# THE HISTOLOGY OF IATROGENIC KERATITIS BULLOSA

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ABSTRACT

Histological examination can differentiate between Fuchs' dystrophy of the cornea and the bullous keratopathy which occurs after cataract extraction, with or without the implantation of an artificial lens. The differences are apparent in Descemet's membrane and the endothelium. In 89% of cases there was agreement between the histological and the clinical diagnosis.

## INTRODUCTION

Between 1977 and 1979 perforating keratoplasty was performed on 65 patients on account of a Fuchs' keratitis bullosa following cataract extraction with or without the implantation of an artficial lens. A histological study was performed on the resemblances and differences between Fuchs' corneal dystrophy and the iatrogenic keratitis bullosa. On the basis of the findings two lists of anomalies were compiled and the material was reexamined, this time without knowledge of the clinical history. The characteristic differences are mainly to be found in Descemet's membrane and endothelium. In 89% of cases the histological diagnosis was in agreement with the case history.

## MATERIAL

Of the 65 patients, on whom keratoplasty was performed for keratitis bullosa, 17 had clinically a primary Fuchs' corneal dystrophy, 18 had keratitis bullosa following cataract extraction and 30 had keratitis bullosa following cataract extraction and the implantation of various types of intraocular lenses.

## METHOD

The corneal discs, trephined during the keratoplasty, were fixed in 10% neutral buffered formalin, laminated and embedded in paraffin, and routine 5$\mu$ microscopical sections were made. This work was carried out in the Pa-

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Fig. 1. Epithelium in keratitis bullosa following lens implantation: irregular structure, intracellular oedema (arrows), intra-epithelial bulla (b). Bowman's membrane (between broad arrows) is intact. Stroma (s) more or less normal. HE.


Fig. 2. Epithelium in Fuchs' dystrophy: irregular structure, intracellular oedema (arrows). Bowman's membrane (between broad arrows) intact. Stroma (s) scanty keratocytes. HE.

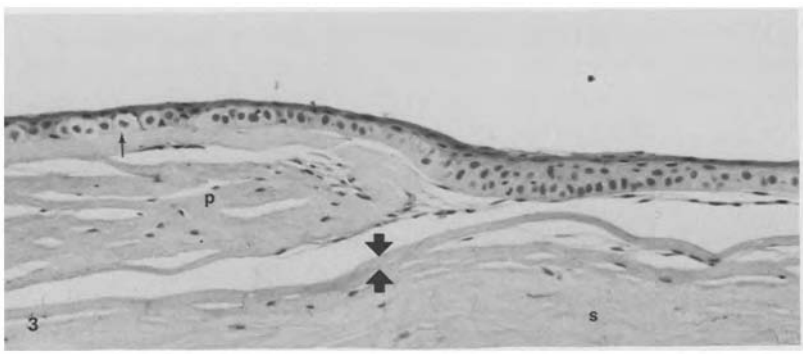


Fig. 3. Prolonged keratitis bullosa following cataract extraction: irregular epithelial structure, intracellular oedema (arrows), pannus (p), s= stroma. Bowman's membrane (between broad arrows) intact. HE.

thology Department of the State University in Leiden. The sections were stained with haematoxylin and eosin (H.E.) and in a few cases with the periodic acid-Schiff stain (P.A.S.) When the sections were examined attention was paid to the criteria drawn up in the following 2 tables.

Table 1. Fuchs' corneal dystrophy.

| | |
|---|---|
| epithelium | – irregular structure |
| | – thin |
| | – intracellular oedema |
| | – bullae |
| | – subepithelial connective tissue (= pannus) |
| Bowman's membrane | – intact |
| stroma | – few nuclei |
| | – irregular thickness of fibres |
| Descemet's membrane | – wart-like excrescences |
| endothelium | – scanty |
| | – between the warts |
| | – flattened |
| | – intracellular pigment |

Table 2. Corneal dystrophy following intraocular operations.

| | |
|---|---|
| epithelium | – irregular structure |
| | – thin |
| | – intracellular oedema |
| | – bullae |
| | – subepithelial connective tissue (= pannus) |
| Bowman's membrane | – intact |
| stroma | – few nuclei |
| | – irregular thickness of fibres |
| Descemet's membrane | – puckered |
| | – smooth or slightly wavy |
| | – double |
| endothelium | – scant and atrophic or absent |
| | – intracellular pigment |
| | – proliferation retrocorneal membrane |

When the histological diagnosis had been made it was compared with the clinical history and the description of the clinical picture.

Table 3. Clinical picture compared with histological diagnosis.

| | Clinical | Diagnosis correct | Diagnosis incorrect |
|---|---|---|---|
| Fuchs' dystrophy | 17 | 15 (88%) | 2 (12%) |
| Intraocular surgery | 48 | 43 (90%) | 5 (10%) |
| Total | 65 (100%) | 58 (89%) | 7 (11%) |

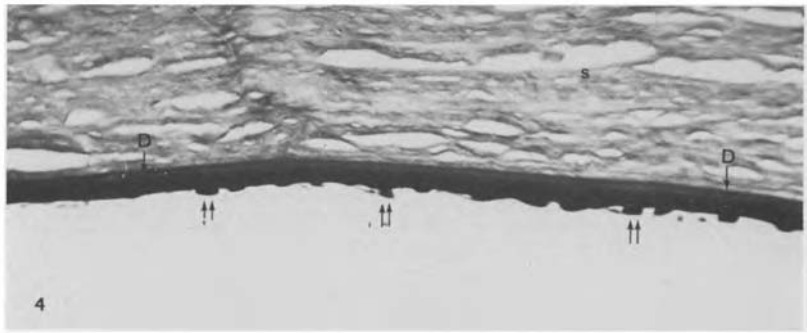


Fig. 4. Fuchs' corneal dystrophy. Characteristic wart-like excrescences (double arrows) on Descemet's membrane (D). PAS.

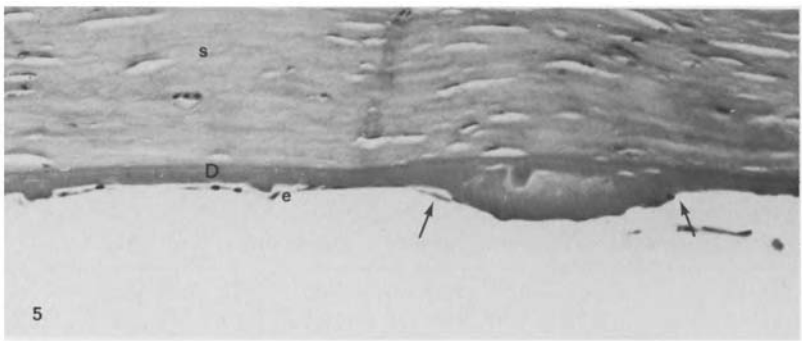


Fig. 5. Fuchs' corneal dystrophy. Confluent wart-like excrescences (between arrows) on Descemet's membrane (D) in the centre of the cornea. Endothelium (e) scanty and atrophic. HE.

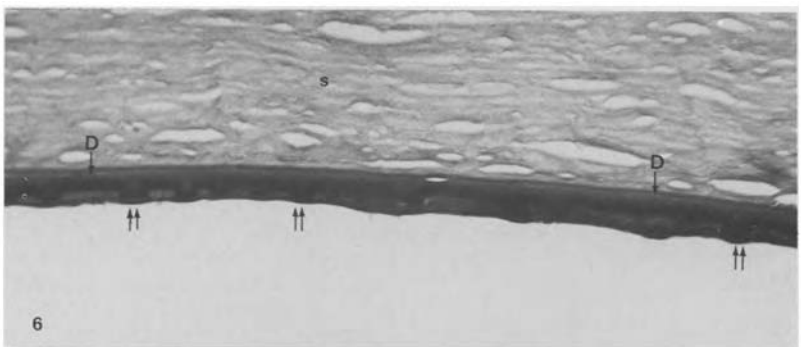


Fig. 6. Fuchs' corneal dystrophy. Greatly thickened Descemet's membrane (D). The wart-like excrescences (double arrows) can be seen as shadows. PAS.

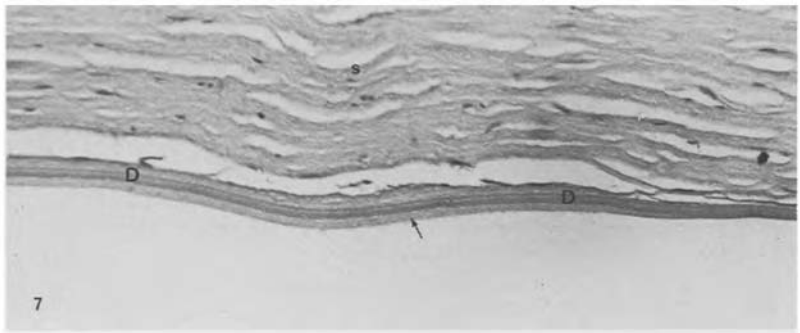


Fig. 7. Cornea after lens implantation. The original Descemet's membrane (D) is covered with a layer which is nearly as thick (arrow). HE.

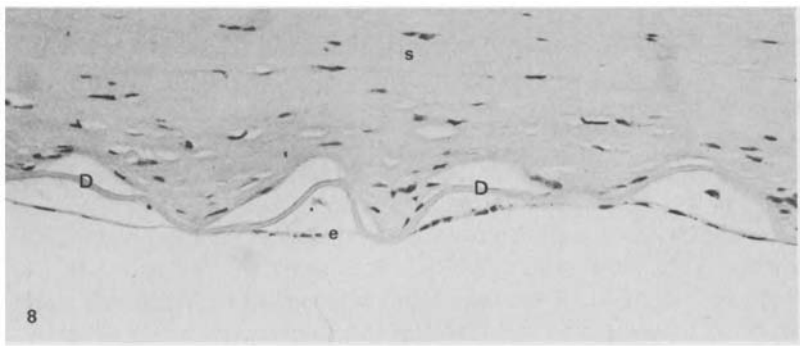


Fig. 8. Cornea after lens implantation: folds in Descemet's membrane (D), atrophic endothelial cells (e) with pigment. HE.

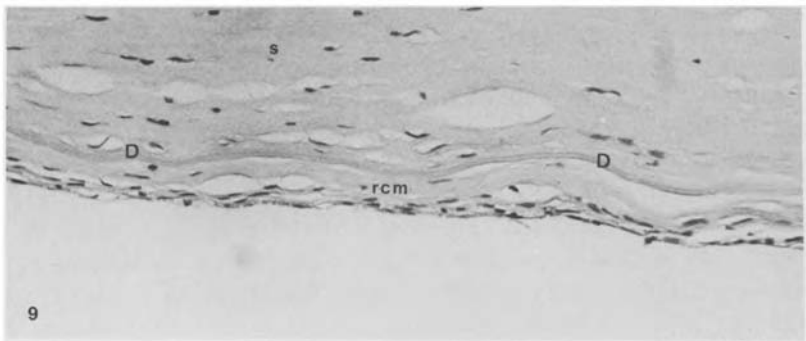


Fig. 9. Cornea after cataract extraction: on Descemet's membrane (D) a retrocorneal membrane (rem) has formed. HE.

## RESULTS

In 15 (88%) of the 17 cases it was possible to recognize Fuchs' corneal dystrophy. In 14 (78%) of the 18 cases iatrogenic dystrophy following cataract extraction was diagnosed. In 29 (97%) of the 30 cases iatrogenic dystrophy following lens implantation was found (see Table 3).

Table 4. Bullous keratopathy following intraocular surgery.

| Clinical picture compared with histological diagnosis. | | |
|---|---|---|
| Clinical – cataract extraction | 18 | |
| – lens implantation | 30 | |
| total iatrogenic | 48 | |
| histologically in complete agreement with Table 2 | | 34 |
| guttata picture also present, but combination recognizable | | 14 |

The diagnosis was incorrectly made in 2 cases of Fuchs' dystrophy, in which Descemet's membrane was very thick and the characteristic wart-like structures had disappeared through confluence and filling of the intermediate clefts with Descemet material (Fig. 6); the endothelial cells in these cases were very scarce.

The incorrect diagnosis in the cases of iatrogenic keratitis bullosa were due to the fact that wart-like excrescences on Descemet's membrane were present and it was not clear histologically that this was a combination of two pictures. In those cases in which this combination was present the simultaneous occurrence of the two groups of anomalies of Descemet's membrane could be recognized in 7 (50%) of the 14 cases (see Table 4). It was not possible to ascertain whether the guttata condition of the cornea had been present before the operation.

## DISCUSSION

Fuchs' dystrophy, also called epithelial-endothelial dystrophy of the cornea, is a tendency, which may be hereditary (Krachmer et al., 1978), for the endothelium to show functional regression with age; the characteristic picture of cornea guttata then develops. This picture can be seen on slit-lamp examination and with the specular microscope (Kaufman et al., 1966).

When some critical point has been passed, corneal oedema, dystrophy of the epithelium and bulla formation occur. The condition is mainly seen in people above the age of 50 years and rather more frequently in women than in men.

Studies with the specular micrsocope (e.g., Kaufman & Katz, 1977), scanning electron microscope (Sugar et al., 1978) and animal experiments (Katz

et al., 1977; Völker-Dieben, 1979) have shown that the endothelium can be damaged during cataract extractions and intraocular lens implantations and that the number of endothelial cells decreases. The resulting functional insufficiency is only in a limited number of cases so great that the clinical picture of keratitis bullosa, which is the same as that of Fuchs' dystrophy, can develop. Jaffe (1975) reports that 5.5% of the 450.000 cataract extractions per year in the U.S.A. are followed by corneal dystrophy. Nordlohne (1975) reports 9.2% corneal lesions, of which half are corneal dystrophy following intraocular lens implantation. So far only a few publications have been made on the histology of corneal dystrophy following intraocular surgery, and usually only a few cases are described (Arentsen et al., 1977). The light-microscopical findings, however, are similar to those in our material. The extensive study by Chi et al. (1962) covers primary Fuchs' dystrophy, but the findings are not compared with keratitis bullosa following intraocular surgery.

Snip et al. (1975) give a histological description of 8 cases in which a retrocorneal membrane formed on contact between the vitreous and the cornea. A guttata picture is not found and endothelial cells are absent.

The findings in this iatrogenic corneal dystrophy demonstrate a final state of the processes occurring during and after surgery. Clinical particulars of the situation during cataract extraction and the lens implantation are usually absent in our material because the patients were only referred to us when keratoplasty was indicated. The cornea was sometimes so opaque that it was impossible to determine whether there was contact between vitreous in the anterior chamber and the cornea in the case of intracapsular lens extraction, or between the intraocular lens, a foot of the lens or the iris suture, and the cornea in the case of an intraocular lens.

In a few cases the artificial lens had dislocated – in which case contact had certainly taken place – and operative repositioning had been necessary. Katz et al. (1977) described severe damage to the endothelium from contact between methacrylate lenses and the corneal endothelium. In many cases the iatrogenic keratitis bullosa occurred bilaterally.

As the group of patients becomes larger it may become possible to say which factors tip the balance in the direction of keratitis bullosa. The time interval between the intraocular surgery and the corneal dystrophy must be noted, and whether there are differences in this interval dependent on whether or not a lens is implanted, as suggested by Kaufman (1977).

In those cases in which histology showed the typical Descemet warts together with the endothelial reaction caused by the operation, it was possible to recognize this combination in 50% of cases.

Where there is a pre-existing cornea guttata, decompensation of the endo-

thelial function must be taken into consideration, when a classical cataract extraction is proposed as well as when an intraocular lens is to be implanted.

It is not yet clear why in some cases an intraocular operation leads to marked reduction in the number of endothelial cells, while in other cases proliferation of endothelial cells occurs with the formation of a retrocorneal membrane.

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