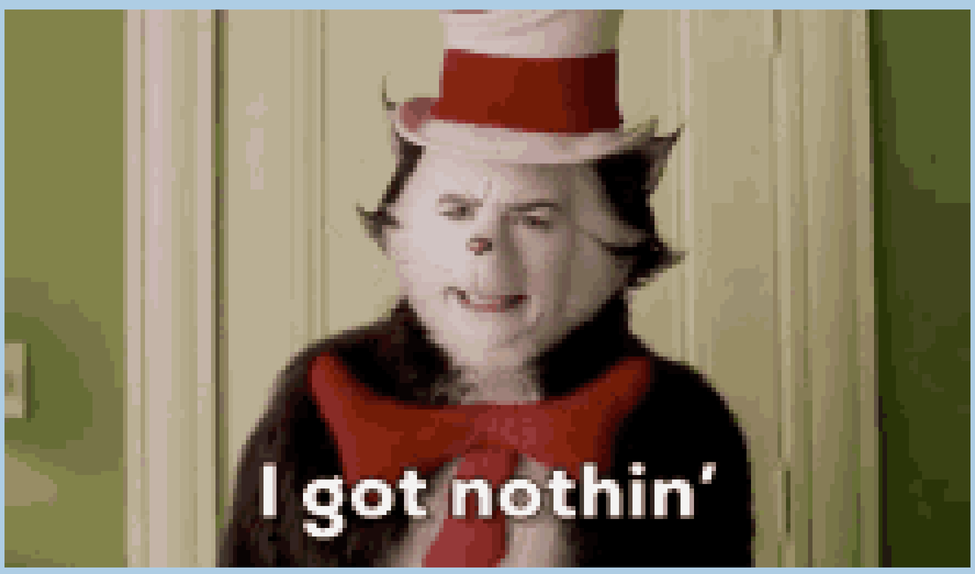
Time to defrost:
Review of frostbite injuries

Disclosures



Objectives

01 Participants will be able to define frostbite.

02 Describe the pathophysiology of frostbite

03 Operate the clinical tool used to grade severity of frostbite.

04 Identify elements of the non-pharmacological mgmt of frostbite

05 Identify elements of the pharmacological mgmt of frostbite

06 Post-injury care

Wilderness
Medical
Society

Developed by the British Columbia Provincial Nursing Skin & Wound Committee in collaboration with NSWOCs/WCs from:

CANADIAN FROSTBITE CARE NETWORK

PUBLIC HEALTH PROFESSIONALS RESOURCES ABOUT CFCN CONTACT

FROSTBITE PATHOPHYSIOLOGY
RECOGNIZING FROSTBITE
MANAGING FROSTBITE
FROSTBITE CLINICAL PRACTICE GUIDELINES AND CARE PROTOCOLS
CONNECT WITH A FROSTBITE CARE PROVIDER

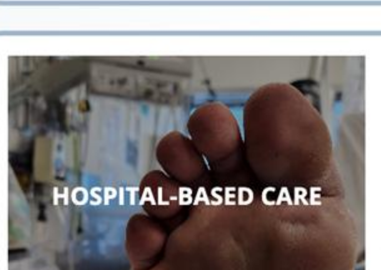
PRE-HOSPITAL CARE
HOSPITAL-BASED CARE
POST INJURY CARE

Managing frostb

PRE-HOSPITAL CARE

…JURY

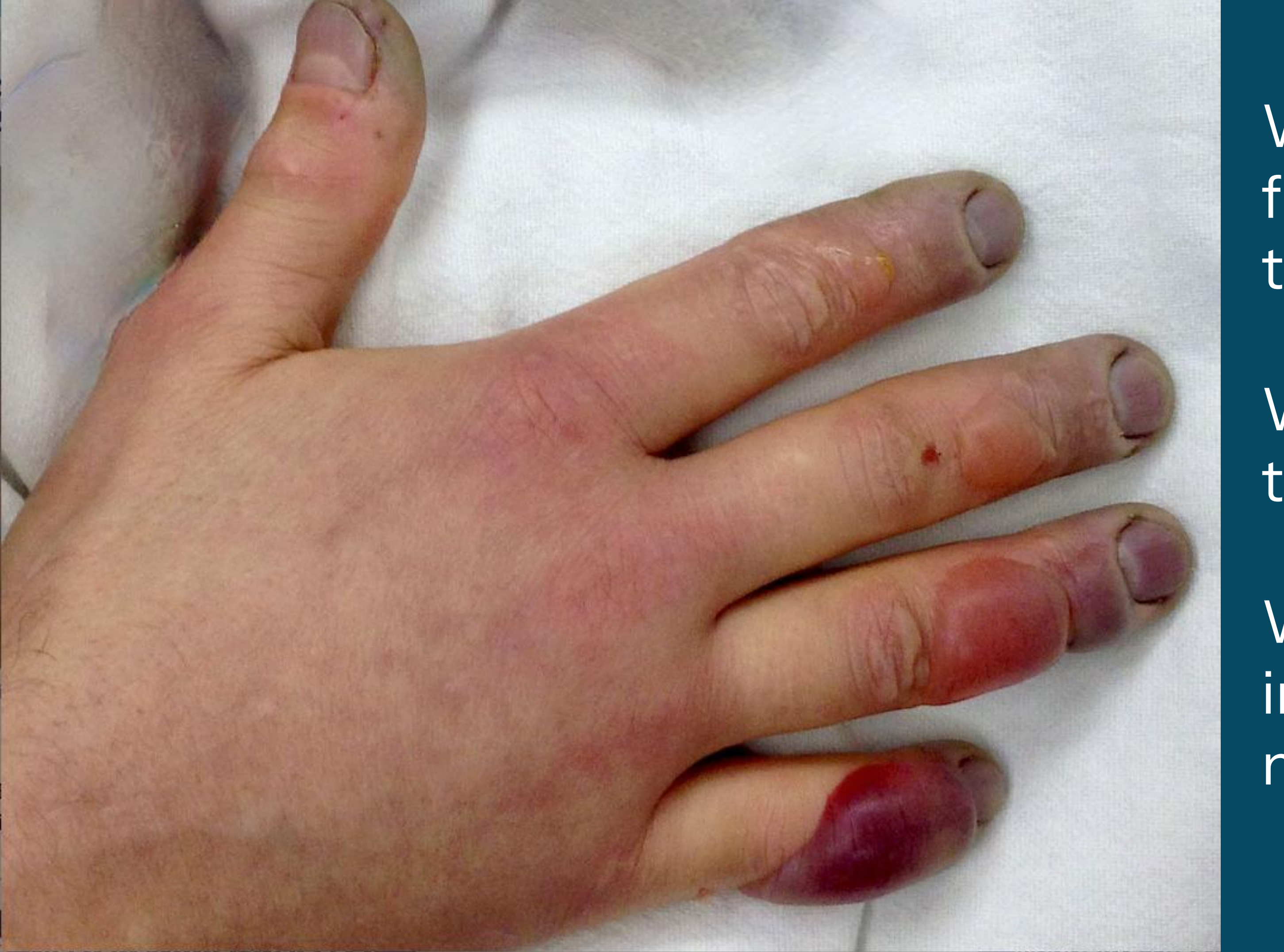
Get out of the cold. Prioritize hypothermia treatment. Remove any constricting, clothing, footwear, or jewelry. Consider early treatment with ibuprofen or aspirin, and aloe vera. Make a rewarming decision: if less than 2 hours from advanced care do not rewarm on site.



PREVENTING AMPUTATION

Rapidly rewarm in water (36-40°C). Minimize warm ischemia time, avoid delays in advanced treatment when indicated. Grade the injury (clinically, consider bone scan/angiography). Begin treatment based on injury grade: antithromboxanes (aloe vera, Ibuprofen), prostacyclin (iloprost) and/or thrombolysis, consider hyperbaric oxygen if available, initiate wound care.

https://frostbitecare.ca/health-professionals/managing-frostbite/hospital-based-care



What grade of frostbite is this?

What does that change?

What is the initial management?

01 Defining frostbite

- *Frostbite is a condition caused by freezing of the skin and ultimately, if it progresses, freezing of deeper tissues.
- Frostbite is an extremity threatening injury while hypothermia is a life threatening injury
- Ranges from reversible changes upon rewarming to irreversible cell damage
- Typically affects the face, ears, fingers and/or toes.

Defining frostbite

Suspect frostbite in a patient who presents with a history of :

- Exposure to temperature < 0 degrees Celsius for several minutes to hours
- Inadequate protection (i.e. – exposed skin, thin/damp clothing, clothing not warm enough)
- Pain/tingling/loss of sensation in their digits or extremities.
    - *The skin may appear normal or pale and there may be a line of demarcation where the frostbite progressed to. *

02

Pathophysiology of frostbite

Two main mechanisms lead to tissue damage in the acute phase of frostbite injuries:

1. immediate cellular death during cold exposure
2. progressive dermal ischemia leading to deterioration and necrosis.

During freezing extra and intra-cellular ice crystal formation may lead to cell damage and circulatory stasis. A cascade of events occur at this point leading to further cell damage, thrombosis and vasoconstriction. Thrombosis and vasoconstriction are mediated by metabolites of the arachidonic acid pathway including thromboxane A2 (TxA2), prostaglandin F2α and thromboxane B2. Leads to intravascular coagulation, sustaining reperfusion injury and potentially causing microthrombi showers that damage the microvasculature, along with thrombus formation in larger vessels

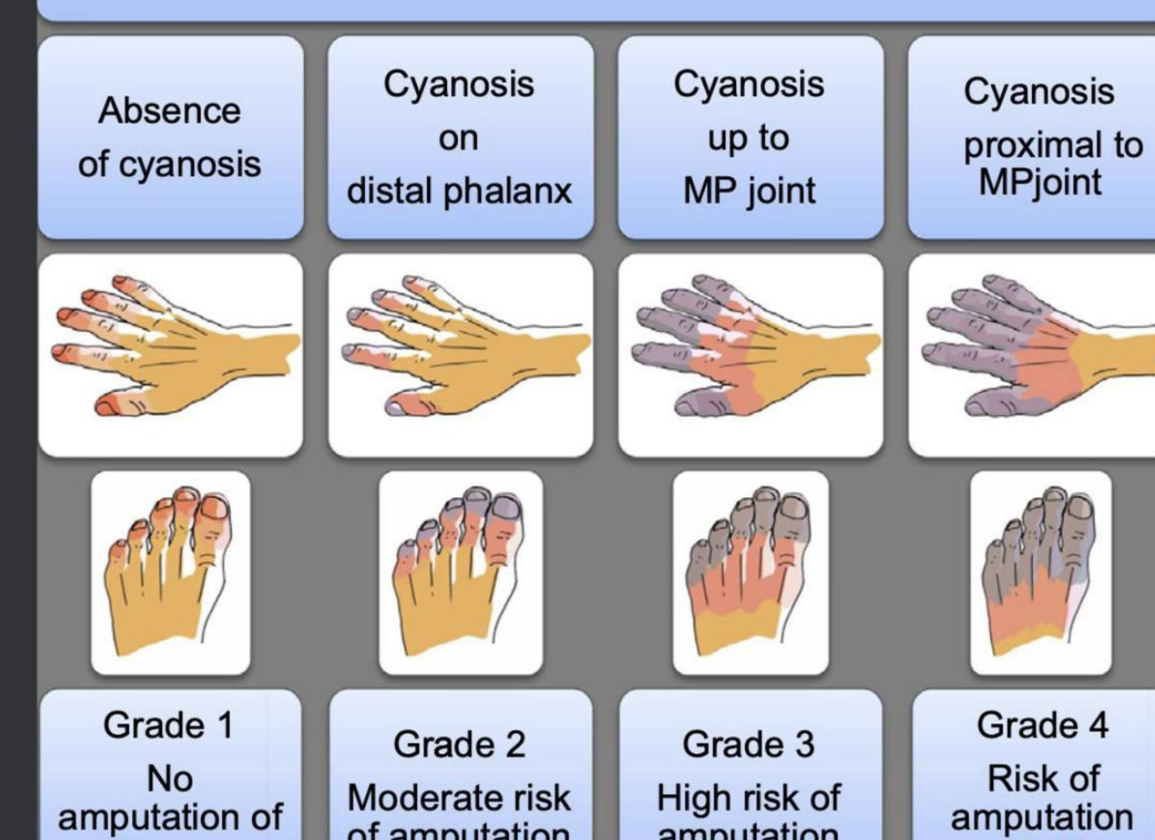
- Reperfusion injury can lead to the generation of radical oxygen species and an inflammatory reaction, further damaging tissues.

Grading severity

Frostbite can be classified by both its depth and by grade, best applied **after the skin has been rewarmed**, as the tissue will appear different before and after rewarming. If skin looks and feels normal after rewarming to normal temperatures, frostbite is unlikely. The appearance of frostbite will also evolve over time with the most severe changes such as greyish skin or blisters taking 24-48h to appear.

Many healthcare providers use the Cauchy grading scale:

- correlate well with findings on bone scan and amputation rates.
- It reflects the fact that as the cyanotic injury progresses proximally the risk of amputation increases.
    - provides early prognostication for the risk of a functionally important amputation
    - easiest for clinicians to use to guide therapy.

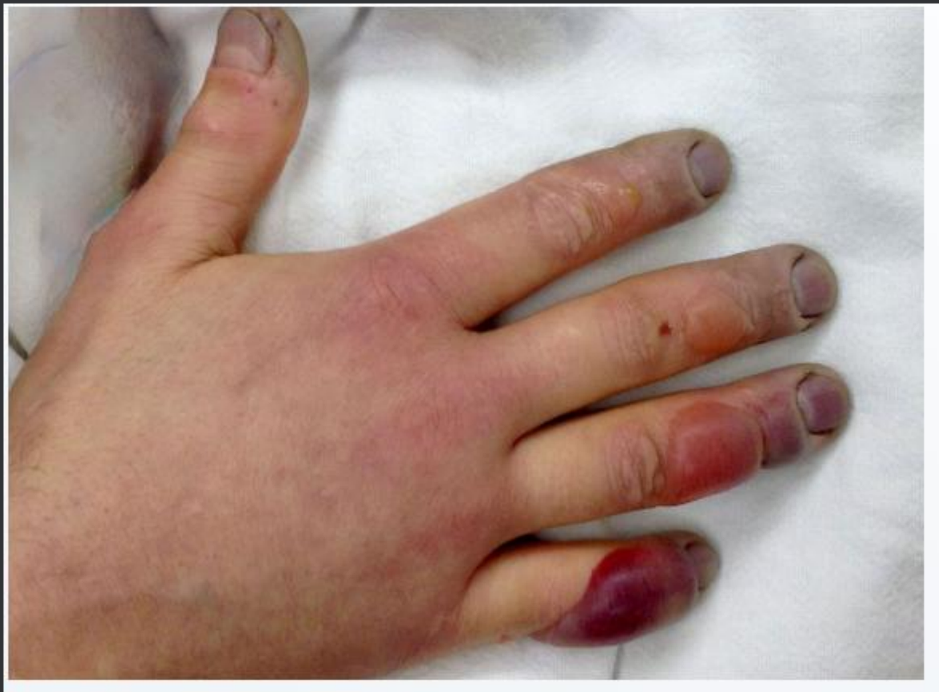


Grading severity of frostbite after rewarming
Absence of cyanosis
Cyanosis on distal phalanx
Cyanosis up to MP joint
Cyanosis proximal to MPjoint
Grade 1
No amputation of bone
Grade 2
Moderate risk of amputation
Grade 3
High risk of amputation
Grade 4
Risk of amputation 100%

Table 1. Cauchy 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 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 $\pm$ systemic involvement $\pm$ sepsis
	No sequelae	Fingernail sequelae	Functional sequelae	Functional sequelae

Reproduced from: Cauchy E, Chetaille E, Marchand V, Marsigny B. Retrospective study of 70 cases of severe frostbite lesions: A proposed new classification scheme. *Wilderness Environ Med.* 2001;12(4):248–255.



Click image for larger view.

Grading injuries based on the most proximal level of cyanosis or hemorrhagic blistering is demonstrated in this photo.

Thumb: The thumb is clearly a grade 2 with cyanosis involving only the distal phalanx.

Index and long finger: Both the index and long fingers have cyanotic changes abutting the middle phalanx, so a certainly a Grade 2 and arguably a Grade 3.

Ring finger: The ring finger is more convincingly a grade 3 with cyanosis and likely hemorrhagic blister into the middle phalanx.

Fifth finger: The fifth finger has unquestionably cyanosis and hemorrhagic blistering into the middle phalanx; clearly a grade 3 injury.

Overall, the above injury is best assessed and treated as a Grade 3 injury based on the most severe extent of injury.

03 Grading severity

- Angiography
- Bone scan
- SPECT/CT

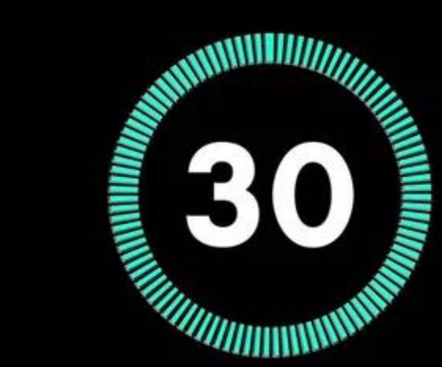
Only recommended by one of 3 major resources- WM (Weak recommendation, low-quality evidence.)

Non-pharmacological mgmt

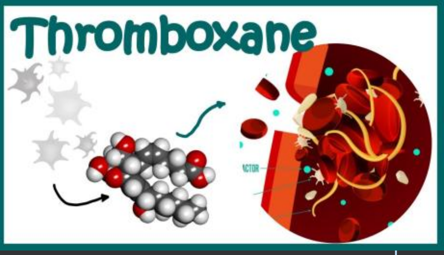
Rapid rewarming with warm water bath immersion: better outcomes than slow rewarming. Water temp should be between 37 and 39 C.

- Rewarming is complete when involved part is red/purple and becomes soft and pliable to touch (approx 30min)
- Allow to air dry/ blotting technique (avoid rubbing)

Spontaneous/passive thawing: a good option while in the field if rapid rewarming not available



04/05 Non-pharmacological/pharm mgmt



The role of thromboxanes in frostbite was identified by Heggers and al, who aspirated blisters of frostbite patients and found high concentrations of thromboxanes:

- Thromboxanes promote vasoconstriction and clot formation
- Prostacyclin is believed to be beneficial to frostbite by promoting vasodilation and inhibiting clot formation.
    - Iloprost, as a synthetic prostaglandin analogue, may mitigate this loss.

As known vasoconstricting agents an antithromboxane protocol was thought to be of value and was validated in a case control study in the 1980s demonstrating a decreased amputation rate relative to historic controls.

Thrombolytics or recombinant tissue plasminogen activators (rtPA) are also used for local fibrinolysis and prevents enlargement of blood clots in frostbitten extremities. *Because fibrinolysis can have a procoagulant effect (clot extension and reformation), anticoagulants such as unfractionated heparin (UFH) and low-molecular weight heparins (LMWH), have been used as adjunctive therapy in thrombolytics protocols.*

04 Non-pharmacological mgmt

Blisters:

Current approach -(weak recommendation, low quality evidence)

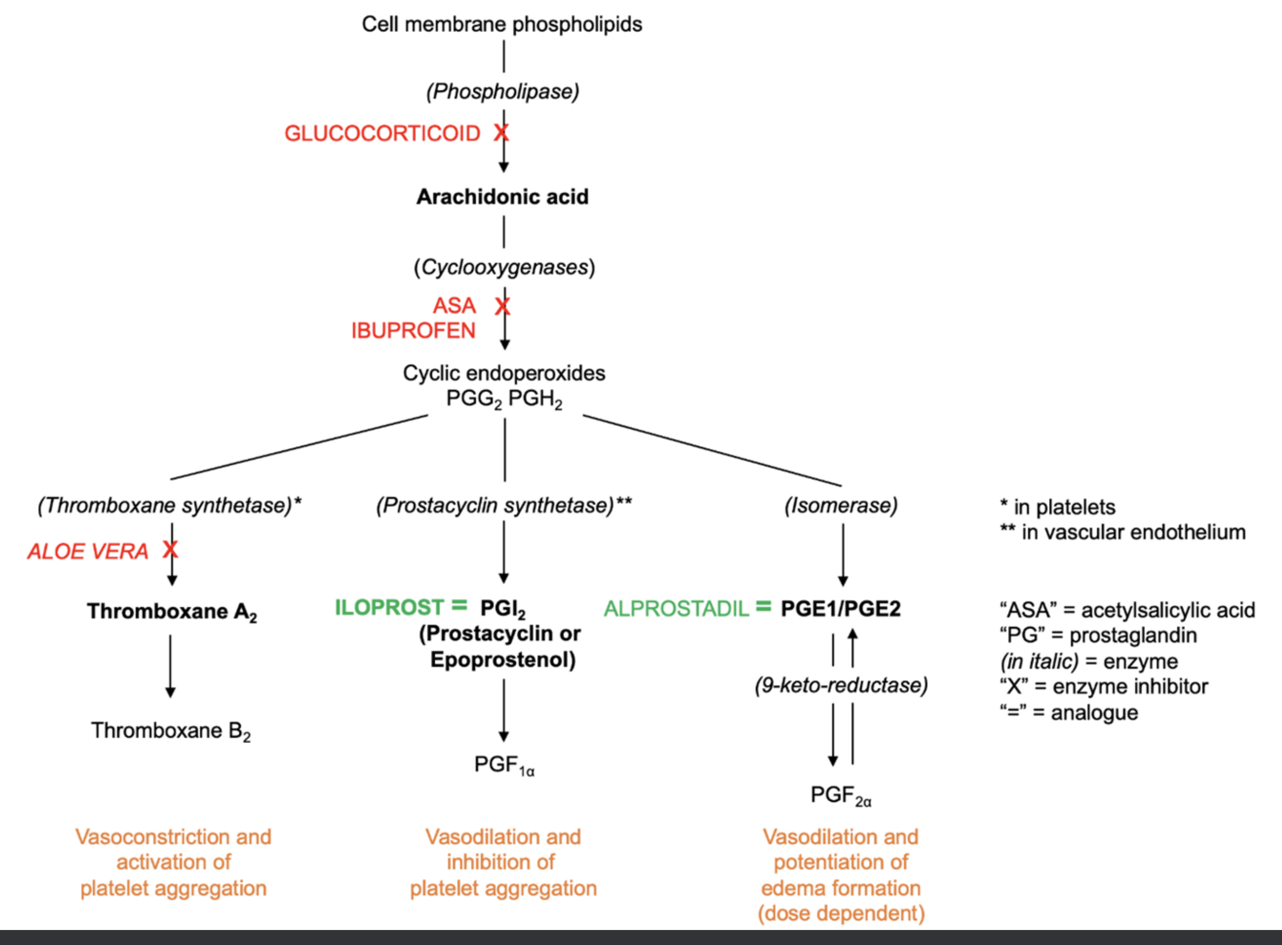
Clear blisters which may harbour thromboxanes may be gently aspirated or debrided if beginning to fall apart. Hemorrhagic blisters are a sign of a deeper injury and are best left alone unless inhibiting joint movement.

Fasciotomy:

- Thawing results in reperfusion of ischemic tissue- sometimes results in elevated pressures within closed soft-tissue compartments.

Compartment syndrome clinically manifests as tense, painful distention with reduced movement and sensation.

If elevated compartment pressures are present, prompt surgical decompression is indicated for limb salvage.


Cell membrane phospholipids
(Phospholipase)
GLUCOCORTICOID X
Arachidonic acid
(Cyclooxygenases)
ASA X
IBUPROFEN
Cyclic endoperoxides
PGG_2 PGH_2
(Thromboxane synthetase)*
(Prostacyclin synthetase)**
(Isomerase)
* in platelets
** in vascular endothelium
ALOE VERA X
Thromboxane A_2
ILOPROST = PGI_2
(Prostacyclin or
Epoprostenol)
ALPROSTADIL = PGE1/PGE2
"ASA" = acetylsalicylic acid
"PG" = prostaglandin
(in italic) = enzyme
"X" = enzyme inhibitor
"=" = analogue
(9-keto-reductase)
Thromboxane B_2
$PGF_{1\alpha}$
$PGF_{2\alpha}$
Vasoconstriction and
activation of
platelet aggregation
Vasodilation and
inhibition of
platelet aggregation
Vasodilation and
potentiation of
edema formation
(dose dependent)

Pharmacological mgmt

Iloprost (potent vasodilators):
- inhibiting platelet aggregation, down regulation of lymphocyte adhesion to endothelial cells and may have fibrinolytic activity

-In the absence of large-scale randomized trials and in light of available evidence, intravenous iloprost should be considered a first-line therapy for Grades 3 and 4 frostbite <48 h after thawing, and possibly for up to 72 hours

-The optimal duration for iloprost therapy has not been established. Clinical reports vary in duration from one day to 48 days, with most reports using 5 to 8 days. Considering the lack of robust data, a reasonable approach is to use iloprost for 5 to 8 days,

Thrombolytic therapy: either IV or intra arterial can be considered for severe frostbite (Cauchy grade 3 or 4) within 24hrs of injury

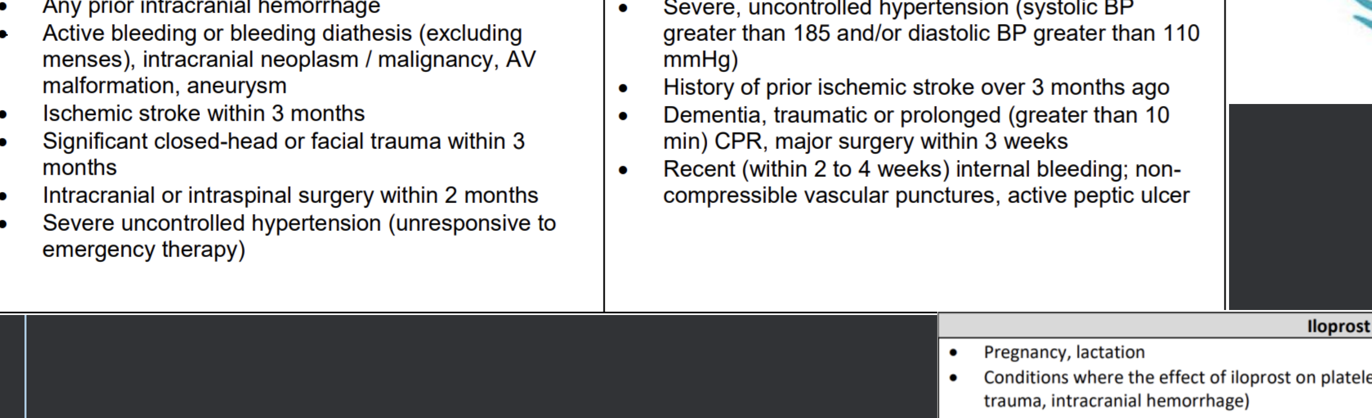
-Evidence is better if administered within 12 hrs

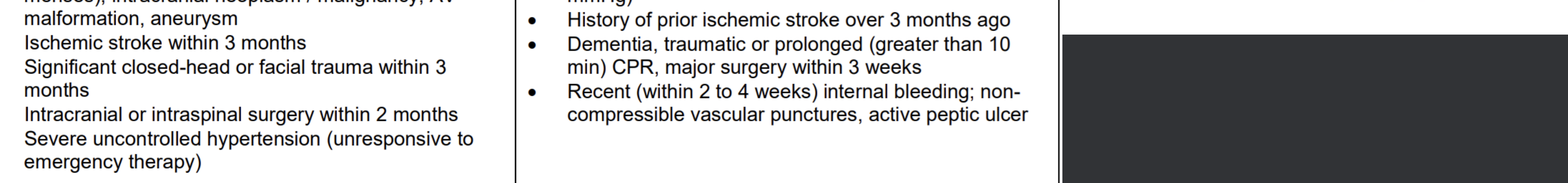
-No RCT's on this topic, only retrospective: found a risk reduction of 31% in digital amputation rates

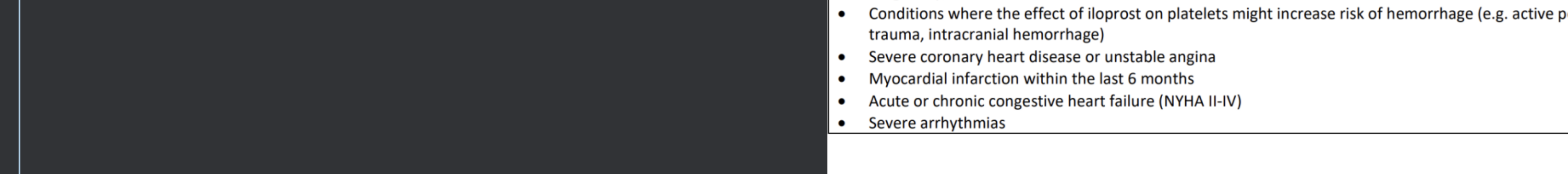
-to be considered for patients who do not have access to centers with iloprost (some use in addition to)

THROMBOLYTIC THERAPY

ABSOLUTE CONTRAINDICATIONS (Do **not** use if any of the following are present)	RELATIVE CONTRAINDICATIONS
➢ Hypersensitivity to tenecteplase or any component of the formulation • Any prior intracranial hemorrhage • Active bleeding or bleeding diathesis (excluding menses), intracranial neoplasm / malignancy, AV malformation, aneurysm • Ischemic stroke within 3 months • Significant closed-head or facial trauma within 3 months • Intracranial or intraspinal surgery within 2 months • Severe uncontrolled hypertension (unresponsive to emergency therapy)	• History of chronic, severe, poorly controlled hypertension • Severe, uncontrolled hypertension (systolic BP greater than 185 and/or diastolic BP greater than 110 mmHg) • History of prior ischemic stroke over 3 months ago • Dementia, traumatic or prolonged (greater than 10 min) CPR, major surgery within 3 weeks • Recent (within 2 to 4 weeks) internal bleeding; non-compressible vascular punctures, active peptic ulcer







Iloprost contraindications
• Pregnancy, lactation • Conditions where the effect of iloprost on platelets might increase risk of hemorrhage (e.g. active peptic ulcers, trauma, intracranial hemorrhage) • Severe coronary heart disease or unstable angina • Myocardial infarction within the last 6 months • Acute or chronic congestive heart failure (NYHA II-IV) • Severe arrhythmias

Iloprost special precautions
• Surgery should not be delayed in patients requiring urgent amputation (e.g. in infected gangrene) • Iloprost elimination is reduced in patients with hepatic dysfunction and in patients with renal failure requiring dialysis • In patients with low blood pressure care should be taken to avoid further hypotension and patients with significant heart disease should be closely monitored • Monitor for possible orthostatic hypotension in patients getting up from the lying to an upright position after the end of administration • For patients with a cerebrovascular event (e.g. transient ischemic attack, stroke) within the last 3 months a careful benefit-risk evaluation should be undertaken • Currently only sporadic reports of use in children and adolescents are available • The paravascular infusion of undiluted iloprost can lead to local changes at the injection site • Oral ingestion and contact with mucous membranes must be avoided. On contact with the skin, iloprost may provoke long-lasting erythema

05 **Pharmacological mgmt**

Nsaids

Ibuprofen 600mg every 6 hours for 5 days (Do NOT give if tenecteplase and enoxaparin ordered)

-American guidelines call for BID dosing

- Improved frostbitten tissue survival in an animal study
- Prevented significant tissue loss in one observational study conducted in patients in Chicago.
- Case-controlled study in Detroit, patients treated with ibuprofen as part of a protocol had less amputation and reduced hospital length of stay
- Literature with slight preference of Ibuprofen over aspirin but no head-to-head studies

05 Pharmacological mgmt

Antibiotics- for patients with significant trauma, other potential infectious sources, or signs and symptoms of cellulitis or sepsis.

- Not supported by evidence for prevention alone (Not an infection prone injury)

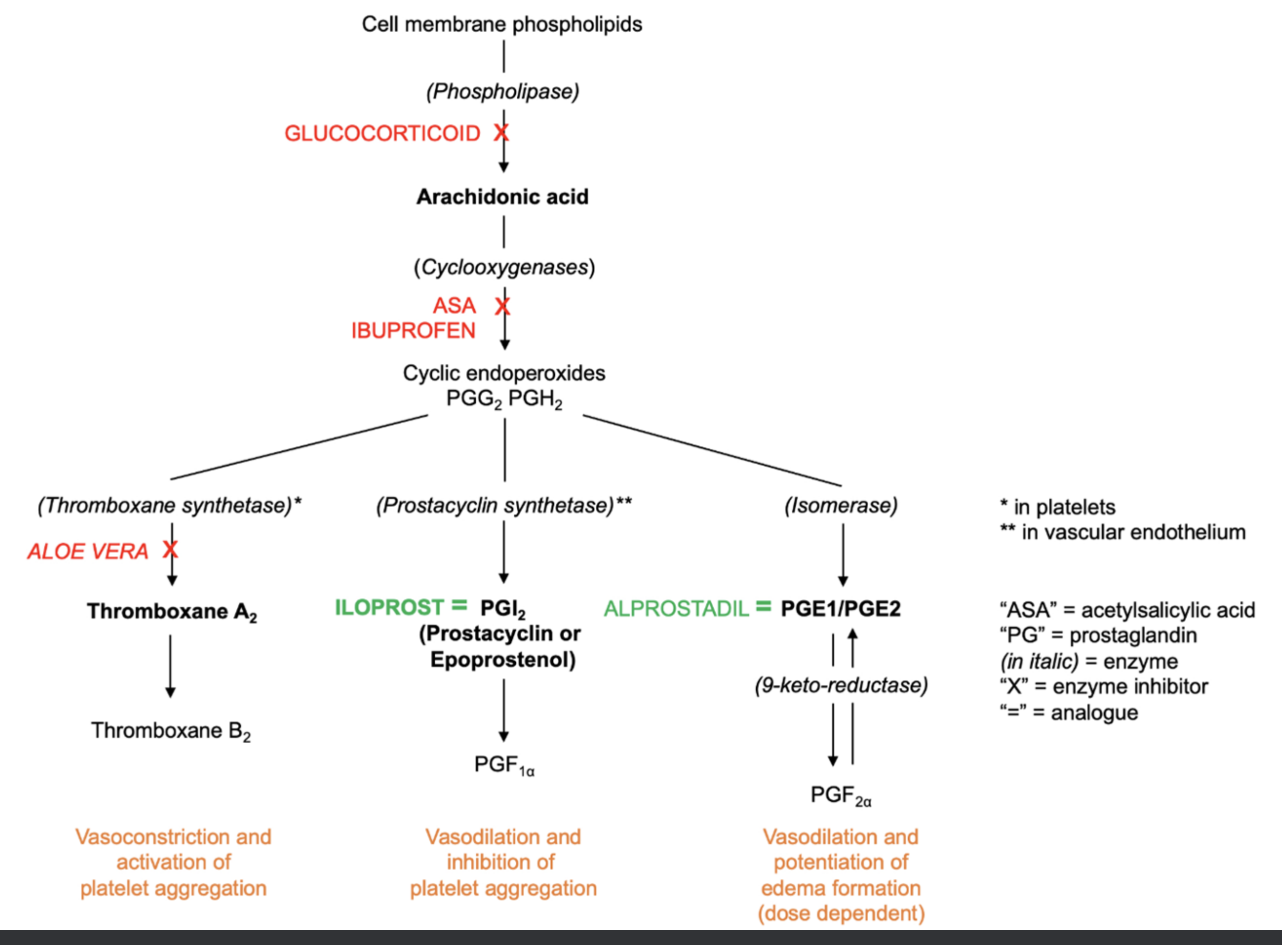
Tetanus prophylaxis should be administered according to standard guidelines.

Heparin: no evidence supports low molecular weight or unfractionated heparin-further studies required

Aloe vera:

- All grades of frostbite
- Q6H-Minimum of 70% aqueous extract of aloe
- Improves outcome by reducing thromboxanes-problem is similar to all topical products- poor penetration. Should be applied before dressings (reapplied with drsg changes)

Drsg: Bulky gauze drsg for protections. Avoid tight circumferential due to anticipated edema



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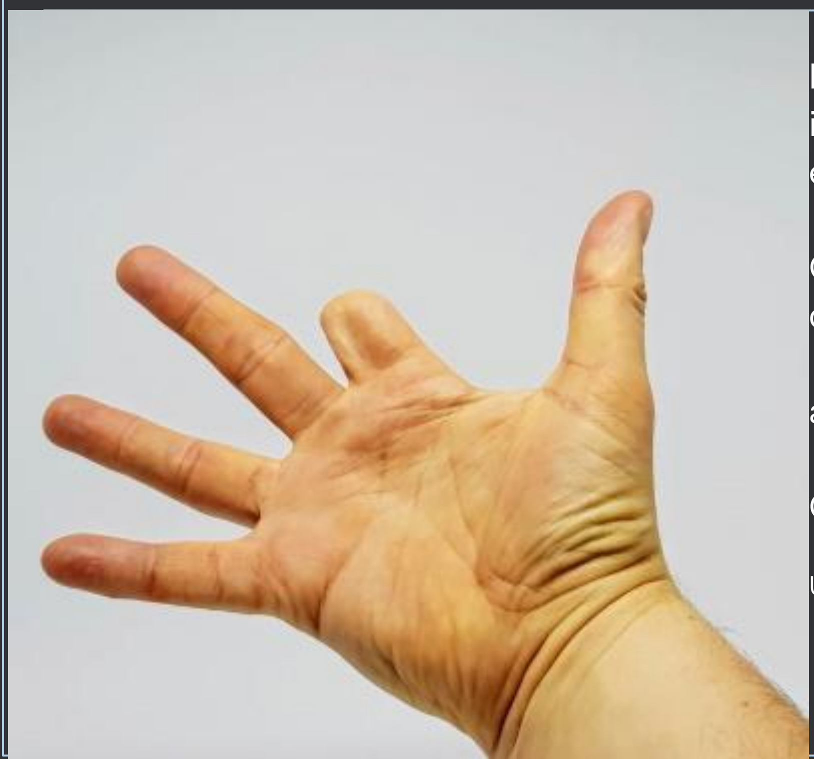
Cyclic endoperoxides
PGG_2 PGH_2
(Thromboxane synthetase)*
(Prostacyclin synthetase)**
(Isomerase)
* in platelets
** in vascular endothelium
ALOE VERA X
Thromboxane A_2
ILOPROST = PGI_2
(Prostacyclin or Epoprostenol)
ALPROSTADIL = PGE1/PGE2
"ASA" = acetylsalicylic acid
"PG" = prostaglandin
(in italic) = enzyme
"X" = enzyme inhibitor
"=" = analogue
(9-keto-reductase)
Thromboxane B_2
$PGF_{1\alpha}$
$PGF_{2\alpha}$
Vasoconstriction and activation of platelet aggregation
Vasodilation and inhibition of platelet aggregation
Vasodilation and potentiation of edema formation (dose dependent)

06 Post-injury care



If the patient exhibits signs and symptoms of sepsis related to infected frostbitten tissue- amputation should be performed expeditiously

Otherwise, amputation should be delayed until definitive demarcation occurs.
Significant morbidity may result from unnecessary and premature surgical intervention

Complete demarcation may take between 1-3 months

Use of imaging??*

06 Post-injury care

Hospital admission/discharge -determined on an individual basis.

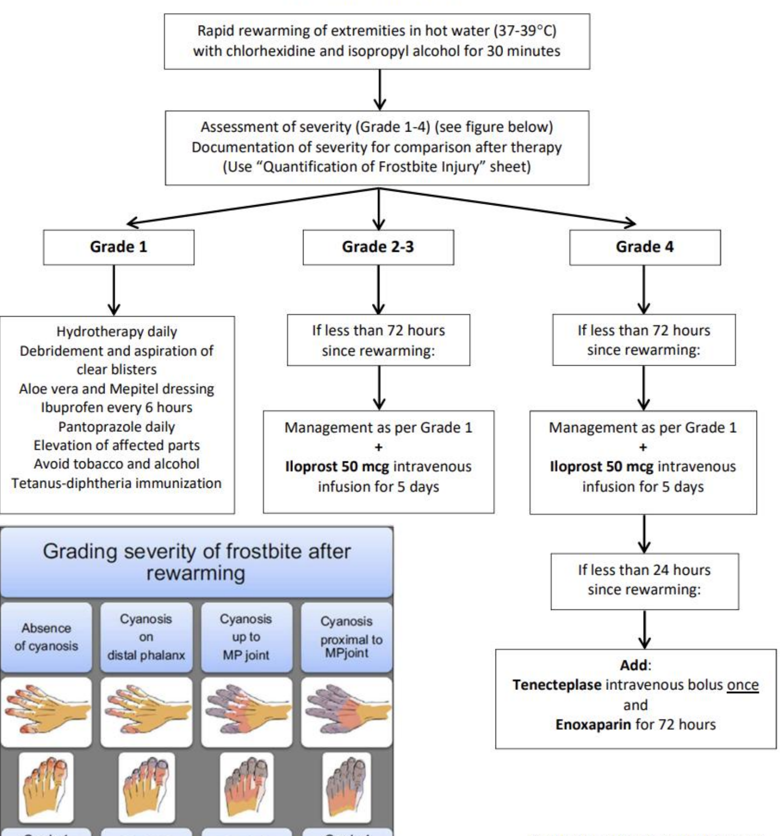
- Factors should include severity of the injury, coexisting injuries, comorbidities, and need for hospital-based interventions (tPA, vasodilators, surgery) or supportive therapy, as well as ease of access to appropriate community medical and nursing support.
- Significant swelling should prompt evaluation for compartment syndrome and admission for observation.
- Patients with superficial frostbite can usually be managed as outpatients or with brief inpatient stays followed by wound care instructions. Initially, deep frostbite should be managed in an inpatient setting.

06 Post-injury care

Wound care:

- Drsg + aloe for at least 5 days
- Avoid maceration (managing web spaces between digits)
- Elevating extremity- swelling
- Hyperbaric oxygen therapy: well studied for wound care but not for treatment of frostbite- no recommendation regarding use
- Hydrotherapy:
  - The water bath supports cleansing of open areas, removal of slough/necrotic tissue, mobility of the joints and comfort.
  - The length of immersion, frequency and timeframe is to be determined by care team, (e.g., 30 min. daily for first 1-2 weeks) based upon the need for wound cleansing, (e.g., the development of eschar), joint mobility and comfort.

FROSTBITE PROTOCOL



You may consult Dr. Alex Poole and Clinical Pharmacist Josianne Gauthier for guidance

Table 3. Summary of initial hospital management of frostbite

1. Treat hypothermia or serious trauma.
2. Rapidly rewarm in water heated and maintained between 37 and 39 °C (98.6 and 102.2°F) until area becomes soft and pliable to the touch (approximately 30 min).
3. Ibuprofen (12 mg kg^{-1} per day divided twice daily).
4. Pain medication (eg, opiate) as needed.
5. Tetanus prophylaxis.
6. Air dry (ie, do not rub at any point).
7. Debridement: selectively drain (eg, by needle aspiration) clear blisters and leave hemorrhagic blisters intact.
8. Topical aloe vera every 6 h with dressing changes.
9. Dry, bulky dressings.
10. Elevate the affected body part if possible.
11. Systemic hydration.
12. Thrombolytic therapy: consider for deep frostbite at the distal interphalangeal joint or proximal if less than 24 h after thawing; use angiography for prethrombolytic intervention and monitoring of progress. Consider intravenous thrombolysis if angiography is not available.
13. Iloprost therapy: consider for deep frostbite to or proximal to the proximal interphalangeal joint, within 48 h after injury, especially if angiography is not available or with contraindications to thrombolysis.
14. Clinical examination (plus angiography or technetium-99 bone scan if necessary) to assist determination of surgical margins. Evaluation by an experienced surgeon for possible intervention.

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10