

would seem to be no reason why equal quantities of adrenalin and novocaine should not be used as a solvent for routine purposes. As for the frequency of application, results in the rabbit suggest that when 50,000 units are used injections should be given at intervals of 6 hours.

Summary

1. Substantial concentrations of penicillin in the ocular tissues, many times the usual therapeutic level, can be obtained by the subconjunctival injection of crystalline penicillin in a dose of 50,000 units. Adequate levels persist for 6 hours.

2. The concentrations are distinctly higher if adrenalin 1:1,000 is used as the solvent for the penicillin.

3. Observations on 5 human eyes support the findings obtained experimentally.

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LOCAL PENICILLIN THERAPY OF HYPOPYON FORMATION: WITH SPECIAL REFERENCE TO THE USE OF SUBCONJUNCTIVAL INJECTION*

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INDICATIONS for the use of penicillin and optimal methods for its employment locally have still to be determined. Drops require to be instilled at frequent intervals; lamellae have not proved satisfactory and ointments have presented difficulties as to the best base to be employed. For hypopyon ulcer Juler and Young (1945) have found penicillin effective and have advocated the application of solid penicillin to the infected ulcer. The present study on the

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value of penicillin in the different varieties of hypopyon formation also attempts an assessment of subconjunctival injection as a method of application.

Clinical Data

1.—Infected cornea ulcer with hypopyon

1. *Infected corneal ulcer with hypopyon.*—Hardly any of the 39 cases of infected corneal ulcer with hypopyon conformed to the text-book picture of serpiginous ulcer. The ulcer itself was generally irregular in shape, the base and margin being infected to a variable degree; interstitial infiltration around the ulcer was present in 8 cases, whilst iritis was noted in 21 cases, though probably present in a subclinical form in all cases. In only one instance was the pneumococcus found. The clinical data of these cases are shown in Table I.

The following are the salient features :—

1. *Sex distribution.*—There were 30 men and nine women.
2. *Age distribution.*—This is shown in the following summary table.

Age	Number of Cases	
	M.	F.
0-9	—	—
10-19	2	1
20-29	1	—
30-39	3	—
40-49	2	2
50-59	10	—
60-69	9	5
70 and over	3	1

It will be noted that 28 out of the 39 patients were over 50 years of age.

3. *Trauma.*—In only 18 cases was there a clear history of antecedent trauma.

4. *Organisms.*—In 11 cases no bacteriological examination was carried out and in 9 more it was negative; the remaining 19 cases showed this distribution : staphylococcus albus 11, staphylococcus aureus 6, Morax-Axenfeld bacillus 1, pneumococcus 1.

5. *Degree of hypopyon formation.*—Using the arbitrary designations of minimal, $\frac{1}{4}$ of anterior chamber, $\frac{1}{3}$ and $\frac{1}{2}$ and total, the following distribution was observed :

Minimal	13 cases
$\frac{1}{4}$	22 „
$\frac{1}{3}$	2 „
$\frac{1}{2}$	1 case
Total	1 „

6. *Response to treatment.*—The following summary table shows that in 12 out of 39 cases there was a poor response to treatment or a relapse after initially satisfactory response. In the successfully treated cases recovery was generally rapid, judging by relatively short duration of in-patient treatment.

Treatment in days	Number of cases
up to 7 days	4
8 to 14 days	12
15 to 21 days	7
22 to 28 days	4
Poor response or relapse	12

7. *Response in relation to the patient.*—Three of the 12 patients with poor response or relapse, ultimately gave good functional results, 2 having vision of 6/6 and the third vision of 6/12. Two of these patients (Nos. 19 and 25) showed relapse; in the first patient after subconjunctival injections, in the second after oily drops. Ultimately a satisfactory end result was obtained by exclusive subconjunctival penicillin treatment. The third patient (No. 19) treated initially and unsuccessfully for 48 hours with subconjunctival injection, responded well to combined general sulphonamide and local penicillin therapy.

There are therefore 9 patients to consider. Of these the end results were fairly good in five in so far as useful vision was retained; in three more patients there was extensive opacification of the cornea, and 1 patient lost his eye altogether. Apart from the fact that these 9 patients contained a high proportion of women (4 out of 9) the age distribution and other clinical data were not dissimilar to those of the series as a whole. Three of these patients showed staph. aureus, 1 staph. albus, 1 no organisms and in 4 a culture was not taken. One patient had acne rosacea and one rheumatoid arthritis (Nos. 32 and 33 respectively). There was no history of trauma in three patients.

8. *Response in relation to the mode of treatment.*—As can be seen from Table I, subconjunctival injection was the main (or only) treatment in 21 cases. Other forms of local penicillin treatment were given in 12 more cases, whilst local penicillin treatment

combined with general sulphonamide therapy was employed in 4 cases. In 2 cases general sulphonamide therapy was used exclusively.

The following summary table shows the number of cases responding to treatment in relation to the mode of application.

Duration of in-patient treatment	Subconjunctival injection	Other local penicillin therapy			Combined penicillin and sulphonamide therapy	Exclusive oral sulphonamide therapy
		Concentrated ointment	Drops	Painting		
Up to 7 days ...	2	1	—	—	—	1
8 to 14 days ...	8	—	1	1	1	—
15 to 21 days ...	3	1	—	3	1	—
22 to 28 days ...	4	—	—	—	—	—
Poor response or relapse ...	4	1	1	3	2	1

Four failures out of 21 cases treated with subconjunctival injections compare favourably with 8 failures in 18 cases treated by other methods. The disproportion is, however, not quite so marked, for one of the failures with combined penicillin and sulphonamide treatment received subconjunctival injections. In all, 25 patients received subconjunctival injections (three also receiving sulphonamides simultaneously—Nos. 33, 34, 36, and one receiving it after unsuccessful application of drops—No. 25); five failed to respond satisfactorily, against 7 out of 16 treated initially by other methods.

That the advantage would indeed seem to lie with subconjunctival injections is suggested from a study of the cases showing poor response, and from the end results as regards vision for the series as a whole.

8. *Cases showing poor response.*—(a) *Poor response to subconjunctival injection* (Nos. 18—21). In two of these patients (Nos. 20 and 21) the end result was poor in spite of general sulphonamide therapy in both, and intramuscular penicillin therapy in one, after three days treatment exclusively with subconjunctival injections. In the two other cases the end result was good; in one case (No. 18) full vision was obtained by exclusive subconjunctival therapy after two relapses; in the last case (No. 19) a good result was obtained by the addition of general sulphonamide therapy.

(b) *Poor response to other forms of local penicillin therapy.*—(Cases Nos. 24, 25, 31, 32 and 33.) In one case, treated exclusively with concentrated penicillin ointment, the eye came to

excision (No. 24). In one case, treated exclusively with weak penicillin ointment, corneal scarring reduced vision to 6/24 (No. 31). In two further cases (Nos. 32 and 33) treated with weak penicillin ointment, oral sulphonamide had to be administered, combined in one case with one subconjunctival injection. In the one case in this series that did well (No. 25) with resultant vision of 6/12, a good response was obtained only after two subconjunctival injections.

(c) *Poor response to sulphonamide treatment.* (Nos. 36, 37 and 39). The end result as to vision in these three cases was H.M., 6/60 and 6/18. As these patients had received a variety of treatment in addition to the sulphonamide therapy (to which they did not respond) it is difficult to indicate which was the favourable factor in the one case with useful vision. It may, however, be of some significance that this patient (No. 36), is the only one of the three who had received subconjunctival injections.

10. *End-results as to vision.*—The following summary table shows the end obtained in the 18 cases treated exclusively by subconjunctival injections, compared with the 14 cases in which no such injections were used. In 7 cases (6 of which were cases with poor response) a variety of treatments had to be combined.

Vision at end of Treatment	Subconjunctival injections		Other methods
	Used exclusively	Together with other treatment	
6/9—6/5 ...	10	2	6
6/18—6/12 ...	1	2	2
6/60—6/24 ...	5 (a)	—	4 (c)
H.M.—P.L. ...	1	3	1
No. P.L. ...	—	—	1
Not recorded ...	1 (b)	—	—
	18	7	14

(a) 4 cases had pre-existing visual defect.

(b) Cornea clear.

(c) One had pre-existing visual defect.

It will be noted that in only 3 out of 18 cases treated exclusively by subconjunctival penicillin was corneal damage sufficiently

severe to reduce vision to less than 6/9. In contrast 7 out of the 14 cases treated by other methods gave an end result of vision less than 6/9.

2.—*Hypopyon with herpetic or neuropathic corneal lesion*

As can be seen from Table II there were 12 patients—9 men and 3 women—with hypopyon associated with a herpetic or neuropathic corneal lesion. There was an infected corneal ulcer in all but four cases, and the cornea was intact in only one case. All but one patient had some degree of iritis.

The hypopyon was minimal in 5 cases, occupied $\frac{1}{4}$ of the anterior chamber in 3, and $\frac{1}{3}$ of the anterior chamber in 4 more. In three patients herpes ophthalmicus was present; one patient had had an alcohol injection into the Gasserian ganglion for trigeminal neuralgia. Dendritic ulcer, or a history of it, was present in five patients. In the remaining three patients the cornea was insensitive. Treatment consisted of sub-conjunctival injections in 8 patients. Penicillin ointment 4-800 units per gram was used in 4 patients, in one of whom the ulcer was also painted with penicillin 2,500 units per c.c. Oral sulphonamide was used in 6 patients, "carbolicisation" with methyl salicylate in two, and concentrated penicillin ointment in 7 cases. Generally several modes of treatment were used in combination or in sequence.

In only two patients (Nos. 43 and 45) could the response to treatment be designated as good, though only in relation to the hypopyon and not as regards the end result for vision.

One ended in enucleation, and the corneae in the remaining cases all showed dense leucomata. Recovery was slow. The duration of in-patient treatment was generally prolonged as can be seen from the following summary table.

No. of inpatient days	No. of cases
Up to 7 days	—
8-14 days	1
15-21 days	1
22-28 days	3
29-35 days	3
36-42 days	3
43-49 days	1
50 days and over	3

3.—*Glaucomatous eyes with hypopyon*

In a series of 5 cases of old-standing glaucoma complicated by hypopyon (Table III), 3 eyes ended in evisceration or enucleation for rapidly developing panophthalmitis; 2 of these three eyes were treated intensively by subconjunctival injections of penicillin in addition to oral sulphonamide. One patient responded unexpectedly well to two subconjunctival injections of 50,000 units of penicillin followed by the instillation of penicillin ointment 8,000 units per gm. for 14 days. One further patient did not respond to penicillin "carbolicization" and the application of penicillin ointment 800 units per gram; there was a moderately good response to oral sulphonamide.

4.—*Hypopyon iritis*

Ten patients present 13 instances of hypopyon iritis, one patient having had a bilateral attack and recurrence in one eye, and another patient had recurrence of a unilateral attack (Table IV). Two of these ten patients showed infected corneal lesions. In them (Nos. 57 and 60), as in the remaining 8 patients, the essential lesion was, however, iritis, generally recurrent. In contrast to the sex distribution in patients with infected corneal ulcers, and with neuropathic keratitis (Tables I and II) there was no difference in the sex distribution in this group, men and women being equally represented. The hypopyon was minimal in 6 eyes, $\frac{1}{4}$ in 5, $\frac{1}{3}$ in one, and $\frac{1}{2}$ in one more.

As can be seen from Table IV response to treatment was good in all but one patient. However, it was only in relation to the hypopyon that response could be regarded as satisfactory. In relation to vision the results were not good in 8 out of the 11 eyes treated. This, however, must be ascribed to the pre-existing iritis rather than to the immediate attack of hypopyon formation, as is suggested by the fact that the 3 patients with a first attack (Nos. 61, 63 and 65)—all young people aged 26, 31 and 25 years respectively—recovered full vision.

The treatment adopted was atropine exclusively in 2 cases, oral sulphonamides in 2, subconjunctival injections in 4, combined local penicillin and oral sulphonamide therapy in 2, and these latter measures with additional measures in 3 more.

TABLE I.—INFECTED CORNEAL ULCER
(a) Treated by Subconjunctival injection of Penicillin (50,000 units)

No.	Sex	Age	History of trauma	Culture	Lesion other than infected ulcer	Hypopyon	Response	Days in hospital	Treatment.			End result
									No. of injections	Additional Penicillin in ointment form. Concentration U/gm. used	Treatment other than Penicillin	
1	M	66	Yes	Staph. albus.	—	‡	Good	7	12	—	—	V = 6/5
2	M	66	Yes	Morax-Axenfeld Bacillus.	Onyx	‡	Good	28	14	—	—	Faint corneal nebula V = 6/9
3	M	64	No	Staph. Albus.	—	Minimal	Good	16	2	—	—	V = 6/9
4	F	47	Yes	Staph. Albus.	—	Minimal	Good	8	10	—	—	V = 6/6
5	M	56	No	—	—	‡	—	14	7	25,000	—	V = 6/6
6	M	85	No	Staph. Aureus.	—	‡	Good	10	10	25,000	—	Cornea practically clear. Died from operation for enlarged prostate
7	M	54	No	Nil	Severe iritis	‡	Good	24	2	25,000	—	Faint nebula central. V = 6/12
8	M	68	Yes	Nil	—	1/3	Fair	25	20	50,000	—	Central corneal nebula
9	M	34	No	Pneumo-coccus	—	Minimal	Good	12	16	50,000	—	V = 6/9

TABLE 1.—Continued.

No.	Sex	Age	History of trauma	Culture	Lesion other than infected ulcer	Hypopyon	Response	Days in hospital	Treatment.			End result
									No. of injections	Additional Penicillin Treatment in ointment form. Concentration U/gm. used	Treatment other than Penicillin	
10	M	16	Yes	Not done	Interstitial infiltration	‡	Good	12	16	50,000	—	V = 6/6
11	M	59	No	Staph. Albus.	Interstitial infiltration	Minimal	Good	12	10	100,000	—	Old nebula both V = 6/36
12	M	76	(Spastic entropion)	Staph. Albus.	Severe iritis	‡	Good	14	15	100,000	—	Iris bound down Peripheral nebulae. V = 6/24
13	F	43	(Leucoma since childhood)	Not done	Moderate iritis	Total	Good	20	9	100,000	—	P.L. (as before)
14	M	59	No	Staph. Albus.	Interstitial infiltration	Minimal	Good	12	1	100,000	—	Old mustard gas keratitis. V = 6/36
15	M	40	Yes	Staph. Albus.	Interstitial corneal infiltration and mild iritis	Minimal	Good	7	4	100,000	—	Old nebula. Amblyopic V = 6/60
16	M	65	?	Nil	—	Minimal	Good	11	4	100,000	—	Barely perceptible scar V = 6/24

TABLE I.—continued.

No.	Sex	Age	History of trauma	Culture	Lesion other than infected ulcer	Hypopyon	Response	Days in hospital	Treatment			End result
									No. of injections	Additional Penicillin in ointment form. Concentration U/grm. used	Treatment other than Penicillin	
17	F	62	4 previous attacks; rheumatoid arthritis	Staph. Aureus.	Severe iritis	±	Fair	25	3	100,000	—	V = 6/9
18	M	45	Yes admission	Staph. Albus.	—	±	Good but 2 relapses	7	18	50,000	—	Barely perceptible scar V = 6/6
								16	6	50,000		
19	F	18	Yes	Nil	Severe iritis	±	Poor (to penicillin)	19	8	50,000	Oral sulphonamide additional to penicillin after 48 hrs	Barely perceptible scar V = 6/6
								77	19	100,000		
20	M	32	Yes	Staph. Aureus.	Interstitial infiltration Severe iritis	±	Poor	57	12	100,000	Oral sulphonamide additional to penicillin after 3 days	Cornea perforated; leucoma adherens
21	M	63	Yes	Nil	—	±	Poor	57	12	100,000	Oral sulphonamide and intramuscular penicillin after 3 days	Cornea opaque

TABLE I—continued.
 (b) Treatment by concentrated Penicillin Ointment.

No.	Sex	Age	History of trauma	Culture	Lesion other than infected ulcer	Hypopyon	Treatment		Response	Days in Hospital	End result
							Concentration used: U/gm.	Frequency of application			
22	M	58	Yes	Staph. albus.	Moderate iritis	‡	100,000	3 hourly	Good	7	Central corneal scar. V.=6/60
23	M	51	No	Not done	Mild iritis	Minimal	100,000	4 hourly	Good	18	V.=6/5
24	M	68	Yes	Staph. aureus	Interstitial infiltration with moderate iritis	‡	50,000	Hourly for 2 days	Good at first. Relapse after two days. Rapidly developing panophthalmitis	12	Eye excised
25	M	60	No	Nil	—	—	—	—	—	—	—
25	M	60	No.	Nil	—	‡	10,000 (only)	Hourly for 4 days	Poor	26	—
25a	Second admission				—	—	(Relapse 10 days; cleared by two subconjunctival injections)		Good	—	V.=6/12
26	F	65	No	Not done	Mild iritis	‡	2,500	‡; ‡; 1 hourly, then 2 hourly	Good	11	Barely perceptible scar. V.=6/9

(c) Treatment by Penicillin Drops

TABLE I—continued.
 (d) Treatment by daily "carbolicising" the Ulcer with Penicillin 2,500 units c.c. and subsequent application of dilute penicillin ointment (400-800 U/gm.).

No.	Sex	Age	History of trauma	Culture	Lesion other than infected ulcer	Hypopyon	Treatment		Response	Days in hospital	End result
							Concentration of ointment used: U/gm.	Frequency of application of ointment			
27	M	52	No	Nil	—	Minimal	800	Hourly	Good	15	V. = 6/9
28	M	73	Yes	Nil	Moderate iritis	Minimal	800	Hourly	Good	10	Barely perceptible scar. V. = 6/24
29	M	52	Yes	Staph. albus	—	‡	800	4 hourly	Good	19	Faint nebula. V. = 6/9
30	M	52	Yes	Nil	Mild iritis	Minimal	800	4 hourly	Good	19	Scar. V. = 6/18
31	F	81	Yes	Not done	Severe iritis and interstitial infiltration	‡	800	4 hourly	Poor: two relapses	27	V. = 6/24
32	F	61	No (Acne rosacea)	Staph. aureus	Mild iritis	‡	(a) 800 (b) Course of oral sulphona- mide	Hourly	Poor Good	19	Scar. V. = 6/18
33	F	60	No (Rheumatoid arthritis)	Not done	Severe iritis	‡	(a) 1,000 (b) One subconjunctival in- jection, and course of oral sulphonamide	4 hourly	Poor Poor	64	Central corneal scar. V. = 6/36

TABLE I—continued.
(e) Combined local Penicillin and general Sulphonamide Therapy.

No.	Sex	Age	History of trauma	Culture	Lesion other than infected ulcer	Hypopyon	Mode of local penicillin therapy	Response	Days in hospital	End result
34	M	13	Yes	Staph. aureus	Severe iritis	1/3	Ung. 25,000 U/gm., 4 hourly, and subconjunctival injections 6 hourly	Good	15	V. = 6/9
35	M	69	No	Not done	Mild iritis	Minimal	12, insillations of gutt. 2,500 U/c.c. at 5 mins. intervals Subsequently Ung. 800 U/gm. hourly	Good	12	V. = 6/9
36	M	58	Yes	Not done	—	±	(a) 27 subconjunctival 6 hourly. (b) T.A.B. subsequently	Poor	39	Moderate central opacity. V. = 6/18
37	M	22	Yes	Staph. aureus	Moderate iritis; interstitial infiltration	Minimal	(a) "Carbolizing" with penicillin 2,500 U/c.c. and Ung. 800 U/gm. hourly. (b) T.A.B. subsequently	Fair	34	V. = 6/60

(f) Exclusive General Sulphonamide Therapy.

No.	Sex	Age	History of trauma	Culture	Lesion other than infected ulcer	Hypopyon	Treatment	Response	Days in hospital	End result
38	M	33	Yes	Not done	Moderate iritis	±	Sulphamezathine	Good	7	V. = 6/9
39	F	61	No	Not done	Iritis; corneal abscess on 12th day	±	(a) Sulphamezathine followed by Penicillin 800 U/gm. hourly (b) Ung. Penicillin 800 U/gm. hourly	Poor	58	V. = H.M.

TABLE II.
Neuropathic or herpetic keratitis with hypopyon.

No.	Sex	Age	History	Lesion	Hypopyon	Culture	Response	Days in hospital	Treatment (apart from atropine)	End result
40	M	64	Herpes ophthalmicus 2 years before	Infected ulcer. Mild iritis	Minimal	—	Poor	35	(1) For 3 days daily "carbolic acid" with penicillin 2,500 U/c.c.; ung. penicillin 800U/gm. hourly and methyl salicylate cauterizing. Then (2) Oral sulphamezathine, and Ung Albucid.	Enucleation
41	M	82	Herpes ophthalmicus	Infected ulcer and mild iritis	1/3	Staph. aureus.	Poor	59	Oral sulphamezathine (for 4 days) together with ung. penicillin 800 U/gm. 2 hourly, and methyl salicylate cauterizing daily.	Descent of ocele on 14th day. Total corneal opacity. V = P.L.
42	F	84	Herpes ophthalmicus Spastic entropion	No corneal lesion. Severe iritis	1/2	—	Fair	34	Operation on entropion, and instillation of ung. penicillin 50,000 U/gm. 3 hourly. Also subconjunctival penicillin 50,000 units 3 in the first week and 2 each in the second and third weeks.	V = 6/18 p.
43	M	34	Alcohol injection of Gasserian ganglion for tic douloureux	Infected ulcer and mild iritis.	Minimal	Nil.	Good, but relapse 12 days later	26	(1) Three subconjunctival penicillin injections 50,000 units 6 hourly followed by ung. penicillin 100,000 units 4 hourly. (2) Seven more injections on relapse, followed by tarsorrhaphy.	Dense leucoma

TABLE II.—continued.

No.	Sex	Age	History	Lesion	Hypopyon	Culture	Response	Days in hospital	Treatment (apart from atropine)	End result
44	M	46	Recurrent dendritic ulcer. 4 or 5 attacks.	Infected ulcer. Mild iritis	±	—	Poor	16	(1) Subconjunctival penicillin 50,000 units 4 hourly and ung. penicillin 100,000 U/gm. 4 hourly for 2 days. Then (2) Oral sulphamezathine 30 gms.	Dense leucoma V = 2/60
45	M	76	4 months—persistent superficial punctate staining. Cornea anaesthetic	Infected ulcer. Mild iritis	±	—	Good	9	12 subconjunctival injections of penicillin 50,000 units 6 hourly.	V = P.L.
46	M	49	5 years—intermittent dendritic corneal ulceration. 3 weeks—recurrence	Infected ulcer	Minimal	Nil.	Poor	51	In succession: (1) 12 subconjunctival injections and penicillin 50,000 U/c.c. 6 hourly, and ung. penicillin 100,000 U/gm. 4 hourly. (2) Oral sulphamezathine 30 gms. (3) Milk injections. (4) Short wave therapy.	Dense leucoma
47	F	61	10 months previously a dendritic ulcer. Started as iritis and developed corneal stain on 24th day of treatment	Interstitial infiltration. Moderate iritis	Minimal	—	Poor	35	(1) Ung. penicillin 400 U/gm. 4 hourly for 6 days. Then (2) Sulphamezathine 30 gms.	Spontaneous improvement after cessation of all treatment

TABLE II.—continued.

No.	Sex	Age	History	Lesion	Hypopyon	Culture	Response	Days in hospital	Treatment (apart from atropine)	End result
48	M	19	Gradual onset over 3 weeks. Poor sensation	Interstitial infiltration resembling disciform keratitis. Moderate iritis	Minimal	—	Poor	25	(1) 20 subconjunctival injections of penicillin and ung. penicillin 100,000 U/gm. 4 hourly. (2) Tarsorrhaphy.	Relapse. V=6/36. Under treatment
49	M	57	One week gradual onset of pain in eye. Cornea insensitive	Infected corneal ulcer and severe iritis	1/3	Nil.	Poor	46	20 subconjunctival injections of penicillin 6 hourly, and ung. penicillin 100,000 U/gm. 4 hourly.	Total corneal opacity. Iris bound down. V=P.L.
50	M	60	Similar attack 10 years ago. Cornea insensitive. Sore 3 weeks	Infected ulcer and severe iritis	1/3	—	Poor	54	Ung. penicillin 800 U/gm. hourly and drops 2,500 U/c.c. at 15 minutes—1 hour for 8 days. Subsequently oral sulphamezathine.	Dense leucoma
51	F	60	Tarsorrhaphy in the past. Broken down corneal scar; 3 days later hypopyon ulcer. Cornea insensitive	Interstitial infiltration and moderate iritis	1/3	Nil.	Poor	24	Ten subconjunctival injections of penicillin, and ung. penicillin 100,000 U/gm. 4 hourly. Subsequently repeated. A.C. wash out and milk injections.	Dense leucoma



TABLE III.
Glaucomatous eyes associated with hypopyon.

No.	Sex	Age	History	Culture	Lesion	Hypopyon	Response	Days in hospital	Treatment	End result
51	F	85	For 5 years a blind glaucomatous eye	—	Large corneal abscess	+	Poor	18	(1) Penicillin drops 2,500 U/c.c. hourly for 6 hours followed by ung. penicillin 800 U/gm. 4 hourly for 5 days. Albuclid drops subsequently for 4 days	Enucleation on 9th day
52	M	62	Old iritis, secondary glaucoma	—	Iris bombé	+	Poor	32	Twelve subconjunctival injections of penicillin followed by 2 intravitreal injections 5,000 units penicillin and oral sulphamezathine	Evisceration
53	M	41	Bilateral buphthalmos c. iridectomy at age of 10. Eye hit with twig 5 days ago	Staph. aureus at evisceration	Infected corneal ulcer	+	Poor	48	(1) 44 subconjunctival injections together with ung. penicillin 100,000 units 2 hourly. (2) On 4th and 6th days intravitreal injection of penicillin 5,000 units with sulphapyridine from 4th day onwards. Paracentesis on 6th day.	Evisceration. Hypopyon had disappeared after 24 hours but panophthalmitis rapidly developed
54	F	64	A blind eye due to chronic glaucoma	Pneumococci	Infected ulcer and moderate iritis	+	Good	37	Two subconjunctival injections penicillin 50,000 units. Ung. penicillin 8,000 U/gm. hourly	Corneal nebula
55	F	74	Blind eye from long standing chronic glaucoma	Nil.	Infected ulcer and mild iritis	+	Good	19	(1) "Carbolization" with penicillin 2,500 U/c.c. and ung. penicillin 800 U/gm. hourly for 3 days. Then (2) oral sulphamezathine	Corneal nebula

TABLE IV—Hypopyon Iritis

No.	Sex	Age	History	Lesion other than iritis	Hypopyon	Response	Days in hospital	Treatment (apart from atropine)	End result
57	F	40	Recurrent bilateral iritis. Congenital spastic paraplegia	Interstitial infiltration right cornea	1/3	Poor	40	In succession:—(1) Subconjunctival penicillin 50,000 units 6 hourly, and Urog. penicillin 25,000 U/gm. 4 hourly for two days. (2) Oral sulphamezathine. (3) Short wave therapy	R.V. = P.L. L.V. = 6/60
58	F	82	Influenza 14 days before admission. Old rheumatoid arthritis	—	‡	Good	15	(1) Two subconjunctival injections of penicillin 50,000 units; followed by oily penicillin 10,000 U/c.c. 2 hourly	Cornea clear. Atrophic iris. V. = H.M. Lens opaque
59	F	27	Recurrent bilateral iritis	—	Right minimal. Left ‡	Good	21	Subconjunctival penicillin 50,000 units 4 hourly for 4 days	R.V. = 5/60 L.V. = C.F. at 1m.
59a	Second admission		ditto	—	Right minimal	Good	6	As before	—
60	F	63	Diabetic iritis, rubeosis and secondary glaucoma	Infected corneal ulcer	‡	Good	22	(1) Subconjunctival penicillin 50,000 units 6 hourly, and Urog. penicillin 100,000 U/gm. 4 hourly for 3 days, followed by (2) Oral sulphamezathine and short wave therapy	—
60a			ditto	ditto	‡	Good	26	(1) Subconjunctival penicillin 50,000 units 6 hourly, and Urog. penicillin 100,000 units 4 hourly for 3 days followed by (2) Short wave therapy	Dense corneal scar. Occluded pupil

TABLE IV—Hypopyon Iritis—(continued).

No.	Sex	Age	History	Lesion other than iritis	Hypopyon	Response	Days in hospital	Treatment (apart from atropine)	End result
61	M	26	Acute iritis	—	Minimal	Good	18	Ung. penicillin 8,000 U/gm. 4 hourly and oral sulphamezathine simultaneously	Eye normal. V. 6/6
62	M	8	Endophthalmitis following an infectious illness a year ago. Blow on eye 4 days ago	Endophthalmitis	Minimal	Good	43	(1) Two subconjunctival injections of penicillin 50,000 units; also ung. penicillin 25,000 U/gm. 2 hourly, with oral sulphamezathine simultaneously	Sbrunken eye
63	F	31	Acute iritis	—	Minimal	Good	8	Oral sulphamezathine	Eye normal. V. 6/6
64	M	61	Recurrent iritis	—	Minimal	Good	10	Sulphamezathine 30 gms., mydricine and short wave therapy	V. = 6/18
65	M	25	Acute iritis	—	‡	Good	19	Heat	Eye normal. V. 6/6
66	M	57	Left iritis 5 years ago. Recurrence now with hypopyon	—	‡	Good	0	Mydricine daily	Hypopyon disappeared within 3 days. V. 6/24

Discussion

1. *Causes of hypopyon formation.*—Hypopyon as a complication of infected corneal ulcer, and hypopyon associated with iritis are clearly recognised as distinct clinical entities. The fundamental difference is, of course, that in the first group the cornea is the seat of the primary lesion, and in the second the iris lesion is the responsible factor. This distinction is important and generally valid, but the presence of a corneal lesion in two of the cases of hypopyon iritis (Nos. 57 and 60) shows how difficult it may be in individual cases to assess the type of hypopyon with which one is dealing—a difficulty all the more real as severe iritis is not infrequent in hypopyon corneal ulcers. The diagnostic difficulties are complicated still further by the occurrence of hypopyon in the group of cases shown in Table II. Both iritis and corneal ulcer were present in most of these cases, which, however, constitute a distinct entity of their own in that the primary lesion appeared to be neither of these affections, but loss of corneal sensation of a trophic or possibly virus origin. This group does not appear to be well recognised, but the therapeutic response no less than the disturbed corneal sensation leave no doubt that it must be regarded as distinct from the others. In a final group, glaucomatous degeneration of the eye appeared to have been the primary disturbance, with the hypopyon formation as the result of either an iris reaction or a corneal lesion.

As distinct from these four types, there were cases of hypopyon formation following an operation, or on infection carried into the eye by trauma. These cases have not been considered in the present study because their fulminating course and response to treatment would suggest that they are true infections as distinct from aseptic inflammatory reactions and require detailed consideration on their own.

2. *Response to treatment.*—It is clear from the data in Tables I-IV that generally speaking infected corneal ulcers (as tabulated in Table I) respond well to local penicillin therapy, and that hypopyon formation secondary to herpetic or neuropathic corneal lesions gives no response. It would also seem that whether a response is obtained in hypopyon formation in glaucomatous eyes depends upon the condition of the eye, and possibly also whether the hypopyon is septic in origin. In contrast to the efficacy of penicillin in infected corneal ulcers, and its uselessness in the herpetic and neuropathic hypopyon formation, is the lack of need of penicillin in hypopyon iritis. From the data shown in Table IV it is seen that hypopyon iritis responds well to treatment by atropine, and nothing else is required.

Reduced to general terms one may perhaps say that an infected

corneal ulcer is sterilised by the action of penicillin; this explains the value of penicillin in these cases—the hypopyon disappears when the primary infection is brought under control. In contrast, hypopyon formation secondary to virus or neuropathic corneal lesion does not respond to penicillin, presumably because the virus is penicillin-resistant, and that in a neuropathic lesion there may be no infecting agent at all. Finally in hypopyon iritis control of the inflammatory iris reaction by atropine brings about absorption of the hypopyon; penicillin is unnecessary as there is no bacterial exciting factor. As in infective lesions generally, so in hypopyon reactions, penicillin can give results only when the exciting cause is infective in character and susceptible to penicillin.

3. *Mode of use of penicillin: theoretical considerations.*—It has been shown elsewhere (Sorsby and Ungar, 1946) that subconjunctival injection of 25,000 units of penicillin gives higher and more sustained aqueous levels than the administration of 50,000 units intravenously, or 40,000 units in beeswax intramuscularly, or of the insertion into the conjunctival sac of ointment containing 100,000 units per gm. The simpler procedures of the instillation of drops, and of ointments containing a low concentration of penicillin are inapplicable if an adequate intra-ocular level of concentration is to be reached (Struble and Bellows, 1944). Nothing is known of the concentration in the aqueous on the application of penicillin in solid form to the surface of an infected corneal ulcer as advocated by Juler and Young.

On theoretical grounds it would therefore seem that subconjunctival injection is the method of choice for obtaining and maintaining high intra-ocular levels of concentration of penicillin. It is superior to both systemic administration and to other methods of local application. The detailed studies of Andrews (1947) and of Sorsby and Ungar (1947) have confirmed the high intra-ocular levels of concentration reached by this mode of administration of penicillin. It would furthermore appear that the addition of adrenalin to the penicillin materially increases both the levels reached and the levels maintained, as can be seen from the following summary table (Sorsby and Ungar, 1947).

Level of penicillin in the aqueous and the cornea of the rabbit after subconjunctival injection of 50,000 units pure penicillin with and without adrenalin

Hours	$\frac{1}{4}$	$\frac{1}{2}$	1	2	3	4	6
Aqueous: Without adrenalin	24	19	17	9	3	0.75	0.56
Aqueous: With adrenalin ...	>32	>17	>32	>32	>20	20	1.25
Cornea: Without adrenalin	950	97	76	25	18.75	4.87	1.5
Cornea: With adrenalin ...	>860	>200	>1,440	925	450	65	2.5

The clinical use of massive doses of penicillin subconjunctivally only became possible with the advent of purified penicillin. With such penicillin, injections of 50,000 units are well tolerated, even when repeated frequently. (Sorsby and Ungar, 1946.)

4. *Management of hypopyon corneal ulcer susceptible to penicillin.*—Theoretical expectations are borne out by the results recorded for the cases summarized in Table I. Subconjunctival injection of penicillin proved superior to several other modes of applying penicillin. The relative value of subconjunctival penicillin and oral sulphonamide cannot be assessed, as no substantial studies on the effect of the sulphonamides on hypopyon keratitis appear to be available.

As this work was progressing a standard method of treatment began to emerge. At the moment the routine used consists of the following steps:

(1) After a smear is taken for culture purposes the eye is irrigated with half normal saline at room temperature to remove any organic matter.

(2) The conjunctiva is anaesthetised by the instillation of two drops of 4 per cent. or 5 per cent. cocaine hydrochloride solution, repeated if necessary.

(3) Into an ampoule containing 100,000 units of white crystalline penicillin 0.5 c.c. of 2 per cent. novocaine and 0.5 c.c. of adrenalin 1:1,000 is injected. 0.5 c.c. is now withdrawn and injected subconjunctivally.

(4) Drops of atropine are instilled into the conjunctival sac and the eye is bandaged.

(5) Injections are repeated at 6-hourly intervals for three days, so that a total of 12 injections are given in all cases. Where response appears to be halting another four injections are given over an additional day.

(6) When injections are suspended penicillin ointment in a concentration of 100,000 units per gm. is instilled at four-hourly intervals day and night. The ointment should be made up with a specially prepared base of petroleum jelly and liquid paraffin 90 and 10 parts of each respectively. The penicillin is incorporated into this base without dissolving it in water. The ointment is continued for 48 hours after apparent clinical cure.

Whilst normally the solvent for the penicillin injected subconjunctivally is an equal quantity of 1:1,000 adrenalin and of 2 per cent. novocaine, it is possible to use either solvent by itself. Novocaine helps to overcome the discomfort some patients experience on repeated subconjunctival injections; adrenalin is



well tolerated by most patients. Sterile water can be used, but saline should not be employed as it produces a hypertonic solution which is distinctly uncomfortable on injection. It is feasible to replace either of these solvents by mydracaine where the iritis is particularly intense. Adrenalin solution, because of its low pH, tends to destroy penicillin *in vitro* (Cameron, 1945). Clinically this deleterious effect does not seem to be substantial; in the tissues subconjunctivally the adrenalin is apparently rapidly buffered; in solution *in vitro* the amount of penicillin destroyed would appear to be small.

Where no substantial response is obtained with subconjunctival injections at the end of 48 hours, further treatment on these lines is useless.

Subconjunctival injections of penicillin as a method of treating hypopyon formation secondary to infected corneal ulcer give gratifying results. The management of the occasional resistant case is still a problem of some difficulty. A full exploration of the possibilities of oral sulphonamide would seem to be desirable.

Summary

1. Results of treatment, mainly with penicillin, are recorded for 66 patients with hypopyon.

2. This series included 39 cases of infected corneal ulcer; 18 of these were treated by subconjunctival injections of penicillin in doses of 50,000 units with or without the application of penicillin ointment in concentrations of 25,000 to 100,000 units per gm. Other methods of local penicillin therapy were employed in 12 patients. Oral sulphonamide treatment was used in two cases and local penicillin therapy combined with general sulphonamide therapy in four more. In three patients general sulphonamide therapy was used when subconjunctival injections of penicillin proved inadequate.

Twelve patients with hypopyon formation associated with herpetic or neuropathic corneal lesions were treated by various applications of penicillin locally, with or without general sulphonamide therapy.

There were also five cases of old-standing glaucoma showing hypopyon as a complication.

A final group of 10 patients presented 13 instances of hypopyon iritis.

3. Infected corneal ulcers responded well to treatment. Hypopyon seen in herpetic or neuropathic keratitis gave no response. Hypopyon iritis appeared to require no treatment other than atropine.

4. A detailed analysis of the cases of infected corneal ulcers with hypopyon treated by different methods of penicillin therapy shows subconjunctival injections to be the method of choice. It was successful in 18 out of 21 cases so treated.

5. The mode of treatment is described. It consists essentially of 12 to 16 subconjunctival injections each of 50,000 units of penicillin (dissolved in 0.25 c.c. of 2 per cent. novocaine and 0.25 c.c. of 1:1,000 adrenalin) at intervals of six hours, followed by the 4-hourly instillation of penicillin ointment in a concentration of 100,000 units per gm.

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THE LAMINA CRIBROSA AND ITS NATURE*

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THE present knowledge of this subject is based mostly on the work of E. Fuchs (1916) as there have been no newer researches in this field. The cribriform lamina is generally taken to be a semi-independent structure. The dimensions of its anterior and posterior planes, its thickness and backward curve and other dimensions have been already measured. In cases of glaucoma the possibility of the cribriform lamina being pushed backward by the raised intra-ocular pressure has been generally accepted.

Birnbacher and Czermak (1885—1886) have likened the cribriform lamina to a membrane of India-rubber which can bulge under

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