

CLINICAL NOTES

THE TREATMENT OF HERPES SIMPLEX AND ZOSTER WITH TERRAMYCIN

J. I. MARAN, M.R.C.S., L.R.C.P., S. S. LAWSON, M.R.C.S., L.R.C.P., A. FENTON HILL, M.B., B.S., M.R.C.S., L.R.C.P., and J. SELWYN BALL, M.B., B.S., M.R.C.S., L.R.C.P.

Westminster

THE TREATMENT OF HERPES SIMPLEX in either the sporadic, isolated case or else in the individual who has regular recurrent attacks is unrewarding and unsatisfactory. Herpes simplex is caused by an easily isolated virus. Sixty per cent of the population are stated to be infected and are either carriers or have recurrent attacks.

Previous work

Topical application of 5 iodo-2-deoxyuride as a 0.1 per cent solution or 0.5 per cent ointment produced marked resolution of eruption within 24 to 72 hours (Hall-Smith *et al.* 1962). It was noted that lesions would normally persist for seven to 21 days, or longer, untreated.

Similar treatment for herpes simplex of the female genitalia suggested in a limited series, that there was relief within 24 to 48 hours (Sceyen *et al.* 1965).

Previous treatments by local antibiotics, or x-rays, have been shown to be ineffectual or locally damaging, although x-rays have sometimes produced a reduction in the incidence of recurrent attacks.

Lesions characteristically reappear on the same site, e.g. on the lips, usually at the junction of skin and mucous membrane—around or within the nares—on the cheeks. Genital lesions are common. Small areas of infection can, however, be seen anywhere on the body and are not uncommon within the auditory meatus.

Subjectively the lesion is characterized by a tense feeling at the site with an irritant tingling, which is not relieved by scratching. Within a few hours the vesicles make their appearance and are raised on a plateau of indurated tissue that is tense and painful. At this stage the total area involved is usually sharply demarcated and unless other specific areas erupt the lesion is limited. The progression is then an increase in the size of the vesicles which coalesce. Within 48 hours the indurated base resolves, the local lymph nodes become tender and the lesions crust, becoming secondarily infected and producing a disfiguring scab, which dries off leaving no scars. Once the vesicle has formed the average duration of disfigurement to the final separation of the scab is 10–14 days.

In carriers, the precipitating factors for an attack are well known, fever being the main cause but other agents such as exposure to strong sunlight, cold drying winds, local trauma, all act as precipitating causes.

Recurrent attacks seem to have no obvious cause except in the case of pre-menstrual herpes.

The rare dangers are ocular involvement, or generalized eruption in infants who have atopic eczema. Neonatal deaths have occurred in infants of women with acute genital herpes at the time of delivery. Despite these serious complications, herpes simplex is, of course, in the vast majority of cases, of no danger to the patient. Attacks are only cosmetically disfiguring and depressive.

TABLE I
HERPES SIMPLEX

<i>Age and sex</i>	<i>Single attacks</i>	<i>Recurrent attacks</i>	<i>Results</i>	<i>No. of days to complete resolution</i>
Fem. 61		*	Excellent	4
Fem. 55		*	No further lesions	1
Fem. 27		*		1
Fem. 54	*		Good	4
Fem. 30	*		Dramatic	6
Male 27		*	Dramatic. Subsequent attacks less	4
Fem. 19		*	Dramatic	2

TABLE II
HERPES ZOSTER

<i>Age and sex</i>	<i>Treatment started: number of days after onset</i>	<i>Results</i>	<i>Residual pain</i>	<i>No. of days to complete resolution</i>
Fem. 82	Same day	Progressed to severe vesiculation	Yes	Weeks
Male 75	Fourth day	Dramatic	Yes	4 to 5
Fem. 32	First day	Normal progression	?	30
Fem. 28	First day	Resolved	None	5
Male 33	Three days	Resolved	None	9
Fem. 49	Three days	Natural progression	Pain	? 28
Male 47	First day	Natural progression — extensive vesiculation	?	Not known
Male 56	Same day	Dramatic — vesiculation resolved	None	9
Fem. 74	Tenth day	Normal progression	Yes	Not known
Fem. 73	Seventh day	Immediate relief of pain	None	7
Fem. 48	Third day	Excellent	Yes	Not known
Male 52	First day	Progressed to normal vesiculation with eye involvement	None	14

Investigation

The present series was undertaken for the following reason. A patient who had recurrent herpes for many years, on the lips, developed a typical lesion subjectively and objectively, two days prior to a wedding. She was given Stoss therapy of 2.5 G. oxytetracycline (terramycin), a total of ten tablets. The rationale being that the skin vesicle concentration of terramycin would be high enough to prevent secondary infection and possibly the lesion would clear more rapidly. The patient reported that within two hours all the irritation and discomfort ceased, the herpes did not progress to a full scale lesion and resolved within four days. This was an unprecedented occurrence for her. She has had no further attacks for the past two years.

Stoss therapy is a method of treatment by a single massive dose of drugs or drug. For this trial 2.5 G. was chosen; the dose used by Stoker (1962) for the treatment of bacillary dysentery. With this dose he found no significant side-effects. Sayer (1951) shows that above 1 G. doses there is relatively little difference in the serum level of the antibiotic. The skin concentration is 70 per cent of the serum level (Gould *et al.* 1952). The trial was extended to include cases of herpes zoster partially as a method of control and primarily as it is a related disease and a more serious condition, and we felt any observations either negative or positive would be of value.

Results

Herpes simplex

In the few cases treated within the first 24 hours of onset the results were dramatic, and followed the pattern described in the initial case.

Case 1. An S.R.N. aged 56 with severe recurrent attacks, approximately three to four times a year for the past 20 years, had a complete resolution of an attack and remained free of further attacks for two years.

Case 2. A girl of 19 who had pre-menstrual herpes ever since ménarche, resolved dramatically, and had no attacks for the subsequent three periods for which she was followed up.

Case 3. One of us had complete resolution within two days, and no further attacks for a year. Subsequent attacks were less severe, but did not respond so dramatically to Stoss therapy, although the duration of the attacks were reduced and all resolved within seven days. Previously resolution had taken up to 14 days.

Herpes zoster

The results here are not so easy to interpret in so small a series. Some cases were treated within the first 24 hours and progressed as classical cases to extensive eruptions and were obviously not influenced. Others showed dramatic relief from pain and rapid drying of the lesions with resolution in a shorter time than normal.

Case 1. An 82-year-old female presented with a classical herpes over the left eye and was treated within the first 24 hours, and proceeded to an extensive attack that involved the eye and necessitated hospitalization.

Case 2. A male aged 56 treated the day of onset for a rash on the inner

aspect of the left thigh. The result was dramatic with complete reduction in vesiculation and just a few dry spots which were completely healed within a week. The pain continued for the first three or four days, but within a week the pain completely resolved.

Case 3. A 56-year-old male treated two days after the onset of the attack of a left frontal herpes zoster, had considerable pain and the rash was fully developed. It was dry within four days and had cleared completely within a few days. He still had residual pain one month later.

Side-effects

These were negligible and amounted only to transient nausea for two to three hours in two cases. No bowel disturbances were noticed.

Discussion

Herpes simplex

The diagnosis of herpes simplex in the patient who has recurrent attacks is unquestionable. The clinical and subjective response to treatment was clear cut, and the marked reduction in further attacks was also an obvious factor.

The explanation of the clinical and subjective improvement is obscure. It is unlikely that the antibiotics had any effect on the virus itself as previous work would have demonstrated this sensitivity. The improvement appeared to be prior to the period during which secondary infection can be forecast, and although the suppression of this is certainly an advantage, it is not the whole explanation.

Whether it is a rational procedure to use a blunderbuss method of therapy such as this for a minor condition such as herpes simplex is a matter for individual consideration. Certainly in recurrent cases starting prior to an important social function, it may help the patient both physically and mentally. The facial disfigurement can be far more upsetting than is generally appreciated. What constitutes a minor condition from the point of view of the doctor is often a major problem to the patient.

Herpes zoster

The diagnosis of herpes zoster is more difficult as the patient has no experience of previous attacks, and the preceding pain is often ignored. Most of the cases treated were seen after several days, and the dramatic results recorded may well be the natural variance of the condition.

The figures on so small a number can only be misleading. The clinical impressions which must be the precursors to scientific study lead us to believe that herpes simplex and herpes zoster were both definitely influenced by treatment.

It is perhaps significant that half the cases of zoster responded extremely well or even dramatically, with rapid regression of the lesions and rapid disappearance of the often incapacitating pain. This would seem to be a definite improvement on pre-existing methods of treating this condition.

Summary

Cases of herpes simplex and herpes zoster were treated with Stoss

therapy of 2.5 G. terramycin. The results suggest that the course and recurrence rate of herpes simplex is favourably influenced, and that in herpes zoster many cases run a shorter and far less painful course.

We feel this pilot study should be followed by more extensive trials.

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THE TREATMENT OF IRON-DEFICIENCY ANAEMIA OF PREGNANCY

A. P. J. WYNNE-JONES, M.A., M.R.C.S., L.R.C.P., M.C.G.P.

Crawley, Sussex

IT IS GENERALLY RECOGNIZED THAT the treatment of iron-deficiency anaemia of pregnancy presents special problems to the general practitioner and these notes are the result of a study made of the problem following an evaluation carried out with a new preparation of ferrous sulphate administered as a slow-release tablet. Assessment of the efficacy of such preparations during pregnancy is made difficult by the haemodilution which occurs, and estimates of haemoglobin concentration will only give a rough indication of the degree of anaemia. For this reason, MCHC readings were made in all cases, the accepted normals being 34.2 per cent between the 10th and 15th week of pregnancy, 32.9 per cent between the 26th and 35th week and 32.5 per cent between the 36th week and full term. On these criteria it will be seen from the tables that, though initially below normal, in the majority of cases, satisfactory haemoglobin concentrations were attained and were thereafter well maintained on oral iron therapy. The incidence of side-effects experienced with the preparation used, Ferro-Gradumet, at a dosage of one tablet daily, was low.

Pregnancy imposes a substantial burden on the female. In contrast to the iron requirements of about 336 mg. over an equivalent period when non-pregnant, the pregnant female must mobilize about 550 mg. of iron. These increased requirements are largely limited to the last six months