Perhaps the precipitation of fibrinous shreds depended on an hereditary predisposition or on the particular strain of spirochaete.

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Summary

Three cases are described of hyaline membranes; one of them a consequence of developmental arrest, one due to birth trauma and the third following uveokeratitis. Their aetiology is discussed.

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LOCAL APPLICATION OF UREA FOR THE TREATMENT OF DENDRITIC ULCER*

BY

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HYPERTONIC solutions applied in an eye-bath are believed to have a favourable influence on marginal ulcers of the cornea. One obvious advantage of an eye-bath is that the medication is kept in the conjunctival sac. A series of cases of dendritic ulcer was treated with a corneal bath containing a 25 per cent. solution of urea in 1942-44 at the Central London Ophthalmic Hospital and the results in over 30 cases were encouraging.† The same treatment has been carried out in a new series, and the results are reported here. It

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† M. Klein. Results unpublished, as the notes of these cases were lost during the war.

appears that urea, though widely used in other branches of medicine, has not been employed in ophthalmology.

Historical.—The effect of urea on bacteria has been known for many years. Ramsden (1902) noted that urea inhibited putrefaction. According to Peju and Rajat (1906) urea added to a nutritive medium produces abnormal morphological forms, and if the concentration is increased the growth of bacteria stops altogether. Wilson (1906) noted that 1.5 to 3.5 per cent. of urea in the medium caused pleomorphism, and an addition of 8 per cent. urea prevented the growth of *B. coli*. In 1915 Syms and Kirk observed that 25 per cent. or stronger solutions of urea killed *B. typhosus*, and local applications of crystalline urea resulted in the sterilization of wounds. Foulger and Foshay (1935) treated purulent otitis media by local application of saturated solutions of urea, and McKay and Schröder (1936) found that concentrated urea solutions inactivated rabies and poliomyelitis virus in a relatively short time. The use of urea gained popularity recently when it was found that it increased the activity of locally applied sulphonamides, and a dusting powder consisting of urea and sulphonamide was widely used for wound treatment during the late war. Weinstein and his co-workers (1944-1947) studied the antibiotic activity of urea and its related compounds (urethane and thiourea) and found that the antibiotic effect of these preparations is considerable and is mainly directed against Gram-negative bacteria. Gram-positive bacteria are affected only by exposure to higher concentrations and for longer periods (Weinstein and co-workers). Some of the urea derivatives, especially phenylurethane, can be regarded as poisons acting directly on the cell. Spores soaked in 0.5 per cent. urethane show effects similar to irradiation with 1,000 r X-rays (Haddow 1948). Urethane has also been administered in leucaemia and the effect is said to be comparable to that of deep X-ray therapy. (Paterson *et al.*, 1946.)

Properties of urea and its derivatives are as follows: Urea forms white hygroscopic crystals. Solutions must be kept sterile as they are liable to undergo ammoniacal decomposition if contaminated. Urea is a normal constituent of tissues and blood. It is not toxic, and if it is applied to wounds, healing is not interfered with. Thiersch grafts do not necrose in the presence of urea. Urea solutions are neutral and their antibiotic activity is retained in acid or alkaline media. Urea penetrates cells readily, *e.g.*, red blood cells, and the urea content becomes similar within and without. It does not cause haemolysis. The break-down products of tissues are dissolved in a solution of urea, a point of importance in the local use of sulphonamides. Clinically urea

solutions have proved useful in chronic purulent wounds; they stimulate healing and help in the separation of sloughs (Williams, 1946 and Robinson, 1936). Urea can be used with advantage in combination with sulphonamides, as it enhances their solubility and contributes its own bactericidal effect. It can also be used in combination with penicillin, and, according to Weinstein, urea limits the production of penicillinase. Derivatives of urea which have been used or investigated for antibiotic effects are: allantoin, urethane and phenylthiourea. The action of urea on wounds is the rationale of the present study.

LOCAL USE OF UREA IN CASES OF DENDRITIC ULCER

As in the preliminary series, the following method of treatment was used in the present series. The eye was anaesthetised with two instillations of 0.5 per cent. amethocaine hydrochloride B.P.

FIG. 1.

(a) Contact shell applicator. (b) Eye bath.

The contact lens applicator* was placed over the eye (Fig. 1a and Fig. 2) and filled with a freshly made solution of 25 per cent. urea to which 2 drops of amethocaine was added to each 5 ml. solution. The application was well tolerated and treatment was done either in the sitting or recumbent position. Through the transparent plastic contact applicator the eye was watched during treatment, and if the ulcer was not covered by the fluid the appli-

* Made by G. Nissel & Co., Ltd.

cator was replenished. The duration of the treatment was 5 minutes. Immediately after treatment the cornea usually showed diffuse staining round the dendritic ulcer, and very often a large adjacent area became denuded of epithelium.

In some cases there was difficulty in the use of the contact applicator, and a bakelite eyecup, the bottom of which was removed, was used instead (Fig. 1b and Fig. 3). After placing the cup over the open eyelids, the urea solution was poured into the cup. By

FIG. 2.

Contact shell applicator inserted without fluid. Condensation shows up the raised corneal portion.

a slight pressure with the edge of the cup the palpebral fissure was kept open so that the cornea was bathed with the fluid. With this treatment the patient had to be in a recumbent position.

The urea treatment was followed by instillation of 1 per cent. atropine drops, yellow soft paraffin was placed in the lower fornix and the eye bandaged. The dressing was changed after 24 hours, when the staining area was found to have diminished or completely healed over. A second or third urea treatment could be given with an interval of 24 hours between each treatment. A mild ointment such as yellow soft paraffin was useful in preventing the breaking-down of the newly formed epithelium.

FIG. 3.

Eyebath in use. The edges of the cup hold the palpebral fissure open.

RESULTS

Thirty-three cases were treated in this series arbitrarily divided into three groups according to the severity of the lesion. Group I included all the cases in which there was a well localized dendritic

TABLE I
Data on individual cases

No.	Age	Sex		Severity			No. of urea applications	Healing time in days	
		M.	F.	I	II	III			
1	45	M.	—	—	II	—	1	13	—
2	70	M.	—	—	—	III	—	40	See Remarks
3	30	M.	—	—	II	—	2	14	—
4	28	M.	—	—	—	III	2	28	See Remarks
5	35	—	F.	—	II	—	2	42	Healed 12 days after urea, See Remarks
6	71	M.	—	I	—	—	1	2	—
7	58	M.	—	I	—	—	1	2	—
8	46	M.	—	I	—	—	1	4	—
9	67	M.	—	I	—	—	1	3	See Remarks. Urea treatment was given 4 weeks after onset and 3 weeks after other treatment had failed.
10	62	M.	—	I	—	—	1	10	History of previous dendritic ulcers 1933, 1943, 1946.
11	63	M.	—	I	—	—	1	5	—
12	60	M.	—	—	II	—	1	28	History of previous dendr. ulc. See Remarks.
13	25	M.	—	—	II	—	1	7	Came to Hospital 1 month after onset.
14	62	M.	—	—	II	—	1	9	History of previous dendritic ulcer.
15	19	—	F.	I	—	—	1	7	—
16	38	M.	—	I	—	—	1	7	—
17	48	—	F.	—	II	—	1	28	Transient punctate staining of cornea. Hist. of prev. dendritic ulcer.
18	45	—	F.	I	—	—	2	16	Transient punctate staining of cornea.
19	61	M.	—	I	—	—	1	15	Transient punctate staining of cornea History of prev. corneal ulcers, ? nature.
20	24	M.	—	I	—	—	2	5	—
21	51	M.	—	I	—	—	1	7	—
22	51	M.	—	I	—	—	1	7	—
23	39	M.	—	I	—	—	1	10	—
24	64	M.	—	I	—	—	1	11	—
25	70	M.	—	I	—	—	1	5	—
26	68	M.	—	—	—	III	1	42	See Remarks
27	69	M.	—	—	II	—	1	13	Transient punctate staining.
28	52	—	F.	I	—	—	1	—	No response to urea, transferred to Radiotherapy.
29	38	—	F.	I	—	—	1	7	—
30	38	—	F.	I	—	—	1	9	—
31	44	M.	—	I	—	—	1	17	—
32	53	M.	—	I	—	—	1	13	—
33	56	M.	—	I	—	—	1	6	—

figure, Group II those in whom the lesion was more extensive, and Group III those with deeper lesions marked either by infiltrations of the deeper layers of the cornea, or by cells in the anterior chamber, or by hyperaemia and swelling of the iris without patent herpetic iritis.

REMARKS

(2) Recurrent dendritic ulcer; attacks almost every year since 1933. No response to treatment. Iodised six times, carbolised twice, urea applied three times, vaccinated, sulphacetamide locally applied, retrobulbar alcohol injected. Eventually the eye became quiet after tarsorrhaphy. Duration 40 days. Urea ineffective.

(4) First urea treatment on the fourth day after onset. The eye made a slow recovery and on the 21st day the ulcer recurred, for which a second treatment with urea was given. Two days later there was no staining. Received two urea treatments; healed in 28 days.

(5) October 17, 1947. Carbolised and local penicillin applied: October 20, 1947, vaccinated. One month after treatment had failed urea was applied, and 10 days later repeated. Rapid healing followed in a few days. A fortnight later a small staining area was noted, urea treatment was given again and healing followed.

(9) Iodised twice, local albucid applied, without success. Three weeks after treatment had failed, urea was applied and 3 days later there was no staining. Four weeks after discharge there was a relapse which healed without treatment in one week.

(12) After the first urea treatment the condition improved but the epithelium was constantly breaking down. Patient was treated with albucid, healing was slow, taking 4 weeks. History of dendritic ulcers previously.

(26) Had one urea treatment. After some improvement, the ulcer broke down and did not heal until intravenous ascorbic acid (500 mg. daily for 7 days) was given.

Group I was the largest with 22 cases. The number of days needed for healing varied between 2 and 16 after the application of urea, with an average of 8 days. In 20 cases one application of urea proved sufficient. The average healing period of 8 days applies to cases in which 6 or 8 days after the urea treatment, punctate staining appeared. In these cases the time was recorded when the corneal condition was completely healed.

Group II contained 8 cases. Healing time was protracted in two cases owing to a recurrence of the staining area. In the remaining cases of this group the healing time was from 7 to 14 days with an average of 15.5 days for the group as a whole.

TABLE II
Classified data on the patients in group

	Healing time in days			Distribution of age			Total	Distribution of sex	
	average	min.	max.	under 35	36-55	56 & over		Male	Female
Group I 199	8	4	16	2	11	9	22	18	4
Group II	15.5	7	42	3	2	3	8	6	2
Group III	36	28	42	1	—	2	3	3	—
				6	13	14	33	27	6

Three cases fell into Group III. The healing period was in one case 28 days, in the other two 6 weeks.

Discussion

In this series, dendritic ulcer was predominantly a disease of males, and mostly of the older age group, as can be seen from Table II. In those cases giving a history of one or more attacks of dendritic ulcer in the past the tendency to healing was poor. On the other hand, where the dendritic ulcer developed upon corneal scars of other than dendritic origin, the healing time was the same as on a previously healthy cornea. After urea treatment the epithelium quickly regenerated, and the ulcer healed, but there was a tendency to relapse, a well-known characteristic of dendritic ulcer. It was therefore deemed important to give protection to the corneal epithelium by placing in the lower fornix a mild lubricating ointment and to keep the eye bandaged for 6 to 10 days after complete epithelialization. Patients were then advised to continue the pad and bandage at nights only, for another 3 weeks.

An important factor in the healing of dendritic ulcers is the general condition of the patient; the most severe cases appeared to be in poor physical condition, and the corneal lesion healed only after general treatment was given. In two severe cases, 500 mg. ascorbic acid was given intravenously daily for 7 days, and rapid healing was observed. It appears that the essential points in the treatment are (1) the favourable effect of locally applied urea followed by (2) protection of the healed area by a lubricant and a bandage, and in severe cases by (3) general treatment in order to improve the physical condition of the patient.

The punctate staining which was seen in a few cases following urea treatment may have been caused by the use of urea from a stock solution; it is advisable to use solutions freshly made. Recently in the treatment room, packets of 1 gm. urea powder have been kept ready, and the solution made by adding 4 ml. distilled water immediately before use.

Summary

The use of 25 per cent. urea solution applied as a corneal bath by means of a contact applicator or an eyecup is suggested as a method of treating dendritic ulcer. This application lasts from 5 to 10 minutes. The urea solution should be freshly made. The urea treatment is combined with treatment by atropine, yellow soft paraffin and bandaging of the eye.

No damage was observed from the application of urea. Results of 33 cases are reviewed. The milder cases generally healed after one application.

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THE RELATIVE IMPORTANCE OF DIRECT AND INDIRECT OPHTHALMOSCOPIC EXAMINATION IN THE TREATMENT OF RETINAL DETACHMENT*

BY

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It is essential to employ both methods of ophthalmoscopy to obtain the highest possible percentage of successes in the surgical treatment of retinal detachment. I have seen on my travels that many colleagues employ one method to the exclusion of the other, and that in some countries the majority of the ophthalmologists use one method almost exclusively. If we grant the enormous importance of ophthalmoscopic examination in the treatment of retinal detachment, we must also make as complete an examination as possible by this method. I have seen colleagues who, though excellent clinicians and surgeons, only reached 55 per cent. of successes in these operations, owing, in my opinion, to the exclusive use of direct ophthalmoscopy as a mode of operative orientation.

These facts decided me to prepare the statistics of 200 unselected cases of my own, which I had classified in the following four groups:—

The *first* group includes those cases in which tears were visible to either method of examination. In the *second* group tears were visible only to indirect ophthalmoscopy, and in the *third* only visible

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