Liquid Nitrogen Cryotherapy in the Treatment of Benign Skin Lesions

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This article summarizes the use of liquid nitrogen as a cryotherapeutic modality in the treatment of various benign skin lesions. Deep cryosurgery also has been effectively instituted for the treatment of malignant cutaneous lesions, but this article will not describe the latter in detail.

Liquid nitrogen is equally as effective as other conventional modalities. Superiority of this treatment is attributed to the simplicity of its application and lack of disfigurement and scarring.

Cryotherapy is a method of producing tissue necrosis by freezing. It has been used in the treatment of various cutaneous lesions since the turn of the century. However, in the last decade, it has made remarkable advances, particularly in the instrumentation, assessment of movement of cold in depth (especially applicable in the treatment of malignant lesions), and understanding of the etiopathogenesis of cold injury.

The use of refrigeration therapy with carbon dioxide snow for certain dermatologic disorders was recommended by Pusey in 1907.[1] In 1928, the efficacy of liquid air in the treatment of verrucae was mentioned by Irvine and Turnacliff.[2] Liquid nitrogen was first used by a neurosurgeon, Irving Cooper, in 1961.[3] He described a closed system liquid nitrogen apparatus attached with a cryoprobe which could destroy tissue at a depth of several centimeters. The Cooper apparatus, although primarily designed for surgical and neurosurgical purposes, can be effectively used in treating skin lesions. However, its size and cost make it impractical for dermatologic office procedures. This article will describe current methods of using liquid nitrogen in the treatment of benign skin lesions.

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Mechanism of Cryonecrosis

The exact mechanism of cellular death by freezing is not completely understood. Cryonecrosis of the cell and tissue alike is complex and depends upon the type of cryogen, the rate of cooling and thawing, and the ultimate temperature achieved in the tissue.

It is thought that cryonecrosis works in the following manner:

1. *Effect on cells* – Rapid freezing induces dehydration as a result of the formation of extracellular and intracellular crystals. This ultimately leads to an abnormal increase in the intracellular concentration of electrolytes. Rupture of the cell membrane takes place as a result of denaturation of lipid proteins, and this brings about the biological death of the cell.[4]

2. *Effects on the vascular system* – The effects of cryogen on the blood vessels and lymphatics were first mentioned by Kreyberg.[5,6] Damage to the blood vessels following freezing is important in determining the extent of the tissue necrosis. The degree of injury is roughly proportionate to the intensity of freezing.

The effect on the blood vessels may range from the temporary interruption of circulation in the smaller vessels, followed by vascular dilatation and edema, to irreversible vascular occlusion due to the accumulation of erythrocytes. This occlusion results in the formation of thrombi and diapedesis of blood elements, eventually causing necrosis of tissue.

Other factors that are also important in the production of cryonecrosis include the conductivity and "specific heat" of a tissue. Specific heat is defined as the ability of the tissue to absorb the quantity of heat supplied. Tissue elements vary in respect to this property. Thus, the character and thickness of the epidermis, the

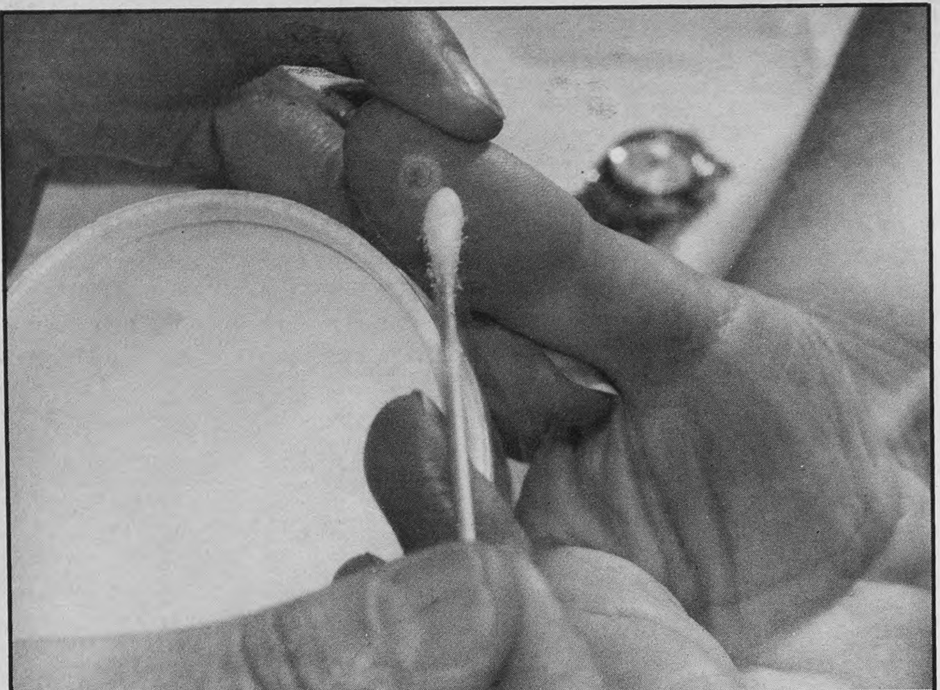

Figure 1. Liquid nitrogen is delivered to the lesion by a cotton applicator. It should be repeatedly applied until the freezing part extends to 1 to 2 mm around the tissue. In this picture, a wart is being treated with this modality.

dermis, the subcutaneous tissue, the water content, and the blood flow in the area are significant factors in determining the quality and quantity of response to the application of a cryogenic agent.

Types of Cryogen and Methodology

Cryogenic agents are easy to apply, usually do not require any type of anesthesia, and leave minimal or no scarring. Freezing capacity is inversely proportionate to the boiling temperature of the cryogen. The boiling points of some of the cryogens used are as follows:

1. Ethylchloride +13 C
2. Frigiderm +4.0 C
3. Freon +3.6 C
4. Carbon Dioxide Snow (dry ice) −78.5 C
5. Liquid Nitrogen −194.0 C

Solid carbon dioxide (CO_2) snow has been used in dermatologic practice for a long time and enjoys the advantages of wide availability and ease of storage. It has the disadvantage that collecting and forming the CO_2 mass to the size and shape of the lesion to be treated may be somewhat cumbersome and time-consuming. Moreover, it lacks the capacity of penetration of cold deeper into the tissues.

Liquid nitrogen, which is readily available from medical and industrial sources, is inexpensive, noncombustible, and has the lowest boiling temperature, as indicated above. It has, therefore, become a standard therapeutic agent. Freezing with liquid nitrogen is accompanied by a stinging and burning pain which attains its peak during thawing, about two minutes after the treatment is over. Local anesthesia is usually not required. Pressure of application increases both the rate and depth of freezing.

Liquid nitrogen is relatively easy to obtain and, in most instances, it can be purchased from a company distributing industrial gases. I have two containers for the storage of liquid nitrogen. A thirty-liter tank is adequate for two to three weeks' need for the average dermatologist. It can be fitted with a special withdrawing unit which may be used for transferring nitrogen to a smaller container of ten liters, which can be easily transported. These containers are manufactured by various companies and are moderately priced.

Treatment of lesions on hands, feet, lips, ears, and eyelids is relatively painful. A triple response of Lewis characterized by redness, wheal, and surrounding flare occurs a few minutes following the treatment; a blister may form three to six hours later, and it may flatten uneventfully in two to three days. Complete healing occurs in two to three weeks. The post-treatment lesions require no dressing and secondary infection is extremely rare.

The treatment is achieved by dipping a loosely wrapped, cotton-tipped applicator into the nitrogen and promptly placing it on the lesion (Figure 1). Larger cotton swabs such as those used for sigmoidoscopy or gynecological examinations will hold greater amounts of nitrogen. When these are used, the cotton tips should be shaped into a point slightly smaller than the lesion under treatment. A five to thirty-second application is adequate for small superficial growths on thin skin. Most other benign lesions such as warts, actinic keratoses, and seborrheic keratoses require a thirty to ninety-second application. This application is done repeatedly until the white freezing point extends one to three millimeters onto the margins of the normal skin.

The zone of freezing reaches a depth of one to two millimeters within one minute of the initiation of application and does not advance significantly further. An optimum treatment produces a blister at the dermo-epidermal junction resulting in the formation of a subepidermal blister which separates the lesion with no damage to the underlying tissue. With some experience, treatment frequently can be limited but still be adequate to cause drying and shedding without the formation of a blister.

Cryotherapy for Large Benign Lesions

For benign skin lesions larger than one centimeter, treatment can be rendered by a spraying system. There are many spraying systems available commercially, but I prefer to use C-21 Zacarian unit (Figure 2). This apparatus is relatively efficient and easy to handle. It holds 250 cc's of liquid nitrogen and allows a free spray for up to five minutes. It also permits the treatment of a number of benign or cancerous skin lesions at one sitting. This unit contains two safety valves which permit the escape of liquid nitrogen and is supplied with interchangeable needles and metallic discs of various sizes. Interchangeable needles allow a generous delicate flow of the refrigerant. The hub and shaft of the needle are made of plastic to avoid the accumulation of moisture and ice crystals which may enhance plugging during freezing.

Metallic discs which are provided with escape vents may be used for the treatment of intraoral lesions and in areas where the spray should be kept away from the adjacent normal delicate tissue. This spray device is housed in a compact unit including the pyrometer with two microthermocouple needles (Figure 3). The whole set can be easily transported from one place to another. Microthermocouple needles and the pyrometer are primarily used for the treatment of cancerous lesions. The detailed description of microthermocouple needles and the pyrometer may be obtained from the listed references.[7-12]

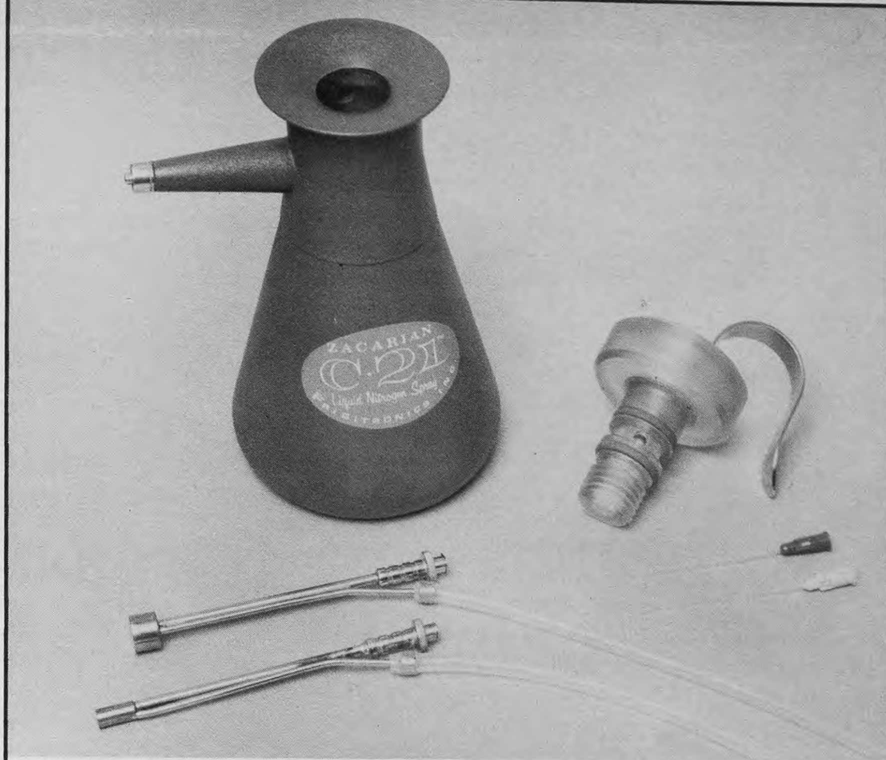

Figure 2. C-21 (Zacarian) liquid nitrogen container shown with lid, metallic discs, and plastic needles. This spray unit is a part of the compact cryosurgical system provided with pyrometer and microthermocouple needles.

Indications

The following lesions are amenable to liquid nitrogen treatment:

1. Verruca vulgaris
2. Plantar warts
3. Periungual warts
4. Condyloma acuminata
5. Actinic keratoses (solar keratoses, senile keratoses)
6. Seborrheic keratoses
7. Molluscum contagiosum
8. Superficial angiomata
9. Cutaneous tags
10. Granuloma pyogenicum
11. Chondrodermatitis nodularis chronica helicis

All of the above mentioned lesions are benign in nature. Deep cryotherapy has been effectively used for the treatment of various skin cancers, but this role is beyond the scope of this article. Further information on this subject can be obtained in the various texts and references which are listed.[7-12]

One should be alert to exclude

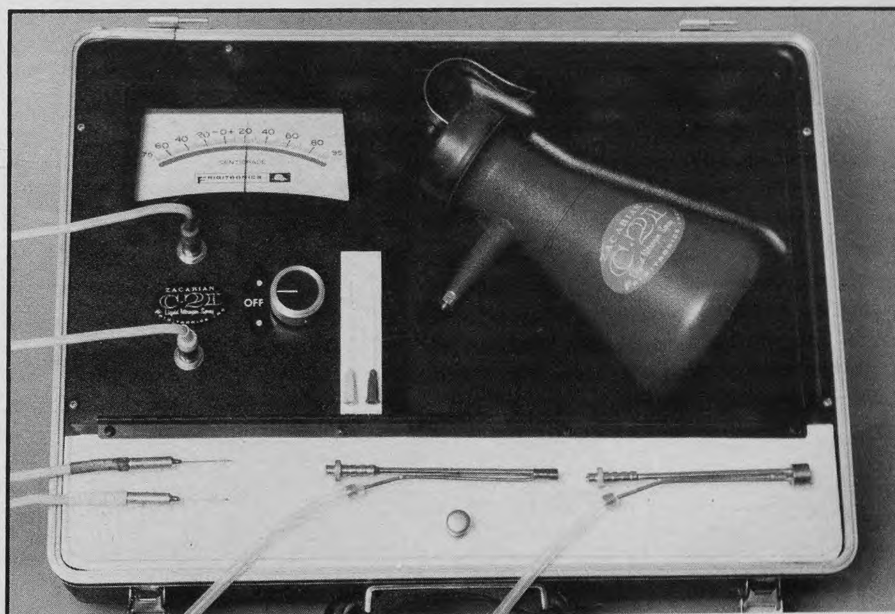

Figure 3. Spray unit with microthermocouple needles and pyrometer. The latter are primarily used for the treatment of cancerous lesions.

malignancy by performing a biopsy prior to treatment, as the morphology of the lesion may be grossly altered by the application of liquid nitrogen. In cases of pigmented lesions, the possibility of basal cell epithelioma and melanoma should be ruled out on the basis of biopsy before instituting treatment.

Complications of Liquid Nitrogen Treatment

As mentioned above, freezing produces stinging and burning which may be followed by a throbbing pain. In some patients, analgesics may be required. Local anesthesia, while itself painful, protects during treatment and the period of maximum discomfort, and may be advantageous. However, the injected anesthesia alters freezing characteristics of the tissue and, therefore, a longer freezing period or increased pressure may be required. Hemorrhage may sometimes occur into blisters which may follow liquid nitrogen treatment. It is advisable to inform the patient of this complication to alleviate concern.

Ulceration may ensue if the treatment is prolonged or excessive pressure is used, especially on thin or devitalized skin. Permanent scarring occurs following healing in these cases. Keloids may sometimes form following ulcers. Neuropathy induced by liquid nitrogen has been described by Nix,[13] and is thought to be caused by injury to superficial nerves underlying the sites of application of liquid nitrogen. Fortunately, this complication is uncommon. Secondary infection is seldom seen with this treatment. The judicious use of topical antibiotics, especially for lesions on sites prone to injury or irritation, will minimize this complication.

Atrophy and hypopigmentation seldom occur. When they do occur, they are usually less than would have resulted if the lesions had been treated by another modality.

Concluding Remarks

Cryotherapy is a useful method in the treatment of benign skin problems. Liquid nitrogen, when available, is the cryogenic agent of choice in most instances. It is easily applied to an area of uneven surface and irregular outline. Multiple lesions are easily and rapidly treated. Most often only a container, liquid nitrogen, an applicator stick, and a watch are required.

Freezing causes some pain but is usually tolerated without anesthesia. Reactions tend to heal more rapidly than those produced by other methods of surgical destruction. After-care is simple and complications are infrequent. A family physician may find this treatment modality rather useful and timesaving. Paramedical staff, such as a nurse or a physician's assistant, can be easily trained to perform this procedure.

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