**Trench Foot (Immersion Foot)**

**Pathophysiology**

Continuous exposure to a cold, wet environment causes skin breakdown, directly cools nerves in the area of exposure, and causes prolonged vasoconstriction. NFCI is primarily caused by prolonged vasoconstriction, which in turn causes direct injury to the vessels (and endothelium) that supply blood to nerves, fat, and muscle cells. Pain, fear, constrictive footwear, and immobility interact in maintaining vasoconstriction through a heightened sympathetic nervous system response or by mechanically limiting blood flow (Figure 7-1). Nerve cooling has been suggested as a contributing factor in the development of NFCI. Large myelinated fibers (C fibers) are most susceptible to prolonged cold exposure. In severe nonfreezing cold injury, there is characteristic peripheral nerve damage and tissue necrosis. Clinical sensory tests indicate damage to both large- and small-diameter nerves. The prolonged cold injury affects blood vessels serving these large myelinated fibers, with subsequent ischemia causing decreased oxygen to the nerve, resulting in the appearance of a primary nervous system injury (Figures 7-2 to 7-5).

![Figure 7-1 Schematic of factors and mechanisms that contribute to nonfreezing cold injuries.](image-url)
FIGURE 7-2  Laser Doppler mean nerve blood flow (NBF) in control and experimental animals at 10-minute intervals during nerve cooling and rewarming (up to 250 minutes) and at follow-up examination immediately before sacrifice (at various times up to 5 days). Note that the nerve blood flow falls steeply over 20 minutes and reaches its nadir (25% of baseline) 180 minutes after the onset of cooling. Nerve blood flow remains significantly reduced up to 5 days after cold injury. (Modified from Jia J, Pollock M: The pathogenesis of non-freezing cold nerve injury: Observations in the rat, Brain 120:631, 1997.)

FIGURE 7-3  Sciatic nerve epineurial microvessels before, during, and following nerve cooling (1° to 5° C [33.8° to 41° F]). A, Normothermia. Arteriole (A), venule (V), and metarterioles (M) have a normal appearance. B, One hour after the commencement of nerve cooling the diameter of both the arteriole and venule are reduced by approximately 40%. Under a dissecting microscope, erythrocytes present a granular appearance in both vessels (arrows). Note occlusive aggregations (open arrow) in metarteriole and the suggestion of leukocyte clumping in the venule (arrow head). C, Two hours after nerve cooling, segmental occlusive aggregates are seen in the venule (arrows). The arterioles contain prominent rouleaux (open arrows). D, Three hours after nerve cooling, there is stasis of flow in both vessels. An occlusive aggregate (arrow) is now seen in the arteriole, and those in the venule have extended (open arrows). E, After 1 hour of nerve rewarming (37.5° C [99.5° F]), the venule still exhibits multiple segmental occlusions (arrows). Erythrocyte granulations (open arrows) in the arteriole indicate poor reperfusion. Bars represent 100 mm. (From Jia J, Pollock M: The pathogenesis of non-freezing cold nerve injury: Observations in the rat, Brain 120:631, 1997.)
FIGURE 7-4  Electron micrographs of endoneurial vessels in cooled sciatic nerve. A, An empty capillary with a degenerating pericyte 1 hour after nerve rewarming. Bar represents 2 µm. B, Aggregating platelets (arrows) 24 hours after cooling. Bar represents 2 µm. C, Platelets, adherent to the endothelium of a venule, show varying degrees of degranulation without pseudopod formation, 48 hours after nerve cooling. Two red blood cells are trapped within this platelet thrombus. Bar represents 1 µm. D, A thrombus formed of platelets, red blood cells, and fibrin 5 days after nerve cooling. The blood vessel wall is necrotic. Bar represents 2 µm. (From Jia J, Pollock M: The pathogenesis of non-freezing cold nerve injury: Observations in the rat, Brain 120:631, 1997.)
FIGURE 7-5  Electron micrographs of cooled sciatic nerve fibers. A, A rat sciatic nerve fiber, 12 hours after nerve cooling, illustrating myelin unraveling and intramyelinic edema (arrow). B, A rat sciatic nerve fiber 2 days after cooling, exhibiting a shrunken axon and marked periaxonal edema. Bars represent 1 µm. (From Jia J, Pollock M: The pathogenesis of non-freezing cold nerve injury: Observations in the rat, Brain 120:631, 1997.)

Vasoconstriction is mediated by presynaptic vesicle release of norepinephrine and neuropeptide Y from sympathetic nerve fibers that interact postsynaptically on smooth muscle at α<sub>2</sub>C<sup>6.18</sup> and Y1<sup>95</sup> receptors. Recent work<sup>100</sup> demonstrated that cold-induced vasoconstriction is mediated by Rho kinase. The prolonged decrease in blood flow caused by vasoconstriction causes direct injury to capillary endothelium. Studies indicate that the endothelial lining separates from underlying cells, leaving “gaps.”<sup>31</sup> Leukocytes and platelets fill in these gaps and accumulate to further decrease capillary blood flow, leading to ischemia and eventual tissue hypoxia (Figure 7-6, online). The degree and duration of cold exposure determine severity of the injury.

FIGURE 7-6  Proposed hypothesis for the etiology of non-freezing cold injuries. α<sub>2</sub>, Norepinephrine (NE) α-adrenergic receptor; Ca<sup>2+</sup>, calcium; DAG, diacylglycerol; IP<sub>3</sub>, inositol triphosphate; Y1, neuropeptide Y (NPY) receptor.

Animal models have been developed to understand the underlying pathophysiology of NFCI. Thomas and co-workers<sup>99</sup> developed a rat model of NFCI by immersing the tail in 1° C (33.8° F) water for 6 to 9 hours and characterized the loss of CIVD and a prolonged decrease in tail blood flow followed by an increase in blood flow above baseline. This pattern is similar to that clinically observed in humans during the prehyperemic phase followed by the hyperemic phase. In rats, absence of CIVD with prolonged cold exposure is similar to this prominent and consistent finding of NFCI in humans.

Stephens and associates<sup>95</sup> used the rat tail model in an attempt to elucidate possible mechanisms that cause vascular endothelial damage. Their preliminary data suggest that acute cold-water exposure causes loss of nitric oxide–dependent
endothelial function and possibly a change in smooth muscle contractility. Using a rabbit hind limb model, Irwin \[53\] demonstrated that cold-water immersion damaged large myelinated fibers while sparing small myelinated and unmyelinated fibers.

Nonfreezing cold injuries affect many different types of tissue. Pathologic examination of specimens displays a variety of lesions in skin, muscle, nerves, and bone. \[8,9,38\] Muscles exhibit separation of cells and damage to muscle fibers, described as acidophilic and hyalinized (Zenker's hyaline degeneration). The myoplasm within muscle loses its cross striation, and the healing muscle appears to undergo fibrous tissue replacement.

One of the major pathologic processes in cold injury is progressive microvascular thrombosis following reperfusion of the ischemic limb, with cold-damaged endothelial cells playing a central role in the outcome of these cold-injured tissues. \[71\] Reperfusion of previously ischemic tissues causes free radical formation, leading to further endothelial damage and subsequent edema. With restoration of blood flow, there is reintroduction of oxygen species within cells that further damages cellular proteins, DNA, and the plasma membrane. Free radical species may also act indirectly in redox signaling to initiate apoptosis. Leukocytes may accumulate in small capillaries, obstructing them and leading to more ischemia. \[59\]

In an in vivo rabbit hind limb model subjected to 16 hours of cold immersion (1° to 2° C [33.8° to 35.6° F]), there was reduction in the number of myelinated nerve fibers of all sizes, most marked in large-diameter fibers, a feature consistent with ischemic neuropathy and reperfusion injury. \[54\] Unmyelinated fibers showed only minor damage. The resulting evidence has suggested that both of these mechanisms may contribute to the nerve injury. There is further extensive supporting evidence that established NFCI is associated with histologic and/or clinical evidence of nerve damage. \[27,30,59,76\]

Das and colleagues \[25\] demonstrated that quinacrine, an antioxidant, decreased damage to cell membrane phospholipids upon rewarming and reperfusion, although more recent studies \[97\] have shown no benefit from antioxidant use. Most importantly, both these studies used models that assumed that cold-induced nerve injury, rather than capillary or endothelial damage, is the primary cause of NFCI.

**Clinical Presentation**

Trench foot and immersion foot are clinically and pathologically indistinguishable but have different etiologies. The term trench foot originated during the trench warfare of World War I, \[110\] when soldiers wore wet boots and socks for prolonged periods. \[5\] Immersion foot was first medically documented during World War II among shipwreck survivors whose feet had been continuously immersed in cold water. \[21\] Both injuries occur when tissue is exposed to cold and wet conditions at temperatures ranging from 0° to 15° C (32° to 59° F). Colder temperatures decrease the time required to induce NFCI. \[10,92\] Severe nerve damage from immersion foot has been seen after exposure periods of 14 to 22 hours. \[103,104\] Immersion foot injury may extend proximally and involve the knees, thighs, and buttocks, depending on the depth of immersion. \[111\] Clinically, NFCI is insidious in onset, with progression from initial exposure through three distinctive phases (prehyperemic, hyperemic, posthyperemic). These phases have variable time courses and may overlap.

**Prehyperemic Phase**

During the prehyperemic phase, the affected limb, both during and immediately after cold exposure, appears blanched, yellowish white, or mottled but seldom blistered (Figure 7-7). \[104\] Whayne and DeBakey \[110\] state that the degree of edema during this prehyperemic stage is less severe if the feet are intermittently rewarmed during the course of exposure. Whereas muscle cramps are common, pain is rare. \[43,92\] The single most important diagnostic criterion is loss of a sensory modality, most typically complete local anesthesia, which is distinct from premonitory feelings of extreme cold in the affected periphery, almost invariably in the feet although hands can also be affected. With further exposure, the cold sensation leads to complete anesthesia with loss of proprioception, resulting in numbness and gait disturbances. This sensation has been described as “walking on air” or “walking on cotton wool.” \[104\] Capillary refill is sluggish, and pedal arterial pulses are usually absent, except through Doppler examination. \[70\] Intense vasoconstriction is the predominant feature of this stage. \[46\]
Hyperemic Phase

Within several hours after rewarming, the extremities become hot, erythematous, painful, and swollen (Figures 7-8 to 7-11; Figure 7-9, online), with full bounding pulses. [109] Impairment of the microcirculation is evident through delayed capillary refill [98] (Figure 7-12, online) and petechial hemorrhages. [45] Sensation returns first to proximal regions and then extends distally, rapidly progressing to a severe, burning, or throbbing pain and reaching maximal intensity in 24 to 36 hours. [103,104] Affected areas have marked hyperalgesia to light touch. This pain is aggravated by heat and dependent positioning and often worsens at night, when even the pressure of sheets may become unbearable. [46] After 7 to 10 days, the nature of the pain changes to “shooting or stabbing.” [103] The sensory deficits usually diminish, but paresthesias continue, and anesthesia may be extensive on the toes and plantar foot surfaces. [111] Vibratory sensation is reduced or lost, whereas proprioception is usually retained. Anhidrosis coincides with the extent of sensory loss. [98]
FIGURE 7-10 Hyperemic phase of immersion foot. The characteristic redness of the stage is absent because of the pigmented skin, but the feet are swollen and painful. (British Crown Copyright/MOD.)

FIGURE 7-11 Hyperemic phase in moderately severe nonfreezing cold injury. Swollen, red, and persistent pain in the feet of an infantry soldier from the Falklands War. (British Crown Copyright/MOD.)
Vascular injury is evident in vessel reactivity. Skin temperature gradients are absent, with digits often as warm or warmer than the groin or axillae. When the affected limbs are lowered, blood pools, turning the extremity a deep purple-red color, whereas blanching occurs when the limb is raised. Tense edema becomes marked during this stage. Blisters containing serous or hemorrhagic fluid may form, indicating more severe injury. The superficial epidermis becomes thick, indurated, and desquamated. Eschars form (Figures 7-13 and 7-14) and eventually slough, leaving a pink dermis (Figure 7-15). In more severe cases, the skin may become gangrenous (Figure 7-16). This is rare, and with appropriate care, gangrene is usually minimal. [1,109,110]
FIGURE 7-13  Severe nonfreezing cold injury. This Argentinian soldier had been unable to care for his feet for many weeks. (British Crown Copyright/MOD.)

FIGURE 7-14  Severe nonfreezing cold injury in an Argentinian mine layer who wore his boots for 47 straight days during the Falklands War. (Courtesy M.P. Hamlet.)
Muscles may show weakness with impaired electrical responses, slowing of plantar deep tendon reflexes, and intrinsic muscle atrophy.\cite{103,104} In milder cases, this stage peaks at 24 hours; in more severe cases, the hyperemic phase may take 6 to 10 weeks to resolve.\cite{98}

**Posthyperemic Phase**

The posthyperemic phase lacks obvious physical signs. In mild cases, this phase may be absent \cite{104}; in other cases, it may last weeks, months, or years after the hyperemic phase has subsided.\cite{70,103} The extremities transition from a consistent warmth to noted coolness, with affected areas becoming cold sensitive, remaining so for hours after exposure despite normal warming processes.

After 6 to 10 weeks, patients often complain of spontaneous hyperhidrosis, and sweat rashes are common in areas with heavy perspiration.\cite{103} On a warm day, socks are quickly soaked; extremities may sweat excessively, even when cold. Hyperhidrosis predisposes to chronic paronychial infections. Sweating may be more pronounced at the margins of anhidrotic and analgesic areas.\cite{104}

During the posthyperemic phase, the paresthesias and extreme pains typical of the hyperemic phase have usually resolved, replaced by dull aches and anesthesia that may persist for months to years.\cite{110} Recurrent edema of the feet, return of
paresthesia, and further blistering are common, especially after long walks. Intrinsic muscle and ligament atrophy tend to resolve,[104] but in severe cases, fibrous scarring may lead to rigidity and permanent contracture of the toes.[111] Decalcification of bones similar to that seen with osteoporosis is frequently observed.[102] Immobility and pain in severe cases may lead to prolonged convalescence of 6 or more months.[111]

In the most severe cases, gangrene can develop, and ablative surgery in the form of amputations of digits or even major lower limb amputation becomes necessary. Neuropathic tissue is susceptible to local trauma, ulceration, and eventually local osteomyelitis and sinus development (Figures 7-17 to 7-19). Appearance and behavior of the neuropathic foot have many similarities to those of the diabetic foot. In the diabetic foot, infections tend to be polymicrobial with *Staphylococcus aureus*, *Staphylococcus epidermidis*, and *Enterococcus* and *Streptococcus* species being most commonly isolated from bone culture. However, aerobic gram-negative rods (such as *Pseudomonas aeruginosa*) and obligate anaerobic species may be found.[52] Partial foot amputations may result in significant alterations in functional biomechanics of the foot. Because this is often associated with alterations in the sensory nerve supply to the feet, ongoing disabling problems can persist (Figure 7-20).[52]

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**FIGURE 7-17** Patient 24 months after nonfreezing cold injury. Amputation of third, fourth, and fifth toes on the left foot. (*Courtesy Christopher H.E. Imray, MD.*)

**FIGURE 7-18** Same patient as in Figure 7-17, 24 months after nonfreezing cold injury with chronic discharging sinuses from osteomyelitis of the first metatarsal. (*Courtesy Christopher H.E. Imray, MD.*)
FIGURE 7-19  Magnetic resonance imaging scan of the patient in Figures 7-17 and 7-18, 24 months after nonfreezing cold injury with chronic discharging sinuses from osteomyelitis of the first metatarsal head. (Courtesy Christopher H.E. Imray, MD.)

FIGURE 7-20  A guillotine transmetatarsal amputation of the left foot was undertaken 6 months after severe nonfreezing cold injury. The patient was treated with delayed primary split-skin grafting. This photograph was taken 12 months after the original injury and shows that the split-skin graft has taken, but is now ulcerated as a result of the shear forces generated by walking on the insensate tissue. A, Transverse view
More Severe Injuries

NFCl can vary in severity from mild to severe. In severe cases, cold sensitization is so serious that individuals are unable to work outside. There is often persisting edema and hyperhidrosis, making the individual susceptible to fungal infections. Chronic pain may resemble causalgia or reflex sympathetic dystrophy. The profound sensory neuropathic foot can develop ulcerations and tissue loss, ultimately resulting in either minor or major lower limb amputation. Ongoing care with a foot specialist who can arrange for custom-made shoes and insoles appears to improve functional outcome. Multidisciplinary team approaches to coordinating care leading to healing of the ulcerated neuropathic foot using patella weight-bearing orthoses has been described. NFCI pain is often so severe as to require tricyclic antidepressants, which may need to be instituted at an early stage. Failure to do so increases the risk for developing severe chronic pain resistant to all subsequent treatment modalities. Early involvement of pain specialists is important. It is essential to control pain following NFCI at the earliest opportunity.

Treatment

Hypothermia

The treatment required for the general effects of cold is different from that needed for localized NFCI. Core temperature must be raised while the extremities are kept cool. Injured feet should be elevated and exposed to steady cool air from a fan. Extremity cooling lowers metabolic requirements to a point where vascular oxygen supply can sustain tissue demand. Continuous cooling brings rapid improvement in pain, edema, and vesiculation. Local cooling should be continued until pain is relieved, circulation has recovered, and hyperemia subsides. The affected extremities should never be rubbed, which may compound the injury.

Rewarming

Treatment is limited to symptomatic relief and reversing ischemia while minimizing progression of disease. Rewarming injured tissues increases metabolic demand of damaged cutaneous cells to a greater extent than can be provided by the supply capability of the injured subcutaneous blood vessels. Tissue anoxia and endothelial cell injury, coupled with reflex vasodilation, lead to fluid transudation, increasing edema, skin necrosis, and worsening pain.

Sympathectomy

Recovery during the posthyperemic phase may be hastened with physiotherapy and exercise to rehabilitate atrophied intrinsic muscles. Lumbar sympathectomy has been theorized to reduce disabling contracture by decreasing vascular tone, increasing circulation, and hastening collagen and fibrous tissue absorption. In severe cases of NFCI exhibiting atrophic rigid feet, small case studies have shown symptomatic improvement after sympathectomy, but other clinicians feel that there is little therapeutic advantage to the procedure.

Tissue-Freezing Complications

Frostbite and NFCI injuries do not necessarily occur in isolation, so when assessing an individual, both diagnoses need to be entertained. Following exposure to severe cold, careful appraisal of the injury allows selection of optimal treatment.

Drugs

Diagnosis of NFCI is often difficult or delayed. In view of involvement of the α-receptors in the control of peripheral circulation and the apparent noradrenergic sensitization, it was believed that vasodilators or α-blocking drugs might be beneficial. However, there is no evidence to support this approach.

Because painful rewarming and persistent pain are features of NFCI, it is important to attempt to alleviate pain at an early stage. Although simple analgesics may be of benefit, Thomas and Oakley observed that quinine sulfate (200 to 400 mg, given at night) appeared more successful than regular analgesics, although others have since commented that they are not useful. Since 1982, the standard treatment in the armed forces of the United Kingdom, first proposed by Riddell, has been amitriptyline hydrochloride, in doses of 50 to 100 mg given at night. Incremental increases in dosage may be required with both drugs if pain breaks through after initial relief.

Assessing the Severity of Nonfreezing Cold-Induced Injury

Following the initial injury, there develops increased sensitivity to cold. There are often few objective clinical signs of a
nonfreezing cold injury. A careful history of cold exposure, clear history of the typical rewarming symptoms and signs, detailed examination, and special investigations combine to build a case consistent with NFCI. Corroborative evidence of an appropriate cold exposure and symptoms consistent with NFCI from medical records is vital.

Special Investigations

Infrared thermography can be used to assess the individual's response to a standardized cold stress and may be helpful in confirming the diagnosis, assessing the severity of injury, and monitoring recovery from NFCI (Figure 7-21). Although the infrared thermography test is used extensively by the UK military, it is not widely used elsewhere. There appears to be significant intraindividual variability in the responses of some individuals to the current infrared thermography test. As a result, interest is shown in the use of gentle exercise before the infrared thermography cold sensitivity test and also in the use of laser Doppler flowmetry to try to improve the assessment used to classify nonfreezing cold injury. Careful experimental design to validate any potential new tests against suitable controls, both preexposure and postexposure, will be required.

**FIGURE 7-21** Infrared thermography in the assessment of the consequences of nonfreezing cold injury. The upper sequence of three images was taken from an uninjured, asymptomatic control; the lower sequence from a patient who had sustained nonfreezing cold injury and subsequently complained of sensitivity. In both the control and patient, the first (left) image was taken after resting in ambient air temperature of 30°C (86°F). The second (center) image was taken immediately after the foot had been immersed in water at 15°C (59°F) for 2 minutes. The final (right) image was taken 5 minutes after removal from the water, again in 30°C (86°F) air. The upper series shows feet that were warm at rest, which rewarmed briskly after mild cold stress, and recovered almost completely within 5 minutes after removal from the water. The lower series shows a severe degree of cold sensitization; the feet were much colder than the surrounding air at rest, and once cooled, took a long time to rewarmed, remaining much cooler than the control foot at 5 minutes after immersion. The scale at far right indicates the color-temperature relationship. (Copyright British Crown Copyright/MOD. Reproduced with the permission of Her Britannic Majesty's Stationery Office. From Thomas JR, Oakley HN: Nonfreezing cold injury. In Pandolf KB, Burr RE, editors: Textbook of military medicine: Medical aspects of harsh environments, vol 1, Washington, DC, 2002, Office of the Surgeon General, Borden Institute, pp 467-490.)

Prevention

The simplest way to prevent NFCI is to avoid prolonged exposure to cold, wet environments. This can be difficult to achieve. During military conflict, completing the assigned mission may require performing in a cold, wet environment for sustained periods of time in cramped, immobile positions. During mountain rescues, individuals may be so focused on helping to save others that they do not take adequate care to prevent NFCI.

Prevention can be achieved by encouraging activities that promote blood flow to the feet, rotating personnel out of cold, wet environments on a regular basis, keeping feet dry by early changing of wet socks, maintaining core body temperature by limiting sweat accumulation into clothing and dressing in layers, and by educating people about the early signs and symptoms of nonfreezing cold injuries. Changing socks two to three times during the day is mandatory in cold, wet environments. The military suggests that optimal care entails air drying feet for at least 8 hours out of every 24. Vapor-barrier boots do not allow sweat to evaporate, and in some situations, this increases maceration. These boots should be taken off each day, wiped to remove moisture and debris, and allowed to dry. Footwear should not constrict blood flow; sizing is important as is educating the user not to tie his or her shoelaces too tightly.
Prophylactic treatment with topical skin silicone preparations (antiperspirants) has proved effective. [40] The effect is believed to be caused by prevention of hyperhydration of the stratum corneum. [14,28] However, stickiness, adherence of sand and grit to the foot, and product bulkiness make this technique marginally acceptable to infantry soldiers in combat situations. [40] In small clinical trials, silicone ointment applied only to the sole of the foot instead of to the entire foot (thus reducing surface area exposed to dirt retention, amount of material transported by the soldier, and expense) was sufficient to prevent NFCI. [28]

As a consequence of the apparent increasing incidence of NFCI in the British military, preventive steps are being taken. These include improved education of recruits and existing personnel about prevention measures and equipment and early recognition. Well-designed equipment, supplied to appropriate personnel, and used in a timely and appropriate way should reduce the incidence of injury.

The severity of current UK military NFCI events appears to be relatively mild in comparison with civilian NFCI injuries (see Figures 7-17 to 7-19) and military historical controls (see Figures 7-13 to 7-16). This raises the question of whether (1) there is a continuous spectrum of disease, (2) there is a bimodal distribution of the disease with milder and more severe forms of NFCI, or (3) the commonly presenting form is the same disease process that has been investigated in the past. Perhaps the lack of clarity lies in the UK military's decision to use infrared thermography as one of the bases for diagnosis, severity, and progression of NFCI. There appears to be a lack of published control data on subjects’ prior response to cold exposure, so that the test cannot be compared with the normal variability in the population.

One approach would be to screen potential recruits. This requires a test with high sensitivity and specificity. However, individual variation in the control of peripheral blood flow is so great that no assessment currently available meets these requirements. [12,22,24,98]

Reducing the incidence of cold injury in military training requires striking a delicate balance between training, realism, and safety. Training in demanding environments runs real risks of injuring personnel, but the benefits to soldiers in their necessary field skills are vital if they are to avoid future NFCI. [98]

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