

# Cold damage to the extremities: frostbite and non-freezing cold injuries

C Imray,<sup>1,2</sup> A Grieve,<sup>3</sup> S Dhillon,<sup>2</sup> The Caudwell Xtreme Everest Research Group<sup>2</sup>

<sup>1</sup>UHCW NHS Trust and Warwick Medical School, Coventry, UK; <sup>2</sup>Centre for Altitude Space and Extreme Environment Medicine, Institute of Human Health and Performance, University College London, London, UK; <sup>3</sup>General Practice Vocational Trainee, Defence Postgraduate Medical Deanery, ICT Centre, Birmingham Research Park, Birmingham, UK

Correspondence to: Professor C H E Imray, Warwick Medical School, UHCW NHS Trust, Coventry CV2 2DX, UK; [chrisimray@aol.com](mailto:chrisimray@aol.com)

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## ABSTRACT

The treatment of cold injuries to the periphery has advanced substantially in the last 10 years and optimal outcomes are only likely to be achieved if a multi-disciplinary team uses the full range of diagnostic and treatment modalities that are now available. The internet and satellite phones with digital images allow immediate access by patients from remote geographical locations to hospital based specialists who can assess cold injuries and advise on early field care. The severity of frostbite injuries can now be assessed with triple phase bone scanning, allowing early prediction of likely subsequent tissue loss. Early hyperbaric oxygen therapy appears to improve outcome and the use of intravenous drugs such as synthetic prostaglandin analogues infusions and tissue plasminogen activator have been shown to reduce amputation rates. In non-freezing cold injuries the early administration of analgesia, the avoidance of secondary exposure, and the use of infrared thermography to assess the injuries are among newer approaches being introduced.

Frostbite and non-freezing cold injuries (NFCI) were once primarily military problems, but are becoming increasingly prevalent among the civilian population. In the last 20 years, there has been a growing interest in outdoor activities such as skiing, hiking and mountaineering, and coupled with a sharp increase in the numbers of homeless, there has been a rise in frequency of cold exposure among the civilian population.<sup>1</sup> The effective treatment of frostbite and NFCI has therefore become more of an issue, not only for the rural physician in polar climates, but also for many urban hospitals in Great Britain. Knowledge of the management of cold injuries is therefore important to both the military and civilian medical practitioner.

Frostbite injuries to the extremities can have disastrous effects. The injuries frequently affect those who are active and in the prime of their lives; fit people such as agricultural workers, mountaineers, cross-country skiers, expedition members and climbers. The spectrum of injury is enormous, varying from minimal tissue loss with mild long term sequelae, to major necrosis of the distal limbs with subsequent major amputations and resultant phantom limb pain. Studies into the epidemiology of civilian frostbite have identified several risk factors that may aid the clinician in the diagnosis and management of frostbite.

Cold injuries result from the limited capacity of homeothermic humans to cope with cold exposure. The law of conservation of energy requires that, when heat loss exceeds heat production, there is a

net loss of heat, reflected by a fall in tissue temperature. Physiological responses to whole body cold exposure include peripheral vasoconstriction, resulting in increased intrinsic insulation, and increased metabolic rate, particularly shivering. The adverse consequence of whole body cooling, hypothermia, is thus not infrequently concomitant with local freezing or non-freezing cold injury of the peripheries.

Frostbite is defined as true tissue freezing caused by heat loss sufficient to cause ice crystal formation in superficial or deep tissues.<sup>1</sup> The severity of frostbite injury depends on environmental temperature, the wind chill factor and the length of exposure. Research into the pathophysiology of frostbite has revealed notable similarities with the inflammatory processes seen in burn injuries and ischaemia/reperfusion injury. Evidence for the role of thromboxanes and prostaglandins has resulted in a more active approach to the medical treatment of frostbite.<sup>1</sup> Yet the roles of many of the potential adjunctive therapies remain to be determined.

## SEARCH STRATEGY AND SELECTION CRITERIA

References for this review were identified through a search of Pub Med from 1969 to November 2008, with the terms “frostbite” and “non-freezing cold injury” forming the basis for the article. Abstracts from recent international scientific meetings were also included. Priority was given to recent publications, particularly those published since 2005.

## HISTORICAL PERSPECTIVE

In 218 BC Hannibal lost nearly half his army of 46 000 to cold injuries in 15 days when they crossed the Southern Alps to reach Italy. During the second world war it was reported that the German army alone performed more than 15 000 amputations for cold related injuries on the Russian front in the winter of 1942.

Baron Dominique Larrey, surgeon-in-chief of Napoleon's army during the invasion of Russia in the winter of 1812–1813, gave the earliest description of the pathophysiology of frostbite. Larrey introduced the concept of friction massage with ice or snow. He recognised that warming was beneficial, but not by using the excessive heat of fires. He also noted the deleterious effects of the freeze–thaw–refreeze cycle with men re-freezing their feet while marching on successive days. These approaches were the mainstay of treatment for over 140 years until 1956 when Hamill described rapid rewarming in a patient with hypothermia and frostbite.<sup>1</sup> Rapid rewarming has subsequently become the mainstay of treatment in all severities of frostbite.

## EPIDEMIOLOGY

A 12 year study into inpatient frostbite injuries in the northern prairies of Saskatchewan, Canada<sup>2</sup> revealed the following predisposing factors: alcohol consumption (46%), psychiatric illness (17%), vehicular failure (19%), and drug misuse (4%). Alcohol consumption is particularly devastating as it causes heat loss through peripheral vasodilatation and clouds judgement. This may lead the victim not to seek adequate shelter which may in turn lead to a more severe injury. The need to amputate injured parts in most studies was closely correlated with the duration of cold exposure rather than the temperature.<sup>2</sup> Studies clearly reveal evidence of the anatomic sites most at risk from frostbite. The feet and the hands account for 90% of injuries reported.<sup>3 4</sup> Frostbite also affects the face (nose, chin, earlobes, cheeks and lips), buttocks/perineum (from sitting on metal seats) and penis (joggers). Further risk factors for frostbite are listed in box 1.

Although the elderly and young children are potentially at high risk from sustaining frostbite injury, the published epidemiological studies show that frostbite is uncommon in these age groups and instead tends to affect adults between the ages of 30–49 years.<sup>2 3</sup>

Waterless ointments applied to the skin have traditionally been used by the Finnish to protect against frostbite. They hypothesise that an additional lipid layer on the skin forms a protective barrier against the elements. A recent epidemiological study indicated, however, that the use of ointments in the cold may be a considerable risk factor in development of frostbite of the face and ears.<sup>5</sup>

## 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 “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 thawing rate. Mills proposed a simplified scheme of injury<sup>6</sup> with two phases: the cooling–supercooling–freezing stage; and a vascular stage that includes thawing (rewarming) and post-thaw.

Skin sensation is lost around 10°C. With further cooling, vascular contents become more viscous, there is microvascular constriction and transendothelial leakage of plasma. Arteriovenous 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 arteriovenous shunts resulting in an avascular environment which protects the core from further heat loss.<sup>7</sup>

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.<sup>6</sup>

Depending on the method of rewarming, hyperaemia, ischaemia, cyanosis, or total circulatory failure develops. Blisters 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 F<sub>2α</sub> (PGF<sub>2α</sub>) and thromboxane A<sub>2</sub> (TXA<sub>2</sub>) cause platelet aggregation and thrombosis which results in ischaemia. Robson and Heggers found notably elevated concentrations of PGF<sub>2α</sub> and TXA<sub>2</sub> in frostbite blister fluid.<sup>8</sup> These eicosanoid derivatives have been heavily implicated as mediators of progressive dermal ischaemia in burns, frostbite and ischaemia/reperfusion injuries.<sup>9</sup>

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 PGF<sub>2α</sub> and TXA<sub>2</sub>. A rabbit ear model demonstrated increased tissue survival after a blockade of the arachidonic acid cascade at all levels.<sup>9</sup> The most notable tissue salvage resulted when specific TXA<sub>2</sub> inhibitors were used. This has now been shown to be effective clinically.<sup>10</sup>

## CLINICAL PRESENTATION AND CLASSIFICATION

Classically frostbite has been described by its clinical presentation. Initially it is often difficult to predict the extent of frostbite injury.

### Box 1 Factors that increase risk for frostbite

#### Behavioural

- ▶ Inadequate clothing and shelter
- ▶ Alcohol and other drug use
- ▶ Psychiatric illness
- ▶ Smoking

#### Physiological

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

#### Mechanical

- ▶ Tightly constrictive clothing (too many socks)
- ▶ Contact with heat conductive materials
- ▶ Rings on fingers
- ▶ Immobility (military situations)

## Symptoms

Severity of symptoms is usually related to the severity of injury. At first most patients describe a cold numbness with accompanying sensory loss.<sup>4</sup> The extremity will feel cold to the touch and patients often complain that it feels clumsy, "like a block of wood".

Thawing and reperfusion are often accompanied by intense pain. A throbbing pain begins 2–3 days after rewarming and may persist for weeks or months, even after the tissue becomes demarcated. A residual tingling sensation beginning after 1 week has also been described. This is probably due to an ischaemic neuritis.<sup>11 12</sup> A variation in onset of symptoms exists, with some victims never noticing pain (for example, diabetics with previous neuropathic damage). In victims without tissue loss, symptoms usually subside within 1 month, whereas with tissue loss, disablement may exceed 6 months. In all cases, symptoms are exacerbated by a warm environment. Other sensory deficits include spontaneous burning and electric current-like sensations. Usually frostbite victims experience some degree of sensory loss for at least 4 years after injury, perhaps indefinitely.<sup>12</sup>

## Signs

The initial appearance of frostbite seen in the emergency department may be deceptively benign. In the majority of patients some degree of thawing has already taken place. Frozen tissue may appear mottled blue, violaceous, yellowish-white or waxy. Following rapid rewarming, there is an initial hyperaemia, even in severe cases.<sup>15</sup>

Favourable prognostic signs include: retained sensation, normal skin colour, and clear rather than cloudy fluid in the blisters, if present. Early formation of oedema and clear blisters that extend to the tips of the digits are a good sign.

Poor prognostic signs include: non-blanching cyanosis, firm skin, lack of oedema, and small, proximal, dark haemorrhagic vesicles (indicates damage to the subdermal vascular plexus).<sup>3</sup>

However, no prognostic features are entirely predictive and weeks or months may pass before the demarcation between viable and non-viable tissue becomes clear.

## Classification

There are two classes of frostbite injury: mild or superficial (no tissue loss) and severe or deep (with loss of tissue)<sup>12–14</sup> (box 2).

Cauchy *et al*<sup>15</sup> recognised that frostbite classifications were based on retrospective diagnoses and could not predict the extent of final tissue loss and prognosis for the patient. The 3–6 week waiting period often necessary to determine the severity of the lesion and resultant need for amputation often causes mental anguish for patients. They suggest a new classification system that begins at day 0 (just after rewarming) which is based mainly on the topography of the lesion and on early bone scan results. This appears to be a very useful classification for both doctor and patient, in that it allows accurate determination at a very early stage of the likely extent of subsequent tissues loss.

## IMAGING AIDS TO DIAGNOSIS

Several diagnostic tests have been used to help predict the severity and prognosis of the frostbite injury including plain radiographs, infrared thermography, angiography, triple phase bone scanning, laser Doppler studies, digital plethysmography and magnetic resonance imaging/magnetic resonance angiography (MRI/MRA). The most promising studies have used triple phase bone scanning<sup>16</sup> and MRI/MRA.<sup>17</sup> Triple phase bone

## Box 2 Classification of cold injury according to severity

### Superficial

#### 1st degree

- ▶ Partial skin freezing
- ▶ Erythema, oedema, and hyperaemia
- ▶ No blisters or necrosis
- ▶ Occasional skin desquamation (5–10 days later)

#### 2nd degree

- ▶ Full thickness skin freezing
- ▶ Erythema, substantial oedema
- ▶ Vesicles with clear fluid
- ▶ Blisters, desquamation and black eschar formed

### Deep

#### 3rd degree

- ▶ Full thickness skin and subcutaneous freezing
- ▶ Violaceous/haemorrhagic blisters
- ▶ Skin necrosis
- ▶ Blue-grey discoloration

#### 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

scanning (using <sup>99m</sup>technetium) has now become the standard study used within the first few days after injury. This technique assesses tissue viability in an effort to allow early debridement of soft tissue and early coverage of ischaemic bony structures.<sup>18</sup>

## TREATMENT

Treatment of frostbite can be divided into three phases: pre-thaw field care phase, immediate hospital care phase, and post-thaw phase.

### Field care

If caught out in the field and there is a possibility of onset of frostbite one should move out of the wind and seek shelter.<sup>19</sup>

One should: drink warm fluids, remove boots (consider problems with replacement if swelling occurs), remove wet gloves and socks and replace with dry ones, warm the cold extremity by placing in companion's armpit or groin for 10 min only, replace boots, and take aspirin (75 mg) for its antiplatelet effect and ibuprofen (800 mg) for its anti-prostaglandin effect.<sup>19</sup>

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 over 4000 m, give supplementary oxygen.

Field rewarming should only be attempted if there is no further risk of refreezing.<sup>12</sup> Tissue which is thawed and then refrozen almost always dies. Consequently, the decision to thaw the frostbitten tissue in the field commits the provider to a course of action which may involve pain control, maintaining warm water baths at a constant temperature, and protecting tissue from further injury during rewarming and eventual transport. If rewarmed in the field, frostbitten extremities cannot be used for ambulation.

### Immediate hospital care

The standard approach to the initial treatment of frostbite is the strategy originally outlined by McCauley and Heggers<sup>20</sup> (box 3). Hypothermia and concomitant injury should be evaluated first. Systemic hypothermia should be corrected to a core temperature of 34°C before frostbite management is attempted.<sup>12</sup> Rewarming should be carried out in a whirlpool (recirculating water) with a mild antibacterial agent (povidone-iodine or chlorhexidine). The State of Alaska Cold-injury Guidelines recommend a lower temperature waterbath of 37–39°C which decreases the pain for the patient while only slightly slowing rewarming.<sup>21</sup> The time period recommended for rewarming varies from 15–30 mins<sup>20</sup> up to 1 h.<sup>19</sup> Rewarming should continue until a red/purple colour appears and the extremity becomes pliable. Active motion during the rewarming period is beneficial but care should be taken to prevent the extremity from touching the sides of the whirlpool. Intravenous fluid resuscitation is not usually required for frostbite. If the patient has been at altitude then it is more likely that they are dehydrated; moreover, if they are also hypothermic they may exhibit a cold diuresis, due to suppression of antidiuretic hormone. This often requires correction with intravenous fluids.

### Post-thaw care

Blisters containing clear or milky fluid should be debrided and covered in aloe vera, a potent anti-prostaglandin agent, every 6 h. Splinting, elevating, and wrapping the affected part in a loose, protective dressing should follow the administration of the aloe vera cream. Padding should be put between the patient's 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, opiate analgesia and ibuprofen are all indicated. Ibuprofen (400 mg orally, every 12 h)<sup>12</sup> is useful as it provides systemic anti-prostaglandin activity that limits the cascade of inflammatory damage. Aspirin is less beneficial as it prolongs blockade of all prostaglandin synthesis, including some prostacyclins that are

#### Box 3 Treatment protocol for frostbite (after McCauley and Heggers<sup>20</sup>)

1. Admit frostbite patient to specialist unit if possible
2. Evaluate for hypothermia, concomitant injury, or complicating problems
3. On admission, rapidly rewarm the affected areas in warm water at 37–39°C (99–102°F) for 15–30 mins or until thawing is complete
4. Debride clear or white blisters and apply topical aloe vera (Dermaide aloe) every 6 h
5. Leave haemorrhagic blisters intact and apply topical aloe vera every 6 h
6. Splint and elevate the extremity
7. Administer antitetanus prophylaxis (toxoid or immunoglobulin (Ig))
8. Analgesia: opiate (intravenously or intramuscularly) as indicated
9. Administer ibuprofen 400 mg orally every 12 h
10. Administer benzyl penicillin 500 000 U every 6 h for 48–72 h
11. Administer daily hydrotherapy in 40°C water for 30–45 mins. Do not towel dry affected tissue
12. Prohibit smoking

beneficial for wound healing. The role of clopidogrel in frostbite has yet to be assessed.

When the skin is oedematous penicillin is administered as oedema inhibits the skin's own streptococcal properties.<sup>1</sup> If there are further signs of infection, further antibiotic use is indicated. Almost all patients should be admitted to hospital; given that alcohol intoxication, psychiatric illness, and homelessness are common features of the frostbite patient, immediate discharge is rarely prudent.

Goals of hospital treatment include keeping the patient comfortable, well nourished, well hydrated, and pain free. Wound care must be meticulous and further secondary trauma must be avoided. Injured extremities should be elevated above heart level to avoid oedema. Physiotherapy is important and the patient should be encouraged to mobilise as soon as possible.<sup>12</sup> Extremities are treated with clean, dry dressings and twice daily whirlpool baths with added chlorhexidine. This encourages the eschars from the blisters to separate from the underlying healthy tissue. Escharotomy or fasciotomy may be performed if circulation is impaired or a compartment syndrome develops.

### SURGERY

Early surgical intervention, in the form of fasciotomy, in the immediate post-thaw scenario, is required for compartment syndrome. Occasionally early amputation is indicated if liquefaction, moist gangrene, or overwhelming infection and sepsis develops. There is rarely any urgency to intervene, and so it should be undertaken by a surgeon with appropriate experience usually 6–12 weeks after the injury. In the vast majority of cases it is the failure to delay surgery that is a major source of avoidable morbidity. The functional end result of any surgery needs to be considered and ideally, where major limb loss is foreseen, the early involvement of a multidisciplinary rehabilitation team will produce better long term functional results. However, some clinicians are now advocating a more aggressive approach with the advent of <sup>99</sup>technetium scintigraphy<sup>18</sup> and MRI scanning<sup>17</sup> since with better imaging more accurate prediction of viable tissue is possible.

### ADJUNCTIVE THERAPIES

More recent studies have assessed the role of adjunctive therapies in the treatment of frostbite. These include surgical lumbar sympathectomy, intra-arterial reserpine, brachial plexus blockade, oral nifedipine, hyperbaric oxygen, low molecular weight dextran and thrombolytic agents such as tissue plasminogen activator (tPA). Many have only been tested in animal models, and further randomised trials in humans are needed.

#### Hyperbaric oxygen therapy

The role of hyperbaric oxygen therapy (HBO) therapy in frostbite has had mixed acceptance among authors. Several animal studies have demonstrated it to be of no benefit,<sup>1</sup> yet two recent studies in humans have yielded excellent results.<sup>22 23</sup> HBO increases the deformability of erythrocytes, diminishes oedema formation in burned and post-ischaemic tissues and has a bacteriostatic effect.<sup>22</sup> It also may act as an antioxidant.<sup>23</sup> Its role in frostbite therapy warrants further investigation as it is a relatively safe and inexpensive treatment.

#### Sympathectomy

The role of sympathectomy, either surgical (open or minimally invasive) or chemical, has yielded mixed results. Early sympathectomy, performed within the first few hours of injury, is

said to increase oedema formation and leads to increased tissue destruction. However if performed 24–48 h after thawing it is thought to hasten resolution of oedema and decrease tissue loss.<sup>24</sup> Sympathectomy may have a role in preventing some long term sequelae of frostbite such as pain (often due to vasospasm), paresthesias and hyperhidrosis.<sup>24</sup> However, since a sympathectomy is irreversible, great caution should be exercised when considering its use, particularly since the advent of alternative intravenous vasodilators, and some would argue there is now no role for its use in frostbite.

### Vasodilators

Iloprost is a prostacyclin analogue with profound vasodilatory properties and has been used with some success.<sup>12</sup> It is used in arterial surgery to mimic the effect of a sympathectomy. Intra-arterial reserpine has been used in frostbite to prevent vasospasm. The use of pentoxifylline,<sup>25</sup> a methyl-xanthine derived phosphodiesterase inhibitor, has yielded some promising results in human trials. It increases blood flow to the affected extremity, decreases platelet hyperactivity, and helps normalise the prostacyclin to TXA<sub>2</sub> ratio. It has been clinically proven to enhance tissue survival. The  $\alpha$ -blocker buflomedil has been used to increase peripheral blood flow.<sup>15</sup>

### tPA

A small study assessing the effectiveness of tPA in reducing amputation rates in frostbite has recently been reported.<sup>26</sup> Among the six patients who received tPA within 24 h of injury, six of 59 (10%) affected fingers or toes were amputated, compared with 97 of 234 (41%) among those who did not receive tPA. It is postulated that rapid clearance of the microvasculature improves tissue salvage.

### Long term sequelae

The long term sequelae of frostbite are less well studied. The functional use of extremities following a partial amputation is variable and injury specific. Partial foot amputations radically alter the biomechanics of the foot, and this combined with frostbite induced neuropathy means specialist custom made footwear is required to maximise the functional result and minimise secondary injuries. Major lower limb amputations, while rare, are occasionally necessary and appropriate multi-disciplinary care is essential. Tissue that has recovered from frostbite is more susceptible to further injury and this needs to be born in mind when advising individuals about a return to environments where they may be at risk. Preventative measures remain the mainstay to primary and secondary treatment.

### Internet and satellite phone

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.<sup>27</sup> The UK based service can be accessed via the Diploma in Mountain Medicine or the British Mountaineering Council websites. The service is run by Diploma Faculty Members and is being increasingly used by climbers and physicians worldwide, often to obtain a second opinion or to seek more specialised advice. 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.

### Box 4 Prevention of frostbite

- ▶ Good experience base of core survival skills
- ▶ Protective clothing should be worn—layers, loose, heat insulating
- ▶ Avoid constriction of body parts with clothing
- ▶ Stay dry
- ▶ Wind protection
- ▶ Hands:
  - wear mittens instead of gloves
  - chemical hand heaters
- ▶ Feet:
  - avoid tight fitting boots
  - triple layer extreme altitude boots
  - electric heated insoles
- ▶ Adequate nutrition
- ▶ Maintain hydration
- ▶ Aspirin (if not contraindicated)
- ▶ Supplementary oxygen at extreme altitude

### NON-FREEZING COLD INJURY

NFCI occurs when tissue fluids do not freeze (usually at about  $-0.5^{\circ}\text{C}$ ), but local temperatures remain low for several hours or days. The true prevalence of the injury is likely to be much higher than currently believed, because it often goes unreported and is often under-diagnosed. There is often a history of the affected individual having been cold and wet for a sustained period, often having been unable to dry out satisfactorily. On rewarming, it becomes apparent that the limb (most commonly the lower leg) has developed a localised sensory neuropathy. Three phases were described by Ungley.<sup>28</sup> On rewarming there is a short period of pale cyanosis. Once fully re-warmed there is hyperaemia, with redness, swelling, full pulses and onset of pain. This pain is much more prolonged than the rewarming pain normally experienced in freezing cold injury, and is the most common reason for presentation. The last phase can last up to many months after initial injury, during which time persisting long term sequelae may become apparent. Following the initial injury there develops an increased sensitivity to cold. There are often surprisingly few objective clinical signs. Infra-red thermography can be used to assess the individual's response to a standardised cold stress, and may be helpful in confirming the diagnosis, assessing the severity of the injury, and finally monitoring the recovery or otherwise from the NFCI.<sup>29</sup> However, although the infra-red thermography test is used extensively by the UK military, it is not widely used elsewhere. There appears to be a significant variability in the response of some individuals to current infra-red thermography test. As a result, interest is being shown in the use of gentle exercise before the cold sensitivity test, and also in the use of laser Doppler flowmetry to try to improve the assessment used to classify non-freezing cold injury.<sup>30</sup> Careful experimental design to validate any potential new tests against suitable controls both pre- and post- exposure will be required.

NFCI vary in severity from mild to severe. In severe cases the cold sensitisation is so serious that individuals are unable to work outside. There is often persisting oedema and hyperhidrosis making the individual susceptible to fungal infections. Chronic pain resembling causalgia or reflex sympathetic dystrophy is reported. The profound sensory neuropathic foot can develop ulceration and tissue loss, ultimately resulting in either minor or major lower limb amputation. Ongoing care within a specialist foot clinic using custom made shoes and

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insoles appear to improve functional outcome. Multidisciplinary team approaches such as healing of the ulcerated neuropathic foot using patella bearing orthoses has been described.<sup>31</sup>

NFCI pain is often so severe as to require tricyclic antidepressants, and this should be instituted at an early stage. Failure to do so increases the risk of developing severe chronic pain resistant to all subsequent treatment modalities. Early involvement of pain specialists is important. Sympathectomy usually results in longer term deterioration. It is thus essential to control pain following NFCI at the earliest opportunity.

Unlike freezing cold injury, NFCI should be allowed to re-warm slowly. It is possible that hyperbaric oxygen may have value in early treatment too, although no trials appear to have assessed that use. Gross tissue damage following NFCI is relatively rare in peacetime experience, and after initial slow rewarming, management should follow the standard conservative protocol employed in freezing injury.

With the likelihood of chronic sequelae and only limited potential for treatment, the most effective approach to NFCI is to try to prevent its occurrence. There is a need to raise awareness to those most susceptible, particularly junior military recruits, for example. Ultra-early recognition of NFCI, even in the field, might be possible by the introduction of a simple field scoring system (not dissimilar to the Lake Louise Scoring System currently used for field assessment of acute mountain sickness). Although almost all cases of NFCI involve the feet, as many as 25% may also have injured hands. Afro-Caribbeans appear to have a significantly increased susceptibility to NFCI as well as freezing cold injury.<sup>32</sup> This may be a result of an impaired or reduced cold induced vasodilatory response in Afro-Caribbeans as compared to Caucasians.<sup>33</sup> These ethnic differences remain when Afro-Caribbeans move to colder areas.

## CONCLUSION

Although still potentially a disastrous injury associated with a high morbidity, frostbite and NFCI can now be treated more

### Key learning points

- ▶ Prevention is vital for both frostbite and non-freezing cold injury (NFCI).
- ▶ Early recognition and treatment will limit the extent of the injury.
- ▶ Frostbite: warm quickly, defer surgery.
- ▶ NFCI: warm slowly
- ▶ Seek early advice from experts if in doubt: [http://medex.org.uk/diploma/diploma\\_holders.php](http://medex.org.uk/diploma/diploma_holders.php) <http://www.thebmc.co.uk/>
- ▶ Sensory neuropathy is a major cause of long term morbidity particularly in NFCI.

### Research questions

- ▶ Development of improved protective clothing .
- ▶ Increase understanding of the importance of individual's responsibility in injury avoidance.
- ▶ Determine the role of newer adjunctive treatments such as tissue plasminogen activator and anti-tumour necrosis factor.
- ▶ Improve post-injury care with particular focus on the local neurological sequelae.
- ▶ Improve early assessment and treatment of non-freezing cold injury.

### Key references

- ▶ Cauchy E, Chetaille E, Marchand V, *et al.* Retrospective study of 70 cases of severe frostbite lesions: a proposed new classification scheme. *Wild Environ Med* 2001;**12**:248–55.
- ▶ Syme D (for ICAR Medical Commission). Position Paper: On-site treatment of frostbite for mountaineers. *High Alt Med Biol* 2002;**3**:297–8.
- ▶ McCauley RL, Hing DN, Robson MC, *et al.* Frostbite injuries: a rational approach based on the pathophysiology. *J Trauma* 1983;**23**:143–7.
- ▶ Bruen KJ, Ballard JR, Morris SE, *et al.* Reduction of the incidence of amputation in frostbite injury with thrombolytic therapy. *Arch Surg* 2007;**142**:546–51.
- ▶ Oakley EHN. In: Tooke JE, Lowe GD, eds. *A textbook of vascular medicine*. Arnold UK, 1996

effectively to ensure tissue loss is minimised and functional outcome maximised.<sup>34</sup> With adequate preventative measures (box 4) the risk of frostbite injury can be reduced. With the rising prevalence of frostbite and NFCI, 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. Understanding of the role of inflammatory mediators, such as PGF<sub>2</sub> and TXA<sub>2</sub>, has led to new active medical regimens such as the use of ibuprofen and aloe vera. Improved imaging assessment using MRA, infrared thermography 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 and NFCI. However, prevention, early warming, early medical treatment and delayed surgery are likely to remain the mainstays of treatment for the foreseeable future.

### MULTIPLE CHOICE QUESTIONS (TRUE (T)/FALSE (F); ANSWERS AFTER THE REFERENCES)

1. Frostbite is more common in the young and old rather than fit active individuals.
2. It is now possible to predict within a few days of a frostbite injury the level of any amputation based upon a combination of clinical assessment and <sup>99</sup>technetium bone scanning.
3. Like frostbite, rapid re-warming of a non-freezing cold injury is advised.
4. Following a non-freezing cold injury, the resulting neuropathic injury means that an individual is at a greater risk of a subsequent cold injury.
5. The eicosanoid derivatives PGF<sub>2α</sub> and TXA<sub>2</sub> have been heavily implicated as mediators of progressive dermal ischaemia in burns, frostbite and ischaemia/reperfusion injuries.

**Competing interests:** None declared.

**Patient consent:** Obtained.

**Provenance and peer review:** Not commissioned; externally peer reviewed.

## Case report

In December 2006 a surgeon was climbing in Antarctica with a guided party. Retreating in a storm, he fell into a crevasse and lost his gloves. The party spent a night out in a blizzard in subzero temperatures at altitude and they had to be rescued by other parties. At a tented field hospital he underwent primary treatment before being evacuated back to the UK for treatment of his frostbitten hands (figs 1–6).

"I went back to work at beginning of April 2007, had hand surgery (under LA - very interesting!) in May and have been doing full operating exactly as pre injury from July 2007, so quite lucky ...."



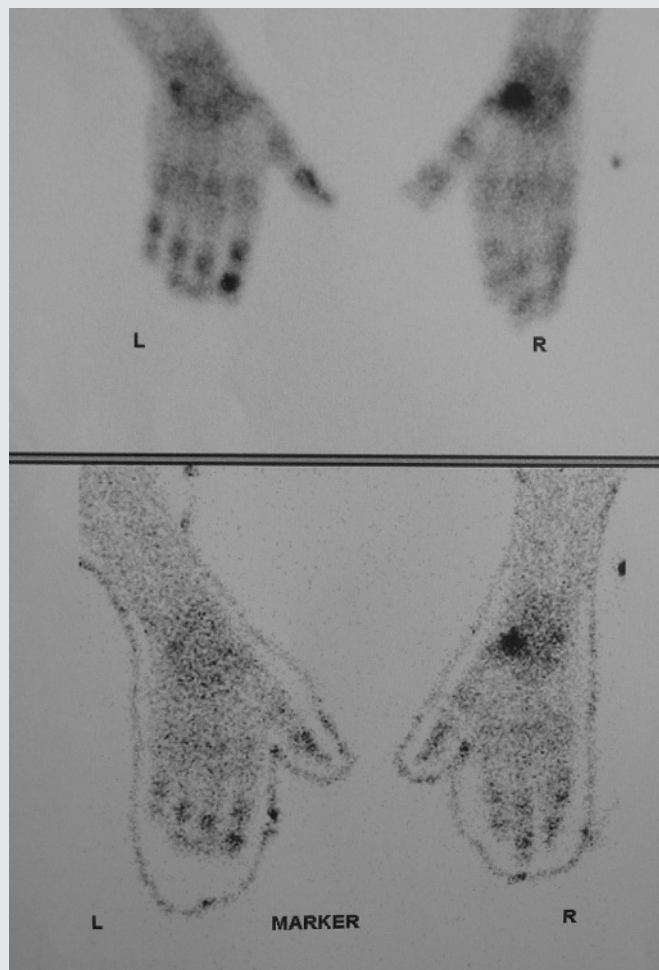
**Figure 1** Frostbitten left hand of a climber, taken 36 h after injury, while climbing in Antarctica. Note discoloration and blister formation, iodine warming bowls and aseptic techniques used in tented field hospital. The digital image was reviewed within 6 h by CHEI in the UK, and management advice given over the internet.



**Figure 2** Frostbitten hands of same climber shown in fig 1.



**Figure 3** Condition of hands on patient's arrival in the UK, 5 days after initial injury.



**Figure 4**  $^{99m}\text{Tc}$  bone scan performed on arrival in the UK. The scans show minimal perfusion to the terminal phalanges in the left hand, suggesting that amputation of the distal phalanges is likely to be necessary.



**Figure 5** Dorsal surfaces of hands after 5 days of intravenous iloprost.



**Figure 6** Palmar surfaces of hands after 5 days of intravenous iloprost.

## REFERENCES

- Murphy JV**, Banwell PE, Roberts AHN, *et al.* Frostbite: pathogenesis and treatment. *J of Trauma* 2000;**48**:171–8.
- Valnicek SM**, Chasmar LR, Clapson JB. Frostbite in the prairies: a 12-year review. *Plast Reconstr Surg* 1993;**92**:633–41.
- Pollard AJ**, Murdoch DR. *The high altitude medicine handbook*. Abingdon: Radcliffe Medical Press, 2003.
- Reamy BV**. Frostbite: review and current concepts. *J Am Board Fam Prac* 1998;**11**:34–40.
- Lehmuskallio E**. Cold protecting ointments and frostbite. *Acta Derm Venereol (Stockh)* 1999;**79**:67–70.
- Mills WJ**. *Clinical aspects of freezing cold injury in medical aspects of harsh environments, the textbook of military medicine*. US Surgeon Generals Office, 2002:429–67.
- Washburn B**. Frostbite. *N Eng J Med* 1962;**266**:974–89.
- Robson MC**, Heggers JP. Evaluation of frostbite blister fluid as a clue to pathogenesis. *J Hand Surg (Am)* 1981;**6**:43–7.
- Raine TJ**, *et al.* Antiprostaglandins and antithromboxanes in the treatment of frostbite. *Surg Forum* 1980;**31**:557–8.
- Marsigny B**. Mountain frostbite. *ISSM Newsletter* 1998;**8**:8–10.
- Oakley EHN**. In: Tooke JE, Lowe GD, eds. *A textbook of vascular medicine*. Arnold UK, 1996.
- West JB**, Schoene RB, Milledge JS. *High altitude medicine and physiology*. Hodder Arnold, 2007.
- McCauley RL**, Smith DJ, Robson MC, *et al.* Frostbite. In: Auerbach PS, ed. *Wilderness medicine*, 4th ed. Mosby, 2001.
- Biem J**, Koehncke N, Classen D, *et al.* Out of the cold: management of hypothermia and frostbite. *Can Med Assoc J* 2003;**168**:305–11.
- Cauchy E**, Chetaille E, Marchand V, *et al.* Retrospective study of 70 cases of severe frostbite lesions: a proposed new classification scheme. *Wild Environ Med* 2001;**12**:248–55.
- Bhatnagar A**, Sarker BB, Sawroop K, *et al.* Diagnosis, characterisation and evaluation of treatment response of frostbite using pertechnetate scintigraphy: a prospective study. *Eur J Nucl Med* 2002;**29**:170–5.
- Barker JR**, Haws MJ, Brown RE, *et al.* Magnetic resonance imaging of severe frostbite injuries. *Ann Plast Surg* 1997;**38**:275–9.
- Greenwald D**, Cooper B, Gottlieb L. An algorithm for early aggressive treatment of frostbite with limb salvage directed by triple-phase scanning. *Plast Reconstr Surg* 1998;**102**:1069–74.
- Syme D (for ICAR Medical Commission)**. Position paper: on-site treatment of frostbite for mountaineers. *High Alt Med Biol* 2002;**3**:297–8.
- McCauley RL**, Hing DN, Robson MC, *et al.* Frostbite injuries: a rational approach based on the pathophysiology. *J Trauma* 1983;**23**:143–7.
- Anon**. State of Alaska Cold-Injury Guidelines. Rev 11/03. [www.chems.alaska.gov](http://www.chems.alaska.gov).
- Heimbarg D**, Noah ME, Siekmann UPF, *et al.* Hyperbaric oxygen treatment in deep frost bite of both hands in a boy. *Burns* 2001;**27**:404–8.
- Findlerle Z**, Cankar K. Delayed treatment of frostbite injury with hyperbaric oxygen therapy: a case report. *Aviat Space Environ Med* 2002;**73**:393–4.
- Taylor MS**. Lumbar epidural sympathectomy for frostbite injuries of the feet. *Mil Med* 1999;**164**:566–7.
- Hayes DW**, Mandracchia VJ, Considine C. Pentoxifylline: adjunctive therapy in the treatment of pedal frostbite. *Clin Podiatr Med Surg* 2000;**17**:715–722.
- Bruen KJ**, Ballard JR, Morris SE, *et al.* Reduction of the incidence of amputation in frostbite injury with thrombolytic therapy. *Arch Surg* 2007;**142**:546–51.
- Imray CHE**, Hillebrandt D. Telemedicine and frostbite injuries. *BMJ* 2004;**328**:1210.
- Ungley CC**, Blackwood W. Peripheral vasoneuropathy after chilling. 'Immersion foot and immersion hand'. *Lancet* 1942;**2**:447–51.
- Oakley EHN**. Cold injury. In: Tooke JE, Lowe GDO, eds. *A textbook of vascular medicine*. London: Arnold, 1996:353–70.
- Eglin C**, Golden F, Tipton M. The effect of gentle exercise prior to a cold sensitivity test used to classify non-freezing cold injury. In: *Prevention of Cold Injuries* (11-1-11-6) Meeting Proceeding RTO-MP-HFM-126, Paper 11. <http://www.rto.nato.int/abstracts.asp>.
- Khaira HS**, Coddington T, Drew A, *et al.* Patellar tendon bearing orthosis- application as adjunctive treatment in healing lower limb tissue loss. *Eur J Vasc Endovasc Surg* 1998;**16**:485–8.
- Sumner DS**, Cribblez TL, Doolittle WH. Host factors in human frostbite. *Mil Med* 1974;**141**:454–61.
- Iampietro PF**, Goldman RF, Buskirk ER, *et al.* Responses of negro and white males to cold. *J Appl Physiol* 1959;**14**:798–800.
- Imray CHE**, Oakley EHN. Cold still kills: cold-related illnesses in military practice. Freezing and non-freezing cold injury. *R Army Med Corps J* 2006;**152**:218–22.

## Answers

1. F; 2. T; 3. F; 4. T; 5. T.



## Cold damage to the extremities: frostbite and non-freezing cold injuries

C Imray, A Grieve, S Dhillon, et al.

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