PENICILLIN TREATMENT OF OCULAR INFLAMMATION*

BY

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DURING the last nine months we have used penicillin in the local treatment of any superficial ocular infections in which it was thought that beneficial results might follow.

A brief note is given of a series of thirty-eight such cases, and also of one case of perforating injury (Part I) and two of Eales' disease (Part II).

Part I.—Procedure

All cases were treated in Hospital, with the exception of case No. 47, who was working in the eye department.

A bacteriological examination, including penicillin sensitivity, was made before commencing treatment; as a rule treatment was commenced on admission, without waiting for bacteriological report.

In the later cases cultures were taken as a routine every forty-eight hours, and treatment was continued for a few days after negative cultures were obtained.

For most cases a solution of the sodium salt was used, containing 500 units per c.c., occasionally 250 units, three or four drops being instilled every four hours. In eight cases lamellae of the calcium salt, containing 180 or 100 units, were applied four-hourly.

The one case of perforating injury received an injection of 1,250 units of the sodium salt in 0.25 c.c. sterile distilled water, into both the anterior chamber and the vitreous.

A summary is shown in tabular form.

Results

Blepharitis.

Most cases were of long duration. Of the twenty cases treated nine showed apparent clinical cure, and of the others all but two were greatly improved; the exceptions being the cases 46 and 47. From the former, penicillin resistant organisms were recovered from one eye: there was no apparent difference in the progress of the two eyes.

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BLEPHARITIS

Serial No.	DIAGNOSIS	Bacteriological Report before treatment	Penicillin Treatment	Clinical Progress	Bacteriological Report after treatment
5	Blepharo-conjunctivitis R.L. 13 years.	Staph. aureus P.S.*	Guttae (500 u/c.c.) 4 hourly for 12 days.	Cured.	Sterile after 14 days.
6	Chronic blepharitis R.L. 6 years. Other treatment unsuccessful.	Cocco-bacillus, Neisser positive.	Ung. (250 u/gramme) in Eucerin and water a.a.	Only slight residual hyperaemia of lids—improved.	Sterile after 11 days.
15	Chronic blepharitis R.L. Many years.	Staph. aureus P.S. = O.S.†	Lamellae (100 u) 4 hourly for 8 days.	Cured; follow up—no relapse 2½ months later.	Sterile after 5 days. Scanty growth staph. albus 2½ months later. Sterile after 5 days.
16	Chronic blepharitis R.L. 4 years.	Staph. aureus P.S. Morax-Axenfeld P.S. less than O.S.	Lamellae (100 u) 4 hourly for 8 days.	Much improved—slight residual crusting.	Sterile after 5 days.
17	Chronic blepharitis R.L. 20 years.	Staph. aureus P.S. Morax-Axenfeld P.S. less than O.S.	Lamellae (100 u) 4 hourly for 8 days.	Cured.	Sterile after 5 days.
18	Chronic blepharitis R.L. 4 years.	Staph. aureus.	Lamellae (100 u) 4 hourly for 8 days.	Much improved, slight hyperaemia and scaling. Follow up 5½ months later—improvement maintained.	Sterile after 5 days.
23	Chronic blepharitis R.L. Many years.	Staph. aureus P.S.	Guttae (500 u/c.c.) 4 hourly for 15 days.	Much improved—slight residual hyperaemia.	Sterile after 13 days.
24	Chronic blepharitis R.L. Many years.	Staph. aureus P.S.	R.E. lamellae (180 u) 4 hourly. L.E. Guttae (500 u/c.c.) 4 hourly for 7 days.	Much improved—slight residual hyperaemia.	Sterile after 2 days.
25	Chronic blepharitis R.L. 2 years.	Staph. aureus P.S.	Guttae (500 u/c.c.) 4 hourly for 16 days.	Apparent cure till 13th day when developed conjunctivitis L.E. (? artefacta). Follow up—no relapse 3 months later.	Both eyes sterile 6th and 8th days. On 13th, 17th, 21st days L.E. staph. albus P.R.† 23rd day both sterile.
30	Chronic blepharitis R.L. Many years.	Staph. aureus P.S.	Guttae (500 u/c.c.) 4 hourly for 18 days.	Much improved—slight residual hyperaemia.	Sterile after 3 days till 12th day when R.E. staph. aureus P.S. = O.S. L.E. staph. albus P.S.

BLEPHARITIS—continued

Serial No.	DIAGNOSIS	Bacteriological Report before treatment	Penicillin Treatment	Clinical Progress	Bacteriological Report after treatment
34	Chronic blepharitis R.L. Many years.	Staph. aureus P.S. and few Gram neg. diplococci.	Guttae (500 u/c.c.) hourly for 20 days.	Much improved—slight residual scaling and hyperaemia. Follow up—lids normal 2 months later.	Sterile 11th day R.E. 15th day L.E.
36	Blepharo - conjunctivitis. Acute R.E. Sub-acute L.E. 10 months L.E.	R.E. no growth. L.E. Staph. albus P.S.	Guttae (500 u/c.c.) hourly for 7 days.	Apparent cure. Follow up—no relapse 2 months later.	Sterile after 5 days.
37	Chronic blepharo-conjunctivitis, R.L. 6 years.	R.E. Staph. aureus P.S. L.E. Staph. aureus P.R.†	Guttae (500 u/c.c.) hourly for 10 days.	Apparent cure. Follow up—lids normal 2 months later.	6th day R.E. Staph. albus P.R. sterile. 10th day R.E. sterile.
38	Chronic blepharitis R.L. Many years.	Gram + coccus P.R.	Guttae (500 u/c.c.) hourly for 15 days.	Much improved, slight residual crusting.	14th day R.L. Staph. albus P.R.
39	Blepharo - conjunctivitis R.E. Conjunctivitis L.E. 5 weeks.	R.L. Staph. aureus P.S.	Guttae (500 u/c.c.) hourly for 19 days.	Apparent cure. Follow up—no relapse 2 months later.	Sterile after 10 days.
42	Chronic blepharitis R.L. Many years.	Staph. aureus P.S.	Guttae (500 u/c.c.) hourly for 6 days.	Apparent cure.	8th day R.E. sterile. L.E. Staph. aureus P.S. 12th day sterile.
43	Chronic blepharitis R.L. Many years.	Staph. aureus P.S.	Guttae (500 u/c.c.) hourly for 13 days.	Much improved—slight residual crusting and hyperaemia.	10th day sterile.
44	Chronic blepharitis R.L. Many years.	Staphylococcus P.S.	Guttae (500 u/c.c.) hourly for 2 weeks.	Much improved—slight residual scaling. Follow up—improvement maintained 3 weeks.	
46	Chronic blepharitis R.L. 2 years.	R.E. staph. aureus P.R. L.E. Staph. albus P.S.	Guttae (500 u/c.c.) hourly for 7 days. R.E. 10 days L.E.	Only slight improvement in both eyes after penicillin. Further improvement with silver nitrate paint and ungt. of brilliant green and gentian violet. Follow up—relapse in 3 weeks.	6th day R.E. Staph. aureus P.R. L.E. Staph. aureus P.S. 11th day R.L. sterile. 13th day R.E. Staph. aureus P.R. L.E. sterile.
47	Chronic blepharitis L.R. Many years. Seborrhoea.	Staph. albus P.S. = O.S.	Guttae (250 u/c.c.) 4 or 5 times daily for 6 days (out-patient) local irritation.	Improved after subsidence of local reaction to penicillin. Follow up—gradual recurrence.	6th day R.E. Staph. albus P.S. L.E. Staph. albus P.R.

* Penicillin Sensitive.

† P.R. = Penicillin Resistant.

‡ O.S. = Oxford standard.

CONJUNCTIVITIS

Serial No.	DIAGNOSIS	Bacteriological Report before treatment	Penicillin Treatment	Clinical Progress	Bacteriological Report after treatment
19	Acute conjunctivitis R.E.	Staph. aureus P.S.	Lamellae (180 u) 4 hourly for 9 days.	Cured in 3 days.	7th day sterile.
26	Acute recurring conjunctivitis R.E.	Staph. aureus P.S.	Guttae (500 u/c.c.) 4 hourly for 6 days.	Cured in 3 days.	2nd day sterile.
31	Acute conjunctivitis L.E.	Staph. aureus P.S.	Guttae (500 u/c.c.) 4 hourly for 6 days.	Cured in 6 days.	6th day sterile.
41	Acute conjunctivitis L.E.	Staph. albus P.R.	Guttae (250 u/c.c.) 4 hourly for 16 days.	Cured in 16 days—doubtful if penicillin of benefit.	4th day Staph. aureus P.S. 10th day sterile. 13th day Staph. aureus P.S. 17th day sterile.

CONJUNCTIVITIS WITH KERATITIS OR CORNEAL ULCER

3	Conjunctivitis and catarrhal ulcer L.E. resistant to other treatment for one month.	Staph. aureus and albus both P.S.	Guttae (500 u/c.c.) 4 hourly for 8 days.	Cured.	5th day sterile.
8	Conjunctivitis and punctate keratitis L.E. Other treatment for 5 weeks.	Staph. aureus (P.S. not tested).	Guttae (250 u/c.c.) 4 hourly for 16 days only.	Cured after 2½ months. No apparent benefit from penicillin.	11th day sterile.
9	Conjunctivitis with severe marginal ulcers R.L.	Staph. aureus P.S.	Guttae (250 u/c.c.) 4 hourly for 9 days R.E. 7 days L.E.	Rapid cure in 1 week. The L.E. was treated with albucid drops for first 48 hours, the improvement of L.E. during this period was not so rapid as R.E. which was receiving penicillin.	12th day sterile.
20	Conjunctivitis, small catarrhal ulcers L.E.	Staph. aureus R.L. Morax-Axenfeld R.L. Both P.S.	Guttae (500 u/c.c.) 2 hourly L.E. 4 hourly R.E. for 3 days.	Cured. Follow up 17 days later—no relapse.	3rd day sterile.
28	Mild conjunctivitis R.E. Conjunctivitis with marginal keratitis L.E.	Staphylococci P.S.	R.E. guttae (500 u/c.c.) 4 hourly. L.E. lamellae (180 u) 4 hourly for 7 days.	Rapid cure in 3 days. Drops and lamellae equally good.	3rd day R.E. sterile. L.E. Staph. albus P.R.
33	R.L. conjunctivitis. L. slight superficial punctate keratitis recurring.	Staph. aureus P.S.	Guttae (500 u/c.c.) 4 hourly for 10 days.	Cured.	9th day sterile.

CONJUNCTIVITIS WITH KERATITIS OR CORNEAL ULCER—continued

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Serial No.	DIAGNOSIS	Bacteriological Report before treatment	Penicillin Treatment	Clinical Progress	Bacteriological Report after treatment
35	R.L. conjunctivitis. L. slight superficial punctate keratitis 2 days.	Staph. aureus P.S.	Guttae (500 u/c.c.) hourly for 18 days.	Cured in 20 days. Also had antritis R.L. Doubtful if penicillin of benefit.	4th day Staph. aureus haemolytic Strep. 16th day sterile.
40	L.E. acute conjunctivitis and catarrhal ulcers.	Staph. albus P.S.	Guttae (500 u/c.c.) hourly for 13 days.	Cured in 18 days. Doubtful if penicillin of benefit.	6th day Gram negative bacillus P.S. 11th day sterile.
CORNEA					
7	R.E. conjunctivitis and catarrhal ulcer. Dermatitis of eyebrows.	Staph. aureus P.S.	Guttae (250 u/c.c.) hourly for 7 days.	Cured in 5 days.	5th day sterile.
13	R.E. corneal ulcer, with development of small hypopyon later. No trauma.	Staph. aureus P.S. almost = O.S.	Guttae (250 u/c.c.) hourly for 6 hours, then 4 hourly for 16 days.	Small hypopyon developed on 4th day. Unsatisfactory progress with penicillin. Sulphathiazole by mouth (24 gms.) + local application of iodine paint. Healing commenced after penicillin stopped, and after administration of milk intramuscularly. Cured in 8 days.	No culture taken.
21	L.E. Marginal ulcer 10 days.	Staph. aureus P.S.	Guttae (500 u/c.c.) hourly for 10 days.	Cured in 12 days.	9th day sterile. 15th day sterile.
22	L.E. diffuse superficial keratitis 3 weeks.	Staph. aureus P.S.	Lamellae (180 u) 4 hourly for 10 days.	Cured in 8 days.	11th day sterile.
25	R.E. deep keratitis with superficial ulceration for 6 weeks.	Staph. aureus P.S. Morax-Axenfeld P.S.	Lamellae (180 u) 4 hourly for 15 days.	Quiet in 2 months. No apparent benefit from penicillin.	9th day and after sterile.
32	R.E. superficial punctate keratitis recurring for some months.	Scanty growth. Bacillus of haemophilus group. P.S. = O.S.	Guttae (500 u/c.c.) hourly.	Cured in 7 days.	6th day and after sterile.
INJURIES					
2	R.E. perforating wound cornea with small F.B. in posterior chamber: no response to magnet.	None taken.	1250 units into both anterior chamber and vitreous on 4th and 5th day.	Hypopyon 3rd day. 8th day improved, no hypopyon. Gradual deterioration thereafter. 16th day—on section purulent infiltration of vitreous. Penicillin probably only alleviated acute inflammation.	5th day culture from stab wound into vitreous (made for penicillin injection). Staph. albus only.

The second case was of interest on account of marked local reaction to penicillin treatment: there was moderate oedema of the eyelids of both eyes commencing on the third day of treatment. After six days, treatment was discontinued on account of the discomfort. When the reaction had subsided two or three days later, the condition of the lids was much better than before treatment was started. In three weeks time, as the blepharitis was recurring, treatment was re-commenced with a solution of penicillin (250 u/c.c.) of a different make, but again had to be stopped owing to a more severe local reaction.

Major D. G. Freshwater, Command Dermatologist, carried out sensitisation tests with penicillin.

1. Patch test with penicillin (Pfizer brand)—strength 250 u/c.c.
a. Moist patch:—no reaction after 48 hours. b. Patch remoistened every three hours:—positive after 48 hours.

2. Patch test with another make of penicillin (Glaxo)—strength 500 u/c.c. a. Moist patch:—positive reaction after 18 hours. b. Patch remoistened every three hours:—positive after 12 hours.

3. Intramuscular injection of 10,000 units (Upjohn brand) caused no febrile reaction or general upset.

4. Patch tests with 10,000 u/c.c. (Upjohn):—positive reaction in five hours.

5. a. Patch tests with penicillin 10,000 u/c.c. which had been autoclaved—negative. b. Patch test with penicillin 10,000 u/c.c. with penicillinase—no reaction in 24 hours—positive in 48 hours.

In view of the notorious liability of blepharitis to relapse, an attempt was made to re-examine all cases treated. This was only possible in ten cases, owing to the inevitable movement of troops. Eight cases re-examined at intervals ranging from one to five and a half months after cessation of treatment, showed no relapse. Of the remaining two, one, No. 46, has already been mentioned as showing little response to penicillin treatment, and the other, No. 47, was the case which was allergic to penicillin.

Acute conjunctivitis. Of the four cases treated all were cured.

Conjunctivitis with lesion of Cornea. Of the eight cases treated, five were cured: three showed no apparent response to penicillin.

Keratitis or Corneal ulceration. Of the six cases treated, four were cured: the remaining two did not respond to penicillin, and required other treatment.

Perforating injury. One case: failure.

Comments

Lamellae.—These were used in nine cases. As compared with a solution of penicillin they have these advantages: easy storage, no necessity for refrigeration and immediate availability. The lamellae are highly deliquescent, and on this account the container must be

kept tightly corked. Those containing 100 units caused a little more discomfort than a solution of 500 units/c.c., but it was found that the 180 unit lamellae did cause considerable smarting and slight conjunctival injection for about ten minutes. It was thought that lamellae of both strengths and a solution of 500 units/c.c. were equally effective.

The cases of blepharitis responded well to penicillin, and the results seem more favourable than those obtained with any other treatment. When penicillin is more generally available, it is hoped that its early use in blepharitis of childhood may effect a complete and early cure, and prevent recurrent and chronic infection. In the few cases of acute conjunctivitis treated, it is thought that penicillin accelerated the cure in cases from which a penicillin sensitive organism was recovered. The response of cases Nos. 9 and 28 (conjunctivitis with marginal ulcers, and keratitis) was most striking. The one case of hypopyon ulcer (No. 13) developed hypopyon while under penicillin treatment: it should be noted, however, that the penicillin was not used in the energetic manner described by Juler and Young (1945).

The intra-ocular use of penicillin in one case of perforating injury was unsuccessful: this was not unexpected, as the foreign body was not removed.

Part II.—“Eales Disease”

D.S.—Male, aged 32 years. History of sudden loss of vision of right eye, May, 1944.

On admission October 26, 1944, the right eye showed much vitreous opacity and the vision was reduced to counting fingers at two feet. The left eye showed recent haemorrhages, and exudate from old haemorrhage along the course of the inferior temporal vessels. L.V. = 6/6.

Investigations as to cause.—The following examinations revealed no abnormality:—blood Kahn, blood culture, red and white counts, dental, nasal sinuses, X-ray of chest, urine, urea concentration, bleeding time—2 minutes, clotting time—4 minutes, B.S.R. 3 mm. Mantoux, weak positive for 0.0001 c.c. of old tuberculin.

Treatment included full doses of vitamins A, B, C, D, K, P, at various times: autohaemo-therapy, calcium and ostelin, and 24 grammes sulphathiazole. An acute attack of tonsillitis on December 7, due to a haemolytic streptococcus, responded well to 14 grammes of sulphanilamide. A repeat of blood count at this time showed R.B.C. 6,300,000 and W.B.C. 11,000.

A course of old tuberculin was commenced on November 14, 1944, and ended on June 10, 1945, the initial dose being 0.000,005 c.c., and final dose 0.06 c.c. By December 19 nearly all the lower

half of the left retina showed haemorrhages; there was oedema of the macula; the veins of the upper half of the retina were engorged and showed marked sacculation, and at points were obscured by periphlebitis, with no haemorrhage yet to be seen. L.V. 6/36.

The right vitreous was still very opaque, and vision was only hand-movements.

On December 23 a course of penicillin was commenced, 12,500 units intra-muscularly every three hours for ten days—a total of 1,000,000 units.

Two days before the course was finished, it was thought that the superior retinal veins of the left eye were less congested and their calibre more even. Improvement in the appearance of the veins continued, but on January 21 haemorrhages were noted peripherally along one tributary of the superior temporal vein. Since then repeated haemorrhages have occurred at this site, and occasional more profuse haemorrhages into the right vitreous. At the present date, June 22, the right vision is counting fingers at 8 in. and the left 6/12.

A.W.—Male, aged 24 years. Recurring haemorrhages into vitreous of both eyes for ten months prior to administration of penicillin, as in the preceding case. A similar complete clinical and bio-chemical examination showed no abnormality, with the exception of Mantoux which was strongly positive to 0.0001 c.c. of old tuberculin, and positive to 0.00001 c.c.

Treatment.—Vitamins as in the previous case, and a course of old tuberculin therapy from 0.000,001 c.c. to 0.01 c.c. over a period of seven months: penicillin as already detailed.

He has been under observation for five months since receiving penicillin, and haemorrhages continue to recur in both eyes.

While in the case D.S. definite improvement occurred towards the end of the course of penicillin, we feel this was probably a coincidence: in the case A.W. there was no appreciable effect.

Comment

Though penicillin has not been of benefit in these two cases of Eales' disease, it may be worth investigating its use in those cases of acute perivasculitis of the retina where it is thought that a mild septicaemia may be the cause.

Summary

A report has been made of:—

Thirty-eight cases of superficial ocular inflammation treated by local application of penicillin, and of one case of perforating injury treated by intra-ocular injection of penicillin.

Two cases of Eales' disease, treated by intra-muscular injection of penicillin.

We wish to thank Colonel J. S. K. Boyd, Lt. Colonel A. Sachs, Major C. E. Van Rooyen and Miss M. E. Davies for kindly carrying out the bacteriological investigation, and to Dr. I. M. M. Mears of the Astley-Ainslie Institution for supervising the treatment.

REFERENCE

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THROMBIN TECHNIQUE IN OPHTHALMIC SURGERY

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THE perfect form of wound repair must, we take it, be that, which follows most closely on Nature's methods, and if it were possible in ophthalmic surgery—where the structures dealt with are so delicate—to find some method of wound repair which would obviate the need for sutures and yet help wounds to heal quickly and firmly, then we should be approaching the ideal.

It was speculation on the above lines that led us to think that the use of thrombin for ophthalmic wound repair might be of value and it was decided to try it out on a number of cases.

The use of thrombin is well established in plastic surgery. It is an extract of blood platelets and its action is to reduce the bleeding time at any raw surface, thus securing quick and firm adhesion between two raw areas of tissue such as wound edges brought together in apposition, or where tissue flaps or grafts are placed on a prepared bed. Thrombin is capable of reducing the bleeding time from the normal 6-8 minutes to 15 seconds. There are two commercial preparations in circulation which we have used: thrombin topical (Parke-Davis) and thrombin coagulant (Maw). The preparation is made up in powder form in sealed ampoules and solutions are made from the ampoules of the strength required. This solution must be used immediately and will not keep for any appreciable length of time. Extract of platelets was used systemically before on the assumption that parenteral administration of such extract would enable the body to reduce its own bleeding time. Coagulin (Ciba) was probably the widest known commercial preparation of this type.

Plastic Surgeons apply thrombin to the actual surfaces of the graft and bed and it is generally agreed that the adhesion of such