Retinopathy of prematurity

ROP and neurodevelopmental disabilities

G E Quinn

The dilemma in premature babies

There are essentially three ways in which blindness from retinopathy of prematurity (ROP) can be prevented, including elimination of premature birth, changes in neonatal care, and improved detection and treatment of established sight threatening retinopathy. It is on the latter that the attention and efforts of the ophthalmic community have been focused, leaving the first two to the paediatricians, perinatologists, neonatologists, nurses, and others who care for these tiny babies. What Darlow et al have done in the paper in this issue of the BJ O (p 1592) is direct our attention to the second possibility—that is, neonatal care may be able to be altered to decrease the incidence of potentially blinding disease.

Darlow et al document a remarkable variability in the prevalence of severe ROP among the nurseries in the neonatal intensive care units in the Australian and New Zealand Neonatal Network. Such variability is generally expected when morbidity or mortality results are compared across centres, even in an essentially population based study that this report represents (the four tertiary paediatric care referral centres are excluded from the analysis reported by Darlow et al). The variability in such reports can usually be explained by a combination of several factors, including case mix, assessment of the primary outcome measure, viability considerations by neonatologists at the various centres, and variations in clinical practice among nurseries, leading to more at-risk deliveries may differ dramatically among nurseries, which blindness from retinopathy of prematurity (ROP) can be prevented, including elimination of premature birth, changes in neonatal care, and improved detection and treatment of established sight threatening retinopathy. It is on the latter that the attention and efforts of the ophthalmic community have been focused, leaving the first two to the paediatricians, perinatologists, neonatologists, nurses, and others who care for these tiny babies. What Darlow et al have done in the paper in this issue of the BJ O (p 1592) is direct our attention to the second possibility—that is, neonatal care may be able to be altered to decrease the incidence of potentially blinding disease.

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Deep lamellar keratoplasty was the first form of corneal transplantation attempted, with a history over a century, and has been regarded mainly as a therapeutic technique. Lamellar grafting offers several advantages over penetrating keratoplasty, including the elimination of allograft rejection and the avoidance of intraocular complications. In addition, more donor cornea can be used in lamellar keratoplasty since the procedure does not require donor endothelium. This is particularly important in countries where donor corneas are scarce. However, the use of lamellar keratoplasty has been limited by difficulties such as irregularity and scarring of tissue interfaces, leading to poor visual outcomes compared with penetrating keratoplasty, as well as technical difficulties and prolonged operating time. Penetrating keratoplasty has thus been the most common corneal transplantation procedure for visual restoration for many years. Although penetrating keratoplasty has been shown to be effective and safe for most anterior segment pathologies, there are persistent long term risks such as endothelial failure and immunological graft rejection.

Deep lamellar keratoplasty (DLK) is a logical step in the surgical management of corneal stromal opacification in the setting of functional endothelium. In DLK, pathological stroma is excised down to Descemet’s membrane, and offers the promise of better visual outcomes compared with conventional lamellar grafting. Since this procedure was first reported by Arichita in 1985, several large case series have described favourable visual results after DLK. A report of 120 cases by Sugita and Kondo demonstrated that corrected visual acuity improved by 0.09 to 0.6 on average after DLK. Anwar and Teichmann reported that 89% of 181 eyes treated by DLK achieved visual acuity of 20/40 or better. More recently, Shimazaki and associates performed a randomised prospective trial of DLK versus penetrating keratoplasty, showing that visual function after DLK, as measured by corrected visual acuity, contrast visual acuity, the glare test, and corneal topography, was comparable to that achieved in penetrating keratoplasty. It should be noted that DLK was superior to penetrating keratoplasty in measures of operative morbidity such as continuous endothelial cell loss and intraocular complications. These results suggest that DLK is a safe alternative to penetrating keratoplasty in eyes without endothelial abnormalities. These findings underscore the importance of overcoming technical challenges such as achieving thorough stromal tissue excision without perforation of Descemet’s membrane.

Deep lamellar keratoplasty is a logical step in the surgical management of corneal stromal opacification in the setting of functional endothelium. Most corneal surgeons have confronted the technical challenge of deep lamellar dissection and the attendant risk of puncturing Descemet’s membrane during DLK. To facilitate the dissection of stromal tissue while reducing the risk of perforation, Arichita and Price employed an air injection technique to separate tissue planes. Sugita and Kondo and Amayem and Anwar used hydrodelamination to separate the deep stromal fibres from Descemet’s membrane. More recently, Shimazaki and associates used a hyaluronic acid for viscoelamination. These dissection techniques promises to make DLK easier, safer, and less time consuming.

Trends in keratoplasty have been changing over the past decade. Ocular surface reconstruction, consisting of limbal transplantation combined with amniotic membrane transplantation, has enabled us to improve the management of cicatrising diseases. Posterior lamellar keratoplasty, also referred to as deep lamellar endothelial keratoplasty, was developed for patients with endothelial dysfunction. These procedures are based on the concept that only the pathological part of the corneal endothelium, should be replaced by donor tissue, leaving the healthy portion of the host cornea intact. DLK is consistent with this paradigm, and can be viewed as a procedure designed to remove pathological stroma from healthy corneas. With continued improvements in surgical technique, including the advance described by Senoo and associates in this issue, DLK may become the procedure of choice for keratoplasty in most eyes without endothelial abnormalities.
Age related macular degeneration

Mouse models may provide new insight into the relation between cholesterol and age related macular degeneration

J L Duncan

With the goal of preventing vision loss from this disease, it is important to identify modifiable risk factors that may be targets for intervention

Age related macular degeneration (AMD) is the leading cause of severe vision loss among the elderly in the United States, Europe, and Australia. However, the cause of this blinding disease remains a topic of active investigation. Most agree the pathogenesis of AMD is multifactorial and that it results from the interaction of genetic, environmental and ageing effects. Evidence from population based studies has supported a role for heredity in the pathogenesis of AMD. Recent studies have identified a polymorphism in the pathogenesis of AMD. Recent studies has supported a role for heredity effects. Evidence from population based studies have found no consistent association. Increased dietary consumption of saturated fat, monounsaturated and polyunsaturated fat and vegetable fat has been associated with early and late AMD in various studies. Some recent studies have identified an association between use of cholesterol lowering medications, such as statins, and reduced risk of early or late AMD, while others have found no such association. Although total serum cholesterol has been associated with neovascular AMD in a large case-control study, many large population based studies have found no association. Some studies have suggested an association between different lipoprotein polymorphisms and risk of AMD, including apoE, apo B, and apo A1. Certainly the relation between cardiovascular risk factors, lipid metabolism, and AMD remains confusing.

The findings described in LDL receptor deficient mice may provide insight into the mechanism of early AMD

Insight into the role lipid metabolism has in the development of early AMD has come from the study of preclinical models. Although no murine model exists that exactly replicates the phenotype seen in human AMD, studies have shown that C57BL/6 mice fed a high fat diet and briefly exposed to blue-green light develop basal laminar deposits, a histological feature of human eyes with AMD. Mouse with null mutations in apoE have shown basal linear deposits and thickened Bruch’s membranes, similar to findings in human eyes with AMD. However, neither of these models develops choroidal neovascularisation or geographic atrophy, the stages
of AMD associated with vision loss in patients, limiting our understanding of the mechanisms responsible for these sight threatening complications.

In this issue of the Br J Ophthalmol (p 1627), Rudolf and colleagues present novel information about mice with a null mutation for the low density lipoprotein (LDL) receptor, which have been studied as a murine model of atherosclerosis. Further ultrastructural analysis of the lipid composition of Bruch’s membrane in LDL receptor deficient mice, using previously described methods to preserve neutral lipids, may provide insight into whether these deposits result from elevated plasma lipid levels or an intraocular source.36 Further ultrastructural analysis of the lipid composition of Bruch’s membrane in LDL receptor deficient mice, using previously described methods to preserve neutral lipids, may provide insight into whether these deposits result from elevated plasma lipid levels or an intraocular source.36

Even in the absence of correlates of late AMD, the findings described in LDL receptor deficient mice may provide insight into the mechanism of early AMD. The fact that the mice develop abnormally thickened Bruch’s membranes, similar to early AMD, and demonstrate VEGF upregulation suggests that ischaemia or oxidative stress occurs even in early stages of AMD, perhaps as a result of compromised diffusion from the choriocapillaris to the outer retina. LDL receptor deficient mice will provide a useful model of early AMD and may allow investigators to determine the part abnormalities of cholesterol metabolism may play in its pathogenesis. Whether or not deficiencies in the LDL receptor are associated with AMD in humans, the ocular phenotype of LDL receptor deficient mice described in the present work should encourage investigators to study murine models of atherosclerosis with careful attention to the eyes.

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