LUPUS VULGARIS*

A NOTE ON A NEW METHOD OF TREATMENT BY
INTRADERMAL INJECTION OF PHENYL-
ETHYL HYDNOCARPATE

BY

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(With Special Plate)

The similarity between leprosy and tuberculosis has frequently been noted, and has led to remedies for leprosy being used in lupus vulgaris. In 1933 Rogers¹ reported successful results in the treatment of the latter disease with sodium morrhuate and creosoted moogrol (ethyl esters of hydno-*carpus* oil with 4 per cent. creosote) injected intradermally into the lesions, a technique originally devised by workers in the Philippine Islands,² and widely used in the treatment of cutaneous leprosy.³ Muende has also treated cases of lupus vulgaris with creosoted moogrol,⁴ but he found that the injections caused considerable pain and local reactions. His results were good in adults, but not in children. Further cases of lupus in adults treated by Muende and Cochrane with creosoted moogrol have confirmed these observations.⁵

Owing to the pain caused by the creosoted ethyl esters Cochrane suggested to the chemical research department of Burroughs Wellcome and Co. that some preparation might be made which would be less painful. Hydno-*carpus* oil is chiefly composed of a mixture of glyceryl esters of chaulmoogric and hydno-*carpic* acids. "Glyceryl" is the radical derived from ordinary glycerin or glycerol, and may be replaced in hydno-*carpus* oil by other radicals, such as "ethyl" from ordinary alcohol or "methyl" from wood alcohol. After much research, in the course of which many preparations of this type were made from hydno-*carpus* oil, it was found that phenylethyl esters, in which the replacement radical is "phenylethyl"—derived from phenylethyl alcohol, a bland substance having a slight local anaesthetic action—proved to be one of the least irritant preparations, and to be as easily absorbed as any other kind of hydno-*carpus* ester.

It has long been known that some samples of hydno-*carpus* oil are more irritant than others, and that this may persist in esters made from such oil. The source of this extra irritation has been traced to a constituent in the small uncrystallizable portion of the total fatty acids derived from the oil.⁶ It is possible to eliminate this material, and this has been done in preparing the phenylethyl esters used in this investigation. A convenient name for the preparation is "phenylethyl hydno-*carpate*." The preparation, after a limited trial, was found not to be of greater efficacy in the treatment of leprosy as compared with the ordinary preparations, but it was much less painful. Cochrane therefore suggested to me, a little over a year ago, that this preparation should be tried in cases of lupus vulgaris.

In this report are recorded the results of treatment in eleven cases. The preparation is injected intradermally into the lesion.

Case Records

CASE 1

E. S., male, aged 26 years. Operation on cervical glands at age of 3 years. "Skin disease" affecting left side of neck and chin for as long as he can remember. Sought advice from me for the first time on April 26th, 1934. Prior

to this had had treatment with chemical caustics, α rays, radium, and carbon dioxide snow. On left side of neck, angle of jaw, and chin there was a large scar with hyperkeratosis in the centre and telangiectases; nodules of lupus vulgaris were present all around the edge of the scar.

Treatment.—11/5/34: Some of the nodules infiltrated with phenylethyl hydno-*carpate* (0.5 c.cm.). 18/5/34: All nodules infiltrated (2 c.cm.). 25/5/34: All nodules infiltrated (2 c.cm.). 1/6/34: All nodules infiltrated (3 c.cm.). 8/6/34: All nodules infiltrated. 20/6/34: Lesions flatter; nodules on posterior margin infiltrated (1 c.cm.). 29/6/34: Nodules on chin, front of neck, and upper part of posterior margin infiltrated (2 c.cm.). 3/8/34: Nodules on chin and front of neck infiltrated (2 c.cm.). 28/8/34: No nodules visible. 4/9/34: Some nodules on lower margin; these were infiltrated (1 c.cm.). 30/10/34: No nodules present. 27/3/35: No nodules present. 5/6/35: No nodules present. 17/7/35: No nodules present.

From May to September, 1934, the patient had weekly carbon-arc ultra-violet light baths, and was taking ostomalt three times a day.

CASE 2

H. B., male, aged 15 years. Patch of lupus on right side of neck for ten years. No previous treatment (see Fig. 1 on Special Plate).

Treatment.—11/5/34: Phenylethyl hydno-*carpate* 0.5 c.cm. injected intradermally. 18/5/34: Whole patch infiltrated (1 c.cm.). 25/5/34: Whole patch infiltrated (1 c.cm.). 1/6/34: Whole patch infiltrated (2 c.cm.). 8/6/34: Patch is paler and somewhat indurated (0.5 c.cm. injected). 20/6/34: Patch almost flush with surrounding skin (2 c.cm. injected). 29/6/34: Injection (1 c.cm.). 3/8/34: No nodules visible; area previously affected now quite flat and flush with surrounding skin. 28/8/34: No nodules visible. 30/10/34: Two very small nodules (0.5 c.cm. injected into these). 9/1/35: Two pinhead-sized nodules (0.25 c.cm. injected). 13/2/35: Injection (1 c.cm.). 20/3/35: No nodules visible; Fig. 2 on Special Plate shows result of treatment. 15/5/35: No nodules visible. 5/6/35: No nodules visible. 17/7/35: No nodules visible.

From May to December, 1934, the patient was given weekly carbon-arc baths, and was taking ostomalt three times a day.

CASE 3

G. P., male, aged 38 years. Multiple patches of lupus vulgaris on face, body, and limbs since the war. Four patches were treated with intradermal injections of phenylethyl hydno-*carpate*.

1. *Patch on Right Shoulder: Treatment.*—15/6/34: Whole patch infiltrated (2 c.cm. injected). 22/6/34: Almost clear except at the medial border (1 c.cm. injected). 17/8/34: Injection (2 c.cm.). 31/8/34: Injection (1 c.cm.) into remaining nodules. 5/9/34: No nodules visible. 21/11/34: Three nodules present, which were infiltrated. 19/12/34: Injection (1 c.cm.). 6/2/35: Three nodules present—infiltrated. 20/3/35: Three nodules still present—infiltrated. 3/4/35: No nodules visible. 15/5/35: No nodules visible. 19/6/35: No nodules visible. 17/7/35: No nodules visible.

2. *Patch in Right Axilla.*—No previous treatment (see Fig. 3 on Special Plate). *Treatment:* 16/1/35: External half of lesion infiltrated (3 c.cm.). 21/1/35: Whole area infiltrated (3 c.cm.). 6/2/35: Whole area infiltrated (2.5 c.cm.). 21/2/35: Whole area infiltrated (2 c.cm.). 6/3/35: Injection (1 c.cm.). 20/3/35: Nodules only present at edge of patch—infiltrated. 1/5/35: No nodules present; Fig. 4 on Special Plate shows progress. 17/7/35: No nodules present.

3. *Patch on Left Forearm.*—Previous treatment elsewhere with α rays and chemical caustics. *Treatment:* 5/9/34: Nodules on inner margin infiltrated (5 c.cm.). 12/9/34: Nodules on inner margin and upper part of patch infiltrated. 19/9/34: Injection (2 c.cm.). 10/10/34: Injection (2 c.cm.). 23/10/34: Injection (1 c.cm.). 7/11/34: Injection into outer edge of patch (1.5 c.cm.). 5/12/34: Injection into inner edge of patch (2 c.cm.). 19/12/34: Injection into outer edge of patch (1 c.cm.). 9/1/35: Injection into inner margin of patch (1.5 c.cm.). 22/1/35: Inner margin infiltrated. 13/2/35: All nodules infiltrated (3 c.cm.). 27/3/35: All nodules infiltrated (2 c.cm.). 3/4/35: All nodules infil-

* A paper read at the Ninth International Congress of Dermatology and Syphilology at Budapest, September, 1935.

trated (1 c.cm.). 17/7/35: Very few scattered nodules present—infiltrated.

4. *Patch on Left Side and Front of Neck.—Treatment:* 29/5/35: Vertical limb of patch infiltrated (2 c.cm.). 19/6/35: Vertical limb of patch infiltrated (2 c.cm.). 3/7/35: Horizontal limb infiltrated (2 c.cm.). 17/7/35: Horizontal limb infiltrated (4 c.cm.). Vertical limb now free from nodules.

From November, 1934, to April, 1935, this patient was given weekly carbon-arc baths. He is taking radiomalt three times a day.

CASE 4

M. M., female, aged 21 years. Multiple patches on face, chest, and limbs followed measles in childhood. Patch on left side of chest was treated by intradermal injections of phenylethyl hydnicarbate. Fig. 5 on Special Plate shows condition before treatment.

Treatment.—7/11/34: Whole patch infiltrated (0.75 c.cm.). 21/11/34: Patch is flatter (1 c.cm. injected). 11/12/34: Part of patch infiltrated (1 c.cm.). 9/1/35: Whole patch infiltrated. 13/2/35: Whole patch infiltrated. 20/3/35: Part of patch infiltrated. 19/6/35: Affected area is flush with the surrounding skin, and only two nodules are visible—infiltrated. 24/7/35: Two small nodules only are present—infiltrated (0.1 c.cm.). Fig. 6 on Special Plate shows progress made.

CASE 5

S. O., female, aged 65 years. Face affected for over twenty years. Has had very little treatment. When first seen (January 16th, 1935) lupus nodules were present on cheeks, nose, upper lip, hard palate, and gum of upper jaw. Ulceration present on both cheeks, and an epithelioma present on tip of nose. Fig. 7 on Special Plate shows condition prior to injection.

Treatment.—16/1/35: Radium applied to epithelioma on nose (full strength, 20 mg. flat applicator, screened with 2 mm. of lead, applied for forty-eight hours). Hydrarg. ammon. 1 per cent. in zinc paste used for dressing ulcerated areas on the cheeks. 20/1/35: Injection (1 c.cm.) into nodules on lower half of left cheek. 6/2/35: All nodules on left cheek infiltrated (2 c.cm.). 13/2/35: All nodules on right cheek infiltrated; 1 c.cm. injected into gum of upper jaw. 5/3/35: Injection into gum of upper jaw (1 c.cm.). 26/3/35: Nodules on right cheek infiltrated (1 c.cm.). 17/4/35: Only a few nodules present on skin—infiltrated. Injection into gum of upper jaw (0.5 c.cm.). Ulcerated areas have healed; considerable improvement in mucous membrane lesions. Fig. 8 on Special Plate shows the result of treatment.

The patient was unable to attend hospital for further treatment owing to the distance of her home from Bristol.

CASE 6

G. H., male, aged 48 years. Lupus vulgaris on right side of face since infancy. Has had much previous treatment, including x rays. Large scar with some telangiectases on the right side of the face, with a few lupus nodules at the medial border.

Treatment.—27/6/34: Nodules infiltrated. 10/10/34: All nodules infiltrated (2 c.cm.). 15/10/34: Swelling on right side of face. 24/10/34: Swelling has subsided. 20/3/35: Nodules on right side of nose infiltrated (0.5 c.cm.). 10/4/35: Nodules on right side of nose infiltrated (0.5 c.cm.). 29/5/35: Nodules on right side of nose infiltrated (0.25 c.cm.). 17/7/35: Definite improvement, but some nodules still present—infiltrated.

From November, 1934, to March, 1935, this patient was given weekly carbon-arc baths.

CASE 7

A. C., female, aged 27 years. Patches of lupus on right side of face and nose for several years.

Treatment.—15/5/35: All nodules infiltrated. 25/5/35: All nodules infiltrated. 3/7/35: All nodules infiltrated (1 c.cm.). 17/7/35: Some induration in lower patch; upper patch and patch on the nose are flatter; nodules in two latter patches infiltrated (0.5 c.cm.). 24/7/35: All patches are now flat; induration in lower patch diminished but still present; upper patch and patch on nose infiltrated (0.5 c.cm.).

The patient has had weekly carbon-arc baths since beginning treatment, and has taken malt three times a day.

CASE 8

A. F., male, aged 31 years. Lupus vulgaris affecting right side of face over an area of four square inches for several years. Had been under treatment since 1932 with pyotrocin. Large numbers of scattered nodules present in the scar.

Treatment.—6/3/35: All nodules infiltrated. 27/3/35: All nodules infiltrated (1 c.cm.). 17/4/35: All nodules infiltrated (0.75 c.cm.). 29/5/35: All nodules infiltrated. 17/7/35: Very few pinhead-sized nodules now visible. Affected area is smooth and flush with general skin surface.

CASE 9

M. B., female, aged 36 years. Patch of lupus vulgaris on right thigh three inches by one inch since childhood. First seen on May 31st, 1934, and treated with the Kromayer lamp with compression. She was also put on a salt-free diet.

Treatment.—20/5/35: Whole patch was flush with the surface, and only four nodules remained at the margin of the lesion. Phenylethyl hydnicarbate (1.5 c.cm.) was injected into the remaining nodules. 3/6/35: Considerable swelling and induration of the whole patch; patient complains of irritation. 17/6/35: Irritation subsiding, but still present. 1/7/35: Induration almost completely subsided; no nodules present.

CASE 10

R. D., female, aged 4 years. Patch of lupus vulgaris on flexor aspect of left arm present for about a year.

Treatment.—10/7/35: Patch infiltrated. 17/7/35: Patch has become almost level with surrounding skin; some scalliness present, and induration following injection not yet completely subsided; general carbon-arc baths are being given once a week, and the child is taking radiomalt three times a day. 24/7/35: Induration disappeared—lesion infiltrated (0.1 c.cm.).

CASE 11

W. E., male, aged 34 years. Patient first seen on May 2nd, 1934. Had been having treatment elsewhere for lupus vulgaris of the nasal mucosa on the right side for four months. Some swelling present on the right side of the nose.

Treatment.—2/5/34 to 7/11/34: Local treatment with Kromayer lamp and general carbon-arc baths. 29/6/34: Examined by Mr. Gordon Scarff, who reported, "Active lupus vulgaris is present in the right nostril." 7/11/34: Again examined by Mr. Scarff, who reported, "Active lupus is still present in the nasal mucosa." 28/11/34: Phenylethyl hydnicarbate (0.25 c.cm.) injected into lesion. 12/12/34: Injection (0.25 c.cm.). 9/1/35: Injection (0.25 c.cm.). 8/2/35: Injection (0.75 c.cm.). 22/2/35: Injection (0.75 c.cm.). 15/3/35: Examined by Mr. Scarff, who reports a very definite improvement—0.25 c.cm. injected. 19/7/35: "No lesions visible in mucous membrane."

Comment

It will be seen from the reports detailed above that in Cases 1 to 5 the average number of treatments necessary to clear up the affected areas was between eight and nine. In Case 3, "patch 1" was clear, except at one edge, after one treatment, while half of "patch 4" was clear after two treatments only. In Case 9 the nodules which remained after treatment with ultra-violet light cleared up after one injection, while in Case 11 the lesions in the nasal mucosa cleared up after six injections. Cases 6, 7, 8, and 10 are still under treatment. In Case 6 treatment was somewhat irregular, and on one occasion there was rather a severe local reaction. A similar reaction, but more intense, was observed in Case 9, which only received one injection. (Cochrane tells me that similar reactions are occasionally seen in leprosy.) In Case 9 no lupus nodules were visible when the reaction had subsided. In the remaining cases the induration was relieved in a few days. Less improvement has been noted in Case 6 than in the other instances. Case 10 is of interest in view of Muende's failure to obtain good results in children with creosoted moogrol. This case has only just come under treatment, but the reaction following the first injection is comparable with that seen in adults. Cases 5 and 11 show the value of

the treatment affecting the mucous membranes. Mr. Scarff, assistant surgeon to the ear, nose, and throat department, Bristol General Hospital, who co-operated with me in the treatment of Case 11, is so far very favourably impressed with the result of this method. Those cases still under treatment are making satisfactory progress.

The advantages of this method of treatment are: (1) comparatively little pain is experienced by the patient; (2) the treatment sessions are of short duration; (3) the technique of treatment is simple; and (4) after treatment very little scarring is present, the skin being quite supple. It would, of course, be unwise at this stage to make any extravagant claims for this method, but the results so far obtained do, I think, indicate that it is worthy of a more extensive trial.

Summary

1. A new method of treatment of lupus vulgaris is described, consisting of intradermal injection of phenylethyl hydriocarpate into the lesions.

2. The results of treatment in eleven cases are recorded. In seven cases clinical cure of affected patches was obtained. The other four cases are still under treatment, and are making satisfactory progress.

3. Comparatively little pain is experienced by the patient.

4. It is suggested that these results indicate that a more extensive trial of the method should be made.

I wish to express my thanks to Dr. Cochrane for suggesting the method of treatment; to Dr. Henry of Messrs. Burroughs Wellcome and Co., who prepared the phenylethyl hydriocarpate; to Dr. Price, my former house-physician, for taking most of the photographs; and to Miss K. Whitton, my clinic nurse, whose help has been of the greatest assistance.

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CONGENITAL CYSTIC LUNG

BY

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(With Special Plate)

The term "congenital cystic lung" is used for cases in which occlusion cysts appear in the lungs—that is, cysts which have no communication with the bronchi—and for cases of congenital bronchiectasis in which the dilated bronchi appear as cysts. The condition is not common. Koontz,¹ in 1925, collected 108 cases of congenital cystic lung (including many of congenital bronchiectasis) from the literature. He also describes a case of his own of bronchiectasis (obviously congenital) in a twelve-days-old child. A case of congenital cystic lung in an eight months foetus, described by Sydney Smith,² is quoted by Wood,³ but in this instance the cysts did not communicate with the bronchi. Wood³ records a case of his own of congenital bronchiectasis in a youth of 18, and Morlock and Pinchin⁴ have seen several cases in young adults.

Case Report

The following is a case of congenital bronchiectasis. Its chief interest lies in the fact that an opportunity was obtained of studying it both clinically and at necropsy.

A female child, aged 10 months, was admitted to hospital on December 4th, 1934, for constipation and malnutrition with the following history. A first child; normal delivery at full term. Father and mother well. Weight at birth not known; breast-fed for ten weeks, then given various artificial foods—namely, Ostomilk, Cow & Gate, Nestlé, and finally cow's milk and Blakey's oatmeal. She was apparently a healthy child until 6 months bld, when she had pneumonia. It was not known whether this was lobar pneumonia or bronchopneumonia, but the illness was severe and lasted ten days. A week later she developed pneumonia again; this time it lasted two weeks, and was again severe, but the type was not known. After this the child had persistent cough and failed to gain weight satisfactorily. There were never any attacks of dyspnoea or cyanosis. She suffered from constipation and occasional vomiting.

CLINICAL NOTES

On admission the child weighed 11 lb. 12 oz., and was pale, lethargic, and undernourished. Coarse rhonchi all over chest, but especially on left side; otherwise no abnormality. Temperature 99° to 100° F. for a few days, but later this settled

to 98° F. Crepitations often heard at the bases, especially on the left side. Cough persisted, but the bowels moved normally and there was no vomiting. She gained weight slowly, and was discharged a fortnight after admission, her weight then being 12 lb. 9 oz.

Readmitted a fortnight later; had lost 2 lb. History of frequent loose brown stools commencing soon after discharge and persisting till readmission. Temperature 101° F. Toxic and dehydrated. Crepitations all over chest, but especially on left side. No other abnormality. For a few days the patient had one loose green stool daily and occasional vomiting, but the stools soon became normal and vomiting ceased. She had a persistent loose cough, and the temperature fluctuated from 98° to 100° F. daily. The crepitations grew louder and more bubbling in character. She became dyspnoeic and more cyanosed, and died twelve days after admission.

NECROPSY NOTES

A thin infant. Small sore over sacrum. The right pleura and pleural cavity were normal. The right lung showed a few small areas of collapse, but no pneumonia and no cysts. The left lung was adherent to the chest wall and to the diaphragm by tight fibrous adhesions. There was consolidation of most of the left lower lobe, especially at the base. The left upper lobe was divided into two: the upper part was normal; the lower part consisted of a number of thin-walled vesicles of varying sizes, the maximum being about 1/3 inch in diameter. (See Plate.) The heart, and the stomach, intestines, and other abdominal viscera were normal. The brain and meninges were not examined.

Before the lungs were sectioned they were removed complete with trachea, and a solution of barium sulphate (such as is used for a barium meal) was injected through the larynx by means of a Higginson syringe. An x-ray photograph was then taken, which showed that the barium had entered and outlined the cysts. (See Plate.)

PATHOLOGICAL REPORT

The following is the report on the microscopical examination of the left lung. *Upper lobe.*—The "cysts" are obviously dilated bronchi, and for the most part lined by a layered bronchial mucosa. In places the mucosa is missing and the "cysts" are then lined by inflammatory granulation tissue, in which are numerous large cells having a markedly vacuolated cytoplasm and which appear to be macrophages. Pus is present in some of the cysts, together with remnants of injection material. Alveoli are present, but tend to be collapsed; some of them are lined by cubical epithelium suggesting that they were not functioning. *Lower lobe.*—Acute bronchopneumonia with early fibrosis in parts. Bronchial and cervical lymph glands; oedema and hyperaemia; there are none of the giant cells described by Collins.⁵

NORMAN BURGESS: LUPUS VULGARIS

FIG. 1.—Case 2. Lesion of neck. Before treatment.

FIG. 2.—Case 2. The same lesion after treatment.

FIG. 3.—Case 3. Patch in right axilla. Before treatment.

FIG. 4.—Case 3. The same patch after treatment.

FIG. 5.—Case 4. Lesion of chest wall. Before treatment.

FIG. 6.—Case 4. The same lesion during treatment.

FIG. 7.—Case 5. Lesion of face. Before treatment.

FIG. 8.—Case 5. The same lesion during treatment.