CONTINUING MEDICAL EDUCATION

CRYOSURGERY IN DERMATOLOGY

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The first recorded use of cold as a physical modality for the treatment of medical conditions was mentioned in the Edwin Smith Surgical Papyrus as early as 3000 BC. Hippocrates described the use of snow and ice for relieving pain and arresting haemorrhage (400 BC). However, freezing has achieved popularity as a recognised treatment only in the past 100 years.[1-10] Liquid air,[2-4] liquid oxygen,[5,6] and carbon dioxide snow,[7,8] were used in the beginning of the 20th century. In 1899, White[2] used liquid air by the method of dipping a cotton-tipped applicator and applying it to the surface of the lesion to be treated. Pusey (about 1907)[8] developed another method in which carbon dioxide (CO_2) sticks of various shapes were applied to the skin lesions. On the same principle, later, Kiddle apparatus, for making carbon dioxide applicators whenever desired, was developed. Both these methods are popular even now, but their use is limited to the treatment of superficial lesions with a depth not more than 2 mm. In the year 1950, Allington[9] described the use of liquid nitrogen (LN_2) as the freezing agent, obtaining excellent results in the treatment of a variety of skin lesions. The liquid nitrogen swab technique was very popular with the dermatologists till mid 1960s,[10,11] when a cryoprobe technique was introduced by Cooper[12] for neurosurgery and subsequently simplified for dermatological therapy by Torre.[13] Soon thereafter, Torre also introduced a spray technique.[14] Zacarian,[15] developed a copper disc cryoprobe technique which is useful for the treatment of both superficial and deep, as well as benign and malignant lesions. The effective depth of destruction can be as deep as 10 mm. Since then, particularly, in the last decade, many sophisticated cryosurgical units, portable as well as table models have become available.

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Pathogenesis of cryo-necrosis

A minimum temperature of - 25°C within and below the lesion is essential for effective cryo-necrosis. This effect can be achieved with the use of cryogens.[16] The 99% of the water content of the tissue turns into a solid compartment of ice under the effect of the cryogen. This mass of ice sends waves of cold energy downwards and peripherally. This effect is partly counteracted by the homeostatic response of the underlying circulation, thus influencing the depth and extent of the cryo-lesion. The rate of freezing and subsequent thawing are the other important considerations. The more rapid the freeze and slower the thaw, the greater is the degree and the magnitude of tissue necrosis.[17] Cryogenic temperature affects two anatomic sites; the cells[18-20] and the microvessels.[21-24] Cell injury and death is probably caused by a combination of events such as extracellular and intracellular ice formation, high ionic strength surrounding the cells, leading to hypertonic damage and cell shrinkage. The microvessels on the other hand, undergo stasis and thrombosis with infarction and necrosis of the pathological tissue which extends even to the surrounding normal tissue. Though, cancer cells can withstand extreme cold,[25] these cannot survive the effect of circulatory arrest.[24]

Histopathological changes become visible within 30 minutes of freezing. Cells show pyknotic nuclei, oedema, and coarsely granular and often vacuolated cytoplasm. Vascular damage and oedema appear within one hour. Later on, cellular infiltrate appears in the acutely ischaemic areas, and consists of mainly polymorphonuclear leucocytes, some lymphocytes and plasma cells. Resolution of the cryogenic lesion usually begins within 3 days and complete healing occurs without scarring.[26,27]

Cryogens and techniques of application

Cryogens in current use are : (1) liquid nitrogen (LN_2), (2) carbon dioxide (CO_2) snow and CO_2 slush, (3) nitrous oxide (N_2O), and (4) freon sprays.

1. Liquid nitrogen : [9-11, 13-15, 28-30, 32, 33] Liquid nitrogen is the most ideal refrigerant. It is readily available, non-explosive, and an extremely cold cryogen having a boiling point of -195.8°C. This boiling point is important for the treatment of malignant tumours of the skin, because it destroys the micro-circulatory barriers of the integument and allows the ice front to develop and extend into the subcutaneous tissue and beyond. LN_2 is stored in vaccum-insulated dewars. The better the insulation, the lesser the loss of LN_2 due to its daily evaporation and hence lower the expenses. These are available in different capacities, but if refilling is available nearby, a portable hand-held spray unit is all that is needed. An ordinary glass thermos bottle can be utilized for one day storage. It can be obtained from suppliers of welding gas. Refilling of the cylinder is usually done by direct pouring. The pouring requires extreme caution, because if it spills on the face, hands or other exposed parts of the body, it will produce ulcers. So pouring should be air-tight without allowing it to leak.

Liquid nitrogen can be used with cotton swabs, copper-disc cryoprobes, sprays or closed cryoprobe technique. The selection of the technique will depend upon the site, size and depth of the skin lesion, and of course on the choice of the dermatologist.

Cotton swab method is used when the depth of the freeze needed is only 2-3 mm, as in actinic keratoses, warts, lentigenes, cystic acne etc. A proper sized swab is chosen and after dipping it in a thermos or styrofoam cup containing LN_2, it is applied on the surface of the lesion. Since LN_2 vaporizes quickly, the container should be closed immediately after removing the swab. It can be dipped again in the same manner, if required.

Copper-disc cryoprobe technique is not only useful for the lesions treated with the cotton swab method but also for those having a depth upto 4-5 mm. Since the disc gets heated up again, it cannot be used for too deep lesions or malignant lesions. A proper sized disc with an insulated handle is placed in LN_2 and when it has attained the temperature of LN_2(indicated by cessation of bubbles) it is applied to the lesion till the lesion and a little halo of normal tissue are frozen.

Spray is used for treating a great majority of the skin lesions especially the large and the deep lesions. Liquid nitrogen is sprayed over the surface of the lesion until the desired depth of freezing is obtained. Accuracy in limiting the size of the frozen area can be achieved by varying the pressure in the system and selecting a proper sized nozzle.

Closed cryoprobe technique consists of using various modern cryogenic units and applying cryoprobes of different shapes and sizes. The coolant, LN_2 is allowed to circulate through a closed probe. These units are available in portable as well as table models, with or without built-in measurement devices. Models with measurement devices are very useful in treating malignant tumours. However, each model of LN_2 spray/cryoprobe apparatus has relative advantages and disadvantages in respect of its storage capacity, ease of handling, portability, control of flow and character of the spray, and built-in measurement device etc.

2. Carbon dioxide snow : [7,8,13-15,23-20,32,33] It has two major advantages, wider availability and easy storage. It can be obtained as solid chunks or blocks from the commercial gas suppliers or it can be produced in the snow form from CO_2 cylinders. This snow can be compressed into pencils. The commonly used apparatus for making CO_2 pencils is the Kiddle apparatus. It uses small disposable cylinders which when punctured, discharge crystals. These crystals can be given various shapes by pressing through moulds of different shapes. The solid chunk of pencil thus obtained is directly applied to the surface of the lesion including an adequate margin of the surrounding normal tissue. Yet, it has its own limitations. Since it has a minimum temperature of only –78.5°C, the destructive effect is limited. Therefore lesions which need freezing of upto 2-3 mm depth only, can be successfully treated with it.

Carbon dioxide is also used in the form of slush. Slush is prepared by placing C_2O chunks/snow in a container and adding acetone or alcohol with continuous stirring until a slush (paste) of a desired consistency is obtained. This should normally be comparable to a sharbet. This is applied with a cotton tipped applicator to the lesion. It is slower in freezing than the liquid nitrogen. Slush is useful for the treatment of large flat lesions, but not thicker than 3 mm.

3. Nitrous oxide (N_2O): [27,30,33] This cryogen also is quite commonly used by the dermatologists, gynaecologists, ophthalmologists and surgeons. It can be stored for indefinite periods. It has got a boiling point of – 90°C and thus has a lethal effect on tissue cells to a limited depth only; it is a little more than CO_2 but less than LN_2. So its indications are more or less the same as for CO_2. It can be used in two ways, (i) cryoprobe system, and (ii) spray. Cryoprobe systems are available in different models and some of them can be used both for CO_2 as well as N_2O. Though, it is possible to produce a liquid N_2O spray, it is of a poor quality as compared to that of liquid nitrogen. When liquid N_2O is sprayed, the droplets either solidify into crystals due to the lowered atmospheric pressure of the N_2O, or fly off in all directions, freezing areas of the surrounding normal skin as well. To rectify this defect, Torre[13] designed a cup-shaped device to isolate N_2O spray from the air. With further modifications, it has become suitable for treating superficial lesions such as actinic keratosis, seborrhoeic keratosis and acne.

4. Freon spray : [30,33,34] Freons have so far been applied for cooling only the cryo-probes. The cryosurgical units are available for other medical specialities like ophthalmology but not for dermatology. However, majority of the benign skin lesions can be treated by utilizing the wide range of temperatures produced by various freons, the lowest being – 90°C which can be achieved by using a blower aid. Freons if inhaled are known to produce cardiac toxicity. Therefore, these have to be used with proper protective devices and applicators.

Treatment guidelines[28-31,33]

Before venturing in for cryosurgery, it is better to evaluate the following facts : (i) a proper assessment of the pathological lesion to be treated i.e. its site, size, surface, depth and type (benign/malignant), (ii) possible complications, functional integrity of the part and cosmetic results after cryosurgery;, (iii) lethal temperature, freezing and thawing time and freeze-thaw cycle, (iv) interface, and (v) the effect of freezing on different tissues such as nerves and melanocytes. Rapidly growing cells are more easily damaged than tissues like stroma of blood vessels, cartilage and bone.

In most cases clinical judgement of the dimensions including the depth of a lesion can be achieved by observation, palpation and ballotment. The amount of freezing carried out is based chiefly upon this judgement. The freeze time is the length of time necessary to freeze the lesion to the required depth and temperature, and it is quite a difficult factor to determine in cryosurgery. It varies tremendously with, (i) the type of application, probe or spray, (ii) character of the spray, (iii) type of the instrument, (iv) the cryogen, (v) lesion characteristics, and (vi) anatomical site. The most practical clinical method of judging whether or not a lesion has been adequately frozen is the thaw time. Thaw time is defined as the time that elapses from stopping application of the spray or the cryo-probe till the entire lesion is thawed. This end point is detected by the disappearance of the white frosted appearance of the surface and/or disappearance of the hard area on palpation. When measuring the halo surrounding the lesion, it is preferable to wait for 3-5 seconds after stopping the spray so that the very superficial peripheral frosting of the keratin layer gets thawed. To get the desired depth of freeze, it is sometimes necessary to repeat the process of freezing and thawing every 3-5 seconds. This process is known as freeze-thaw cycle. Formation of ice in the lesion does not guarantee destruction. For destruction of the tumour cells, $-25°C$ temperature is a frequently used figure, but it is arbitrary. The actual lethal temperature varies with the type of cell being frozen. The rate of freezing and thawing and the number of freeze-thaw cycles also influence this particular lethal temperature.

The depth of freeze can be time-related where the cryo-probe maintained at a specific temperature is used. This is applicable only where the tissue being frozen is homogenous and the interface between the cryo-probe and the tissue is good. Therefore, irregularity of the surface and variations in the pressure, alter the interface contact in actual practice and limits the value of this method as compared to spray.

Follow-up care

Once the patient has undergone the cryotherapy, he should be followed-up as follows :

The patient is asked to report within 24 to 48 hours after the treatment, to see if a satisfactory reaction has developed. If it has not, a second treatment may be given at that time. In experienced hands, usually it is not necessary to see the patient again until healing is complete. It is not necessary to open and drain the blisters or remove their roofs. The blister top should be left in place. This makes the after-care simpler since secondary infection rarely occurs and dressings are not required immediately after the operation. It is usually possible to tell whether or not the treatment is successful. If a lesion has not completely disappeared,it will be smaller and shallower. Re-treatment at this time is more likely to complete the removal than if it is delayed.

In an occasional case, the blister continues to spread beyond the frozen area due to the pressure of the vesical fluid. This occurs most commonly over the joints or pressure points. When it happens, the vesicle may be cleansed and opened with a sterile needle or the top may be removed and a sterile dressing applied. It is advisable in some cases, especially in the treatment of plantar warts, to remove the blister top shortly after it forms. This will not only prevent undue enlargement but may also lessen discomfort.

Treatment of benign and premalignant[28-33,35-39] skin lesions

Actinic keratoses[10] : These are the best suited lesions for cryosurgery. Multiple lesions can be treated in a single session. The lesion is sprayed until it turns completely white, including a 1 to 2 mm halo of normal tissue. The time required to achieve this usually varies from 15 to 45 seconds.

Seborrhoeic keratoses : Thin lesions are sprayed evenly until the entire lesion and a 2 to 3 mm halo of normal tissue is frozen. Very thick lesions are usually best treated by curettage preceding cryosurgery. Thick lesions may need retreatment.

Lentigo/Lentigenes : These are superficial and thus minimal freezing is required. The lesion and a narrow halo (1 to 2 mm) of normal tissue is frosted by brief spurts of liquid nitrogen through a small nozzle or application of a flat probe smaller than the lesion, for 3 to 6 seconds. When treating multiple lesions, all the lesions may not be completely eradicated but are at least lightened considerably.

Sebaceous hyperplasia : The liquid nitrogen pointed probe is inserted into the punctum or a fine spray directed at the punctum, and freezing is continued until the punctum and a 1 to 2 mm collar of normal tissue is frozen. Many lesions disappear without a trace, but some may need re-treatment at 4 to 6 week intervals.

Leukoplakia : The lesion is sprayed until it is quite firm. Thawing should take 45 to 90 seconds, since lips are quite vascular and require more freezing than expected. Only half of the lip or the entire lip may be frozen at one sitting by starting at one end and painting to the other end. When spraying inside the mouth, the vapour clouds may become a problem. Ask the patient to breathe-in through the nose and breathe-out through the mouth, and use intermittent spray (this also prevents nitrogen hypoxia). The use of extension tubes (plastic syringe barrels) is helpful in limiting the sprayed surface area, and it allows extra-oral venting of vapour. Dental suction devices are also helpful. When using probes, care should be taken that the probe wall doesn't touch the tongue or other tissues, not meant to be frozen. To prevent sticking to the tissues, allow the probe to be pre-chilled before contact and twist it gently after contact.

Keratoacanthoma : Multiple lesions or small recurrent lesions can be frozen with the spray or the probe until at least 3 to 4 mm of normal tissue surrounding the lesion are frozen. Thaw time should be well over one minute. Double freeze-thaw cycles increase the cure rate. Single lesion is best treated by surgical excision.

Verruca vulgaris :[41] These lesions are sprayed with a fine nozzle and intermittent flow, so as to freeze throughout including a thin rim of normal tissue. For thick or deep warts (on the palm), limiting devices such as the neoprene cones or pressure rings with disposable pads are helpful for confining the spray. The swab technique is particularly useful for treatment of multiple warts in children. Several swabs should be dipped in a styrofoam cup containing liquid nitrogen. Swabs are then placed on the warts and held in place for about 20 seconds before being replaced by a new swab. About one minute total treatment time per wart is necessary. This is also applicable to the periungual warts.[42] When using probes on warts, to improve inter-face conduction, the wart should be soaked in water by application of an aqueous solution or K-Y jelly. The probe is then applied on the wart until the entire wart and a 2 to 3 mm halo of normal tissue is frozen. A carbon dioxide pencil may be used on the smaller warts.

Verruca plantaris : Cryosurgical treatment of verruca plantaris is fairly painful. Preoperative analgesics or use of subcutaneous anaesthesia is usually indicated. Postoperative pain should be anticipated in some cases, and appropriate analgesic prescribed. Cold compresses or soaks are also helpful. Povidone-iodine solution should be used to wash the feet twice daily following treatment. When spray is used, a limiting device such as neoprene cone is almost always necessary so that the proper depth can be reached without too much lateral extension of the freeze. The entire lesion along with a 3 mm halo should thus be frozen. When using probes, pare off the callous or pre-treat the lesion with salicylic acid plaster to remove the callous and better defining of the wart. Select a probe smaller than the lesion being treated, apply K-Y jelly to the wart surface, and freeze until the entire wart and a 2 to 3 mm halo of normal tissue is frozen.

Verruca digitata : A very fine liquid nitrogen spray should be directed on the shaft of the wart, till the entire wart and a 1 to 2 mm halo of normal tissue is frozen.

Verruca plana : Bunney[43] believes that it is the treatment of choice for facial warts as it leaves no scarring. Apply a 1 to 2 mm size probe to each individual lesion so that the lesion and a 1 mm halo of normal tissue is frozen. When spray is used on an individual lesion, a very fine aperture must be used. For numerous, closely packed lesions, a broad (door-knob-type) applicator, chilled with liquid nitrogen, can be used.

Mosaic warts : Cryosurgery has little to offer in the treatment of this persistent and troublesome condition. However, when used, the involved area is pared off and then sprayed with liquid nitrogen or nitrous oxide. Freezing the entire depth of the wart is usually quite painful, but brief freezing until the lesion turns white, seems to be of some benefit when combined with various chemical procedures.

Condyloma acuminatum : Podophyllin has been considered the first choice in the treatment of genital warts. Recently, however, the success rate of podophyllin for the treatment of genital warts reported in some studies has been disappointing.[44-46] Cervical cryotherapy for condylomata acuminata during the second and third trimesters of pregnancy was very effective and had no adverse effect on pregnancy, labour or delivery.[47,48]

Acne : [31,49,50] Papules and pustules can be sprayed individually for a brief period until the lesion blanches. Thaw time should be less than 10 to 15 seconds. Cystic lesions are frozen longer, and may take 20 to 30 seconds to thaw. Various probes or a CO_2 pencil can be used to produce the same degree of blanching. When the Door-knob applicator is used, it is kept in motion over the area being treated until the papules and pustules are frozen. Normal tissue between the lesions remains unfrozen. It is also useful in acne conglobata.[51]

Acne scarring : [31,49,50] When treating ice-pick scars, a fine spray is directed into the orifice or a pointed probe is placed in the orifice, and the individual scar is frozen until a 2 mm halo of freezing appears around the scar. A very small (2 mm) cone is helpful in limiting the lateral extent of freezing. When treating hypertrophic scars, a probe or carbon dioxide pencil is applied to each scar until it is completely frozen with a 2 mm to 3 mm halo of normal tissue. Torre technique of liquid nitrogen spray for acne scars comprises of back and forth paint-brush application of spray gradually covering the area to be treated and the thaw time is 10 to 30 seconds. Recently, a simple technique using Freon 12, by Cryokwik, has been used experimentally with a great reduction in the time required for application. By spraying a thin film on the surface with a Cryokwik spray and letting it evaporate, an entire cheek can be frozen in about 5 to 15 seconds. Caution must be exercised to avoid pooling of the liquid and consequent over-freezing.

Hidradenitis : Cryosurgery is beneficial for the small lesions. In the combined therapy, following marsupialization, gelatinous contents can be curetted before tract linings are frozen with liquid nitrogen spray.

Angioma : [52,53] For strawberry angiomas, a very mild treatment with freezing may induce the process of resolution. Small adult angiomas and Osler-Rendu-Weber-type lesions respond fairly well to freezing with a small tip or application with pressure of a pointed probe. Only a few lymphangiomas have been treated with favourable results. Cherry angioma treated with the cryo-currettage method has given cosmetically excellent results.

Chondrodermatitis : [54] Where intralesional triamcinolone has failed, treatment with spray freezing is useful. Direct the spray at the centre of the lesion and continue until the tissue is well frozen with a 2 mm halo of normal tissue. Thaw time varies from 30 to 60 seconds. Retreatment may be necessary.

Dermatofibroma : [55] When using a probe, select a probe which is two-thirds the size of the lesion, and freeze until a 2 to 3 mm halo around the lesion is frozen. When spraying, use a surface restricting device (neoprene cone) with a diameter approximately two-thirds that of the lesion and freeze in the same way. The average thaw time is about 1 minute. When treating large lesions, remove a central plug with biopsy punch and spray into the cavity. Re-treat at a 6 to 8 week interval, if necessary. An average lesion requires two to three treatments.

Keloid : Small, immature keloids frequently respond well to freezing. Freeze the entire lesion along with 2 mm of the normal tissue. Several treatments at 4 to 6 week intervals are usually required. Freezing may be combined with triamcinolone injections. Cryosurgery may be helpful in some large keloids as well.

Pyogenic granuloma : Cryosurgery without biopsy is advocated only in small, recurrent and multiple or satellite lesions. Lesions are frozen with a 2 to 3 mm halo of normal tissue. When using combined therapy, the lesion is removed for biopsy with a sharp curette, haemostasis is achieved by application of Monsel's solution, trichloroacetic acid or electro-coagulation, and the base is frozen with spray or probe until a 3 mm halo of normal tissue is frozen.

In general, cryotherapy has also been advocated in the management of adenoma sebaceum,[29] inflammatory linear verrucous nevus,[28] acute cutaneous leishmaniasis,[56] psoriasis,[57] oral lichen planus,[58,59] herpes simplex,[60] prurigo nodularis,[61] erythroplasia of Queyrat,[62] pseudopyogenic granulomata, junctional nevi,[63] cutaneous tags, discoid lupus erythematosus, larva migrans, lymphangioma, molluscum contagiosum, porokeratosis of Mibelli, sebaceous cyst, trichoepithe lioma, syringoma, xeroderma pigmentosum, carbuncle, granuloma annulare, leiomyoma and lupus vulgaris.

Treatment of malignant tumours of the skin : [23,28,29,34-39,54]

Cryosurgery was reinforced in the early 60s by treating malignant tumours such as basal cell carcinoma, squamous cell carcinoma and lentigo maligna. Once the diagnosis is made, the skin around the lesion is marked with a skin marking pencil or gentian violet solution, taking in at least 4-5 mm of the normal skin. The area is then anaesthetised by infiltrating with xylocaine and a thermocouple needle is introduced obliquely at an angle of 25° until its tip lies in the normal tissue underneath the middle part of the tumour. Then fix the needle in place with sticking plaster. The thermocouple needles are delicate and have to be used with care. These can be re-used after autoclaving. Liquid nitrogen is sprayed into the centre of the lesion for 1-2 seconds and repeated at intervals of 1 second, till the entire neoplasm is frozen and its edges extend to the previously outlined margins of the lesion. Freezing is continued till the pyrometer records -25° to -30° C. Then complete thawing is allowed and freezing begun again a second time for about half the duration of the first time.

After the second thawing, the needle is removed, and the tumour is bandaged. For complete freezing, 1-2 minutes are needed for an average tumour but the duration has to be determined by recording the temperature. Local anaesthesia by causing vasoconstriction, facilitates more rapid extension of the ice-front. A template can facilitate more accurate measurement of the temperature. The nose and ear where irradiation therapy for malignancy is contra-indicated, cryosurgery serves as the ideal physical modality of choice. At least 1/3rd of the skin cancers involve the nose and ears. The underlying cartilage tolerates freezing well. Cryo-necrosis, if it occurs, is not beyond repair. Early epidermal carcinoma of the lip with no evidence of metastasis to the regional lymph nodes responds satisfactorily to cryosurgery. Skin cancers on eyelids, especially the lower lid are a challenge to cancer therapists, because the recurrence rate is high. Cryotherapy is very effective in such cases.[64-69]

Untoward reactions and complications [10,27]

Pain : Cryosurgery is comparatively painless, though a burning or stinging sensation may be felt occasionally during the application or during the thaw period. Some areas like palms, soles and paronychial sites where the space for oedema is limited, forehead, temporal areas, anterior scalp (migraine-type headache) and mucous membrane lesions are more painful.

Pain may be managed through the following measures : (1) Infiltration of 2% xylocaine should be used in those areas known to be painful, or when the patient complains of pain. (2) Post-operative analgesics may be needed in some cases. (3) Mucous membrane lesions may be pre-operatively anaesthetized by 4% lignocaine gel. (4) Cold packs or compresses post-operatively give some relief. (5) Clobesterol propionate ointment reduces inflammation after cryotherapy.

Infection : It can occasionally occur in thick or deep lesions when the dead tissue takes a long time in sloughing off. It is more commonly seen in a hot and humid climate. Systemic antibiotics are recommended for the treatment of lesions if the infection is present at the time of cryosurgery. Prophylactic use of systemic antibiotics is indicated only in those patients who have little or no resistance to infection especially those with leukemia or receiving immuno-suppressive therapy.

Haemorrhage : It is rare. Bleeding can occur in blisters formed after cryosurgery. Cryosurgery dissolves the tumour cells including those that have invaded blood vessels. Thus delayed haemorrhage can occur as a consequence. Friable lesions or lesions concurrently biopsied may bleed if not provided with proper haemostasis. Inform patients about possibility of black blisters and delayed bleeding.

Scarring : Hypertrophic scarring is also rare. It may occur in lesions which heal very slowly or become secondarily infected. Atrophic scarring is uncommon but over-treated lesions such as dermatofibroma and tumours in which the normal tissue has been replaced by tumour cells which disappear on cryosurgical treatment can cause atrophic scarring. A patient hypersensitive to cold can react and develop an excessive inflammatory reaction and scarring. Therefore to avoid scarring, do not over-treat benign lesions. It is always better to under-treat and repeat if needed. Intralesional triamcinolone is helpful in treating hypertrophic scars. In addition, take a detailed history about cold hypersensitivity before treatment. If possible, rule out cold urticaria, cryoglobulinemia, cryofibrinogenemia etc. If in doubt about cold sensitivity, test a small area before the treatment is carried out.

Nerve damage : Nerve tissue itself is quite sensitive to cold, though the stroma of the nerve sheath is resistant to cold. It may result in localized anaesthesia or paraesthesia which in most of the cases is temporary because regeneration should be expected following cryosurgery. Areas such as sides of the fingers, angle of the jaw, posterior or lateral tongue, and elbows, where nerves are superficial and susceptible to injury, care should be taken in treating lesions present on these sites. In some instances, injecting normal saline or 1% xylocaine solution between the nerve and the overlying lesion to be treated may add to the safety margin.

Hypopigmentation : Melanocytes being more sensitive to cold than keratinocytes, temporary hypopigmentation is to be expected in areas treated writh cryosurgery, though repigmentation occurs in most instances.

Hyperpigmentation : This appears to be a non-specific post-inflammatory phenomenon, and occurs most frequently in the dark-skinned individuals. Also hyperpigmentation is frequently seen after treating seborrhoeic keratoses on the trunk and skin tags on the neck. Alternate methods are advisable in dark-skinned patients. Sunscreens may be of help in diminishing post-inflammatory hyperpigmentation.

Miscellaneous : The skin adnexal glands are sensitive to freezing, and thus temporary hair loss and hypohidrosis are common, but can occasionally be permanent. Delayed healing, recurrence of benign and malignant lesions and rarely pyogenic granuloma may occur at the site of cryotherapy.[69]

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