indebted to the medical staff of Harefield Hospital, to whose sanatorium wards three of the patients were admitted.

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TREATMENT OF OPHTHALMIC ZOSTER WITH PREDNISONE

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Herpes zoster affecting the first division of the trigeminal nerve is a severe and painful condition, particularly in elderly patients. In many cases it is complicated by ophthalmic lesions and is often followed by intense neuralgia. There is usually considerable oedema of the face in the early stages, and some of the pain occurring before, during, and after the eruption may be peripheral in origin. It is possible that the cellular reaction to the zoster virus both intraneurally and extraneurally accounts for some of the pain, and, if so, any successful control of this reaction would be useful.

Suppression of cellular reaction by corticosteroid drugs is seen to best advantage in the allergic hypersensitivity states, but it is also known that these drugs can inhibit primary tissue responses to infection, and it was therefore thought justifiable to try their effect on ophthalmic zoster. To avoid sodium and water retention due to treatment, prednisone rather than cortisone was used.

Material and Method of Treatment

Fifteen consecutive cases of herpes ophthalmicus were treated during 1956, eight of them in the Ashford Hospital, Middlesex, and seven in their homes. Details of the treatment are as follows:

Systemic.—(1) Prednisone, 10 mg. six-hourly by mouth for four days, followed by 10 mg. eight-hourly for the next three days. The dose is then reduced by 5 mg. each day until it is discontinued on the fifteenth day. (2) Tetracycline, 250 mg. six-hourly by mouth for seven days. (3) Vitamin-B complex ("becosym"), two tablets three times a day for seven days.

Local.—(1) To the rash, oxytetracycline cream 1% daily. (2) To the eye: atropine 1%, sulphacetamide 30%, hydrocortisone 1%, applied as drops six-hourly for the first week and then according to the condition of the eye.

Results

The results of treatment in these patients, although the follow-up times were short and varied from 18 to 6 months,

were sufficiently satisfactory to consider that the natural history of ophthalmic zoster had been altered for the better. A previous group of 44 cases of zoster, including by chance exactly 15 cases of ophthalmic zoster, had been reported by one of us (Barham Carter, 1951), and this group was thought to be similar enough to act as a reasonable control series.

TABLE I.—Comparison of Control and Treated Groups

	No. of Patients	M.	F.	Average Age	Average Age of Rash on Admission
Control group, 1951 ..	15	8	7	64 years	4.3 days
Treated group, 1956 ..	15	7	8	66 "	4 "

Table I compares the two groups regarding age, sex, and duration of illness before admission to hospital. Both groups were nursed in the same wards of the same hospital under the care of the same physicians. The criteria chosen for comparison were: time of subsidence of oedema; time taken for drying of rash; appearance of fresh lesions; degree of scarring; percentage of ophthalmic complications; and severity and duration of pain, including occurrence of post-herpetic neuralgia. Tables II and III show in detail the results and progress of the two groups.

Subsidence of Oedema.—In the control series the peri-orbital oedema lasted from 8 to 17 days, and in the prednisone series its duration depended entirely on when treatment was begun. In Cases 5 and 13 treatment was started on the second day of the pain and within 24 hours of the rash, and no oedema appeared at all, and in Case 6 prednisone was started on the third day of the rash and the oedema lasted only for five days. In contrast one patient was admitted on the 16th day of her illness and her oedema

Scatter diagram showing relationship between improvement of rash and time of treatment. O = First day of dry rash (15 patients). X = First day free of oedema (13 patients, as Nos. 2 and 5 had no oedema).

persisted until the 24th day. A scatter diagram relating the time from onset of illness to treatment with the time from onset to first day oedema-free shows a steady correlation (see Chart). Two patients are omitted, as they had no oedema on admission to hospital.

Drying of Rash.—A similar relationship was seen between drying of the rash and inception of treatment, and this has been plotted and incorporated in the Chart. An interesting observation was that the rashes were more haemorrhagic than in the control series and pustulation in the early treated cases was minimal.

Appearance of Fresh Lesions.—In the control group fresh vesicular lesions appeared in all the patients admitted within 72 hours of the rash, and continued to appear up to the eighth day of the eruption. In the treated group 10 patients were admitted within 72 to 96 hours of the rash, and no fresh vesicles were seen in any of these patients 24 hours after prednisone had been started.

Degree of Scarring.—It is accepted that in all patients with ophthalmic herpes of any severity scarring is to be expected, and in most cases this will be deep and its extent will be in accordance with the extent of the rash. To us one of the surprising effects of the corticosteroid therapy was the remarkable lack of scarring in those patients treated within four days of onset of rash. There were 10 of these patients, and in seven of them it is now difficult to find scars without close examination, and on superficial inspection the site of the lesion cannot be identified. In the control series nine patients were admitted within four days of the rash, and seven of these are scarred sufficiently to be noticed.

Ophthalmic Complications.—All patients in both groups showed conjunctivitis, and in the treated series six patients had keratitis with some evidence of iridocyclitis. In one of these it was severe enough to require tarsorrhaphy and one patient had a panophthalmitis and lost all vision. This patient was not admitted until the 16th day of her illness,

and the tarsorrhaphy patient was first treated on the seventh day, the rash appearing on the fourth day. In the control group eight patients had keratitis and iridocyclitis; two required tarsorrhaphy and two had corneal scarring sufficient to impair vision severely. No patient became completely blind in the affected eye.

Incidence of Pain and Post-herpetic Neuralgia

Herpetic and pre-herpetic pain is universal in this complaint except in the mildest of cases, and post-herpetic pain is said to occur in 1 patient in 10 (Ritchie Russell, Espir, and Morganstern, 1957). The pain of post-herpetic neuralgia is usually a continuation of severe herpetic pain, often at its maximum in the stage of vesiculation; and Tatlow (1952), in a series of 58 unselected cases, found that 7 out of 29 examined from 5 to 10 years after the illness had severe pain or painful paraesthesiae. Only one case had needed any surgical treatment for the pain, and the rather surprising impression obtained by the author from this series was that the incidence of post-herpetic neuralgia was very small, that it bore no relation to age, and that the patient who continued to have pain after herpes zoster was of the introspective, worrying type. Ritchie Russell *et al.* (1957), however, think that this complication cannot be correlated with the severity of the illness but is much more likely in the elderly—the patients actually being over the age of 60 and often over 70. They also make the point mentioned by Taplow that post-herpetic neuralgia is commoner in those who sit at home doing little but nursing and protecting the sensitive area, and suggest that prevalence in the elderly is correlated more with their inactivity than with their age. Peet (1929) considered post-herpetic neuralgia "exceptional" in his experience, and in a series of trigeminal neuralgia cases found only 3 out of 400 due to this. Similarly, Cushing (1920) and Frazier (1921) considered that this condition produced only 1% of all cases of trigeminal pain.

TABLE II.—Details of Progress. Treated Group

No.	Sex and Age	Side	First Day From Onset of Rash to Following				Scarring	Ophthalmic Complications	Strongest Analgesics Used	Post-Herpetic Neuralgia	Time of Follow-up in Months
			Pred-nisone	Oedema-free	Pain-free	Full Drying of Rash					
1	F 75	R	16	21	30	23	Severe	Iritis; keratitis; blind	Omnopon	Severe	8
2	F 78	R	7	Nil	11	9	Moderate	Iridocyclitis; punctate keratitis	Codeine	Nil	14
3	F 59	L	6	8	8	10	Nil	Nil	Nil	"	17
4	M 45	R	3	6	7	8	Minimal	"	Nil	"	12
5	M 45	L	1	Nil	2	6	Nil	"	Nil	"	18
6	F 68	L	2	5	18	8	Minimal	"	Pethidine	"	10
7	M 58	L	3	10	8	11	Nil	Iritis; keratitis	Codeine	"	18
8	F 75	R	2	8	8	10	"	Nil	Nil	"	16
9	M 68	L	4	9	6	12	"	Iridocyclitis; keratitis; tarsorrhaphy	Omnopon	"	11
10	M 84	L	2	5	6	8	Moderate	Nil	Nil	"	14
11	F 49	R	6	12	8	14	Severe	Keratitis	Pethidine	Mild	12
12	M 72	R	2	6	4	8	Nil	Nil	Nil	Nil	13
13	F 76	L	1	5	3	5	"	"	Codeine	"	11
14	F 63	L	2	7	5	10	Minimal	Keratitis	"	"	9
15	F 67	L	3	8	7	10	"	Nil	Pethidine	Moderate	6

TABLE III.—Details of Progress. Control Group

No.	Sex and Age	Side	First Day From Onset of Rash to Following				Scarring	Ophthalmic Complications	Strongest Analgesics Used	Post-Herpetic Neuralgia (6 Years After)
			Admission	Oedema-free	Pain-free	Rash Dry				
1	M 59	L	4	8	10	14	Severe	Keratitis; iridocyclitis	Omnopon	Nil
2	F 73	R	6	10	9	13	Moderate	Nil	Codeine	Dead
3	F 43	R	7	12	11	15	Severe	Keratitis	Omnopon	Nil
4	M 79	R	2	8	16	17	Minimal	Nil	Pethidine	Dead
5	F 66	L	1	8	12	13	Moderate	Keratitis	"	Nil
6	M 54	L	3	10	14	14	Severe	Iridocyclitis	Omnopon	Moderate
7	M 63	R	5	9	9	12	Moderate	Nil	Codeine	Nil
8	F 43	L	10	17	18	20	Severe	Keratitis	Pethidine	"
9	M 64	R	6	10	9	12	Minimal	Nil	"	"
10	M 47	R	4	8	6	9	Nil	"	Nil	Moderate
11	M 82	L	4	9	10	12	Moderate	Iridocyclitis	Omnopon	Dead
12	F 74	L	7	13	12	14	"	Nil	Codeine	"
13	M 70	R	3	8	12	15	Severe	Keratitis; iridocyclitis	Omnopon	"
14	F 69	L	2	9	14	14	Nil	Keratitis	Codeine	Nil
15	F 63	R	2	9	12	12	Severe	Nil	Pethidine	"

In our treated series 3 patients out of the 15 still complain of pain. One has mild pricking sensations, one has occasional annoying jabs, and one persistent pain causing some disability eight months after the attack.

In the control series only 10 out of the 15 patients can be traced owing to deaths, and two of these find their pain still annoying six years later, but "think they have got used to it." Taking the two groups together our impression is that a combination of old age, severity of attack, and severity of secondary infection is likely to result in prolongation of herpetic pain into post-herpetic neuralgia. We found little evidence of psychological disorder as a cause, but agree that some elderly patients complain more about pain than others.

Discussion

If it is agreed that any comparison can be made between two such small groups, then it appears that the use of prednisone has only in some respects modified the patient's response to ophthalmic zoster for the better. Disappearance of oedema is quicker, drying of the rash occurs earlier, and scarring is reduced to a minimum. No fresh vesicles appeared once treatment was established, and pain during the course of the illness was less. Treatment seemed to have no effect on the incidence of post-herpetic neuralgia, but, as the incidence of this is low in any case, a much larger series is necessary to draw any conclusions. Moreover, treatment with prednisone seemed to have no effect on the incidence of ophthalmic complications, but there seems to be plenty of evidence that it has a beneficial effect on these when they occur.

Duke-Elder (1951) treated four cases of zoster iridocyclitis with cortisone and found improvement, and Olson *et al.* (1951) had a similar experience with corticotrophin. Poulin (1952) described four cases of ophthalmic herpes treated by corticotrophin and suggested that the ocular complications could be controlled thereby. Doenges (1954), in a series of 15 cases of herpes zoster, treated 11 with cortisone alone, 3 with chloramphenicol, and 1 with no specific drug. His criteria were drying of the rash, occurrence of fresh vesicles, and the relief of pain. Only one of these cases was ophthalmic, and it did well, but the author concluded that the cortisone had not changed the course of the illness. Gelfand (1954) treated five cases, of which two were ophthalmic, with good results, and Marshall (1955) had one excellent result in a severe iridocyclitis and keratitis with local hydrocortisone. Appelman (1955) treated four cases of ophthalmic zoster with corticotrophin and had good results; and finally an encouraging report comes from Scheie and Alper (1955) of 11 cases of ophthalmic zoster with iridocyclitis treated with cortisone or corticotrophin in which relief of pain was prompt in all, occurring within 24 to 36 hours of treatment. In all these cases the ocular lesions improved, and in none was there any permanent loss of vision. From the literature it appears established that the ocular complications responded to local or systemic corticosteroid drugs, but there is nothing to suggest that these drugs influence the incidence of these complications.

From the present series it is evident that the earlier prednisone is begun the better the result, and it is probably useless to use it after the first 10 days, except locally for the eye. The necessity for continuing treatment after early improvement is shown in Case 6.

Case 6.—A woman aged 68 was admitted to hospital with the story that 11 days before admission she had been talking over the fence to her next-door neighbour, who developed shingles on the following day. Five days later the patient experienced pain in the left forehead, and two days after that a rash appeared. Five days after the pain began she was admitted to hospital with her left eye closed by oedema and with a severe vesicular rash. Prednisone, 10 mg. six-hourly, was given for three days, and on the second day the eye was open, the rash was haemorrhagic, and she was free from pain. Prednisone was reduced gradually to 10 mg. daily by the ninth day of her stay in hospital, but she then complained of severe pain and her forehead looked swollen

and red around the haemorrhagic rash. Full dosage of prednisone was resumed, and was continued for three days; a more gradual withdrawal then followed. The pain disappeared two days after recommencing prednisone, and she was discharged after 30 days. Ten months later she was well.

It would be wrong to suggest that all our cases were severe ones, as zoster differs in its virulence of attack and people differ in their response to infection, but prednisone seemed to abort an attack of zoster in Case 13.

Case 13.—A woman aged 76 was admitted to hospital for investigation of anaemia. On her left-hand side in the next bed was a woman with a right ophthalmic zoster; a week later the patient complained of pain in the left side of her head, and next day developed a left ophthalmic herpes which was immediately treated with prednisone. The vesicles coalesced quickly into a haemorrhagic crusting and pain was minimal by the third day. No fresh vesicles appeared, and although a little discharge was seen from the eye no conjunctivitis occurred. The rash was dry by the fifth day, when all oedema had disappeared; the crusts had completely separated on the eighth day of her illness. She was then entirely free from pain, showed hardly any scarring of the forehead at all, and had no sensory changes. She was re-examined 19 weeks later and had no complaints. There were four small scars of her illness present on the left side of her forehead and no anaesthesia between them. Her corneal response was normal.

The course of this patient's illness differed from the usual pattern in that all stages were telescoped into a much shorter time than usual.

Dangers of Treatment

It is well known that the corticosteroid drugs are not without danger in their use, particularly in elderly patients.

However, by the use of prednisone rather than cortisone, and by restricting the course of the treatment to a fortnight and keeping the dosage relatively low, no complications were encountered. We consider the use of antibiotics essential when using prednisone in these cases, as without them septicaemia might well be a complication of the secondary skin infection. One possible danger is that the treatment might produce a lowering of naturally produced cortisone for a while after the patient's discharge from hospital, so that during this time any further trouble in the damaged eye might produce a severe panophthalmitis. However, this has not occurred in any of our cases, and presumably this danger is largely theoretical.

Summary

Fifteen consecutive patients with ophthalmic zoster have been treated with prednisone and antibiotics. The results of treatment are compared with a similar group treated with prednisone in 1951. No conclusions regarding the efficacy of this treatment can be drawn owing to the small numbers treated, but in the prednisone group oedema was less, drying of the rash quicker, and scarring considerably reduced. Fresh vesicles did not appear after 24 hours of treatment, and herpetic pain was much less.

No effect was found on the incidence of ophthalmic complications or of post-herpetic neuralgia.

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