Brit. J. Ophthal. (1968) **52**, 659

ANTERIOR CORNEAL MOSAIC*†

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THE corneal anatomy has received intensive study in recent years, but an aspect of its structure which is readily observed clinically has received little attention in the literature.

In all normal corneae, after the instillation of fluorescein into the conjunctival sac, a striking mosaic pattern may be observed on the surface of the corneal epithelium after massage of the cornea through the lids. This pattern will be referred to as the anterior corneal mosaic. It was first observed by the author in patients whose eyes had been padded for corneal disease. It was noted in some that a mosaic pattern appeared after the instillation of fluorescein. This pattern disappeared in a short period of time, but could readily be re-induced by pressure on the cornea through the lids. It is the purpose of this paper to describe the characteristics of the anterior corneal mosaic and to discuss its significance. This pattern was studied by Fischer (1928), and has since been re-studied by Schweitzer (1967).

Methods

Induction of the Mosaic

A drop of 2 per cent. fluorescein is instilled into the conjunctival sac and the cornea is viewed with the cobalt beam of the slit lamp. If necessary the fluorescein is diluted to produce a bright fluorescence. A thumb is placed on the upper lid of the eye under examination and with the eye in the straight-ahead position, the lid is moved up and down over the cornea with light or moderate pressure applied to the globe.

A delicate mosaic pattern, traced out in the fluorescein of the tear film, appears immediately over the area of pressure application. By altering the point of application of pressure during massage of the cornea, the pattern may be made to appear over any area of the cornea, though the ease with which it appears varies from eye to eye.

In a proportion of patients, particularly those with soft eyes, the mosaic pattern may be seen without pressure over the lids.

Fluorescence Photography

This was carried out with a Pentax Spotmatic camera carried on an adjustable table (Photomont-Soper-Houston) which was attached to a Haag-Streit-900 slit lamp. The camera was arranged to be par-focal with the slit-lamp beam. With three standard extension rings a 1 : 1 magnification of the subject was achieved. A Prinz "Saturn" electronic flash was used on one side of the subject at the lens-subject distance. A Wratten 47B gelatin (Kodak) was placed as exciter filter over the flash unit. A Wratten 58 gelatin (Kodak) was placed as barrier filter over the lens of the camera. Final focusing adjustments were made by moving the camera fowards or backwards with the joy-stick of the slit lamp. Exposure was achieved using a cable shutter release. The film used throughout was Agfa Isopan Record which has an approximate A.S.A. rating of 1200. Development was for 2½ minutes in Ilford D19B. The camera aperture was f 2.0 throughout.

* Received for publication December 15, 1967.
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Some photographs in colour have been taken with a Praktica Camera using Kodachrome II film, and with the Zeiss Photo slit lamp using high speed Ektachrome-Daylight film.

Material

Over 500 normal corneae have been examined, and a study of diseased corneae has also been made.

Results

Normal Corneae

Appearance.—The pattern is seen as a mosaic of interconnecting fluorescent lines picked out on the surface of the corneal epithelium and forming a series of polygonal figures lying side by side. In many eyes an appearance of regularity is produced so that the pattern resembles a honeycomb (Fig. 1). In other eyes the polygons may be elongated in one direction so that the mosaic possesses a main axis which may be vertical (Fig. 2), oblique (Fig. 3), or more rarely horizontal.

There is variation in the size, shape, and number of sides of individual polygons in different areas of cornea. Nonetheless, the polygons may be of sufficiently similar size to differentiate a fine pattern in one cornea and a coarse pattern in another. The mosaic pattern is quite different in the two eyes of the same subject. The pattern may be induced over the whole cornea to a point just within the limbus, though in many it is more difficult to induce peripherally than centrally. There is marked variation in the ease with which the pattern can be induced in different corneae by the present method; in some it appears faint, in others brilliant. The pattern is seen whether fluorescein is instilled before or after massage of the cornea. The ease with which it is seen depends on the nature of the stain as well as on other factors. The pattern is poorly seen if rose Bengal is used or if the fluorescein is not fluorescing brilliantly.

The lines of the pattern are not due to staining of the epithelium with fluorescein. This is shown by the fact that if, after induction of the mosaic, the fluorescein is washed out the pattern disappears completely. However, if fluorescein is then replaced in the conjunctival sac, the pattern may be seen once more without further massage of the cornea. The pattern has been noted after the removal of corneal microlenses (Dixon, 1964; Ruben, 1967).

Incidence

The pattern has been induced in all normal corneae in over 500 eyes. It is seen in both sexes and in Caucasians and non-Caucasians. The youngest subject examined was 18 months and the oldest 85 years old.

Duration following induction

The time taken for the pattern to disappear after its induction over the whole cornea is variable. This has been studied in twenty eyes. In some eyes the pattern fades completely within a minute, but in a few it lasts over ten minutes. To some extent the duration is related to the ease of induction, so that the pattern is seen for longer in the eyes in which the mosaic is readily induced. Also it is possible to increase the duration of the pattern by repeated massage of the cornea and in some subjects blinking of the lids is sufficient to make the pattern remain longer.

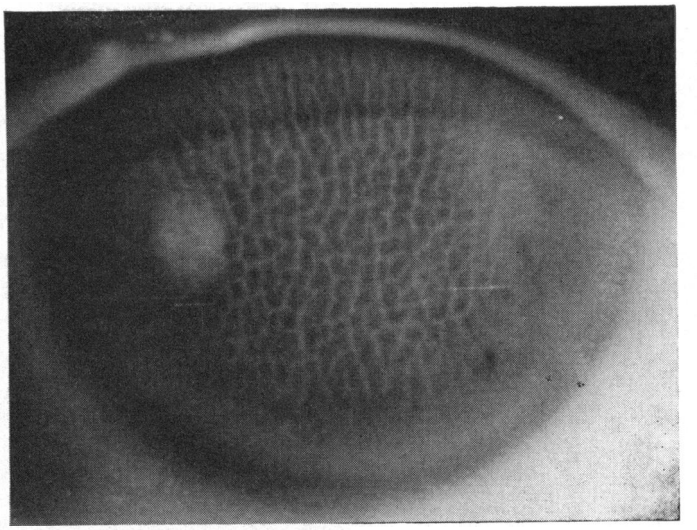

FIG. 1.—Anterior corneal mosaic. Normal eye showing honeycomb pattern.

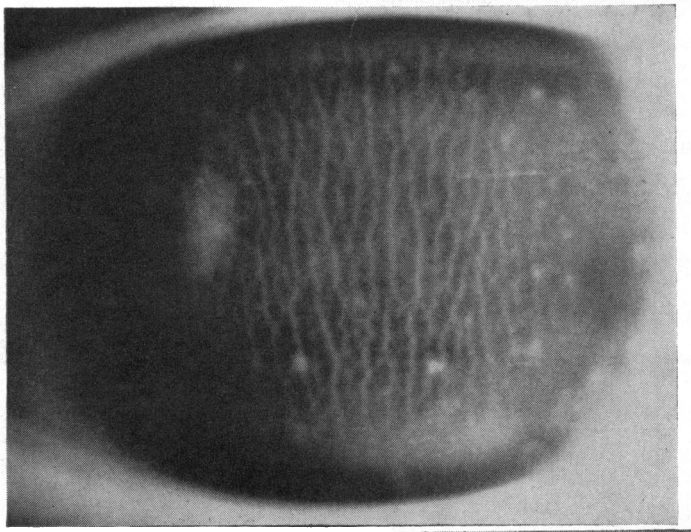

FIG. 2.—Anterior corneal mosaic. Normal eye showing vertical pattern.

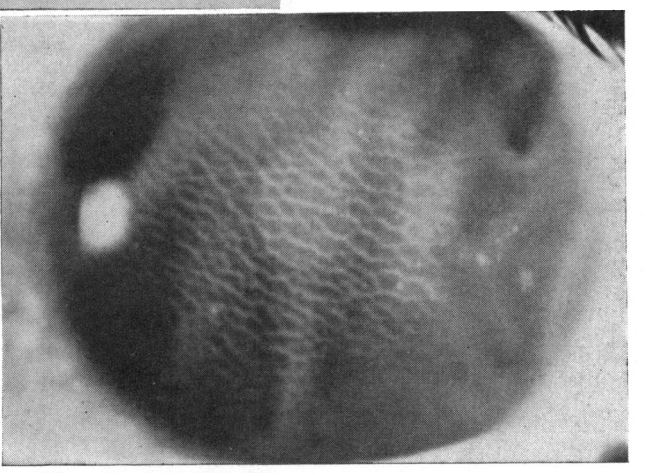

FIG. 3.—Anterior corneal mosaic. Normal eye showing oblique pattern.

Stability of the Mosaic

For this study the mosaic was induced in a cornea, photographed, and then allowed to fade completely. The mosaic was then re-induced after varying intervals and re-photographed. Comparison between the mosaics induced at different times was then made by projecting the patterns onto sheets of paper at the same magnification, and copying them. The copies could then be aligned one with the other and the exactness of registration assessed. Only small areas of cornea could be compared, mainly because of technical problems such as bubbles in the tear film, reflexes from the cornea, and slight differences in direction of gaze at different times. The intervals between photographs varied in different subjects. Ten corneae were studied.

It has been possible to show with the current technique that in a given cornea the mosaic pattern maintains its shape and dimensions after re-induction. This has been shown for periods ranging from 10 minutes to 8 weeks in different subjects (Table I).

Fig. 4 (opposite) shows the superimposed mosaics of the right eye of a 19-year-old girl, the second having been induced 2 months after the first. The correspondence of the two patterns is very exact except at a few points, and here the absence of a line from one photograph which is shown in another is readily explained by the difficulty in obtaining an even film of fluorescein at all times. Pools of fluorescein may frequently obscure portions of the pattern. For this reason, multiple photographs are always taken of each eye.

The mosaics have been found to be stable so far in ten eyes. This is taken by the author to imply that the mosaic reflects the presence of a structurally constant component of the superficial cornea. It remains to be seen from the results of more extensive studies whether the pattern represents a permanent "corneal-print" for each eye.

TABLE I

Subject No.	Sex	Age (yrs)	Eye	Time between Inductions of Anterior Corneal Mosaic
1	M	19	R	3 min.
2	F	65	R	8 min.
3	F	30	L	10 min.
4	F	67	R	15 min.
5	M	20	L	3 days
6	F	32	R	9 days
7	M	28	R	7 wks
			L	7 wks
8	F	19	R	8 wks 3 days
9	M	33	R	16 wks 2 days

TABLE II
CORNEAL DISORDERS STUDIED

Disorder	No. of Eyes
Corneal abrasion	10
Recurrent erosion	12
Linear abrasions and punctate erosions	14
Superficial corneal nebulae due to minor trauma	50
Penetrating grafts	8
Lamellar grafts	2
Healed full-thickness corneal laceration	1
Calcareous band degeneration	8
Vogt's crocodile shagreen	2
Irregularities of Bowman's membrane	16
Reis-Bücklers' corneal dystrophy	7
Total	130

Diseased Corneae

The effect of a number of disease processes on the mosaic has been studied. Table II shows the numbers of eyes studied in each disease category.

Corneal Oedema.—It is difficult to demonstrate the mosaic well in eyes showing gross epithelial corneal oedema. Also, the mosaic cannot be seen if the fluorescein is used over areas of corneal staining, because fluorescein staining is denser than the fluorescence of the mosaic.

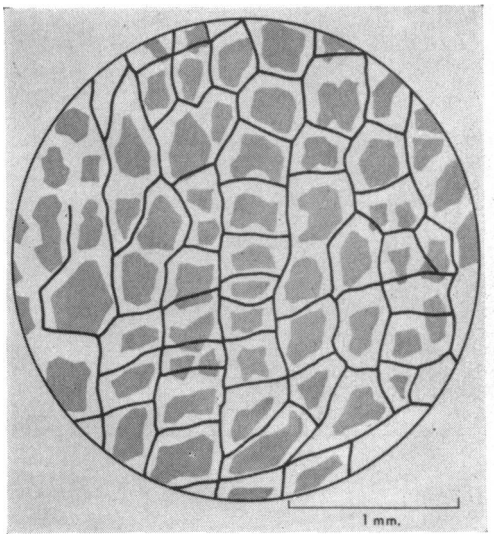

FIG. 4.—Superimposed tracings of a portion of the corneal mosaic of the right eye of a 19-year-old girl. First trace (broad pale lines) 2 months before second trace (narrow black lines).

Abrasions.—Study of corneal abrasions gives some idea of the depth of the structure responsible for the mosaic. After a simple corneal abrasion caused by physical or chemical trauma, the pattern may be induced up to the margin of the abrasion, but cannot be seen over the abrasion itself by the fluorescence method.

However, once the epithelium has healed over an abrasion and the site no longer stains, the mosaic pattern may be induced once again. It may be added that the mosaic over the healed abrasion site appears normal in configuration, does not stand out from the neighbouring pattern, and is contiguous with it.

Erosions.—Punctate epithelial erosions and linear epithelial stainings do not respect any boundaries represented by the mosaic pattern, but may run across it at any angle.

In a proportion of patients examined after the healing of recurrent erosions, no disturbance of the corneal mosaic has been found at the site of the previous erosions.

Trauma to the Superficial Stroma and Bowman's Membrane.—This has a different effect on the pattern. This is readily studied after the removal of small foreign bodies lying at the level of Bowman's membrane. It is found that the mosaic can no longer be induced over the nebulae left by such traumata. This is so even though the healed epithelium is smooth and the tear film uninterrupted.

The surrounding mosaic is often, but not always altered. When altered, the lines of the mosaic pattern are drawn in towards the centre of the nebula to form a stellate figure the centre of which is free of any mosaic pattern. It appears as though the structure which gives rise to the mosaic pattern has been involved in a scarring process (Fig. 5, overleaf).

A Full-thickness Corneal Wound.—Once healed, this may produce very little deviation of the neighbouring mosaic, though the pattern will be absent over the stromal scar. This is probably best exemplified by a penetrating corneal graft (Fig. 6, overleaf).

Band Keratopathy.—The effect of corneal nebulae on the pattern contrasts with that produced by calcareous band keratopathy. In band keratopathy too, it may be impossible to induce the pattern over the site of the lesion. But here, the pattern outside the band is

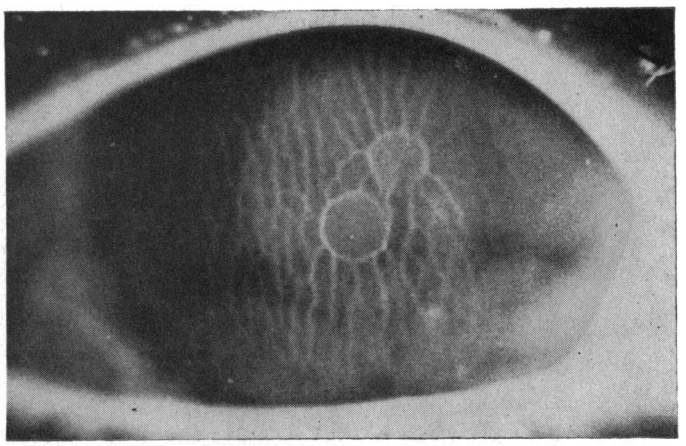

FIG. 5.—Effect of two superficial corneal nebulae on mosaic pattern. (see text).

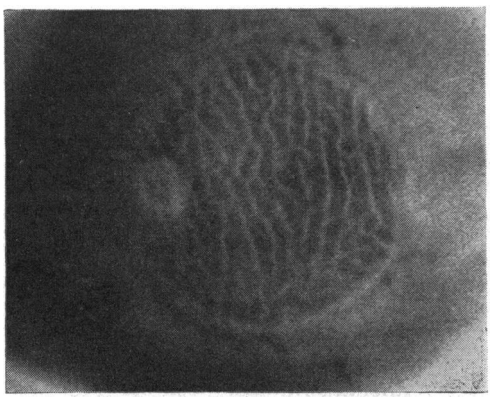

FIG. 6.—Corneal mosaic in a clear penetrating corneal graft carried out 11 years before. The pattern is lacking outside the graft.

unaffected. It is merely interrupted abruptly at the edge of the keratopathy. The obliteration of the mosaic over the band occurs in the presence of an apparently smooth and normal-looking epithelium. In some eyes only a portion of the pattern is lost.

Bowman's Membrane.—Induction of the mosaic pattern is also disturbed by another more delicate affection of Bowman's membrane. The condition of fingerprint lines and irregularities of Bowman's membrane (Kaufman and Clower, 1966) does not affect vision in its stationary form. The changes seen are so fine that even with the slit lamp they may often be noticed only by retro-illumination of the cornea or by examination by scleral scatter. Sixteen corneae with this condition have been examined. In one no mosaic could be induced. In another, the mosaic was represented by a few lines only. In three others portions of the mosaic were missing over the affected areas. In the remaining corneae, a normal pattern could be induced over the whole cornea, but the lines were less distinct than usual in all but two. The appearance was of particular interest in one eye in which only the central cornea was affected. Here it was found that a normal mosaic was induced outside the margin of the disordered Bowman's membrane, but only a few lines were induced over the diseased membrane itself.

Stroma.—Stromal disease in the absence of a primary affection of the epithelium may cause gross changes in the induced mosaic pattern. A cornea diffusely scarred by inter-

stitial keratitis and in which the epithelium is clinically healthy may yet show complete absence of the mosaic. Other cases of interstitial keratitis may show a partial loss of the pattern with gross distortion of the remaining mosaic. It can be noted that the pattern is seen only over areas of cornea showing the least stromal scarring. The same loss of pattern has been seen in the stromal scarring of keratoconus.

Grafts.—A clear corneal graft may show a perfectly normal mosaic pattern though the opaque host cornea shows no pattern (Fig. 6). A superficial stromal opacity in the graft alters or obliterates the mosaic over the affected cornea. The pattern may appear normal whether the graft was lamellar or penetrating, as long as the anterior cornea is clear, and even as long as 11 years after grafting.

Animal Corneae

Some pilot studies have been made on animal corneae. So far the pattern has not been observed in the rabbit, cat, or baboon. It has been observed in the monkey (cynomolgous). Both the monkey and baboon possess a Bowman's membrane.

Discussion

It is probable that the anterior corneal mosaic has been known to exist as an entoptic phenomenon for years. Bull (1894) referred to a pattern observed entoptically after applying pressure to the cornea through the lids. He spoke of "tigred" or "net-like" markings which he thought were due to a wrinkling of the corneal epithelium. He was able to induce the pattern with a glass rod also. His single drawing greatly resembles the mosaic described in this paper. He noted that the pattern remained unchanged from day to day.

Other authors have also observed patterns entoptically after corneal massage (Helmholtz, 1909; Esser, 1926; Duke-Elder, 1962) and have remarked on their constancy. Hirschberg (1901) described a "groove-pattern" in the cornea after rubbing through the lids and observing the cornea against the red reflex of the fundus. Stähli (1915) identified a mosaic pattern in the epithelium as a slit-lamp phenomenon, and thought that this was due to the epithelial cell borders. It was evidently a finer pattern than that described here. Vogt (1921) later regarded this pattern as due to corpuscular elements in the tear film. Fischer (1928) described the "groove pattern" in greater detail in an interesting monograph in which the pattern was recorded by the technique of reflectography. In this, the catoptric image of a light source was focused onto a photographic plate. This permitted accurate recording of subtle changes in the corneal surface. Both normal and diseased corneae were examined and the latter included corneal scars and erosions. This method has been improved by Schweitzer (1967) who has been able to photograph the pattern in fine detail. It is evidently the same pattern that is described here.

The anterior corneal mosaic is not merely an imprint of lid structures upon the corneal surface. The morphology of the mosaic is the same whichever direction the lids are moved over the cornea. Also, as has been noted, it may be induced by the pressure of a contact lens on the cornea.

The constant morphology of the pattern in a given eye suggests that it is due to a relatively fixed anatomical structure. Though to the author's knowledge no such structure is described in the literature, it is of interest to speculate upon its possible situation in the cornea.

In normal human corneae in the absence of fluorescein, the pattern induced by massage is not seen by focal illumination of the epithelium with white light even at a magnification of ×40. However, if the procedure is repeated using retro-illumination through the dilated pupil, a mosaic may be seen as a dark pattern against the red fundus reflex. This may be observed with the ophthalmoscope (Hirschberg, 1901; Cogan, 1951) or the slit lamp. It may readily be confirmed by the instillation of fluorescein that this pattern corresponds exactly to the anterior corneal mosaic. The pattern may be photographed with the Zeiss slit-lamp camera (Fig. 7). Cogan (1951) commented that the lines of the ophthalmoscopically observed pattern were " . . . apparently in the basal layer . . . " of the corneal epithelium.

It is evident, however, that some surface change must occur in the epithelium after massage. Otherwise the pattern would not be demonstrated by fluorescein. On the basis of his reflectographic studies, Fischer (1928) believed the pattern to lie in grooves on the corneal surface. Certainly such an appearance is seen if the tear film is observed after massage over the area of the catoptric image of the slit lamp bulb. This is seen best with the blue light of the slit lamp. With focal illumination of the epithelial surface the change is not seen.

An observation apparently conflicting with the above may be made with the applanation tonometer. In a proportion of applanated subjects a mosaic pattern may be seen over the applanated surface of the cornea within the half circles of the fluorescein meniscus. The distribution of fluorescein is the reverse of that seen after massage through the lids. The polygonal islands are found to be brightly fluorescent, while the intervals between them are non-fluorescent and dark. Such a pattern would be expected only if the epithelium were raised into ridges over the lines of the mosaic.

It can be shown that the applanation mosaic is the same as the anterior corneal mosaic. If a flat plate of glass is pressed against the cornea after the instillation of fluorescein, a brilliant mosaic pattern appears, identical to that seen during applanation (Fig. 8). However, when the slide is removed, the fluorescein runs into the centre of the previously

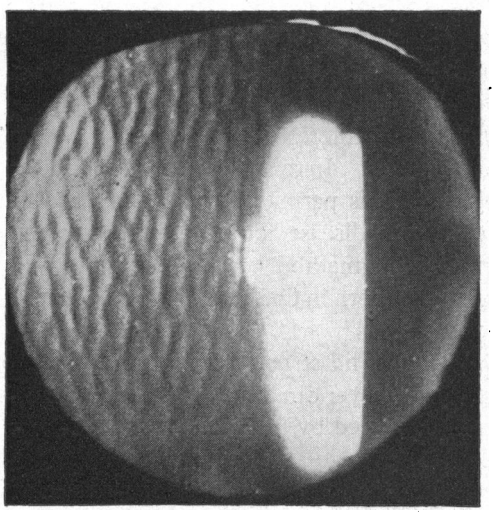

FIG. 7.—Retro-illumination of corneal mosaic seen against the fundus reflex in a normal eye. (Zeiss photo slit-lamp picture. Black and white copy of colour transparency).

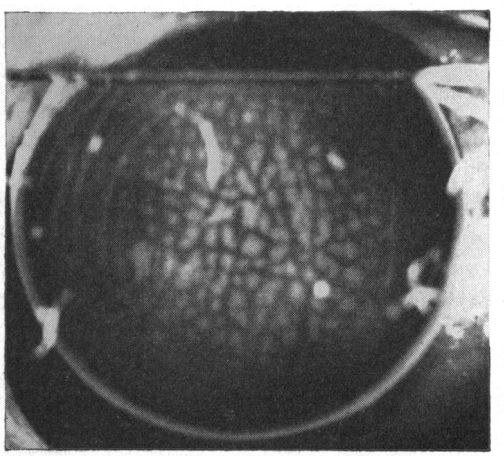

FIG. 8.—Mosaic corneal pattern seen during applanation of cornea with a glass slide. The eye is anaesthetized and fluorescein instilled, and the pattern is viewed with a blue light. (Zeiss photo slit-lamp picture. Black and white copy of colour transparency).

applanated cornea and the mosaic takes up the form seen after massage through the lids; that is, the lines are fluorescent and the islands less so. At this stage one can only speculate on the course of this reversal of appearances.

The occurrence of these epithelial phenomena after pressure on the cornea does not imply necessarily that the structure giving rise to them lies in the epithelium itself. Certain other possibilities exist. It is possible that a sub-epithelial structure could produce the same effects by reason of its attachments to the deep aspects of the epithelium. Such a hypothetical structure might lie in the basement membrane of the epithelium, in Bowman's membrane, or in other sub-epithelial structures such as nerve fibre networks or tissues connecting the epithelium to Bowman's membrane.

Certain of the observations made in diseased corneae support a sub-epithelial site for this structure.

The anterior corneal mosaic over a healed abrasion site can be seen with fluorescein as soon as the epithelium has ceased to stain. In fact the pattern is seen patchily while the epithelium is still taking stain. At this stage the new epithelium is only a few cells thick. This would imply that the mosaic structure lies at least in the deepest part of the epithelium. Also, the fresh pattern is similar to that of the neighbouring cornea with which it is contiguous. If the mosaic structures were in the epithelium this would imply a remarkable ability on the part of the re-surfacing epithelium growing in, to reproduce the general morphology of the previous mosaic pattern. It seems more reasonable to suppose that the epithelium is growing over a mosaic structure just deep to the epithelium. This is supported by observations in three subjects with large abrasions, in whom it was possible to induce a mosaic pattern in the base of the lesion visible by retro-illumination. These abrasions were still staining densely at this time so that it is clear that epithelialization was incomplete. However, in other abrasions, no definite mosaic pattern has been seen and in no instance has the pattern been induced on the first day of abrasion. An even stronger argument in favour of a sub-epithelial structure responsible for the mosaic pattern, is provided by the findings in corneal grafts. The pattern is present on a clear graft even when it is absent from the host cornea. Since the graft button is epithelialized with host epithelium within a few days of grafting and since the host shows no pattern itself, it is unlikely that the pattern seen is of host epithelial origin.

The effect of a corneal nebula on induction of the mosaic pattern is very different. If Bowman's membrane is affected, whether the cause be herpes, interstitial keratitis, keratoconus, or foreign bodies, the induced mosaic is absent or distorted over the site of the lesion. This contrasts with the failure of pure epithelial lesions to interfere with the subsequent induction of the mosaic. It provides indirect evidence suggesting that the mosaic arises in a subepithelial structure.

Further support for the concept is provided by observations in disorders of Bowman's membrane. The anterior mosaic may be completely absent over portions of a band-shaped dystrophy. It may be added that after removal of the band with versene the mosaic pattern remains absent despite re-growth of the epithelium. It might be argued in these cases that failure to induce the mosaic over the lesion is due to secondary epithelial changes. However, the anterior corneal mosaic may also be absent over irregularities of Bowman's membrane (Kaufman and Clower, 1967) in which, in the forms examined in this study, secondary epithelial changes would be less likely. The absence of the mosaic could be due to the absence of a structure in or related to, Bowman's membrane. In keeping with the

above findings, the pattern was found to be absent in the eyes of two patients with Reis-Bücklers' corneal dystrophy, and difficult to induce in the eyes of two other patients so affected. Reis-Bücklers' corneal dystrophy is predominantly an affection of Bowman's membrane though marked epithelial changes do occur.

The observations quoted above may imply a subepithelial origin for the structure giving rise to the mosaic pattern. But it cannot be excluded that the structures lie in the deepest part of the epithelium. The point must await histological study. It would be of great interest to know whether the mosaic pattern over a healed abrasion is identical to that present before the abrasion. The opportunity for confirming such a possibility must be infrequent in clinical practice, but it may be provided by a long-term follow-up in patients with recurrent erosions. The monkey cornea may provide an appropriate model system for animal experiments along these lines. This paper is devoted mainly to the normal anterior corneal mosaic and to alterations known to be produced in it by disease. However, other mosaic patterns have been described in diseased cornea, and it will be of interest to discuss these briefly in relation to the present study.

Vogt (1921) described in his slit-lamp atlas a senile form of mosaic degeneration occurring in both corneae of an 80-year-old man. This anterior crocodile shagreen is made up of polygonal, grey opacities in the axial region of Bowman's membrane. The drawings are very similar in appearance to the patterns made by the anterior corneal mosaic. Juvenile, hereditary, and post-traumatic forms of this condition are described (Duke-Elder and Leigh, 1965). Vogt (1921b) also described a polygonal pattern developing in herpetic scars, certain corneal dystrophies, and in band keratopathy, giving a honeycomb appearance to the lesion. It is tempting to suggest that these patterns arise on the basis of the structure responsible for the normal anterior corneal mosaic. This is strongly supported by the observation of an exact correspondence between the fluorescent mosaic pattern and the pattern in both eyes of one patient with anterior crocodile shagreen and in three eyes showing the peripheral form of the disorder.

The condition of keratoconus and its effect on the mosaic pattern is still being studied, but one interesting observation may be noted here. In one patient with marked keratoconus, a reticular opacity was seen near the base of the cone infero-nasally in each eye. When the fluorescein mosaic pattern was induced, it could be seen that the part of the mosaic overlying the opacities corresponded exactly in position and form to the opacities themselves, which were just subepithelial.

Until the anatomical basis for the mosaic is known, it is impossible to speculate on its physiological significance. It may be hoped that further study will yield this information, and perhaps shed some light on the natural history of certain obscure progressive corneal disorders such as keratoconus and band keratopathy.

Summary

A mosaic pattern may be induced in normal corneae by pressure through the lids. The term anterior corneal mosaic has been used to describe this, and embraces both a groove pattern seen on the surface of the epithelium and the same pattern seen deeper in the epithelium by retro-illumination. Photographic study shows that the pattern is constant in a given eye up to a period of months. The alteration of the pattern by a variety of corneal disorders has been studied. These include abrasions, recurrent erosions, corneal

nebulae, band keratopathy, fingerprint lines and irregularities in Bowman's membrane, keratoconus, and interstitial keratitis. From such observations it is suggested that the pattern arises in a structure just deep to the epithelium or in the basal layers of the epithelium itself. In pilot studies a similar mosaic pattern has been seen in the cynomolgous monkey but not in the baboon, cat, or rabbit. The relationship between the anterior corneal mosaic and certain mosaic corneal disorders is discussed.

I am indebted to the Surgeons of Moorfields Eye Hospital for free access to their patients and to Mr. C. M. Ruben and Dr. P. Hansell for advice and encouragement.

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