COMMUNICATIONS

A CONTRIBUTION TO THE PATHOLOGY OF BOWMAN'S MEMBRANE *

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THE function of the ocular glass membranes is not fully under-stood. The two elastic membranes, Descemet's and Bruch's, may contribute to the firmness of the globe and counterbalance the vary-ing intra-ocular pressure. Besides this essential function they may control the metabolism of tissues linked with them. The cornea, lens, and retina demand a very constant constitution of the lymph-stream. These glass membranes may fulfil a special filter function. It may be that observation of pathological changes of these struc-tures may contribute to the knowledge of their function.

Thirty years ago Ernst Fuchs (*Arch. f. Ophthal.*, Vol. LXXXIX, p. 337) described a case of familial corneal dystrophy, in which Bowman's membrane divided the corneal incrustations into two layers. That in front of Bowman's membrane was acido-(eosino) phil, the granules posterior to Bowman's membrane being Giemsa blue and basophil. The acidophil substance was flat and structureless, while the blueish basophil granules of varying size and shape were prised between the corneal lamellae (Loewenstein, *Amer. Jl. Ophthal.*, Vol. XXIII, p. 1,229, 1940). The two kinds of

incrustation are separated according to their pH concentration by a membrane. This is an unusual occurrence in histological studies. Another peculiarity of the ocular glass membranes is the fact that they undergo a change due to age, for example, the appearance of Henle's warts, drusen of Bruch's membrane and the fatty impairment of Bowman's membrane in arcus senilis. Wear and tear of life seems to damage glass membranes at an earlier term than the surrounding tissues. A metabolism inferior to that of vascularised tissues is likely in glass membranes.

I.—Band-shaped corneal degeneration

Metabolic changes in the eye may lead to the gross change in Bowman's membrane known as band-shaped corneal degeneration. Physical and chemical conditions basic to this condition are unknown.

The specimen which we wish to discuss was sent by Dr. Magnus of York. A married woman, aged 67 years, suffered from uveitis for several years. There was no history of infantile rheumatism. General investigations were negative except for a strongly positive Mantoux reaction. A course of tuberculin treatment was given. In 1942 a bilateral iridectomy was carried out. Broad prominent band-shaped incrustations with numerous tears and clefts were removed from the left eye in January, 1945. They had the appearance of broken ice. A conjunctival bridge flap was used to cover the defect. A similar procedure was carried out in the right eye without a conjunctival flap. Both eyes settled down without reaction. Vision R. and L. 6/60. Three pieces of the specimen were sent to me; two were embedded in paraffin and the third in gelatine. Fat staining proved to be negative. The paraffin slides were stained with haematoxylin and eosin, van Gieson, Mallory, Masson and von Kossa (for lime).

In front of Bowman's membrane there was eosin-staining tissue which appeared to be whorled. The eosined mass was loose in some areas and compact with empty holes at others. Where the epithelium had gone, the acidophil mass covered the front of Bowman's membrane (Fig. 1) and was three or four times the normal thickness of epithelium. The red areas were the shape of onion peelings lying between preserved corneal epithelium (Fig. 2). At some places the acidophil mass was poised as a flat structureless smooth layer in front of Bowman's membrane (Fig. 3) and was reminiscent of the findings in familial corneal dystrophy. There was an indistinct, slightly red mass with few nuclei at some places subepithelially (Fig. 1), at others a connective tissue was found (Fig. 4) not unlike that found in old degenerative pannus. Bowman's membrane was calcified throughout the whole specimen.

No gas bubbles arose on adding 50 per cent. HCl, but the substance of Bowman's membrane was melted away to a considerable extent. Von Kossa's reaction was strongly positive and therefore a Ca compound was present; this may have been calcium phosphate (Fig. 5).

Not all the granules in Bowman's membrane and the neighbouring lamellae were brownish black with von Kossa's reagent as some granules appeared safranin red. We may conclude that calcification is a later stage of the regressive process. The safranin stained granules may be a protein precipitate, a possible forerunner of calcification. Bowman's membrane appeared equally granular and stained a dark purple with haematoxylin; at other places it was split into thin platelets like mica (Fig. 6). The anterior lamellae were the thickest and darkest. Elsewhere the whole thickness of Bowman's membrane was broken into smaller fragments. The preserved epithelium grew between the gaps into the corneal lamellae (Fig. 1). The unequal distribution of lime was shown at other places by very small and patchlike purple staining.

Splitting of Bowman's membrane in parallel platelets was due to pathological changes, and it is likely that we have to deal with a peculiarity which is based on a preformed physiological structure. According to Salzmann, Eisler, Wolff and others, there is no structure recognisable in Bowman's membrane. Its fibrils are supposed to be closely interwoven. Nevertheless the appearance of mica-like regular platelets in the calcified tissue is hard to explain otherwise than by physiological preformation. Bruch's membrane for instance appears in routine examination as an entity, but is split pathologically or can be split by special histological methods. In cases of lipoid infiltration Descemet's membrane is affected only in its anterior third (Loewenstein, *Trans. Ophthal. Soc., U.K.,* Vol. LXII, p. 159, 1942), the posterior two-thirds being fat free.

How can one explain the establishment of lime incrustation in Bowman's membrane with a scattering in the superficial lamellae? Fischer (*Arch. f. Augenheilk.,* Vol. CII, p. 146, 1929) has shown that cornea with preserved epithelium and endothelium is permeable to water from the conjunctival side. Oxygen can diffuse through the cornea towards the aqueous and CO_2 only outwards towards the air. It seems that a certain equilibrium of gas metabolism is necessary to keep Bowman's membrane intact. We know that calcium phosphate is precipitated if the pH concentration of the tissue fluid changes from the acid to the alkaline side. That may happen when CO_2 escapes. As the fibrils of Bowman's membrane are very closely interwoven, a minor exchange of fluid is more probable than in the looser tissue of the parenchyma, where lymph circulates under better conditions. We may assume that a

reduced metabolism leads to alkalosis of the corneal tissue. Calcium phosphate is precipitated from the corneal tissue fluid in the part of the cornea which has the slowest metabolism—that is in Bowman's membrane. It may be that the direction of the fluid stream causes the deposit in Bowman's membrane and not in Descemet's membrane.

It is easily understood that permeability of Bowman's membrane suffers by calcification and the fluid stream from the epithelial side towards the anterior chamber is impeded thus explaining precipitation in front of Bowman's membrane. We cannot offer an explanation why those precipitates are eosinophil. It is not blood which produces the acidophil mass, for in slides stained with Mallory or Masson, red blood corpuscles appear orange while the acidophil areas are an intensive red. The appearance of this difference in front and behind the frontal layer of Bowman's membrane in familial corneal dystrophy and in band-shaped corneal degeneration is remarkable.

We would expect the calcified Bowman's membrane to lose its elasticity, to break up in many places, and the epithelium might grow into the corneal lamellae. We conclude from the histological appearance that the abnormal position of the calcified broken ends is bound to create a chronic irritation. Improvement is possible by operative removal of the prominent sharp edges.

The question of lime precipitation in the cornea was discussed by Axenfeld, in his last paper : Dystrophies of the corneal parenchyma (*Klin. Monatsbl. f. Augenheilk.*, Vol. LXXXV, p. 493, 1930). The primary disease, according to Axenfeld, is located within the cement substance between the corneal lamellae. This substance may be impregnated with lipoidal bodies as in fatty, symmetrical, primary corneal dystrophy, or in corneal arcus lipoides. It may be an impregnation with hyaline or mucinous material or finally with lime, each of these substances causing a different kind of corneal dystrophy.

Axenfeld considers that light may produce precipitation of lime salts in the cornea. This idea may be especially productive in the explanation of the establishment of calcium salts in Bowman's membrane in cases of band-shaped corneal degeneration, as they are restricted to the part of the cornea, almost always, exposed to air and light. It is more than likely that a slowed down corneal metabolism, as it might occur, and is supposed to occur, in chronic iridocyclitis, may be prone to be influenced by light rays.

Finally I want to mention that I have observed two cases of young girls (aged 8 and 10 years) with chronic uveitis of both eyes and rheumatic affections of the lower extremities. Both showed a well developed icy band-shaped corneal degeneration in each eye. In spite of the softness of the painless unirritated eyes the vision

was still 6/36 and 6/24 respectively. Calcium was not increased in the blood. The band-shaped corneal degeneration in the lid fissure is assumed in these cases to be due to local metabolic deterioration. The influence of light may have facilitated the establishment of the precipitates in Bowman's membrane. Calcium opacities in Axenfeld's case of calcareous corneal dystrophy were influenced favourably by dense light filters worn for a long time (dark auto-goggles). It is worth while to try a similar therapy in those cases of calcareous deposits in Bowman's membrane. It might be tried in other cases of corneal dystrophies as well, as a similar modus of precipitation may come into consideration.

Our speculation is that there is a slowing down of the corneal metabolism in band-shaped corneal dystrophy which leads to alkalosis. Calcium phosphate is precipitated in Bowman's membrane. The calcified Bowman's membrane is a barrier to the transfer of fluid from the epithelium through the corneal tissue. Thus an eosinophil mass is established in front of Bowman's membrane. These greyish white masses are responsible for the broken ice appearance of band-shaped corneal degeneration. Calcified Bowman's membrane loses its elasticity and breaks up under the stress of wear and tear.

II.—Bowman's membrane in glaucomatous eyes

If this idea is correct, we may expect changes in Bowman's membrane whenever corneal metabolism is damaged by increased intraocular pressure. It is really astonishing that such a frequent appearance as the hemispherical bodies in Bowman's membrane in glaucomatous eyes were overlooked before E. von Hippel (Cornea in Wessely's Pathology of the Eye, Vol. 1, p. 322, Springer, 1928) described them without giving an explanation. E. Wolff and Lyle (Proc. Roy. Soc. Med., Vol. VI, p. 701, 1982 and Talbot, Brit. Jl. Ophthal., Vol. XXII, p. 210, 1938) have confirmed their presence in glaucoma cases. We have seen these bodies very frequently (Fig. 7) in cases of primary and secondary glaucoma and also in hydrophthalmos. Garrow and Loewenstein (Brit. Jl. Ophthal., Vol. XXV, p. 514, 1941) infer that they are an indication of disordered corneal metabolism in glaucomatous eyes.

The fluid stream towards the anterior chamber reaches the rigid scaffolding of the globe after passing the loose epithelial covering. We assume that an obstacle is created by the increased intra-ocular pressure and precipitation occurs where the fluid stream is checked, that is, at the outer, the epithelial side of Bowman's membrane, where the hemispherical bodies are found exclusively. The presence of hemispherical bodies has nothing to do with the cause of primary glaucoma, but is a corollary only of the increased intra-ocular pressure. It is found in different kinds of secondary glaucoma.

III.—Concretion in Bowman's membrane in a case of hypertensive retinopathy

.   We have found another kind of precipitation in Bowman's membrane in both eyes of a patient with hypertensive retinopathy, undescribed so far. .These precipitates were discovered in the periphery whereas the glaucomatous hemispherical bodies show no predilection for any part of the cornea. This second type were not round, but ragged (Fig. 8) and many were polyhedric (Fig. 9). They are bigger and extend throughout a whole thickness of Bowman's membrane. Some of them find a continuation in the superficial corneal lamellae. Similar concretions were present in the basal layers of the epithelium of the sclera and in the fibres of the episcleral tissue (Fig. 10). We have not found any description of this kind of concretion so far. Elschnig's drusen of Bowman's membrane (*Klin. Monatsb. f. Augenheilk.*, Vol. XXXIII, p. 453, 1899) and Loewenstein's colloid droplets in the anterior corneal lamellae (*Klin. Monatsb. f. Augenheilk.*, Vol. L, p. 513, 1912) are different in appearance. This observation seems to prove that senile changes and other regressive processes linked with hypertensive retinopathy might create another disturbance of corneal metabolism which differs from that seen in glaucoma.

IV.—Bowman's membrane in a case of late changes of mustard gas injury of the eye

It may be that the corneal metabolism suffers by direct chemical damage and that this may happen in a clinically normal or nearly normal cornea. We know for instance that the cornea can recover more or less completely after a mustard gas injury. A breakdown of corneal tissue may occur many years after. I. Mann and B. D. Pullinger (*Proc. Roy. Soc. Med.,* Vol. XXXV, p. 229, 1942) have shown experimentally in rabbits that a lipoid change precedes the corneal breakdown. We do not want to go into details of the clinical or histological side of mustard gas poisoning but mention briefly the histological appearance of a late stage of corneal changes 27 years after the gas injury, as these changes fit well into our material and conclusions.

There was no clinical similarity between this case of greyish patchy opacities and a band-shaped corneal degeneration. We found in slides of the excised corneal opacity that Bowman's membrane (Fig. 11) was full of lime granules which were spread in a loose distribution in the anterior corneal lamellae. There was a whorled mass (Fig. 12) in front of Bowman's membrane which showed eosinophil staining and suggested the changes in band-shaped corneal degeneration described above. A calcified Bowman's membrane is fractured at many places. Calcification of Bow-

man's membrane in our case is a late sequel to mustard gas poisoning and may occur without corneal breakdown. We assume that the corneal damage by mustard gas poisoning may have been due to the pericorneal injury. Damage of pericorneal vessels is described in many fresh cases of mustard gas poisoning. There may have been a certain equilibrium achieved by corneal fluid exchange in spite of the reduced metabolism which may suffice to preserve corneal translucency. A slight slowing of the corneal metabolism creates the mechanism suggested above as the basic cause of calcification of Bowman's membrane and the secondary establishment of an eosinophil substance in front of the calcified Bowman's membrane. The nature of this process is necessarily progressive which is in accordance with clinical experience.

Conclusion

1. Precipitation of lime in Bowman's membrane in the form of calcium phosphate may be due to a slowing down of corneal metabolism. CO_2 escapes, alkalosis sets in and calcium phosphate is condensed in the tissue with the slowest metabolism which is Bowman's membrane. The influence of light in this process of precipitation is likely.

2. Calcified Bowman's membrane is an obstacle to the normal fluid exchange from epithelium to the anterior chamber. Its sequel is the establishment of an amorphous eosinophil substance in front of Bowman's membrane which was found in a case of band-shaped corneal degeneration and in a late, progressive case of macular corneal opacities after mustard gas poisoning.

3. Increased intra-ocular pressure may be a further obstacle to the entrance of fluid into the inner eye. The frequency of hemispherical bodies in Bowman's membrane in cases of primary and secondary glaucoma may be due to the precipitation at this border zone.

4. A case of arterial hypertension is described in which another form of purple staining concretions was present in Bowman's membrane and also in the superficial scleral layers. The precipitation may be a general metabolic deterioration of the ocular walls.