Non-freezing Cold Injury (NFCI)

Dr Silviya Doneva and Lauren Binnie
King Edward VII’s Hospital and Medical Advisory Committee (MAC)

Prepared by the Health of Veterans’ Research Team (HVRT)
28/06/18
1. Introduction

The purpose of the present report is to provide a brief summary of what is currently known about non-freezing cold injury (NFCI), with a particular focus on UK Service Personnel. The presented information herein has been drawn from academic research, official MoD reports and guidelines on cold weather injuries (CWI) and NFCI, including the Non-Freezing Cold Injury report, prepared by the NFCI Review Group (1), which is considered the most comprehensive review of the condition up to date. The present document provides information on the definition, symptoms, clinical features, pathogenesis, epidemiology, risk factors, prevention and management of the condition. Furthermore, it recognises the number of gaps in the study of NFCI, such as a lack of official definition and clear classification of the condition, unreliable data on incidence, as well as the limitations of the current tests used for diagnosis. In line with these, at the end of this document we also outline some recommendations for future research.

Importantly, throughout the report we refer to the condition only by NFCI, although a variety of terms, found in the literature, are often used as synonymous with the disorder. The latter, namely trench foot, paddy foot (2) and immersion foot (3,4), in fact, represent more severe forms, with a different aetiology to NFCI where the condition has most likely progressed due to help not being sought for a prolonged period of time.

2. Definition of NFCI

Cold weather injuries (CWI) produce a spectrum of cold-related disorders, including hypothermia, freezing cold injury (FCI) and non-freezing cold injury (NFCI) (1). Hypothermia develops when prolonged exposure to lowered temperature results in a reduction in deep body temperature of below 35°C (95°F). It may impair health and performance, and in some cases can result in death (1). FCI, or frostbite, results when tissue is cooled at below 0.55°C for long enough that it leads to the freezing of tissue fluid (1). By contrast, NFCI is a pathological state resulting from damage caused to peripheral tissues exposed to
cold temperatures between 0.55°C and 20°C (33°F-68°F) for a prolonged period of time (5). Therefore, surprisingly, NFCI does not involve tissue freezing but instead a slow decrease in temperature, which distinguishes it both clinically and pathologically from FCI (1). NFCI is often associated with exposure to persistent wetness, and it is usually the combination of cold and wet that leads to the development of the condition (5).

### 2.1 NFCI affecting Civilians

NFCI tends to be associated with the military; however it can also occur in civilians, particularly those who work or partake in outdoor activities (6). Hikers, mountaineers, fishermen, construction workers and cyclists, for example, may be exposed to cold and wet conditions for a prolonged period of time resulting in wet socks and boots, exhaustion, dehydration and cold, which can ultimately result in NFCI (6–8). Others who may be at risk of developing NFCI include the homeless, older adults and alcoholics (9), as they may not have the facilities or ability to remain dry and warm after exposure to a wet environment (7).

Importantly, it should be recognised that in the UK NFCI occurs fairly rarely in civilians and some groups in particular (e.g., the homeless) are difficult to reach and engage in research.

### 2.2 Clinical Features

Early examination (within a few weeks) of NFCI reveals an impairment of large and small nerve fibres, whereas a late examination (weeks/months) shows a recovery of large nerve fibres but small nerve fibre impairment may persist, frequently resulting in neuropathic pain and cold alldynia¹ (5). Additionally, cold sensitivity can persevere due to abnormal sensory and vascular reactivity (5,8). Often recovery occurs before the chronic phase of NFCI where patients will experience an alleviation of symptoms. Although variability between cases is likely, efforts have been made to construct a guideline of the presentation of symptoms at different stages of NFCI (see Section 2.3 below).

---

¹ Pain caused by a normally innocuous stimulus.
2.3 Symptoms and signs of NFCI

NFCI varies in presentation and symptoms are dependent on its severity and time course (5). Some symptoms may be minor and return to normal over subsequent weeks, however, long-term symptoms can be intractable and debilitating (see b) below). NFCI occurs more often to the legs than the arms, however, the fingers and toes are the most affected areas (5).

The disorder is known to have four distinct stages in the evolution of symptoms. These have been presented below together with some of the possible long-term consequences of NFCI.

a) Stages (1,4)

ACUTE NFCI

Stage 1 (Injury phase): occurs during cold exposure (0-20°C, 1 day - 1 week)
- Loss of sensation/complete local anaesthesia
- Gait and stumbling may occur
- Extremities initially bright red then paler/white
- Pain and swelling unlikely

Stage 2 (Immediate post-injury): occurs when the limb is warmed (hours to days)
- Early, small increase in peripheral blood flow
- Extremities change from white to mottled pale blue
- Cold and numbness, loss of sensory and motor function
- Initial oedema², weak peripheral pulse

Stage 3 (Hyperaemic¹ phase): can last from 2 weeks - 3 months, usually 6 - 10 weeks
- Abrupt onset, extremity becomes hot and flushed
- Peripheral pulse full and bounding, microcirculation becomes sluggish
- Intense pain that is worse at night, no vasomotor activity
- Oedema becomes obvious, may blister

CHRONIC NFCI

Stage 4 (Post hyperaemic Phase): weeks to lifelong

² A build-up of fluid in the body causing the affected tissue to become swollen.
³ Excess blood in vessels.
• Lack of physical signs, inflammatory response reduced
• Increased cold sensitivity, persistent pain, hyperhidrosis
• Abnormal sensation (i.e., paraesthesia)

**b) Potential long-term consequences (10)**
• Inability to work outdoors due to cold sensation.
• Increased susceptibility to fungal infections due to persisting oedema and hyperhidrosis.
• Dependence on tricyclic antidepressants to alleviate chronic pain.
• Ulceration, muscle atrophy, deformity of the knee (i.e., flexion contracture), minor or major lower limb amputation.

3. **Epidemiology of NFCI**
To our knowledge there is currently no reliable data on the incidence of NFCI in the UK. Additionally, the clinical pattern of the condition has changed substantially since its most major recorded outbreak during the Falklands conflict of 1982:

**a) During the Falklands conflict 20% of the evacuated British causalities were due to NFCI (11), and 98% of the military personnel on the front line suffered NFCI (12). Importantly, almost all casualties were UK-born Caucasian males of the Royal Marines (5) and interestingly, a very few claims were lodged for NFCI from the Falklands veterans as a consequence.**

**b) Since then the clinical pattern of the condition has changed. According to the 2013 Report on the Health of the Armed Forces records in 2012/2013, 604 new cases of suspected cold injury were referred to the Institute of Naval Medicine Cold Injury Clinic (INM CIC; see Section 3.1 ), the majority of which were in the UK Army (13). Furthermore, unlike during the Falklands conflict, these more recent NFCI casualties are of a foreign or Commonwealth descent (e.g., British born Afro-Caribbeans or Caucasians born and raised in Africa; (5).**

---

4 Abnormal sweating (See Section 6.2 for more information).
5 Usually indicative of damage to the peripheral nerves.
c) Importantly, at present NFCI is not a major disabling disorder among UK Service Personnel with the numbers of compensation claims currently decreasing. One possible reason for this is that in July 2013⁶ the MoD made the residency requirements for Commonwealth recruits who wished to join the UK Armed Forces more stringent (14). This in turn reduced the number of Commonwealth citizens joining the Army and therefore possibly the compensation claims for NFCI.

3.1 The Cold Injury Clinic Audit
Dr EHN Oakley (Former Head of Survival and Thermal Medicine, Institute of Navy Medicine) ran the Institute of Naval Medicine Cold Injury Clinic (INM CIC) and assessed up to 1000 patients a year with suspected NFCI. In 2014, Dr EHN Oakley conducted an unpublished audit of 644 NFCI new cases; of these cases, there were 271 where injury was sustained before the 1st of September 2012 (15). The average time interval between injury and the date seen in the CIC was 7.8 months, with a range of 2 to 15 months. Medical diagnoses other than cold injury were recorded in 89 cases, with the majority having primary Raynaud’s disease⁷.

Of the 284 winter 2012/13 NFCI cases identified, the majority were Army junior ranks with an average age of less than 30 years; most of these injuries occurred in the UK and half developed NFCI on their hands and feet (16). Mixed freezing and non-freezing cold injuries occurred, but were rare.

The prevalence can be affected by factors such as age and ethnicity. See Section 6 for more information.

4. Pathogenesis of NFCI
First, it should be noted that the pathogenesis of the condition is not well-understood at present (1). Knowledge of how NFCI develops following exposure to cold stimuli is largely based on animal models and personal accounts, since

---

⁶ These have been relaxed again as of September 2016.
⁷ Raynaud’s disease is a cold-induced vasospastic disorder (limiting blood circulation to affected areas).
longitudinal data and human skin biopsies\(^8\) are lacking. However, one recent clinical study examined 30 soldiers with cold exposure and persisting sensory symptoms using sensory testing, nerve conduction studies and skin biopsies (8). It was found that 20 (67%) out of the 30 soldiers who took part, had an abnormal pinprick sensation in the feet, while 67-83% experienced abnormalities of thermal thresholds to the different modalities (8). Furthermore, a range of abnormal skin biopsy markers were identified in 90% of the soldiers suggesting that skin biopsy assessment with a range of markers is a useful tool for the diagnosis of peripheral neuropathy in NFCI (8). This study concluded that ‘increased blood vessels after tissue ischaemia\(^9\)/hypoxia\(^10\), with disproportionate density of associated nerve fibres, may underlie pathogenesis of NFCI and result in a painful vaso-neuropathy’ ( (8), p.14).

It is currently assumed that due to vasoconstriction\(^11\), cold temperatures impair microvascular flow which leads to neurovascular damage, resultant upon ischaemia. Furthermore, the vascular and neural components possibly also interact (i.e., microvascular damage causes neural ischaemic injury, and damage to microvascular innervations, in turn leads to further ischaemia. Further evidence suggests that cold exposure can directly cause nerve fibre damage, which is independent of vascular damage (1,17).

### 4.1 Cold induced vasodilation (CIVD)
Cold induced vasodilation (CIVD) predominately occurs in extremities, possibly as a protective mechanism after exposure to temperatures of around 10°C or less, however, deep body temperature must be at a normal level. For instance, when exposed to cold, vasoconstriction occurs to reduce heat loss, which consequently cools extremities significantly. After 5-10 minutes of cold exposure, blood vessels in the distal portions of limbs begin to dilate due to decreases in neurotransmitters. The CIVD subsequently increases the

---

\(^8\) A procedure in which a sample of skin tissue is removed, processed, and examined under a microscope.

\(^9\) A restriction in blood supply to tissues, causing a shortage of oxygen and glucose needed for cellular metabolism.

\(^10\) The deprivation of oxygen at the tissue level.

\(^11\) The narrowing of blood vessels resulting from contraction of the muscular wall of the vessels.
temperature of the area exposed to the cold through an increase in blood flow. Therefore, impaired CIVD may place individuals at a higher risk of NFCI (18). One study showed that Caucasians, compared with other ethnicities, were at a lower risk of NFCI due to higher resistance indexes for frostbite, a measure based on CIVD response. Smokers, on the other hand, were found to be at an increased risk for NFCI (19) (see Section 6).

5. Diagnosis of NFCI

A diagnosis of NFCI should take into consideration history (timing, circumstances and clinical features), examination (cutaneous\textsuperscript{12}, neurological and peripheral) and laboratory tests/investigations (1).

Currently there is no accurate test of appropriate sensitivity for NFCI, however, the most widely used tests for diagnosing NFCI are infra-red thermography and the thermal sensory threshold test.

5.1 Additional Tests

Tests currently used to diagnose NFCI:

a) \textit{Infra-red thermography} uses thermal imaging to compare infra-red energy emitted from a cold injured limb before and after a standardised cold stress test. Those extremities with NFCI will likely take longer to rewarm following cooling which will be evident from the imaging. Problems with this test include a wide normal range and possible abnormal results in patients with no history of cold exposure. Exercising prior to immersion in water is thought to isolate peripheral injury for improved test accuracy; however, the test is still not regarded as diagnostic (5,6). Infra-red thermography has also been suggested as able to predict the future risk of NFCI, since repeated cold exposures are likely to increase NFCI susceptibility, but again there is a lack of evidence (1).

b) \textit{The thermal sensory threshold test} is used to assess small nerve function by the ability to detect incremental changes in skin temperature, using the Middlesex Thermal Testing System. Values are obtained for the thermal perception threshold of warm and cold temperatures. However, problems

\textsuperscript{12} Relating to or affecting the skin.
with this test include the potential for invalid results that are based on subjective perception (1).

c) *Nerve conduction* studies can provide information with regards to large motor and sensory nerve fibre conduction. No systematic studies of nerve conduction have been performed for NFCI (1).

5.2 Further tests, likely to aid diagnostic accuracy (20):

a) *Quantitative multi-modal sensory testing (QST)* tests how well nerve endings work. A thermal threshold test measures the response of small fibres to temperature changes and a vibration test measures large fibres’ sensory thresholds for vibration (exists but not conventionally used for NFCI).

b) *Skin biopsy* can quantify intraepithelial nerve fibre density. Since nerves are damaged in NFCI, a lower density of nerves would be expected (exists but not conventionally used for NFCI).

c) *Genetic screening* is hoped to provide a potential basis for ethnic differing, however, no markers exist as of yet (test to be developed in the future).

6. Risk Factors

Below follows a list of some of the risk factors predisposing to the development of NFCI. Although a definitive view of these is not available, both experience and a limited number of peer-reviewed articles offer useful insights into the potential risk factors of the condition.

6.1 Situational Conditions

a) Intuitively, the main predisposing risk factor for CWIs, in general, is having to endure cold weather conditions for a significant proportion of time (e.g., NFCI: 12 hours to 4 days; (21)).

  • More specifically for NFCI, damp environments, and especially the combination between cold and wet conditions, are known to be a key risk factor (1,5,21,22). NFCI has, however, also been reported to

---

13 Within the tissue that lines organs and vessels.

14 A gene or DNA sequence with a known location on a chromosome that can be used to identify individuals or species.
develop in warm climates, up to 20 degrees C, following prolonged foot immersion (1,5).

b) Conditions that further lead to a reduction in body temperature such as exposure to moving water or air (e.g., swimming, travel in an open-topped vehicle) have also been identified as a risk factor (1).

c) Inadequate clothing and footwear (in terms of coverage, water-, wind-proofing and insulating properties) and malnutrition are risk factors as these contribute to heat generation loss and therefore, reduced body temperature (1).

d) Certain individuals are at a heightened risk of developing NFCI because of their occupation (e.g., the military, fishermen, sailors and cold storage workers), their engagement in outdoor activities (e.g., skiing, mountaineering) or poverty (the homeless; (23)).

6.2 Individual Differences

a) Slower rewarming response – Variations have been reported in one’s ability to rewarm after cold exposure. Brändström et al. (24) found that indeed NFCI was more common in their group of so called ‘moderate’ to ‘slow’ rewarmer, as these individuals were characterised by a decreased cutaneous blood flow.

b) Emotional stress and anxiety have also been suggested to be a potential risk factor, especially in a combination with reduced cutaneous blood flow (see above) and increased perspiration.

c) Gender – there is mixed evidence on the prevalence of NFCI as a function of gender (25,26). Some have reported that CWIs are more widespread among males (26), however, these findings might be confounded by the fact that men are more likely to be exposed to the situational conditions that put one at risk, including their occupational choice (22). At the same time African-American women seem to be more protected than African-American men with respect to developing NFCI (27).
d) Ethnicity – A retrospective UK military study examined whether peripheral cold injury\(^{15}\) in soldiers of African-American, Pacific-Islander\(^{16}\) and Gurkha descent differed in incidence and severity, compared to Caucasians (28). Results revealed that as opposed to Caucasians, cold injury was 30.3 times more prevalent in African Americans (who also developed more severe injuries), 2.6 times in Pacific Islanders, while Gurkhas were protected. Finally, ethnic differences have also been reported in the chronic sequelae\(^{17}\) of NFCI, with 95% of Caucasians developing vascular sequelae, while the neurological sequelae of the disorder is more characteristic of around 1/4th of the Afro-Caribbeans (5).

e) Hyperhidrosis is a medical condition, characterised by excessive perspiration in the armpits, palms, soles of the feet, face, scalp, and/or torso. It has been reported as a risk factor for the development of NFCI and cold injuries in general (1). This is so as logically, sweating leads to a reduction in one’s insulation from the environmental conditions, and therefore further cools down the body. Importantly, hyperhidrosis is also one of the chronic sequelae that may develop in Stage 4 of NFCI (29) (See Section 2.3).

6.3 Other Factors
Other factors that have been suggested to contribute to the development of the condition (1) are listed below. It should be remarked that many of these have not been conclusively confirmed by research:

a) Prior history of NFCI;
b) Sleep deprivation;
c) Dehydration;
d) Immobility;
e) Cigarette smoking, upright posture and reduced physical fitness;
f) The wear of skin creams;

---

\(^{15}\) 74% of the participants in this sample suffered from NFCI, while 24% - from freezing cold injury.

\(^{16}\) Pacific-Islanders are: Polynesians, Melanesians and Micronesians.

\(^{17}\) Sequela (plural sequelae) is an abnormal condition resulting from a previous disease.
g) Age – conflicting evidence on the effect of age has been reported. While, some data suggests that CWI are more widespread among young and untrained Service Personnel (16-19 years) (17), others (1) have found that CIVD becomes impaired with age, which is in turn associated with an increased risk of cold-injury.

7. Psychosocial Aspects

Employment, family life and general quality of life may suffer as a consequence of NFCI.

a) Employability – There is evidence that NFCI can restrict one’s employment and occupational outcomes (1,32) and even be the primary reason for unemployment (33). For example, even if sufferers remain in the military, they are often downgraded due to restricted abilities following NFCI diagnosis. In support, Vale et al. (32) reported that from their sample of 42 UK military veterans that had developed NFCI in Service, 53.3% remained unemployed, while 71% of the new patients seen between 2005 and 2006 at the Institute of Naval Medicine Cold Injury Clinic (INM CIC) had a restriction in duties following their injury (28). Furthermore, often, adjustments to the sufferers’ environmental exposure are needed due to the condition. For instance, only once treatment has been received and symptoms have subsided, individuals may be employed in sheltered environmental conditions, such as working indoors in heated buildings only (17). Patients who are completely asymptomatic can progressively be re-introduced to the cold, however if symptoms return, then this should be immediately terminated (17). Exposure to cold and/or wet conditions should be considered when returning to work, as well as restriction to working indoors, wearing warm hand-wear, footwear and clothing, and daily or frequent use of a foot spa to rewarm feet (17).

b) Family Function – Chronic pain and cold hypersensitivity both prove to be damaging symptoms of NFCI that affect sufferers’ everyday lives. Vale et al. (32) found that tasks, such as testing water temperature might be

---

18 We are referring to British Army soldiers.
impaired, causing problems for seemingly simple everyday tasks such as bathing one’s children. Furthermore, tasks at home that involve varying temperatures like using a fridge or freezer can cause exacerbation of symptoms.

c) Long-term consequences – NFCI is associated with a number of quality of life reducing long-term consequences such as chronic neuropathic pain, hyperhidrosis and cold hypersensitivity (described in b)). More specifically, research has shown that neuropathic pain could be particularly debilitating. Ionescu (33), for instance, described the case of a 41-year old veteran who had lost complete mobility since he sustained a NFCI 20 years ago. Furthermore, neuropathic pain could lead to a number of additional undesirable outcomes such as social isolation, limited function, relationship difficulties and substance misuse (34,35). Furthermore, reduced sleep, a high prevalence of major depressive disorder (MDD) and anxiety disorder have also been reported in a high number of neuropathic pain sufferers (36).

Finally, apart from affecting one’s job and everyday functioning, hyperhidrosis might also impact on the sufferer’s recovery and long-term management of NFCI (5).

Unfortunately, there is limited work examining the long-term consequences of NFCI. In our search we found only one published study that measured the sufferers’ quality of life after sustaining the condition (32).

8. Prevention

Cold injuries may be preventable through appropriate strategies in line with the Chain of Command19.

For effective NFCCI prevention, commanders need to be fully aware of the risks, hazards and conditions that subordinate personnel are exposed to (See Section

19 A system in an organisation, in this case the military, by which instructions are passed from one person to another.
6 on Risk Factors). Additionally, preventative measures should aim to include the maintenance of a normal core body temperature and the protection of vulnerable body parts, such as extremities, in order to help sustain good peripheral blood flow (See Section 3.5 of the JSP-539; (17)). Sections 4.5 and 4.6 of the Ministry of Defence Joint Service Publication 539 (JSP-539 (17); See Section 9) provide a broad outline of the various preventative measures that can be utilised to maintain peripheral perfusion\(^{20}\) and to increase protection from the cold, for all cold injuries, including NFCI, and these can be found in Appendix 2.

Medical history should also be taken into consideration, alongside environmental aspects, since certain medical problems can increase the risk of NFCI. This can be supported by medical personnel who should be trained in preventative measures and highlight at risk individuals to the Chain of Command (See Sections 4.4 and 4.43 of the JSP-539 (17)).

Additionally, individuals themselves should be aware of the risks of NFCI through adequate briefing prior to an at risk activity (See Section 3.7c of the JSP-539 (17)). Personnel at a heightened risk of NFCI, such as African-Caribbean and Pacific Islanders, should be extra vigilant in upholding appropriate measures to prevent NFCI and commanders should be prepared to make extra kit and equipment available if necessary (See Sections 3.10 and 4.43 of the JSP-539 (17)).

### 9. Treatment and Management

There is no conclusive research evidence to inform best practice in the treatment of NFCI. Rather than active therapeutic interventions, currently acute NFCI is managed by avoidance of the triggering factors (i.e., removing the extremity from further exposure to a cold and wet environment), foot spa therapy and rewarming (5,22).

#### 9.1 Clinical Care Pathway

The Joint Service Publication 539 (i.e., JSP 539 (17)) is the Ministry of Defence official document, endorsed by the Defence Authority for Healthcare and Medical,  

\(^{20}\) The delivery of blood to peripheral tissues, such as the feet and hands.
providing guidance for the initial medical management and treatment of climatic casualties (heat illness and cold injury) up to Secondary Health Care\textsuperscript{21} (17). According to it, once a cold injury is suspected, personnel should follow the clinical care pathway guidelines of JSP, outlined in Appendix 1 in the present report and the Defence Primary Healthcare (DPHC) Guidance Note No. 10/17. Below in Fig. 1 is a summary of the main actions that need to be taken once NFCI is suspected.

\begin{center}
\textbf{Non Freezing Cold Injury (NFCI) Management}
\end{center}

For use in the primary care setting or by those with limited experience of treating cold weather injuries.

<table>
<thead>
<tr>
<th>Evacuate Patient from cold environment</th>
</tr>
</thead>
<tbody>
<tr>
<td>NFCI should be evacuated from the cold environment as quickly as possible.</td>
</tr>
</tbody>
</table>

\begin{center}
\textbf{Initial Management}
\end{center}

- Slow Rewarming: exposure to warm air alone.
- NFCI \textit{must not be immersed in warm water.}
- Analgesia: Amlopidyl, should be titrated upwards as necessary.
- Regional Analgesia (spinal or epidural) may give complete pain relief temporarily.

\begin{center}
\textbf{Further Management}
\end{center}

- Review: Either in local Primary care or specialist Cold injury centre*.
- Surgery: Should be avoided until advised by specialist Cold injury centre*.

* e.g. Cold Weather Injury Clinic, Institute of Naval Medicine.

Fig.1 Summary of current practices in NFCI management in a primary care setting. Reproduced from (22).

\section*{9.2 NFCI Referral Pathway}

The NFCI referral pathway differs depending on whether the patient is a Serving or Ex-serving Personnel.

For Service Personnel, advice can be sought from the Defence Primary Healthcare (DPHC) regional Cold Injury Advisor, or at the Cold Injury Clinic Institute of Naval Medicine (CIC INM; see Section 3.1). However, depending on the severity of the case, some may be referred onto pain clinics, specifically via the Defence Medical Research Council (DMRC) (37). If the case is mild, then a Cold Injury Advisor should be employed (see Section 2.3). In addition to the CIC INM, the MoD has recently commissioned an NFCI service at the Hammersmith Hospital in London for Serving Personnel. Professor Praveen Anand will be

\textsuperscript{21} Managed by clinical staff.
leading this NFCI service with a primary focus on pathophysiological and chronic pain syndromes (8). This new service at the Hammersmith Hospital will be managed by the Defence Primary Healthcare (DPHC). Furthermore, one of the datasets from which the numbers of Armed Forces Personnel, suffering from NFCI could be estimated is the Defence Patient Tracking System (DPTS). The DPTS records the patient care pathway from the clinical intervention until the patient no longer requires specialist treatment. It monitors the progress of Armed Forces patients undergoing specialist treatment for long-term conditions, such as for NFCI (38).

NFCI in veterans is managed by 'main stream' NHS England services, however referrals are conducted, as appropriate, to local pain clinics as well as local neurological and vascular services (37). Referrals from main stream services can also include escalation to tertiary or national services as clinically indicated (see Appendix 1). In England, these services are funded by the Clinical Commissioning Groups (CCGs) as, at present, no specific national service for veterans exists (38).

The aim of NFCI care and referral pathways should be focussed on early recognition in order to prevent prolonged and repeated exposure, as well as screening for neuropathic pain and also provision of therapeutics targeting neuropathic pain (32).

### 9.3 Drugs to manage neuropathic pain

Amitriptyline22 and/or pregabalin23 are often prescribed to treat the neuropathic pain, associated with NFCI. However, as before, there is little evidence to suggest that these represent the most optimal pharmacotherapy for NFCI (5,22,33). Importantly, the latter have been associated with a number of

22 Amitriptyline is often prescribed to treat persistent pain. It belongs to the group of medicines called tricyclic antidepressants that are also used to treat depression (39).

23 Pregabalin is mainly used to treat nerve pain, such as burning, shooting or stabbing pain. It belongs to a group of medicines called anticonvulsants, which are also used to treat epilepsy (40).
adverse effects, patients should be aware of. Amitriptyline, for example, may cause marked drowsiness as well as hypertension, suggesting that patients’ blood pressure should always be checked before administration (17).

9.4 Other drugs

There are several reported attempts to treat the disorder with alternative drugs (32–34). For example, in a recent case study by Ionescu et al. (33) a 41-year old white veteran, diagnosed with NFCI was administered iloprost on two occasions, 3 months apart to target his severe pedal pain and improve his mobility (the patient was walking with crutches). Furthermore, iloprost was trialled as standard analgesics (e.g., pregabalin) could not alleviate the debilitating pain this patient was experiencing. Results revealed that although the drug was successful in ameliorating the symptoms on the first occasion, these returned after 6 weeks from the initial dose and the patient even worsened after the second administration of iloprost (33).

9.5 Specialist Treatment Centres

At present there is one specialised Cold Injury Clinic in the UK - the Institute of Naval Medicine Cold Injury Clinic (INM CIC), located in Gosport, Hampshire. This clinic was established in response to the many CWIs sustained in the Falklands war in 1982. The clinic is open to Service Personnel only (veterans are not treated; 36). Patients are also referred to DMRC Headley Court for pain management and the NHS for specialist neurological assessment (17);

9.6 FCI or NFCI

As explained above there are differences in the pathological processes involved in FCIs and NFCIs and therefore these follow a different treatment regimen. Where the two conditions co-occur, treatment should focus first on the freezing cold injury and only after on the nonfreezing cold injury (44).

10. Armed Forces Compensations due to NFCI

10.1 Costs, associated with NFCI

Up to 2013, some 200 claims had been settled at an overall cost to the MoD of approximately £16 million, according to data from The MOD Common Law

24 Ilprost is prescribed to patients with blood circulation problems. It is the synthetic equivalent of a chemical produced by the human body, called prostacycline (43).
Claims and Policy (CLC-P) unit (1). Furthermore, the UK Defence Statistics\textsuperscript{25} stated that the financial cost, associated with NFCI so far, is £17.2 million in damages and £11.3 million claimant legal costs; the latter figure also includes those who have claimed for civil damages\textsuperscript{26} (5). Additionally, there is a human resource cost, related to the number of medical discharges. Between the 6\textsuperscript{th} April and 31\textsuperscript{st} December 2014 there were 518 medical discharges due to NFCI, of which 330 have been given an award from the Armed Forces Compensation Scheme (AFCS; see below for more information) (5).

- Descriptors for NFCI

Since April 2005, UK Armed Forces Personnel who experienced an injury (among which NFCI), illness or death caused by service make no fault compensation claims under the Armed Forces Compensation Scheme (AFCS). Currently the severity of NFCI of claimants under the scheme is assessed through three descriptors, suggested by the Independent Medical Expert Group (IMEG\textsuperscript{27}).

Since January 2011, the IMEG descriptors and payment tariffs are (in an ascending order of compensation; (5), p. 25):

- **Item 65 Level 14** - Non-freezing cold injury which has caused, or is expected to cause, neuropathic pain and significant functional limitation or restriction at 6 weeks with substantial recovery beyond that date.
- **Item 55 Level 13** - Non-freezing cold injury which has caused or is expected to cause neuropathic pain and significant functional limitation or restriction at 26 weeks, with substantial recovery beyond that date.
- **Item 27 Level 10** - Non-freezing cold injury with persistent local neuropathic pain and severe compromise of mobility or dexterity, and evidence of permanent damage to small nerves on thermal threshold testing.

\textsuperscript{25} The Ministry of Defence publishes national statistics on a range of defence related topics. UK Defence Statistics is the annual statistics compendium of the Ministry of Defence.

\textsuperscript{26} A civil damages claim in negligence can be paid in addition to the AFCS claim. This claim provides financial support based on calculating the loss incurred by the injury on future earning potential and living costs. A civil damages claim often exceeds awards made under the AFCS.

\textsuperscript{27} IMEG is a non-departmental public body that advises the MOD on the Armed Forces Compensation Scheme (AFCS).
These are evolving in order to increase identification of the condition.

- Compensation under the AFCS

Since the beginning of the scheme in April 2005, a total of 1,910 awards have been given, with 118 over the last year (2016/2017). Between 2005 and 2010, only 134 individuals received a compensation for NFCI. The number of compensations due to NFCI dramatically increased to 355 in 2011/2012 from the previous year when only 165 were awarded (45).

10.2 Caution when interpreting the numbers

Importantly, the reported information above should be interpreted with caution as the seen increase in claims and costs, associated with NFCI is most likely due to other reasons, rather than an actual increase in NFCI cases. Some possible reasons are:

a) As the AFCS was only introduced in 2005, the number of claims was fairly low in the first 4-year period, taking off in 2011 when presumably there was more awareness about the scheme.

b) As noted above, the IMEG revised the AFCS descriptors in 2011 which resulted in changes in the eligibility criteria.

c) In 2013 the MoD made the residency requirements for Commonwealth recruits who wished to join the UK Armed Forces more stringent (14). This in turn reduced the number of Commonwealth citizens joining the Army and therefore possibly the compensation claims for NFCI (See Section 3).

11. Recommendations for Research

As stated previously, most of what is known about the condition has been derived from experience and limited research literature. There should be certain areas research concentrates on in order to effectively progress with diagnosing and treating NFCI. Below follows a list of some of these key research areas, particularly from a military perspective (1):

<table>
<thead>
<tr>
<th>Research Areas</th>
<th>Proposed Research Study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence</td>
<td>Assessment of the prevalence of NFCI in military and matched civilian controls.</td>
</tr>
</tbody>
</table>
Assessment of the prevalence of current symptoms suggestive of past NFCI.

Longitudinal studies of NFCI prevalence during training and onwards.

Pathogenesis

Large cohort study of the vascular response to cooling.

Large cohort study of peripheral vascular response to cooling in normal individuals.

Diagnostic Tools

Identification of markers for small fibre damage in skin biopsies.

Validation of thermographic testing.

Pharmacological Advances

Investigation of possible preventative and therapeutic pharmacological approaches, including neuropathic pain treatment.*

Trials of pharmacotherapy, such as a comparison of analgesics.

*Iloprost warrants further investigation into its pharmacotherapeutic uses for NFCI (Section 9.4) (33)

12. Conclusion

NFCI is a Cold Injury Disorder defined by local cooling of tissues at a temperature range from just above freezing to 20°C, characterised by four stages of symptom development. The disorder, however, varies widely in its presentation, severity, chronic sequelae and time course. Despite its pathogenesis not being well-understood, case reports and animal models data suggest that NFCI occurs due to either a vascular or nerve fibre damage or the interaction between the two. Furthermore, its most common potential long-term consequences are cold allodynia, cold hypersensitivity, hyperhidrosis and chronic neuropathic pain, which have all been associated with a reduction in one’s quality of life in terms of the suffer’s employment opportunities, family function, mental and physical health. Additionally, none of the currently used diagnostic tests can accurately identify the presence of NFCI or its severity, making compensation claim settlements for the disorder particularly challenging. Due to the uncertainty surrounding NFCI, unsurprisingly, no best practice guideline is available to inform the treatment and management of the condition. Future research should focus, in particular, on further investigating the prevalence, pathogenesis, diagnostic tools and medication of NFCI.
References


14. Ministry of Defence. The government has announced that UK residency rules for new Armed Forces recruits have been reviewed. [Internet]. [cited 2017


Appendix 1

Clinical Care pathway for the management of NFCI, recommended by (17).

**Tier 1A - NFCI field care.**

(1) **Management.** If NFCI is suspected, you should:

(a) Remove the patient from the risk environment. Shelter the patient and dry affected feet and/or hands replacing wet socks or gloves as needed. Provide supplementary whole-body insulation.
(b) Intake of fluids may help peripheral perfusion where dehydration is a contributory factor to its impairment. ‘Sweet fluids’, by increasing calorie intake, may help improve perfusion and ability to generate heat though exercise or shivering where this is a factor.
(c) In contrast to patients with FCI, those with NFCI should always have their affected parts re-warmed **slowly**, by exposure to warm air alone, and **should not be immersed in water**. If necessary, only use paracetamol and/or ibuprofen for pain control. If there is any visible evidence of tissue damage, protocols for FCI should be followed.
(d) Alert the Chain of Command that there has been a cold injury during the activity - others may also be at risk.
(e) Evacuate the patient to safety immediately. Do not allow them to return to the cold environment even if they appear to have recovered.
(f) Arrange a routine appointment with a MO, preferably one with experience in managing NFCI. If the patient has significant skin changes, cannot walk or their pain is not controlled by paracetamol and/or ibuprofen alone an urgent appointment is required.

(2) **Recording.** You should record the episode on the DMICP NFCI template:

**Tier 1B - NFCI primary care.**

(1) **Management.**

(a) Manage pain.
(b) Advise the patient to use warm foot/hand spas (30 min / 40°C / twice daily), if appropriate.
(c) Advise the patient on appropriate use of clothing and footwear.
(d) Authorise issue of extreme cold weather (ECW) hat and mittens.
(e) Advise smokers on benefits of cessation.
(f) Request bloods: FBC, U&Es, LFTs, random glucose, HbA1c, B12, folate, thyroid screen, auto-antibody screen and (if appropriate) haemoglobinopathy screen.
(g) Advise on appropriate occupational restrictions and consider amending JMES in accordance with JSP 950 Part 1 Leaflet 6-7-7 Joint Manual of Medical Fitness
Section 5 Annex N Other Conditions. Issue the NFCI specific PAP10 App 9 (Army only) in accordance with clinical progression.

(h) Prompt the Chain of Command to complete a single Service incident form (patient consent required).

(i) Where there is not recovery within one week refer the patient to the DPHC NFCI Clinics (including INM CIC as tier 2), using a DMICP e-referral. Existing photographic records should be sent separately to the latter. Suspicion of compromised tissue viability should be discussed with the DPHC NFCI Clinic and local surgical services as a matter of urgency.

(j) Thereafter, review as clinically indicated and await DPHC NFCI Clinic appointment.

(k) At any time, consider referring the patient into the Defence Medical Rehabilitation Programme.

(2) Recording. The episode should be recorded on DMICP.

**Tier 2 - DPHC NFCI or INM CI clinic.**

(1) Management. If NFCI is suspected:

(a) You should make a working diagnosis of NFCI.

(b) You should make recommendation to award the appropriate JMES, if not already done (to be discussed with ROHT).

(c) Patients should be issued with a NFCI Patient Information Leaflet.

(d) After establishing a baseline of any cold damage/sensitisation, patients should be followed up as appropriate (at 6-12 weeks, 26 weeks and 1 year post-injury) to assess the progress of recovery, provide advice on likely long-term residual sequelae and inform future employability limitations. If the patient is seen more than one year following the index injury then only one attendance may be needed.

(e) Arrange for referral to a Specialist if needed.

(f) Consider referring the patient into the Defence Medical Rehabilitation Programme.

(2) Recording. The episode should be recorded on DMICP.

**Tier 3 - specialist referral.**

Cases with mild to moderate signs and symptoms of NFCI may be managed locally by suitably experienced medical staff utilising the ROHT or nominated DPHC Regional Lead for advice. More severe cases, or those in which symptoms are persistent, should be referred for tertiary assessment and care as appropriate, including: DMRC Headley Court for pain management; the NHS for specialist neurological assessment; or to the Cold Injury Clinic (CIC), INM. Referrals to these clinics should be arranged by DPHC NFCI or INM CI Clinics only and in accordance with DPHC Guidance Note No. 10/17.

(1) Clinical assessment against the criteria below will indicate which patients need onward referral where sequelae are persistent or problematic to treat, or where there remain questions over employment limitations:
(a) Persistent numbness or neuropathic pain, particularly overnight or other symptoms of persistent sensory loss especially temperature sensation. Sensory loss is sometimes indicated by a change of gait or evidence of a functional limitation or restriction.

(b) Evidence of tissue damage, such as skin discolouration changes and trophic changes to nail-beds.

(c) A newly acquired cold sensitivity, i.e. increased sensation of cold on exposure to a cold environment.

The above criteria are not exhaustive and further advice can be provided by INM or DPHC Leads.

(2) **Cold Injury Clinic, INM.** Those patients referred to the CIC will undertake a standardised prognostic test battery, including a neurological examination and assessment, thermal sensory thresholds and cold sensitivity to help inform the patient’s future medical employability.
Appendix 2

The following information has been taken from Sections 4.5 and 4.6 of JSP-539 (17).

5. Maintaining peripheral perfusion. Preventive measures to ensure local tissue perfusion include:

a. Maintaining adequate core temperature and body hydration.
b. Minimising effects of known diseases or medications and drugs that may decrease perfusion.
c. Covering all skin and the scalp to avoid vasoconstriction where practicable.
d. Minimising restriction in blood flow, such as constrictive clothing, footwear, or immobility.
e. Ensuring adequate nutrition.
f. Using supplemental oxygen in hypoxic conditions (eg >4000 m).

6. Protection from cold. Measures should be taken to minimise exposure to cold. These measures include the following:

a. Avoiding environmental conditions with a risk of cold injury, specifically below –5°C even with low wind speeds.
b. Protecting skin from moisture, wind, and cold.
c. Avoiding perspiration or wet extremities.
d. Increasing insulation and skin protection by layering clothes appropriately.
e. Ensuring personnel are able to take the appropriate behavioural response to changing environmental conditions (eg, not being under the influence of drugs or alcohol or suffering extreme hypoxemia).
f. Using chemical hand and foot warmers and electric foot warmers to maintain peripheral warmth (note: warmers should be close to body temperature before being activated, and should not be placed directly against the skin nor constrict flow if used within a boot).
g. Performing “cold checks” if an individual experiences extremity numbness or pain or is concerned that FCI may be developing.

h. Recognising frostnip or superficial frostbite before it becomes more serious.

i. Minimising duration of cold exposure.

The time that a digit or extremity can remain numb before developing FCI is unknown; thus, paresthesia should be addressed as soon as possible. An extremity at risk for frostbite (eg, numb, poor dexterity, pale colour) should be warmed with adjacent body heat from the person or a companion, in the axilla, or on the abdomen.