Ocular defects in infants of extremely low birth weight and low gestational age

Priscilla Burgess, Ann Johnson

Abstract
The eyes of 49 babies who weighed less than 1000 g at birth or who were born at or before 28 weeks gestation were examined at the age of 4 years. Twenty-one children were normal. The remaining 29 children (59%) had ocular abnormalities which ranged from mild ambylopia to blindness from retinopathy of prematurity. The need to examine children at risk is stressed.

The recent increase in survival of babies of extremely low birth weight (ELBW), that is, weighing less than 1000 g, and infants of low gestational age (28 weeks or less) has led to increasing concern about their long term outcome. Overall less than half of these babies survive, though survival rates as high as 63% are achieved in some areas. A recent meta-analysis of a large number of follow-up studies of ELBW infants has shown that just over a third of all survivors (36%) were impaired. Most of this impairment is of neurological origin — that is, cerebral palsy, sensory deficit, and learning difficulties. The most serious ocular defect in these babies is retinopathy of prematurity (ROP), and several studies have confirmed that the risk of ROP is inversely related to birth weight. In particular, cicatrical, binding ROP is more common in infants weighing under 1 kg at birth.

The literature contains little information on the outcome of babies of low birth weight and low gestational age from the ophthalmological as distinct from a developmental standpoint. Saigal et al described the findings at the age of 2 years of a group of ELBW infants from a geographically defined region in Canada. She noted an overall incidence of ROP of 38%. There were eight children with one or both eyes blind from ROP from a population of 110 survivors (7%). Two children had reduced vision due to optic atrophy (2%), 17 were myopic (16%), 13 had strabismus (12%), and one had nystagmus (1%). Keith and Kitchen in a similar study noted ocular lesions in 33% of survivors: 10% had cicatrical ROP, 3% had optic atrophy, 17% had considerable refractive error, and 19% had squint. Hungerford et al in a study of babies born before 33 weeks of gestation found ocular pathology in 15%. The commonest problem was refractive error; 8% had ROP, and 5% had delayed visual maturation. Both these studies were hospital based and described survivors from one centre.

In 1984 a study was undertaken of all infants born to mothers resident in the Oxford Region and who weighed less than 1000 g at birth or who were born at or before 28 weeks' gestation. The eyes of 72% of this cohort of ELBW babies were also examined. The main purpose of this report is to give a detailed description of the ocular findings.

Patients and methods
Sixty-eight of 127 (54%) babies born alive to mothers in the Oxford Region and who weighed less than 1000 g or who were born at or before 28 weeks' gestation survived to their fourth birthday. The eyes of 49 of the 68 survivors were examined during a two-year period from June 1987 to June 1989. The mean age of the children (25 girls, 24 boys) at the time of visual assessment was 4 years 4 months (range 3 years 8 months to 4 years 11 months).

The ocular assessment consisted of the following: The parents were questioned about eye disease either in the child or in the family, with particular reference to strabismus and myopia. A detailed neonatal history was available from the hospital notes. The ocular motility was assessed, and examination included pursuit and saccadic eye movements, and a cover test for near and distance. Visual acuity was measured where possible with a linear Snellen chart or linear Sheridan Gardner or Kay pictures. In non-verbal children the ability to fix and follow small targets was assessed. We also undertook confrontation visual field tests using finger counting in the quadrants; TNO tests (named after authors — Toegepast, Natuurrwenschappeljik, Onderzoek to measure stereopsis; Slit-lamp examination; and refraction and indirect ophthalmoscopy following the instillation of cyclopentolate 1%).

Not all children were examined by an ophthalmologist as neonates. Whether or not such an examination was performed depended on the intensive care unit in which the child was treated.

Results
The ocular findings in 21 to 49 (43%) children were normal. The remaining 28 children (59%) were found to have a variety of ocular abnormalities (Table 1).

<table>
<thead>
<tr>
<th>Retinopathy of prematurity</th>
<th>Number of children</th>
<th>Percentage of children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strabismus</td>
<td>12</td>
<td>25</td>
</tr>
<tr>
<td>Myopia</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>Optic nerve head abnormalities</td>
<td>5</td>
<td>10</td>
</tr>
</tbody>
</table>

Table 1 Ocular defects
ROP. The first was born at 26 weeks’ gestation and weighed 720 g. She suffered from respiratory distress syndrome, was ventilated until the fifth day of life, and had supplemental oxygen in a headbox until the sixteenth day. She also had a patent ductus arteriosus which was treated with indomethacin. At 6 months of chronological age she was noted to have roving eye movements and was found to have bilateral closed funnel retinal detachments. At age 4 years she was blind in both eyes and entirely retarded, with a severe communication disorder.

The second child with severe cicatricial ROP was born at 24 weeks’ gestation and weighed 632 g. She was ventilated for six weeks and sustained an intraventricular haemorrhage. When assessed the right eye was normal, but the left was divergent and had an eccentric macula with a dragged disc and temporal vasculature. Interestingly this eye was highly hypermetropic and astigmatic. This child had made good developmental progress, and neither child with ROP had associated cerebral palsy.

Another child when seen during the neonatal period had acute ROP (grade 2 maximally) but was normal when seen at age 4. A further child had mild mid peripheral retinal pigmentary speckling as her only abnormality at age 4.

**Table 2** Associations found with strabismus

<table>
<thead>
<tr>
<th>Number</th>
<th>6</th>
<th>1</th>
<th>1</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myopia</td>
<td>5</td>
<td>1</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Amblyopia</td>
<td>5</td>
<td>1</td>
<td>3</td>
<td>1</td>
</tr>
</tbody>
</table>

**Table 3** Optic nerve head abnormalities

<table>
<thead>
<tr>
<th>Number of children</th>
<th>Bilateral</th>
<th>Unilateral</th>
<th>Neurological defects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optic atrophy</td>
<td>2</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Optic nerve hypoplasia</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Optic disc drusen</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Tilted discs</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

**Discussion**

This study has been largely concerned with the detection of anatomical and functional defects of the visual system in a group of ELBW babies delivered to residents of a geographically defined area. The high incidence of ocular morbidity of 59% could have been due to bias in the sample, because children with known or obvious defects were more likely to be available for ophthalmic examination. The group of children not seen did not differ from those who were seen in mean birth weight or mean gestational age (Table 4). Neither did the proportion of children with an
impairment differ in the two groups. All 19 infants not seen were screened by health visitors; seven of 19 were referred to specialist eye services. None of these referred children were found to have an ophthalmic abnormality. If we assume that, although other systems were impaired, all 19 children were ophthalmologically normal, the incidence of ocular defect in this population is 43% (29/68).

RETNOPATHY OF PREMATURITY
The two children with cicatricial ROP had several of the recognised risk factors for this condition, namely extreme prematurity, extremely low birth weight, severe respiratory distress syndrome, and intraventricular haemorrhage. Several studies from the United States have shown that the incidence of blindness from ROP in infants with birth weights of less than 1.5 kg ranges from 1.8% to 4%, but the distribution is markedly skewed towards those weighing less than 1 kg. Cicatricial disease occurs in 22–42% of these smallest survivors, whereas 5–11% of them are blind. Ng et al claimed that infant death is well recognised. They suggest that this may be partly due to racial factors. The incidence of cicatricial disease in our study may be underestimated owing to the difficulties of examining the peripheral fundus of children of this age. Indeed three of the myopic children had straightening of the temporal vascular arcades and probably had ROP. If these children are included, the incidence of cicatricial ROP was 5/49 or 10%.

Table 4 Birth weight, gestational age, and impairment code of all survivors to 4 years

<table>
<thead>
<tr>
<th>Children seen</th>
<th>Children not seen</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>49</td>
</tr>
<tr>
<td>Male</td>
<td>25 (51%)</td>
</tr>
<tr>
<td>Birthweight (g), mean (SD)</td>
<td>1009 (201)</td>
</tr>
<tr>
<td>Gestational age (weeks), mean (SD)</td>
<td>27.9 (1.9)</td>
</tr>
<tr>
<td>Number of children with impairment coded 3 or 4*</td>
<td>27 (55%)</td>
</tr>
</tbody>
</table>

* Impairment code 3 = impairment in one or more areas resulting in mild to moderate disability. Impairment code 4 includes cerebral palsy, severe sensory loss, total developmental delay. † Impairment codes not available for seven infants (unavailable for assessment because overseas, etc.)

babies without ROP, and 5% in a comparable group of full-term babies. Anisometropia inducing strabismus and amblyopia only partly explains these findings. The incidence of strabismus in this study (24%) is higher than in similar studies, where incidences of 12% and 19% have been noted. One explanation for this is the older population seen in the Oxford study, with an increased risk of accommodative esotropia and consecutive divergence.

In this study one-third of the squints were divergent, a much higher proportion than that seen elsewhere in similar but not strictly comparable groups and again may be due to the age of the population examined. In Black's study of visual disorders associated with cerebral palsy he also noted a convergence/divergence ratio of 2:3:1.

The strong association between myopia and convergent squint has also been noted by Keith and Kitchen; the mechanism is presumably a type of sensory deprivation esotropia. The incidence of squint is higher in children with neurological deficit, especially cerebral palsy. The mechanism for this is not fully explained, but children with the spastic type of cerebral palsy are the most likely to have ocular defects. In them the pathology is extensive and diffuse, with periventricular and subcortical haemorrhage and cortical atrophy.

OPTIC NERVE ABNORMALITIES
The association between cerebral palsy and ocular morbidity is well recognised. The 4% incidence of optic atrophy in this study compares with reported incidences of 2% and 3%. Possible mechanisms for optic atrophy are that it is secondary to hydrocephalus and also is associated with cerebral palsy. In the same study hypoplastic discs were seen in 3/20 (2.5%) children with severe spastic cerebral palsy; our child with hypoplastic discs also had severe spastic cerebral palsy. There were two cases of relatively innocuous disc abnormalities (one tilted disc and buried drusen) which have not previously been recorded as a feature of low birth weight.

CORTICAL BLINDNESS
Diffuse cortical deficit may be associated with visual impairment without any abnormality of the eyes or anterior visual pathways. The acuity in these children is usually limited to counting
fingers or less. Colour vision and the ability to perceive movement is better than form perception. There is a broad spectrum of disability in this condition. It has recently become apparent that visual acuity in children who were born prematurely is less good than in full term controls. This seems to be the result of some other factor associated with prematurity.\textsuperscript{19,20} It may be that the five children in our study with decreased acuity without any ophthalmic explanation have the latter type of cortical visual impairment.

**MYOPIA**

There is a well recognised relationship between myopia and ROP.\textsuperscript{11–19} Myopia has been described as a feature of all grades of ROP but occurring in up to 80% of patients with cicatricial disease.\textsuperscript{20} Asymmetrical myopia can result in severe anisometropic amblyopia in an eye with only minimal cicatricial changes. Several studies have reported that the myopia is not solely due to increased axial length but may have lenticular and corneal components.\textsuperscript{25–28}

Because of the high incidence of ocular morbidity in ELBW babies it is recommended that such children should not only be examined by an ophthalmologist in the nursery to detect ROP but also followed up during early childhood to detect, and if possible treat, any associated ocular disorder. Some of these children have multiple handicaps, and visual defects may be overlooked, with serious visual and educational implications. Babies of extremely low birth weight contribute minimally to the total ocular pathology seen in early childhood. However, the risk of abnormality is high, and they warrant thorough ophthalmic assessment and care.

The authors thank Mr J J Kansi and Dr Andrew Wilkinson for their help in the preparation of this paper. Action Research for the Crippled Child funded the neurodevelopmental part of the study.