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Editorials

The impact of low birth weight on the visual pathway

It is well known that the survival of babies born prematurely has increased greatly in the recent past and that low birth weight carries a significant morbidity for ophthalmic problems. However, the impact of low birth weight on childhood vision impairment in epidemiological terms is largely unknown.

The article in this issue of the *BjO* (p 9) by Crofts and colleagues is therefore particularly welcome. Using the Oxford Register of Early Childhood Impairment, these authors gathered information on all babies with severe vision impairment born in the 4 years commencing January 1984. We are told that this population is reasonably representative of the UK as a whole. Vision impairment was defined as an acuity of 6/18 or less in the better eye identified by 5 years of age. From this database the birthweight specific rate of severe vision loss was calculated. The overall rate of severe vision impairment was 1.25/1000 births, but those of birth weight less than 1500 g contributed to 17.5% of the cohort and for this group the rate was 26 times that for babies of 2500–3499 g birth weight. The prevalence of associated impairments was high for all birth weights (60%), but highest for those under 1500 g (72%), decreasing with increasing birth weight to 44% for those over 3500 g.

The time of origin of the disorder was estimated, as best as possible, according to three major categories—prenatal, perinatal, and postnatal, and each of these contained 60%, 24%, and 10% respectively (5% were unclassifiable). Thus, 84% of childhood vision impairment has its origins at birth or before, and once the perinatal period has passed, from the vision impairment point of view, the visual pathway is more likely than not to remain unscathed. The aetiological front runner was cortical vision impairment which accounted for 36% of all childhood vision impairment, and was followed by optic atrophy (13%) and cataract (10%), with nystagmus, retinal dystrophy, and retinopathy of prematurity (ROP) all accounting for 6% each. Mindful that most childhood vision impairment affects parts of the visual pathway other than the eye, significant reduction of childhood vision impairment in the future has to come from preventing neurological prenatal and perinatal maldevelopment and/or damage.

It is of interest that ROP accounts for such a small proportion of severe vision impairment in this low birthweight population, particularly as this study predated the introduction, in 1988, of treatment for severe disease. Here, Oxford does not accurately reflect the worldwide situation for there is a rising incidence of severe disease associated with increased survival of preterm babies in middle

income countries such as Latin America and eastern Europe, all of which have less than ideal standards of care.¹ Thus, 54% of babies requiring treatment in Lithuania² had birth weights over 1500 g and the birth weight of some of the treated babies in Hungary was over 2000 g.³ In the UK and USA, severe ROP is virtually confined to babies under 1500 g and less than 32 weeks gestational age, hence the use of these criteria for the UK national screening guidelines.⁴ Clearly, however, these are not internationally appropriate and it is ironic that those countries with sparse resources have the greatest screening load. Both ROP and cataract are important for they are two of the few conditions about which the clinician can influence outcome.

So far we have concentrated on severe vision impairment, but babies born prematurely are also at risk of developing a range of less severe sequelae of the visual pathway. These include low acuity, colour and contrast sensitivity deficits, field defects, as well as the better known refractive errors and strabismus.⁵⁻¹⁶ A number of factors might play a role, such as an abnormal prenatal period, the neonatal environment, and illnesses suffered during the perinatal period.¹⁷⁻¹⁸ Some of these can be directly attributed to ROP and/or neurological insults, although in many instances it is not possible precisely to tease out their individual contributions.⁸ Over the past decade or so we have learned much about the visual pathway complications of prematurity, but as yet we know little about the mechanisms by which they occur, or about their functional implications. Fascinating glimpses of future research directions come from the finding that advanced ROP can be associated with a missense mutation of the Norrie gene,^{19,20} or at a neurological level that intrauterine stress and preterm birth could impair wiring and impede neuronal migration.^{21,22}

Epidemiological data are essential if we are to learn about the types of vision impairment and their frequency in the community, but they give no insight into the functional impact of visual disability, mindful that most children have more than one handicap. Here the term “disability adjusted life years” (DALYs) is helpful, for it reminds the clinician of the lifelong challenges that lie ahead for the child and family, with education and employment, social interaction, and leisure. We have now entered a difficult area. For all clinicians, telling parents that their baby has a severe vision impairment is a difficult and daunting experience. But, it is nothing compared with what the parents have to face thereafter, and giving the appropriate information sensitively is an essential prerequisite to ensure that the baby and family get the best possible support. A recent survey of parents of impaired

children sought information about the support they received at the point of diagnosis—it does not make comfortable reading for the medical profession. However this report, *Taking the Time*,²³ makes several important and positive recommendations of which the following are but a few. If possible, giving the diagnosis of severe vision impairment should be done in private. A review appointment should be offered within a couple of weeks to provide another opportunity for discussion, recognising that this is not strictly medically necessary. Try to give parents written information which can be updated according to progress, this may be in the form of a personal letter. The care of the visually disabled child requires multiprofessional input and links with the community support services, such as the peripatetic teaching service, should be established as soon as possible. Do not forget the value of client based parents' support organisations. Finally, while the ophthalmologist has to be the bearer of bad news, he or she also has the first opportunity to take positive supportive steps for the family, one which must not be missed. Hopefully by being open with the family and other professionals, the parents will come to regard the clinician as an advocate and ally to work with.

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Is there a role for computerised image analysis in glaucoma management?

The key elements in glaucoma diagnosis and follow up are measurement of the intraocular pressure, assessment of the optic disc, and examination of the visual field. In the 1920s, Ransom Pickard wrote about the benefits of drawing the optic disc to outline the disc and cup boundaries, placing emphasis also on the depth of the cup.^{1,2} In addition, he used a grid to measure the size of the cup relative to the disc, and his results of serial drawings over many years show an increase in cupping with the passage of time.³

Armaly⁴ popularised the use of the cup:disc ratio in the 1960s, particularly in epidemiology studies, but the term was later adopted by clinicians and to this day is the most commonly used clinical method of describing the glaucomatous optic disc. In a classic paper by Lichter in 1976,⁵ the poor agreement in cup:disc ratio estimation by a number of leading glaucoma specialists clearly illustrated that it is an “inexact method of recording the status of the disc” and “is probably not reliable in checking for small disc changes”. The level of within observer agreement is considerably greater than the degree of between observer agreement at describing optic disc features.⁶ The weakness of this form of disc assessment is the subjective estimation by the observer of the boundary of the cup edge relative to

the edge of the disc. Secondly, the size of the optic disc determines the physiological size of the cup.

The usefulness of perimetry in glaucoma is somewhat limited by the subjective nature of the patient's response when presented with a test target in the field of vision. This weakness is true of both manual and automated methods and for static and kinetic test strategies. The subjective aspect of the test invariably results in a measurement error which can on occasions be so large as to invalidate the test result. Consequently the signal to noise ratio can be so small that it becomes difficult to identify real change over time. Steps are being taken to reduce this source of error which will lead to more reliable results.

As a result, long term glaucoma management is undermined by the clinician's subjective assessment of the appearance of the optic disc and by the subjective nature of a patient's response when performing perimetry. There is a need to have more objective methods to help make more realistic decisions about progression of the disease. The measurement of optic disc topography with image analysis techniques (initially described by Nagin and Schwartz⁷) offers the potential of an objective test. The recent introduction of confocal laser scanning ophthalmoscopy

(CLSO) represents one of the latest development in imaging technology in glaucoma.

However, before any computer image analysis system can be introduced into the clinical setting, it is essential that certain requirements are fulfilled. These include that the image acquired and the topography measurements are accurate, clinically meaningful, and reproducible. By accuracy is meant that the resolution of the imaging system produces an accurate contour of the structure under investigation. It is important too that the topographic variables quantified (for example, neuroretinal rim area, cup shape, retinal nerve fibre layer thickness) provide useful clinical information about the disease. Ideally we need to identify those topographic features which predict subsequent change in the visual field. It is pointless acquiring volumes of quantitative data if the measurements have little or no bearing on the disease.

The issue of reproducibility with CLSO has two key elements—namely: (1) the ability of the imaging system to acquire the same topography contour at independent imaging sessions when no anatomical change has occurred⁸⁻⁹ (which is related to the issue of accuracy of image acquisition described above); and (2) the reliability of the operator and imaging system to generate the same topographic measurements on repeated measurements of the “same image”.¹⁰⁻¹² In this issue of the journal (p 14), Geyer and colleagues examine reproducibility of topography measurements with the TopSS CLSO in a group of glaucoma patients whose optic discs were imaged at two independent sessions 30 minutes apart. Using a number of statistical tests to examine reproducibility, the study identified three (out of 14) disc variables with a high degree of reproducibility which were suggested to be sufficiently robust topography features to be useful for long term monitoring of the optic disc. These features were cup depth, cup volume, and cup area halfway between the surface of the disc and the floor of the cup. We do not know if these same variables are equally reproducible in non-glaucomatous optic discs—for example, in ocular hypertension, or over longer time intervals such as 6 months apart. We do know that previous work shows a significant correlation between cup volume and visual field loss in glaucoma,¹³⁻¹⁴ and therefore at least one of these variables might provide valuable clinical information. Secondly, cup shape is capable of detecting early glaucomatous visual field loss with a high degree of sensitivity and specificity.¹⁵

In addition to the above prerequisites, instruments such as the CLSO (and other glaucoma image analysis techniques such as nerve fibre layer polarimetry¹⁶ and opti-

cal coherence tomography¹⁷) should generate data which discriminate between two or more groups, and measure change over time. The challenge to those involved in this area of clinical research is to demonstrate the usefulness of this type of objective assessment of the optic disc and retinal fibre layer during long term follow up over 5 to 10 years. It remains to be seen whether any of the markers of cup shape identified by Geyer *et al* turns out to be sufficiently robust in terms of accuracy and reproducibility, and also clinically meaningful in detecting disc change before field progression during glaucoma follow up. Only then can we consider the use of such expensive equipment in routine glaucoma management.

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Striving for the perfect keratoprosthesis

The ideal keratoprosthesis (KPro) should have all the advantages of but none of the problems associated with allografting. It should have specifiable aspheric optical variables, it should block ultraviolet radiation, and it should allow full visual field. The optical zone should be sufficiently rigid to avoid optical aberrations and astigmatism from buckling but sufficiently elastic to allow measurement of intraocular pressure by applanation.¹ Full wound healing (biointegration—a form of “biocompatibility”)²⁻³ should take place at least at the periphery of the artificial cornea, allowing defence against intraocular infection, epithelial downgrowth, as well as eye

rubbing and minor trauma. Artificial materials used should be non-toxic and not degrade in the lifetime of the patient.

It should allow host corneal epithelium to grow over its anterior surface and to adhere to it thus making a wettable and self renewing surface; therefore, proteinaceous materials would not be deposited onto its anterior surface and giant papillary conjunctivitis would not develop. Penetration by topical medication is important as steroids, pupil dilating and constricting drops, as well as antiglaucoma drops are used frequently. The formation of a retroprosthetic membrane has been a major cause of failure of many KPros, so its posterior surface should be highly polished

and non-sticky. The prosthesis should be flush with the rest of the ocular surface to enhance comfort and to reduce mechanical shearing forces on it. It should be sufficiently soft for suture needles to pass through but strong enough so that suture materials do not cheesewire. Last but not least, the prosthesis should be inexpensive.

This is a tall order indeed, but if met, would solve the problem of worldwide shortage of corneal donors, as well as the two major complications of allografting—graft astigmatism and rejection. How close are we to this? The related field of contact lenses, where safe extended wear has proved to be a tantalisingly difficult goal that has not yet been achieved despite considerable commercial investment, suggests just how complex the problem is likely to be.

In this issue, Hicks *et al* (p 18) demonstrate to us the need for a multidisciplinary approach to the development of such a biomedical device. Previous workers have used a range of biomaterials incorporated into a range of design features. The common feature that characterises almost all these attempts, however, is the fact that the materials selected have been chosen because of their availability and their susceptibility to fabrication techniques appropriate for the specific KPro design employed, rather than for their ability to interact appropriately with the specific biological environment in question. One significant feature that sets the development work on the Chirila prosthesis apart from other published work in this area is the fact that in its initial stages it sought to make use of a polymer that is significantly more hydrophilic than the generality of those previously employed in KPro design—namely, poly(2-hydroxyethyl methacrylate) or poly-HEMA. Then, having elegantly harnessed established principles of behaviour of the material in the formation of a two part prosthesis with porous skirt and clear core,⁴ the group has recognised that the literature on cellular interaction with hydrogels predicts that some modification to the chemical structure of the porous skirt will inevitably be necessary in order to manipulate and optimise biological integration.⁵ This paper contains the first report of the initial exploration of the effect of small changes in the chemical structure of the prosthesis. It represents a significant stage in what will inevitably be a long road towards the achievement of a

KPro whose chemical and physical features produce an acceptable level of biocompatibility to support long term success.

In terms of long term retention results, we must not forget the osteo-odonto-keratoprosthesis (OOKP) which has been in existence for over 30 years.⁶⁻⁸ Following modifications by Falcinelli, the modern technique has a track record of close to 20 years. Well over 90% of Falcinelli OOKPs are retained in the long term and three quarters of patients achieve 6/12 vision or better.⁹⁻¹¹ OOKP is not without its problems—its complexity, relatively poor visual field (30°–40°), and having to sacrifice oral structures. However, it can withstand a hostile ocular environment and future generations of KPros will inevitably be judged against the grandfather of KPros when they come to clinical use.

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