

# TREATMENT OF LUPUS VULGARIS WITH DIETHYL DITHIO-LISOPHTHALATE ('ETISUL')\*

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Although cases of lupus vulgaris are not very common in our clinic we do see a certain number, some 12 cases on an average being recorded in a year, out of between 15 and 20 new cases of skin diseases seen daily. Though all the recognised clinical types of lupus vulgaris are seen, the nodular and fibrous types are more common.

The sufferer from this disease has to face a serious social disability; particularly if the lesions are present on the exposed parts of the body, because of the tissue destruction, scarring and disfigurement associated with this condition. Hence the objective of treatment should be to minimise destruction of the tissues and the scarring which follows.

The therapeutic response to specific chemotherapy with INH and streptomycin has been promising, and has radically changed the prognosis of lupus vulgaris. In this report we present an account of the therapeutic activity of 'Etilsul' (diethyl-dithio-lisophthalate) a dithiol ester derivative, in lupus vulgaris. The work was undertaken because 'Etilsul' is administered as an inunction and thus the anti-tubercular effect of the remedy was applied directly to the site of infection, although it should be noted that 'Etilsul' also has systemic activity (Goburn and Marsden, 1960). In this trial an attempt is made to assess the effectiveness of 'Etilsul' alone as a topical treatment, without addition of any oral chemotherapy. The patients were given *only* local therapy and had been observed for a period of 12-16 weeks at the time of our first evaluation.

'Etilsul' has been used as a therapeutic agent against leprosy, as an inunction, and has raised considerable interest. The original clinical trial was conducted by Davey and Hogerzeil (1959) and revealed that if the inunction of extensive areas of the body was carried out using 3-6 g. of 'Etilsul' twice daily the effect in the first 2-3 months of treatment was variable but in certain cases very marked indeed.

Davies and Driver (1959) have demonstrated a marked inhibitory action of 'Etilsul' on intracellular *Mycobacterium tuberculosis*. This effect was comparable to that of INH or streptomycin. However it was found to be less active in guinea pigs. Our present study was started in 1961.

## METHODS AND MATERIAL

Ten cases of lupus vulgaris from the out-patient clinic of the hospital have been studied. Eight were admitted as in-patients and two were treated as out-patients. Out of these 10 cases, 5 were males and 5 were females. One case

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( No. 1 ) had received some irregular unspecified anti-tubercular treatment before being seen by us. The history of the duration of the disease in our cases varied from three months to 2 years.

The patients were instructed to rub 'Etisul' ointment into the affected areas, twice a day. In all cases photographic record along with detailed clinical histories were maintained. Notes on clinical progress were made from time to time and biopsies repeated wherever possible. The duration of the treatment varied from 8 to 16 weeks.

The lungs were screened in every case and skiagrams were taken in addition whenever the results of the screening were doubtful. None of the cases showed any evidence of pulmonary lesions. The tuberculin test ( 1 : 1000 ) was done in all cases and was found to be negative excepting in one ( No. 7 ).

Case histories of the patients studied are detailed below :

*Case No. 1.* A Hindu female aged 25 years had the lesions for 2½ years. The lady's face had a typical parrot beak appearance. She also had a nodular lesion on the right arm and a warty one on the sole of the left foot.

She had received inadequate streptomycin and INH therapy from time to time. After 'Etisul' therapy for 12 weeks, good improvement was visible on the face and arm lesions. However the lesions on the sole did not show the same progress.

*Case No. 2.* A boy aged 14 years had a small circular lesion consisting of numerous dry papules. Some of these were covered with crusts and scales, and some oozed serosanguinous discharge, causing stains on the clothes. There was no history of previous antitubercular therapy. A biopsy report was confirmatory of the clinical diagnosis. He received 'Etisul' therapy for 12 weeks.

Result: Much improvement was observed, discharge was reduced; however, clinically it cannot be said that patient is yet completely cured.

*Case No. 3.* A female aged 30 years, lupus vulgaris on the dorsum of the right hand 3 months duration.

'Etisul' inunctions twice a day for 10 weeks.

Result—overall improvement was noticed after 4 weeks; discharge and itching ceased after 2 weeks.

*Case No. 4* A female aged 60 years had lupus vulgaris of nodular type with marked scarring of 2 years duration.

'Etisul' therapy—8 weeks.

Result—improvement seen. Signs of healing but further trial was not possible as this patient left Poona.

*Case No. 5* A young girl aged 12 years, lupus vulgaris on dorsum of the left leg. Fibrous variety with marked scarring.

'Etisul' therapy—8 weeks.

Result—no improvement. Erythematous rash appeared on the surrounding skin, and the treatment was terminated at 8th week.

*Case No. 6* A boy aged 6 years had the nodular variety of the disease on the lateral aspect on the right side of the thigh; 8 months duration. He also had the warty type of lesions on the sole of the left foot.

'Etisul' therapy—12 weeks.

Result—marked improvement in both the lesions, the itching and discharge disappearing within 2 weeks.

*Case No. 7* A female aged 20 years, with scrofuloderma on the right side of neck and right axilla for  $1\frac{1}{2}$  years. Lupusvulgaris on chest wall; duration 6 months. Discharge was marked; tuberculin test positive.

'Etisul' therapy—12 weeks.

Result—discharge stopped within 3 weeks, itching subsided within a week. Marked improvement within 12 weeks. Patient is still improving with therapy.

*Case No. 8* A 7 year old child had hypertrophic lupus on the chest for 4 months. 'Etisul' therapy—16 weeks.

Result—improvement very poor, but on continuation of the treatment for 12 weeks the lesion faded.

*Case No. 9* A boy aged 12 years; lupus vulgaris, nodular type, with typical nodules at the periphery of the lesions and healing in the centre, rosy colour; some scarring present at the centre.

'Etisul' therapy—18 weeks.

Result—initial improvement after 4 weeks, but later on no further response was observed.

*Case No. 10* A male aged 45 years, warty type of lupus vulgaris on the left heel, of 3 months duration.

Secondary infection was present.

'Etisul' therapy—12 weeks.

Result—no response, but the lesion remained constant in size and shape.

## RESULTS

Ten cases were studied, presenting various types of lupus lesions, and their clinical response to 'Etisul'. Clinically, the results have been satisfactory in 7 cases. The response has been particularly good in the nodular type of the disease though one case (No. 9) failed to improve. The result in the warty type of lesions was found to be poor. It may be said that the symptoms and signs were well relieved within 2 weeks time in almost all the cases.

## DISCUSSION

This is a preliminary report of a clinical trial of a new compound diethyl dithiolisophthalate ('Etisul') with an action against *M. tuberculosis* and *M. leprae*.

The results of the percutaneous inunction of the drug are promising and are good cosmetically. The improvement is good in the early cases and in the nodular type, where the fibrosis and the scarring are minimal. The results are poor where the lesions were of long standing and where fibrosis was marked. The rapid action of the drug is thought to be due to liberation of ethyl mercaptan locally, after inunction (Davies et al., 1956).

However, it is thought that this drug should be used in combination with specific antitubercular and/or Charpay's therapy for perfect results.

The standstill in the process of healing after continued use of the drug alone indicates the possibility of resistance or tolerance of the mycobacterium to the drug after prolonged use. Such a cessation of the progress is also known to develop in cases of leprosy when 'Etisul' has been given alone.

The drug was applied over the affected areas from which absorption is likely to be variable. We think it will be worthwhile studying the effects on the lesions, when inunctions are directed to areas of healthy skin.

## SIDE EFFECTS

1. Garlic odour in the breath was present in all cases. To combat this smell patients were advised to use scented soap and a deodorant tooth paste.
2. An erythematous rash was observed in one case. This was possibly due to local sensitivity.
3. Itching increased in one case, in all other cases it was controlled.
4. Vomiting and nausea were present in early days of treatment in a few cases, probably of a psychological nature, due to the penetrating odour when first met with. The liquid 'Etisul' formulation which we have not yet used is said to be much better in respect of this odour (Browns, 1961; Molesworth 1961).

## SUMMARY

1. Ten cases of various clinical types of lupus vulgaris have been treated with 'Etisul' 3-5 grammes applied locally into the lesions, as an inunction twice a day for a period of 12-16 weeks.
2. The overall results have been satisfactory.
3. A local inunction of this anti-tubercular agent (ethyl thiol ester derivative) is a new approach in the therapy of lupus vulgaris, but further detailed studies are needed before any final conclusions are drawn. Our own trials with this agent in liquid form are continuing.

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## REFERENCES

1. Brown, S. G., (1961): Lep. Rev. 32, 83.
2. Coburn, J. C. and Marsden, C. W. (1960): Brit. J. Dermatol. 72, 192.
3. Davies, G. E., Driver, G. W., Hogarth, E., Martin, A. R., Faige, M. F. E., Rose, F. L. and Wilson, B. R. (1956): Brit. J. Pharmacol, 11, 351.
4. Davies, G. E. and Driver, G. W. (1957): Brit. J. Pharmacol, 12, 434.
5. Davies, G. E. and Driver, G. W. (1956): Nature, 182, 664.
6. Davey, T. F. and Hogerzeil, L. M. (1959): Lep. Rev. 30, 61.
7. Davey, T. F. (1959): Lep. Rev. 30, 141.
8. Molesworth, B. D. (1961): Lep. Rev. 32, 150.
9. Naguib, M. and Robson, J. M. (1956): Lancet i, 411.


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