Freezing and non-freezing cold weather injuries: a systematic review

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Abstract

Introduction: The debilitating impact of cold weather on the human body is one of the world’s oldest recorded injuries. The severe and life-changing damage which can be caused is now more commonly seen recreationally in extreme outdoor sports rather than in occupational settings such as the military. The diagnosis and treatment of these injuries need to be completed carefully but quickly to reduce the risk of loss of limb and possibly life. Therefore, we have conducted a systematic review of the literature surrounding cold weather injuries (CWIs) to ascertain the epidemiology and current management strategies.

Sources of data: Medline (PubMED), EMBASE, CINHAL, Cochrane Collaboration Database, Web of Science, Scopus and Google Scholar.

Areas of agreement immediate field treatment: The risk of freeze thaw freeze injuries. Delayed surgical intervention when possible. Different epidemiology of freezing and non-freezing injuries.

Areas of controversy: Prophylactic use of antibiotics; the use of vasodilators surgical and medical.

Growing points: The use of ilioprost and PFG2a for the treatment of deep frostbite.

Areas timely for developing research: The treatment of non-freezing CWIs with their long-term follow-up.

Key words: cold weather injuries, frostbite, frost nip, non-freezing cold weather injury, freezing cold injury
Introduction
The debilitating impact of cold weather on the human body has been evident since man first ventured to climates outside of the tropical. The oldest documented case of frostbite was discovered in a 5000-year-old mummy in the Chilean mountains.\(^1\) Although equipment, training and medical understanding have evolved over the many centuries since, injuries caused by exposure to the cold have been ever present.

Cold weather injuries (CWIs) have historically been associated with occupational settings such as the military, fishermen and cold storage workers (butchers, meat processors). However, over the last 20 years, there has been an increase in the number of civilians who have sustained these injuries.\(^2\) This may be related to the increasing popularity of activities with a high risk of CWIs such as skiing and winter mountaineering.\(^2,3\)

CWIs is a term that can be used to describe both injuries that have a central effect such as hypothermia and ones that primarily affect the peripheries such as frostbite. Injuries affecting the peripheries can be subdivided into freezing cold injuries (FCIs) and non-freezing cold injuries (NFCIs).\(^4\)

FCI is defined as the damage sustained by tissues while subject to temperatures below their freezing point at approximately \(-0.55^\circ°C\). NFCIs occur when tissue fluids are continuously exposed to low temperatures between 0 and 15°C for several hours or days. NFCIs have been historically referred to as ‘trench foot’ or ‘immersion foot’. However, NFCIs are not restricted to the feet and may occur elsewhere in the body.\(^4\)

We provide a systematic review of the epidemiology of FCI and NFCI and assess the influence of treatment modality on the outcome of these injuries. Study quality was assessed using the American College of Chest Physicians (ACCP) intervention grading. ACCP intervention grading has been used in the past to assess the quality of studies reporting treatment modalities in the management of CWIs.\(^5–13\)

Methods
A comprehensive literature search was performed in February 2015 using Medline (PubMed), EMBASE, CINHAL, Cochrane Collaboration Database, Web of Science, Scopus and Google Scholar. This was to identify articles published in English peer-reviewed journals, reporting data and information on CWIs.

All potential studies were retrieved in full and their relevance to the research question further assessed. The bibliographies of all articles retrieved in full print were also reviewed to identify articles not included in the first electronic search.

The search was performed using the keywords ‘frost-bite’, ‘frost nip’, ‘non-freezing cold injuries’ and ‘freezing cold injuries’ with no limit for year of publication and level of study evidence.

ACCP grading has previously been extensively used for the classification of evidence in anti-thrombotic therapy, a modality also used in the treatment of frostbite. The ACCP criteria are defined in Table 1.

Results
Search—study selection
Figure 1 illustrates the initial search results returned from the various databases used. One hundred and seventy papers investigating freeing and non-freezing CWIs were found with 100 of these being excluded because of inappropriate methodology or lack of relevance.

The epidemiology of FCIs and NFCIs
A significant number of papers in the English language describing CWI came from military publications, which may reflect the captive population that military training has. Although this does provide useful information on CWI, it does bias the data away from the civilian epidemiology.

In a retrospective study by DeGroot \textit{et al.},\(^14\) CWI cases that required hospitalization were studied to establish the prevalence of CWI. This meant that a significant proportion of CWI patients who did not require this level of care were excluded from the study. The hospitalization rate was 38.2/100 000 in 1985, dropping to 0.2/100 000 at the end of the study in 1999. The authors conclude that the high occurrence of CWI during military training could
<table>
<thead>
<tr>
<th>Grade of recommendation</th>
<th>Benefit vs. risk and burdens</th>
<th>Methodologic quality of supporting evidence</th>
<th>Implications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strong recommendation, high-quality evidence, Grade 1A</td>
<td>Benefits clearly outweigh risk or vice versa</td>
<td>Consistent evidence from randomized controlled trials (RCTs) without important limitations or exceptionally strong evidence from observational studies</td>
<td>Recommendation can apply to most patients in most circumstances. Further research is very unlikely to change confidence in the estimate of effect</td>
</tr>
<tr>
<td>Strong recommendation, moderate-quality evidence, Grade 1B</td>
<td>Benefits clearly outweigh risk and vice versa</td>
<td>Evidence from RCTs with important limitations (inconsistent results, methodological flaws, indirect or imprecise), or very strong evidence from observational studies</td>
<td>Recommendation can apply to most patients in most circumstances. Higher quality research may have an important impact on confidence in the estimate of effect and may change the estimate</td>
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<tr>
<td>Strong recommendation, low- or very low-quality evidence, Grade 1C</td>
<td>Benefits clearly outweigh risk and burdens or vice versa</td>
<td>Evidence for at least one critical outcome from observational studies, case series or from RCTs with serious flaws or indirect evidence</td>
<td>Recommendation can apply to most patients in many circumstances. Higher quality research is likely to have an important impact on confidence in the estimate of effect and may well change the estimate</td>
</tr>
<tr>
<td>Weak recommendation, high-quality evidence, Grade 2A</td>
<td>Benefits closely balanced with risks and burden</td>
<td>Consistent evidence from RCTs without important limitations or exceptionally strong evidence from observational studies</td>
<td>The best action may differ depending on circumstances or patient or society values. Further research is very unlikely to change confidence in the estimate of effect</td>
</tr>
<tr>
<td>Weak recommendation, moderate-quality evidence, Grade 2B</td>
<td>Benefits closely balanced with risks and burden</td>
<td>Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise) or very strong evidence from observational studies</td>
<td>Best action may differ depending on circumstances or patient or society values. Higher quality research may well have an important impact on confidence in the estimate of effect and may change the estimate</td>
</tr>
<tr>
<td>Weak recommendation, low- or very low-quality evidence, Grade 2C</td>
<td>Uncertainty in the estimates of benefits, risks and burden; benefits, risk and burden may be closely balanced</td>
<td>Evidence for at least one critical outcome from observational studies, case series or RCTs, with serious flaws or indirect evidence</td>
<td>Other alternatives may be equally reasonable. Higher quality research is likely to have an important impact on confidence in the estimate of effect and may well change the estimate</td>
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</table>
have been prevented, and they continue to suggest that the later drop in incidence is due to ‘multi-factorial’ reasons, but specific details of these are not elaborated on by the authors. The follow-up period for this study was 19 years which allowed a large amount of data to be collected. However, it was limited by the use of coding data, which relies on the correct diagnostic code being recorded. A study by Hsia et al.\textsuperscript{15} demonstrated an error rate in clinical coding of 20.8\% in a group of Medicare patients. Campbell et al.\textsuperscript{16} demonstrated an accuracy rate of 91 and 82\%, respectively, in studies of discharge coding in England and Wales and Scotland, respectively. Therefore, the error rate of the use of coding data must be considered when viewing the results of this paper.

Cattermole\textsuperscript{17} performed a 10-year study on the epidemiology of CWI in British Antarctic Survey personnel from 1986 to 1995. This study had an incidence rate of 65.6/1000 per year, which accounted for 2.5\% of all new consultations. Ninety-five per cent of injuries were due to frostbite, 3\% were hypothermia and 2\% ‘trench foot’. A limitation of this study was that it was a retrospective search of medical documents to determine incidence and aetiological factors for CWI.\textsuperscript{17} This study was not clear about whether or not a formal diagnostic protocol was used, although it clearly demonstrated that individuals who had a previous CWI were at a significantly increased risk of another CWI ($P < 0.001$). Most of the injuries (78\%) occurred during recreational activities such as skiing. Wind chill and
temperature were not found to be associated with an increase in severity of frostbite.

Questionnaire-based studies have also been used to identify the epidemiology and predisposing factors of CWI. A study by Harirchi et al. used a questionnaire which was given to mountaineers in a cross-sectional study looking back over their previous 2 years of mountaineering. The study gave an incidence of 366/1000 population per year in 637 respondents. This study was reliant on self-reporting and accurate recall of events over 2 years which may have caused bias in the results. Additionally, the study used self-diagnosis of frostbite and relied upon individual responses to develop a background incidence which may have caused further bias. Lehmuuskallio et al. performed a prospective study on the incidence in frostbite of the face and ears in Finnish conscripts. They limited the study by only looking at young males (average age 19 years). The incidence of frostbite was reported to be 1.8/1000 conscripts. This figure is less than would be expected considering 913 conscripts were affected in the period 1976–89. The total population at risk data was not provided by this study.

Ervasti et al. studied a similar group of 5893 Finnish men entering military service between July 1995 and January 1996. They attempted to calculate lifetime and annual occurrence rates for frostbite in this population, by using a self-reporting questionnaire. Lifetime occurrence was reported to be 44% and annual occurrence 2.2%. This study also reported a lifetime incidence risk of 65% and an annual occurrence of 22% in reindeer herdsmen.

A study by Reynolds et al. assessed risk factors for CWI following an 18-day US Marine Corps winter mountain exercise, using a questionnaire in addition to a clinical assessment. This study reported on a cohort of 365 Marines. A final foot examination of 141 Marines demonstrated that 11.9% had suffered frostnip. This study was not clear on the definition of ‘frostnip’ or why only 141 Marines had a final foot inspection, which may be a limitation in this study.

To identify the epidemiology of NFCI, Tek and Mackey only reported on NFCI in their study on a US Marine infantry battalion during a peacetime military exercise. They reported 38 cases (11%) from an exposed population of 358. Again this study has a notable bias as it only identified patients who were admitted to hospital and so they may have under-reported the absolute number of NFCI cases.

Daanen and van der Struijs identified CWI retrospectively, using cold-induced vasodilation as criteria. They found that 54 out of 1080 Marines had sustained a CWI after exercising in Norway.

The previously mentioned studies have all looked at relatively high-risk individuals. We have not been able to identify any large-scale studies that describe the epidemiology of CWI in a normal population.

### Risk factors

#### Ethnicity

DeGroot et al. found that African American men and women are 3.7 and 2.2 times, respectively, more likely to suffer CWI than their Caucasian counterparts. Additionally Candler and Ivey found that African American males are significantly more susceptible to frostbite than Caucasian males in their study of soldiers (RR = 3.94; 95% CI 2.77–5.59).

Interestingly, Tek and Mackey found no difference in prevalence of CWI between black people and non-black people while Reynolds et al. found white ethnicity a risk factor for developing any foot injury in cold climates but not necessarily CWI.

A paper by Daanen and van der Struijs found that Caucasians had higher ‘Resistance Index of Frostbite’ (RIF) scores than non-Caucasians, although this was not statistically significant.

#### Smoking

In the study by Daanen and van der Struijs, they found that smokers had higher RIF scores than non-smokers. This suggests that smoking may be protective against CWI as a higher RIF score is considered to reduce the likelihood of CWI in the subsequent analysis.

However, Tek and Mackay reported a non-significant increase rate of CWI in smokers (14%) versus non-smokers (9%) (P = 0.09) and Ervasti
et al.\textsuperscript{20} found a significantly increased risk of CWI among smokers. Taylor\textsuperscript{25} found no association between CWI and smoking in a retrospective study of 220 cases presenting to an Evacuation Hospital in Germany. Similarly, Lehmuskallio \textit{et al.}\textsuperscript{19} assessed smoking in their questionnaire-based study but reported ‘no correlation’ between frostbite and smoking, with no statistical data given.

**Gender**

The prevalence of CWI is greater in men than in women, with a ratio of 10:1.\textsuperscript{12} This may be due to most of the studies being conducted in the military service and based upon cold weather sportspeople, where in both settings there tends to a greater proportion of males compared with females.

A study by Taylor\textsuperscript{25} found there to be no difference between gender and the probability of developing a CWI though they did not specify if this was for FCI or NFCI. DeGroot \textit{et al.}\textsuperscript{14} reported there to be similar numbers of men and women per 100 000 (13.9 and 13.3, respectively) acquiring a CWI when all races were taken into account.

A study by Juopperi \textit{et al.} (2002)\textsuperscript{26} looked at the hospital admission of patients with frostbite as a primary or secondary diagnosis, from 1986 to 1995 in Finland. A total of 1275 patients were identified aged between 0 and 89 years. The incidence of frostbite in males was higher at all ages compared with female admissions. The overall incidence of frostbite in the civilian population in this study was 2.5/100 000 population per year.

**Age**

Juopperi \textit{et al.} (2002)\textsuperscript{26} demonstrated a linear increase in frostbite with increasing age in male patients admitted to hospital with only a slight increase in age for females.

**Previous CWI**

Cattermole\textsuperscript{17} found a significant ($P < 0.001$) association between previous CWI and subsequent CWI in his 10-year study on CWI experienced by the British Antarctic Survey. In his dissertation on cold-induced illnesses among the military in mid-Wales between November 1992 and April 1994, Richards\textsuperscript{27} noted that 12.5\% of individuals who suffered cold-induced illness had previously suffered cold injury. Level 1B

**Clothing**

Inadequate clothing is cited by Harirchi \textit{et al.},\textsuperscript{18} Candler and Ivey,\textsuperscript{24} Nagpal and Sharma\textsuperscript{28} and Murphy \textit{et al.}\textsuperscript{12} as a risk factor for acquiring a CWI. Lehmuskallio \textit{et al.}\textsuperscript{19} looked specifically at this and noted that ear frostbite occurred when not wearing ear flaps down on hats (Odds ratio 18.5), ears and cheeks (frostbite) when not wearing scarf (odds ratio 2.1 and 3.8, respectively) and frostbite of cheeks when transported in open top vehicles (Odds ratio 2.2) Level 2B

**Fatigue**

Castellani \textit{et al.}\textsuperscript{29} demonstrated a significantly ($P < 0.05$) reduced core body temperature in 10 subjects following exhaustive exercise and subsequent cold exposure compared with the same 10 subjects undergoing cold exposure having been artificially warmed. This suggests that exhaustive exercise is a risk factor for an altered thermoregulatory response, predisposing to hypothermia. Level 2B

**Cold water immersion**

The human thermoregulatory response to serial cold immersion has been studied by Castellani \textit{et al}.\textsuperscript{30} In this study, eight subjects were immersed in water at 20°C on three occasions in 1 day (‘repeat exposure’). As a ‘control’ group, the same eight subjects were immersed only once, 1 week after the initial repeat exposure. Compared with the ‘control’ group, the study group demonstrated significantly ($P < 0.05$) lower rectal temperature, lower metabolic heat production and higher metabolic debt as a result of repeated cold water immersion. This study concluded that repeated cold water immersion may impair the ability of the body to thermoregulate to maintain its core temperature, possibly due to a fatigue mechanism. Level 1B
Dehydration

O’Brien et al.31 studied the effects of both hypertonic and isotonic dehydration in nine subjects who were subsequently exposed to a cold environment. Hypertonic dehydration was achieved by induced sweating in the study subjects. Isotonic dehydration was achieved by giving subjects a diuretic. Hyper and isotonicity were confirmed by blood testing. A euvoletic group acted as a control.

The study was conducted in an artificial environment and found a non-significant impairment of the cold vasoconstrictor response in the hypertonic/dehydrated group (which mirrors the type of dehydration found following exercise). Numbers in this trial were too small for statistical analysis. Otherwise, the trial appeared well thought out and important physiological variables were taken into account. Level 2C

Diagnosis

Frostnip and frostbite can be recognized clinically; however during the initial stages, it can be a challenge to determine the severity and extent of the injuries. It can take weeks before the full extent of damaged is apparent.

Patterns of freezing and non-freezing injuries are hard to predict as they ‘may coexist in a single individual or limb’, ‘although the dominant form of injury will usually be apparent’.32

Often the context and environmental conditions will give a reasonably reliable indication of the likely type of injury which is to be expected. For example, a 1986 study of Royal Marines33 found that most FCIs occurred in ambient temperatures of between −9 and −19°C. These FCIs occurred in individuals who were prepared for the environment and so are not indicative of a lay population. However, anecdotally it would appear that a colder temperature would usually be required to produce FCIs.

In a civilian population, FCIs rarely occur outside of those who partake in activities or employment that increases their risk of injury (mountaineering, refrigerated environments workers and fishermen).1 The homeless or those trapped outside in winter, especially around the festive season, are always at increased risk of FCIs.

The homeless are also at increased risk throughout the year of NFCIs, which does not involve tissue freezing, distinguishing it both clinically and pathologically from FCIs.2 NFCIs are seen regularly in soldiers, but may also present in anyone who spends extended periods with cold wet feet. This may include those working outside such as farmers or hillwalkers, but could also include festival goers or police personnel.

Hota and Singh3 described a series of 234 CWIs. They decided that the mildest form of injury was frost nip and could be detected by a change in pallor and numbness. The military definition of frost nip is ‘a white blanched area with paraesthesia which returns to normal following 30 min of infeld warming’.34

The authors continued to describe chilblains as localized lesions that are cyanotic or red and painful after rewarming. The UK military, however, would categorize these symptoms as mild frostbite. To define frostbite, Hota and Singh3 used four grades: the first degree was oedema and redness in the absence of necrosis. The second degree was the formation of blisters and eschar at 2–3 weeks. The third degree was complete necrosis of skin, with a thick gangrenous eschar at ∼2 weeks and the fourth degree was when the entire thickness of skin was involved and appendages (toes, fingers) may have been lost. When this is the case, spontaneous amputation usually happens at ∼2 weeks post-injury.

Further classification is seen in Table 2; it relies on the appearance of the tissues after rewarming. It is very difficult to ascertain the depth and extent of frostbite prior to the tissues being rewarmed, because the appearance looks similar regardless of the grade of the injury. This classification system is useful for research purposes, but it is not particularly useful in predicating the likely outcome of tissues. As a result, many publications categorize frostbite as superficial, which would correspond to the first and second degree frostbite in Table 2. Deep frost bite corresponds to third and fourth degree and therefore is regarded as involving the muscles, bones and joints.12

Imaging

Due to the difficulties in assessing the depth and extent of tissue damage at early stages, many forms
of imaging have been used to try and assess viable tissue. Plain radiography, laser direct imaging (LDI),\textsuperscript{35} bone scanning,\textsuperscript{36,37} magnetic resonance imaging (MRI)\textsuperscript{38} and angiography have been all trialled. The most useful have been triple-phase bone scanning and MRI/MRA. Triple-phase bone scanning (using \textsuperscript{99}Tc) has become the standard modality used soon after injury (2–3 days). A retrospective review by Cauchy \textit{et al.}\textsuperscript{36} at the 2-day point suggested \textsuperscript{99}Tc scanning was an accurate predictor of the level of amputation in 84\% of cases.

At an earlier stage after injury (first 24 h), a case report from 2011\textsuperscript{39} concluded that magnetic resonance angiography (MRA) was superior to bone scan and has the potential benefit of being able to illustrate the degree of occlusion of vessels along with the viability of surrounding tissue.

At present, no large-scale studies have taken place that prove the need for early imaging by any of the modalities mentioned above. Because of this, the use of complex imaging in minor cases of FCIs is not recommended.\textsuperscript{2} In the case of suspected severe FCIs in which tissue preserving surgery or thrombolysis may be required, then it is recommended that complex imaging should be sought at the earliest opportunity.\textsuperscript{2} This should take the form of a \textsuperscript{99}Tc Bone Scan or more likely an MRA due to its greater availability and increasing trend of use in this manner.\textsuperscript{39}

### Non-freezing cold injury

NFCIs occur when tissues are subjected to prolonged cooling insufficient to cause freezing. It is thought that exposure to temperatures below 15°C are needed for NFCIs to develop\textsuperscript{4,37} (though similar injuries may occur at warmer temperatures).

Although both FCIs and NFCIs can co-exist, for the purposes of treatment, the predominant injury takes precedent, as the treatment regimen is not the same for FCIs as for NFCIs. The pathological process involved in NFCIs appears to depend on prolonged immersion in water as opposed to just cold temperatures.\textsuperscript{40} Paddy Foot is a related injury that occurs after extended periods of immersion in water at temperatures up to 29°C. The term ‘cold injury’ may therefore be inappropriate for some recognized syndromes.

NFCIs are regarded as having four distinct stages in the evolution of symptoms. The four phases are the injury phase or cold exposure, the immediate post-injury phase, a hyperaemic phase and the post hyperaemia phase; this is illustrated in Table 3.\textsuperscript{41–43}

### Management of freezing and non-freezing CWIs

It is important to identify whether a patient has an FCI or NFCI. Field rewarming can be attempted for 30 min using axillary warmth to identify whether the patient has frostnip or frostbite. If there is complete resolution of symptoms after half an hour field rewarming with no skin changes or paraesthesia, the patient can be regarded as having sustained a frostnip and requires no further treatment other than continual prudence to ensure no further injuries.\textsuperscript{34} However, if the patient has a second episode of frostnip in the same digit, they should be regarded as having sustained a frost bite and treated accordingly.\textsuperscript{34} Apart from this diagnostic field rewarming, no attempts should be made to defrost the patient in

<table>
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<tr>
<th>Degree of frostbite</th>
<th>Appearance after rewarming</th>
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<tr>
<td>First degree frostbite</td>
<td>Numb central white plaque surrounded by erythema but no blistering</td>
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<tr>
<td>Second degree frostbite</td>
<td>Blister formation surrounded by erythema and oedema. Blisters filled with clear or milky fluid in first 24 h</td>
</tr>
<tr>
<td>Third degree frostbite</td>
<td>Death of skin and subcutaneous tissues forming haemorrhagic blisters resulting in black eschar 2–3 weeks later</td>
</tr>
<tr>
<td>Fourth degree frostbite</td>
<td>Tissue necrosis, gangrene and eventually full thickness tissue loss; initially body part is hard, cold, white and numb post rewarming</td>
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the field as multiple freeze thaw cycles have been demonstrated to adversely affect the patient outcome.\(^4^4\) If there is no evidence of frozen tissue, the patient should be regarded as having a NFCI and treated accordingly. Once the diagnosis of FCIs or NFCIs is made, they should be treated according to the diagnosis. However, if FCIs and NFCIs occur simultaneously, treatment should focus on the freezing injury initially followed by treatment of the non-freezing cold injury subsequently.\(^3^4\)

**Freezing cold weather injury management**

Current protocols are largely reflective of the study by McCauley *et al.*\(^4^5\) Hypothermia should be corrected prior to the treatment of frostbite as well as dehydration with either oral or intravenous fluids.\(^4\) Level 1B

There is a correlation between the length of time tissue is frozen and the amount of time it takes to thaw. However, there is no direct correlation between length of time tissue is frozen and tissue damage. Therefore, rapid evacuation to a field hospital is vital. During evacuation, the patient should be kept away from radiators or camp fires until definite rewarming can be achieved to avoid any risk of refreezing as this is related to considerably worse outcomes than would be expected from the initial injury alone.\(^3^4\) Level 1B

Active motion should be encouraged during rewarming but no active massage. It has been recommended that a whirlpool bath can be used with a temperature between 37 and 39°C, to decrease the pain felt by the patient. The end of vasoconstriction is indicated when skin takes on a red/purple appearance and the tissue takes on a pliable texture.\(^2^,1^2,4^5\) This can take between a quarter of an hour to an hour to achieve dependent upon the extent of the frostbite.\(^4^5^–^4^7\) The non-steroidal anti-inflammatory (NSAID) advised is ibuprofen 400 mg BD, which has largely replaced aspirin. Aspirin is thought to be inferior for the treatment of frostbite because of its non-selective prostaglandin blockade, including some prostacyclins, advantageous in wound healing.\(^4^8^,^4^9\) Thawing is associated with pain so appropriate analgesics must be prescribed and tetanus prophylaxis must be administered if appropriate.\(^4\) Level 2B

Protection of tissue against further damage during treatment is of particular importance during the demarcation period which may be prolonged. The digits should be protected from abrasive damage from adjacent structures; this can be reduced by placing soft dressings between them.\(^4\) Padded accommodative footwear should be sought from the orthotics department to protect the foot while maintaining the function of the limb. Early orthotic intervention in the event of amputation is also important as chronic regional pain is common post frostbite; it will also reduce sensitivity to touch in a third of patients.\(^5^0\) Custom made footwear, prosthesis and orthotics will also reduce the likelihood of the development of chronic ulcers which may become malignant in the susceptible, poor quality tissue. Level 1B

<table>
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<th>Stage of NFCI</th>
<th>Characteristics</th>
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<tr>
<td>Stage 1: Injury phase</td>
<td>Patient undergoes vasoconstriction with tissue being cold and numb. There is</td>
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<td></td>
<td>a degree of local anaesthesia and loss of proprioception in the limb. Limb</td>
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<td>may either be red or completely white, there is no pain.</td>
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<tr>
<td>Stage 2: Immediate</td>
<td>Occurs when the limb is warmed, it will change from white to blue but remain</td>
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<tr>
<td>post-injury</td>
<td>cold and numb and can be associated with mild swelling and an absence of</td>
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<td></td>
<td>peripheral pulses.</td>
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<td>Stage 3: Hyperaemic phase</td>
<td>This can last between 2 weeks to 3 months and the limb becomes hot red with</td>
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<td>dry skin, the limb becomes painful and has a degree of paraesthesia, in heavy</td>
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<td>cases blistering and demarcation of the skin may occur.</td>
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<tr>
<td>Stage 4: Post hyperaemic</td>
<td>This phase may last for the rest of a patient’s life, and the patients may</td>
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<tr>
<td>phase</td>
<td>have increased sensitivity to the cold, hyperhidrosis and ongoing paraesthesia</td>
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<td></td>
<td>and pain. In severe cases, flexion contracture, claw deformities, muscle</td>
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<td>atrophy and ulceration may occur.</td>
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</table>
There is controversy over the routine prescribing of antibiotics and debridement of blisters. Antibiotics should be considered prophylactically in severe injuries particularly in second and third degree frostbite where there are blisters and open tissue damage. However, in the presence of trauma, cellulitis or known infection antibiotics are required. The evidence for treatment and the de-roofing of blisters is weak. If blisters are restricting movement, then the benefits of aspirating blisters that are not haemorrhagic may outweigh any risks. Debridement of blisters should not be conducted in a field environment to decrease the chance of infection as well as enable the accurate assessment of the soft tissue damage.

Adjuvant therapies

Over the years, many adjuvant therapies have been trialled to try to prevent the progressive dermal ischaemia seen in the post-thaw phase. The mechanism of these has been to interrupt vasoconstriction, vascular stasis, thrombosis and endothelial injury. Studies on burn wounds in the 1970s and 1980s found that the main agents in progressive dermal ischaemia were the breakdown products of the prostanoïd cascade, prostaglandin E2 and F2 and in particular thromboxane (TxA2). Robson and Heggers demonstrate that these mediators are also present in frostbite blister fluid. It follows that any medication or intervention which inhibits this cascade may be beneficial in reducing dermal ischaemia and subsequent tissue loss. NSAIDs are used for this reason blocking the synthesis of prostaglandins and thromboxane.

As well as for blocking the synthesis of prostaglandins, NSAIDs can be used for pain relief. The process of rewarming is very painful, and therefore non-steroidal and opiates should be used for patient comfort. The use of aspirin should be considered for its analgesic and antplatelet properties.

Aloe vera

Aloe vera has been used for its anti-thromboxane effects. Heggers et al. used a modified protocol for treatment of frostbite incorporating Aloe vera for its local anti-thromboxane effects and ibuprofen for its systemic control of prostanoid production. When it was used, the overall tissue loss and amputation rate was reduced. This was a heterogeneous population, representative of patients who would present to a clinician.

Hyperbaric oxygen

Experimental and human case studies emerged using hyperbaric oxygen (HBO) therapy in the late 1960s. Theoretically, it is an attractive modality due to its ability to increase dissolved oxygen supply to tissues and its association with increased capillary formation and white cell function. However, while some individual human case studies and series have shown promise, its use remains controversial as results have been mixed with some animal studies in mice and rabbits showing no increased tissue survival. In one study, 32 pairs of rabbits underwent hyperbaric treatment or control after freezing of their hind leg over a range of temperatures and allowing slow rewarming. This study showed no benefit in terms of tissue loss. The same author repeated the experiment with rapid rewarming, and again hyperbaric oxygen made no significant difference to tissue loss. Increased tissue survival was seen in rabbit tissue if hyperbaric oxygen was given for 2 h daily, and better still survival was demonstrated if it was given within 24 h of the event. However, as with most of the treatments for FCIs, lack of injury uniformity, time to presentation and field treatment make it hard to assess this modality’s efficacy.

Thrombolysis

Considering the main source of tissue damage in frostbite is due to thrombosis of damaged vessels causing ischaemia, it is logical that preserving the blood flow would alleviate some of this potential tissue damage.

Treatments that have been previously used are intravenous (IV) heparin, surgical and medical sympathectomy and low molecular weight (LMW) dextran. Experimental studies looking at tissue survival in rabbits used IV thrombolysis with streptokinase.
One particular study found that it was additive to rapid rewarming, and unlike rapid rewarming its beneficial effect was sustained at 12, 24 and 48 h. As this showed promising results, it has been largely replicated in human case series with retrospective comparison to older cases.

Sheridan et al. have attempted to develop an algorithm for which patients are suitable for the use of thrombolitics. They suggest that an angiography should be done before consideration of thrombolysis combined with the use of tissue plasminogen activator (tPA) and that angiography should be repeated every day after treatment to evaluate the ongoing response to treatment.

General consensus is tPA when used early (preferably within 24 h and after rapid rewarming) significantly reduces tissue loss and subsequent amputation. One study showed no significant difference between intra-arterial (IA) or IV thrombolysis in terms of tissue survival; however, they experienced side effects in relation to the IA tPA. It is recommended that the tPA is used in conjunction with heparin to reduce the recurrence of microvascular thrombosis.

It must be kept in mind that reperfusion of ischaemic tissue can cause tissue oedema which may lead to fasciotomies. Patients undergoing thrombolysis should be managed in a high dependency or intensive care setting.

**Vasodilators—medical and surgical sympathectomy**

Original studies have given contradicting views for sympathectomy, relating to the time it should be performed at post-injury. Regional sympathetic blocks and gangliectomy were proposed by French authors in World War II. However, some studies have shown that early sympathectomy may have a detrimental effect. Usually, this has involved the use of reserpine or tolazoline with an immediate onset of action via blockade of the alpha adrenergic receptors of tolazoline and the subsequent noradrenergic depletion caused by reserpine. One study in rabbits found that these agents could be useful in those presenting late in whom rapid rewarming had been missed. However, unlike IV thrombolytic agents, these were not superior to rapid rewarming alone, but they did have an improved effect in combination. The authors found that the IA usage of these drugs resulted in a regional block and less systemic effects. Level 2B

Iloprost is an alternative to surgical sympathectomy and has been demonstrated to reduce the risk of amputation in digits from 40% down towards 3%. Iloprost has the advantage over tissue plasminogen factor, because it can be administered on a general ward and does not need any radiological input when administering it. Additionally, it can be used in patients who have sustained concurrent trauma and can be started beyond 24 h without a decrease in the efficacy of the drug. Level 1B

**Surgery**

Early surgery is rarely required. As with any burns surgery, the estimation of devitalized tissue can be difficult and evolves. Auto-amputation is an attractive option with revision as required later on. However, a strong indication for surgical intervention is for wet gangrene and uncontrolled infection. The obvious drawback to this is extended hospital stay and loss of work days with the risk of super-added infection and this is where imaging modalities such as radionucleotide angiography with bone scanning have proved attractive in the early assessment of viability to achieve early debridement and coverage of bone. Level 2B

Despite this it is often documented in the literature that white or clear blisters, more superficial in nature, containing PGF2a and TXA2, should be debrided to prevent further damage to the sub-dermal plexus. However, haemorrhagic blisters do not hold this risk and should be left intact. Although the fluid could be aspirated, debridement may allow desiccation to the underlying tissue and conversion to full thickness.

Other surgical input which may be required involves escharotomiesubder or fasciotomies to relieve compartment syndrome and improve distal circulation. These are rarely required, but surgeons deploying to these environments must be aware of this possibility. Level 1B (Fig. 2)
Treatment of non-freezing CWIs

As with freezing CWIs, the immediate treatment is to remove the limb and patient from the cold wet environment. The evidence behind the treatment of NFCIs is far less than for its freezing counterpart; however the evidence suggests that:

Slow rewarming at 37–39°C is required as rapid rewarming can exacerbate the injury.\(^4\) Again surgery should be avoided until the extent of the injury is understood, and amputation may be required to remove areas of gangrene. Level 1B

The recommended analgesia to be given is amitriptyline with or without pregabalin as traditional opioids and NSAIDs and gabapentin do not have the same efficacy. There is evidence that early intervention with amitriptyline may reduce the sequelae of chronic intractable pain.\(^4\) Level 2B.

Sympathectomy by medical or surgical means should be avoided as it has been demonstrated to cause medium- to long-term deterioration in patient symptoms.\(^4,34\) Level 2B (Fig. 3)
Conclusion

In the last 20 years, a growing interest in outdoor recreational activities coupled with a sharp increase in the numbers of homeless has resulted in a rise in frequency of both FCI and NFCI exposure among the civilian population. FCI has a significant morbidity which can be minimized if patients are treated early and using an initially conservative approach will reduce the amount of soft tissue loss. All treatment modalities should be aimed at decreasing the amount of tissue loss and optimizing the function of the residual limb. The governing principle is to avoid early surgical intervention if possible while protecting life and limb.

It is impossible to ascertain the severity of injury in the early phase and where necessary additional imaging modalities should be sought. In some circumstances, medical teams should consider administering iloprost or thrombolysis. However, in inexperienced hands, further iatrogenic injury can be caused; therefore, advice should be sought from institutions with appropriate experience either via telemedicine or in person.

Further research into the management of NFCIs is required to improve the management of this debilitating condition.

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