PENICILLIN THERAPY IN TRACHOMA*

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IN an earlier paper (Gilkes, Smith, and Sowa, 1958a), the effect of large systemic doses of penicillin on the presence of Halberstaedter-Prowazek inclusions in cases of trachoma was described. Recently the opportunity arose to follow up three of the small series of five cases then described. 18 months after the original course of treatment, and with no further local or systemic therapy, all three patients were found to be inclusion-free. The conjunctivae were clinically normal apart from scanty fine papillae in one case. The cytological appearance of the conjunctival scrapings was normal in each case.

These observations, taken in conjunction with the reported action *in vitro* of penicillin on the T'ang virus (T'ang, Chang, Huang, and Wang, 1957), together with the experience of Smith (1958) and other observations made by the writer, appeared to justify the treatment with penicillin of a further series of cases of inclusion-positive trachoma.

Methods

The cases were similar to those described in the earlier investigation. All were Africans of Mandingo or Jola extraction. The clinical criteria of trachoma, as set out by WHO, were present, and many Halberstaedter-Prowazek inclusions were visible in the conjunctival scrapings.

The patients were admitted to hospital and conjunctival scrapings were taken a day or so before and after the course of treatment. To eliminate the possibility that the presence of inclusions might be affected, intermediate scrapings were not taken.

Where possible, the clinical details were confirmed by slit-lamp examination. The inclusions were identified in scrapings using the iodine-staining method of Gilkes and others (1958b).

Treatment Schedules

Eight cases were treated with phenoxymethyl penicillin (Distaquaine) orally, 250 mg. 4-hrly for 5 days (total dose 7.5g.).

Four cases were treated with phenoxymethyl penicillin orally, 125 mg. 4-hrly for 5 days (total dose 3.75 g.).

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Two cases with the clinical signs of trachoma but no inclusion bodies were treated with phenoxymethyl penicillin orally, 250 mg. 4-hrly for 5 days.

No other local or general treatment was given. The penicillin was administered at least 45 min. before a meal.

Results

The results obtained are summarized in the Table. Cases 11 and 12 were re-admitted one week after the completion of the course of oral penicillin. Inclusions were then still present. Both were given a course of injections of 900,000 units of Avloprocil procaine penicillin, daily for 5 days, after which they became clinically normal and the scrapings were inclusion-negative.

TABLE

RESULTS OF ORAL PENICILLIN THERAPY IN FOURTEEN CASES OF TRACHOMA

Case No.	Age (yrs)	Stage of Trachoma	Inclusions	Oral Penicillin (mg. 4-hrly)	Results after One Week	
					Clinical	Inclusion
1	4	I	+	250	Normal	0
2	7	II	+		Few follicles	0
3	4	II	+		Normal	0
4	4	II	+		Normal	0
5	3	II	+		Normal	0
6	13	III	+		Residual papillae	0
7	17	III	+		Normal	0
8	13	III	+		Normal	0
9	2	I	+	125	Improved	+
10	12	II	++		Normal	0
11	2	II	++		Improved but still active	+
12	8	II	+		Improved	+
13	2	I	0	250	Improved	0
14	10	III	0		Slight improvement only	0

Cases 3, 6, and 8 had been treated with local penicillin and streptomycin ointment during the course of the investigation described in the previous paper (Gilkes and others 1958a), with no permanent effect on the presence of inclusions.

In the very young children some difficulty was experienced in the administration of tablets and an elixir would have helped.

Discussion

In discussing these results the particular characteristics of Gambian trachoma must be borne in mind. These have been discussed elsewhere (Gilkes, 1958). The disease presents a low incidence of scarring and corneal involvement and the sequelae of such lesions. The elimination of the virus by means of penicillin appears therefore to permit a speedy recovery of the conjunctiva to a normal appearance with minimal residual scarring even in

cases of stage three trachoma. That the disease is trachoma is borne out by the presence of inclusion bodies, which have been shown by the work of T'ang and others (1957) and of Collier and Sowa (1958) to be present usually, though perhaps not invariably, in cases from China and the Gambia, in which the virus has been isolated.

From the results in the previous series it would seem that the disappearance of inclusions from conjunctival scrapings, where these have previously been present, may be taken as presumptive evidence of cure of the disease. It will be apparent that, where there have been specific physical changes in the conjunctiva, removal of the specific infective agent will not cause these changes to disappear. It may be that where there is gross thickening of the submucous layer of the conjunctiva with crypt formation, this is pathologically self-perpetuating even in the absence of the virus or of any other specific infective agent.

The incompletely resolved chronically-inflamed tonsil and appendix appear to present similar examples of this process at other sites.

It would therefore be illogical to expect that in trachoma the therapeutic effects of any agent can be assessed on purely clinical grounds. It may well be that the disappearance of inclusions from scrapings is an insufficiently reliable indication of cure and that this should be confirmed by negative chick embryo culture.

With these reservations the results described in this and the previous paper appear to indicate that:

(1) Systemic administration of penicillin is more efficacious than local administration in the treatment of trachoma associated with Halberstaedter-Prowazek inclusions.

(2) A dosage of 900,000 units procaine penicillin daily by parenteral injection for 5 days appears to be curative.

(3) Oral dosage of phenoxymethyl penicillin, 250 mg. 4-hrly for 5 days is curative, but a dose of 125 mg. for the same period results in only 25 per cent. of cases being cured.

Using the results of Brown, Kennedy, Reed, and Stephens (1957), it appears that, allowing for variation of absorption and excretion of penicillin in individuals, a blood level of at least 0.4 to 0.7 $\mu\text{g./ml.}$ must be attained and maintained for 3 or 4 days and probably longer in order to effect a cure.

The sulphonamides apart, it has been the practice to regard the treatment of trachoma, and indeed of most of the conjunctivitis, as a matter for the local administration of drugs. Why this is so is a matter for conjecture, and may be due to the simplicity of administration by this route. The practice would seem to have the same justification as the treatment of throat conditions with pigments. The local application of substances to the conjunctival sac can have only a relatively evanescent effect before being leached away by

the tears and inflammatory secretions; where the submucosa is thickened with crypt formation it is unlikely that the substance administered will ever reach much of the infected epithelium.

The known sensitivity to penicillin of the other members of the trachoma virus group, lymphogranuloma and psittacosis, lends support to the suggestion that, used rationally by an effective route, this antibiotic merits considerable further investigation in the cure of trachoma.

An effective concentration of penicillin in the blood will not only result in adequate tissue fluid concentrations but also raise the excretion in the tears to a sufficient level to have an appreciable local effect.

Both oral and parenteral routes of administration present advantages, but the difficulties likely to arise in administering large numbers of tablets to patients with varying diets and potential alimentary pathologies (*e.g.* infestations, malnutrition), make daily systemic injections over a short period the method of choice.

Summary

The late results of the treatment of a small series of cases of inclusion-positive trachoma with large doses of systemic penicillin are described.

The treatment of a further series of similar cases with oral and systemic penicillin and the apparent curative effects of the methods and dosages used are described. Some aspects of the therapy of trachoma bearing on these results are discussed.

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