[89] resulting in cell volume reduction and solute concentration in the extracellular spaces and interstitium.

As freezing continues, there is an elevated concentration of electrolytes, protein denaturation, intercellular and extracellular pH changes, intercellular and extracellular dehydration, freezing of extracellular water, loss of protein-bound water in the cells, and destruction of essential enzymes.[18] As further cooling and freezing continue, cell membrane damage occurs, with impairment of microvascular function and increased cell wall permeability, and with critical endothelial cell injury and endothelial separation from the internal elastic lamina of the arterial wall.[18,58] At this time, severe injury to chondrocytes may occur because cartilage, particularly epiphyseal cartilage, is susceptible to freezing damage. Further insult causes ultrastructural capillary damage, mitochondrial loss in muscle cells, and injury to other intracellular structures.[49]

The Thawing (Rewarming) and Postthaw Stage

Depending on the method of thawing, postthaw hyperemia, ischemia, cyanosis, or even total circulatory failure usually develop.[37,80,90] Proximal blebs, distal blebs, or no blebs appear. The usual event is that of vasodilation, edema, and stasis.[43,67] Corpuscular aggregation begins with thawing, often associated with progressive ischemia or with hyaline plugs in the vascular tree.[56,58,80] Occasionally, because of associated or combined injury, increased pressures may develop in soft-tissue compartments.[6] Changes related to reperfusion injury occur, with formation of oxygen-derived free radicals, neutrophil activation, and other inflammatory events.[81] An early response in the thawing stage, and perhaps in cooling too, is the arachidonic acid cascade, liberating prostaglandins and thromboxane, and predisposing to vascular clotting.[75,91] Proteolytic enzymes are produced, with increased membrane permeability.

Eventually, (*a*) vascular reconstitution and clot dissolution begin or (*b*) capillary and peripheral vessel collapse occurs, followed by microvascular and macrovascular thrombosis, venule and arterial obstruction by thrombosis, tissue ischemia, necrosis, and gangrene, resulting in loss of the affected part or area. Following thawing, should refreezing occur, intracellular ice formation is most probable, resulting in the destruction of cells and vital organs. Thawing in this usually deep injury results in unrelieved thrombosis, stasis, failure of cell repair, and loss of body parts usually near or at the level of the second freeze.[7,15,27]

DESCRIPTION OF THE COLD-INJURED PART

In general, the cold-injured or frozen body part may be described as in two states, frozen or thawed. In the frozen state the part is hard, cold, and usually white and apparently bloodless, but is occasionally pale yellow. The part frozen often represents the condition of the extremity at the time of the injury (eg, one that was partially cyanotic would remain so, with a purplish hue in the frozen state). The digits are usually rigid, obviously anesthetic, and generally immobile at the interphalangeal joints and often at the metacarpal- or metatarsal-phalangeal junction (although as a mass the fingers or toes might move, owing to the function of the long flexor or extensor tendons). The surface appears solidly frozen, as do the total digits, even in areas where freezing may actually be superficial. The thawing is usually painful, particularly when accomplished rapidly. Delay in thawing is associated with less pain and may account for the popularity of ice, snow, or ice water as a thawing medium in many areas where self-care is practiced. The area frozen, as well as being hard, insensitive, and cold or white, is occasionally covered with frost particles and, occasionally, has a yellowish cast or areas that are obviously avascular, depending on skin pigment. The outer shell of the skin (epidermis and dermis) is rigid and pulses are absent. Pain generally is nonexistent in that area.

In the thawed state, the clinical pattern often depends on (*a*) the method of thawing, (*b*) the duration of freezing, and (*c*) the depth of injury. Following thawing the part becomes flushed, often with

an ominous purple hue, particularly if extremes of temperature are used. With rapid rewarming, the part is usually flushed pink or red and occasionally a violaceous hue. The thawed extremity is usually edematous with large, serum-filled blisters (ie, blebs) developing an hour to several days following thawing. The formation of blebs often gives an indication of the severity of the injury and perhaps is a result of the thawing method. If the blebs are small, dark, or hemorrhagic, and are present above the interphalangeal joints, the prognosis is generally poor. On the other hand, if the blebs are clear or yellowish, even pink-tinged, and extend clear to the tips of the digits, that usually is an indication of an adequate response to thawing and good prognosis. It may also indicate a lesser depth of freezing than much more proximal blebs. Unless accidentally broken, the blebs will remain intact until the 4th to the 10th day, when resorption of fluid begins and spontaneous rupture of the blebs may occur. As these blebs dry, a hard eschar develops throughout and circumferentially on the injured surface. This eschar may be quite black, giving a false impression of deep gangrene. However, within 14 to 21 days, the eschar begins to separate spontaneously, revealing delicate but healthy tissue below. This eschar, once formed, should be carefully incised and split down to newly forming epithelial tissue so that joint motion is permitted, and also exposing the underlying, newly epithelializing tissues for massage and whirlpool therapy.

Patients have generally described initial feelings of cold discomfort in the extremity, then often loss of pain or discomfort, followed by a sensation of tingling or numbness, then followed by a complete loss of all sensation, including pain. It is presumed that at this point the tissues are frozen. Anesthesia lasts until thawing occurs. Some individuals describe walking on a numb foot, or feeling almost as if they had a "wooden leg." On the other hand, it is not uncommon for those who are inured to the cold, particularly American Indian and Eskimo individuals, to have had none of the warning signs usually demonstrated by black or white people and not be entirely aware of the frozen state, particularly of the toes, until they are changing their boots or mukluks. Again, because of the anesthetic nature of all cold injuries, patients often say that they were unaware that they were developing FCI.

For additional information about and illustrations of the cold-injured part, interested readers can consult the Pictorial Atlas of Freezing Cold Injury at the end of this textbook.

Traditional Classification of Injury (by Numerical Degree)

Because some physicians and many manuals still describe FCI by the degree of injury, it is included and described here for the sake of completeness; another classification method follows.

First Degree

First-degree injury is considered to be very superficial freezing, usually of short duration, with few residual findings and only occasional blisters, if any. In first-degree injuries, erythema and edema, along with transient tingling or burning, are early manifestations. The skin becomes mottled blue-gray and red, and hot and dry. Swelling begins within 2 to 3 hours and persists for 10 days or more, depending on the seriousness of the injury. Desquamation of the superficial epithelium begins in 5 to 10 days and continues for as long as a month, but no deep tissue is lost. Paresthesias, aching, and necrosis of the pressure points of the foot are common sequelae. Increased sensitivity to cold and hyperhidrosis may appear, especially with repeated first-degree injuries. It should be noted that it is difficult to differentiate first-degree frostbite from the abrasion produced by the insulated vapor barrier boot; medical personnel must be cognizant of the difference, as both injuries occur in the same clinical setting.

Second Degree

Second-degree injury is considered true freezing, demonstrated by pallor of the skin, very little pain, and loss of sensation with freezing of the skin and subcutaneous tissues. Second-degree FCI begins as does first-degree, but progresses to blister formation, anesthesia, and deep color change. Edema may form but it disappears within days. It should be noted that if the part is hard, cold, and white, it is very difficult to determine the degree of injury; because the part is frozen, the segment is immobile and usually without joint motion; only after thawing may further change be identified. Vesicles appear within 12 to 24 hours. They generally appear on the dorsum of the extremities, and when these vesicles dry, they form an eschar. Blisters are a good clinical sign as long as they are filled with clear fluid. If the fluid is hemorrhagic, the prognosis is often poor. As these vesicles dry, they slough cleanly with pink granulation tissue demonstrated beneath, or they may form a cover of black eschar involving

primarily the dermis and epidermis. Throbbing and aching pain occur 3 to 10 days after this injury. Hyperhidrosis is apparent at the second or third week. Early rupture of the blisters with subsequent infection often occurs in second-degree FCI. This infection, if present, significantly increases the severity of the injury. It is the purpose of the whirlpool treatment (described later in this chapter) to completely wash the fractured blebs and dilute the bacteria if any are present.

Third Degree

Third-degree injury involves full skin thickness and extends into the subcutaneous tissues. Vesicles are smaller and may be hemorrhagic. Generalized edema of the extremity may occur, but it usually abates within 5 to 6 days. Subfascial pressure increases and compartment syndromes are common in third- and fourth-degree FCI. If pressure rises significantly with loss of distal blood flow, then fasciotomy along with vasodilators are indicated for therapy. The skin soon forms a black, hard, dry eschar, usually thicker and more extensive than that of second-degree FCI. When the eschar and area of involvement finally demarcates, sloughing with some ulceration occurs if there is no complicating problem of infection. Patients often complain of burning, aching, throbbing, or shooting pains beginning on the fifth day and usually lasting through 4 to 5 weeks. Hyperhidrosis and cyanosis appear later, and extreme cold sensitivity is a common postinjury sequela (discussed later in this chapter).

Fourth Degree

In fourth-degree injury there is destruction of entire thickness of the part, including bone, resulting in extensive loss of tissue. After rewarming, tissue is cyanotic and insensitive, and blister formation, if present, is hemorrhagic. Severe pain on rewarming, along with deep cyanotic appearance, regularly occurs. In rapidly frozen extremities or the freeze-thaw-refreeze injury, dry gangrene progresses quickly, with mummification occurring as rapidly as 4 to 5 days and up to 7 to 10 days. With slower freeze injury, there is some early swelling and deep pain and demarcation takes much longer to occur. The line of demarcation becomes obvious at 20 to 36 days and extends into the bone in 60 or more days. Because freezing is usually deep, and occurs often over an extended period of time, tissue damage in fourth-degree injury is irreversible, with major necrosis and gangrene, and often associated with severe infection.

Modern Classification of Injury (by Depth)

Because of the difficulty in clinically differentiating the various degrees of FCI, the diagnostic nomenclature that specifies freezing injury by degree needed to be simplified. As a result, Mills, Whaley, and Fish[3–5] proposed the terms "superficial" and "deep" injury instead of the traditional degrees:

- *superficial* injury is defined as FCI limited to the skin, and corresponds to the traditional first- and second-degree injuries.
- *deep* injury is defined as FCI involving tissues beneath the skin, including muscle, tendon, nerve, blood vessel, and bone; it is comparable to the traditional third- and fourth-degree injuries.

It is important to note that under the traditional classification, some of the first- or second-degree injuries, depending on the depth of treatment, could, as a result of abnormal warming, infection, or trauma, suddenly become third- or fourth-degree injuries.

Following a clinical examination of patients with FCI using all the usual means and proper tools, medical officers may find that other diagnostic modalities are useful in diagnosing thermal injury (Exhibit 14-3).

EXHIBIT 14-3

DIAGNOSTIC TOOLS FOR COLD INJURY

- Sensory measurement utilizing sterile needles, or equipment for measuring two-point discrimination and tests for proprioception
- Thermography
- Electromyographic and nerve-conduction studies
- Examination for pulses, by manual and by Doppler examination
- Measurement of tissue compartment pressure
- Examination for carpal and tarsal tunnel pressures
- Examination of tissues by radiographic means, including routine flat-plate anteroposterior roentgenograms, computed axial tomography, magnetic resonance imaging, and radioisotope examination (technetium 99m) for the status, presence, or absence of cellular perfusion
- Arteriography if required

MANAGEMENT OF FREEZING COLD INJURY

For armed forces medical personnel, management of cold-injured service personnel depends on the military situation at the time that cold-injured individuals are seen and rescued or treatment begins.[92] Medical care will also be determined by the type of facilities available for treatment or for transfer elsewhere, from the foxhole, the tent, the battalion aid station, or upward in the echelon system of the military medical services. Exhibit 14-4 contains examples of the kind of questions that medical officers must ask themselves before they begin the first of two categories of medical management of cold-injured casualties: field treatment and care after rescue and evacuation.

Despite all we have listed as causative elements in the sequence of freezing, little has been said of the other factors that are so important in determining the final result in the human. These variables—often difficult to anticipate, measure, or predict—are in the realm of weather, inadvertent accident and trauma, and individual human physiology and anatomy. The state of health and physical condition of the victim are also vital, and include the associated factors of alcohol and drug use and mental state at the time of exposure. The individual's neurovascular integrity in peripheral areas is also a major factor if disease states such as diabetes, arteriosclerosis, vasculitis, labile vasomotor disturbances, and Raynaud's syndrome or Buerger's disease are present.

Associated trauma that precedes freezing, such as extremity strain, sprain, or fracture, pose major problems, as do penetrating wounds, blunt trauma, or blood loss from any cause. FCI is further influenced by the degree of hypovolemia or dehydration present, causing further distal vascular deficiency prior to the onset of freezing. Rescue and survival often result in refreeze injury and perhaps result in the irreparable trauma that occurs at the junction of frozen-nonfrozen tissue, as "brittle" tissue segments are stressed when the victim with FCI must walk to survive a wilderness catastrophe.

Once the victim of any cold injury (eg, immersion NFCI, FCI, hypothermia, separately or in any combination) is evaluated, an effort must be made to avoid further cold exposure. As soon as the patient has been sent to an adequate care area, total physiological control should be attempted—which means monitoring the cardiovascular system, blood gases, electrolytes, and airway care, as in any emergency care.

In the absence of hypothermia, victims of immersion-type NFCI or of true FCI are seldom in a life-threatening condition, unless the condition is associated with hemorrhage from battle trauma, the onset of infection, or the presence of associated trauma to vital areas. With those exceptions, extremity FCI or NFCI rarely results in death unless accompanied by hypothermia, with or without other trauma, or unless—even with hypothermia—total physiological control is not obtained. In the absence of total physiological control of systemic hypothermia or extremity cold injury, death may result from potassium release after warming, causing cardioplegia and cardiac arrest.

At present, as this chapter is written, we are reviewing nearly 1,500 cases of cold injury, all seen by or consulted on by the author. Only one death in more than 1,000 cases of FCI occurred during hospitalization after rescue. That patient, a man older than 80 years of age, died from pulmonary embolism more than 1 month after he was hospitalized after freezing all four extremities. The analysis of case records is not yet complete, but a preliminary review indicates that of 250 cases of hypothermia with associated cold injury, death occurred much more frequently and was related primarily to the depth of hypothermia. When hypothermia and

EXHIBIT 14-4

EXAMPLE QUESTIONS FOR MEDICAL OFFICERS

1. What are the battle conditions in the field? Are your forces in attack mode or retreat? Are they pinned down by enemy fire or able to move freely?
2. From previous troop education, can the injured combatant care for himself, or will he need help from a squad member or leader?
3. For further care of the combatant with frozen lower extremities particularly, is transport care available if necessary by stretcher, ground vehicle, or helicopter to rear areas such as the company medical area or the battalion aid station or even farther?
4. For the casualty with severe injuries, is a helicopter or fixed-wing vehicle available for rapid transport to mobile hospital units, hospital ships, or permanent hospital facilities established elsewhere?

freezing occurred in the same patient, no deaths resulted if the patient was treated by *total physiological control* and warmed either by rapid rewarming in a tub or by peritoneal dialysis for treatment of hypothermia and simultaneous tub treatment of the freezing injury.

Field Care and Prehospital Management

In the field, the military situation may dictate the method of care and transfer or return to duty after the initial examination, especially if it is militarily necessary that the troops remain on line or participate in retreat. If possible, instruction should be instituted concerning the care of hands and feet, change of stockings, and reiteration of all methods of detection and avoidance of cold injury. Weather–continued cold–wet or freezing–may hamper care. No matter the environmental condition, it is expected that if thawing an extremity is proper, then refreezing should not occur. The decision must be made as to whether thawing or warming be done on the spot or after transfer to a rear area. If evacuation is intended, instruction for care during transport should be given. This is especially so to avoid refreezing, and also to avoid further trauma to the part frozen.

Other factors must be considered, including the diagnosis of cold injury, whether freezing or nonfreezing; diagnosis of hypothermia; and the presence of combat injury including gunshot or shrapnel wounds, or open wounds with hemorrhage, which must then take priority for treatment over the cold injury. It becomes necessary, therefore, to practice triage at all echelons. An adequate triage examination must be performed so that other or more-severe medical problems besides cold injury be identified, and so that essential care be given at that time and during rescue.

Some controversy may exist regarding initial and continuing basic battlefield care, because there is no adequate definition between the care rendered in the field, where so little aid is available, compared with the ultrasophistication of modern hospital care, where so much in the way of personnel and equipment is at hand. Whether at the discovery site or in the field, there may be many field-care variables, including

- the rescue experience of the discovery party;
- the number of victims found, and the stress of combat conditions;
- more pertinent, the depth and duration of hypothermia of the victims or the cold injury;
- the associated injuries or medical problems of the victims, including FCI, NFCI, and battle wounds; and
- even more pertinent, the local weather, which may hinder not only the rendering of care but also the care itself.

If hypothermia is present along with other injuries, the victim may have been in that state for quite awhile. The first responder usually has time to view the area, consider the problem, and assess the condition of the victims before rushing forward. Not the least consideration is an evaluation of the discovery site to determine whether rescuers can safely work there, and if not, whether they can take precautions with whatever equipment is at hand to make the area safe. Immediate transport of the casualties may be indicated. Even without a low-reading thermometer, the first responder can make an assessment of the victim's hypothermic state. The onset of hypothermia in the field may be sudden (eg, immersion in cold or icy water) or insidious, or a result of exposure to wind, rain, snow, falling temperatures–all perhaps under the pressure of combat conditions. *Penetrating wounds and hemorrhage may be leading causes of hypo-thermia.*

Not too many years ago, the treatment of the frozen extremity was fraught with controversy. The differences of opinion ranged from varying methods of thawing, a paucity or a plethora of aftercare methods, and debate regarding utilization of drugs of all types and uses, and debate, too, over the need for invasive techniques or surgical procedures. At the least, the approach to care of the casualty with FCI should be purposeful and systematic, utilizing all treatment that is now known to be helpful. Treatment should be offered in an orderly and proper sequence from initial thawing to demonstrable conclusion, with or without immediate sequelae. This sequence may be listed briefly as follows:

1. Avoid further trauma to frozen or, in the event of thawing, injured parts.
2. The trauma to be avoided includes exposure to excessive heat or mechanical trauma, or any factor causing loss of circulation to the involved limb (for instance, in the use of a tourniquet if a compress will suffice).
3. Prevent refreezing of thawed extremities, in the rescue or initial care or transport.
4. Carefully insulate the involved extremities to avoid further injury from helicopter wash, which acts as an increased chill factor, as refreezing under those conditions is likely to occur.

5. Recognize and treat the associated trauma, realizing the need for immediate care for the condition of hypothermia, if present, along with freezing injury.
6. In the process of triage, be vigilant for trauma more severe and life-threatening than extremity freezing. Penetrating trauma, including hemorrhage, must be treated to avoid worsening any circulatory loss to the frozen, now thawed, extremities.

The squad leader or medic or field surgeon should look for and be prepared to treat problems of hypovolemia, dehydration, and electrolyte and acid–base imbalance. The diagnosis of other problems may require selective triage and rear-echelon hospitalization where laboratory facilities are available.

If transport is not available and the soldier with frozen extremities must walk without stretcher or vehicle support–especially if large numbers suffer freezing cold injury–it is important that they ambulate on frozen, nonthawed extremities rather than thawed, which usually results in painful, edematous feet with decreased circulation, which increases the likelihood of refreezing injury. The decision in the field to have troops walk on frozen feet rather than to rewarm them is difficult for troop commanders and medical personnel alike.

Definitive Treatment in a Hospital

It is convenient to describe the definitive care phase in two stages: before thawing and after thawing. The frozen part must be protected to avoid trauma and the risk of irreversible injury at the frozen-nonfrozen interface, which may result if motion occurs at that level, fragmenting partially frozen tissue. This may be beyond the control of the treating physician, if it has been necessary for the injured individual to walk in order to survive. The frozen part should then be thawed using the approaches described below. The thawing is completed when the distal tip of the thawed part flushes. The thawed part should not be massaged.

Postthaw treatment including surgical procedures should be carried out in a hospital, where pain can also be managed if necessary. Many medical inpatient treatment modalities proposed in the past have not proved particularly effective (eg, sympathetic blockade, sympathectomy, anticoagulants, vasodilators, alcohol, and enzymes). This may well be because of the development of thromboses or corpuscular aggregation in vessels that have not permitted an increase in circulation because of a blocked transport system. The same consideration applies to the use of hyperbaric oxygen. In the past, on a single occasion, the use of a single-man hyperbaric oxygen chamber delivering 2 atm pressure appeared beneficial in postthaw frostbite. However, hyperbarism is not likely to be helpful if the oxygen transport system is blocked by vessel thrombosis or destruction of the vascular endothelium. Finally, smoking is forbidden. Alcohol may be given in moderation if requested by the patient.

Prethaw Treatment and Rewarming

In caring for patients with FCI, it is important that a system of care be utilized and that all treatment modes be purposeful. If the extremity is still in the frozen state, it must be thawed. *How* warming is achieved becomes of paramount importance. Some warming methods may be entirely out of the control of medical personnel, as warming, by one means or another, often may have occurred prior to rescue or prior to the patient's being seen by medical personnel. Many thawing methods are utilized by the victims or by helpful rescuers. *Not all are appropriate.* Generally, the victim presents to the rescuers or emergency department and is treated with one of the methods of thawing discussed below, in decreasing order of effectiveness:

1. Rapid rewarming in warm water, 32°C to 41°C, in a tub or whirlpool bath or by means of a crane-lift platform in a Hubbard tank. Rapid rewarming by external means appears to produce the best results but does not always give protection from tissue loss, especially where the injury is deep or of long duration. This method has also been used to warm and thaw the combined injury of hypothermia with extreme freezing.
2. Gradual, spontaneous thawing at room temperature (which varies from 7°C to 32°C owing to cabin heat); or thawing occurring in travel by foot, by vehicle, or during rescue; or thawing due to the warmth of a sleeping bag, often in the wilderness, at altitude, or both. Spontaneous thawing gives variable results, which are often determined by the depth of injury; the duration of freezing; and the patient's activity during survival, rescue, and thawing.

The following two methods are presented for completeness but are not recommended:

3. Delayed thawing using ice and snow, cold water, and friction massage. Warming by cool methods, usually at temperatures near freezing in warm areas, often give poor results.
4. Thawing by excessive heat, such as from a campfire, oven, or engine exhaust (temperatures < 50°C). This method generally results in heat injury (burning) to a part already injured by cold. The final results are disastrous, resulting in great tissue loss and usually major amputation, usually with spontaneous demarcation after the third to the eighth day.

At present, rapid rewarming is favored, this method seeming to demonstrate the greatest tissue preservation and the most adequate early function, especially in deep injury. Results by gradual thawing vary in deep injury, but seem satisfactory in patients with superficial injuries. Ice- and snow-thawing give variable results, most often poor, with marked loss of tissue. The use of excessive heat as a thawing method has resulted in disaster in most cases, especially with dry heat at temperatures of 66°C to 82°C (150°F–180°F), for example, as with the use of a diesel exhaust, wood fire, or stove heat.

An early diagnostic clue as to the exact freezing event is the condition of the digital tips when the patient is first seen. If spatulate mummification occurs within the first 3 to 5 days after thawing, the diagnosis is usually that of a freeze-thaw-refreeze injury, or thawing by excessive heat. Freezing and thawing modes generally seen without the two conditions of excessive heat or refreeze injury usually demonstrate necrotic or avascular changes from the 10th to the 21st day.

It has often been stated that rapid rewarming by internal means (through either arm intravenous or arterial line), administered at temperatures of 37.1°C to 41.1°C (100°F–106°F), is more physiological and may be a method of choice in dissolving ice crystals and restoring cellular hydration. Although this method appears most logical and seems to be a new consideration on the horizon of care, in fact, since the mid 1980s in Alaska and elsewhere, it has been a method of choice in the treatment of combined hypothermia and freezing injury, by both adding heat and restoring fluid volume. The results, however, are still no better than by rapid rewarming. In addition, the development of an arterial line, especially in the areas of ankle and wrist, may cause local arterial spasm and further decrease digital perfusion. The ideal method is obviously not yet at hand, at least for the thawing of the frozen part, but tissue loss is less now than it was in past decades, regardless of thawing method.

Postthaw Treatment

When the injury is severe and deep and hospitalization is required, the extremities are kept on sterile or clean sheets, with cradles over the frostbitten part to avoid trauma and pressure. This is not necessary for the upper extremities, which may be placed on sterile or clean sheets and placed over the chest or trunk. If edema is present or, as required, arms and hands are often elevated in stockinette sleeves to permit drainage and encourage digital motion and decrease dependent edema. The injured part should be protected from maceration with cotton pledgets placed between the digits. In the presence of severe digital edema, however, pledgets or cotton swabs may compress digital vessels, further compromising the circulation. The treatment is open, not occlusive, without the use of wet dressings, unguents, ointments, or petrolatum gauze. Whirlpool baths are utilized twice daily for 20 minutes per bath, at temperatures of 32°C to 35°C (90°F–95°F). In addition, a program of bedside digital exercises of all the joints is initiated and should be done through the entire waking day. Buerger's exercises for the lower extremities are recommended four times daily at least. Biofeedback training can, and has, been utilized to enhance postthaw blood flow to the cold-injured extremity. This technique has demonstrated much benefit, especially in the early stages of injury. Even more interesting is its probable aid to the rifleman in the cold, where biofeedback training might help to avoid vasoconstriction and onset of cold injury.[93]

Surgical soaps, such as hexachlorophene or 4% chlorhexidine gluconate and povidone iodine, are employed in the whirlpool. Occasionally, following the methods of Moyer and colleagues[94] for treatment of burns, 0.5% silver nitrate solution may be lavaged over the area of frostbite. The result is similar to that produced by the surgical soap; with Moyer's solution epithelialization is similar with one outstanding difference: pain is reduced and infection, even superficial, is much less obvious using the silver nitrate solution. The whirlpool clears the debris from the injury and removes superficial bacteria. The tissues are debrided without trauma by the whirlpool action at a time when they are physiologically prepared for the separation of the viable tissue from the overlying eschar.

Occasionally, when severe drying and premature

rupture of blisters have occurred, 1% silver sulfadiazine solution has been utilized on open wounds secondary to freezing injury, usually followed by superficial infection. Blebs are usually left intact because their contents are usually sterile, as is the underlying tissue; they are debrided or trimmed only if they are infected and contain purulent material. Others believe that the bleb fluid should be removed. In the event that aspiration of the fluid is performed, it should be done under sterile conditions.

Over the years, multiple drugs have been recommended for prethaw and postthaw treatment of cold injuries, especially of the extremities. Some of these drugs are listed in Exhibit 14-5, grouped under their principal functions, including plasma volume expanders, vasodilators, hypotensive agents, calcium channel blockers, sympatholytic agents, anticoagulants, thrombolytic enzymes, cryoprotectors, antiinflammatory agents, hyperbaric oxygen, antibiotics, and surgical soaps.

Surgical Procedures

Over the years many surgical procedures have been proposed for postthaw care of the frostbitten extremity. The benefits of surgery should always be weighed against possible injury to the regional vascular structures in the injured area. If possible, the surgical approach should improve the prognosis by relieving compartment pressure, increasing joint mobility, limiting infection, or increasing vascularity. Surgical procedures appropriate to treating FCI are listed in Exhibit 14-6.

Fasciotomy to Relieve Compartment Pressure. Severe FCI, with or without rapid rewarming, often includes signs of increased compartment pressure. Various methods of measuring compartment pressure have been utilized in the past, but the Stryker stick apparatus (295 Intra-Compartmental Pressure Monitor System; manufactured by Stryker Surgical, Kalamazoo, Mich), is one of the favored methods at the present time. Experience has dictated that although capillary pressures greater than 37 to 40 mm of mercury are suspect, we must consider fasciotomy in the presence of clinical evidence of vascular compromise. In 1973 and later, Mills[6] described fasciotomy as a method of relieving the lethal tissue effects of increased compartment space pressure. This mode of decompression was further investigated in 1978 by Franz and colleagues[95] on laboratory dogs, demonstrating its effectiveness.

Several imaging modalities may help supplement clinical judgment and compartment pressure measurement. Most common are arteriography, or the injection of radioisotopes such as technetium 99m that demonstrate the state of cellular perfusion. Isotope studies have been performed as an indicator of cellular perfusion for more than 30 years in Alaska. Doppler ultrasound has also been used as a vascular study tool. Interestingly, at Providence Hospital, Anchorage, Alaska, patients in the Thermal Unit with Doppler evidence of good pulses in the distal extremities (digital vessels) have had conflicting isotope evidence, showing failure of extremity perfusion in the same area. In all cases but one, the isotope study was the accurate one. Evidently, large digital vessels may remain patent for a short while even when the deep capillary system is blocked.

The ultimate decision to do the fasciotomy rests with the attending physician or surgeon, and that judgment often may demand compartmental pressure release regardless of pressure readings. This is important to note, because unless the compartment pressure reading is on a continuous monitor, a near-normal pressure may, in 8 to 24 hours, change to destructive pressure levels and cause severe tissue necrosis, especially in muscle, in a short period of time. If an extremity has remained in a frozen state for some considerable time, even rapid thawing and general supportive care may not be effective in restoring the circulation, and a condition similar to anterior tibial compartment syndrome may be clinically demonstrated. This problem may require fasciotomy.

Failure of sophisticated tools has also been demonstrated in the use of devices for measuring compartment pressure. If one's clinical judgment and experience suggest that an immediate fasciotomy is required, whereas the pressure transducer indicates that the pressure is high but not lethal or indicates a marginal reading, it is often better to trust one's own judgment. A later measurement may indicate sudden pressure increase. A delay in performing the fasciotomy may be disastrous. This diagnostic problem may be avoided by the use of continuous pressure monitoring. However, there are many pitfalls. The monitoring device is still only a machine, and if one's own studied opinion is that the fasciotomy should be performed, then it may be best to rely on one's own surgical judgment and release the pressure. An example of a situation in which even the best clinical judgment in conjunction pressure measurements is inadequate to make the correct diagnosis is the individual with what appears to be a straightforward, superficial, or deep freezing injury who, after rapid rewarming in warm water at the recommended or even lower tempera-

EXHIBIT 14-5

THERAPEUTIC DRUGS USED TO TREAT FREEZING COLD INJURY

- ***Plasma Volume Expanders***
  Low molecular weight dextran (dextran 40), when given intravenously, has a major effect of plasma volume expansion. Dextran 40 also enhances blood flow through correction of hypovolemia (often present in freezing injury owing to marked peripheral vasoconstriction of the arterial capillary tree) and improves microcirculation. It is considered to diminish or reverse erythrocyte aggregation. A good beginning dose may be 25 mL/h given by intravenous infusion or pump.

- ***Vasodilating Agents***
  Tolazoline hydrochloride (Priscoline hydrochloride*) and isoxsuprine hydrochloride (Vasodilan†) presumably function by relaxing vascular smooth muscle. Priscoline is administered intravenously and Vasodilan is administered orally. Generally the dose of Vasodilan is 10 to 20 mg, 3 or 4 times daily. Priscoline is also given subcutaneously at a dose of 10 to 50 mg/d, 4 times daily, beginning with low doses.

- ***Hemorheological Agents***
  Pentoxifylline (Trental*) is said to increase vascular blood flow in patients with peripheral vascular disease by correcting pathologically altered platelet reactivity. It is administered orally or intravenously. The drug exhibits an inhibitory effect on platelet aggregation and on disseminated intravascular coagulation. Males usually are given oral doses of 400 mg three times daily.

- ***Hypotensive Agents***
  - Guanethidine monosulfate is said to produce a selective block of efferent peripheral sympathetic pathways, and is given orally, initially at a dose of 10 mg/d.
  - Reserpine, an ester alkaloid from certain *Rauwolfia* (plant) species that causes sympathetic inhibition resulting in vasodilation and increase cutaneous flow with flushing. It is given orally, 0.05–0.1 mg initially and then 0.1 mg every other day.

- ***Calcium Channel–Blocking Agents***
  Nifedipine (Procardia*) presumably functions by inhibiting calcium ion influx. Nifedipine inhibits the contractile processes of cardiac and vascular smooth muscle, thereby dilating the main coronary and systemic arteries. It is given orally, 30–60 mg once daily.

- ***Sympatholytic Agents***
  Phenoxybenzamine hydrochloride (Dibenzyline*) blocks a-adrenergic receptors. The drug acts on vascular smooth muscle to block epinephrine-induced vasoconstriction and induces peripheral vasodilation. Dosage initially is 10 mg twice daily, increased to 20 mg twice daily after 24–48 h. The hypotensive effects require increased intravenous or oral fluid intake. The drug is effective as a "medical sympathectomy." Dibenzyline and low molecular weight dextran are among the most effective postthaw drugs in the drug armamentarium.

- ***Anticoagulating Agents***
  Heparin was used often in past decades, particularly for its antithrombotic effects. There is no substantial evidence of its effectiveness in freezing injury as compared with other drugs.

- ***Thrombolytic Enzymes***
  Streptokinase, urokinase, and tissue plasminogen activator. Although great promise has been held out for all three enzymes, at present, patients with intracranial or intraspinal injury, or other trauma that would permit increase of local or systemic bleeding, cannot receive them. Using these drugs in patients whose cold injury has caused endothelial or capillary wall injury may cause further local bleeding and increased compartment pressure. Ongoing research[1–3] involving these drugs in selected patients and centers may eventually determine an adequate, safe protocol for their use.

(**Exhibit 14-5** *continues*)

Exhibit 14-5 *continued*

- ***Industrial Solvent***
  Dimethyl sulfoxide (DMSO) has long been used by cryobiologists and animal researchers. It is a cryoprotective agent, a penetrating agent that may someday hold promise in bringing needed drugs to areas via the skin, which cannot be readily reached otherwise because of small vessel or capillary thrombosis. It is said to have vasodilating properties. Its use has been frowned on by the Food and Drug Administration, although DMSO is available in some states by prescription, and it has been used to a great extent in veterinary medicine.

- ***Antiinflammatory Agents***
  Acetylsalicylic acid and ibuprofen, both nonsteroidal antiinflammatory drugs (NSAIDs), are recommended because of their ability to interfere with the arachidonic acid cascade in trauma including freezing cold injury by inhibiting the formation of prostaglandin and thromboxane, thereby aiding and avoiding intraluminal clot formation in small vessels.

- ***Hyperbaric Oxygen***
  In a single case, the use of hyperbaric oxygen in a single-man unit (Union Carbide type), at 2 atm twice daily, was believed to be helpful in a patient with bilateral severe injury of hands and feet. The problem arises if the blood transport system, arteries, and venous channels are destroyed or plugged with intraluminal clots so that oxygen cannot be brought to the cellular level by an adequate blood flow. Then the oxygen, regardless of the atmospheres applied, will be of little help. The absorption of oxygen in this fashion, despite the blocking by thrombus or by aggregated corpuscles, is made even more difficult if the endothelial lining of the vascular tree is severely traumatized or destroyed.

- ***Antibiotics***
  - Moyer's solution,[‡] 0.5% $AgNO_3$, has been utilized as an agent in burns to overcome superficial and even deep infection of the involved extremity.[4]
  - Silvadene, a drug used in burn therapy, has been helpful in the treatment of digital freezing injury, particularly after bleb loss or rupture. Although salves and ointments have not been considered helpful in treating freezing cold injury because they prevent lavage of the injured tissue with whirlpool therapy, hexachlorophene detergent cleanser (pHisoHex[*]), povidone-iodine (Betadine[*]), chlorhexidine gluconate (Hibiclens[*]), or benign surgical soaps have all been helpful.

[*]Manufacturing and availability information: Tolazoline hydrochloride (Priscoline hydrochloride; mfg: Ciba Pharmaceutical Co, Summit, NJ); Pentoxifylline (Trental; mfg: Hoechst-Roussel Pharmaceuticals, Somerville, NJ); Nifedipine (Procardia; mfg: Pfizer Inc, New York, NY); Phenoxybenzamine hydrochloride (Dibenzyline; mfg: SmithKline Beecham, Philadelphia, Pa); pHisoHex (hexachloraphene detergent cleanser; mfg: Sinofi Winthrop Pharmaceuticals, New York, NY); Betadine (povidone-iodine; mfg: Purdue Frederick, Norwalk, Conn); Hibiclens (chlorhexidine gluconate; mfg: Stuart Pharmaceuticals, Wilmington, Del).
[†]Not often used; listed in *AHFS Drug Information*. Bethesda, Md: American Society of Health-System Pharmacists, American Hospital Formulary Service; 1999.
[‡]The solution is made fresh by the hospital pharmacy on request. Moyer's solution was developed by Moyer for burn care at St Louis University School of Medicine, Department of Surgery, St Louis, Mo. It is good for superficial infection in frostbite too, and it also lessens pain.
FCI: freezing cold injury
Sources: (1) Salini Z, Wolverson M, Herbold D, Vas W, Salini A. Treatment of frostbite with IV streptokinase: An experimental study in rabbits. *AJR Am J Roentgenol.* 1987;149(Oct):773–776. (2) Tuomey J. An open label pilot study to evaluate the efficacy and safety of intra-arterial tissue plasminogen activators (TPA) in the treatment of severe frostbite. Minneapolis, Minn: Trauma Center, Henepin County Medical Center; December 1989. Letter. (3) Zdeblick T, Field G, Shaffer J. Treatment of experimental frostbite with urokinase. *J Hand Surg Am*. 1988;13A(6):948–953. (4) Mills WJ. Frostbite: A discussion of the problem and a review of an Alaskan experience. *Alaska Med*. 1973;15(2):31,32.

tures, gradually develops tissue demarcation and gangrene, requiring amputation of the part. Severe endothelial damage or reperfusion injury is probably the reason for the bad outcome.

Escharotomy. Escharotomy should be performed on the dorsum or lateral aspect of the digits when the eschar is dry and has firmed sufficiently to have a cast effect on the digits, limiting their joint motion. Digits will be debrided further in the whirlpool, without prematurely exposing underlying

EXHIBIT 14-6

SURGICAL PROCEDURES FOR POSTTHAW CARE OF EXTREMITIES WITH FREEZING COLD INJURY

- Escharotomy and escharectomy
- Bleb, bullae, and wound debridement
- Fasciotomy
- Arteriotomy
- Vascular wound repair
- Dermal graft procedures:
  - Reverdin (Davis) pinch grafts
  - Split-thickness skin grafts
  - Split-thickness skin graft (mesh)
  - Free, full-thickness skin graft
  - Cutaneous pedicle flap graft
  - Muscle, musculocutaneous vascular flap transfer with associated nerve supply
  - Very early digital debridement with vascular cutaneous flaps
- Controlled subcutaneous balloon tissue expansion, often fraught with danger because of pressure over the small vessels in the region
- Modified guillotine amputation
- Closed amputation with or without suction irrigation
- Closed or open reduction of fractures and dislocations
- Joint contracture releases, joint excision, and replacement and joint fusion
- Soft-tissue and web-space releases
- Surgical regional sympathectomy
- Periarterial sympathectomy, microdigital sympathectomy
- Excision of sinus tract for the presence of squamous-cell carcinoma (a rare occasion)
- Tissue compartment releases, carpal and tarsal tunnel syndromes

epithelializing tissues.

Sympathectomy. In patients with apparently equal bilateral injury, results of sympathectomy within the first 24 to 48 hours have demonstrated that although there is no further preservation of tissue, there is

- decrease in pain;
- marked decrease in edema;
- much less infection, both superficially and deep; and
- early and more proximal tissue demarcation.

Pharmacological sympathetic blockade may be considered as an alternative. Particularly effective has been the use of phenoxybenzamine hydrochloride (Dibenzylene; manufactured by SmithKline Beecham, Philadelphia, Pa), given 10 mg daily and increased to 20 to 60 mg/d, depending on the effect and need. This drug is used for vasospasm and appears to be an effective α-adrenergic blocking agent. It is important that the patient be well hydrated after surgical or chemical sympathectomy. *Sympathetic blockade is especially effective if accompanied by fasciotomy in casualties with severe FCI, who have associated increased tissue compartment pressure.* Lumbar block for the lower extremities and stellate ganglion block for the upper extremities are appropriate, with an epidural approach to the former being especially useful. Epidural blockade is often given in the continuous mode and may be repeated as necessary. The treatment is seldom maintained for longer than 4 days but has been highly effective in relieving the severe pain, edema, and pallor often associated with NFCI.

Debridement and Amputation. Debridement or amputation, if required, should be delayed until sufficient time (often 15–45 d) has elapsed to demonstrate

a line of demarcation, mummification, and tissue death; and with no danger of further retraction of tissues. It should be emphasized that premature amputation during the edematous stage often results in further retraction of tissue that could be utilized to cover the residual stump. Overwhelming infection, often found in freeze-thaw-refreeze injuries or in extreme extremity trauma complicated by freezing, may result in overwhelming sepsis, requiring immediate amputation to avoid toxic shock.

Skin Grafts. The grafting of split-thickness skin to large granulating areas or areas where skin cover is considered proper may be carried out from the 3rd to the 14th day. The results of skin graft are best when it follows thawing by rapid rewarming. The pedicle grafting of full-thickness skin is a late procedure. The use of a mesh skin graft at the time of fasciotomy, or soon after, reduces the morbidity, lowers the incidence of scarring and infection, and allows proper draining through the mesh openings.

Infection. Antibiotics are not necessary except where infection is deep. Common bacterial organisms found in the injured tissues include staphylococci, streptococci, and *Pseudomonas* species, and often an abundance of Gram-negative species. Clostridia species are occasionally found. Routine cultures and sensitivity studies are taken, and at the first indication of nonsuperficial infection that is not cleared by whirlpool washing, aggressive antibiotic therapy by oral, intramuscular, or intravenous methods is utilized. Particularly for injuries that occurred in the field and are associated with frostbite, and for frostbite alone, it is helpful to utilize the toxoid booster; in the event of no booster being available, antitoxin may be given.

Pain Management

Narcotics are used sparingly in uncomplicated cases after initial thawing; tranquilizers or aspirin will generally suffice, although pain obviously varies with each individual. Pain also varies with the type of injury, the degree of edema, and the presence or absence of infection. Pain is lessened by immediate physiotherapy, activity, and whirlpool bath. In severe cases of immersion injury, with edema prior to fasciotomy, or with high-level extremity freezing (postthaw), pain relief is provided with continuous epidural block for 24 to 48 hours. Requests for pain medication often increase when it is apparent that necrosis of tissue is eminent or present–pain and distress having both a physical and a psychological cause. The discomfort, too, is lessened by a healthy doctor–nurse–patient relationship; by adequate physiotherapy and occupational therapy; and by whirlpool baths and analgesia as required.

In severe cases of FCI, and particularly so with the acute stage of postwarming immersion injury, pain relief may be provided with continuous epidural block, the use of a long-acting anesthetic such as Marcaine (bupivacaine hydrochloride; manufactured by Sanofi Winthrop Pharmaceuticals, New York, NY), for 24 to 48 hours, and repeated if necessary. This treatment is especially effective if accompanied by fascial release in severe cases of freezing or immersion injury, when increased compartment pressures are present. Helpful to these patients is an anesthesiologist or pain center physician. Choices of epidural medication usually are 0.25% Marcaine in a bolus or with an infusion pump. Marcaine is utilized with the axillary or stellate blockade to achieve a long-acting effect; occasionally, indwelling axillary catheters are utilized with an infusion pump or 1.5% Xylocaine (lidocaine hydrochloride; manufactured by Astra USA, Westboro, Mass), occasionally supplemented with a steroid such as Depo-Medrol (methylprednisolone acetate; manufactured by The Upjohn Company, Kalamazoo, Mich).

Prognosis

Prognosis for recovery depends on the extent of freezing, other associated trauma, the manner and timing of thawing, and if freeze-thaw-refreeze or reperfusion injury has occurred. After FCI, the prognosis for a good result with the least number of complications occurs if

- the frozen state is of short duration and the depth of injury is minimal;
- thawing is by rapid rewarming;
- blebs develop early and are very distal or pink and large;
- blebs extend to the distal tips;
- in the process of rescue, trauma has been minimal and refreezing has been avoided; and
- there is an early and rapid return of capillary perfusion, especially as demonstrated by technetium 99m radioisotope studies.

Prognosis for an adequate result is uncertain if

- the frozen state is of long duration;
- the depth of freezing is deep;
- thawing is spontaneous or delayed (other than rapid rewarming); and
- freezing is superimposed on fracture or dislocation, or associated with moderate to se-

vere hypothermia.

The prognosis is almost certain to be poor and with complications if

- thawing is delayed (by means of ice, ice water, snow, friction massage);
- thawing is by excessive heat (> 49°C, 120°F);
- postthaw blebs are proximal, dark, hemorrhagic, and do not extend to the distal phalanges;
- necrosis is early, with early advent (4–5 d) of mummification or liquefaction necrosis of the involved part;
- freeze–thaw–refreeze injury has occurred;
- there is obvious loss of cellular perfusion, as identified clinically and confirmed by technetium 99m studies, on early and repeated views; and
- reperfusion injury is suspected.

Throughout all our experience with cold injuries obvious unsolved problems have remained, namely, the poor results when FCI is superimposed on immersion injury or hypothermia; when the epiphyseal plates of children are subjected to freezing; and one of the most disastrous events of all, when freeze–thaw–refreeze injury occurs. This latter injury is of major consequence at altitude, where, in addition to the refreeze injury, compression injury may also occur above the level of 15,000 ft or in aircraft, and particularly so at altitude in arctic mountains. At that altitude and latitude, the barometric pressure–different from on mountains near the equator–is nearly 0.5 atm and permits expansion of cellular stocking or boot-liner material, such as neoprene stocking material. Nonpliable leather or plastic outer boots, unable to expand, allow the increased pressure from the underlying cellular expansion to be directed downward against the soft tissue of the foot. This compressive force deprives the foot of required microcirculation; ischemia soon develops, followed by local circulatory failure and freezing.

SEQUELAE OF COLD INJURY

Tissue freezing is almost always followed by some residual loss of anatomy or function, slight though that loss may be. The sequelae of cold injury may be categorized as transient or long-standing; before we list the sequelae of FCI and especially of NFCI, it is pertinent to list their present importance. As previously noted, in World War II, especially during the Battle of the Bulge and the winter campaign of 1944/45 in Europe, severe cases of FCI and NFCI occurred. These injuries are well documented in a volume of the official history of the US Army Medical Department in World War II, published by The Surgeon General.[19]

In the Korean War that followed, especially during the 1950 winter months of November and December and during the 15-day retreat from the Chosin Reservoir, many more cold casualties were obtained as the beleaguered troops—US Marines, US Army, US Air Force observers, and allied support, including the Royal British Marines and the South Korean forces—fought back to the sea, surrounded by more than 150,000 Red Chinese troops, who had just entered the war. The allied group numbered 15,000 and despite the overwhelming odds managed to reach the sea, carrying their wounded with them, marching, many of them, with cold-injured extremities (Exhibits 14-7 and 14-8).

For years, this group was told that for purposes of compensation, cold injury was considered a nonservice–incurred event. This decision has since been overruled by the US government and the Department of Veterans Affairs. Beginning in the fall of 1996, veterans of World War II and the Korean War began to be evaluated, 45 to 55 years after the injury for service-incurred disability. Most are aged 60 to 70 years, and a few are 80 or more years of age. On physical examination, many of these survivors demonstrate signs of sequelae (Exhibit 14-9). As more veterans are evaluated, the demonstration of cold-injured sequelae becomes more apparent—so much that it may be said that any significant FCI or NFCI will demonstrate some residual finding, often increasing as the veteran ages and time goes by.[96]

In examining the cold-injured patient for sequelae, first thought should be directed to an adequate history of exposure (eg, the patient's having been a member of the 84th Infantry Division, Battle of the Bulge, 1944/45; or a member of the 1st Marine Division in their march to the sea from the Chosin Reservoir in Korea, November or December 1950). A further history should include the type and the duration of exposure, the apparent type of injury as FCI or NFCI, and medical verification by the medical records, if they still exist. In the march south from the Chosin Reservoir, many of the records of the beleaguered troops were lost or destroyed, adequate medical history was taken on very few, and unfortunately, according to their current history, very few had a discharge physical examination.

All these details would be helpful: the duration

EXHIBIT 14-7

THE RETREAT FROM CHOSIN RESERVOIR: A MEDICAL OFFICER'S EXPERIENCE

The Chosin Reservoir is a large, lakelike reservoir in northeast North Korea, one of a chain of lakes used to create hydroelectric power for that area. Then a lieutenant in the Medical Corps, US Navy, I served as a battalion surgeon in the 2nd Battalion, 7th Marines, in the Chosin Reservoir Campaign in November/December, 1950. Temperatures at that time were some of the lowest ever recorded in North Korea, reaching –30°F and –40°F on occasion. My battalion aid station was located in Hagaru-ri, a small village on the south end of the Chosin Reservoir. On the northeast side of the reservoir were stationed US Army units that had been placed in an isolated geographic location, with only a single winding road offering supply and evacuation possibilities. On the west side of the reservoir was located a small town called Yudam-ni, approximately 10 miles over rugged terrain north of Hagaru. As we marched into Hagaru-ri, the temperature was well below zero. Marines were forced to stand in line for long periods while the area in front of our troops was cleared. It soon became apparent that men were freezing while standing still, with white discoloration of the nose, cheeks, and ears. I assigned my corpsman the job of going up and down the standing line of troops to establish a buddy system, so that each Marine would monitor his buddy for frostbite. Despite this, many of the troops developed redness and blistering of their faces and ears that day.

The Marines were assigned positions in the mountains surrounding Hagaru. The Chinese had come into the war. Unfortunately, with the first contact with the Chinese, some of our troops were bayoneted in their sleeping bags. This story was quick to spread throughout the entire battalion. As a result, many of the men were unwilling to even get into a sleeping bag, using it as a blanket instead. We were assigned shoepac boots. These contained a 3/4-inch felt innersole. A spare innersole was issued to the soldier or Marine; this was to be kept against his body inside his undershirt. The theory behind this special boot was that body heat would evaporate any perspiration in the innersole, and at night the shoes could be taken off, the toes massaged and possibly powdered, and a fresh, dry, warm innersole would be inserted into the boot. The other perspiration-laden innersole was to be removed and placed against the body for evaporation. Unfortunately, the men in the field were unable to take off their boots, especially if they were not sleeping in their sleeping bags. In –30°F weather, the shoepacs froze. This caused a layer of ice to form across the sole of the shoepac, causing freezing of the feet, painful walking, and, when boots were removed, swelling to a point that boots could not be placed back on the feet. The soles of these men's feet looked like raw meat. Many had bloody blisters on one or more toes. In addition, some sustained cold injury to the fingers and hands from outdoor contact with metal weapons.

At the time the 1st Marine Division moved into northeast Korea, General Douglas MacArthur's headquarters had issued statements that, for practical purposes, the war was over and that we would be home by Christmas. The issuance of winter gear was delayed until late in November, since there was no reason for issuing gear if we would be out of there in such a short time. Unfortunately, the weather was already below freezing before we received winter parkas, heavy gloves, and shoepac boots.

No education regarding frostbite prevention was even attempted. In fact, the medical personnel were lacking in knowledge of short-term effects of frostbite and how best to treat this. Fortunately, in our aid station we had several petty officers who had served in World War II and had some cold weather experience. They gave us advice as to slow warming of frozen tissue versus rapid warming, dry warming versus immersion in water, and so forth.

A small airstrip was bulldozed out of the ice in Hagaru. This strip was able to take small, propeller-driven airplanes, which could evacuate only 28 stretcher cases or about 32 seated casualties at a time. Evacuation of many of the frostbite victims would have been desirable. This certainly would have allowed them to get to Japan, where the weather was warmer and where slow thawing of tissue and proper treatment could have been administered. Unfortunately, we were overwhelmed with severe combat casualties, many of them from the 31st and 32nd Infantry Regiments, which had been stationed east of the Chosin Reservoir. Many of their officers were killed, and the Chinese took their time to destroy this trapped fighting unit. Many soldiers crawled across the ice of the Chosin Reservoir to try to reach Marine positions. A tank infantry team was organized to place drivers on trucks that had been stalled on the single-lane road. These trucks were brought into Hagaru-ri, and many of the casualties were assigned to my battalion aid station. We treated hundreds of casualties

(**Exhibit 14-7** *continues*)

Exhibit 14-7 *continued*

over the next 3 to 4 days. Many of the casualties had multiple gunshot wounds, fractures, skull injuries, sucking chest wounds, and the like. All of these soldiers were frozen. We had to cut their boots off their feet. Initially when we tried to remove the boots, some of the toes would come off in the boot. We found we could do less damage by cutting the leather boots and slowly removing the foot, almost dissecting the foot out of the boot, in an attempt to preserve tissue. With these multiple, severe, life-threatening injuries, the evacuation of Marines and soldiers with simple frostbite had a lower priority. In fact, we had orders to keep all troops in the line who could ride "shotgun" and protect the driver by riding in the right front seat, even though they could not walk! At this same time, Marines were returning from Yudam-ni, having successfully escaped from Chinese encirclement. All of these troops had experienced prolonged outdoor exposure to freezing weather and snow. All had some degree of frostbite of toes and, in many cases, hands and ears.

After the march back from the Chosin Reservoir to board ships at Hungnam to move to Pusan, South Korea, many of the troops who had blistered feet found that the fluid was absorbed and that the tissue returned to "normal." These men stayed in the line and no record of frostbite was ever documented in their medical records. Now, years later, many of them suffer the long-term effects of cold injury. One interesting observation after we reached Masan, South Korea (where the weather was warm), we suddenly found our sick-call line two city blocks long! These men had upper respiratory infections with nasal congestion, cough, and sneezing. Apparently, while they were in North Korea with its subfreezing weather, the common cold virus somehow did not cause trouble. We did see respiratory illness, such as bronchitis and even some cases of pneumonia, but even these were not common. The sudden emergence of upper respiratory infections certainly was somehow associated with exposure to a warmer environment.

Lessons Learned From My Chosin Reservoir Experience

1. The shoepac boot theoretically could prevent cold injury, if properly used. In a combat experience where replacement of perspiration-laden innersoles is impossible, however, they contribute to severe cold injury.
2. While it is impossible to anticipate all medical problems, the possibility of exposure to harsh winter conditions should have prompted the leaders of the medical departments of the US Navy and Army to offer educational seminars on how to handle these injuries. We spent 2 weeks patrolling north and south in the Yellow Sea, while the largest mine field in history was cleared from Wonsan Harbor in North Korea. This would have been ample time to brief the medical departments on what might be in store. Perhaps we could have prevented some of the severe cold injury with this information.
3. A constant review of equipment for harsh weather conditions should be mandatory in the armed services. Our troops deserve the best possible equipment, which should not be compromised for financial reasons.

Exhibit prepared for this textbook by Stanley I. Wolf, MD; formerly, Lieutenant, Medical Corps, US Navy Reserve; Second Battalion, 7th Marines, Hagaru-ri, Chosin Reservoir, North Korea, November/December, 1950; currently, 7213 Greentree Road, Bethesda, MD 20817-1507.

of exposure, depth of injury, diagnosis of degree of injury or description of the injury as superficial or deep. Did a refreeze injury occur? What was the appearance of the extremity? Was there associated trauma including gunshot wound?

An ongoing medical history and physical examination are in order to determine or rule out specific or general systemic diseases that might affect the sequelae. For example, preexisting or present diabetes, arthritis, peripheral vascular or neurovascular disease such as Raynaud's syndrome or labile vasomotor changes, small-vessel disease from any cause, or neurovascular loss all might cloud the picture when evaluating for sequelae. Equally, the sequelae may be altered by, or actually be arthritic, or undergoing musculoskeletal change. The appearance of edema, swelling from any cause, skin-color change, dependent rubor and elevation pallor or loss of pedal pulses-any and all of these are pertinent findings during the examination.[97] Specifically, the general appearance of the limb should be noted, including skin-color and musculoskeletal changes (muscle atrophy or limitation of joint motion, digital deformity, scarring, edema, and swelling).

It is wise to have the patient go through a range of motion of the fingers and to have gait evaluation by heel-toe walking, as well as examining the appearance of the toes, looking carefully for onycho-

EXHIBIT 14-8

THE RETREAT FROM CHOSIN RESERVOIR: A CORPORAL'S EXPERIENCE

I joined the US Marine Corps Reserves on 6 March 1948, and was then attached to B Company, 11th Infantry Battalion. On 5 August 1950, I was called into active duty along with the rest of our reserve unit from Aberdeen, Washington, Grays Harbor County. At that time we consisted of about 350 Marine Reserves. I was sent to Camp Pendleton, California, where I received overseas medical shots; in mid September I was sent with a work party to San Diego, California, where we spent about 12 days loading winter gear onto a ship that was to go to Korea. On 29 September I boarded the *General Nelson M. Walker* with about 2,000 other troops and about 15 October docked at the port of Yokahama, Japan. We trained in Japan about 2 weeks at the Marine base in Otsu, Japan, then boarded the USNS *Aiken Victor*y on 3 November and arrived in Won Son, Korea, on 6 November 1950. We were the first replacements for the 1st Marine Division. We were told that winter gear awaited us at our units and that everything would be distributed there. But when we arrived and were assigned to our outfits, there was no winter gear.

Later, six other Marines and I were sent to B Battery, 11th Marines, as replacements. It was nearly dawn when we arrived. We immediately began to dig our foxholes but the ground was frozen solid—almost like digging into solid rock. We were told at the time that the temperature was –42°F. Along with my best friend from Aberdeen, Leland Godfrey, and one other GI, I got up every 2 hours during the night to do calisthenics to keep warm. The next morning the four other replacements, who had slept straight through the night, were sent back to the hospital in Seoul, South Korea, where they were treated for frostbitten feet, hands, ears, face, and buttocks. The three of us who had exercised to keep warm were OK. After 2 days and nights of freezing weather we were finally issued winter clothing. Later that morning we were informed that the decision had been made: we would fight our way out of the trap. We thought we had protection on our flanks: the 8th Army on one side and a division or so of the Republic of Korea (ROK) Army covering the other. Unbeknown to us, however, the 8th Army had been overrun and had fled down the mountain. They had been ambushed and had left all their equipment (many of the trucks still running) along the treacherous road. Also unbeknown to us, the ROK forces covering our opposite flank had also been overrun and annihilated. We were unprotected, alone, and surrounded by almost 120,000 Chinese troops. Within the Chosin Reservoir, our own forces consisted of two battalions of the Army's 7th Infantry Division and the 1st Marine Division: 20,000 men. We were outnumbered 6 to 1.

All troops were ordered to rendezvous at Yudam-ni, and from there the battle would begin. Because we Marines are trained first in infantry, many of us volunteered to fight with the 7th Marines. I was placed in a group of 20 other GIs from the 7th. While on patrol, we were attacked by (from what we could tell) about 75 Chinese troops. We were all huddled together and were able to kill most of them. We took 14 back with us as prisoners. They were wearing shoes that looked like tennis shoes. A foot of one of the prisoners had come off his leg just above the ankle; it had been frozen and gangrene had set in. I don't know how he remained alive.

I had been with the 7th Marines only 3 or 4 days when I was sent back to my artillery unit from the 11th. Things went fairly smoothly while I was with the artillery. But we each took our turn on the front lines as a forward observer, whose job was to pinpoint targets for the artillery and give the coordinates over the radio. And regardless of what our position may have been, we were poorly equipped. Our carbines froze, our M1s and 105-mm howitzers were left over from World War II, and our thermoboots left much to be desired. As long as we were moving, our feet stayed warm and even sweated; but as soon as we were still, the sweat would freeze and so would our toes. But we accomplished what we needed to: our howitzers wreaked havoc on the Chinese troops and enemy equipment. (Each Chinese soldier carried simple but effective equipment: a backpack, which held a straw mat and a white sheet. In a field of grass, they would cover themselves with the straw mats, then with the sheets. In snow, the white sheets blended perfectly and they were able to hide entire divisions.)

The enemy demolished every bridge to keep us from withdrawing from the trap, so we were forced to find other means of crossing waterways and valleys. Huge roadblocks were placed in our path to buy time for the opposing forces. Between Yudam-ni and Toktong Pass we had 30% casualties. The Chinese constantly shelled us with white phosphorus, and even lobbed phosphorus grenades into truckloads of wounded Marines. The fighting at Hagaru-ri was fierce. We had a makeshift airstrip there, which was used to evacuate the wounded

(**Exhibit 14-8** *continues*)

Exhibit 14-8 *continued*

and victims of extreme frostbite. The enemy wanted that airstrip and concentrated all their strength there. Being outnumbered (now nearly 9 to 1), we could not hold. We had previously carried all our dead with us but now would be forced to leave them; we used bulldozers to push the bodies of several hundred men into a mass grave. We then loaded our wounded and almost all our equipment (destroying the little we could not take) and withdrew from Hagaru-ri.

We were fighting not only the enemy but also the weather, and we lost as many men to frostbite as we did to the Chinese. We were not used to such cold conditions; during the winter it was never above –20°F. The enemy had lived all their lives in this weather, however, and benefited from that. Our artillery could not recoil it if got too cold, and our carbines were worthless. The M1 rifle was our best weapon. It took 10 to 15 days for us to fight completely out of the trap. We lost nearly half our men and more than half of those to the cold weather. Most of the troops had not been able to sleep since the rendezvous at Yudam-ni and had little to eat because our C rations were completely frozen. On the last leg of our retreat, when we were headed for the collection center at Hamhung (the port of evacuation was at Hungnam), the Chinese had set up roadblocks all along they way and fired on our left flank from machine gun nests along the way. Men were slaughtered; we had no defense. I tried to return fire but my fingers were so frozen that I couldn't even pull the trigger on my M1. As the Chinese continued to fire on us, a group from the 7th Marines came up from behind and destroyed their guns. By the end of the battle we had lost just over 12,000 troops: 3,000 men were dead; 6,000 were wounded; and 3,000 more had frostbite. When we finally arrived at Hungnam, the Marines there had prepared hot food and warm tents for us. The next day we boarded troop transports, carriers, freighters, and fishing boats, which had been held for our retreat.

The battle from the Chosin Reservoir was called "the Christmas Miracle" by the Koreans. Because we had been able to hold out so long, we were able to take more than 100,000 North and South Korean refugees out with us. I have been told that this was one of the largest rescue operations in history; never before had so many enemy civilians been rescued in the midst of battle. Although some historians are said to have called this the "most savage battle of the 20th century," I believe that we would have been at least 50% more effective if our military had known how to train us properly for such battle conditions. The training and equipment provided now, half a century later, far surpass nearly everything we had during the Korean War.

Exhibit prepared for this textbook by Wayne F. Cotton; formerly, Corporal, US Marine Corps Reserves; currently, 333 West Lake Forest Lane, Shelton, Washington 98584

mycosis or onychogryposis. Range of motion of ankle and toes should be examined, with evidence of intrinsic muscle loss of hands or feet noted, and consideration given for the presence of tarsal or carpal tunnel syndrome, which are often sequelae of freezing injury.[98] Instruments are available to measure range of motion, both flexion and extension, lateral and medial deviation, and claw toe or hammer toe, for which small goniometers are available and helpful. For assessing sensation, a pin wheel may be utilized to measure hyperesthesia, normal sensation, hypesthesia, or anesthesia. For determining nerve function, a tuning fork is helpful; a tape measure is useful for measuring circumference to determine the presence of edema; and a palpable examination is necessary to determine the presence of pitting edema. An anesthesiometer measuring 2-point discrimination is helpful, and a telethermometer recording in Centigrade or Fahrenheit is useful, particularly for comparing extremities. Ultrasound Doppler for measurement of pulses not palpated manually is also helpful.

EVALUATION OF MILITARY PERSONNEL FOR RETURN TO DUTY

The range of disability varies following FCI and, depending on the degree of injury, may vary from very little to a large amount. A greater degree of disability precluding return to normal duty may follow NFCI (trench foot) than FCI (frostbite). In both cases, sequelae may begin to demonstrate themselves in 6 to 18 months and thereafter. The ultimate in loss, amputation, may not preclude the patient's return to duty, full or limited, depending on the level of amputation and the ability of the soldier to function in the field. These factors can readily be determined by examination or actual ac-

EXHIBIT 14-9

SEQUELAE OF COLD INJURY

Transient sequelae
- Hyperhidrosis
- Hypesthesia or anesthesia of digits
- Limitation of motion of the interphalangeal and metatarsal or metacarpal joints
- Swelling of the interphalangeal and metacarpophalangeal joints
- Edema of digits, hands, and feet
- Thin, fragile epidermis in involved areas
- Nail loss
- Intrinsic muscle atrophy
- Fat pad loss from distal tips of digits
- Pain from injury to peripheral nerves and small vessels as a result of ischemia

Late, long-lasting, or increasing degree of sequelae
- Deep, fixed scars over the affected area
- Atrophy or fibrosis of the affected musculature
- Flexion, extension deformity of distal joints especially involving the toes, often with hammer toe or claw toe deformity
- Volar fat pad loss of fingers and toes
- Hyperesthesia of distal tips of digits, with increased sensitivity to heat and cold
- Residual hypesthesia of digital tips
- Decreased proprioceptive sense of digital tips
- Permanent nailbed deformity, as onychogryphosis, often with associated onychomycosis
- Roentgenographic evidence of subarticular and periarticular lytic destructive changes of bone and cartilage, especially in phalangeal joint areas
- Avascular necrosis of bone, especially in the phalanges, metatarsi, and tarsi (eg, the calcaneus)
- In children or young adults, epiphyseal necrosis or total destruction of physis or epiphysis (growth plate destruction) with joint or phalangeal angulation deformity or shortening
- Chronic ulceration, infection, or osteomyelitis in area of cold injury
- Loss of fibrocartilage of ears and external ear part loss
- Decreased capillary perfusion by isotope examination (indicative of endothelial cell loss)
- Rare findings of carcinoma (usually squamous cell) in long-standing draining sinus tracts, or with chronic wound infection or osteomyelitis
- Interphalangeal joint immobility, marked limitation of joint motion or fusion of interphalangeal joints
- Carpal and tarsal tunnel syndromes (seen in acute stage, too)
- Variable findings or hyperhidrosis, hypohidrosis, anhidrosis
- Intermittent or consistent pain in hands or feet, often extending in the lower extremities to levels above the apparent injury level
- The ultimate in long-standing sequelae, or the result of severe early cold insult, namely, amputation of the involved part at any level

tivity under field conditions. Pain, swelling, neurological loss, poor vascular supply, and the presence of wounds that fail to heal properly usually preclude return to full duty.

Generally, problems of cold sensitivity may limit duty in arctic or subarctic or mountainous regions. Following FCI, sequelae usually are not debilitating enough to demand medical discharge and the

sequelae may consist of only hyperhidrosis, lack of proprioceptive sense, and limited capillary perfusion. Should thermography be available, this could determine the degree of superficial circulation. Studies using radioisotopes such as technetium 99m could determine deep capillary perfusion, and flat-plate roentgenograms could determine any lytic destructive changes near the small joints of the carpal or tarsal areas, as well as the interphalangeal joints. These findings—by roentgenography, thermography, or isotope studies—are often accompanied by physical examination changes, including swelling or limited range of motion.

On the other hand, in NFCI, residual problems of pain, formication, anesthesia of the extremities, or hypesthesia or hyperesthesia are often found to increase as time evolves. Pain along the course of peripheral nerves and digital vessels and marked intrinsic muscle loss or flexion or extension contractures of the interphalangeal joints often occur (see Exhibit 14-7). After FCI or NFCI, exposure to cold *must* be avoided for 6 months following minimal injury and for 12 months following major injury. A second exposure to FCI or NFCI within 6 months or a year may result in major tissue loss-even like those seen in freeze-thaw-refreeze injuries. As is often the case, US Army Medical Manuals; Technical Bulletins, Medicine; and Survey Board Recommendations after examination may help medical officers to decide the wisdom of retention for full or limited duty or separation from the service.

SUMMARY

Freezing cold injury (FCI, the occurrence of ice in and around cells), also called frostbite, has been a frequent source of attrition in mountain warfare and military campaigns fought in the winter. Eight modes of freezing injury can be found in soldiers fighting in a cold environment:

1. true FCI, superficial or deep;
2. a mixed injury: immersion (cold-wet) followed by FCI;
3. freezing, then thawing at any temperature, followed by refreezing;
4. hypoxia; high-attitude environmental injury, usually associated with hypovolemia, dehydration, and extremity freezing;
5. extremity compartment compression from any cause, followed by freezing;
6. extremity fracture or dislocation, followed by freezing;
7. hypothermia, associated with FCI to the extremities; and
8. FCI with superimposed burn injury or burn injury followed by freezing.

FCI leading to cell death has been graded in terms of the magnitude of tissue necrosis both as degree of injury and as superfical and deep. Superficial freezing injury (first and second degree) is manifested as transient hyperemia, edema, and possibly bullae, but there is no permanent tissue loss. Deep freezing injury causes skin necrosis (third degree) or death of underlying tissue (fourth degree), the latter condition frequently leading to amputation.

The principal pathophysiological event of FCI is the formation of ice crystals in the extravascular fluid spaces. Not only may the crystals cause mechanical damage to nearby cells but the loss of liquid water causes extracellular osmotic pressure to increase. The osmotic pressure gradient across the cell membranes draws liquid water from the intracellular space, resulting in electrolyte and acid–base changes that degrade enzymatic functions. As freezing continues, cell membrane damage occurs, especially in the endothelial cells of the microcirculation. On thawing, the initial event is vasodilation, followed by edema and vascular stasis, the latter resulting from intravascular cellular aggregation and consequent microvascular and macrovascular thrombosis. Edema may further contribute to tissue ischemia through mechanical compression of vessels and may be of a severity consistent with the diagnosis of compartment syndrome. During reperfusion of the thawed part, four factors may contribute to the tissue damage seen in cold injury: (1) generation of oxygen-derived free radicals, (2) neutrophil activation, (3) formation of vasoactive prostaglandins and thromboxane from the metabolism of arachidonic acid, and (4) activation of proteolytic enzymes. Tissue damage is especially severe when there is refreezing of a previously thawed part, possibly because of the formation of intracellular ice crystals.

The most important intervention in managing FCI is thawing. Four methods of thawing are commonly seen:

1. rapid rewarming in warm water (37°C–41°C);
2. gradual (spontaneous) thawing at room, cabin, or tent temperature, or in a sleeping bag, so that the thawing range varies;

3. delayed thawing utilizing ice, ice water, or snowpacks, and often accompanied by friction massage; and
4. thawing by excessive heat, which has included car heater, diesel generator exhaust, oven heat, hot water, campfire, or any heat greater than 48°C, often as hot as 65°C to 90°C.

Experience has shown that the first two methods are the least harmful, whereas the fourth is quite deleterious. Systemic hypothermia accompanying FCI can be treated by immersion of the patient in a warm water bath (32°C–37.7°C) and infusion of warm intravenous fluid.

Subsequent management of the freezing cold cold-injured body part includes open treatment (ie, no compressive bandages), whirlpool baths, nonsurgical management of blebs and bullae, fasciotomy when compartment syndrome is diagnosed, and possible use of measures designed to provide vasodilation such as sympathetic blockage or pharmacological vasodilation. Escharotomy should be performed only when an eschar is dry and severely limits motion at a joint. Extensive debridement or amputation should be delayed until sufficient time (often 30–90 d) elapses to allow a stable degree of mummification and tissue death to be reached. Blebs are debrided or trimmed only when infected and containing purulent material. Physical therapy has an important role in determining the functional outcome of a serious freezing injury.

Nonmedical factors that may not be sufficiently appreciated by the clinician are important in determining the final result in the human. These variables are in the realms of weather, inadvertent trauma, and individual human physiology and anatomy, which are often difficult to anticipate, measure, or predict. The state of health and physical condition of the casualty are also vital factors, including the associated factors of alcohol and drug use, mental state at the time of exposure, and the presence of additional injuries. The latter factor is of special importance in soldiers. Trauma preceding freezing, such as extremity strain, sprain, or fracture poses major problems, as does the presence of a penetrating wound, blunt trauma, or blood loss from any cause. FCI is further influenced by the degree of hypovolemia or dehydration present, causing further distal vascular deficiency prior to the onset of freezing. Little considered by most clinicians are problems of rescue and survival, often resulting in freeze–thaw–refreeze injury, and perhaps the irreparable trauma occurring at the junction of frozen and nonfrozen tissue, as "brittle" tissue segments are stressed when the FCI victim must walk, whether out of the wilderness before rescue or during a military retreat (eg, Napoleon's retreat from Russia or US and allied troops at Chosin Reservoir).

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