

A Clinical Review of the Management of Frostbite

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Abstract

Frostbite is a thermal injury that can occur when temperatures drop low enough for tissue to freeze. On rewarming the tissues, an inflammatory process develops which is often associated with tissue loss. The extent of the tissue loss reflects the severity of the cold exposure and includes factors such as temperature, duration, wind chill, altitude, and systemic hypothermia.

This review discusses the epidemiology, the pathophysiological processes involved, and the clinical management of frostbite injuries. Practical advice is given on both the field and hospital management and how to seek expert advice from remote situations. The review also discusses newer developments in frostbite treatment such as intra-vascular thrombolysis and adjunctive treatments such as the use of intravenous vasodilators.

Introduction

The unusually cold winter experienced in early 2010 resulted in a large number of cases of frostbite in the United Kingdom. The prevalence of frostbite amongst the civilian population has risen [1] in part because of an increase in the numbers of homeless, but also because of greater ease of air travel, participation in winter sports, and ascents to high altitude [2]. Frostbite is a thermal injury and the clinical features of frostbite relate to the initial freezing and the subsequent thawing of tissue, and the severity is dependent upon the temperature and duration of exposure. The wide spectrum of injuries observed range from minimal tissue loss and mild long-term sequelae, to extensive necrosis and subsequent amputation. Such severe injuries can have devastating consequences in young, otherwise fit individuals [3]. In this review the presentation and management of frostbite will be discussed, and the evidence for new adjunctive therapies and modern approaches will be assessed.

Historical Perspective

Baron Larrey, Napoleon's surgeon-in-chief during the advance into Russia in 1812-1813, gave the first detailed description of frostbite management [4]. He suggested friction massage with ice or snow and gentle warming was beneficial, but the 'excessive heat of fires should not be used'. Rapid rewarming in waterbaths is now a mainstay of frostbite treatment [5]. Larrey's observations regarding the deleterious effects of the freeze-thaw-refreeze cycle, with soldiers re-freezing their feet whilst marching on successive days, remain pertinent today.

Epidemiology

In a 12-year study into inpatient frostbite injuries in Saskatchewan, Canada [6] revealed certain predisposing factors including alcohol consumption (46%), psychiatric illness (17%),

vehicular failure (19%), and drug misuse (4%). Amputation was more closely correlated with the duration of cold exposure than the temperature. The feet and the hands account for 90% of injuries reported. Frostbite also affects the face (nose, chin, earlobes, cheeks and lips), buttocks/perineum (from sitting on metal seats) and penis (joggers). Although early studies classified the elderly and young children to be at high risk from frostbite injury, prevalence is highest between the ages of 30 and 49 years. Risk factors for frostbite are given in Box 1.

Medical and physiological

- Genetic susceptibility (eg those from warmer climates)
- Dehydration and hypovolaemia
- High-altitude, hypoxia and hypothermia
- Diabetes, atherosclerosis, vasculitis
- Arthritis
- Raynaud's phenomenon
- Vasoconstrictive drugs
- Sweating or hyperhidrosis (↑ heat loss)
- Previous frostbite

Behavioural and mechanical

- Inadequate clothing and shelter
- Alcohol and other drug use
- Psychiatric illness
- Smoking
- Tightly constrictive clothing (too many socks)
- Contact with heat conductive materials
- Rings on fingers
- Immobility (military situations)

Box 1 Factors that increase risk of frostbite

Pathophysiology

The pathophysiological processes underlying frostbite have been studied extensively over the years using both human and animal models. Current opinion is that local cold injury produces a succession of changes which are commonly divided into

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“prefreeze phase”, “freeze–thaw phase”, “vascular stasis phase” and “progressive or late ischaemic phase”. These overlap and the changes depend on the freezing rate, the duration of freezing, the extent of injury and the thawing rate. Mills proposed a simplified scheme of injury with two phases: the cooling–supercooling–freezing stage; and a vascular stage that includes thawing (rewarming) and post-thaw [5].

Skin sensation is lost around 10°C. With further cooling, vascular contents become more viscous, there is microvascular constriction and trans-endothelial leakage of plasma. Arterio-venous anastomoses may develop with shunting of distal blood. As skin cools further (0°C), freezing occurs and frostbite starts to develop. The location and speed of ice crystal formation depends on the rate of freezing. Very low ambient temperatures, wind and moisture accelerate this rate. As skin cools, cold-induced vasoconstriction is followed by cold-induced vasodilatation. This phenomenon, also known as the “hunting response”, protects extremities from cold injury (at the expense of heat loss). It occurs in 5 to 10 min cycles. As the extremity cools further there will eventually be closure of the arterio-venous shunts resulting in an avascular environment which protects the core from further heat loss [7].

Unless freezing is very rapid, ice crystals form first in the extracellular fluid spaces. Extracellular osmotic pressure increases, drawing free water across the cell membrane. This causes intracellular dehydration and hyperosmolality. As freezing continues, there are extra- and intracellular electrolyte and pH changes, dehydration, and destruction of enzymes. Cell volume reduction and possibly direct damage from ice growth occur. Cell membranes are damaged, microvascular function is compromised and endothelial cells are injured, with the endothelium separating from the arterial wall lamina. Cartilage, especially epiphyseal cartilage, is very susceptible to freezing injury. This is followed by ultrastructural capillary damage, loss of mitochondria in muscle cells, and other intracellular damage [5].

Depending on the method of rewarming, hyperaemia, ischaemia, cyanosis, or total circulatory failure develops. Blebs or blisters may appear secondary to vasodilatation, oedema, and stasis coagulation. Platelet and erythrocyte aggregates clog and distort the vessels in viable tissue. Associated injury may cause increased compartment pressures. As is seen in burns, reperfusion injury occurs. This may involve oxygen-free radicals, neutrophil activation, and other inflammatory changes.

Prostaglandin F2a (PGF2a) and thromboxane A2 (TXA2) cause platelet aggregation and thrombosis which results in ischaemia. Robson and Heggors found notably elevated concentrations of PGF2a and TXA2 in frostbite blister fluid [8]. These eicosanoid derivatives have been heavily implicated as mediators of progressive dermal ischaemia in burns, frostbite and ischaemia/ reperfusion injuries [9].

Depending on the degree of microvascular damage, one of two processes occurs: either vascular recovery with dissolution of clots, or vascular collapse which results in thrombosis, ischaemia, necrosis and gangrene. Refreezing after thawing causes intracellular ice formation with extensive cell destruction and further release of prothrombotic, vasoconstrictive PGF2a and TXA2. A rabbit ear model demonstrated increased tissue survival after a blockade of the arachidonic acid cascade [9]. The most notable tissue salvage resulted when specific TXA2 inhibitors were used. This has now been shown to be effective clinically [10].

Clinical Presentation and Classification

Symptoms

Patients initially describe a cold numbness with accompanying sensory loss [11]. The extremity feels cold to touch and it feels clumsy, “like a block of wood”. Thawing and reperfusion is often intensely painful and pain may persist for weeks or months, even after tissue demarcation. Residual tingling sensation starting after one week has been described and may be due to an ischaemic neuritis [12]. Symptoms are exacerbated by warm environments. Other sensory deficits include spontaneous burning and electric current-like sensations and may persist for years after the initial injury.

Signs

Initial appearances are often deceptively benign. However with thawing, frozen tissue may appear mottled blue, yellowish-white or waxy. Following rapid rewarming, there is an initial hyperaemia even in severe cases, often with a purplish discolouration.

Classification

Frostbite injury has been classified as either mild/superficial (no tissue loss) or severe/deep (with loss of tissue) [13], and this classification is based upon final outcome (Table 1). Cauchy et al [14] proposed a predictive classification system that is based on the topography of the lesion(s) and early ⁹⁹technetium bone scanning. Using these techniques it is now possible accurately to predict the likely outcome as early as two days (Table 2).

Frostnip

Skin becomes white and loses sensation. On rewarming becomes hyperaemic and paraesthetic.
Recovers completely. Paraesthesia persists for some weeks.

Superficial frostbite

1st degree - Partial skin freezing
- Erythema, oedema, and hyperaemia
- No blisters or necrosis
- Occasional skin desquamation (5-10 day later)

2nd degree - Full-thickness skin freezing
- Erythema, substantial oedema
- Vesicles with clear fluid
- Blisters, desquamation and black eschar (gangrene) formed

Deep frostbite

3rd Degree - Full-thickness skin & subcutaneous freezing
- Violaceous/haemorrhagic blisters
- Skin necrosis
- Blue-grey discolouration

4th Degree - Full-thickness skin, subcutaneous tissue, muscle, tendon and bone freezing
- Little oedema
- Initially mottled, deep red or cyanotic
- Eventually dry, black and mummified

Table 1: Classification of cold injury according to severity [13]

Treatment

Treatment of frostbite can be divided into three phases: field care, immediate hospital care, and post thaw care. Rapid evacuation

Initial lesion	Radiotracer uptake on bone scan	Skin blisters	Grade
None	Not indicated	None	1
Distal phalanx	Hypo-fixation of radiotracer	Clear fluid	2
Middle phalanx	Absence of uptake on digits	Haemorrhagic on digits	3
Carpal or tarsal	Absence of uptake on carpal/tarsal	Haemorrhagic on carpal/tarsal	4
Grade	Outcome		
1	No amputation, no long term sequelae		
2	Soft tissue amputation with fingernail sequelae		
3	Bone amputation on digit. Functional sequelae		
4	More extensive amputation, may develop thrombosis or sepsis. Functional sequelae		

Table 2: Cauchy predictive classification of frostbite [14]. Cauchy et al proposed a new classification of frostbite lesions involving the extremities and is based upon findings after initial rewarming and on day 2 after admission. Parameters a) initial lesion on day 0 after rapid rewarming, b) radiotracer uptake in bone scan on day 2, c) skin blisters on day 2

by helicopter from mountainside to hospital is often possible in Europe and North America hospital and eliminates the first phase. However frostbite sustained in the Greater Ranges now usually presents in the UK within 7-14 days of the injury. Whilst this is certainly an improvement on Herzog's lengthy and painful evacuation from Annapurna in 1950 [15], there is certainly no room for complacency. If the active management described below is enthusiastically undertaken, the severity of frostbite injuries is likely to be attenuated.

Field care

If there is a possibility of developing frostbite the subject should move out of the wind and seek shelter. A combination of warm drinks, removal of boots (consider problems with replacement if swelling occurs), and replacement of wet gloves and socks with dry ones, warming of the cold extremity by placing in companion's armpit or groin for 10 minutes only, finally putting the boots back on should help. Ibuprofen (400mg) should be given for its anti-prostaglandin effect, reducing the inflammatory process. Do not rub the affected part, or apply direct heat. If sensation returns, one can continue to walk. If there is no return of sensation, go to the nearest warm shelter (hut or base camp) and seek medical treatment. If at high altitude, give oxygen, fluids and descend [16].

Field rewarming should only be undertaken if there is minimal risk of refreezing since refrozen tissue almost always dies [17]. The decision to thaw the frostbitten tissue in the field commits the provider to a complex course of action involving pain control, adequate warming and hydration in a hostile environment and

subsequent protection of frostbitten tissue from further injury during evacuation. Frostbitten extremities cannot be used for ambulation once rewarmed [18].

Immediate hospital care

Hypothermia and concomitant injuries should be evaluated and systemic hypothermia should be corrected to a core temperature of 34°C [12]. Frostbitten extremities should be warmed over 15-30mins [18] to 1 hour [12] in a whirlpool (recirculating water and mild antibacterial agent). The State of Alaska Cold-injury Guidelines recommend water bath temperatures of 37-39°C [18]. Rewarming should continue until a red/purple colour appears and the extremity becomes pliable. Patients are often dehydrated; moreover, hypothermia causes cold diuresis due to suppression of antidiuretic hormone, so intravenous fluids are often advisable.

Post-thaw care

Blisters containing clear or milky fluid should be debrided and covered in aloe vera, a potent antiprostaglandin agent six hourly. The limb(s) should be splinted, elevated (to reduce reperfusion oedema), and wrapped in a loose, protective dressing. Padding should be put between the patients' toes if affected. Haemorrhagic blisters should be left intact to prevent desiccation of the underlying tissue. If they restrict movement they can be drained with their roofs left on. Tetanus toxoid and opiate analgesia should be given if indicated. Ibuprofen (400mg orally, every 12hrs) [10] provides systemic antiprostaglandin activity that limits the cascade of inflammatory damage. Antibiotics should be prescribed if there is any evidence of infection.

Thrombolytic therapy

There is emerging evidence that treatment of severe frostbite injuries with intra-arterial or intravenous thrombolytic agents can improve outcome [19]. In patients presenting within 24 hours of original exposure with apparently severe injuries where digit / limb loss is predicted, thrombolysis may be beneficial. A review of absolute and relative contraindications of tissue plasminogen activator (t-PA) should be undertaken. The aim of the thrombolytic treatment is to clear the occluding microvascular thromboses that accompany acute frostbite injury, and so restore arterial flow to normal [20]. The treatment should be undertaken in an HDU/ITU setting. Use of t-PA in the field is not recommended because it may not be possible to detect and treat bleeding complications [21]. The Utah protocol for intra-arterial t-PA administration has been published [22]. Angiography or technetium scanning should be used to evaluate the initial injury and monitor progress after t-PA according to local protocol and resources. A diagnostic angiogram must be performed and an intra-arterial catheter inserted close to the site of thrombosis. Giving t-PA within 24 hours of injury reduced digital amputation rates from 41% to 10% (P<0.05) in one study [22]. Reperfusion of ischaemic tissue can cause tissue oedema, and if this occurs within a confined space, interstitial pressures may rise and result in a compartment syndrome that requires urgent fasciotomy [21].

Early surgery

Fasciotomy should be performed if a compartment syndrome develops, but amputation should be delayed for up to three months, and certainly until the level of demarcation is clear [23]. However systemic infection resistant to intravenous antibiotics warrants early surgical debridement/amputation

[3]. Technetium⁹⁹ scintigraphy [24] and MRI scanning [25] allows more accurate prediction of the level of bone viability and early plastic/reconstructive surgery to cover viable bone may improve outcome.

Goals include keeping the patient comfortable, pain free, well-nourished and adequately hydrated. Twice daily antibacterial whirlpool baths encourages the blister eschars to separate from underlying healthy tissue. Early mobilisation with help of physiotherapists is beneficial [26] but further trauma to affected tissues must be avoided.

Adjunctive Therapies

Vasodilators

Intra-arterial reserpine has been shown experimentally and clinically to prevent vasospasm but failed to prevent tissue loss [27]. The use of pentoxifylline, a methyl-xanthine derived phosphodiesterase inhibitor, increases blood flow to the affected extremity, decreases platelet hyperactivity and helps normalise the prostacyclin to TXA₂ ratio, enhancing tissue survival. Iloprost is a synthetic prostacyclin analogue and a powerful vasodilator which inhibits platelet aggregation [29,30]. Administered as an intravenous infusion, it mimics the effects of a sympathectomy [31,32]. Chlorhydrate of buflomedil has been used to treat frostbite with success in Chamonix [33].

Heparin

There is no evidence to support the use heparin in the management of frostbite, but in patients with other risk factors for DVT, its use should be considered. Published protocols include the use of heparin in conjunction with thrombolytic therapy to prevent recurrent local thrombosis [19,20,22].

Hyperbaric oxygen therapy

The role of hyperbaric oxygen therapy (HBO) therapy in frostbite is unclear. Several animal studies have demonstrated it to be of no benefit yet two recent studies in humans have yielded excellent results. HBO increases the deformability of erythrocytes, diminishes oedema formation in burned and post ischaemic tissues, has a bacteriostatic effect, and has anti-free radical action [34-36].

Sympathectomy

Since blood flow is determined in part by sympathetic tone, it has been proposed that chemical or surgical sympathectomy in the immediate post exposure phase might to reduce tissue loss. In a rat lower limb model, early surgical denervation (within 24 hours of exposure) reduced tissue loss, but had no effect if performed after 24 hours [37]. However in a rabbit ear model, a *procaine* sympathectomy had no demonstrable beneficial effect [38]. Despite over 80 years of study, the potential benefit of sympathectomy in frostbite continues to be proposed, suggesting most clinicians remain uncertain of the role of sympathectomy in frostbite [39].

Frostbite patients often experience long-term delayed symptoms, such as pain, paresthesias, and numbness. Chemical or surgical (open or minimally invasive) sympathectomy to treat these symptoms has been performed with variable results [40,41]. Surgical sympathectomy has been shown in some studies to reduce duration of pain and expedite demarcation of tissue necrosis. However, it has not been shown to reduce the ultimate extent of tissue loss [42-44].

Acute treatment success with intravenous guanethidine has been reported, however in contrast in a single case no benefit was shown [45]. It has been suggested that sympathectomy may have a role in preventing some of the longer-term sequelae of frostbite such as pain (often due to vasospasm), paresthesias, and hyperhidrosis [46].

Amputation

Failure to delay surgery remains a major cause of avoidable morbidity. Better long term functional results are achieved with the early involvement of a multidisciplinary rehabilitation team. Early mobilisation of patients with partial foot amputations on weight bearing custom made orthoses has shown promising results [47].

Long term sequelae

The long term sequelae of frostbite have been less well studied. The functional use of extremities following a partial amputation is variable and injury specific. Following partial foot or digital amputation(s) the biomechanics of the foot are altered and customized orthotic insoles or footwear are often required to prevent further secondary damage. Previously frostbitten tissue appears more susceptible to further injury. Heated insoles and chemical hand warmers are now available and their use in conjunction with appropriate clothing should be considered following frostbite injury if avoidance of cold exposure is either not possible or acceptable to the patient.

Telemedicine

A recent development in accessing expert advice, which has been driven both by the patient's themselves and also those clinicians with a more limited experience of frostbite, is the use of the internet. A virtual opinion can be sought from anywhere in the world [48]. The UK based service can be accessed via the British Mountaineering Council website (<http://www.thebmc.co.uk/medical>). The service is run by UIAA/IKAR/ISSM[†] Diploma in Mountain Medicine Faculty Members and is being increasingly used by climbers and physicians worldwide, often to obtain a second opinion or to seek more specialised advice. Immediate advice can be given by satellite phone to climbers in the field. It is also possible to follow up patients in a "virtual clinic", reviewing recent digital images and discussing management options either by phone or via email.

Conclusion

Although still potentially a disastrous injury associated with a high morbidity, frostbite can now be treated more effectively to ensure tissue loss is minimised and functional outcome maximised. With adequate preventative measures the risk of frostbite injury can be reduced. With the rising prevalence of frostbite, future research remains important. However, a number of factors mean that progress is likely to be slow. Injuries tend to be variable and unpredictable, presentation is often significantly delayed and often to a wide range of different centres, there is no good animal model for basic research, and apart from the military there is little likelihood of achieving significant funding for research programmes. Research over the past 15 years has led to a new understanding of the pathophysiology of cold injury.

[†]International Mountaineering and Climbing Federation/ International Commission for Mountain Rescue/ International Society for Mountain Medicine

Understanding of the role of inflammatory mediators, such as PGF2 and TXA2, has led to new active medical regimens such as the use of ibuprofen and aloe vera. Improved imaging assessment using MRA, and technetium scintigraphy, coupled with further research into the use of adjunctive therapies such as the use of thrombolytic agents, vasodilators and pre-treatment with anti-tumour necrosis factor (TNF), should herald further advancement in the treatment of frostbite.

However, prevention, early warming, early medical treatment and delayed surgery are likely to remain the mainstays of treatment for the foreseeable future.

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