EDITORIAL

DRUSEN IN AGE-RELATED MACULAR DEGENERATION

Changes in the region of Bruch's membrane have long been implicated in the development of age-related macular degeneration. Correlation of the clinical and functional appearances with the histological and biochemical changes that give rise to neovascularisation or eventual geographic atrophy has proved difficult. Attention has tended to be directed at observable findings such as drusen and disciform response without considering the dynamic process of ageing and the changes it produces. Treatment has, as a result, tended to be empirical and only partially effective.

Clinically visible drusen may be described as hard or soft, discrete or confluent, are symmetrically distributed between the two eyes and appear to be genetically determined. The angiographic characteristics tend to correlate with any ensuing disciform response. There is increasing evidence that the chemical composition of Bruch's membrane deposits and the reactions these provoke are major determinants for the outcome of disease.[1]

The value of clinico-pathological correlation was well shown in Sarks' early paper[2] defining the role of basal linear deposit (BLD) in the development of pigmentary and disciform change. This diffuse membranous deposit appears in the seventh decade, being found on both aspects of the retinal pigment epithelial (RPE) basement membrane. In contradistinction drusen develop much earlier and are focal, lying between the basement membrane of the RPE and the inner collagenous zone of Bruch's membrane. Both drusen and BLD can give rise to similar-appearing soft drusen but fulfil different roles in the development of macular degeneration.

In this issue Sarks describes the lifecycle of drusen, drawing on the clinico-pathological examination of over 500 eyes. Enlargement of drusen may result from the amalgamation of a group of small drusen, consisting of amorphous electron-dense material, to form hard clusters. Such clusters of hard drusen become less electron dense at their base and eventually break down to develop an indistinct border and a softer appearance (soft clusters) and ultimately become confluent (confluent soft clusters/pigment epithelial detachments) possibly due to imbibition of fluid. They are no longer electron dense but contain membranous fragments and other debris. Eventually such change, derived from hard drusen, causes the overlying RPE to fail and atrophy to develop. Angiographically amorphous hard drusen fluoresce brightly and early, but as they break down fluoresce later and less brightly.

In one of the cases presented the soft drusen were clinically identical to those derived from clusters, but due to membranous BLD lying on both aspects of the basement membrane. It is such membranous BLD material that is more frequently associated with neovascular complexes. Separately derived small hard drusen were seen within this material and appeared to anchor the RPE to Bruch's membrane. Cells on the outer aspect of Bruch's membrane seemed to be preferentially related to these drusen.

This study allows a number of hypotheses to be proposed. Whilst hard drusen of themselves tend to give rise to focal atrophy following softening and RPE failure their association with macrophages and giant cells on the outer aspect of Bruch's membrane might encourage the development of new vessels[3] in response to the relative ischaemia produced by the BLD, which would also provide a plane of cleavage into which they could develop. It is unlikely that this will prove to be the final answer but the painstaking effort that this study reflects must contribute to our understanding of this major cause of visual loss and ultimately to the development of new management options for its cure.

I. H. CHISHOLM

References

1. Bird AC. Doyne lecture. Pathogenesis of pigment detachment in the elderly: the relevance of Bruch's membrane change. Eye 1991;5:1–12.
2. Sarks SH. Ageing and degeneration in the macular region: a clinico-pathological study. Br J Ophthalmol 1975;60:324–41.
3. Sarks SH, van Driel D, Maxwell L, Killingsworth M. Softening of drusen and subretinal neovascularisation. Trans Ophthalmol Soc UK 1980;100:414–22.