THE BRITISH JOURNAL

OF

OPHTHALMOLOGY

APRIL, 1946

COMMUNICATIONS

EPIDEMIC KERATO-CONJUNCTIVITIS ASSOCIATED WITH SKIN LESIONS*

BY

W. J. O'DONOVAN, Lieut.-Col.

ADVISER IN DERMATOLOGY, MIDDLE EAST FORCES

and

I. C. MICHAELSON, Major

OPHTHALMIC SPECIALIST

IN a General Hospital in Egypt during the year 1944-1945, 33 cases with associated lesions of the skin and kerato-conjunctivitis were seen. So far as we can discover this concurrence has not been emphasised in either the ophthalmic or dermatologic literature. Apart from the close association with lesions of the skin the kerato-conjunctivitis in these cases was clinically indistinguishable from epidemic virus kerato-conjunctivitis. Indeed it appeared to us only late in the series that the close association of lesions of the skin with some of the cases of kerato-conjunctivitis possibly signified that these cases might be of a nature different from epidemic virus kerato-conjunctivitis. It appears worthwhile to describe these cases and to determine if possible their relationship to epidemic kerato-conjunctivitis. The appearance during the

* Received for publication, August, 1945.

same twelve-month period of an exactly similar number of cases of typical epidemic kerato-conjunctivitis supplied material for comparison. In none of these latter cases was a lesion of the skin present. These will be referred to as the "control group."

The 66 cases constituted 1.1 per cent. of all cases and 19 per cent. of all cases with conjunctivitis seen in one year in the eye out-patient department of the General Hospital. The remaining 81 per cent. of cases with conjunctivitis showed no exceptional incidence of lesions of the skin. Ten of the cases were referred from the skin department of the hospital.

Skin lesions in 66 cases with kerato-conjunctivitis

Number of cases with no affection of the skin ("control cases")	...	...	...	...	...	...	33
Number of cases with affection of the skin	...	...	...	...	...	...	33

Detail of lesions in 33 cases with affection of the skin

Seborrhoeic dermatitis	...	...	...	=	18 cases
Severe acne	...	...	...	=	2 "
Severe acne and impetigo	...	...	...	=	1 "
Chronic blepharitis of the squamous type	...	...	...	=	6 "
Impetigo of the face	...	...	...	=	2 "
Recurrent styes	...	...	...	=	1 "
"Dermatitis septic" of the ear lobe	...	...	...	=	1 "
Generalised arsenical dermatitis	...	...	...	=	1 "
Sycosis barbae	...	...	...	=	1 "

The majority of the cases were of the seborrhoeic type. In all cases the face or head was affected. In a few there was also an affection of the skin of the trunk or limb. The following cases typify those with associated lesions of the skin :—

Case 42 illustrated in Fig. 1 belongs to the seborrhoeic dermatitis group. He is an officer who stated that 3½ years before he had been treated in a General Hospital for impetigo of the face and scalp. Fifteen days before the onset of kerato-conjunctivitis in the right eye the scalp became covered with scabs which spread to the right brow, right upper-lid, and right side of the forehead. After the eye condition had developed the skin appearances were as follows:—scaling and scabbing of the right parietal region; erythema and scanty papulation of right forehead; redness and scabbing of right eyebrow region; erythema and fine scaling of right upper lid and outer canthus, papular rash of right cheek and side of neck and very mild folliculitis of the left cheek. The right eyelid showed ptosis and the right pre-auricular gland was tender but not palpable. There was a watery discharge from the eye and the conjunctiva showed a red "cellophane" surface.

The appearance of the cornea on the 6th day is illustrated in Fig. 2. Superficial flecks of opacity covered the central area. They were best seen by indirect light on slit-lamp examination. More peripherally there were larger dots, several of which stained with fluorescein. On the 11th day he suffered very severe pain in the eye. The eye was more injected and Descemet's membrane

EPIDEMIC KERATO-CONJUNCTIVITIS ASSOCIATED WITH SKIN LESIONS

195

showed numerous folds (see Fig. 3). There was a very pronounced hazing and bedewing of the whole corneal epithelium. On the 16th day the left eye also became red and uncomfortable. The appearance of the cornea of the left eye on the 22nd day is illustrated in Fig. 4. By the 33rd day the condition of the skin and eyes had healed and he was discharged from hospital. The visual acuity of the right eye which on the 11th day had fallen to 3/60 was 6/6 on the day of discharge. The left eye has always been amblyopic. It was very noticeable that the skin and eye conditions varied *pari passu*.

Fig. 5 illustrates the appearance of the cornea of case 35 on the 17th day. His first skin trouble occurred in England two years previously when there

FIG. 4.

Illustrating the left cornea of Case 42 on the 22nd day. There are several peripheral dots of opacity, one of which stains with fluorescein. The neighbouring epithelium is hazy.

were two ulcers of the legs which took six weeks to heal. Two weeks prior to the onset of the kerato-conjunctivitis of the left eye a small septic spot appeared on the chin. It lasted for a few days. Eleven days after the onset of the eye condition an erythema and mild red papular rash appeared on the left cheek. A little later a much milder papular rash appeared on the right cheek. This condition of the skin was not due to atropine, which continued to be used. The cornea showed several large dots, and a large area covered with pinpoint-like opacities clustered and coalesced in grumous fashion. There was tenderness of the left pre-auricular gland and marked drooping of the left upper lid. The condition of the eye and skin cleared together and he was discharged on the 40th day.

Figs. 6 and 7 illustrate the external and corneal appearance of case 66. Unfortunately, the former does not include the scalp, which became affected with a moist attack of seborrhoea 17 days before the eye condition developed. The upper lid drooped. The pre-auricular gland was not enlarged or tender, nor did it subsequently alter. From the beginning the cornea showed peripheral dots and epithelial changes. On the 15th day fine keratic precipitates and faint

aqueous flare appeared. On the 57th day the eye became more red and very painful. The cornea was extremely hazy and showed many folds of Descemet's membrane. The illustration was made on that day. The figure shows that two or three of the peripheral dots had become vascularised, which was unusual in these cases. Some atropine irritation developed, but on the 81st day the eye was completely healed. The skin condition, although improved was, however, still present and the patient was repatriated to the United Kingdom because of its chronicity.

Fig. 8 illustrates the appearance of the cornea of the left eye of case 25 on the 70th day. The condition, which began when the patient was in Liverpool, had already been present for 40 days when first seen in the M.E. The patient stated that small eruptions appeared on his face about the same time as the left eye became painful and red. He had never previously had any skin or eye trouble. When seen here there was a generalised seborrhoea and folliculitis of the face and neck and vestibular rhinitis on the left side. The left cornea in the lower segment showed peripheral scars of healed dots of keratitis. Several of them had coalesced. The most striking feature of the cornea, however, was that almost its entire surface was covered with fine staining pin-points. About the same time the right eye became painful and showed similar but fewer staining pin-points. Ptosis was present and the pre-auricular gland was palpable but not tender. By the 70th day the staining points had become much fewer, as shown in the illustration. It is interesting to note that the final area to be affected was that within the sweep of a trichiatric lash, which occasioned the patient no discomfort. In this case there was again a definite relationship between the varying severities of the skin and eye lesions.

Fig. 9 shows the appearance of case 40. The skin condition of the lid and its margin developed for the first time ten days prior to the onset of eye symptoms. There was a marked thickening and drooping of the eyelid with seborrhoeic dermatitis of the neighbouring skin. The pre-auricular gland was palpable.

FIG. 10.

Illustrating the right cornea of Case 40 on the 11th day. The darker dots are fluorescein staining.

FIG. 1.

Illustrating Case 42. Erythema and papulation of right forehead; redness and scabbing of right eyebrow region; erythema and fine scaling of right upper lid and outer canthus; papular rash of right cheek. Note the ptosis.

FIG. 2.

Illustrating the right cornea of Case 42 on the 6th day. Superficial flecks of opacity best seen by indirect light and larger dots, several of which are stained with fluorescein.

FIG. 5.

Illustrating the left cornea of Case 35 on the 17th day. Several large corneal dots and a large area covered with pin-point like opacities. The latter are not well seen in the figure.

FIG. 3.

Illustrating the right cornea of Case 42 on the 11th day. Numerous folds in Descemet's membrane and generalised epithelial haze and bedewing.

FIG. 6.

Illustrating Case 66. Note the typical ptosis. The affected scalp is not included, unfortunately.

FIG. 7.

Illustrating the right cornea of Case 66, on the 57th day. Note the marked haziness of the cornea and the numerous folds of Descemet's membrane.

FIG. 8.

Illustrating the left cornea of Case 25 on the 70th day. Note the peripheral scar below in which the coalition of large dots can be recognised. Originally covering almost the entire cornea, the staining points are fewer, but still well seen. The remaining ones are within the sweep of a trichiatic lash.

FIG. 9.

Illustrating Case 40. Ptosis with seborrhoeic dermatitis of the neighbouring skin.

There was a profuse watery discharge from the eye. On the 11th day of the eye condition the cornea showed numerous staining and non-staining dots as recorded in Fig. 10. On the 26th day the eye and skin conditions were healed and all treatment was stopped. Some thickening and drooping of the lid were, however, still present when the patient was examined 14 days after discharge.

The following is an analysis of the space and the time relationship between the skin and ocular lesions in the 18 cases with seborrhoeic dermatitis which are taken as an easily investigated sample of all the cases with skin lesions.

Relationship between the eye first affected and the distribution of the skin lesion in 18 cases of seborrhoeic dermatitis.—In 13 cases where the skin lesion was initially unilateral the ipsilateral eyes were affected.

In the other 5 cases the skin lesion was not confined to one side of the face or head at the time of the onset of the eye condition.

In some cases involvement of the second eye was preceded by spread of the skin lesion to that side.

Time relationship between the onset of the skin lesion and the onset of eye condition in 18 cases of seborrhoeic dermatitis.—In 11 cases the skin lesion preceded the eye condition by an average of 10 days, the longest interval being 17 and the shortest 4 days.

In 5 cases the skin and eye conditions occurred coincidentally. In one case the skin lesion occurred on the day following the onset of the eye condition.

One case (No. 35) must be termed doubtful as although the patient gave a history of a chin sore two weeks before the onset of the eye symptoms he states it lasted only 3 days. As already noted a rash appeared on the face left side 11 days after the eye had become inflamed. It is possible that the original chin condition had not completely healed when he first came under observation for his eye condition because he was not then seen by the dermatologist.

It should be noted regarding the 6 cases in which the skin lesion did not appear to precede the eye condition that in all of them reliance had necessarily to be placed on the patient's statement, and that in at least 5 of these cases a small symptomless skin lesion may well have preceded the eye symptoms by a short interval of time. In many cases a deterioration of the skin lesion was associated with a similar change in the ocular one. From a consideration of these facts there appears little doubt that the lesions of the skin and the kerato-conjunctivitis are closely associated and that they probably form integral parts of one condition. The problem that postulates itself is whether the kerato-conjunctivitis in these skin cases is identical with epidemic virus kerato-conjunctivitis or whether it is a different kind of kerato-conjunctivitis due to a different cause. In the absence of animal

and tissue culture experiments it is proposed to investigate the problem by a close clinical comparison of the group of the 18 cases showing seborrhoeic dermatitis with the group of 33 cases which were completely free of any skin or lid margin lesion and are considered as a control group of epidemic virus kerato-conjunctivitis.

(1) *Seasonal incidence.*—Graph (Fig. 11) shows the monthly incidence of the 33 cases without any skin lesion “control cases”

FIG. 11.

and the 18 cases with seborrhoeic dermatitis. In each instance the condition was definitely more prevalent in winter time, in Egypt the rainy season. It should be noted that seborrhoea is more prevalent in winter.

(2) *Bilateral cases.*—In the 33 “control cases” both eyes were involved in 10, i.e., 30 per cent. of cases, while among the 18 cases with seborrhoeic dermatitis both eyes were involved in 11 cases or 61 per cent. of cases. The average interval between the onset in each eye was 10 days in all groups.

(3)

	<i>Duration</i>	<i>Average</i>	<i>Shortest</i>	<i>Longest</i>
33 "Control cases"	...	37 days	8 days	90 days
18 Cases with seborrhoeic dermatitis		46 days	16 days	120 days

(4) *Ptosis*.—This was present in all cases except one of both groups. As Viswalingam has pointed out, the drooping of the lid is present most markedly in the outer 2/3rds of the lid which has the heavy thickened appearance seen with a styne or a wasp sting. The whole thickness of the outer part of the lid appears oedematous in some cases as if there was a tarsitis as well as subcutaneous oedema. Indeed cases 60 and 62 developed a chalazion in that part of the lid.

(5) *Pre-auricular glands*.—In most cases the gland was palpable and tender but taking both groups together in 8 per cent. it was

FIG. 12.
To illustrate Case 63. With the appearance of a large fresh corneal dot, on the 27th day the preauricular gland became much more tender. There was no change in the conjunctiva which had remained white since the 13th day.

enlarged and not tender while in 10 per cent. it was tender but not palpable. These changes occurred as early as the first day. In many cases the enlargement was shotty but more commonly it was diffuse. Variation in tenderness was frequently found to be parallel with variations in the corneal condition. Case 63 showed this in a very marked manner. The conjunctiva became white on the 13th day but the gland remained tender. On the 27th day the tenderness became much more marked coincidentally with the appearance of a large fresh corneal dot, as indicated in Fig. 12. Yet there was no change in the colourless conjunctiva that day except for a mild localised injection close to the fresh corneal lesion. In only one case were the cervical glands involved.

Among the 33 "control cases" the glandular involvement was present in 80 per cent. of the cases.

Among the 18 cases with seborrhoeic dermatitis it was present in 94 per cent. of the cases.

(6) *Conjunctiva*.—In most cases of both groups the conjunctiva showed the red glistening cellophane-like surface seen in cases of epidemic kerato-conjunctivitis together with a watery discharge. In a few cases, particularly of the group with seborrhoeic dermatitis the discharge tended to be muco-purulent. Only 3 cases showed any papillary hypertrophy.

(7) *Corneal lesions*.—These were present in all cases of both groups. As in most of the described epidemics these were very protean. In all cases there were diffuse epithelial changes such as hazing, bedewing, unevenness or fine grey dusting. Often patchy in distribution these epithelial changes tended to encircle within the periphery of the cornea and were nearly always present in the epithelium around the more obvious lesions. Indeed they may be taken as an indication of the activity or otherwise of the latter. These showed most frequently as ill-defined flecks, best, or in some instances only, seen by indirect illumination; as pinpoint-like staining opacities which occasionally coalesced to give a grumose appearance; as well-defined dots of which only a few stained with fluorescein or as fine staining non-branching striations such as Sanyal has described. So frequently do the corneal changes require slit-lamp detection it is recommended to stain with fluorescein and to examine with the slit-lamp as many cases of conjunctivitis as possible and certainly all cases showing drooping of the lid or adenopathy. In this connection it is well to remember that the normal cornea may occasionally show one or two fine staining points which may even be arranged linear fashion and do not wash away with irrigation. If fluorescein is again instilled a few hours later, however, these staining points do not reappear. Tests were carried out on 100 consecutive out-patients attending for visual defects and having no symptoms referable to the cornea or conjunctiva. Of these cases 15 showed the temporary fine pointed staining. There was no relationship between their length of stay in the Middle East and the incidence of these stains. This was further shown by the test being repeated with 36 repatriated allied P.O.W.s within a week of their return to the Middle East from Germany. Five of these cases showed two or three fine temporary staining points.

The larger corneal lesions tended to be peripheral but the faint flecks and points were usually central, in any one case, however, the corneal lesions in their distribution as well as in their type were very frequently mixed.

The following table indicates the frequency of the different corneal appearance among the cases.

EPIDEMIC KERATO-CONJUNCTIVITIS ASSOCIATED WITH SKIN LESIONS

	33 cases without skin lesions ("control cases")	18 cases with seborrhoeic dermatitis
Corneal flecks or dots in ...	27 cases (81 per cent.)	13 cases (78 per cent.)
Corneal points in ...	11 cases (33 per cent.)	8 cases (44 per cent.)
Superficial striae in	4 cases (12 per cent.)	no case
Staining with fluorescein ...	22 cases (66 per cent.)	12 cases (66 per cent.)
Centrally placed lesion in ...	14 cases (42 per cent.)	9 cases (50 per cent.)
Peripherally placed lesions in...	26 cases (78 per cent.)	13 cases (78 per cent.)

There is thus no substantial difference between the corneal appearance in each group with the possible exception perhaps of superficial striation. The small number of such cases, however, makes this observation of no significance.

(8) *Deep corneal or uveal involvement.*—This was indicated in 7 cases by folds in Descemet's membrane, by very fine keratic precipitates, by floating cells in the aqueous or by fine aqueous flare.

	Number of cases with deep corneal and uveal involvement
33 cases without skin involvement "control cases" ...	2 cases (6 per cent.)
18 cases with seborrhoeic dermatitis	4 cases (22 per cent.)

Two of the cases with seborrhoeic dermatitis had folds of Descemet's membrane (see Figs. 3 and 7). It would thus appear that cases of kerato-conjunctivitis with skin affection have a greater tendency for the lesion to spread deeply.

(9) *Corneal sensation.*—This was tested in only 13 cases. It appeared to be diminished in two or three of the cases. This small number was not confined to any group.

(10) *Conjunctival smear and culture.*—Because these had, in reported and personal (Feigenbaum, Michaelson and Kornbluth) experiences of epidemic kerato-conjunctivitis, been nearly always negative, routine tests were not done until late in the series. Six of the seborrhoeic dermatitis group examined by smear and culture showed haemolytic staphylococcus aureus. Of six cases without any skin lesion that were examined, four were negative while one showed non-haemolytic streptococcus and one haemolytic staphylococcus aureus. Although the number is unfortunately small it would appear that the staphylococcus aureus is more prevalent in the conjunctival exudate of cases of kerato-conjunctivitis associated with skin lesions than in those not so associated. Indeed because of the near skin condition that is perhaps to be expected.

The use of penicillin drops (250 units per c.c. every 2 hours for 2 or 3 days) was tried in six cases all of whom showed haemolytic staphylococcus aureus. In three of them there were definite lessening of the patient's discomfort and the amount of discharge from the conjunctiva. It could not be established in any case that the progress of the corneal lesion was affected.

(11) *Non-recurrence*.—Although the period of observation in many cases is short there has been no recurrence in any of the cases of both groups. Not one of the cases, including all of those with skin lesions gave an ocular history in any way suggestive of a previous attack of kerato-conjunctivitis.

Discussion

As the ocular changes in the entire group with skin lesions were similar to those described above in the 18 cases with seborrhoeic dermatitis it may be said that the clinical ophthalmic appearances of the cases with associated lesions of the skin suggested very strongly that they were examples of epidemic virus kerato-conjunctivitis. However, there must be significance in the fact that lesions of the neighbouring skin anticipated or occurred coincidentally with the ocular lesions.

It would appear that lesions of the face and scalp especially those of a seborrhoeic nature may be conducive in some patients in some way to the development of a kerato-conjunctivitis identical with the virus kerato-conjunctivitis occurring in epidemic form, the growing literature on which has recently been fully summarised by Rados. The kerato-conjunctivitis in patients with lesions of the skin is, however, rather more intense as indicated by the greater number with bilateral involvement, adenopathy, and deep corneal spread as well as the slightly longer duration. The certain identity of the kerato-conjunctivitis of these skin cases with epidemic virus kerato-conjunctivitis would require the proof which animal and tissue culture experiments could demonstrate.

It is possible that the virus of epidemic kerato-conjunctivitis can possess dermatotropic qualities as do the viruses of herpes simplex and herpes zoster. In this case the lesions of the skin described in the above cases may be considered to be analogous to those found in the skin of patients suffering from herpes simplex and herpes zoster.

The presence of haemolytic staphylococcus in the conjunctiva of several of our cases with skin lesions probably represents an infection super-added, the organism here having a secondary rôle similar to that which it plays in the seborrhoeic infection. It is significant that the use of penicillin in several of our cases did not appear to have any influence on the corneal lesion although it diminished the muco-purulent discharge if present, as well as

the discomfort of the patient. The function of penicillin therapy in these cases would appear to be comparable to its action in the mixed infection complicating that other virus disease of the conjunctiva and cornea—trachoma.

Summary

(1) Thirty-three out of 66 cases of kerato-conjunctivitis seen in one year in the eye department of a general hospital in the Middle East had a concurrent affection of the skin.

(2) Eighteen of the 33 cases had a seborrhoeic dermatitis.

(3) In all cases with skin involvement the scalp or face was affected.

(4) There was a strong tendency for the skin and eye lesions to be ipsilateral.

(5) In the majority of the cases the onset of the skin lesion preceded that of the ocular one by a definite but short interval of time. The evidence in all the others was hearsay obtained from the patient which consisted of the statement that they "began at the same time."

(6) Detailed consideration of the clinical phenomena was made in, and a comparison established between, the 33 cases of epidemic virus kerato-conjunctivitis without skin lesion and the 18 cases with seborrhoeic dermatitis which were taken as an easily investigated sample of all the cases with skin lesions.

(7) This comparison suggests that the kerato-conjunctivitis in the cases with skin lesions was clinically indistinguishable from epidemic virus kerato-conjunctivitis.

(8) The presence of haemolytic staphylococcus aureus in several cases probably represented a mixed infection.

(9) An analogy has been suggested between the skin lesions present in some cases of epidemic kerato-conjunctivitis and those present in two other virus infections of the conjunctiva and cornea, herpes simplex and herpes zoster.

Conclusion

Lesions of the skin of the face or scalp especially those of a seborrhoeic nature are associated in some patients with kerato-conjunctivitis which, on clinical grounds, appears identical with that described as epidemic virus kerato-conjunctivitis. The possible analogous nature of the skin lesions in herpes simplex, herpes zoster and certain cases of epidemic kerato-conjunctivitis has been suggested though by no means proved.

We wish to express our indebtedness to Col. W. B. Stevenson, Commanding Officer of a General Hospital, and to Lt.-Col. G. I. Scott, Adviser in Ophthalmology, Middle East Forces, for their permission to publish this report.

REFERENCES

- FEIGENBAUM, A., MICHAELSON, I. C. and KORNBLUTH, W.—*Brit. Jl. Ophthal.*, Vol. XXIX, August, 1945.
 RADOS, A.—*Arch. Ophthal.*, Vol. XXXII, p. 308, October, 1944. (Review and full bibliography of epidemic kerato-conjunctivitis).
 SANYAL, S.—*Amer. Jl. Ophthal.*, Vol. XXVI, p. 390, 1933.
 VISWALINGAM, A.—*Brit. Jl. Ophthal.*, Vol. XXV, p. 313, 1941.

THE USE OF CRYSTALLINE PENICILLIN IN CORNEAL AND INTRA-OCULAR INFECTION*

BY

FRANK JULER and G. T. JOHNSON

ST. MARY'S HOSPITAL, LONDON, W.2

In a recent review of the literature concerning the use of penicillin in ophthalmology, Rycroft (1945) makes no mention of the direct application of the undissolved salt to the surface of the eyeball. Sorsby (1945) in a similar review does just mention the method, in referring to a paper by Juler and Young (1945) on infective corneal ulcer, but in a recent annotation in the *Brit. Med. Jl.* (1946) entitled "Penicillin in Ophthalmology" no mention is made of this procedure.

From practical clinical experience we feel that this method is worth emphasis, as affording the maximum concentration of the drug in relation to the infection itself.

The method was suggested to one of us (F. A. J.) by Professor Ida Mann (personal communication, February, 1944) who wrote as follows:—"In a small child with a large corneal abscess an incision was made and some crystals of penicillin were put into the cavity. This was repeated twice a day for three days and, although the cornea perforated it healed completely without synechiae and with a scar which was only slightly opaque."

In the report by Juler and Young (1945) the method was described after an extensive trial, chiefly in senile patients with severe corneal lesions.

In that series it was found that the instillation of drops on the cornea did not suffice in the more heavily infected cases, especially in persons of marked senility, and especially where hypopyon was

* Received for publication, February 11, 1946.