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Editorial

Exfoliation syndrome

In 1917 Lindberg,[1] a Finnish ophthalmologist, gave the first published description of a condition that for a time was known as exfoliation of the anterior lens capsule. Associated with a risk of spontaneous lens displacement, posterior synechiae, and a high level of glaucoma such that about 50% of patients are likely to be affected, the disorder has been shown to have a worldwide prevalence and age-related incidence. Subsequent observers considered that the material accumulating on the lens surface originated elsewhere in the eye, though where that might be was obscure, and the term pseudoexfoliation of the lens capsule came to be preferred. Nowadays, however, because there is evidence of multifocal deposition and, possibly, origin, a cautious retreat to the simple designation exfoliation syndrome is gaining in popularity.

The notion that the abnormal substance observed on the front of the lens and elsewhere in the anterior segment might represent true capsular material is readily dismissed, since, unlike the capsule, which is essentially collagenous, the exfoliation deposits are resistant to collagenase digestion and include almost no hydroxyproline. On the other hand the possibility that they are an alternative product of the lens epithelium has not been ruled out. Thus fibrillar material morphologically indistinguishable from that seen on the lens surface in affected patients can be found beneath the capsule in the anterior equatorial region, sometimes apparently arising from small pits in the underlying epithelium.

We would be in a better position to determine the source of exfoliation material if only we understood its nature. Electron microscopy demonstrates a loose fibrillar structure, with individual fibrils being generally 20–30 nm thick and having a characteristic 50 nm macroperiodicity. On the basis of its ultrastructural appearance, specific histochemical staining reactions, and an affinity for antibody to fibrillin it has been suggested that the disorder is one involving the microfibrillar component of elastic tissue. Of relevance is the fact that the lens zonules have a similar ultrastructural, staining, and immunological properties, which could mean that the exfoliation material represents an overproduction of zonular tissue on the part of the non-pigmented ciliary epithelium and perhaps the equatorial lens epithelium. There are, however, some differences in amino acid composition between the two structures.

Moreover, there is also compelling evidence for the presence of other components which include glycosaminoglycans and non-collagenous basement membrane protein. A claim that amyloid protein, other than a plasma derived moiety, is implicated is not well substantiated. That the syndrome is primarily a disorder of basement membrane metabolism originated with the finding by electron microscopy of exfoliative material adjacent to the various epithelial tissues of the anterior segment and blood vessels of the iris, though it was hinted at as early as 1929 by Trantas,[2] who alluded to involvement of the so-called 'glass membranes.' Deposits have also been observed in the conjunctiva, raising the possibility that the disorder is more than a purely local phenomenon. Now in this issue of the *BJO* Drs Konstas, Marshall, and Lee present evidence showing that the non-collagenous protein laminin is a major constituent of the untoward basement membrane derived material. This particular protein is a complex molecule which helps to hold the membrane together and promote adhesion and regeneration of the overlying cells. The authors also indicate that, in the context of the iris vasculature, pericytes and smooth muscle cells are the probable source of the exfoliated laminin, though it is to be noted that many cell types, including the epithelial layers of the iris, ciliary body, and lens, are associated with similar activity.

So what are we to conclude? If, as now seems probable, the exfoliated material includes, among other things, both the fibrillar component of elastic tissue and the principal non-collagenous component of basement membranes, it is reasonable to suppose that a disturbance of an as yet unknown factor controlling specific aspects of extracellular matrix metabolism is a fundamental issue. Furthermore, since the incidence of the syndrome increases with age, it may be that external influences are concerned in the propagation of the disturbance.

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1 Lindberg JG. Kliniska undersökningar över depigmenteringen av pupillarranden och genomlysbarheten av iris vid fall av ålderstarr samt i normala ögon hos gamla personer. Dissertation, Helsingfors, 1917.
2 Trantas A. Lésions séniles de la capsule antérieure du cristallin et du bord pupillaire. *Arch Ophtalmol (Paris)* 1929; **46**: 482–91.