Liquid Nitrogen in the Treatment of Skin Diseases

H. V. ALLINGTON, M.D., *Oakland*

SUMMARY

Liquid nitrogen is a satisfactory freezing agent in the treatment of such skin diseases as warts, keratoses, superficial hemangiomas, leukoplakia, keloids, superficial scarring and dermatitis venenata. It is available and easily applied. Its use is described and the results of treatment in 154 cases of warts are presented.

THERE have been several articles, the most recent one by Kile and Welch,[1] on the use of liquid gases as cryotherapeutic agents in dermatology. This presentation will briefly review some of the practical aspects of this method of treatment.

Liquid air was the first gas used and may still be used. It contains approximately 78 per cent nitrogen, 21 per cent oxygen, 1 per cent argon and traces of other rare gases.

In recent years the commercial demand for oxygen and nitrogen has led to the production of these elements in almost pure form and in tremendous quantities. The process of manufacture includes the compression and the refrigeration of atmospheric air and then its fractional distillation and chemical rectification.

Because of its easy availability liquid oxygen has been used for a number of years and still is often used. Recently, as liquid nitrogen has become more commonly available, it has partially replaced liquid air or liquid oxygen. It has the advantage of being largely inert and avoids the fire hazard inherent in liquid oxygen. Its only disadvantage is perhaps that it is approximately 13° C., or 7 per cent, colder than liquid oxygen and therefore is lost slightly more quickly by vaporization. This is of little practical importance, however.

The liquid nitrogen used in the Student Health Service clinic at the University of California, Berkeley, is obtained from the physics department in a quart-sized thermos bottle. This is surrounded by cotton waste and set in a plywood box measuring about eight inches square and 12 inches deep. The open mouth of the glass container is covered by a half-inch layer of orthopedic felt. Each clinic morning approximately a quart of the liquid nitrogen is obtained. This has been used in treating as many as 21 cases of warts during a clinic period. Much of the liquid nitrogen is left in the container at the end of the clinic.

For office use the author obtains liquid nitrogen—2.5 liters in a special 5-liter container—from a commercial source. From this container the nitrogen is poured as it is needed into a pint thermos bottle surrounded by cotton waste and enclosed in a small plywood box. This box is provided with a handle for ease in carrying it about the office. The supply is obtained twice a week, on Monday and Thursday mornings, and the rate of evaporation with this care is such that it is usually available continuously throughout the week.

The liquid nitrogen is applied by means of an ordinary cotton swab or applicator stick. In order to pick up the liquid nitrogen, it is important not to wrap the cotton too tightly on the applicator. This is dipped into the liquid and applied to the lesion to be treated. No appreciable pressure is required for most lesions, and freezing is almost instantaneous.

Lesions of considerable depth, such as warts on the palmar or plantar surfaces, require several seconds to become frozen to their whole depth. Pronounced hyperkeratosis results in slower freezing since cornified epidermis is a good insulator for heat and cold.

In applying liquid nitrogen to a small lesion, it is usually necessary to interrupt contact with the applicator. If this is not done, freezing proceeds rapidly to a greater depth and particularly to a greater width than is needed. Thus the treatment usually consists of touching the growth intermittently often enough and long enough to confine the freezing to the area desired for as long a period as required. Often if there are two or three lesions in close proximity, they can be treated coincidentally by alternately transferring the applicator saturated with the liquid nitrogen from one to the other. The desired depth and width of freezing can be determined by the appearance of the lesion, since the area actually frozen is white and easily visible.

The time required to freeze a lesion adequately varies with its depth and thickness, its size and character. To one familiar with this method, accurate timing may not be necessary. However, results are apt to be more uniformly successful if a lesion to be treated is first "sized up" and then the determined period of freezing timed. The time is measured as the period during which the liquid nitrogen is actually being applied. It usually takes fully as long and sometimes longer for the frozen lesion to

Chairman's Address: Presented before the Section on Dermatology and Syphilology at the 78th Annual Session of the California Medical Association, May 8-11, 1949, Los Angeles.

From E. V. Cowell Memorial Hospital, Student Health Service, University of California, Berkeley.

thaw out after the application has been discontinued. No hidebound timing schedule can be outlined. In treating hemangiomas, a period of ten seconds or less may be enough, and more intense freezing may predispose to ulceration. However, in most lesions a period of from 15 to 60 seconds will be used. For small superficial lesions on thin delicate skin such as that on the face and the dorsum of the fingers and hands, and of the forearms in children, 15 or 20 seconds may suffice. Juvenile plane warts and early keratoses may be treated in this manner. Lesions on the tougher thicker skin of most adults, especially on the palmar or plantar surface, require the longer periods. Common warts on the back of the hands, for example, may require 30 seconds. For most lesions on the palmar surface, from 45 to 60 seconds is necessary. If the lesion is cornified or imbedded as are warts on the grasping surfaces, 60 to 90 seconds may be required. Plantar warts are not often treated with liquid nitrogen because their depth makes adequate freezing difficult even with prolonged application.

The freezing produces stinging pain which is usually not considered severe. This persists to lesser degree for two or three hours and then disappears.

Following treatment with liquid nitrogen, redness and swelling develop within a few minutes. Blistering is delayed for several hours and reaches a peak on the second or third day. In treating lesions which are to be destroyed, the desired reaction is one in which a blister is produced in a narrow zone about and beneath the lesion, separating it from the normal surrounding tissue.

The patient should be told to return in 24 to 48 hours after treatment to see if satisfactory reaction has developed. If it has not, the lesion may be retreated at that time.

The author does not usually open and drain the blisters or remove the tops of them. Rather, the blister top is left in place. This makes the after-care simpler since secondary infection rarely occurs and dressings are not required. The blister dries and the top separates and exfoliates spontaneously within about three weeks. Patients are asked to return as soon as this has taken place. It is usually possible then to tell whether or not the lesion has been treated successfully. If a wart has not completely disappeared, it will be smaller, shallower and devoid of horny covering. A second treatment applied then is much more likely to complete the removal than if retreatment is delayed. In an occasional case the blister continues to spread beyond the area frozen. Apparently pressure of the vesical fluid causes this enlargement. It seems to occur most commonly in lesions localized over joints or pressure points. When this occurs the vesicle top should be removed promptly and a sterile dressing applied.

In treating conditions involving larger areas, such as contact dermatitis, scarring in acne vulgaris and patches of lichenified eczema, a somewhat different technique is usually used. A larger applicator is needed. Several of the smaller common 6-inch applicator sticks may be combined, or a sturdier stick can be made by wrapping cotton about the end of a suitable length of quarter-inch doweling. This larger applicator is then dipped into the liquid nitrogen and applied either in a slow rolling or sliding manner. In treating the conditions mentioned, the reaction desired is less intense, and severe blistering is usually avoided. Slowly sliding such an applicator over the skin with moderate pressure may suffice to produce sharp delayed erythema followed by exfoliation. Such mild reactions may be of some value in the treatment of alopecia areata.

The low temperature of the liquid nitrogen causes a rapid condensation of atmospheric moisture on the cotton applicator. Thus, if several lesions are being treated or if several patients are treated in rapid succession, the applicator may become coated with ice. This interferes with its saturation with the liquid nitrogen. Likewise ice collects slowly about the opening of the thermos jug and may float on top of the liquid nitrogen. When all the liquid gas has evaporated, the ice will thaw and collect in the bottom of the thermos as water. Such icing is minimized in the commercial containers made expressly for transportation and storage of these gases by the small size of the opening. The container should be emptied and dried before it is refilled.

Liquid nitrogen has been of greatest use in the treatment of warts of the common and juvenile plane types, and it is frequently used in the treatment of superficial keratoses, both seborrheic and senile types. Although with pressure and increased length of freezing, liquid nitrogen can be made to be quite destructive, the author does not use it where appreciable thickening or infiltration of the base of a keratosis is present. Electrodesiccation is preferred for such lesions. In the author's opinion, freezing with liquid nitrogen is the best method for the removal of permanent freckles commonly seen on the exposed skin in older people, if such removal is desired.

The use of liquid nitrogen in hemangiomas is best confined to the more superficial hypertrophic vascular nevi. Solid carbon dioxide is more often used for such lesions, especially if the tumor is elevated or thickened more than a few millimeters. Liquid nitrogen may be satisfactorily used in treating small senile angiomas and the lesions of nevus araneus. In the latter, electrolysis or a fine electrodesiccating spark may be preferable if the central punctum and individual radiating vessels stand out clearly.

Superficial leukoplakia may be satisfactorily treated with liquid nitrogen. If the lesion is in the oral cavity, the patient should be instructed to hold his breath, since the intense cold fogs the moist atmosphere and obscures vision. Keloids, particularly if small, may be improved by freezing with liquid nitrogen, and the lesions of folliculitis cheloidalis have been improved greatly by freezing. The margins of individual pitted scars may be smoothed by this treatment and diffuse pitted scar-

TABLE 1.—*Results of Treatment of Common Warts with Liquid Nitrogen*†

154 patients; follow-up period 4 to 15 months

	No. of Patients	Per Cent	No. of Warts	Per Cent
Cures	97	63	243*	57
One treatment	60	39	111*	26
Two treatments	24	16	58	14
Three treatments	13	8	74	17
Failures	40	26	110*	25
One treatment	18	12	43*	10
Two treatments	11	7	22	5
Three treatments	3	2	13	3
More than three treatments	8	5	32	7
Partial cures (some warts disappeared, others did not)	17	11	77*	18
Cures				
One treatment			36*	8
Two treatments			10	2
Three treatments			2	....
More than three treatments			....	....
Failures				
One treatment			17*	4
Two treatments			6	1
Three treatments			5	1
More than three treatments			1	....

† Cowell Memorial Hospital, Student Health Service, University of California.

* Number of warts not accurate; represents least number in each category; if all records were complete, totals would be greater.

ring such as follows acne vulgaris may be conveniently treated by less intense repeated freezings with liquid nitrogen.

Acute contact dermatitis such as that produced by exposure to poison oak or ivy has long been treated by freezing with liquid gases. At the Student Health Service clinic at the University of California, this method has been in use for at least 25 years. Although it is difficult to evaluate such treatment by comparison with untreated controls, it is the author's impression that it is of value particularly when applied early to small lesions. When the dermatitis is widespread, use of the method is not practical. Similarly, isolated lesions of stubbornly resistant lichenified eczema and hypertrophic lichen planus have been treated by this method, with perhaps some improvement and relief of itching.

In granuloma annulare and stubborn discoid lupus erythematosus, in which a sharp inflammatory reaction extending to some depth is desired but in which destruction of tissue is to be avoided, solid carbon dioxide may be preferable.

Pyogenic granulomas have been successfully treated with liquid nitrogen, but the results of electrodesiccation and curettage are more uniformly successful.

Liquid nitrogen is of sufficient value in the treatment of warts and keratoses alone to justify keeping it at hand. It is easily and relatively quickly applied and lends itself to use on patients with multiple lesions. The pain involved is not great. After-care is simple. No dressing is used unless the vesicle is broken. Complicating secondary infection is rare and residual scarring is minimal. With superficial lesions no appreciable scar is to be expected. In deeper lesions mild to moderate depigmentation and perhaps slight atrophy result. It produces less scarring than other methods. Atrophy and depigmentation are noticeable only when repeated intense freezing is used, as for example in deep, resistant periungual warts. None of a number of physicians who have used this for years in the clinic and in offices has ever seen a keloid result from its use, even when deep and intense reactions are produced.

In an attempt to evaluate the use of liquid nitrogen in the treatment of warts at the clinic at the University of California, Berkeley, 154 patients, all of whom had common warts, were followed for from four to fifteen months. The results are summarized in Table 1.

While these results leave much to be desired, they are sufficiently good to justify the use of this method at least in selected cases of warts until some more specific treatment becomes available.

In order to visualize what takes place when liquid nitrogen is applied to the skin, two areas of normal skin approximately 0.75 cm. in diameter on the abdomen of an adult white male were frozen with light pressure for 45 seconds. One of these was excised after 30 hours and the second after eight days. Under the microscope a section of the 30-hour specimen showed a vesicle which had raised the epidermis cleanly from the dermis at the dermo-epidermal junction. The dermis was edematous, especially in its upper portion, and showed slight basophilic degeneration. There was a mild infiltrate of inflammatory cells scattered throughout the dermis. The majority of the cells were polymorphonuclears, but some round cells were also present. The section of the eight-day specimen showed the degenerated remains of the old epidermis which constituted the roof of the vesicle. A newly regenerated epidermis, two or three or more cells thick, was already present. Edema and cellular infiltrate were less pronounced than in the 30-hour specimen.

3115 Webster Street.

REFERENCE

1. Kile, R. L., and Welch, A. L.: Liquid oxygen in dermatologic practice, Arch. of Derm. & Syphilology, 57:57, January 1948.