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# Cutaneous Cryotherapy in Maxillofacial Surgery

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A good doctor should be aware of all available approaches to therapy. This applies equally to surgeons and physicians. Cryotherapy is frequently used by dermatologists to treat mucocutaneous disease but many head and neck surgeons, while seeing some of the same diseases, do not have confidence in the use of this technique. This review is intended to reawaken interest in cryosurgery and show that it can be the most appropriate treatment for some conditions. The modern consent form demands that alternative methods of treatment have been discussed. This is another factor that should persuade maxillofacial surgeons to be aware of cryosurgery as a treatment option.

## History of Cryotherapy

Cryotherapy has long been noted as a good technique that, when used correctly, can reduce pain and swelling and destroy lesions with little scarring. The ancient Egyptians, over 4,000 years ago, noticed that cooling reduced both pain and inflammation.[1] Hippocrates recommended the use of cold to reduce swelling, hemorrhage, and pain, while John Hunter in 1777 stated that "the local tissue response to freezing includes local tissue necrosis, vascular stasis and excellent healing."[1] In 1899, White was the first person to use extremely cold refrigerants for medical conditions. He used liquefied air to treat warts, naevi, and other dermatologic conditions.[1] Many refrigerants were tried (Table 1) but liquid nitrogen, the most popular and effective cryogen used today, only became readily available after 1945. Initially, liquid nitrogen was applied via cotton tips, but with improvement in refrigeration technology by the 1960s, open sprays and probes became available for more successful cryotherapy.

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## Biology of Cryotherapy

When a tissue is cooled the rate of the heat exchange is very complex. It depends on several factors including water content, blood supply, thermal conductivity of the tissue, rate of freeze, and the temperature of the refrigerant.

In modern cryosurgery:

- The 2 principal methods of application are through closed probes or by spraying liquid nitrogen directly onto the tissues. Probes support more controlled conditions and may freeze deeper because it is possible to apply pressure on the tissues. Spray methods are more versatile but the 2 methods overlap if spray cones are used to concentrate the spray.
- The contour of the cryolesion is approximately dome shaped down to a depth of approximately 6 mm, but becomes more pyramidal at greater depths.[2] The lateral spread of ice from the edge of the probe or cone is approximately equal to the depth of freeze (Fig 1).[3]
- The isotherms lie closer together when the rate of freezing is rapid. This implies that lethal temperatures are found near the base and lateral margins of the iceball after rapid freezing.[3]
- Temperatures down to −50°C are needed to kill malignant cells,[4] and these can be obtained up to 5 mm below the surface when liquid nitrogen is used.

The mechanism of cell death includes[5]:

- Immediately after cryotherapy ice crystals are seen directly intra- and extracellularly.
- Extracellular ice reduces extracellular water and therefore increases solute concentration and osmolality. This causes fluid shift and disrupts the

**Table 1. SURFACE TISSUE TEMPERATURES ATTAINABLE USING VARIOUS CRYOGENS**

| Cryogen | Temperature (°C) |
|---|---|
| Ice | 0 |
| Salt ice | −20 |
| $CO_2$ snow | −79 |
| $CO_2$ slush | −20 |
| Nitrous oxide | −75 |
| Liquid nitrogen | −196 |

Data from Jackson et al.[1]

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cell membrane. Further damage is produced during the thawing process.

- Intracellular ice damages mitochondria and endoplasmic reticulum.
- Large ice crystals are more damaging than small ones.
- Slow thawing is associated with recrystalization of ice and is more destructive than rapid thawing.

## Cryotherapy Spray Technique

Treatment schedules can only be repeated or reproduced if there is a standard nomenclature. The one advocated is the freeze thaw cycle (FTC). The spray or probe is applied continuously until the required ice field has been created and only then does timing begin. Thus, a 5 second FTC denotes maintaining a given ice field for 5 seconds. It may not be necessary to freeze continuously after establishing the ice field as this may create more cold injury than required. Intermittent spraying will usually maintain the ice field at the required diameter.

The lesion to be treated is outlined with a marker pen. The margin for a benign lesion is usually 1 to 2 mm and 5 mm to 1 cm for malignant lesions. The liquid nitrogen spray tip is held approximately 1 cm from the skin over the center of the area to be treated (Fig 2). Spraying is commenced and the ice spreads outward, forming a circular ice field. Once the required area is frozen, the spraying is continued at sufficient pressure to maintain the ice field. Neoprene cones can be used to concentrate the liquid nitrogen spray and limit lateral spread of the ice field (Fig 3). Alternatively, an auroscope earpiece or adhesive putty may be used to produce an accurate ice field, reducing damage to adjacent normal tissue. For peri-

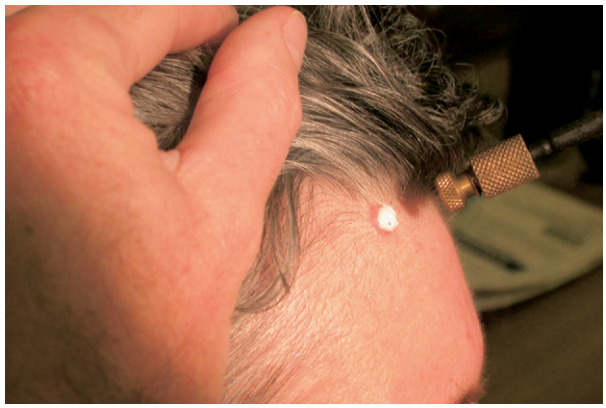

**FIGURE 2.** The cryotherapy spray technique.

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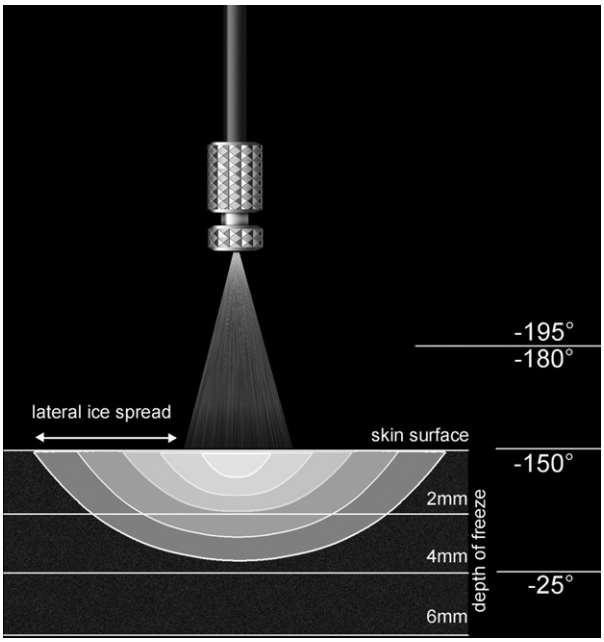


**FIGURE 1.** Shape of the ice field and relationship of lateral spread to the depth of the cryolesion.

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**FIGURE 3.** Neoprene cones used to produce an accurate ice field and protect adjacent normal tissue.

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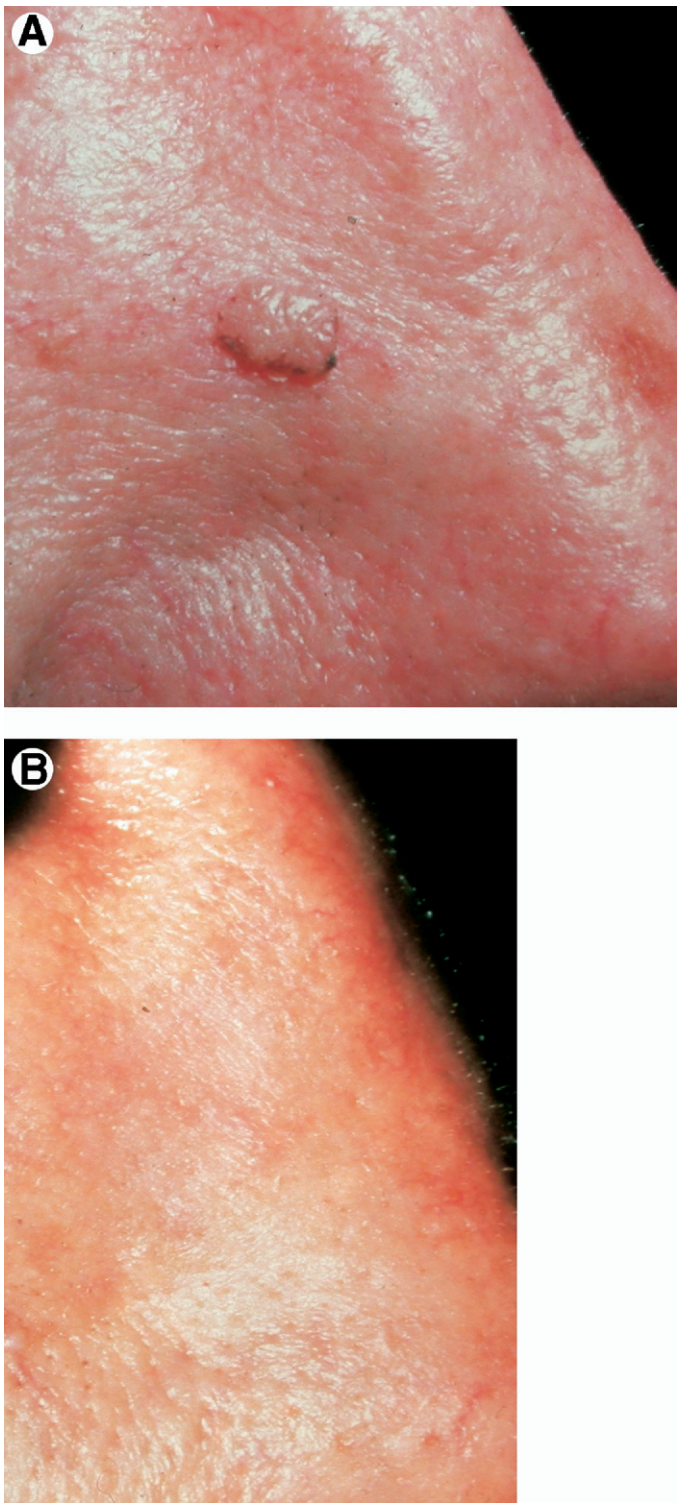


**FIGURE 4.** Seborrhoeic keratosis treated with cryosurgery. *A*, Seborrhoeic keratosis pretreatment. *B*, Post-treatment view showing excellent cosmetic result.

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orbital lesions, a plastic eye protector or a Jaeger eyelid retractor may be used.

Treatment is usually from 5 to 30 seconds depending on the pathology of the lesion. Times greater than 30 seconds may be required, but this can induce scarring.[6] This technique is suitable for treatment of diameters up to 2 cm; beyond this size the temperature at the periphery would be insufficient for reliable

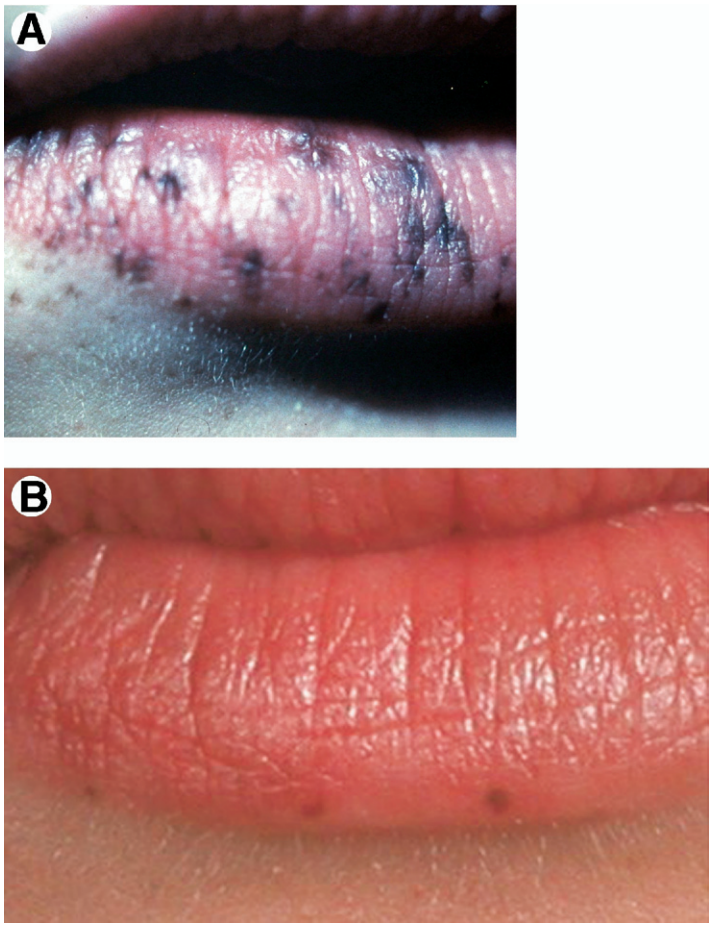


**FIGURE 5.** Melanotic macules of the lower lip treated with cryosurgery. *A*, Preoperative view. *B*, Postoperative view.
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cell killing. In this case, the area can be treated as a series of overlapping circles.

Reproducibility of this technique can be achieved using the FTC concept. However, when treating larger benign lesions it is acceptable to use a random spray pattern over the surface.[7]

## Probe Technique

Most surgeons performing cryotherapy are familiar with the use of cryoprobes. Probe diameters range from 1 mm to several centimeters depending on the size of the lesions being treated. The probe may be applied directly to the lesion or a lubricant jelly may be used as an interface.

## Forceps Technique

Forceps technique is limited to the treatment of skin tags. The forceps are dipped in liquid nitrogen before grasping the stalk of the tag for 10 seconds.

Regardless of the technique used, if 2 or more cycles are required, it is important that thawing is complete after the initial freeze. This can be judged as the time at which the ice has disappeared and can no longer be felt on palpation. This stage may be 3 to 4 times the duration of the freeze time. Significant cellular injury occurs during the thaw phase and complete thawing decreases cell survival.[8]

## Clinical Application of Cryotherapy

Cryotherapy does not provide a tissue sample and indeed it may temporarily improve the appearance of malignant lesions, thus giving the false impression of cure. However, when dealing with clinically benign lesions and most solar keratoses it is not necessary to take a pretreatment biopsy. Experienced clinicians may choose to treat low risk Bowens and basal cell carcinomas on the trunk and limbs without biopsy, but in all other cases a pretreatment biopsy is the wisest choice.

## Benign Lesions

Cryotherapy can effectively treat numerous benign lesions of the skin. Discussion of the treatment of all

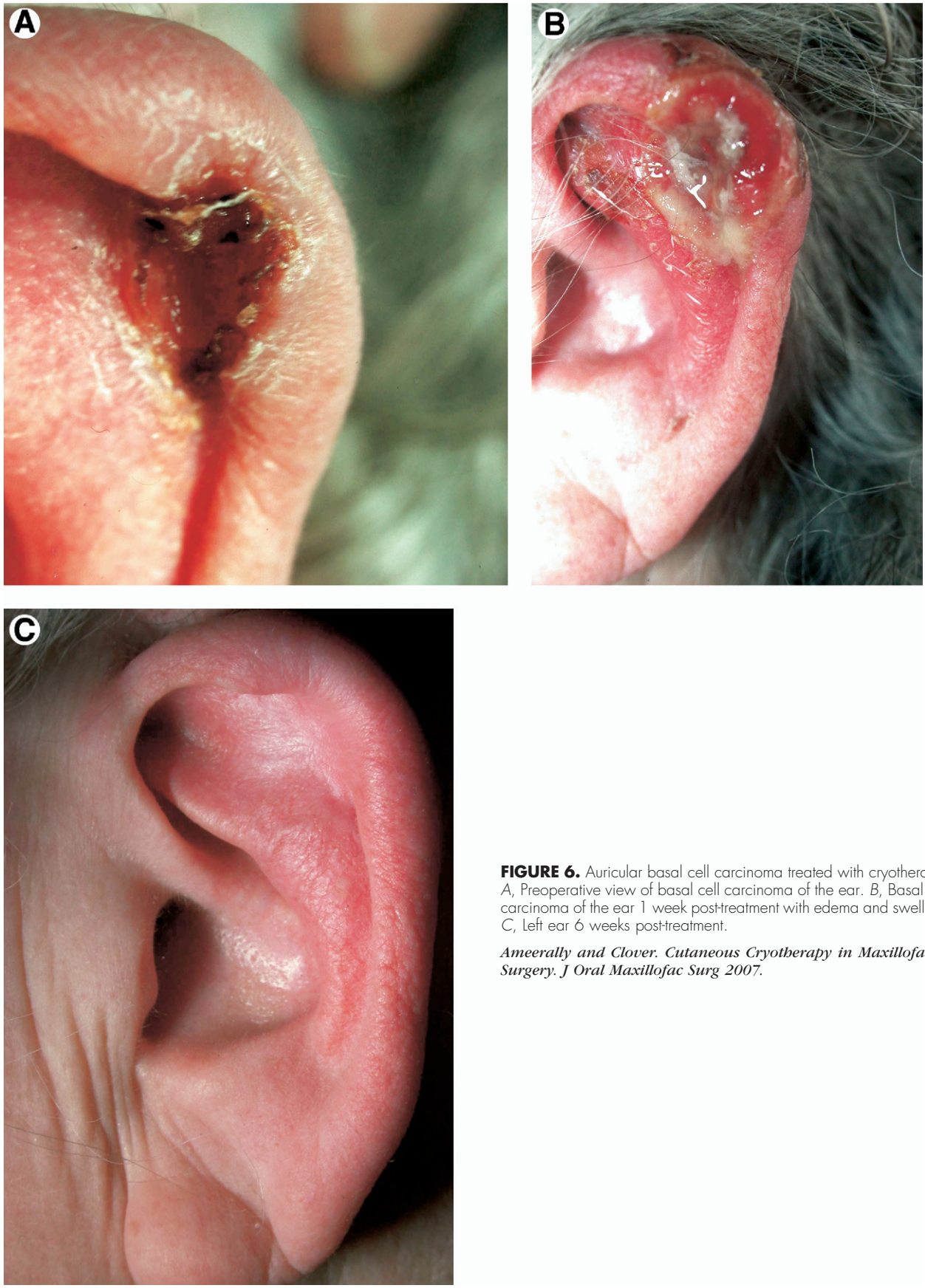


**FIGURE 6.** Auricular basal cell carcinoma treated with cryotherapy. *A*, Preoperative view of basal cell carcinoma of the ear. *B*, Basal cell carcinoma of the ear 1 week post-treatment with edema and swelling. *C*, Left ear 6 weeks post-treatment.

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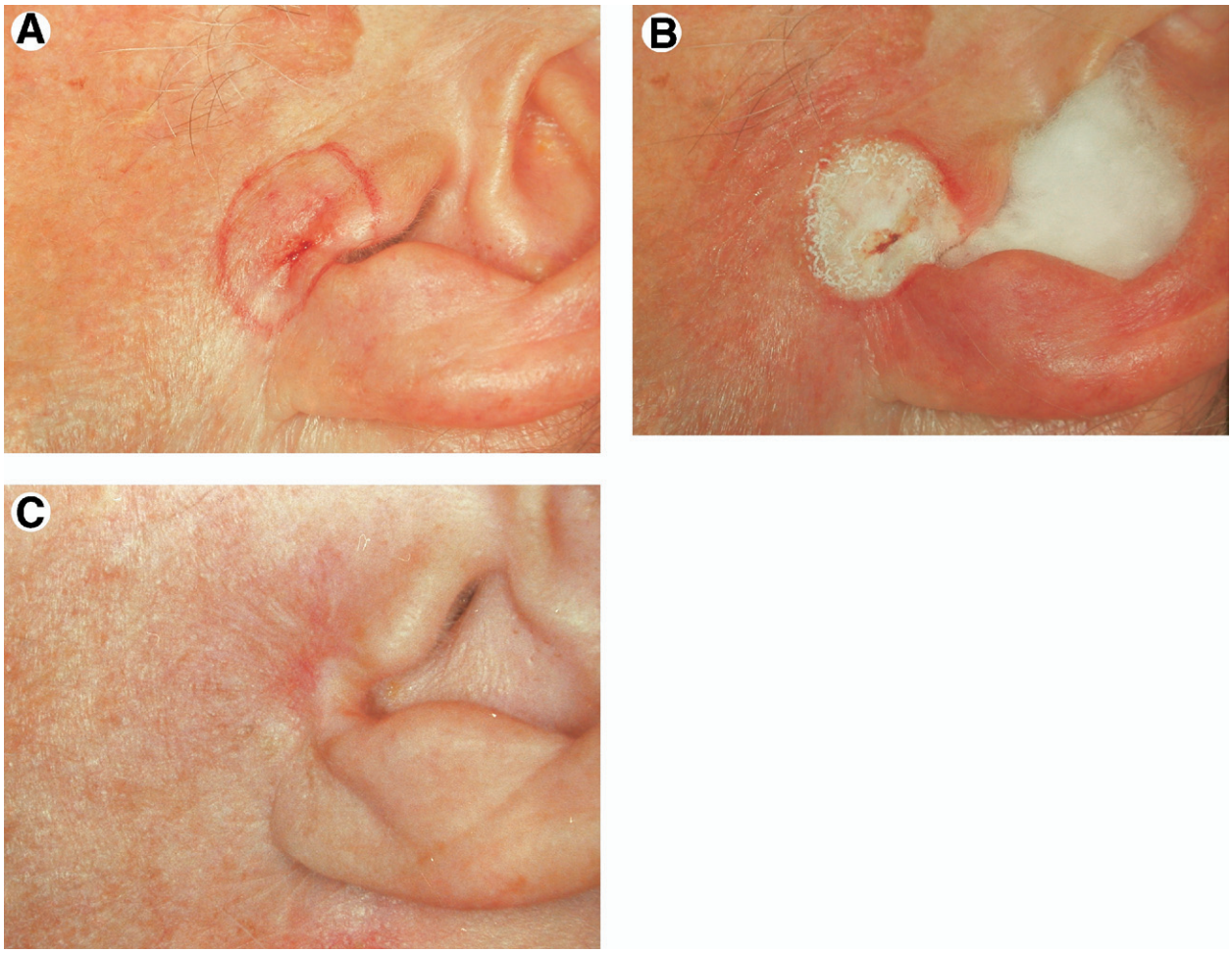


**FIGURE 7.** *A*, Basal cell carcinoma preauricular region (lesion marked with margin of normal tissue). *B*, Basal cell carcinoma preauricular region showing the ice field created to cover the entire marked area. *C*, Preauricular region 6 months post-treatment.

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of these is beyond the scope of this article. In the head and neck region, seborrhoeic keratoses (Fig 4), viral warts, skin tags, and xanthelasmas may be easily treated. Keratin is an excellent insulator and therefore for thick seborrhoeic lesions debulking initially with a scalpel or curette before cryotherapy provides good results.

Bunney et al[9] showed a 75% cure rate for viral warts and the senior author has vast experience in treating seborrhoeic keratoses with cryotherapy. It is invariably successful unless the lesions are grossly hyperkeratotic, in which case they can be managed as mentioned above. Vascular lesions such as spider naevi, pyogenic granulomas, and Campbell de Morgan spots can also be successfully treated with cryotherapy.

Melanocytes are extremely sensitive to cryotherapy. Pigmented lesions such as labial lentigenous macules respond well to cryosurgery (Fig 5). However, care must be taken when managing pigmented lesions because melanomas may initially respond to treatment before recurring.

Cryotherapy is a good treatment method for labial mucoceles.[10] It can be performed without local anesthetic with little risk of infection, low recurrence rate, and no scarring if performed correctly. It is suitable for treating children with these lesions in the outpatient department.

For most of the lesions mentioned above, a single freeze cycle of 5 to 10 seconds is adequate.

## Premalignant Lesions

Premalignant skin lesions are amenable to treatment with cryotherapy. The advantages of this method of treatment for these lesions include:

- All ages may be treated including those with poor health.

- Cryosurgery may be used at sites prone to keloid scarring, such as the shoulder and anterior chest wall.
- Patients on anticoagulants may be safely treated.
- Lesions on sites with poor skin mobility can be easily treated.
- Lesions on previously irradiated skin can be treated with cryosurgery because healing is usually satisfactory.

The main disadvantage of cryosurgery alone for these lesions is that no tissue is available for pathology.

## Bowens Disease

Cryotherapy generally has a good success rate, with recurrence rates of less than 10% at 12 months; however, healing may be slow for larger lesions. This makes cryotherapy less appealing to patients in a study comparing it with curettage and cautery.[11]

## Solar Keratosis

Solar keratoses are common lesions in the sun exposed skin of Caucasians and are usually seen as a field defect on the scalp, face, and hands. Some may disappear spontaneously, but a small proportion undergo malignant change and most skin squamous carcinomas probably arise in a dysplastic lesion.

Cryosurgery is 1 of several methods used to treat these lesions. Other treatment modalities include salicylic acid in paraffin, 5-fluorouracil, topical tretinoin, and curettage and cautery. The choice of treatment depends on the personal experience of the operator and also the nature of the lesions. Curettage and cautery is good for larger lesions and provides tissue for histology. Cryosurgery is useful in patients with a small number of these lesions, especially if they are thin. Widespread changes and multiple lesions are better treated with 5-fluorouracil. A 1 mm rim of clinically normal tissue is included in the ice field. A single 5- to 10-second FTC is appropriate for these lesions. In a series of 1,018 patients with solar keratosis, Lubritz and Smolewski[12] achieved a 99% cure rate. When compared with photodynamic therapy, cryotherapy achieved 75% complete response rates against 69% for photodynamic therapy at 3 months.[13]

**Table 2. TYPES AND CHARACTERISTICS OF TUMORS UNSUITABLE FOR TREATMENT WITH CRYOTHERAPY**

| |
|---|
| Tumors >2 cm diameter |
| Recurrent tumors |
| Tumors with a high recurrence rate (eg, tumors situated on the nasolabial fold and periauricular areas) |
| Tumors with a histopathologic diagnosis of morphoeic, metatypical, or mixed type |

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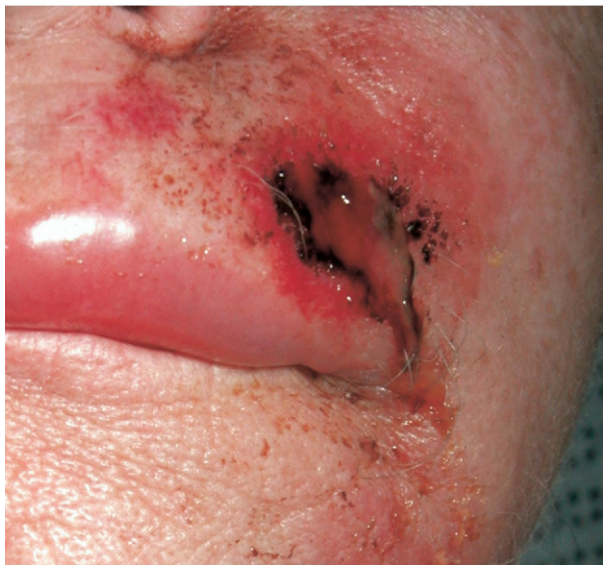

**FIGURE 8.** Edema following cryotherapy.

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## Actinic Cheilitis

Small areas of actinic cheilitis may be treated by cryotherapy. More extensive lesions should be treated by a lip shave procedure.

## Skin Cancers

Although many surgeons may be skeptical of treating skin cancers by nonsurgical methods, there is good evidence that cryotherapy is a successful treatment modality. Several studies have shown a 2% to 5% recurrence at 5 years for basal cell carcinomas,[14-16] and a 1% to 5% recurrence for squamous carcinomas.[15,16] The largest of these studies[16] had a 2.7% recurrence rate and included over 4,000 patients with basal cell and squamous carcinomas. Ninety percent of basal cell carcinomas are 3 mm or less in depth. Cryotherapy is therefore a good modality of treatment for these lesions because, as mentioned above, the depth of freeze is sufficient to destroy these lesions. An ice field should be produced so that it is 3 to 5 mm beyond the tumor margin, which must be produced within 60 to 90 seconds to achieve a temperature of −50°C at 3 mm depth. A double FTC of 30 seconds with a minimum 5 minutes thaw period between each freeze to allow maximum destruction of tumor cells is usually sufficient.

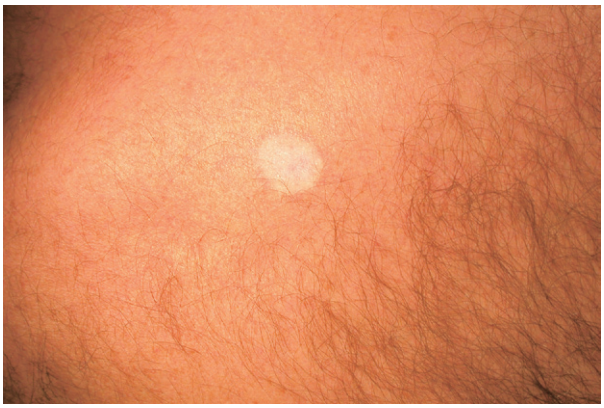

**FIGURE 9.** Hypopigmentation following cryotherapy.

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However, the key to success lies in careful patient and tumor selection and sound technique. It is imperative that any doctor who intends to treat malignant lesions should read widely on the subject and observe an experienced cryosurgeon to learn proper technique. Small, superficial basal cells and well differentiated squamous carcinomas less than 2 cm in diameter with well defined margins are ideal candidates. Tumors of the eyelid, ear, and nose may also suitable because it may avoid potentially difficult reconstruction (Figs 6, 7).

Table 2 shows the characteristics of tumors unsuitable for cryosurgical treatment. There is currently no role for cryotherapy in the curative treatment of melanomas including lentigo maligna. However, it can be very useful in the palliative treatment of melanoma.

## Complications and Side Effects of Cryotherapy

Between 24 and 72 hours following cryotherapy there is edema and sometimes blister formation (Fig 8). After some cases of aggressive cryotherapy, usually following tumor treatment, there can also be hemorrhage and ulceration. Nerve conduction can be affected by cryotherapy and advantage has been taken of this in the management of trigeminal neuralgia and other painful conditions. Hypertrophic, keloid, or contractile scarring is rare and indeed cryotherapy has been used to treat early keloid scars.

Pigmentary changes are the most common long term complications of cryotherapy. Both hypopigmentation (Fig 9) and hyperpigmentation are relatively common and cryotherapy should therefore be used cautiously in those with darker skin types.

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