UDC 616-001.186 616-08 (063)
DOI http://doi.org/10.30978/GS-2023-2-90

ISSN 2786-5584 print
ISSN 2786-5592 online

Methods and pathophysiology of rewarming in case of local cold injury. Literature review

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Nowadays, rewarming of the affected tissues is the primary method of treatment for patients with cold injuries. But the warming manipulation has its own characteristics and limitations, depending on specific circumstances. Untimely and incorrectly performed rewarming can lead to a significant increase in the level of dangerous complications, mortality, and disability. The rewarming strategy is implemented according to one of the two scenarios. If there is a risk of freezing again, the injured area is not actively rewarmed; it is just immobilized, and thermo-insulating bandages are applied. Slow warming with body heat is also acceptable. If the frozen area can be warmed and kept warm without refreezing until the evacuation is completed, a quick warming with warm water or special heating blankets is preferable. Recommendations on the ideal water temperature significantly differ among authors and include a wide range between 37 °C and 43 °C.

The extent of damage to the tissues becomes obvious only after thawing. The traditional classification system of local cold injuries distinguishes four degrees of frostbite. First-degree frostbite presents with superficial damage to the skin; second-degree frostbite involves deep skin damage; third-degree frostbite results in full-thickness skin damage, including the subcutaneous and surrounding tissues; and fourth-degree frostbite causes deep necrosis of the subcutaneous structures. Depending on the extent of damage, patients may experience constant and severe pain during rewarming, so analgesics should be prescribed to relieve it. It is recommended to use topical agents (creams, gels, and ointments) to improve circulation and prevent and treat infection. Tissue necrosis with severe frostbite requires surgical treatment of wounds.

The authors hope that the provided information will be useful to doctors-of-first- contact and in hospital conditions in order to optimize the treatment of local cold injuries.

Keywords
frostbite, local cold injury, pathophysiology, rewarming.

ARTICLE • Received 2023-07-15 • Received in revised form 2023-08-30

Throughout human history, many different methods of rewarming from frostbite have been used. In the 1800s, affected areas were rubbed with substances containing very few calories or thawed in cold water instead of warm water, as there was a belief that cold substances could absorb calories during melting while heat, if applied, could cause rapid development of gangrene. An outdated treatment, slow thawing by rubbing with ice or snow, recommended by Baron de Larrey and considered the standard for more than 100 years, was no longer used [39]. Only in the Second World War did medical professionals start treating military personnel suffering from frostbite by rapidly warming the affected tissues [35]. Employees of Furman University, USA (1947), proved the therapeutic benefit of quickly warming tissues in 40—42 °C water for the management of local cold injuries, and since then this method, with some changes, has become generally accepted in the world [39, 47].

> *The carter, who was running at full speed, shouted to me: «Nose, nose!», some man, grabbing a handful of snow, began to rub my face with all his might, especially my nose. I found this joke not very good.*
> A. Dumas. Fencing Master, 1840.

Snow and ice should not be rubbed into or applied to the frostbitten areas because, firstly, this contributes to even greater freezing of the tissues, aggravating microcirculatory derangements; and secondly, ice crystals damage the affected skin, increasing the risk of infection.

After leaving a cold environment, patients are often able to gradually rewarm on their own, provided that there is no frostbite in the affected area [35].

To date, certain strategies for rewarming tissues have been defined and implemented according to two scenarios [16, 44].

Scenario 1

The frostbitten area can freeze again and is not actively rewarmed. Bandages should only be used if they do not cause any discomfort and do not interfere with the patient's mobility. Bulky, clean, and dry gauze or sterile cotton bandages are recommended to be applied to the frostbitten area and between the fingers. If possible, the frozen limb should not be used for walking or other manoeuvres until proper medical care is provided. While evaluating the affected limb from the point of movement capabilities, the potential for further injury and associated consequences must be taken into consideration in the risk-benefit analysis.

It is not recommended to rub the affected areas [41], except that you can very carefully rub the area of frostbite with a soft woollen glove, but this is rather the exception than the rule. Jewellery and other narrowing and constricting elements (primarily metal) should be removed [39, 41].

If rapid warming under field conditions is not possible or there is a danger of repeated freezing of the tissues, the method of passive slow warming of the cooled limbs using the heat of one's own body or the body of another person is used. A warm hand pressed against a frozen nose, cheek, or chin can change for the better at an early stage. A frozen arm or leg can be warmed by placing it under clothing, directly against the skin under the armpit, or on the stomach of another person [3, 16, 38, 39, 44]. In this case, one should not prevent its gradual spontaneous warming «from the inside outward», which is carried out using thermo-insulating bandages according to O.Ya. Holomidov (1958), who suggested putting a layer of gauze on the affected limbs (from the fingertips to the level 20 cm proximal to the lesion), then a thick layer of cotton, again a layer of gauze, and on top of them, a rubberized fabric. Bandages are applied for at least 12 hours [12, 17, 18].

In comparison to the classic version, the current guidelines for applying thermo-insulating bandages have changed somewhat. Applying them to the affected part of the body or segment of the limb is carried out for a period of at least 24 hours. The bandage should isolate only the areas with a distinct pallor of the skin without capturing the unchanged surface. If this requirement is not followed, the heat from areas with intact blood circulation will penetrate under the bandage, warming the surface tissues affected by the cold, which should not be allowed in any case. The bandages should not be removed until a feeling of warmth appears and sensitivity in the fingers or toes is restored. In this case, the warming of the flooded tissues occurs due to heat transfer with the blood flow from the temperature core, excluding the possibility of the development of the «afterdrop» syndrome, and the vitality of the tissues is restored simultaneously with the restoration of blood circulation. It is important to ensure the immobility of hypothermic fingers and toes, as their vessels become fragile to a large extent and haemorrhages are possible after blood flow is restored. For immobilization, you can use pieces of cardboard, plastic bottles, etc., which are placed on the top of heat-insulating bandages. Immobilization of the hands is carried out in a physiological position, and the ankle-foot area — at a right angle [2, 4—6, 18].

The disadvantage of this technique is the need for a significant amount of material: dressing (cotton) and insulation (rubberized fabric, sacking, etc.).

Currently, many different heat-insulating bandages are offered: dry aseptic thermo-insulating covers and bandages with thermo-accumulating inserts. They also use a thermo-insulating bandage made in the form of a bag made of two layers of cotton fabric and an inner layer of aluminum foil covered with thermo-insulating polystyrene varnish. For thermo-insulation of areas affected by the cold, a thermo-insulating multi-layer container based on porous polyurethane and a double-layer bandage made of polyvinyl chloride film [12, 17] can be used, and the modern method of «wet chamber» is used. The disadvantages of the tool are related to the difficulty of controlling the condition of the affected tissues.

Combined, multi-layered (including foil) shoe covers or mukluks (high fur boots) made of deer or dog skin with fur inside turned out to be the best. Torbases made of deerskin are used only in the regions of the Far North. Combined multi-layer chuns have the advantage of being easily sanitized and reusable.

According to the degree of warming, blood circulation in the distal tissues of the limbs is restored «from the depths» and their temperature and the level of metabolic processes in the cells increase (under this method, the gradual warming of the limbs takes from 5 to 10 hours).

If the affected person arrives with thermo-insulating bandages that have been applied 2—3 hours or more after the cessation of the cold effect, it is advisable not to remove the bandages and to carry out general treatment. After providing first aid, victims with frostbite are evacuated to a multidisciplinary medical facility [2]. In some cases, bandages are removed for 2—3 days after the complete restoration of blood circulation and vital activity of cells, and primary surgical treatment is performed with the closure of postoperative wounds with lyophilized xenoskin [10, 15].

N. B. If the thawed tissue has a chance to freeze again, it is recommended to keep it in a frozen state without heating [45].

N. B. If the affected area has already thawed, rapid warming is impractical [19, 44, 54, 60].

Scenario 2

The frozen area is warmed and kept warm without refreezing until the evacuation is completed. The affected area should not be rewarmed until re-exposure to cold has been ruled out, as alternating freezing and thawing processes can lead to severe thrombosis and ischemia [53]. If the frostbitten tissue is refrozen after thawing, significant cell damage occurs due to the formation of intracellular ice crystals and the sharp release of inflammatory mediators [42]. Rewarming by immersion in a warm water bath can and should be done if adequate resources are available and proper care is over 2 hours away.

It is recommended to avoid other sources of heat (fire, heater, stove, heated rocks) due to the risk of burns.

It has been established that quick warming in a water bath leads to better results than a slow one. Rewarming should be done only if the patient can keep the injured area thawed and warm.

The water temperature should be at the level of 37—39 °C in the presence of a thermometer. In the absence of a thermometer, it is recommended to determine the temperature by placing an uninjured hand for at least 30 seconds to confirm that the water temperature is acceptable and there is no risk of burns. Adding an antiseptic solution (povidone-iodine, chlorhexidine) to the water for warming has theoretical advantages in reducing bacterial infection of the skin. However, there is no evidence for this practice. Adding an antiseptic solution to water when rewarming can reduce the risk of inflammation of the subcutaneous tissue if there is severe swelling in the affected limb. During the warming-up, it is recommended to prescribe anaesthetics (opioid analgesics or non-steroidal anti-inflammatory drugs). Quick warming is recommended. If this method is not possible, it is possible to use the spontaneous or slow warming method, characterized by moving the victim to a warmer place (tent, building) or warming due to adjacent heat (from the patient or caregiver). It is recommended to raise the warmed limbs above the level of the heart, which will reduce the formation of edema [16, 44].

Warming near an open flame, stove, or other heaters for a long time should be avoided, as frostbitten tissues usually become numb and the victim does not feel extremely high temperatures, which can cause an iatrogenic burn [35]. In the field, you can use special thermochemical heating packs, couplings, etc., which are made with the prevention of burns in mind.

At the pre-hospital stage or later in the hospital, when the limb is still frozen but the danger of repeated tissue freezing has passed, rapid rewarming is strongly recommended, which is the first and most important stage of frostbite treatment [3, 16, 24, 28, 44, 51].

Despite current modern standards, some authors continue to adhere to outdated ideas about the harmfulness of rapid heating because, in their opinion, uneven heating is the cause of irreversible damage since rapid external heating leads to an increase in the temperature of the upper layers of tissues and the restoration of tissue metabolism without accompanying recovery blood flow [14], and at the same time, the warming of deeper tissues occurs more slowly, which prevents the restoration of blood circulation; for this reason, the warmed surface tissues do not get nutrition and die. Therefore, the authors believe that in the practical field of providing emergency aid to patients affected by the cold, the main thing is not to commit the rapid warming of the frozen parts of the body because they are adversely affected by warm air, warm water, etc. In their opinion, the best of all would be to warm the limb in warm water, and the temperature of the water should be raised from room temperature (18—20 °C) to body temperature (37 °C) within 20—30 minutes [5, 7, 14]. Other authors suggest the possibility of slowly warming the affected limb only in cases of freezing [53].

According to the outdated standards, it was slow rewarming that was used to prevent the «afterdrop» syndrome, which was really of serious importance in general unintentional hypothermia and was described in detail in our previous works [8, 9]. For quite a long time, it was believed that with rapid rewarming, blood circulation is first restored in the surface layers of tissues, as a result of which it carries cooled blood to the «temperature core of the limb», lowering its temperature, as a result of which it turns from viable to non-viable. But this opinion has been refuted by numerous modern studies because iatrogenic hypothermia of the core during rapid rewarming practically does not occur. Although there is no doubt that the blood circulation in the affected limb is impaired, in consequence of the reflex spasm of blood vessels under prolonged exposure to cold, there is almost no blood in the vessels of the surface layers of the tissues (even more so, dangerously chilled ones).

Numerous studies have shown that the least harmful for tissues is the rapid warming of a frozen limb in warm water with a temperature of 37—39 °C. Slow, gradual rewarming showed the worst results. Higher temperatures should be avoided, as they cause more pain and can lead to burns. Conversely, slow rewarming using lower water temperatures can cause ice crystals to fuse and thus increase structural tissue damage.

It's hard to warm your hands when your soul is still trembling.

M. Zusak, Bridge of Clay, 2004.

At the hospital stage of treatment, the priority is to raise the patient's body temperature. As soon as the core temperature exceeds 34 °C, the local frostbite treatment can be started [53]. After successful correction of the general hypothermia, attention should be switched to local defrosting, and rapid local rewarming should be started. It is recommended to use a water bath with a constant temperature [35] or large containers with circulating water, or a hydromassage bath with the addition of an antiseptic solution (povidone-iodine or chlorhexidine) [30, 34, 41]. The use of oxidizers (potassium permanganate and dyes) is not recommended.

The immersible circulation device «Sous vide» is able to quickly and constantly maintain the temperature of the liquid at a level of 40 °C [56].

If only one limb is thawed, it is necessary to warm both at the same time [30, 34].

During heating, convection movement of water should be ensured, and its temperature should be maintained within the specified level by heating or adding new portions, since the temperature of the water will decrease in the process of thawing the limb. As a result, rescuers should carefully monitor the water's temperature using a thermometer or by feeling it with their hands, and they should carefully and continuously heat the water to the desired temperature. Circulation of warm water around frostbitten tissues will help maintain the required temperature and relieve the patient's pain [30, 34, 35]. Frostbitten skin should not be allowed to touch the walls of the container in which rewarming is carried out in order to prevent tissue trauma. When warming, non-stressful movements in the warming limb will be useful; it is not necessary to massage the tissues [30, 34].

Regarding the temperature of the water for rapid warming, the opinions of researchers diverged. So various authors recommend: 37—38 °C [4, 56]; 38 °C [30, 34]; 37—39 °C [11, 16, 19, 23, 24, 29, 38, 42, 44, 48, 53, 58]; 37—40 °C [21, 41, 52]; 40 °C [56]; 37—42 °C [35]; 37—44 °C [49]; 40—42 °C [39, 47, 55, 59]; 40—43 °C [37].

However, despite the difference in recommended temperature levels, in case of local cold injury, most modern scientists unanimously emphasize the expediency of quickly warming the damaged structures.

Usually, 15 to 30 min are enough for the warming process. The time required for rewarming depends on the extent of the injury but usually lasts from 15 to 60 min [38].

At Providence Hospital in Anchorage (Alaska), Hubbard or Arjo baths are used, in which the entire patient is immersed in water at a temperature of 40—42 °C. This method is used with good results both for peripheral cold injuries and general hypothermia and for a combination of these conditions [39, 47].

The use of a perfused blanket (45—46 °C) on a single forearm and hand in a subatmospheric environment (from –30 to –40 mm Hg) resulted in a 10-fold increase in the rate of rewarming (13.6 °C/h in 5—15 min) in comparison with only external heating (1.4 °C/h). Heating of the limbs under negative pressure caused a rapid cessation of shivering, increased thermal comfort, and a dramatic increase in core temperature to normal values within 15 min [1, 25].

During the cooling phase, microcirculation stasis occurs, which leads to tissue ischemia. Partial thawing and swelling from melting ice originate from warming, depending on the depth of freezing of the skin, nerves, fat, and muscles; bone tissue, nerves, and cartilage may be involved. Loss of mitochondria can occur in muscle cells. Epiphyseal cartilage (involved in the growth of long bones) is particularly sensitive to damage from freezing [38].

The consequences become obvious in the process of warming [18, 39, 46]:

- the temperature rises;
- local inflammatory changes begin with the development of edema, vasodilation, and vascular stasis, the clinical manifestations of which are the formation of blisters and severe pain, which precede the aggregation of platelets and thrombosis;
- adhesion of neutrophils to the damaged endothelium of capillaries.

Between 5 minutes and 1 hour after warming, deposits of emboli are detected in arterioles and venules, and obstruction of blood flow leads to ischemia of surrounding tissues. Thrombosis causes vessel occlusion, damage to endothelial cells, and the formation of oxygen-free radicals [26].

The main pathological processes in the tissues develop during their external heating in the early reactive period, when an increased need for oxygen appears, which coupled with the lack of adequate blood circulation in the limbs, leads to severe hypoxia and necrobiotic changes (reperfusion syndrome). When warming, vascular spasm is replaced by paretic expansion, stasis, and a sharp deterioration of blood flow both in the microcirculatory channel and in the main vessels due to the aggregation of red blood cells and thrombosis [33]. At the same time, the need for oxygen and metabolism in tissues that are no longer in a state of hypothermia increases. This contributes to the formation of deep necrosis a few days after the injury, the prevalence of which increases with thrombosis of the main vessels.

Cellular oxidative stress and inflammation associated with ischemia-reperfusion injury may contribute to further cellular injury and necrosis. Violation of normal blood flow in the vessels due to microvascular thrombosis leads to cellular anaerobic metabolism and subsequent tissue hypoxia. During reperfusion, inflammatory cytokines (thromboxanes, prostaglandins) are released during rewarming, which increases tissue damage. Endothelial cells are affected faster than skin, fat, or connective tissue [38]. These combined factors additionally stimulate the increased release of mediators of the inflammatory process: prostaglandin PGF2 and thromboxane A2 (TxA2). Since they can be considered physiological antagonists of each other, it has been suggested that an increase in the ThA2/PG2 ratio may lead to increased platelet aggregation and thrombosis, and thus achieving a balance between their physiological levels is critical to reducing subsequent tissue necrosis under frostbite. [26, 32, 49]. Neutrophil activation releases oxygen-free radicals; thromboxane A2 and prostaglandins cause vasoconstriction and thrombi formation. There are significant changes in platelet function; reperfusion injury occurs [35, 46].

A secondary effect is the development of postreperfusion edema, which can lead to compartment syndrome due to the increased interstitial pressure [23].

After this process, and depending on the degree of secondary microvascular damage, this sequence can lead to two different situations:

- thrombolysis leading to the formation of viable tissue, or
- vascular collapse under cellular necrosis and the development of dry gangrene.

At this point, tissue damage is irreversible. The result can be the loss of fingers, toes, the tip of the nose, etc. [22, 23, 38].

Re-freezing the tissue causes an even greater release of these mediators, which can lead to significant deterioration. Since the release of thromboxane and prostaglandin is associated with the freeze-thaw cycle, then vasoconstriction, platelet aggregation, thrombosis, and cellular damage follow [45].

Before (or during) warming, the affected area should be carefully observed, and the risk of osteofascial compartment syndrome should be assessed [35]. Patients should be informed about the possibility of increased pain and macroscopic changes in the affected area during this process.

In the traditional classification system of local cold injury, first-degree frostbite causes superficial damage to the skin, which is frostbite per se. After rewarming, the patient will report transient tingling and burning. Noticeable erythema and swelling appear after 2—3 hours [16, 27].

Under second-degree frostbite, the numbness disappears during rewarming, a throbbing sensation appears, and then a slight tingling originates in the affected area. After rewarming, the patient will report throbbing and aching pain that can last from 3 to 10 days after the injury [27, 38]. The presence of pain is a favourable prognostic factor; it is a sign that tissue damage is superficial and not widespread, and the nerve fibers lying under the skin are clearly not damaged [22]. Favourable prognostic factors include preservation of sensation, normal skin colour, and clear, not cloudy, fluid in blisters (if they present) [21].

Third-degree frostbite results in full-thickness skin damage involving subcutaneous and surrounding tissues. Unfavourable prognostic signs after rewarming include [21, 28]:

- non-pale cyanosis;
- elastic skin;
- dark blisters filled with haemorrhagic fluid;
- loss of sensitivity.

The patient will report a burning, throbbing, or shooting pain that occurs in non-frostbitten surrounding tissues on the 5th day and lasts for 4—5 weeks [27, 38].

At fourth-degree frostbite, the victim initially informs us about the insensitivity of the affected area, but during warming, they feel severe pain in the surrounding tissues [27, 38].

The procedure itself is painful for the victim; patients may experience constant and severe pain during rewarming, so analgesics (such as non-opioid or opioid analgesics) should be prescribed to relieve it, depending on the patient's response and drug supply [35]. Sometimes warming is forced to stop earlier than necessary because of the severe pain that occurs [52].

After warming, the white colour of the skin changes to bright redness or cyanosis, and the feeling of pain in the form of paraesthesia or anaesthesia is noticeably disturbing [5]. The frozen part can be considered properly warmed when the nail beds acquire a pink colour; the skin of the thawed area gradually turns red or purple and becomes soft. This process is usually completed in approximately 15 minutes to 1 hour and may require more than 1 hour for complete thawing in some patients [38, 57].

After rewarming, the limb is removed from the water, and the damaged tissue should be allowed to dry naturally in warm conditions or with the help of a towel (soak but not wipe); you can soak with absorbent paper to minimize further damage [19, 30, 34, 35].

Some authors prefer to use ointments of silver sulfadiazine or aloe vera with treatment of wounds with silver sulfadiazine cream. Aloe vera cream or gel should be applied to warmed tissues before dressings are applied, and reapplied with each dressing change or every 6 hours [16, 24, 40, 44, 54, 60].

Volumetric gauze bandages should be applied to the heated parts for protection and wound care. Considerable swelling should be anticipated, so the affected tissues should be wrapped loosely with dry, sterile dressings to avoid excessive pressure, and cotton balls should be placed between the affected fingers and toes to provide protection and reduce friction. In order to reduce swelling, if possible, immobilize the limb in an elevated position [16, 40, 44].

After warming, swelling may begin to appear after 3—5 hours and last up to 7 days. Blisters usually appear within 4—24 hours. The presence of a scab will be evident after 10—15 days, and mummification with a demarcation line may develop after 3—8 weeks [20].

N. B. No prognostic markers are reliable, and weeks may pass before the distinction between viable and non-viable tissue appears [21].

In further treatment, hydrotherapy is aimed at increasing blood circulation and removing surface bacteria and non-viable tissues. A daily procedure with hexachlorophene helps to clean wounds from necrotic elements. It is carried out daily, twice a day, at a temperature of 37—39 °C [16, 23, 44, 52], although some authors recommend warming by immersion in a bath with chlorhexidine water at a temperature of 40—43 °C 5—6 times a day [37] (the latter author seems to like the method much more than the patients).

The basis for effective treatment of frostbite is three rescue ways [52]:

- rapid rewarming to stop freezing;
- increased blood circulation to limit local hypoxia;
- the use of medications to block the release of inflammatory factors.

Warming can protect tissue from freezing and reverse vasoconstriction, while drugs can block the release of inflammatory mediators [50].

With an adequate combination of temperature restoration with restoration of blood circulation and gas exchange, there is a possibility of significant reduction of the necrosis zone [16, 31, 44].

The authors hope that the results of this scientific literature review will be useful to military medics, doctors-of-first-contact, surgeons, combustiologists, anaesthesiologists and rescue service workers in order to optimize the initial treatment of local cold injuries and prevent complications and disability for victims.

Declaration of interests

The authors declare no conflict of interest and no financial interest in the preparation of this article.

Authors contributions

O. V. Kravets: conceptualization, methodology, review and editing; V. V. Yekhalov: conceptualization, methodology, original draft; V. V. Gorbuntsov: review and editing, translation; D. M. Stanin: review and editing; D. A. Krishtafor: review and editing

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Методи та патофізіологія відігрівання при місцевій холодовій травмі. Огляд літератури

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Відігрівання уражених тканин при локальній холодовій травмі — провідний метод лікування цього патологічного стану. Однак зігрівальна маніпуляція має особливості та обмеження залежно від обставин. Несвоєчасно і неправильно виконане відігрівання може призвести до значного підвищення частоти небезпечних ускладнень, інвалідизації або летальності. Стратегію відігрівання застосовують відповідно до одного із двох сценаріїв. Якщо є ризик повторного відмороження, то уражену ділянку активно не зігрівають, лише іммобілізують та вкривають термоізоляційними пов'язками. Припустиме також повільне зігрівання тіла теплом. Якщо відморожена ділянка може бути зігріта та зберігатися теплою без повторного відмороження до кінця евакуації, то бажано швидке зігрівання теплою водою або спеціальними зогрівальними ковдрами. Рекомендації щодо температури води значно відрізняються та передбачають широкий спектр — від 37 до 43 °C.

Ступінь ураження тканин можна визначити лише після зігрівання. У традиційній системі класифікації локальної холодової травми розрізняють чотири ступеня відмороження. Перший ступінь — лише поверхневе ураження шкіри, другий — глибоке ураження шкіри, третій — ураження всієї товщі шкіри із залученням підшкірних та навколишніх тканин, четвертий — глибокий некроз підшкірних структур. Залежно від тяжкості ураження пацієнти можуть відчувати постійний і сильний біль при зігріванні, тому для полегшення болю слід призначити аналгетики. Рекомендовано застосування місцевих засобів (креми, гелі, мазі) для поліпшення циркуляції, профілактики та лікування інфекції. Некроз тканин при тяжкому відмороженні потребує хірургічної обробки ран.

Автори сподіваються, що надана інформація стане в пригоді лікарям першого контакту та в стаціонарних умовах для оптимізації лікування локальної холодової травми.

Ключові слова: локальна холодова травма, відмороження, відігрівання, патофізіологія.

FOR CITATION

Kravets OV, Yekhalov VV, Gorbuntsov VV, Stanin DM, Krishtafor DA. Methods and pathophysiology of rewarming in case of local cold injury. Literature review. General Surgery (Ukraine). 2023;2;90-97. http://doi.org/10.30978/GS-2023-2-90.