

LIQUID AIR IN DERMATOLOGY; ITS INDICATIONS AND LIMITATIONS.*

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During the past year or more I have been particularly struck by the divergence of opinion expressed by my dermatologic confrères in New York respecting the value of liquid air in dermatology. In regard to its efficacy in some affections, there seems to be a general unanimity of opinion, while in others our opinions are strikingly at variance. This is the history of almost every new therapeutic agent, especially if it is a little out of the ordinary, and appears to be due, on the one hand, to a difference in the interpretation of its real powers and therapeutic properties and, on the other, to variations in the technic employed.

This is the position in which we find the *x*-ray to-day; there are few who understand it, hence the great difference in the effects produced and the results obtained. Sabouraud can use it in ringworm with a precision and uniform effect which no other can, apparently, approximate; it is possible that others can do better with it in other directions than he. While liquid air is simplicity itself compared to the intricate and complicated *x*-ray, may it not be possible that this divergence of opinion regarding even so simple a remedy is due to the fact that none of us really understands its powers and capabilities nor how to use it?

It is only by recording our personal experiences with a remedy and comparing the results obtained and technic employed that definite and uniform standards can be obtained in any field. It is for the furtherance of this object that I propose to bring to your attention this short study on liquid air, and the experiences I have had with it in both private and hospital practice, during the past four years. Appreciating fully that this short period of time is entirely inadequate to enable one to judge of its ultimate and radical effects, its immediate and moderately remote effects have been so definite, in some instances, that I feel firmly convinced that we have here a remedy of real worth, in a limited field, at least. With it results may be obtained in some conditions that can not be approximated by other means at our command, and in one instance at least it was the means of arresting a malignant process that was destined, in a few months, to destroy the life of the patient. An agent which can do this, if only in one instance, certainly warrants our most careful attention.

Unlike other means at our disposal, unfortunately, it is not always to be had when most needed, and unless it becomes more generally used for experimental or scientific purposes than it is at the present day it can never take a permanent place in our armamentarium. Commercially it has been proved an impossibility, and our future supply for medical purposes must come from technical and scientific schools and colleges, where it seems to be essential, at present, for the proper carrying out of certain lines of investigation.

We will first consider—though in the briefest manner possible, and only such as are essential to the matter in hand—the varied and peculiar general properties of this agent, together with the gross effects observed on the tissues, in the form of a drop, the spray, or by means of the cotton swab.

GENERAL PROPERTIES.

Physical.—Liquid air is a colorless, odorless, effervescing fluid, emitting a vapor which looks like steam, moderate when quiet, but abundant on agitation or stirring. It is very unstable and must be kept in a loosely-stoppered retainer to allow the escape of its component gases. It is of about the same weight as a given volume of water and has a temperature of 312° F. below zero. It feels dry to the touch and leaves no moisture on any surface with which it comes in contact.

Chemical.—Its component parts, chemically, are essentially nitrogen and oxygen, in the proportion, by weight, of about two and one-half parts of the former to one of the latter, together with a variable quantity of carbon dioxide; about one-eighth of 1 per cent. The nitrogen quickly bubbles away, leaving a liquid composed of almost pure oxygen, as demonstrated by its power to support combustion.

Therapeutic.—The effect of liquid air on bacteria was tested by Parks and White¹ in the Board of Health laboratories in New York some years ago both as regards the extreme cold alone, by incasing the germs in small tubes before immersion, and by placing them directly into the liquid air. Typhoid, anthrax and diphtheria bacilli were tested in tubes and were exposed from thirty to ninety minutes, and anthrax bacilli were immersed directly into the liquid air for over an hour. Pure cultures of all these were subsequently obtained from sterilized bouillon.

Huddleston¹ tested vaccine virus in the same manner and found, after fifteen minutes' exposure to the liquid, that its power to produce vaccination was not at all affected.

Parks² subsequently made further experiments in this same direction, exposing to liquid air almost every kind of germ life, from hay infusion to anthrax bacilli, in pure virulent cultures, for over two hours. It is reported that he found that liquid air killed 98 per cent. to 50 per cent. of these germs, from the weakest to the strongest. It killed 75 per cent. of typhoid germs, 50 per cent. of staphylococcus and 65 per cent. of diphtheria. He states that a two-hour exposure does not completely destroy the virulence of any pure culture of these germs, but suspends their vitality for a long time, and that "they are only brought back to activity by the most careful handling and under the most suitable conditions."

Macfayden,³ in 1902, tested its effect on bacteria extending over a period of six months, using for the purpose *B. typhosus*, *B. coli communis* and *Staphylococcus pyogenes aureus*; in addition to these non-sporing forms he tested a saccharomyces. These were all immersed directly into liquid air and tested from time to time; he found absolutely no impairment of their vitality. The typhoid bacilli retained their pathogenic properties and responded to the agglutination test; the colon bacillus retained its normal properties; *Staphylococcus pyogenes aureus* produced pigment on solid and an active hemolysin in fluid media, while the yeast retained its fermentative powers.

These laboratory experiments, although the results are not exactly uniform, demonstrate pretty conclusively that liquid air is incapable of destroying germ life, and it is reasonable to suppose it is incapable of more than inhibiting the activity of pathogenic organisms in the living tissues.

* Read in the Section on Cutaneous Medicine and Surgery of the American Medical Association, at the Fifty-eighth Annual Session, held at Atlantic City, June, 1907.

1. White: Med. Record, lvi, 1899, 109.

2. White: THE JOURNAL A. M. A., xxxvi, 1901, 426.

3. A. Macfayden: (Proc. Royal Soc., Oct. 31, 1902) Abst. Med., News, Dec. 27, 1902, vol. lxxxi, p. 1215.

To explain the therapeutic properties of liquid air we must look, therefore, to changes in intracellular metabolism rather than to any bactericidal effect. Cell life is manifestly impossible in the prolonged presence of this agent, for the two chief essentials to living protoplasm, viz., heat and moisture, are here lacking. The sudden shock of its application contracts the blood vessels to the highest degree, but the normal temperature is soon resumed, although if frequently repeated a most powerful local stimulation is produced and ultimately endarteritis. The intense inflammatory reaction following its application causes a flooding of the lymph spaces with serous exudate, and to this is due its therapeutic effect in cutaneous cancer, some of whose disordered cells lie in these spaces in the periphery of the growth. By constantly inhibiting the activity of bacteria, in conditions known to be due to such invasion, their pathogenic power is nullified, for a time at least, thus allowing the inflammatory exudate to cope with them, the product eventually being carried off in the lymph stream.

It will thus be seen that liquid air is something more than a caustic, in the true sense of the word, for sloughing and sphacelation are not essential to the accomplishment of its therapeutic effects. I have seen this repeatedly exemplified in the treatment of vascular nevi and angiomas, and in new growths covered with a sound epidermis which was free from moisture.

GROSS EFFECTS ON HEALTHY AND DISEASED TISSUE.

With a full appreciation of the foregoing properties of this agent, it is easy to anticipate its gross and ultimate effects on healthy and diseased tissues, and its indications and limitations can be quite accurately defined. A drop on the sound skin causes a sensation of burning and tingling, and, if allowed to remain in contact a moment or two, will cause a blister. In the absence of moisture no slough nor death of tissue takes place, but on a perspiring skin contact immediately ensues, and a blister is quickly formed; on a denuded or moist surface, a slough with loss of tissue follows.

A mild and short exposure to the normal skin by means of the spray produces blanching, followed by a moderate congestion; a longer exposure thoroughly freezes and anesthetizes the part, but if not distally situated, as the ear, toe, finger, etc., the circulation is slowly restored without affecting its integrity. It is surprising to see how deeply and thoroughly a part may be frozen, either by the spray or by the cotton swab, without ultimately causing any injurious effects. It is a well-recognized fact that extreme degrees of temperature, either of heat or cold, produce deleterious effects on the human organism, in proportion directly to the amount of moisture accompanying them. This property of dryness, therefore, explains the difference in effect of liquid air on the tissues, and much lesser degrees of cold as exhibited, for instance, in frost-bite.

In applications with the swab, the resulting inflammatory swelling varies in degree according to the amount used, the pressure employed, and the location and character of the tissues. If these are firm and well nourished it is often very considerable, while if ill-nourished or in a senile condition, irrespective of the age of the subject, a large dose will cause little or no reaction. These observations are important in the practical use of the remedy, for it enables the physician to confidently tell the patient just what he is to expect. All are more or less mystified by this curious fluid and are often much concerned to know just what it is going to do.

The pain accompanying its application is very slight and rarely lasts long, but in some cases, especially when in proximity to the teeth, it will produce excruciating pain referred to the teeth, sometimes enduring for an hour. In pathologic conditions it relieves pain after a few applications and lessens discharge and odor; it likewise diminishes tendency to hemorrhage, although there is always a surface oozing during the congestive stage, when applied to an open surface. Mild applications will encourage healthy granulation, while stronger ones will destroy exuberant growth. It produces very little, if any, reactionary effect on scar tissue, and in consequence of this property I have found it of distinct diagnostic value in epithelioma, an observation which will be referred to more in detail later on.

ITS INDICATIONS AND LIMITATIONS.

From what has gone before it would naturally be supposed that liquid air is destined to have a very wide range of usefulness in the therapeutics of cutaneous disease. If it were not for the fact that we already have means at our disposal which are always accessible, that possess many of the properties of liquid air, and can fulfil its indications quite as well, or even better in many instances, this might be so. For local anesthesia, the treatment of abscess, bubo, boils, carbuncles, ulcers, warts and various other conditions in which extravagant claims were early made for this agent we have other far more convenient methods of equal or greater efficacy.

In pigmentary, hairy and vascular nevi, angiomas, lymphangioma circumscriptum, lupus erythematosus, lupus vulgaris and epitheliomata (unaccompanied by lymph-gland invasion), however, we have in liquid air a remedy which will often give us better results than we have been in the habit of getting by other means. I say often, rather than always, although the difference, I believe, rests wholly on the matter of technic.

TECHNIC.

Herein lies the kernel, as in almost every branch of practical medicine, but, unfortunately, perfection can not be attained. We can endeavor to approach it, however, and the nearer we do so the more uniform will be our results and, I believe, less divergent our individual opinions respecting the value of liquid air in dermatology.

For practical use liquid air is kept in what is called a "Dewar" bulb, which is a double bulb of glass, one blown inside the other, the space intervening being a vacuum. The surfaces of these bulbs are silvered, and this, together with the separating vacuum, retards the radiation of heat; the whole is incased in cotton wool or thick felt to prevent further radiation. These retainers are made in various sizes, but for office use one containing a liter is most convenient, and this amount, in ordinary room temperatures during the winter, will last six days. In summer it will not keep so long, unless it can be kept in an ice chest. A loose wad of absorbent cotton constitutes the cork.

The spray is obtained by inserting a rubber cork pierced by two glass tubes in the manner employed in the ordinary laboratory wash-bottle, the mouth of the entering tube being closed by the finger. I no longer use this method of applying the liquid, for it is difficult to accurately limit the area of exposure, and, furthermore, the field is constantly obscured by the dense and opaque spray, rendering it impossible to judge of the depth of its action.

The cotton swab is applicable to all conditions, and with a little experience can be used with great precision. Pine sticks of sufficient length to reach to the bottom of the retainer can be so shaped that the liquid may be applied in any quantity desired and to any shape or character of lesion. The end, which should be rather firmly wound with absorbent cotton, can thus be made flat, round, pointed or paddle-shape, as desired.

In making all applications the excess of liquid should be first shaken off, scabs should be completely removed from all lesions to be treated, and thin gauze must intervene between the applicator and all mucous or denuded surfaces, otherwise the swab will freeze fast.

The elements governing the effect produced are (1) the degree of saturation of the swab, (2) the accuracy of contact, (3) the amount of pressure exerted, and (4) the duration of the exposure.

On a thorough appreciation of these four elements, coupled with correct judgment respecting the interval allowed between exposures, which is a variable quantity according to the character of lesion and the effect of an antecedent treatment, depends wholly, I believe, our success or failure in treatment. The amount of pressure and its duration, granting the contact is accurate and saturation adequate, seems to be the keynote to the effect produced in any given application. This is the most difficult element to master and it is undoubtedly the most important. Of almost equal importance, however, is the correct judgment of the time to allow between applications; this may be only a few days or several weeks; if made too frequently disastrous results will follow. As a general rule, the slower the method the better the result.

In some conditions, as lupus erythematosus and port-wine mark, a light pressure with the paddle applicator, of relatively short duration to produce a superficial freezing, is indicated. A second application to the same area is not made until the effect of the first has subsided. In this manner both conditions, if not too extensive, can be successfully removed in a shorter time and with a better cosmetic effect than by our old methods. In pigmented and hairy nevi, angiomas, lymphangioma and lupus vulgaris a medium pressure is indicated, and the same rule applies of waiting until the effect of one application is passed before making another; in treating individual nodules in lupus vulgaris, however, rather severe pressure with the pointed applicator is required.

In epitheliomata firm pressure of considerable duration is essential. In those of the ordinary size that occur on various regions of the face the pressure should be exerted at the periphery rather than in the center, or recurrences may be expected; the same interval rule applies here also. Exactly the same indications obtain for the superficial type of rodent ulcer. It is in this connection that the diagnostic value of the agent previously referred to is apparent. Formerly in curetting what seemed to be small pearly nodules at the periphery of a healed patch one frequently found some of them to be firm cicatricial tissue. Firm pressure with the liquid air applicator, covering several such, freezes only the diseased nodules, no visible effect being observed on the others; I have found it a most valuable aid in this capacity.

In treating indolent eroding epitheliomata very firm pressure is required, particularly at the hard rolled edge, and in this type it generally requires several applications at intervals of two or three days before healing begins,

but when once commenced the same rule of waiting before making further applications should be observed. In rapidly advancing fungating epithelioma the remedy should be used with a very bold hand until recrudescence begins, after which the interval applications should be adopted.

It is here that I have noted in more than one instance a very peculiar and misleading reactionary effect. In a day or two after an interval application a hard, raised, narrow, circinate and pearly border develops, resembling in every respect a typical active epithelioma. This entirely disappears in a few days and is undoubtedly a linear, hard blister formed at the periphery of an over-saturated swab. Were it not for the very sudden development of this condition one might be misled into making a second application, believing that the preceding one had only stimulated the growth; liquid air will do this, as in the case of ordinary caustics, if too mildly applied. In such an event an immediate severe application will usually arrest its progress at once, but in some cases it must be used in a most fearless manner in order to accomplish this effect.

The technic here detailed, based on and developed from an experience gained in the treatment of a fairly large number of cases, I put forth with a considerable degree of confidence, believing that by its careful observance uniform and satisfactory results may be obtained.

Some personal cases are here appended, a portion only of the total treated, but enough to illustrate the value of liquid air in a limited number of diseases and abnormalities. As nearly half of these were in private practice a good opportunity was offered of following most of them to the present time. Three only are at present under treatment, two hospital and one private case:

CASE 1.—*Nevus Pigmentosus*.—J. B., a private patient, a woman aged 50, with a raised, pigmented, non-hairy nevus, elliptical in shape, with dimensions of a half inch by three-eighths, situated on the back of the neck. Three applications with medium pressure successfully removed it, leaving a smooth, whitish cicatrix, scarcely discernible.

CASE 2.—*Nevus Pigmentosus*.—A. R., a girl aged 16, another private patient, with a semi-fleshy, elevated, dark-brown nevus, circular, three-eighths of an inch in diameter, and situated on the left chest below the clavicle. One application with moderate pressure almost entirely removed it; a second lighter application completed its removal, leaving only a small pale spot to mark its site.

CASE 3.—*Nevus Pigmentosus*.—H. B., a 14-year-old boy in hospital practice, with a raised, dark-brown nevus the size and shape of a "butter-bean," situated on the forehead a half inch above the outer end of the right eyebrow. As the tissues were dense and resistant, moderately severe pressure was used, which produced a well-marked inflammatory reaction. The lesion scabbed and healed satisfactorily, but required two subsequent milder applications to complete its removal; the resulting scar was not depressed, and was only slightly noticeable.

CASES 4 and 5.—*Nevus Pilosus et Pigmentosus*.—L. G. and P. M., two dispensary cases, one in a young man aged 17, an elongated hairy mole, three-quarters of an inch in length, situated above the beard line on the left cheek; the other, a mouse-skin lesion, not quite circular, but of about the area of a dime, on the right side of the chin, in a woman over forty. The first was removed in five applications with medium pressure, a slight amount of the pigmentation being left, which successfully masked the smooth cicatrix resulting. Three applications, the first two with moderate pressure, the third a very mild one, were successful in removing the lesion on the chin, leaving only a small non-depressed cicatrix.

CASE 6.—*Nevus Vasculosus*.—M. G. This was situated on

the nose of a woman, aged 40 years, a private patient, and was about the size and shape of a finger-nail. An application was made with sufficient pressure to produce a superficial caustic effect. This was done April 3, 1905, and on the 14th the thin scab that had formed had not fallen, but on the 25th, three weeks after the application, it had entirely disappeared; the scar was smooth and flat. She reported three months later, by request, and there had been no return; the result was apparently permanent.

CASE 7.—*Nevus Vasculosus*.—R. C. The lesion in this case was also situated on the nose, the subject being a dispensary patient, a little girl of 11 years. It was irregular in shape and occupied over twice the area of the preceding case, a so-called port-wine mark. The treatment was begun Jan. 16, 1905, with light pressure applications, and eight of these were made covering a period of about two months. The patch became lighter in color after each application, and in less than three months from the beginning of treatment, nothing remained of it. A very superficial atrophic-looking scar marked its site. No change had taken place seven weeks later, when she reported for observation.

CASE 8.—*Nevus Vasculosus*.—N. H., a young woman, aged 23, a private patient, with an irregularly shaped vascular nevus, situated partially over the angle of the left ramus and adjacent part of the neck. The upper part had been treated by electrolysis leaving a somewhat pitted scar; the remaining patch measured about one inch in its longest diameter. Applications with moderate pressure were begun July 24, 1904. The first was made next to the old scar, but proved to be of little too long duration, as a superficial slough formed. Five other applications were made over the remaining area, covering a period altogether of seven weeks. At the end of two and a half months, none of the nevus remained. The scar was smooth and superficial; the first part treated was slightly depressed, but was perfectly smooth. The patient was seen two years later and there had been no return; the cosmetic effect was satisfactory.

CASE 9.—*Lupus Erythematosus*.—C. S. This patient, a woman, 36 years of age, had been treated at the dispensary for over four months with very little improvement. The disease had lasted three years and consisted of two characteristic patches, one on the left cheek near the wing of the nose, about the size of thumb-nail, the other on the right side of the bridge, a little larger in area. Three applications with mild pressure removed the patch on the cheek, while five or six were required to remove the other completely; the patch on the nose was more deeply infiltrated, being the older of the two. The resulting scars were smooth and quite superficial. She was carefully instructed to return if further troubled. Over a year has elapsed but she has not again reported.

CASE 10.—*Lupus Erythematosus*.—T. K., a man, a hospital patient, 42 years of age, with a patch a little smaller than a twenty-five cent piece, situated on the left temple; duration one year and a half. Six application with moderate pressure were made from time to time in this case, and the patch had almost disappeared when the patient was lost sight of.

CASE 11.—*Lupus Vulgaris*.—M. F. This was a private patient, a girl of 13 years, with a patch nearly an inch in diameter, situated on the right side of the chin; it began as a small papule three years previously. A fairly severe freezing was done which caused considerable reaction. It sloughed and healed under a scab in about five weeks, but only about half of it had been destroyed. A moderately severe and two milder applications were subsequently made, resulting in its complete removal. The scar in this case was smooth and pliable, though slightly depressed. Over a year has now elapsed without any recurrence being reported.

CASE 12.—*Lupus Vulgaris*.—A. M. This is a very old case that I first saw at the hospital Feb. 18, 1895, in a woman then 53 years of age. She had a patch of lupus three inches in diameter on the right cheek, which was then of two and a half years' duration. I scarified it a number of times early in the course of its treatment, and it has been attacked in various ways since. On Jan. 23, 1906, there were five isolated tubercles remaining, the rest of the surface showing a surprisingly small amount of scarring. These were deeply frozen on that day with the pointed applicator; there was a great

deal of inflammatory reaction, but they all disappeared. A week ago, sixteen months having elapsed, the patient thought one of the nodules was returning; it has become red and slightly raised, but it is not yet certain if it is diseased; if so, one application will undoubtedly cure it.

In the following series of fifteen cases of epithelioma, eight private and seven dispensary, there were twelve of that type commonly seen on the head and face. The other three were examples of the indolent eroding, superficial rodent ulcer, and quickly spreading fungating forms. They were all unaccompanied by lymph-gland metastases, the only type of cancer in which I consider this remedy is indicated:

CASE 1.—B. S., woman, aged 41, private patient. A scabbed quarter-inch size lesion, with pearly rolled edge, situated on the left side of the nose, between the bridge and the inner canthus. It began two years previously, from irritation by the nose-piece of her eye-glasses; there was the usual history of scabbing, healing and progression. One application was made with firm pressure Nov. 16, 1905. The crust fell off and it was healed in a little over two weeks. There has been no recurrence to the present time, over one and a half years; the scar is smooth and flat.

CASE 2.—M. M., woman, aged 28, private patient. A lesion of the same character and size as that in the preceding case, situated in the middle of the right side of the nose; it followed the squeezing of a black-head two years previously. Application was made Feb. 27, 1906, and it was entirely healed in three weeks. Thirteen months later, two pin-head size recurring nodules at the lower border of the scar were again frozen. All was healed in ten days, a good flat scar resulting. I attribute this recurrence to the fact that a small piece of the original scab was inadvertently left attached to the lower edge at the time the first application was made.

CASE 3.—C. C., woman, aged 26, private case. The lesion in this case was practically a duplicate of the two preceding ones, but was situated on the bridge of the nose, and followed a traumatism three years previously. One application made April 10, 1906, healed it completely in fourteen days, a good smooth scar resulting. No recurrence to date, a period of thirteen months.

CASES 4, 5, and 6.—L. H., M. P. and M. T. These were three hospital patients, women, aged respectively 24, 59 and 44 years, all with lesions located on the nose, varying in size from a quarter- to a half-inch in diameter. The first was between the left inner canthus and the nasal prominence, and was ten months in duration, developing from a blackhead. The second was two years in duration, located on the right nasal wing, and developed from a mole. The third followed irritation by eye-glasses five months previously, and was on the right side of the nose near the inner canthus. They required one, three and two applications respectively, and smooth superficial scars resulted in all of them. They have not been heard from since and are presumably well, as special efforts were made to impress them with the importance of reporting in the event of any change.

CASE 7.—H. S., man, aged 40, private patient. The lesion was situated beneath the outer canthus of the right eye, was 15 years in duration, and developed from a flat mole. It was nearly circular, three-quarters of an inch in diameter, was covered with a scab, and had a rolled, hard, pearly edge. Applications were begun Jan. 5, 1904, four treatments being necessary to destroy the growth. It was all healed March 12, 1904, two months later, and has remained well to the present time, over three years; he visited me recently for another trouble and a smooth superficial scar marked the site of the old lesion.

CASES 8 and 9.—M. F. and J. P. These were private patients, a man aged 65 and a woman aged 70, both with lesions about the size of a dime, situated on the right cheek, one near the eye, the other lower down. Both developed from flat senile warts, and were three and two years in duration respectively. One application made July 11, 1905, healed the first completely in about three weeks, and it remains well now, nearly two years later. The second required two treat-

ments, Jan. 6 and 29, 1906; it completely healed two weeks after the second application and has not returned, after a year and a half. Good smooth scars resulted in both instances.

CASE 10.—M. R., a man, aged 70, dispensary patient. Lesion behind the left ear, three-eighths of an inch in diameter, six months in duration, and was supposed to have followed the bite of an insect. One severe freezing, April 24, 1905, healed it entirely in less than three weeks. It is now over two years and no relapse has been reported. The scar was a trifle depressed, but smooth.

CASE 11.—H. C., a woman, aged 25, a hospital patient. Typical epithelioma, one-quarter by three-eighths of an inch in diameter, situated on the left breast, one inch above and to the inner side of the nipple; it developed from an injury by a safety-pin one year previously. This was frozen twice, Aug. 15 and Oct. 21, 1904, and was entirely healed in sixteen days after the last application; no recurrence to the present time, nearly three and a half years. The scar was very slight.

CASE 12.—F. S., woman, aged 60, a charity patient. The lesion is located in the center of the forehead and began in a mole last summer. When the first application was made March 26, 1907, it was three-quarters by one-half inch in size. There are still two or three small nodules on the right side of a smooth scar; the case is awaiting another treatment, which will undoubtedly finish it.

CASE 13.—C. M., a woman, aged 72, a private patient, with a rapidly growing fungating epithelioma starting just below the vermilion border of the lower lip, in the median line. It began as a pimple, which was pricked and squeezed, and when first seen, July 20, 1904, six weeks later, there was a round hard growth, a half inch in diameter and elevated the same distance above the surface, slightly ulcerated in the center, with telangiectic vessels coursing over it. This rested on a densely indurated base one inch in diameter, easily felt from inside the mouth. The protruding growth was removed July 25 with acid nitrate of mercury, and the base was exposed to the x-ray two or three times a week, at the hands of another, for four weeks. The patient returned to me August 29, with a fungating growth involving almost the whole width of the lip, and extending inside the mouth. On the same day I applied a large Marsden's paste to the growth below the vermilion line, and the following day another. In seven days the slough came away, leaving a deep excavation. On September 7 the mucous surface was attacked with liquid air, and up to October 22, a period of six weeks, nine severe applications had been made. On October 26 a group of nodules developed on the right side of the chin, at a distance from the original growth; two more applications were made to these and the remainder of the original growth, making eleven in all, the last one being on November 29. On December 20, three months from the first application, all was perfectly healed, with an excellent scar level with the surface. The lip was slightly shortened, but the contour was not affected. She returned on that day to her home in a distant city.

On Jan. 8, 1906, thirteen months from the last application, she returned with a relapsing nodule the size of a pea, on the mucous surface, to the right of the median line. Two applications were made to this, but they were too mild and stimulated it to three times its original size. On January 29 a very severe application was made, freezing the entire thickness of the lip; this was successful, for on March 5 she returned home again, clinically, perfectly well. Strange to say, the contour of the lip was still preserved. There has been no recurrence to the present day, a period of fifteen months, or seventeen since the last application, and the patient is in her 75th year, a fine specimen of physical health.

CASE 14.—D. R., a woman, aged 40, a dispensary patient, with an eroding, indolent, and very painful carcinoma of fifteen years' duration, involving the left side of the nose and adjacent cheek and upper lip. The ala and a portion of the tip have been destroyed, the ulceration extending half way up the side of the nose and to the median line. It has a hard everted border and is devoid of granulations. She received the x-ray three times a week for the past four years, with, the patient says, no beneficial effect. Liquid air has been applied four times between Feb. 3, 1907, and April 1, but inability to

obtain the agent has delayed its further treatment. The pain, however, is very much less, and the upper one-third has healed. I have every confidence that liquid air will eventually heal it.

CASE 15.—S. B., a man, aged 57, a private patient, with a superficial rodent ulcer of about ten years' duration situated on the right temple and forehead. It was successfully healed by the x-ray, but did not remain so, although there is a smooth but thin scar on the temple, three inches in diameter, free from active disease. When first seen, Dec. 5, 1906, the disease was active over the right eyebrow, in the form of a crescentic deep ulceration an inch long, extending parallel to it, and almost exposing the periosteum. There was also an ulcer, three-quarters of an inch in diameter, over the zygoma, and a line of nodular lesions extending anteriorly from this, almost to the outer canthus. A third crescentic ulceration extended upward from this point, almost joining the one above the eyebrow. These have had, altogether, five applications from Dec. 13, 1906, to May 6, 1907, as a result of which all have healed except the ulcer over the zygoma, although this is half gone. The patient is still under treatment and I feel certain one more application will heal the small ulceration remaining. The result to date could have been accomplished in a third of the time had the agent been accessible when wanted and had the patient been more attentive.

It is hoped that the experiences here recorded have justified, in a measure at least, the conviction expressed at the beginning that we have in liquid air a remedy that is not without considerable value in a limited field in dermatology.

The results obtained in the first series of cases, including pigmented, hairy and vascular nevi, lupus erythematosus and lupus vulgaris are certainly better than we have been accustomed to get by our old methods in the same character of lesion. By this method such conditions can be removed with much greater ease and with very little inconvenience to the patient, while with proper care a minimum amount of scarring is produced.

In epithelioma, in the particular class referred to, it must be conceded, I think, that it is distinctly a power for good. It will take time and further experience to determine just all that it is capable of in this direction, but even now, it seems to me, it outranks some of the remedies on which we have placed great reliance. It is generally admitted that excision is not so effective in cutaneous epithelioma as the caustic, or the curette and caustic, for the flooding of the surrounding lymph spaces reaches the outlying cells which the knife can not. It has been shown that liquid air can do more than an ordinary caustic; logically, then, it should take a high place among them.

The x-ray will sometimes heal them, but they are prone to recur, and on a recurrence it is often ineffective. With better technic recurrences after liquid air will be, I believe, less likely, but on these it is as effective as on the primary growth. The cosmetic effect is equally good in both, but it is to be noted that no danger attaches to the use of liquid air either to the operator or to the subject. Finally the matter of time and trouble to the patient should be a consideration, and in treatment by liquid air these are greatly minimized.

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DISCUSSION.

DR. H. W. STELWAGON, Philadelphia, said that he had the pleasure, a few years ago, of seeing Dr. Charles T. Dade demonstrate this method in New York, especially in cases of angioma and lupus erythematosus, in both of which affections there is need of new methods of treatment. In the treatment of angiomata, electrolysis has not proved very serviceable; it very often fails, repeated operations are often necessary, and the treatment is very painful. The usual

methods of treatment in lupus erythematosus are also unsatisfactory, although in some cases the results are fairly good. Those cases in which we do get results are the ones where the disease has remained stationary, has shown no inclination to spread, and in which one is justified in using superficially destructive applications. In the cases of angioma and lupus erythematosus treated with liquid air, there was very little scarring, which, he said, is also a strong argument in favor of this method of treatment.

DR. WILLIAM A. PUSEY, Chicago, stated that the effect of liquid air depends on the fact that it produces almost instantaneous freezing. The objections to it are that it is commercially unobtainable, and is difficult to preserve. After witnessing the demonstration nearly two years ago by Dr. Dade, it occurred to Dr. Pusey that a good substitute for liquid air would be liquid carbon dioxide, which is obtainable anywhere. On investigation, he discovered that the commercial liquid carbon dioxide is liquified under a pressure of about 800 pounds, so that it is not in liquid form at atmospheric pressure, and that when it is withdrawn from a drum it evaporates so rapidly that it freezes into a snow very much in appearance like ordinary snow. Liquid air has a temperature of about -180 degrees C., while solid carbon dioxide has a temperature of about -90 degrees C. Liquid air, therefore, is twice as cold, but both will produce almost instantaneous freezing, and Dr. Pusey was not sure that the temperature of carbon dioxide snow is not better for therapeutic purposes than that of liquid air. In his opinion the usefulness of both of these agents depends on the fact that they are destructive agents whose actions are readily controllable. One can produce an inflammatory reaction which will result in sclerosis, or one can produce destruction of the tissues with them; the effect produced depending on the duration of the application and, to a less degree, on the amount of pressure exerted. Dr. Pusey said that he gained the impression at first that one could produce sloughing with liquid air, but he has since learned that either with liquid air or liquid carbon dioxide one can destroy tissue as completely as with a hot poker. By timing the application of liquid carbon dioxide he has found that the effects can be controlled. With ten seconds there is a moderate reaction, with twenty seconds a fairly severe reaction with blister formation, and so on through longer exposures.

Dr. Pusey has used carbon dioxide in many cases of nevi, to a less extent in lupus erythematosus. In small pigmented nevi, his results have been the same as those of Dr. Whitehouse; the nevi have been removed without difficulty, leaving white pliable scars. He has also used it in one case of a very extensive hairy nevus, involving the face and forehead, in a girl 12 years old. In this case the nevus was covered with long hair, which was first removed by the Roentgen rays; then he began to work on the pigmented area with the carbon dioxide, and he has succeeded, practically, in removing the pigment. The case was demonstrated at a meeting of the Chicago Medical Society and the members present agreed that an equally good result could not be obtained by other means. In cases of vascular nevi the results are also good, but the application must be made with great care, because if the freezing process is overdone, it will result in a perfectly white ivory-like scar. In regard to lupus erythematosus, he demonstrated a case recently in which he obtained good symptomatic results. The lesions involved part of the face and forehead, and the treatment resulted in perfectly white, smooth, flexible scars; in fact, hardly scars at all. At one point there still remains a small area of suspicious tissue. Of course, nothing more is claimed than a symptomatic result, for, as is known, lupus erythematosus is an extremely capricious disease.

Dr. Pusey has not tried the method in the treatment of epitheliomata, except the very superficial lesions accompanying senile keratoses. Senile keratoses, and the beginning epitheliomatous infiltrations which occur with them, can readily be removed by liquid CO_2 much more readily than by other methods. Any amount of tissue can be destroyed with liquid air or with liquid carbon dioxide, so that epitheliomata

can be treated successfully with these agents, but Dr. Pusey does not believe it is the method of choice.

He has applied liquid air on a few nodules of lupus vulgaris, but not with success, undoubtedly, however, because his applications were not vigorous enough. In short, his experience with carbon dioxide snow corresponds exactly with that of Dr. Whitehouse with liquid air. If there is any difference in the results, he is unable to determine them from his description. Dr. Pusey believes the use of both the agents is distinctly worthy of trial.

DR. GEORGE T. JACKSON, New York City, has had a large experience with liquid air at the Vanderbilt Clinic, where Dr. Dade is one of the physicians, and he confirmed the efficacy of this agent, although it is often very painful. He has seen men and women cry with pain during the thawing out of the frozen surface. As regards the methods of applying the liquid air, he has found the swab the most satisfactory, using a sufficient amount of cotton to absorb the liquid. By the applications the tissues are first frozen stiff; then they thaw out and a blister forms which dries up and falls off, leaving a perfectly smooth scar. Liquid air is a destructive agent and will always leave a scar.

In lupus vulgaris he has not had much success with it, but in lupus erythematosus, he thinks it is the best thing we have, in spite of the scar that it leaves. But the disease always leaves scars. In all forms of nevus the result of the treatment has been excellent. In deep-seated angiomas it takes out the color, but does not remove the tumor. In port-wine marks the results have been less satisfactory, on account of the depth of those lesions. In epithelioma he has had practically the same results as those reported by Dr. Whitehouse.

DR. L. DUNCAN BULKLEY, New York City, has had considerable experience with liquid air. In some of the cases, the scars that were left could, he thought, have been rendered less noticeable with a better knowledge of the technic of the applications, especially in lupus erythematosus. He did not understand how Dr. Whitehouse could refer so lightly to the pain caused by these applications. He has known patients to complain bitterly of the pain after severe applications. With repeated and light applications, however, given at distant intervals, as Dr. Whitehouse recommends, one can readily understand that the pain would be comparatively slight.

DR. JAMES D. GOLD, Bridgeport, Conn., has used liquid air to some extent in private practice. In one case of large vascular nevus in the temporal region and involving half of the eyebrow and both upper and lower lids, he made repeated applications, with very satisfactory results. The treatment has left a smooth white scar in the area where there was originally a large, bright red nevus. The patient in this case was a baby, and the treatments were commenced when it was 4 months old. The pain caused by the applications apparently was severe, as the child cried for two or three hours afterward. In cases of lupus erythematosus, his results have also been satisfactory. In one case an excellent result was obtained after two applications. That patient also complained of pain. In another case of lupus erythematosus where the disease was of seven years' standing, the applications failed to arrest the spreading of the lesions.

DR. LEE S. SHONINGER, New York City, stated that one point in connection with this treatment is not entirely clear, and that is the question of scarring. Dr. Whitehouse had a resultant scar in almost every case. It would be of some importance, he thought, if Dr. Whitehouse would dilate on the character of that scar; whether it was atrophic or hypertrophic; the pathologic process involved in the formation of the scar, and also the macroscopic changes taking place in the interval.

DR. WILLIAM S. GOTTHEIL, New York City, stated that liquid air is a curiosity; we can not get it. Carbon dioxide, on the other hand, is obtainable, and, according to Dr. Pusey, it practically answers the same purpose as liquid air. Apparently these applications act by setting up an inflammatory reaction, and they cause scarring. Can not the same thing be done with any cauterizing agent? For instance, with trichloroacetic acid, a very manageable caustic, one can produce

an inflammation, with resulting superficial cicatricial tissue, just as with carbon dioxide.

DR. H. H. WHITEHOUSE, New York City, said he had simply referred to the manner in which the applications should be made if deep scarring is to be avoided. The ordinary scars left by the applications are perfectly smooth and pliable, and he has never seen hypertrophic scars result from its use. What the pathology of the process is, and what the changes are that take place during the intervals of the freezing, he does not know, as most of these lesions are on the face, and it would be difficult to get a section of tissue for examination. As to carbon dioxide, which has about one-half the coldness of liquid air, he thought that one ought to get from it about the results that we get from liquid air. In regard to the pain caused by the application; he stated that while he may have been misled in that respect by some of his patients, he does not think his observations, in the main, were far wrong. After treatment, he has always instructed patients to make cold applications, which apparently were soothing. The better nourished and the younger the patient, the greater the degree of reaction and the greater the pain. In some cases of rodent ulcer the patients scarcely felt the applications, and in none of the cases was pain a prominent symptom. In any event, it could readily be alleviated by the application of an icebag. The interval between the applications, to which Dr. Bulkley referred, is a very important factor in the treatment.

Generally speaking, it takes about a week or ten days, after a mild application, for the little scabs to fall off and the tissues to resume their normal condition. After severe applications, to an epithelioma, for instance, often four to six weeks will elapse before the good effect of an application ceases. In indolent, deeply eroding epitheliomas, several applications, at intervals of a day or two, are necessary to start the healing process, after which three to six weeks will often elapse before another application is needed.

As regards the treatment of deep-seated port-wine marks, his opinions are practically the same as those expressed by Dr. Jackson. In these cases such a deep-seated effect must be obtained that the resulting scar may be worse than the original lesion. The same is true of deep-seated lupus erythematosus, the type generally observed in long-standing cases.

THE VALUE OF TUBERCULIN TR AS A DIAGNOSTIC AND THERAPEUTIC AGENT

IN THE RECOGNITION AND TREATMENT OF TUBERCULOSIS OF THE EYE; WITH REPORT OF CASES.*

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Tuberculosis of the eye and its adnexa is a rather rare disease, though I believe not so uncommon as reported, for its presence is sometimes not recognized from lack of observation. We know that all parts of the eye may suffer secondarily from extension of the disease from lesions elsewhere in the body, yet it is a well-recognized fact that the ocular lesion may be primary, and the only existing focus of infection in the organism. It seems to be a well-established fact that tuberculosis attacks by preference the posterior segment of the eyeball, especially the more highly vascularized portion, like the chorioid, extending to the retina and thence by the blood vessels to the anterior segment of the eye. When the disease spreads from the interior to the exterior, the foci of disease may always be found at the filtration angle. The presence of indurated glands in anterior tuberculosis of the eye is not pathognomonic, but is of great diagnostic value, for statistics show that enlarged glands are found in about 85 per cent. of these cases. The microscopic

examination of these glands does not necessarily render the diagnosis of tuberculosis certain, even if numerous giant cells are found, and the bacteriologic examination must prove the presence of the tubercle bacillus.

DETERMINATION OF NATURE OF LESION.

To determine positively the tuberculous nature of an ocular lesion, we must apply three tests, viz.: 1, histologic; 2, experimental; 3, bacteriologic.

Histologic Test.—The respective value of these tests is well described by E. Treacher Collins,¹ who states that the reaction of the tissues to the tubercle bacillus consists of an aggregation of cells made up of a central giant cell, the so-called Langhans' cell, epithelioid cells, and marginal lymphocytes. These cell aggregations may undergo caseous degeneration or a general cicatricial fibrosis. These three conditions, the cellular aggregation, the giant-cell system and the caseous degeneration, found together in a tissue, make the diagnosis of tuberculosis practically certain; but the presence of any one of them alone is not sufficient proof.

The Experimental Test.—This consists in the inoculation of tuberculous tissue in the eyes of rabbits or guinea-pigs, and the most suitable situation is the anterior chamber. The tissue to be inoculated may be taken from any part of the organ, but must be entirely free from any suppurative organisms. The results of these inoculations of tuberculous material into the anterior chamber have been so generally successful that we have come to look on the experimental test as the most certain of all. The immediate reaction after such an inoculation is very slight. By the end of a week the piece of tissue has been absorbed, and the eye looks normal. After a period varying from ten to twenty days the iris becomes inflamed and shows small gray nodules scattered all over the surface, which grow larger, coalesce and sometimes fill the anterior chamber and invade the cornea. General infection of the animal soon follows.

The Bacteriologic Test.—The presence of the tubercle bacillus in the tissue is conclusive proof of its tuberculous nature, but failure to find the bacillus after the most careful search can not be regarded as disproving the tuberculous nature of a lesion. In some cases the bacilli are limited in number, notably in chronic cases.

MODE OF ENTRY OF BACILLUS IN EYE LESIONS.

The postmortem table has often taught us that many tuberculous lesions exist without giving any clinical evidence of their presence. We know that endogenous infection of the posterior segment of the eye occurs in acute dissemination tuberculosis, and also in connection with the chronic tuberculosis of the skin, bones and joints. But we occasionally see cases of tuberculosis of the eye, both intraocular and extraocular, without the slightest evidence of the disease in any other part of the organism at the time, though they may have developed later.

We are inclined to believe that, except through some perforating wound or loss of substance, the only other port of entry for the tubercle bacilli would be the lymphatic or blood circulation. But we have no positive evidence that the bacilli can enter the blood current, except by direct inoculation or the involvement of the blood vessel in a nodule of the disease. Hence the development of tuberculosis of the eye through the blood is always secondary to a tuberculous focus elsewhere.

We know that tubercle bacilli may pass through the

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1. Ophthalmoscope, January, 1907.