

EFFECTS OF 5-IODO-2'-DEOXYURIDINE AND PHENYLMERCURIC DINAPHTHYLMETHANE DISULPHONATE ON HERPES GENITALIS*

BY

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The successful treatment of thirteen cases of herpes simplex of the skin with 5-iodo-2'-deoxyuridine (5IDU) was reported by Hall-Smith, Corrigan, and Gilkes (1962), and a further series of 22 cases by Jackson (1963). The effects of 5IDU in 43 cases of herpetic keratitis in rabbits compared with an unspecified number of controls have been reported favourably by Kaufman, Nesburn, and Maloney, (1962), and it was recorded that 25 of a further series of 46 patients were cured in 2 to 11 days. This was supported by Corrigan, Gilkes, and Roberts (1962), who reported a favourable response in fifteen patients with dendritic ulceration. Davidson (1962), however, expressed reservations on the effectiveness of 5IDU in dendritic ulceration owing to the high rate of failures and recurrences in a series of 22 patients. Burnett, in a personal communication to Tolman and Wilgram (1962), also expressed reservations on the clinical effectiveness of 5IDU in the treatment of a limited number of recurrent herpes simplex infections in glabrous skin. However, an effective controlled series in the use of 5IDU on herpes simplex skin infections has not been available up to the time of writing.

Hutfield (1963) described the favourable effects of phenylmercuric dinaphthylmethane disulphonate (Penotrane) in twenty cases of herpes genitalis in a comparative trial with an inert compound. The effects of 5IDU in a series of twenty cases of herpes genitalis compared with the twenty cases treated with Penotrane, and a further twenty cases treated with an inert compound used as a control are now described.

Case Management

Herpes genitalis is a manifestation of the herpes simplex virus and the lesions produced often mimic those of a primary syphilitic infection. All cases under trial, therefore, were subjected to three darkfield examinations of the presenting lesions and to serological Wassermann and VDRL (or Kahn) tests to eliminate the presence of *Treponema pallidum*; these tests were negative in all cases.

The sixty patients studied (54 males and 6 females) had an average age of 28·1 yrs (extremes 18–54). A history of previous attacks of herpes genitalis was present in twenty cases, and in one there had been a previous attack of herpes zoster.

The sixty patients were divided into three groups of twenty:

Series A: A 0·5 per cent. preparation of 5IDU in the form of an ointment was applied four times daily. This preparation has been shown to possess antiviral properties owing to its metabolic antagonism to the use of thymidic acid in the synthesis of deoxyribonucleic acid (Prusoff, 1959).

Series B: Penotrane jelly was applied as previously described (Hutfield, 1963).

Series C: An inert preparation supplied in identical tubes was applied four times daily.

All patients were instructed to return at intervals of 2 to 3 days until the lesions had healed, and then monthly for 3 months for serological Wassermann and VDRL (or Kahn) tests.

Results

The results are presented in Tables I, II, and III (opposite).

Table IV (overleaf, p. 212) summarizes the effects of the three courses of treatment on the rate of healing.

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TABLE I
SERIES A TREATED WITH SIDU

| Case No. | Sex | Age (yrs) | Duration (days) | | Previous Attacks | Recurrences |
|----------|-----|-----------|------------------|-----------------|--|--------------------------|
| | | | Before Treatment | After Treatment | | |
| 1 | M | 32 | 4 | 4 | Nil | Nil |
| 2 | M | 24 | 3 | 5 | 3/yr for 2 yrs 7 days' duration | Recurred after 3 mths |
| 3 | M | 19 | 5 | 5 | 8-day attack 6 mths ago | Nil |
| 4 | M | 24 | 14 | 3 | 3/yr for 1 yr 14 days' duration | Nil |
| 5 | F | 21 | 4 | 7 | 6/yr for 2 yrs 10 days' duration | Recurred after 1 mth |
| 6 | M | 21 | 8 | 5 | 2/yr for 1 yr 14-21 days' duration | Nil |
| 7 | F | 22 | 5 | 7 | Nil | Nil |
| 8 | M | 28 | 3 | 2 | Nil | Nil |
| 9 | F | 23 | 5 | 2 | Herpes zoster 1 yr ago | Nil |
| 10 | F | 19 | 14 | 4 | Nil | Nil |
| 11 | M | 30 | 4 | 14 | Nil | Nil |
| 12 | M | 30 | 2 | 2 | 3/yr for 1 yr 4 days' duration | Nil |
| 13 | F | 30 | 1 | 3 | 5-day attack 2 yrs ago | Nil |
| 14 | M | 22 | 4 | 5 | 7-day attack 1 mth ago | Nil |
| 15 | M | 29 | 3 | 3 | Nil | Nil |
| 16 | M | 32 | 5 | 3 | Nil | Nil |
| 17 | M | 24 | 21 | 3 | Nil | Nil |
| 18 | M | 29 | 7 | 5 | Nil | Nil |
| 19 | M | 22 | 4 | 5 | Nil | Nil |
| 20 | M | 23 | 14 | 5 | Nil | Nil |

TABLE III
SERIES C TREATED WITH INERT COMPOUND

| Case No. | Sex | Age (yrs) | Duration (days) | | Previous Attacks | Recurrences |
|----------|-----|-----------|------------------|-----------------|---|-------------------------|
| | | | Before Treatment | After Treatment | | |
| 1 | M | 21 | 21 | 10 | 21-day attack 7 yrs ago | Nil |
| 2 | M | 24 | 1 | 5 | Nil | Nil |
| 3 | M | 22 | 2 | 14 | Nil | Nil |
| 4 | M | 26 | 14 | 5 | Nil | Nil |
| 5 | M | 23 | 4 | 10 | Nil | Nil |
| 6 | M | 32 | 3 | 11 | Nil | Nil |
| 7 | M | 42 | 5 | 5 | 21-day attack 1 yr ago | Nil |
| 8 | M | 32 | 3 | 14 | Nil | Nil |
| 9 | M | 52 | 2 | 4 | Nil | Nil |
| 10 | M | 42 | 2 | 5 | 1/yr for 2 yrs 5-11 days' duration | Nil |
| 11 | M | 36 | 2 | 5 | Nil | Recurred after 1 mth |
| 12 | M | 26 | 3 | 5 | Nil | Nil |
| 13 | M | 24 | 10 | 7 | 14 to 21-day attack 6 mths ago | Nil |
| 14 | M | 49 | 7 | 8 | 6/yr for 2½ yrs 14 to 21 days' duration | Nil |
| 15 | M | 21 | 3 | 5 | Nil | Nil |
| 16 | M | 27 | 1 | 3 | Nil | Nil |
| 17 | M | 24 | 10 | 8 | Nil | Recurred after 1 mth |
| 18 | M | 21 | 3 | 14 | Nil | Nil |
| 19 | M | 23 | 3 | 7 | 10-day attack 1 yr ago | Nil |
| 20 | M | 25 | 14 | 3 | Nil | Nil |

TABLE II
SERIES B TREATED WITH PENOTRANE
(HUTFIELD, 1963)

| Case No. | Sex | Age (yrs) | Duration (days) | | Previous Attacks | Recurrences |
|----------|-----|-----------|------------------|-----------------|-------------------------------------|---------------------------------------|
| | | | Before Treatment | After Treatment | | |
| 1 | M | 23 | 3 | 3 | 1/yr for 2 yrs 10 days' duration | Nil |
| 2 | F | 22 | 14 | 5 | Nil | Nil |
| 3 | F | 18 | 7 | 3 | Nil | Nil |
| 4 | M | 29 | 1 | 5 | 3/yr for 4 yrs 7 days' duration | Nil |
| 5 | M | 46 | 10 | 6 | Nil | Recurred after 1 mth and 2 mths |
| 6 | M | 34 | 7 | 6 | 12/yr for 1 yr 14 days' duration | Recurred after 1 mth |
| 7 | M | 19 | 3 | 4 | Nil | Recurred after 1 mth |
| 8 | M | 22 | 15 | 3 | Nil | Nil |
| 9 | M | 20 | 14 | 3 | Nil | Recurred after 2 mths |
| 10 | M | 24 | 4 | 3 | 3/yr for 1 yr 21 days' duration | Recurred after 1 yr |
| 11 | M | 30 | 14 | 4 | Nil | Recurred after 2 mths |
| 12 | M | 42 | 2 | 2 | Nil | Nil |
| 13 | M | 20 | 5 | 3 | Nil | Nil |
| 14 | M | 29 | 3 | 5 | Nil | Recurred after 6 mths |
| 15 | M | 54 | 5 | 4 | Nil | Nil |
| 16 | M | 29 | 3 | 4 | Nil | Nil |
| 17 | M | 31 | 17 | 5 | Nil | Nil |
| 18 | M | 27 | 2 | 6 | Nil | Nil |
| 19 | M | 44 | 4 | 6 | 7-day attack 15 yrs ago | Nil |
| 20 | M | 24 | 1 | 5 | 3/yr for 2 yrs 7 days' duration | Nil |

Discussion

Published reports have stated that the majority of herpes simplex skin infections treated with SIDU heal within 5 days. This is confirmed by the results in Series A, in which the average healing time was 4.6 days. The results in Series B, in which the average healing time was 4.25 days, demonstrate the close similarity between the effects of the two drugs. SIDU and Penotrane shorten the duration of the lesions after starting therapy by 2.8 and 3.15 days respectively, and the total duration by 1.95 and 2.1 days respectively, when compared with the effects of an inert compound. Analysed statistically, these figures show a significant difference ($P < 0.01$) and indicate that both SIDU and Penotrane possess healing properties superior to those of an inert compound. This observation is supported clinically, in that patients treated with SIDU and Penotrane often remarked on the relief of symptoms which occurred within 24 hours, an effect not often noted with the use of an inert compound.

A critical analysis of results, however, must take into account the extreme variability in duration of herpetic skin lesions in spite of treatment. This variation is illustrated by the fact that ten (*i.e.* half) of the twenty cases treated with an inert compound healed within 5 days, whereas the rest took anything up to 14 days. It should also be noted that in two

TABLE IV
EFFECTS ON RATE OF HEALING

| Series under Test | Duration of Lesion (days) | | | | | | | | |
|--|---------------------------|------|------|-----------------|-----|------|-------|------|--------|
| | Before Treatment | | | After Treatment | | | Total | | |
| | Min. | Max. | Mean | Min. | Max | Mean | Min. | Max. | Mean |
| A Treated with 5IDU | 1 | 21 | 6.5 | 2 | 14 | 4.6 | 4 | 24 | 11.1 |
| B Treated with Penotrane (Hutfield, 1963) | 1 | 17 | 6.7 | 2 | 6 | 4.25 | 4 | 22 | 10.95 |
| C Treated with Inert Com- pound | 1 | 21 | 5.65 | 3 | 14 | 7.4* | 4 | 31 | 13.05* |

* 7.1 and 13.2 days respectively were the figures quoted in a series of ten cases (Hutfield, 1963).

cases treated with 5IDU the lesions persisted for 7 and 14 days, and that in four cases treated with Penotrane they persisted for 6 days. There have been two recurrences within 3 months of using 5IDU and seven recurrences within a year of using Penotrane (up to the date of writing).

It thus appears that the antiviral effects of 5IDU in the treatment of herpes genitalis are in no way superior to the antiseptic effects of Penotrane, but that its healing properties are superior to those of an inert compound.

Summary

The effects of 5-iodo-2'-deoxyuridine (5IDU), phenylmercuric dinaphthylmethane disulphonate (Penotrane), and an inert compound respectively in three series each of twenty cases of herpes genitalis are described.

The results show that 5IDU and Penotrane shorten the duration of the lesions after treatment by 2.8 and 3.15 days respectively, and the total duration by 1.95 and 2.1 days respectively, compared with an inert compound.

A statistical analysis suggests that 5IDU possesses greater healing properties than an inert compound, but does not differ in this respect from Penotrane.

There have been two recurrences within 3 months of using 5IDU and seven recurrences within a year of using Penotrane.

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REFERENCES

- Corrigan, M. J., Gilkes, M. J., and Roberts, D. St. Clair (1962). *Brit. med. J.*, **2**, 304.
 Davidson, S. I. (1962). *Lancet*, **2**, 1326.
 Hall-Smith, S. P., Corrigan, M. J., and Gilkes, M. J. (1962). *Brit. med. J.*, **2**, 1515.
 Hutfield, D. C. (1963). *Brit. J. vener. Dis.*, **39**, 181.
 Jackson, N. (1963). *J. Irish med. Ass.*, **52**, 156.
 Kaufman, H. E., Nesburn, A. B., and Maloney, E. D. (1962). *Arch. Ophthalm. (Chicago)*, **67**, 583.
 Prusoff, W. H. (1959). *Biochim. biophys. Acta*, **32**, 295.
 Tolman, M. M., and Wilgram, G. F. (1962). *Practitioner*, **189**, 445.

Herpès génital traité par la 5-iodo-2'-déoxyuridine (5IDU) et le dinaphthylméthane disulfonate phénylmercurique (Pénotrane)

RÉSUMÉ

On décrit les effets du 5IDU, du Pénotrane, et d'un comprimé inerte dans trois séries de chacune 20 cas d'herpès génital.

Les deux médicaments abrègent la durée des lésions après le traitement de 2,8 et 3,15 jours respectivement, et la durée totale de 1,95 et 2,1 jours en comparaison avec le comprimé inerte.

L'analyse statistique suggère que le 5IDU est plus efficace que le comprimé inerte, mais n'est pas plus efficace que le Pénotrane.

On a noté deux récurrences dans les 3 mois qui suivirent l'emploi du 5IDU, et sept récurrences dans moins d'un an après l'emploi du Pénotrane.

CORRIGENDUM

In the article by D. C. Hutfield in the June issue (*BJVD*, 1964, vol. 40, p. 147), the first sentence in the section headed "Results" should read as follows:

Analysis of results shows that there was a change in the urethral smear findings from the presence of pus to the absence of pus (epithelial cells only), over the 5-day period of treatment with 5 IDU in nine out of the twenty cases (45 per cent.). This resulted in a complete cessation of the discharge . . .