Wolters Kluwer

Frostbite: Emergency care and prevention

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Introduction

Frostbite results from the freezing of tissue. It is a disease of morbidity, not mortality. It is most frequently encountered in mountaineers and other cold weather enthusiasts, soldiers, those who work in the cold, the homeless, and individuals stranded outdoors in the winter [1-4]. Among patients with severe frostbite, timely diagnosis and treatment is essential to maximize tissue salvage.

This topic review will discuss the classification, presentation, diagnosis, and management of frostbite. Severe hypothermia, high altitude illness, and other related illnesses are discussed separately.

- (See "Accidental hypothermia in adults".)
- (See "High-altitude illness: Physiology, risk factors, and general prevention".)
- (See "Acute mountain sickness and high-altitude cerebral edema".)
- (See "High-altitude pulmonary edema".)
- (See "High-altitude disease: Unique pediatric considerations".)

Definitions

Frostbite is a severe, localized cold-induced injury due to freezing of tissue. Immersion foot (also referred to as trench foot) is a nonfreezing cold injury (NFCI) that may also cause tissue

loss and long-term sequelae. Milder forms of injury include frostnip and pernio:

- Frostnip refers to cold-induced, localized paresthesias that resolve with rewarming. There is no permanent tissue damage.

- Pernio, or chilblains, is characterized by localized inflammatory lesions that can result from acute or repetitive exposure to damp cold above the freezing point. Lesions are edematous, often reddish or purple, and may be very painful or pruritic (picture 1). Pernio is most common in young women, but both sexes and all age ranges may be affected [5]. Permanent damage from pernio is uncommon, with symptoms and signs generally resolving within two to three weeks.

- Immersion foot (or trench foot) involves injury to the sympathetic nerves and vasculature of the feet. It was first described in 1914 during World War I trench warfare. It results from prolonged exposure of the feet to a combination of dampness and cold. Tight-fitting boots exacerbate the condition. Feet and occasionally hands are red, edematous, can be numb or extremely painful, and, in severe cases, can be covered with hemorrhagic bullae (picture 2). Tissue loss can occur. (See "Nonfreezing cold water (trench foot) and warm water immersion injuries".)

  Improved foot hygiene including better boot design and frequent sock changes resulted in a much lower prevalence among soldiers by 1917. Not just of historical significance, immersion foot was a major medical issue during the Falklands War of 1982 and still occurs, especially among the homeless [6,7].

Pathophysiology

The tissue destruction of frostbite is due to both immediate cold-induced cell death and the more gradual development of reperfusion-related localized inflammatory processes and tissue ischemia. Following exposure to subfreezing temperatures, ice crystals form extracellularly. If freezing is rapid, ice crystals may also form inside cells. Fluid and electrolyte fluxes cause lysis of cell membranes with subsequent cell death. An inflammatory process ensues mediated by thromboxane A2, prostaglandin F2-alpha, bradykinins, and histamine. This leads to tissue ischemia and necrosis. The initial cellular damage and the subsequent inflammatory processes are made worse in the setting of thawing followed by refreezing of the affected area [3,8].

Classification

A number of systems to classify frostbite have been developed based on initial clinical presentation, findings on scintigraphy with technetium-99m pertechnetate, and outcome [3,9-11].

One classification scheme categorizes frostbite injuries as superficial or deep. As described below, superficial frostbite corresponds to first and second-degree injury, while deep frostbite corresponds to third and fourth-degree injury [12,13].

A more useful clinical prediction tool has been developed for frostbite of the hands and feet, based on the level at which skin lesions are noted after rapid rewarming in warm water. The categories are as follow (table 1):

- Grade 1 frostbite is characterized by no cyanosis on the extremity (picture 3). This predicts no amputation and no sequelae.
- Grade 2 involves cyanosis isolated to the distal phalanx (picture 4). This predicts only soft tissue amputation and fingernail or toenail sequelae.
- Grade 3 frostbite is characterized by intermediate and proximal phalangeal cyanosis (picture 5). This predicts bone amputation of the digit and functional sequelae.
- Grade 4 frostbite involves cyanosis over the carpal or tarsal bones (picture 6). This predicts bone amputation of the limb with functional sequelae [10].

The traditional classification system divides frostbite into four degrees of severity based upon the depth of tissue involvement, in similar fashion to the classification of burns:

- First-degree frostbite is very superficial and is characterized by a central area of pallor and anesthesia of the skin surrounded by edema.
- Second-degree frostbite is recognized by large blisters containing clear fluid surrounded by edema and erythema, developing within 24 hours and extending to or nearly to the tips of digits (picture 7). The blisters may form an eschar, but this later sloughs off, revealing healthy granulation tissue. There is no tissue loss.
- Third-degree frostbite differs from second-degree in that the injury is deeper and the blisters are smaller, hemorrhagic and more proximal. The skin forms a black eschar in one to several weeks (picture 8 and picture 9).

- Fourth-degree frostbite, which extends to muscle and bone, involves complete tissue necrosis. Mummification occurs in 4 to 10 days.

This traditional system gives clinicians a false sense of accuracy. It has caused many to treat frostbite injuries as if they were burns, with suboptimal results. Depending upon rewarming methods and complications, such as infection or trauma, first and second-degree frostbite can unexpectedly become third or fourth-degree.

The Hennepin Score, patterned after total body surface scoring systems for thermal burns, is used for research purposes to describe the extent of tissue involved and quantify tissue salvage rates [14]. It is not a clinical tool.

Risk factors

Frostbite generally develops within minutes to hours depending on circumstances and risk factors. Risk factors for developing frostbite and cold-induced injury include any condition that increases localized heat loss or decreases heat production. Examples include increased convective heat loss due to exposure to wind or conductive heat loss due to contact with metal, the ground, or water [15]. Exhaustion, dehydration, malnutrition, or comorbidities such as peripheral vascular disease, diabetes, or mental illness may limit an individual's ability to respond to a cold stress. Alcohol abuse predisposes to frostbite as a result of acute behavioral changes, increased heat loss from vasodilation, and chronic complications of alcohol consumption [16]. Other sedating or judgment-impairing drugs or medications pose a similar risk. Clearly, risk is greater at low ambient temperatures, when wind chill effects are increased, and at higher altitudes [4,16-20].

Additional risk factors for developing frostbite include smoking, previous cold injury, and exposure of the hands and arms to vibration, which can elicit a Raynaud phenomenon associated with white fingers in some individuals [21-23]. Data from the United States Armed Forces suggest that soldiers who are African-American, female, or younger than 20 years of age are at increased risk [24].

Use of clothing that provides inadequate insulation or coverage, or is damp, too tight, or permeable to wind, can predispose to frostbite, as can use of protective ointments, such as on the face. Studies from Norway in the 1990s showed that ointment use can enhance heat loss in some people and can provide users with a false sense of security, causing them to neglect standard safety measures [25-27]. Excessive sweating of the hands and feet increases an individual's risk of frostbite to those areas, illustrating the importance of

clothing that can wick moisture away from the skin [28].

While generally considered a disease associated with environmental exposure to cold, frostbite has also been reported following direct exposure to freezing materials. As an example, the application of ice packs to reduce swelling from musculoskeletal injuries can cause frostbite [29]. It is important to tell patients to interpose a cloth between the ice pack and their skin, and to limit treatment intervals to 20 minutes with a minute or two break between applications. Fingertip contact with a metal surface at a temp of -15°C (5°F) can lead to frostbite within a few seconds [15].

Case reports describe severe facial, upper airway, and esophageal frostbite from recreational inhalation of halogenated hydrocarbons and nitrous oxide [30]. Contact with Freon, a fluorinated hydrocarbon used as a refrigerant, has been reported to cause third and fourth-degree frostbite of the hand [31-33]. Frostbite of the foot has been described resulting from the discharge of a carbon dioxide fire extinguisher on a sprained ankle in an attempt to reduce edema [34]. Abdominal wall cryolipolysis can cause full thickness tissue loss, likely by frostbite combined with pressure necrosis [35,36].

Some researchers hypothesize that individual variation in cold-induced vasodilation (CIVD) corresponds to the risk of frostbite. The results of one observational study of the Royal Netherlands Navy during arctic training suggested that faster and greater CIVD may decrease risk [37], but subsequent studies have shown no correlation [38,39].

Epidemiology

Because there is no formal reporting system for cases of frostbite, data on incidence and prevalence are derived from selected subpopulations, generally consisting of individuals at greater than average risk [22,28,40]. Based upon such studies, the areas of the body most susceptible to frostbite appear to be the hands, feet, face (including nose and cheeks), and ears.

Clinical manifestations

Areas most frequently affected by frostbite include the ears, nose, cheeks, chin, fingers, and toes (picture 10 and picture 11). Frostbite of the cornea has been reported in individuals who keep their eyes open against very strong winds [7,41]. Patients often complain of cold, numbness, and clumsiness of the affected area [42]. Before rewarming, the

skin is insensate, white or grayish-yellow in color, and hard or waxy to touch (picture 12 and picture 13). Early signs of frostbite may be less conspicuous in patients with darker skin tones. As noted above, bullae containing clear or bloody fluid may develop after thawing (picture 7), depending on the depth of the injury. In cases of delayed presentation to medical care, eschar or other signs of tissue necrosis may be observed (picture 8 and picture 9). Any patient with cyanosis proximal to the distal phalanx of any digit after rapid rewarming is at risk for necrosis of the affected tissue and aggressive therapy (eg, thrombolysis in suitable candidates) may be needed. (See 'Hospital-based management' below.)

Diagnosis

Diagnosis is generally made on clinical grounds, based on the context of the injury, signs, and symptoms. Diagnostic studies–namely bone scanning–are helpful in determining the existence of comorbidities, the extent of frostbite injury, and prognosis. Because frostbite is a disease of morbidity, not mortality, more immediate life-threats, such as coexisting hypothermia, must be identified and addressed first. (See "Accidental hypothermia in adults".)

Imaging studies

Radiologic studies can help to determine the extent of tissue involvement, response to therapy, and long-term tissue viability [43]. The most important study for patients with signs of or at risk for tissue necrosis from frostbite is technetium (Tc)-99m scintigraphy (ie, bone scan). The appropriate role for each modality is described below:

- **Plain radiographs** are not useful initially except to screen for trauma-related fractures. Late (weeks to months) radiographic findings in frostbite include bony destruction and, in children, damage to growth plates [8]. Frostbite arthritis often spares the thumbs, most likely because patients wrap them within clenched fists during the exposure [44].

- **Standard or digital subtraction angiography** can be used to identify patients suitable for thrombolytic therapy [45-47]. Unlike technetium-99m scintigraphy, angiography does not visualize the microcirculation soon after injury, including in bone.

- **Fluorescence microangiography**, a technique that has been used to monitor wound healing, has been used to monitor progression of perfusion in frostbite [48]. A study of

104 frostbite patients, of whom 26 were evaluated with both technetium-99m scanning and microangiography, found that amputation level correlated better with microangiography than with technetium-99m scanning [49].

- **Technetium (Tc)-99m scintigraphy** (ie, bone scan) can be used to identify candidates suitable for thrombolytic therapy [50]. It is also used to predict the long-term viability of affected tissue, with the goal of allowing early debridement or amputation of dead or dying areas while preserving viable tissue [11,14,51,52]. In candidates for treatment with tissue plasminogen activator (tPA), technetium scanning is used immediately after thawing. For patients who are not candidates for tPA, technetium scanning on day 2 following injury may avoid the need for the traditional several-week delay in surgical intervention while awaiting demarcation between viable and nonviable zones. Scintigraphy has also been used to monitor response to a topical therapy protocol by demonstrating the effect of treatment on involved tissue microvasculature [9,53].

- Limited retrospective data suggest that **single-photon emission computed tomography** (SPECT), a nuclear bone scan processed similarly to a computed tomography (CT) scan, combined with conventional CT (SPECT/CT), may be able to identify non-salvageable tissue, allowing more accurate determination of the extent of tissue destruction and autoamputation than a conventional bone scan [54].

- Some researchers claim that **magnetic resonance imaging** (MRI) and magnetic resonance angiography (MRA) may be superior to bone scans in establishing tissue viability. In case reports they have permitted visualization of occluded blood vessels and better demonstrated the line of demarcation between ischemic and nonischemic tissue. However, experience with MRI and MRA in this setting is limited [8,55].

Treatment

Treatment can be divided into prehospital interventions and definitive care. The approach described below is based on animal studies, observational data, clinical experience, and relatively small number of clinical trials. Management of hypothermia is discussed separately. (See "Accidental hypothermia in adults".)

Prehospital care

- Get the patient to a warm environment as soon as possible. Whenever possible, pad or splint the affected area to minimize injury en route.

- Remove wet clothing.
- Avoid walking on frostbitten feet; this can increase tissue damage. If walking is necessary for evacuation, do not rewarm the feet before walking.
- Do not rewarm frostbitten tissue if there is a possibility of refreezing before reaching definitive care. This would result in worse tissue damage.
- If prehospital warming is attempted, options include placing the affected area in warm (not hot) water or warming it using body heat (eg, placing frostbitten fingers in the axillae).
- Do not rub frostbitten areas in an attempt to rewarm them; this can cause further tissue damage.
- Avoid the use of stoves or fires to rewarm frostbitten tissue. Such tissue may be insensate and burns can result [8,41,56].

Hospital-based management — Once the patient has reached the hospital, definitive care consists of rapid rewarming, wound care, efforts to enhance tissue viability, and prevention of complications [20,57-59]. Among patients with severe frostbite, timely diagnosis and treatment is essential to maximize limb and digit salvage [52]. Management of other, more serious conditions, such as severe hypothermia or internal hemorrhage from major trauma, takes priority over the treatment of frostbite. (See "Accidental hypothermia in adults" and "Initial management of trauma in adults".)

Rewarming — Rewarming is most effectively accomplished by immersing the affected area in water heated to 37 to 39°C (98.6 to 102.2°F), ideally in a whirlpool so a steady temperature can be maintained [60]. Gentle active motion of the extremity while rewarming may help. Care should also be taken to avoid trauma to the injured area against the container walls during treatment. Higher temperatures do not warm the injured area appreciably faster and cause the warming process to be much more painful. Dry heat is difficult to regulate and is not recommended.

Thawing is usually complete when the tissue is red or purple and soft to the touch. This usually takes 15 to 30 minutes. Rewarming of frostbitten tissue may be painful. Appropriate analgesia, generally opioids, should be administered.

Time-limited treatments for severe injury

Thrombolysis for severe injury presenting within 24 hours

Indications and general guidance — Because frostbite is associated with vascular thrombosis of affected tissue, administration of intravenous or intra-arterial tissue plasminogen activator (tPA; with intravenous or intra-arterial heparin, or subcutaneous enoxaparin) has been used for therapy [45,50,61,62]. Although high-quality evidence is limited, in patients at high risk for life-altering amputation (eg, multiple digits in a limb, multiple limbs, proximal limb amputation), **without contraindications** to the use of tPA, who present within 24 hours of injury, we suggest treatment with intravenous tPA plus subcutaneous low-molecular weight heparin (eg enoxaparin) or intravenous heparin. The use of intra-arterial tPA with heparin is also reasonable in facilities capable of administering intra-arterial tPA.

Hennepin County Medical Center (Minneapolis, USA) has found that treatment with intravenous tPA and subcutaneous enoxaparin is effective and more easily accomplished than treatment with intra-arterial tPA (see administration regimens below). Controlled trials comparing intra-arterial and intravenous tPA for the treatment of severe frostbite have not been conducted.

The American Burn Association has published guidelines for thrombolytic therapy for frostbite [63]. According to their guidelines, thrombolytic therapy may be used for patients with cyanosis proximal to the distal phalanx (grade 3 or 4 frostbite injury) and demonstrated loss of perfusion at or proximal to the middle phalanx immediately after rewarming.

Whenever possible, treatment should be performed at or in consultation with a center experienced in the use of tPA for frostbite. Patients appropriate for treatment with tPA are also appropriate for treatment with iloprost. (See 'Prostacyclin therapy for severe injury presenting within 48 hours' below.)

The degree of frostbite should be assessed using the extent of cyanosis immediately after rewarming, as described in the classification section [10]. Patients with cyanosis proximal to the interphalangeal joints should be evaluated with technetium scanning or CT angiography. If circulation is absent proximal to the interphalangeal joints, tPA should be given, unless contraindicated. (See 'Classification' above and 'Imaging studies' above.)

Risks and contraindications — Thrombolysis is associated with a small but important risk of dangerous bleeding (eg, intracranial hemorrhage). Contraindications to tPA include, but are not limited to, recent stroke or persistent neurologic impairment, intracranial trauma, recent significant gastrointestinal bleeding, and recent surgery. Before

administering tPA, clinicians must carefully assess the patient's risk for significant bleeding complications. Do **not** give tPA to patients at significant risk for such complications, which are summarized in the following table (table 2) and discussed in detail separately. (See "Acute ST-elevation myocardial infarction: The use of fibrinolytic therapy", section on 'Contraindications' and "Intravenous thrombolytic therapy for acute ischemic stroke: Therapeutic use".)

Administration and dosing — There are no standardized dosing regimens for tPA in the treatment of severe frostbite injury. Reasonable approaches are described below.

As soon as angiography or technetium-99m scanning shows that there is no perfusion to the affected area(s), intravenous (IV) or intra-arterial tPA should begin as soon as possible, but no longer than 24 hours after thawing.

- For **IV administration** of tPA, we suggest the following regimen [52,63,64]:

  Give a bolus dose of 0.15 mg/kg over 15 minutes, followed by a continuous IV infusion of 0.15 mg/kg per hour for six hours. The maximum total dose is 100 mg.

  After tPA has been given, adjunct treatment can be started with IV heparin or subcutaneous (SC) enoxaparin. The dose of IV heparin is 500 to 1000 units/hour for six hours, or targeted to maintain the partial thromboplastin time (PTT) at twice the control value. Enoxaparin can be given at the therapeutic dose (1 mg/kg SC).

- For **intra-arterial administration** of tPA, we suggest the following regimen [45,46,65,66]:

  Give a bolus of 2 to 4 mg, followed by an infusion of 0.5 to 1 mg/hour via the femoral or brachial artery. Repeat angiograms are performed every 8 to 12 hours.

  A few centers give an intra-arterial vasodilator, most commonly papaverine (150 mg), immediately before administering intra-arterial tPA [54,67].

  If more than one extremity is affected, divide the total tPA dose between or among them. Treatment should be continued until perfusion is restored (as demonstrated by angiography or technetium-99m scanning) or a time limit of 72 hours is reached.

  Adjunct treatment with heparin can be given at 500 units/hour via the intra-arterial catheter.

Hennepin County Medical Center, a facility with extensive experience managing frostbite,

uses the following thrombolytic protocol:

- Rapidly rewarm frostbitten tissue in warm (not hot) water until it can be assessed for the presence of hemorrhagic blisters or acral hypoperfusion (cyanosis). (See 'Rewarming' above.)

- Perform a technetium-99m triple-phase bone scan. Patients expected to require significant amputations due to tissue necrosis and who have undergone rewarming within 12 hours injury, without freeze-thaw cycles (ie, repeated episodes of refreezing and thawing), are eligible for thrombolysis in the absence of contraindications.

- For suitable patients at risk for tissue necrosis and with no contraindications, administer a loading dose of alteplase, 0.15 mg/kg intravenously over 15 minutes. Following the loading dose, start an infusion of alteplase, 0.15 mg/kg per hour for 6 hours. (While earlier reports involved intra-arterial administration of tPA and heparin, the Hennepin experience has been that the intravenous route for tPA is also effective and more easily accomplished.)

- Perform another technetium-99m triple-phase bone scan to verify reperfusion.

- After treatment with alteplase is completed, begin treatment with enoxaparin, 1 mg/kg subcutaneously, given twice daily for 14 days.

Clinicians must discuss the relative risks and benefits of thrombolytic treatment with the patient and obtain informed consent. Treatment with thrombolytics assumes the patient is willing to accept a small risk of potentially catastrophic bleeding in return for a greater likelihood of retaining functional digits or limbs. Rates of tissue salvage improve with decreasing time from rewarming to thrombolysis [52].

Evidence in support of thrombolytic treatment of severe frostbite is largely observational but growing [62,64,66,68-70]:

- In a systematic review, data were extracted from 16 studies and case series involving a total of 209 patients with 1109 digits at risk for amputation from frostbite and treated with thrombolytic therapy using either intra-arterial or intravenous tPA [62]. The salvage rate for digits treated with intra-arterial tPA (n = 926) was 76 percent, while the salvage rate for digits treated with intravenous tPA (n = 63) was 62 percent. Although statistical analysis was not possible due to heterogeneity among the studies, it may well be that there is no significant statistical or clinical difference in digit salvage rate between intravenous and intra-arterial tPA. Digital subtraction angiography was used

for the initial evaluation in nine studies, and triple-phase bone scan was used in six. While patient characteristics and study inclusion criteria varied, the authors of the review noted that thrombolytic therapy was less effective in patients with prolonged exposure (longer than 24 hours) or freeze-thaw-refreeze injuries.

- Another systematic review assessed 17 studies involving a total of 1844 limbs and digits with frostbite in 325 patients, 216 of whom were treated with thrombolysis [68]. This review included studies using a number of thrombolytic agents. While limb salvage rates varied from 0 to 100 percent among studies, the weighted average was 79 percent.

The administration of papaverine, a vasodilator, followed by tPA has been associated with good patient outcomes in case reports [69]. However, a controlled trial of tPA with and without papaverine has yet to be performed. Nitroglycerin has also been used as a vasodilator to facilitate treatment with intra-arterial tPA [47].

Prostacyclin therapy for severe injury presenting within 48 hours — Prostacyclin, a vasodilator, shows promise for the treatment of frostbite. Iloprost, a prostacyclin analog (IV formulation not available in the United States), was associated with lower amputation rates among 47 patients treated for severe frostbite compared to those treated with buflomedil in an open label randomized trial [71], and additional case reports of successful treatment with iloprost have been published [70,72].

We suggest treatment with iloprost, with or without tPA, for patients with severe frostbite (Grade 2-4) if given within 48 hours of the initial insult [73]. Iloprost administration may be effective past 48 hours, perhaps up to 72 hours (eg, if a clear history or timeline cannot be established), but supporting data are limited [74]. When used without tPA, administration of iloprost does not require an intensive care setting, nor does it require radiologic intervention. Iloprost should be used alone when tPA is contraindicated, as in frostbite seen more than 24 hours after thawing or in cases associated with trauma. (See 'Classification' above and 'Clinical manifestations' above.)

Iloprost is given by intravenous infusion at a dose 0.5 nanogram/kg per minute, increased every 30 minutes by 0.5 nanogram/kg per minute, to a maximum of 2 nanogram/kg per minute. If the patient develops headache or hypotension, the dose is decreased by 0.5 nanogram/kg per minute. The infusion is given for 6 hours/day for five days at the maximum tolerable rate, up to 2 nanogram/kg per minute [73].

The use of iloprost is safe enough that it can be used in prehospital settings if evacuation to

hospital is not feasible [11]. The dosing regimen is the same, but the infusion is stopped after a total of 50 mcg (one vial) has been given, regardless of the weight of the patient. The patient should be evacuated after the first dose, but if this is not practical, the dose can be repeated daily for a total of three days. A single dose is likely beneficial and should be given even if it is not possible to give subsequent doses.

Wound care — Subsequent management includes application of a bulky dressing to the affected area, elevation to reduce edema, and daily hydrotherapy to improve range of motion. Splinting may be required to prevent contracture formation.

The following practices are important in treating these wounds:

- Maintain aseptic technique during wound treatment.
- Apply nonadherent gauze as the first dressing layer.
- Use sterile fluff dressing.
- Insert pledgets (eg, sterile cotton) between digits to prevent tissue maceration during demarcation.
- Avoid occlusive dressings.
- Protect lower extremity wounds with a cradle and upper extremity wounds with sterile sheets.
- Keep wounds open immediately following water bath or whirlpool treatment and allow them to dry before applying any dressing.
- Blisters – There is no clear consensus on management of frostbite-induced blisters. Some authors suggest that because of the high concentrations of inflammatory mediators in the blister fluid, all should be drained. Others take a more conservative approach. A reasonable compromise is to drain, debride, and bandage large nonhemorrhagic bullae that interfere with movement, such as those over joints. Hemorrhagic bullae of comparable size and location are drained by aspiration but are **NOT** debrided. Hemorrhagic bullae reflect more significant damage to the microvasculature. Other minor bullae should be left intact [8].
- Topical aloe, applied with dressing changes, and oral ibuprofen (adult dose 400 to 600 mg every 12 hours) or aspirin (adult dose 325 mg daily) may limit inflammation associated with frostbite by inhibiting thromboxane and prostaglandins, although

supporting evidence is limited [75,76]. In the absence of contraindications, it is reasonable to use these treatments [77].

Infection prophylaxis

- Tetanus is a reported complication of frostbite. Tetanus prophylaxis is recommended [78].

- Prophylactic antibiotics are controversial, and little evidence exists to guide decision-making. Post-thaw daily or twice daily warm whirlpool treatments are standard therapy to help to reduce bacterial colonization of injured tissue, but infection can develop nevertheless. We do not recommend routine use of prophylactic antibiotics. We suggest giving parenteral antibiotics at the earliest sign of infection. Staphylococci, streptococci, and pseudomonas species should be covered. Topical antibiotics can cause maceration and should be avoided; if given, antibiotics should be administered intravenously. Appropriate antibiotic selection is discussed separately. (See "Acute cellulitis and erysipelas in adults: Treatment", section on 'Acute cellulitis'.)

Surgical consultation — Because frostbite may require long-term wound care, including hydrotherapy, repeated tissue debridement, escharotomy, fasciotomy, and possibly delayed amputation, we recommend early surgical consultation, preferably with an orthopedic surgeon with experience managing frostbite [56].

Unproven therapies: Hyperbaric oxygen, pentoxifylline, heparin without thrombolysis, and others — Several potential but unproven treatments for frostbite have been reported. Hyperbaric oxygen has been proposed as an adjunctive therapy to improve revascularization and healing of injured tissue. Older studies showed no benefit, but subsequent case reports suggest a possible role and describe improvement in symptoms and the microcirculation of affected tissues [79-81]. A retrospective case series of 22 patients reported no definite improvement in the extent of amputations from hyperbaric oxygen therapy [82]. Further study of hyperbaric treatment is needed before it can be recommended. Hyperbaric oxygen therapy is discussed in greater detail separately. (See "Hyperbaric oxygen therapy".)

Pentoxifylline, a drug sometimes used to treat claudication, has been proposed as adjunctive therapy for frostbite because of its favorable effect on blood flow [83]. Although the benefit of pentoxifylline in claudication is limited, animal studies of frostbite have had positive results [84,85]. No controlled studies have been performed in humans. Further data are needed before pentoxifylline can be recommended. (See "Management of claudication due to peripheral artery disease", section on 'Benefit not firmly established'.)

There is no evidence that intravenous heparin **alone** improves outcomes in frostbite. We do not recommend such treatment. For appropriately selected patients, heparin, or enoxaparin, is given along with thrombolytic therapy. (See 'Thrombolysis for severe injury presenting within 24 hours' above.)

Complications

Overview of short and longer term complications — The complications of frostbite are due primarily to peripheral neurovascular injury with associated abnormalities of sympathetic tone. Vasospasm, especially with re-exposure to cold, is common and may be permanent. The severity of complications generally correlates with the severity of the original injury. The sequelae of nonfreezing cold injuries (NFCIs) are similar but often more debilitating than those produced by frostbite [12,86].

Short-term complications include gangrene and infection of the affected area (picture 8 and picture 9). Autoamputation may take many weeks to occur. Therapeutic amputation is necessary if deep infection develops before the autoamputation of nonviable tissue. Rarely, acute compartment syndrome may develop and require emergency decompression.

Throbbing pain that begins two to three days after rewarming may persist for weeks or months, even after nonviable tissue demarcates. Intermittent paresthesias beginning after one week are thought to be due to ischemic neuritis and may last for months. Burning, electric shock sensations may also occur. Hyperhidrosis is common and may be a cause as well as an effect of frostbite.

Cold exposure is contraindicated for six months after minor injury and for at least 12 months after any significant cold injury. Special precautions to protect previously injured tissue may need to be taken for several years if not indefinitely to prevent further damage. (See 'Prevention' below.)

Longer-term complications include hypersensitivity to the cold; patients remain at increased risk for developing frostbite [8,87]. Late and long-term or permanent sequelae include scarring, tissue atrophy, arthritis, bony abnormalities, and peripheral neuropathy, including hyper or hypoesthesia of digits with decreased proprioception and chronic pain. Pediatric patients may develop necrosis of epiphyses, with devastating growth abnormalities. (See 'Complications in children' below.)

Frostbite osteoarthritis — Osteoarthritis caused by frostbite occurs most often in the distal

extremities. There are numerous case reports of frostbite arthritis of hands in adults, usually not associated with loss of soft tissue. Early changes can include flexion contractures of the proximal interphalangeal joints that may improve over several months or become permanent, sometimes with arthrodesis [88]. Joint swelling may also be permanent and associated with osteo-degenerative changes and juxta-articular swelling of the proximal and distal interphalangeal joints (picture 14) [89-92]. In spite of any deformities, good functional outcomes are common [88,89]. The thumbs are usually spared in frostbite arthritis, in contrast to typical osteoarthritis [44,93].

Frostbite arthritis of the feet causing flexion contractures of the toes has been reported [94]. Functional outcomes can be good [95] or debilitating [94]. Frostbite arthritis can occur in patients with underlying connective tissue disorders, such as scleroderma or Sjögren's syndrome, producing a confusing clinical picture, especially if a history of frostbite is not elicited [96].

Frostbite arthritis has been known for centuries but was first described in modern times in a case series of 100 American soldiers who sustained frostbite injuries, primarily in their feet, while in Korea during 1950 to 1951 [95,97,98]. Transient, mostly mild osteoporosis developed in 58 soldiers. Subsequent changes to the bone consisting of sharply defined, punched out defects, usually near joints, were seen in 7 of 62 soldiers who were observed for at least eight months. There was no correlation between the severity of frostbite and the changes in the joints. Only one soldier had long-term clinical sequelae.

Complications in children — Epiphyseal destruction, bone abnormalities, and arthritis are potential sequelae after frostbite of the hands, and occasionally feet, in children [12]. Frostbite need not be severe in order to be associated with damage to the digits. Most reported cases did not involve loss of tissue. Loss of fingernails with subsequent regrowth of normal nails often occurs during the several weeks following injury [99-102]. Multiple nails can be lost with regrowth over months to years [103]. Sometimes, there is sloughing of the epidermis without permanent tissue loss [99,104].

Bone and joint changes usually begin to become evident several months after frostbite injury. Epiphyseal abnormalities, primarily of the distal and middle phalanges, include partial or complete destruction, fragmentation, and premature fusion (picture 15). Thumbs are seldom affected [103,105,106]. In the affected digits, the distal phalanges and sometimes the middle phalanges are shortened. Proximal phalanges and metacarpals are usually normal. Painful or painless joint swelling may occur 6 to 12 months after the injury [107]. Fingers commonly develop painless flexion deformities of the distal and proximal interphalangeal

joints, often with radial deviation of the distal phalanges [102,107] and clinodactyly (curvature of the digits) [108]. Swan neck deformities can also occur [101,108]. Deep frostbite injuries with loss of tissue can cause severe sequelae with markedly limited range of motion of hands or feet [109].

Frostbite sustained at a young age can result in severe, progressive deformity with decreased range of motion and weakness in extension [100,103,105,106,109,110]. Chronic circulatory changes can include cold intolerance and vasomotor instability [108,111]. Deformities often worsen during growth spurts when affected bones fail to grow while unaffected bones develop normally [112]. When patients reach adulthood, radiographs show less specific changes of chronic arthritis with short phalanges [103]. Their hands often have limited dexterity, which can interfere with fine motor skills such as dressing and using a keyboard [103].

There are no specific data to guide treatment of frostbite in children. We recommend treating frostbite in children as for adults. There is no treatment proven to prevent permanent sequelae affecting bones and joints. In the largest published case series (13 patients seen 4 to 50 years after frostbite), none sought surgery to improve function or appearance due to chronic disability [103].

Prevention

Prevention of frostbite includes minimizing predisposing factors, paying attention to weather forecasts, dressing appropriately for the weather, and having an emergency plan when venturing to remote regions [16,17].

- Alcohol consumption and smoking should be avoided, as should exposure to water or metal surfaces.
- Adequate calorie intake and hydration should be maintained.
- Predicted high and low temperatures should be noted, as well as forecasted precipitation and wind chill index. In the setting of extreme cold temperature and high winds, frostbite can develop in a matter of minutes [113].
- Suggested clothing includes a hat, face protection, eye protection under extreme conditions, mittens (as opposed to gloves), warm and water-resistant shoes, and several layers of loose-fitting clothes. The innermost layer should be a wicking material,

such as polypropylene, that will draw moisture away from the skin. The next layer should be of an insulating material such as fleece or wool. The outer-most layer should provide protection against wind, rain, and snow. Wet clothing should be changed as soon as is feasible [41].

- Small chemical heat packs may be placed in gloves or shoes but should be used with caution to avoid burns through direct contact with the skin.
- The practice of applying emollients to exposed skin to prevent frostbite is widespread in many cold regions of the world. However, literature supporting this practice is lacking. In fact, there is some evidence that this may give the user a false sense of security and increase the risk of frostbite. Therefore, we do not suggest the use of emollients as a preventative measure [25-27].
- Individuals traveling in remote areas should, prior to departure, inform others of their anticipated route and carry adequate emergency supplies in case they become stranded.
- Persons frequently exposed to cold environments should be aware of common frostbite symptoms and signs, and should withdraw to warm shelter when these are noticed.

Society guideline links

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Management of environmental emergencies".)

Information for patients

UpToDate offers two types of patient education materials, “The Basics” and “Beyond the Basics.” The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on “patient info” and the keyword(s) of interest.)

- Basics topic (see "Patient education: Frostbite (The Basics)")

Summary and recommendations

- **Classification and risk factors** – Risk factors for frostbite or nonfreezing cold injury (NFCI) include anything that increases localized heat loss or decreases heat production. Examples include increased convective heat loss due to exposure to wind or conductive heat loss due to contact with metal or water. Exhaustion, dehydration, malnutrition, alcohol abuse, or comorbidities such as peripheral vascular disease, diabetes, or mental illness also increase risk. The classification of frostbite and other risk factors are discussed in the text. (See 'Classification' above and 'Risk factors' above and 'Definitions' above.)

- **Clinical manifestations** – The areas most frequently affected by frostbite include the ears, nose, cheeks, chin, fingers, and toes. Patients often complain of cold, numbness, and clumsiness of the affected area. The skin may be insensate, white or grayish-yellow in color, and hard or waxy to touch. Bullae containing clear or hemorrhagic fluid may form after thawing. (See 'Clinical manifestations' above and 'Diagnosis' above.)

- **Imaging** – Technetium-99m scintigraphy (bone scan) can be used to predict long-term viability of affected tissue and help guide decisions about thrombolytic therapy. Other imaging methods (eg, fluorescence microangiography; magnetic resonance angiography) may also be useful for this purpose, but evidence is limited. (See 'Diagnosis' above.)

- **Initial care and rewarming** – Prehospital and hospital care of frostbite is described in detail in the text. Rapid rewarming, meticulous sterile wound care, possible thrombolysis, and early surgical consultation are key interventions. Rewarming is most effectively accomplished by immersing the affected area in a water bath heated to 37 to 39°C. Such water feels warm but not hot to an unaffected hand. (See 'Treatment' above.)

  Tetanus prophylaxis and early, aggressive treatment of possible infection should be provided. Prophylactic antibiotics are not routinely recommended. (See 'Infection

prophylaxis' above.)

- **Thrombolysis and anticoagulation therapy** – In patients at high risk for life-altering amputation (eg, multiple digits in a limb, multiple limbs, proximal amputation), **without contraindications** to the use of tissue plasminogen activator (tPA) (table 2), who present within 24 hours of injury, we suggest treatment with intravenous (IV) tPA plus heparin (**Grade 2C**). Treatment with intra-arterial tPA and intra-arterial heparin is also reasonable in hospitals that prefer this approach. If intravenous tPA is used, subcutaneous low molecular weight heparin (eg, enoxaparin) may be administered instead of IV heparin.

  Whenever possible, treatment should be performed at or in consultation with a center experienced in the use of tPA for frostbite. Clinicians must discuss the relative risks and benefits of thrombolytic treatment with the patient and obtain informed consent. Treatment with thrombolytics assumes the patient is willing to accept a small risk of potentially catastrophic bleeding in return for a greater likelihood of retaining functional digits or limbs. Dosing regimens are provided in the text. (See 'Thrombolysis for severe injury presenting within 24 hours' above.)

- **Prostacyclin therapy** – For patients who present with significant frostbite (Grades 2 to 4) within 48 hours of the initial insult, we suggest treatment with iloprost, a synthetic form of prostacyclin (**Grade 2B**). Iloprost is given by intravenous infusion at a dose 0.5 nanogram/kg per minute, increased every 30 minutes by 0.5 nanogram/kg per minute, to a maximum of 2 nanogram/kg per minute. If the patient develops headache or hypotension, the dose is decreased by 0.5 nanogram/kg per minute. The infusion is given for 6 hours/day for five days at the maximum tolerable rate, up to 2 nanogram/kg per minute. (See 'Prostacyclin therapy for severe injury presenting within 48 hours' above.)

- **Prevention** – Strategies for prevention of frostbite are discussed in the text. (See 'Prevention' above.)

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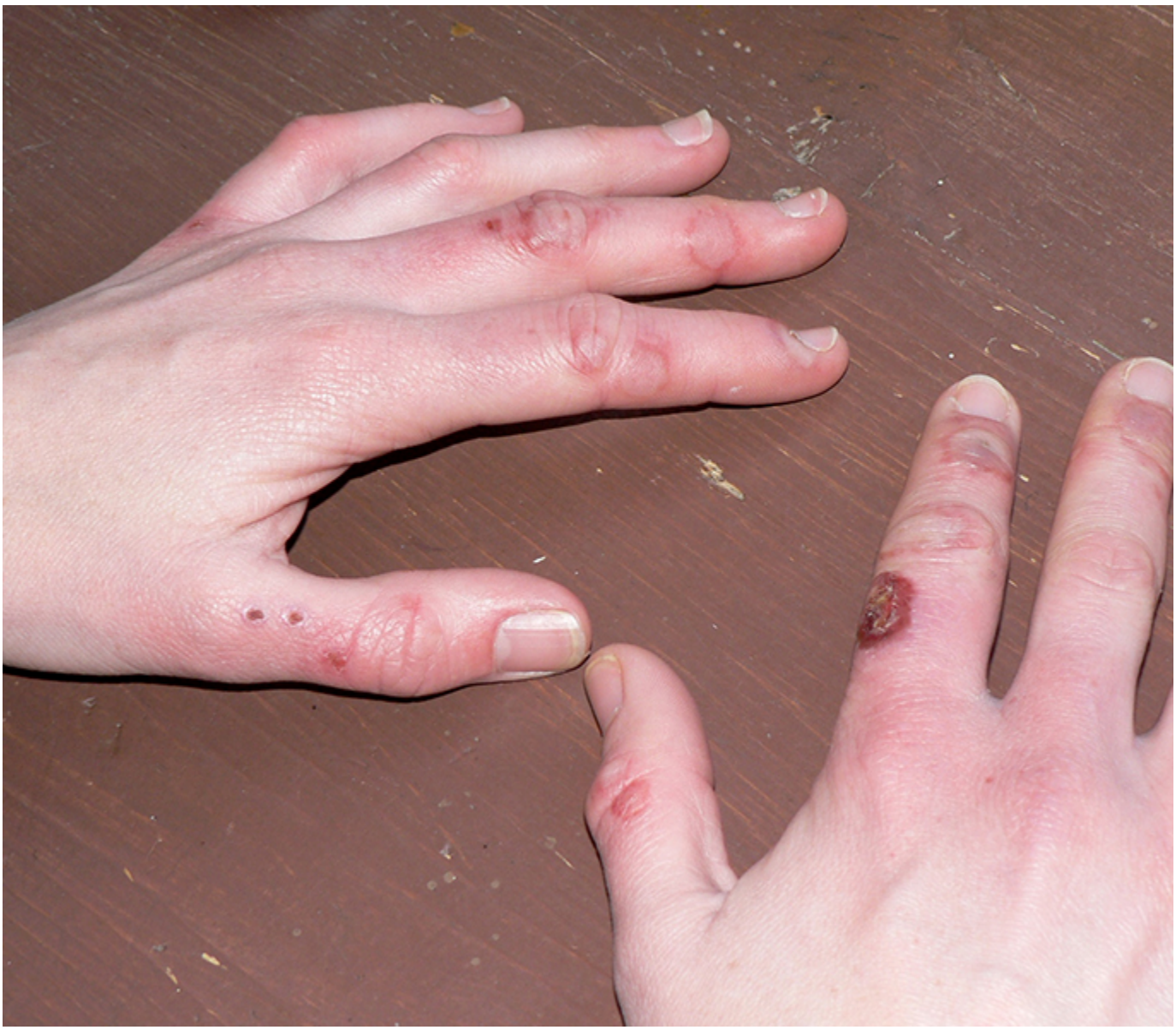
Topic 179 Version 39.0

GRAPHICS

Pernio in a woman chronically exposed to dry cold

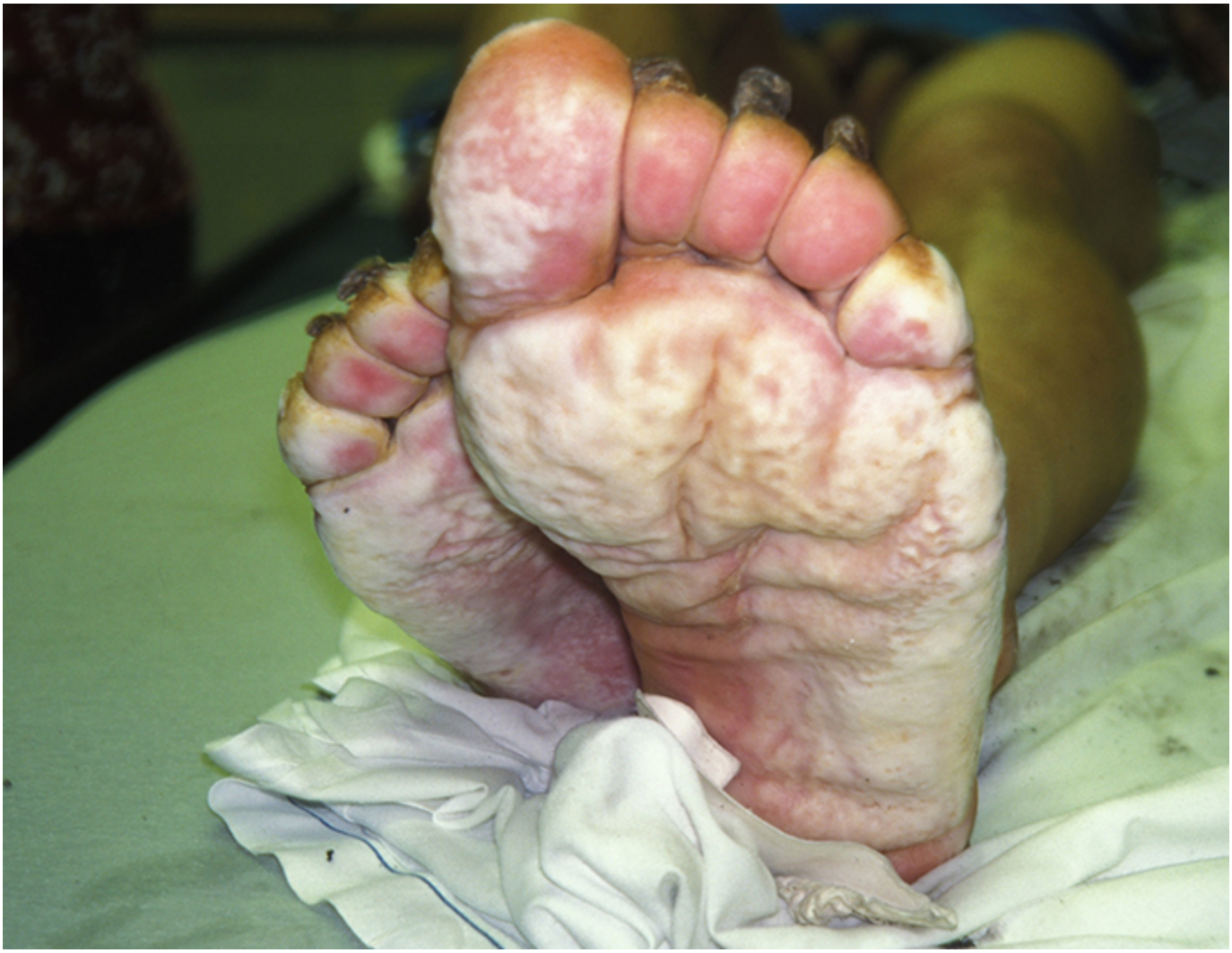


The photo above shows pernio in a woman chronically exposed to dry cold in an austere environment. P
condition.

Courtesy of Alice F Murray, MD.

Graphic 101018 Version 2.0

Nonfreezing cold injury ("trench foot" or "immersion foot")



The photo above shows nonfreezing cold injury ("trench foot" or "immersion foot") in a homeless man sc
presentation to the emergency department after he was found intoxicated outdoors with wet shoes and

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Courtesy of Ken Zafren, MD.

Graphic 101027 Version 1.0

Proposed classification scheme for severity of frostbite injuries

Frostbite injuries of the extremities	Grade 1	Grade 2	Grade 3	Grade 4
Extent of initial lesion at day 0 after rapid rewarming	Absence of initial lesion	Initial lesion on distal phalanx	Initial lesion on intermediary and proximal phalanx	Initial lesion on carpal/ tarsal
Bone scanning at day 2	Useless	Hypofixation of radiotracer uptake area	Absence of radiotracer uptake area on the digit	Absence of radiotracer uptake area on the carpal/tarsal
Blisters at day 2	Absence of blisters	Clear blisters	Hemorrhagic blisters on the digit	Hemorrhagic blisters over carpal/tarsal
Prognosis at day 2	No amputation	Tissue amputation	Bone amputation of digit	Bone amputation of the limb ± systemic involvement ± sepsis
	No sequelae	Fingernail sequelae	Functional sequelae	Functional sequelae

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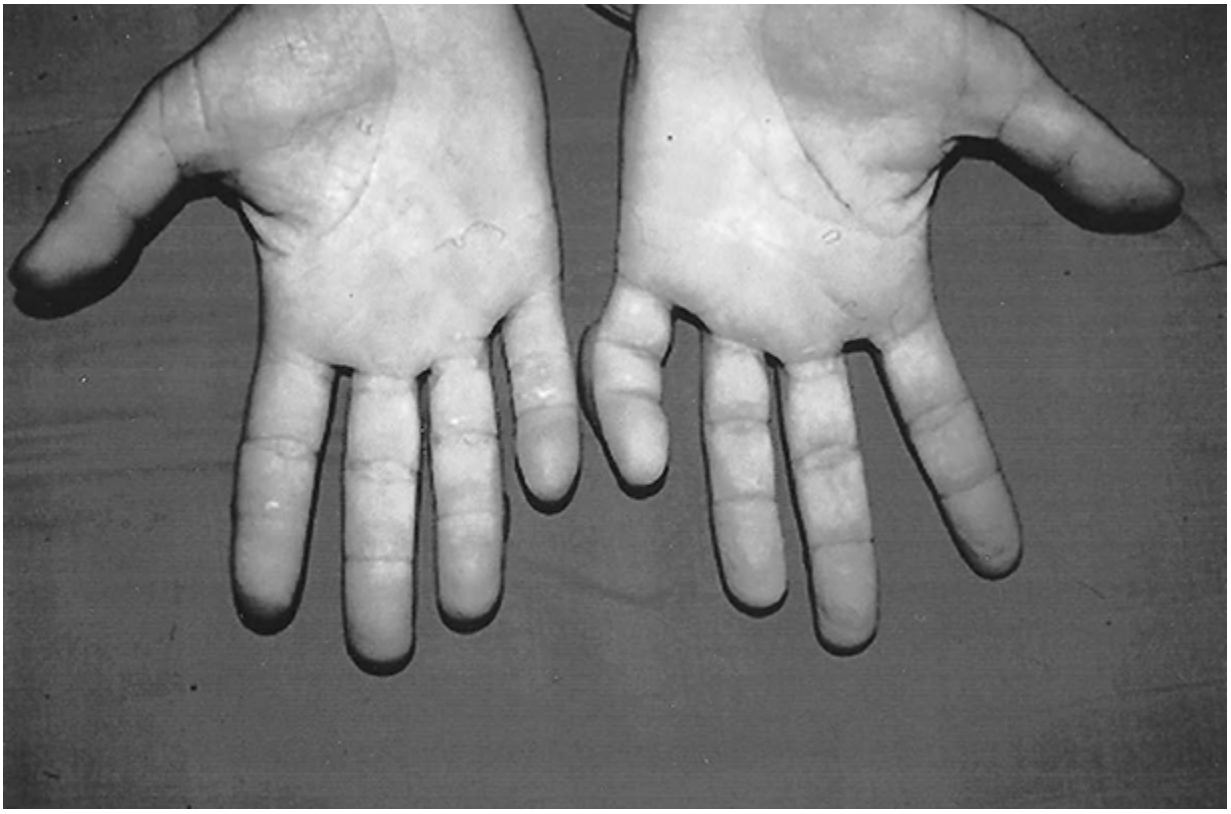
Graphic 111122 Version 1.0

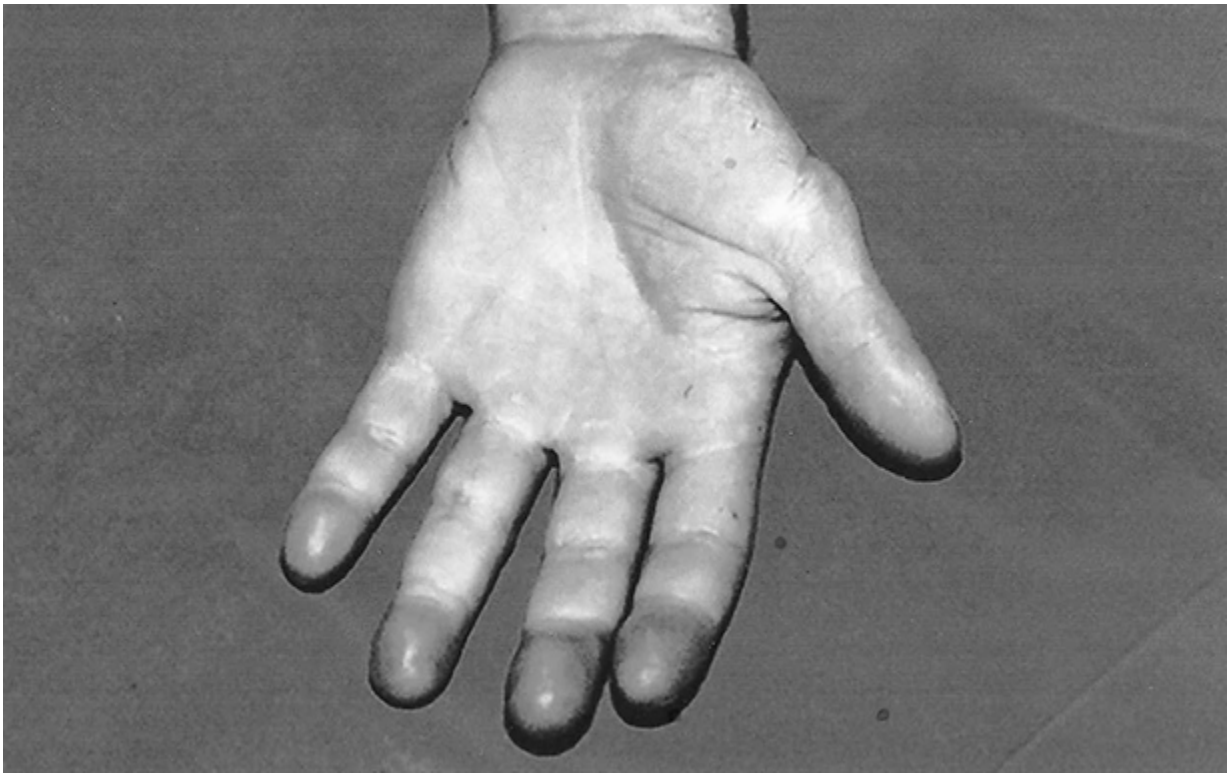
Frostbite injury of the hand - Grade 1



Frostbite injury of the hand at day 0: No initial lesion except erythema (Grade 1).

Graphic 111118 Version 2.0

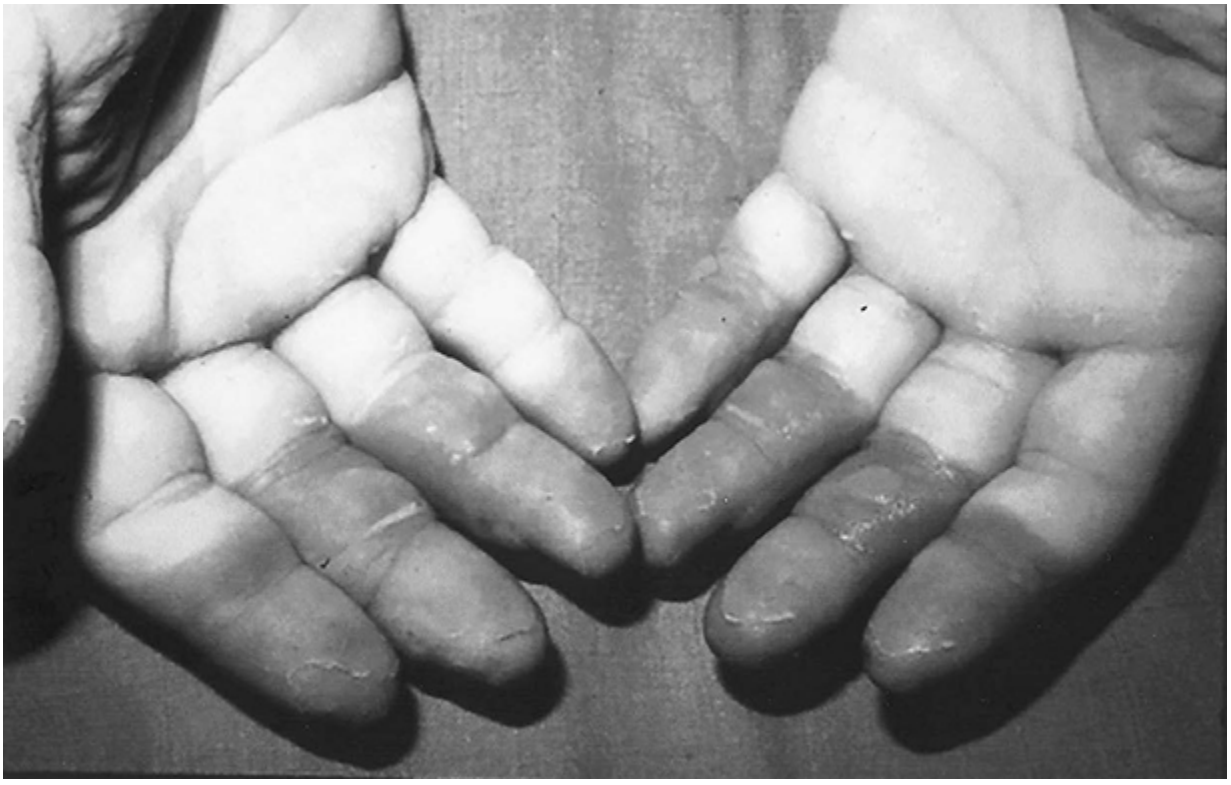
Frostbite injury of the hand - Grade 2



Frostbite injury of the hand at day 0: Initial lesion limited to the distal phalanx (Grade 2). Note the difference in skin color over the distal phalanx of the fingers.

Graphic 111119 Version 1.0

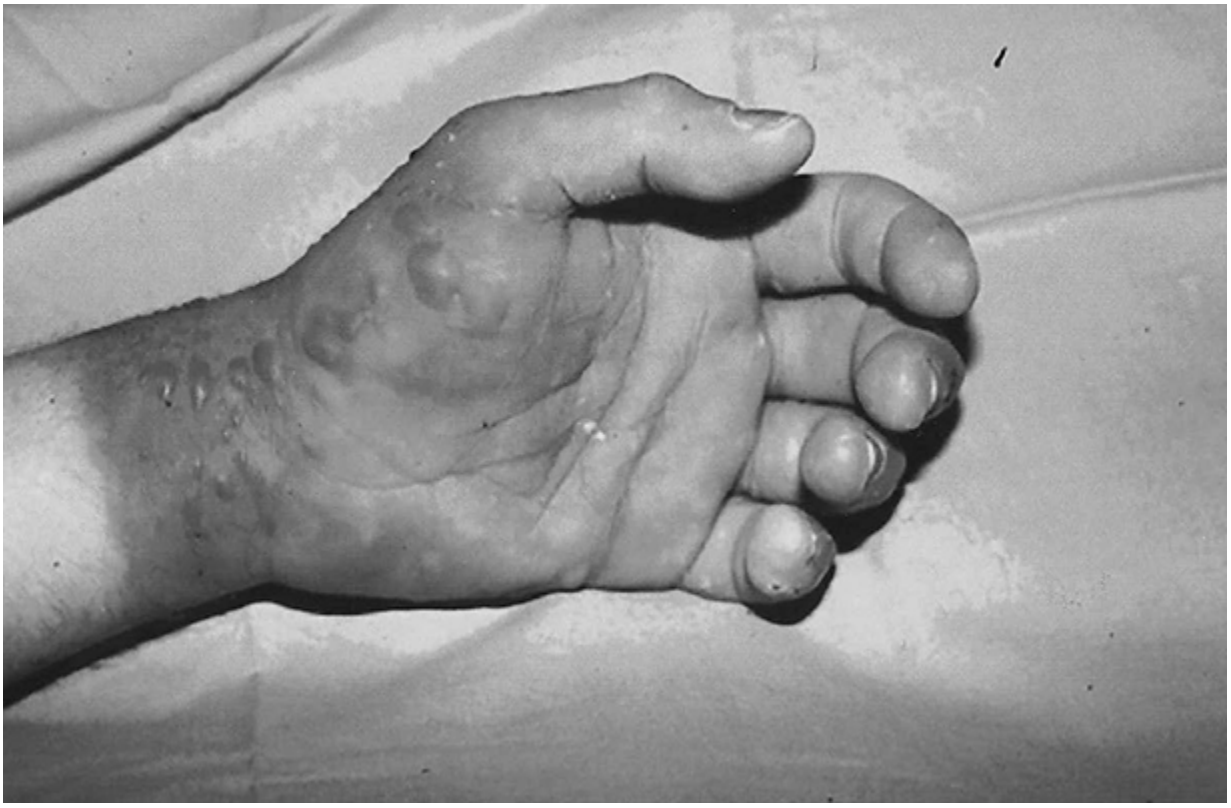
Frostbite injury of the hand - Grade 3



Frostbite injury of the hand at day 0: Initial lesion extends proximally beyond the distal phalanx (Grade 3).

Graphic 111120 Version 1.0

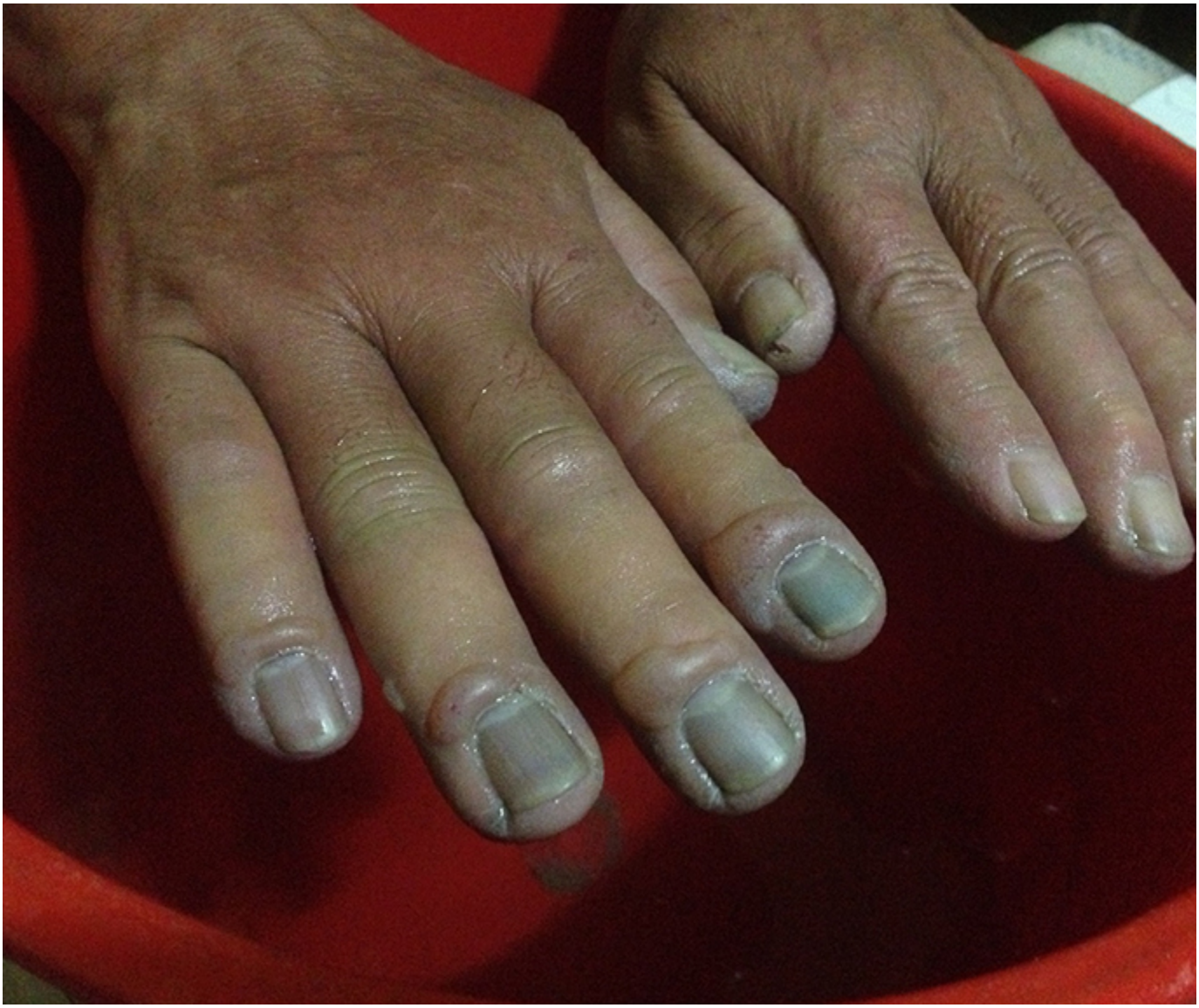
Frostbite injury of the hand - Grade 4



Frostbite injury of the hand at day 0: Initial lesion extending beyond the metacarpophalangeal joints (Grade 4). In the case pictured above, there is involvement of the entire hand, and injury extends just proximal to the wrist.

Graphic 111121 Version 2.0

Frostbite blisters

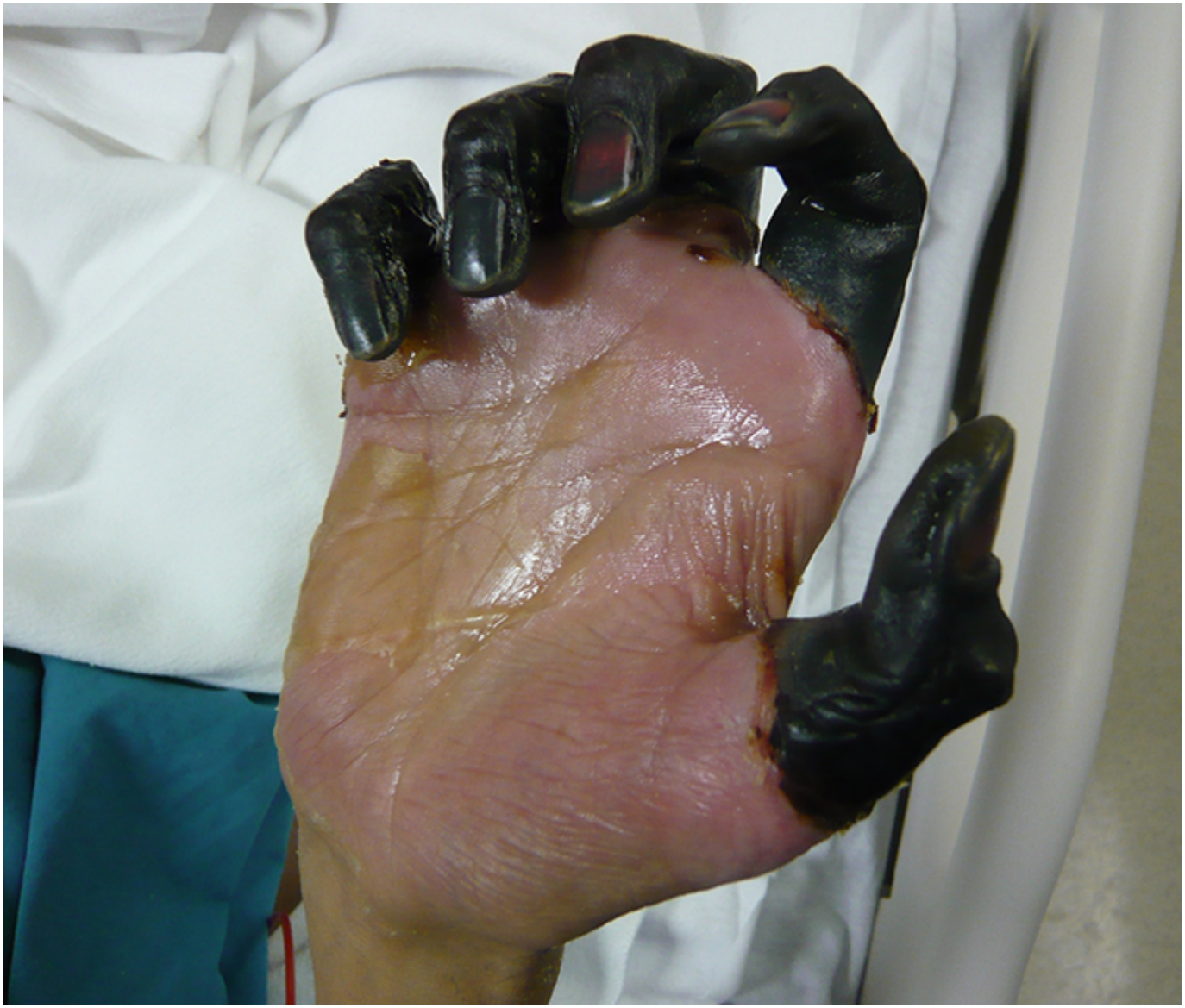


The photo above was taken two days after the patient sustained frostbite from cold exposure in the Him trekker's hands have become edematous and blisters have formed on the distal fingertips. Frostbite blist larger than those shown here.

Courtesy of Nicholas Kanaan, MD.

Graphic 101059 Version 2.0

Severe frostbite of the hand

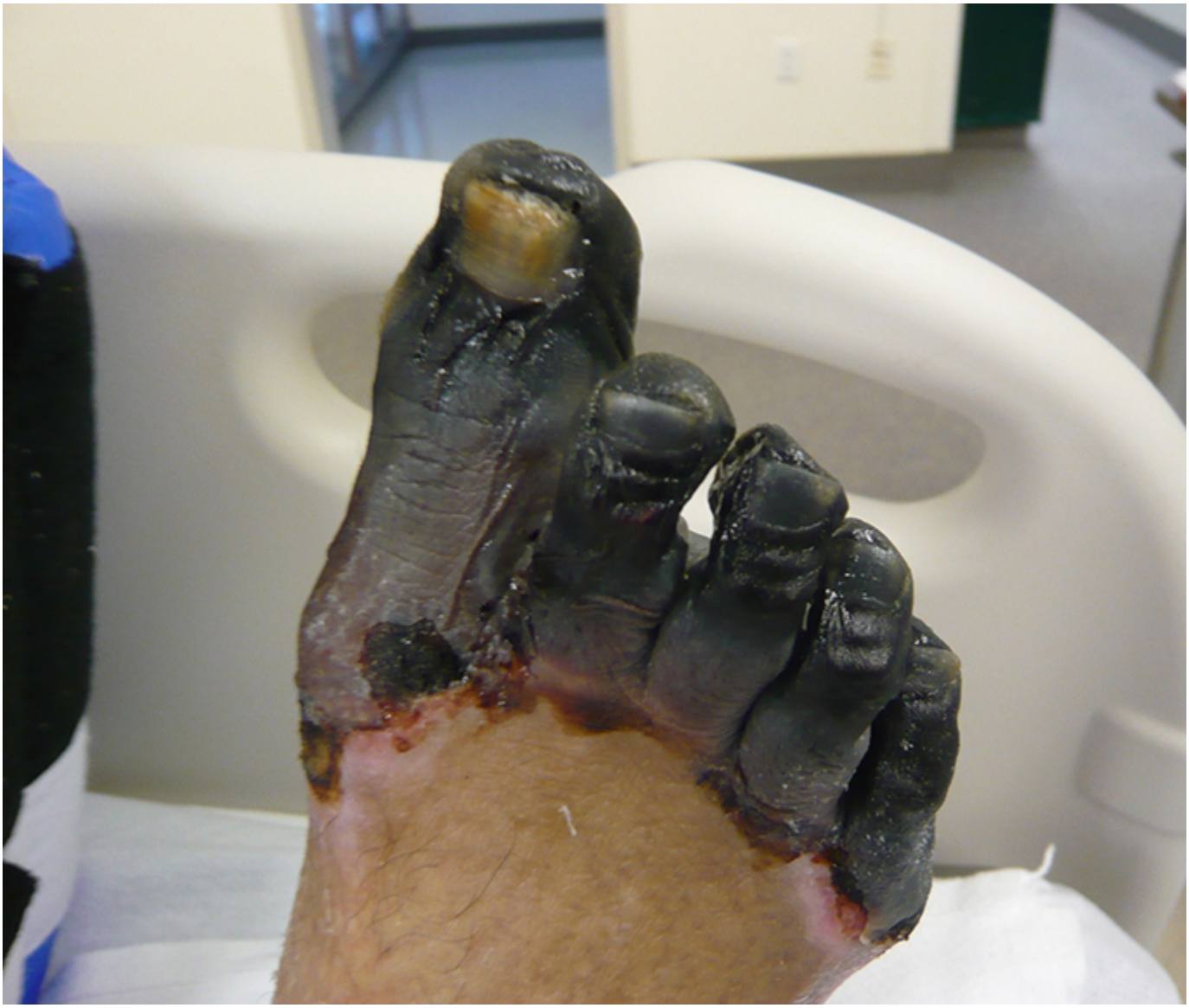


The photo above shows severe frostbite of the hand showing well-demarcated dry gangrene preceding s
loss of tissue.

Courtesy of Ken Zafren, MD.

Graphic 101022 Version 1.0

Severe frostbite of the foot

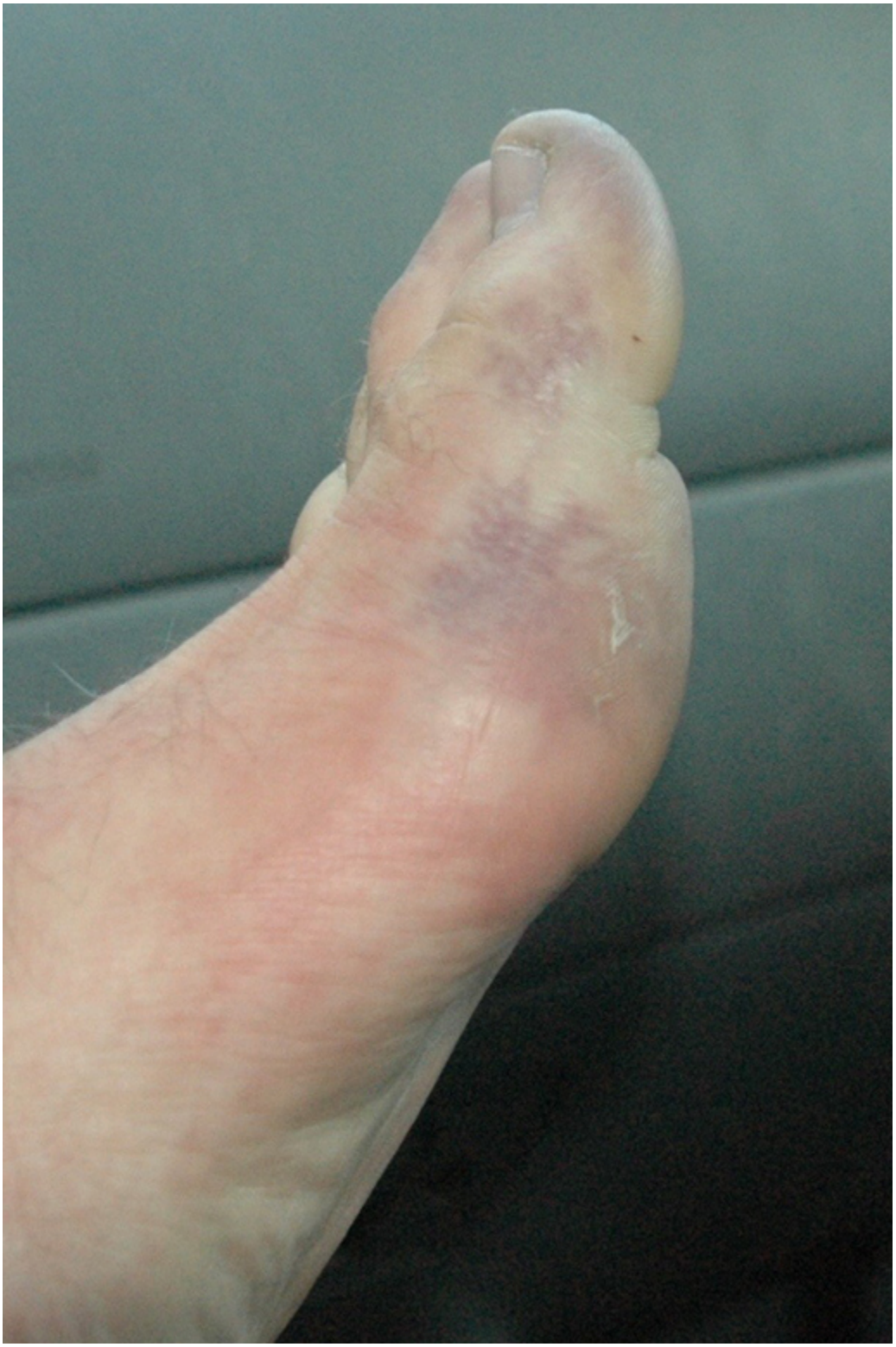


The photo above shows severe frostbite of the foot showing well-demarcated dry gangrene preceding si
loss of tissue.

Courtesy of Ken Zafren, MD.

Graphic 101023 Version 1.0

Frostbite of the foot prior to thawing

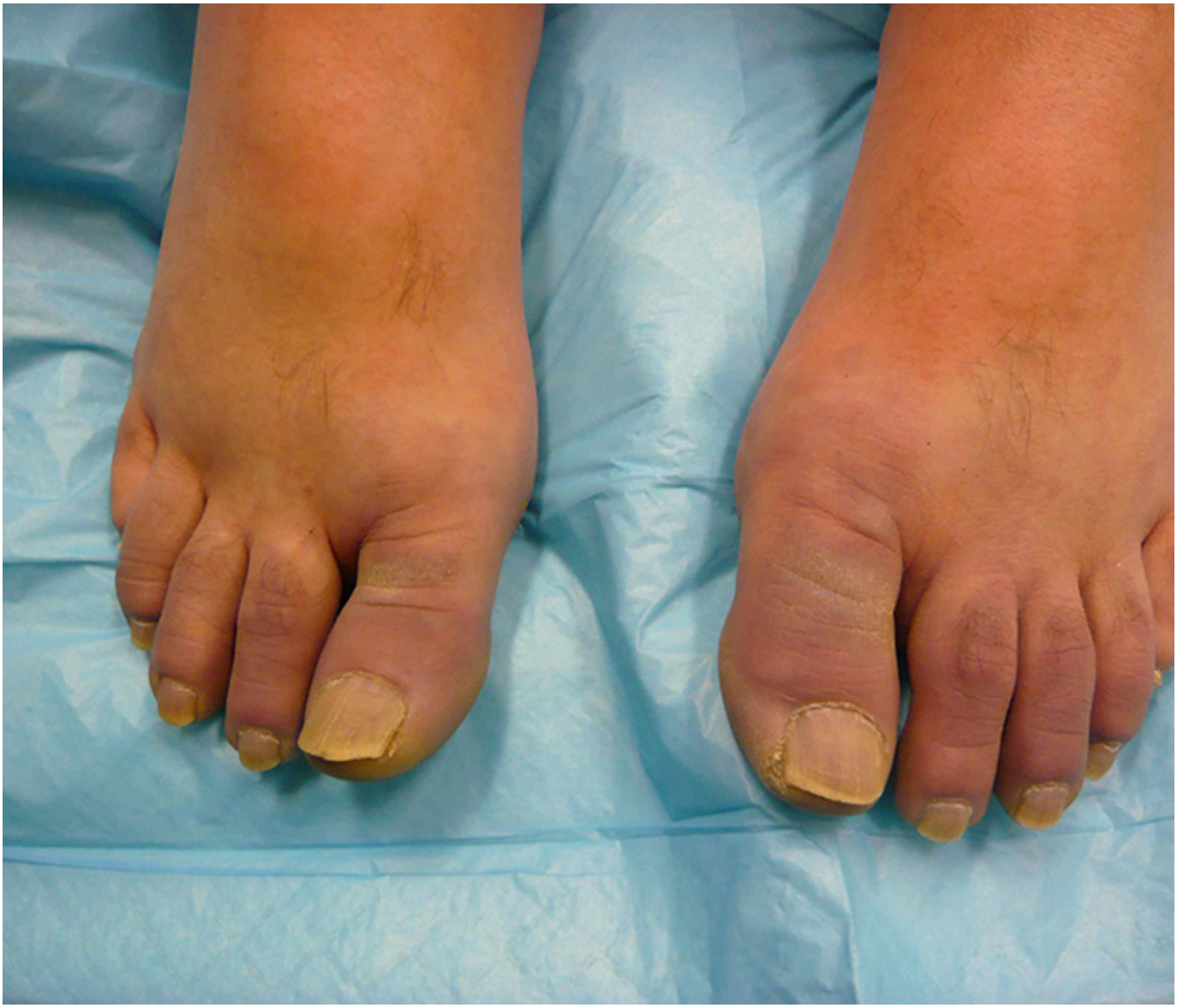


The photo above shows frostbite of the foot at first presentation. Prior to thawing, it is impossible to distinguish mild frostbite from severe.

Courtesy of Nicholas Kanaan, MD.

Graphic 101058 Version 1.0

Early post-thaw appearance of frostbite of the toes

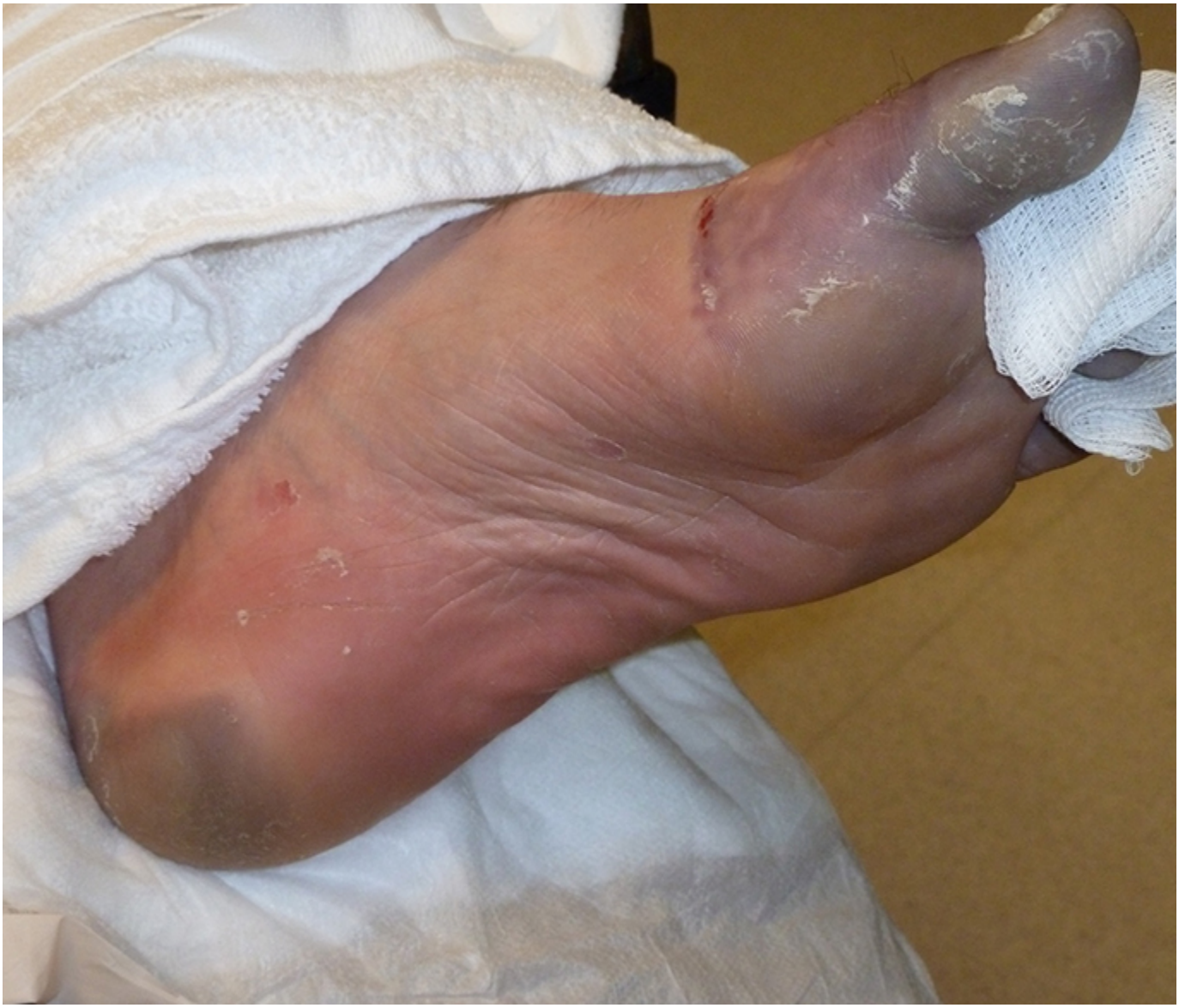


The above photo shows early post-thaw appearance of frostbite of the toes. The lack of swelling and eryt this potentially severe injury appear deceptively benign.

Courtesy of Ken Zafren, MD.

Graphic 101026 Version 1.0

Early demarcation of severe frostbite of the foot

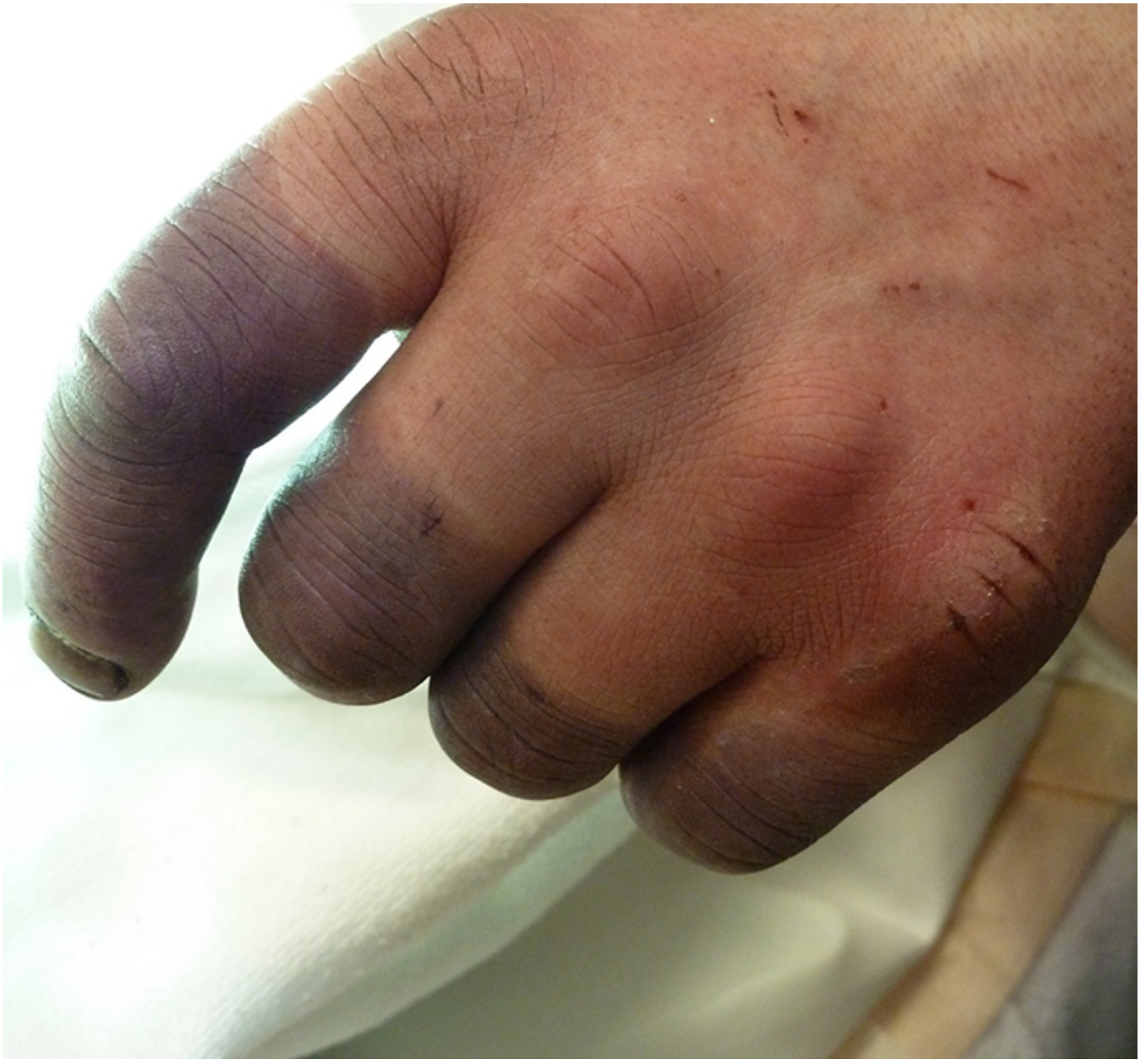


The photo above shows early demarcation of severe frostbite of the foot. The violaceous hue and lack of are grave prognostic signs.

Courtesy of Ken Zafren, MD.

Graphic 101025 Version 1.0

Early demarcation of severe frostbite of the hand



The photo above shows early demarcation of severe frostbite of the hand. The violaceous hue and lack o prognostic signs.

Courtesy of Ken Zafren, MD.

Graphic 101024 Version 1.0

Contraindications to fibrinolytic therapy for deep venous thrombosis or acute pulmonary embolism

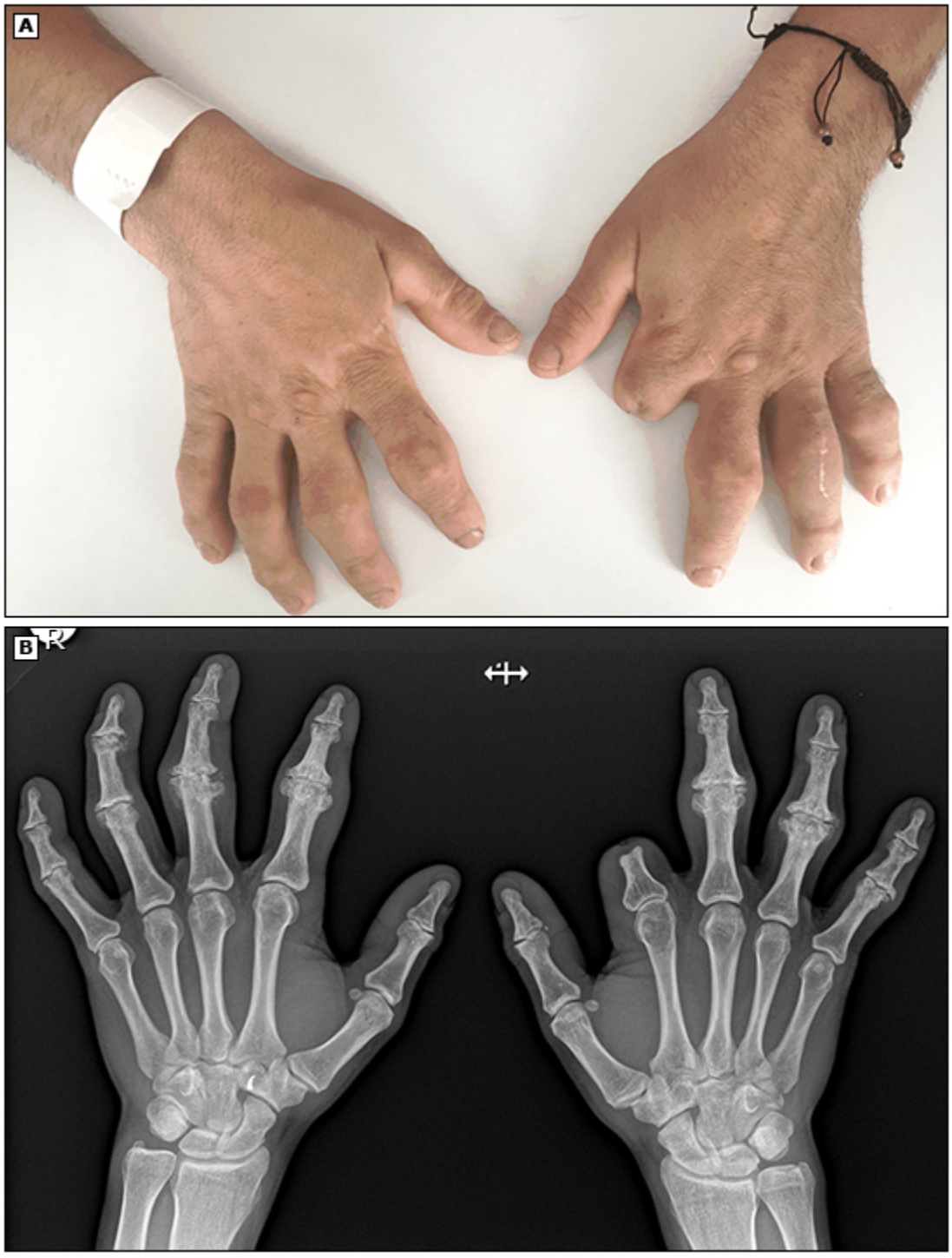
Absolute contraindications
Prior intracranial hemorrhage
Known structural cerebral vascular lesion
Known malignant intracranial neoplasm
Ischemic stroke within three months (excluding stroke within three hours*)
Suspected aortic dissection
Active bleeding or bleeding diathesis (excluding menses)
Significant closed-head trauma or facial trauma within three months
Relative contraindications
History of chronic, severe, poorly controlled hypertension
Severe uncontrolled hypertension on presentation (SBP >180 mmHg or DBP >110 mmHg)
History of ischemic stroke more than three months prior
Traumatic or prolonged (>10 minute) CPR or major surgery less than three weeks
Recent (within two to four weeks) internal bleeding
Noncompressible vascular punctures
Recent invasive procedure
For streptokinase/anistreplase - Prior exposure (more than five days ago) or prior allergic reaction to these agents
Pregnancy
Active peptic ulcer
Pericarditis or pericardial fluid
Current use of anticoagulant (eg, warfarin sodium) that has produced an elevated international normalized ratio (INR) >1.7 or prothrombin time (PT) >15 seconds
Age >75 years
Diabetic retinopathy

SBP: systolic blood pressure; DBP: diastolic blood pressure; CPR: cardiopulmonary resuscitation.

* The American College of Cardiology suggests that select patients with stroke may benefit from thrombolytic therapy within 4.5 hours of the onset of symptoms.

Graphic 95035 Version 4.0

Frostbite arthropathy

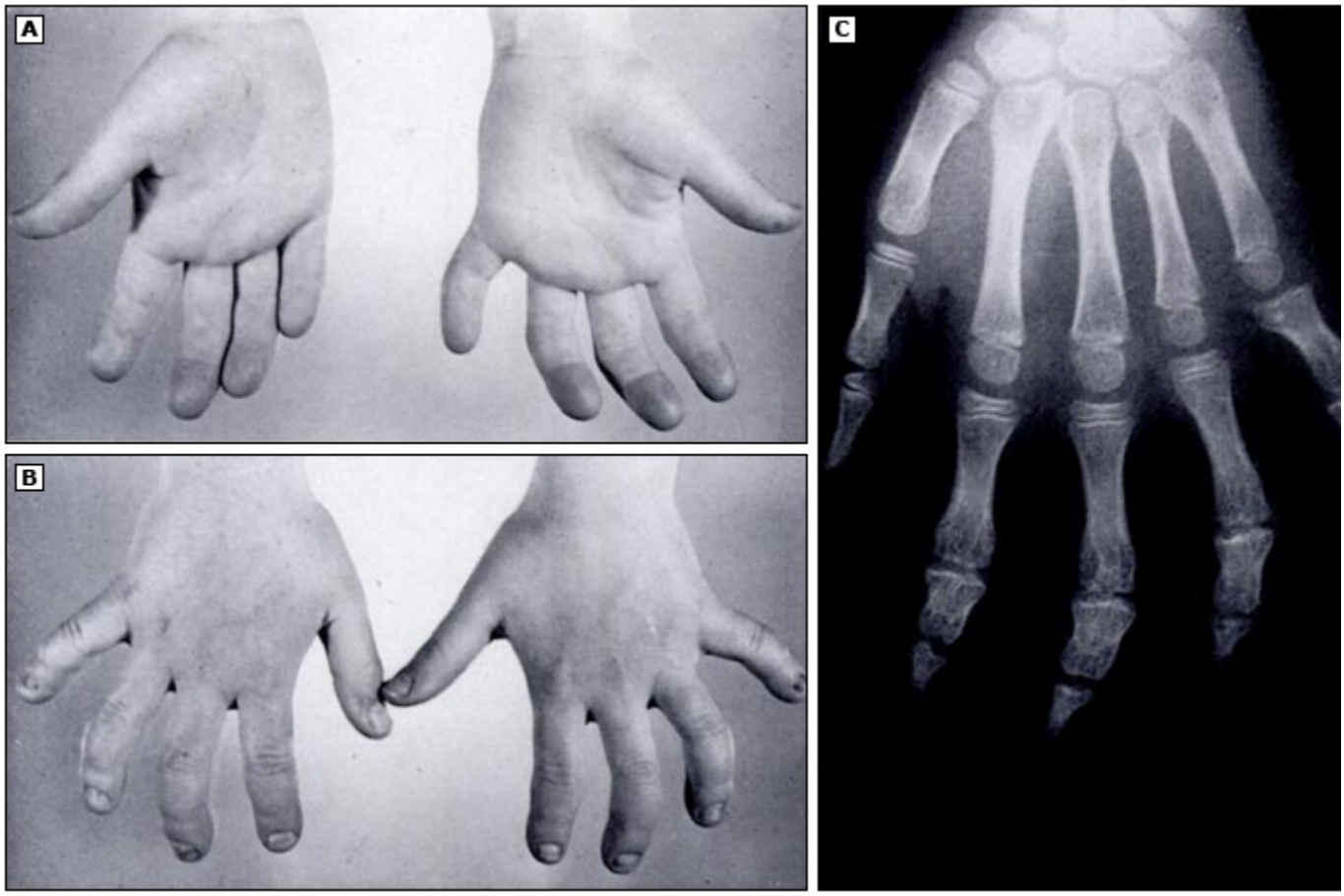


The photograph above (image A) from 2019 shows the hands of a 35-year-old man who sustained severe frostbite in 2002. The left index finger was amputated due to sequala. Progressive swelling of all the remaining proximal interphalangeal joints began in 2012, but the thumbs were spared. The AP radiograph of the hands (image B), also taken in 2019, shows severe degenerative, arthritic changes involving the proximal and distal interphalangeal joints of both hands.

AP: anteroposterior

Graphic 130505 Version 1.0

Frostbite sequelae in fingers: Radial deviation with flexion deformities



The photographs (panels A and B) and plain radiograph (panel C) above are taken of a 12-year-old girl wh sustained severe frostbite at 2 years.

Panel A: Photographs taken soon after thawing.

Panel B: Photographs show radial deviations of the 2nd (index finger) through 4th (ring finger) distal and middle interphalangeal joints of both hands with mild flexion deformities.

Panel C: Plain radiograph of the patient's left hand showing absence of the epiphyses of the distal and middle phalanges of all fingers of the 2nd through 4th fingers.

Graphic 129145 Version 2.0

Contributor Disclosures

Ken Zafren, MD, FAAEM, FACEP, FAWM No relevant financial relationship(s) with ineligible companies to disclose. **C Crawford Mechem, MD, FACEP** No relevant financial relationship(s) with ineligible companies to disclose. **Daniel F Danzl, MD** No relevant financial relationship(s) with ineligible companies to disclose. **Michael Ganetsky, MD** No relevant financial relationship(s) with ineligible companies to disclose.

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