CHILDHOOD CATARACT IN SOUTH INDIA:
AETIOLOGY, MANAGEMENT AND OUTCOME

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Abstract

Background

Cataract accounts for up to 20% of childhood blindness. Despite this, very little is known about the aetiology and visual outcome of children with cataract in the developing world.

Objectives

The aims of this thesis were:

i. to determine the aetiology of childhood cataract in south India and to assess whether the potentially preventable condition of congenitally acquired rubella was a significant cause.

ii. to determine whether examination of saliva for rubella specific IgM would be an equally reliable but less invasive and more practical test for confirming the diagnosis than examination of serum

iii. to determine the most appropriate surgical treatment for children with bilateral cataract in south India.

Methods

An observational and case control study was undertaken to search for associations between events in pregnancy and the development of cataract. Cataract aetiology was determined using interview data, clinical examination and laboratory investigations. Saliva and serum samples were taken from infants with cataract and were analysed for rubella specific IgM by an antibody capture radioimmunoassay.

A randomised clinical trial comparing lensectomy to lens aspiration with a primary capsulotomy (ECCE) was undertaken on children with bilateral cataract.

Results

One quarter of non-traumatic cataracts were hereditary and 15% were due to congenitally acquired rubella. Mothers of children with cataract were more likely to have taken abortifacients than a group of age matched controls.

Congenital rubella infection was confirmed using saliva in 25 out of 95 (26.3%) infants with cataract under 1 year of age.

The clinical trial showed no significant difference between the two surgical groups in rates of complication or of visual outcome 1 year after surgery (p=0.57). If secondary procedures to clear the visual axis had been unavailable, lensectomy would have been the method of choice (p=0.019).

Conclusions

i. Congenitally acquired rubella remains an important and preventable cause of infantile cataract in south India.

ii. Diagnosis using saliva is reliable and is particularly useful in areas remote from testing centres.

iii. Both lensectomy and lens aspiration with primary capsulotomy are effective surgical treatments for bilateral cataract in this population. If surgical intervention is to be kept to a minimum then lensectomy may be preferable.
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The Virus Reference Division, Public Health Laboratory Service, London.
Statement Of Originality And Publications Arising From The Thesis

The work presented in this thesis consists of original research carried out by the author as a contribution to the science and clinical practice of Ophthalmology. The laboratory work, clinical observations and recording and entering of data were all performed by the candidate. All figures, tables, illustrations, graphs and text were prepared by the candidate. All simple statistical analyses were performed by the candidate. Univariate and multivariate modelling were performed by Dr Yoav Ben-Shlomo (Epidemiologist). Dr Darwin Minassian and Miss Jenny Evans advised on the statistical tests required and checked the analyses.

Publications


Foreword

This thesis describes the background, design, conduct, and analysis of clinical and laboratory based studies conducted by the author in India between 1993 and 1996 to determine the aetiology and appropriate management of childhood cataract.
CHAPTER ONE

Introduction and Literature Review

1.1 World-Blindness And Childhood Blindness

1.1.1 Epidemiology of World Blindness
1.1.2 Epidemiology of Childhood Blindness
1.1.3 Childhood Blindness in South India

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1.2.2 The Aravind Eye Hospital

1.3 The Lens

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1.3.2 Embryology
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1.4.3 Susceptibility of Women of Child Bearing Age to Rubella Infection
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1. CHAPTER ONE

Introduction And Literature Review

1.1 World-Blindness And Childhood Blindness

1.1.1 Epidemiology of World Blindness

In 1994 the World Health Organisation estimated that there were 38 million blind people in the world and that this number would continue to increase (Thylefors et al. 1995). By the year 2000 they anticipate that the figure will be between 45-50 million people.

Figure 1 Trends in global blindness 1975-1990

These estimates use the WHO definitions of visual loss (Table 1) where blindness is defined as a corrected visual acuity of less than 3/60 in the better
eye and severe visual impairment a corrected vision in the better eye of 3/60 or better but less than 6/60.

Table 1 Definition of blindness: World Health Organisation

<table>
<thead>
<tr>
<th>Category of visual loss</th>
<th>Visual acuity in the better eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>≥6/18</td>
</tr>
<tr>
<td>Visual impairment</td>
<td>&lt;6/18-6/60</td>
</tr>
<tr>
<td>Severe visual impairment</td>
<td>&lt;6/60-3/60</td>
</tr>
<tr>
<td>Blind</td>
<td>&lt;3/60-NPL</td>
</tr>
</tbody>
</table>

More than 80% of blind people live in the developing world, mostly in Asia (25 million) and Africa (7 million).

Figure 2 Global distribution of blindness 1990

Global Distribution of Blindness 1990
(Total 37.9 million)

As much as 80% of world-wide blindness is potentially avoidable (preventable or curable) but despite this the number of blind continue to increase (Foster, 1993). This is partly due to increased life expectancy and population growth, but largely due to the limited accessibility of eye care services, the relative high cost of these services and the lack of awareness by health personnel and patients that the services exist (Foster and Johnson, 1993).
Cataract, ocular infections and childhood blindness account for three quarters of the total and together these disorders are responsible for more than 200 million person years of blindness (Foster and Johnson, 1993).

**Barriers to Delivering Eye Care in Developing Countries**

1. **Awareness**

   Many blind people in poor areas of the developing world are not aware that they can be helped. Health care professionals may be unaware of the scale of the problem and do not have the knowledge to effectively mobilise their resources.

2. **Accessibility**

   Blind people may have limited or no access to available specialised services due to geographic or social isolation. They tend to be old and this compounds the problem. In parts of Asia and Africa there are few available specialists; in India there is approximately one ophthalmologist per 100,000 population and in Africa one per million. This compares to approximately one per 20,000 in Europe. Specialists tend to be concentrated in large cities and offer only limited services in the rural areas.

3. **Affordability**

   The proportion of Government funding spent on health in developing countries has increased very little over the last 25 years and these countries have become poorer in real terms (UNDP, 1990). The result is that hospitals and doctors have inadequate income from Government sources and expect patients to pay for services. The poor may find the cost of care well beyond their means.
**Prevalence of blindness**

Different countries show wide variations in prevalence of blindness depending on environmental factors which may favour certain blinding diseases.

In Table 2, data from population based surveys performed in Asia are listed. There is a wide distribution from 0.2% to 1.5% with a mean of 0.75%. This compares with a prevalence of blindness of 0.05-0.2% in the USA and Europe (Foster and Johnson, 1990) (Table 3).

**Table 2 Prevalence of Blindness in Population-Based Surveys in Asia**

<table>
<thead>
<tr>
<th>Country</th>
<th>Population (millions)</th>
<th>Number Examined</th>
<th>Prevalence Blindness (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nepal (1980)</td>
<td>16</td>
<td>39,887</td>
<td>0.8</td>
</tr>
<tr>
<td>India (1986)</td>
<td>830</td>
<td>—</td>
<td>0.68</td>
</tr>
<tr>
<td>Indonesia (1982)</td>
<td>160</td>
<td>—</td>
<td>1.2</td>
</tr>
<tr>
<td>China (1982-1984)</td>
<td>1040</td>
<td>433,085</td>
<td>0.2-0.7</td>
</tr>
<tr>
<td>Thailand (1983)</td>
<td>50</td>
<td>19,265</td>
<td>1.1</td>
</tr>
<tr>
<td>Saudi Arabia (1984)</td>
<td>10</td>
<td>16,810</td>
<td>1.5</td>
</tr>
</tbody>
</table>

**Table 3 Estimates of prevalence of blindness and numbers of blind for different continents**

<table>
<thead>
<tr>
<th>Continent</th>
<th>Prevalence Blindness (%)</th>
<th>Number of blind (millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asia</td>
<td>0.8</td>
<td>25</td>
</tr>
<tr>
<td>Africa</td>
<td>1.0</td>
<td>7</td>
</tr>
<tr>
<td>Latin America</td>
<td>0.5</td>
<td>2.5</td>
</tr>
<tr>
<td>The Rest</td>
<td>0.05 - 0.2</td>
<td>3.5</td>
</tr>
</tbody>
</table>

**Causes of Blindness**

Table 4 summarises the causes and epidemiology of world blindness. Adult cataract and trachoma are by far the most common blinding conditions. Childhood blindness accounts for only a small proportion of the total (1.5 million),
however in terms of visual morbidity for the number of years lived and therefore requiring extra care and assistance, the figure is very significant.

Table 4 Epidemiology and Causes of World-wide Blindness (1995)
(Foster and Johnson, 1990; Thylefors et al. 1995)

<table>
<thead>
<tr>
<th>Cause</th>
<th>Number Blind (millions)</th>
<th>Epidemiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cataract</td>
<td>17.0</td>
<td>Everywhere</td>
</tr>
<tr>
<td>Trachoma</td>
<td>5.5</td>
<td>Poor, hot, dry areas</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>5.0</td>
<td>Open-angle glaucoma. Africa, Angle-closure glaucoma, Asia</td>
</tr>
<tr>
<td>Diabetic retinopathy</td>
<td>2.5</td>
<td>Areas with good general medical services</td>
</tr>
<tr>
<td>Childhood blindness</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>Xerophthalmia</td>
<td>0.5</td>
<td>Children</td>
</tr>
<tr>
<td>Onchocerciasis</td>
<td>0.5</td>
<td>West and Central Africa, Latin America</td>
</tr>
<tr>
<td>Age-related macular degeneration</td>
<td>1.0</td>
<td>Areas with elderly populations</td>
</tr>
<tr>
<td>Leprosy</td>
<td>0.25</td>
<td>Asia and Africa</td>
</tr>
<tr>
<td>Others</td>
<td>4.25</td>
<td>Everywhere</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>38</strong></td>
<td></td>
</tr>
</tbody>
</table>

1.1.2 Epidemiology Of Childhood Blindness

Childhood is defined by UNICEF as age 0-15 years. The prevalence of childhood blindness is approximately one tenth that of adult blindness. Although there have been few population based studies the available data suggests a figure of approximately 0.3/1000 children in Western countries, increasing to over 1.5/1000 in children living in poor rural areas of Africa and Asia (World Health Organisation. 1992). Using these data there are an estimated 1.5 million blind children in the world of whom 1 million live in Asia (Table 5). This accounts for approximately 75 million person years of blindness which is similar to the
world-wide visual morbidity from unoperated adult cataract if one makes the bold assumption that children become blind in infancy and have a near normal life span. Figure 4. (Foster, 1993)

Table 5  Estimated number of blind children in the world

<table>
<thead>
<tr>
<th>Region</th>
<th>Population 0-15 years (millions, 1989)</th>
<th>Blindness prevalence (per 1000)</th>
<th>Estimated number of blind children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>240</td>
<td>1.1</td>
<td>264,000</td>
</tr>
<tr>
<td>Latin America</td>
<td>130</td>
<td>0.6</td>
<td>78,000</td>
</tr>
<tr>
<td>North America, Europe, Japan</td>
<td>240</td>
<td>0.3</td>
<td>72,000</td>
</tr>
<tr>
<td>Asia</td>
<td>1200</td>
<td>0.9</td>
<td>1,080,000</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>1810</strong></td>
<td></td>
<td><strong>1,494,000</strong></td>
</tr>
</tbody>
</table>

Figure 3  Number of blind children in different regions of the world
About 75% of all childhood blindness in developing countries is preventable or curable (World Health Organisation. 1992) and the poorer the country the larger the prevalence of preventable disease. The prevalence of childhood blindness in England calculated from blind registrations between 1969-1976 was 0.09/1000 (0-4 years) and 0.23/1000 (5-15 years) (Foster, 1988). In comparison a survey in Bangladesh gave a blindness prevalence of 0.64/1000 (0-5 years) from rural areas and 1.09/1000 for children from urban slums (Cohen et al. 1985).

The causes and time of onset of childhood blindness vary from one part of the world to another (Foster and Gilbert, 1992).

Table 6 and Figure 5 summarises the anatomical cause of blindness using data from prevalence surveys of blind schools in different regions of the world. It is evident that in Africa and Asia, nutritional factors and ocular
infections account for more than half of all childhood blindness. In Asia, diarrhoea is the important predisposing factor for vitamin A deficiency and blindness from corneal scarring, whilst in Africa up to 50% of childhood blindness is associated with recent measles infection. This contrasts with Europe and North America where genetic factors are responsible for 30-50% of cases.

*Figure 5 Anatomical causes of childhood blindness (global)*

The pattern of childhood blindness changes over time and it is important to continue to monitor the causes. For example in Saudi Arabia, acquired childhood diseases accounted for 75% of childhood blindness prior to 1962, while genetically determined diseases accounted for 84% of childhood blindness after 1962 (Gilbert et al. 1995). A new form for recording causes of visual loss in
children has been developed so that a standardised approach to monitor childhood blindness is now possible (Gilbert et al. 1993b).

Table 6 Childhood blindness in different regions of the world by % anatomical cause: 1975-1991

<table>
<thead>
<tr>
<th>Region</th>
<th>Cornea</th>
<th>Lens</th>
<th>Uvea</th>
<th>Retina</th>
<th>Glaucoma</th>
<th>Optic atrophy</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>East Africa</td>
<td>72</td>
<td>6</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>6</td>
<td>10</td>
</tr>
<tr>
<td>West Africa</td>
<td>39</td>
<td>15</td>
<td>6</td>
<td>11</td>
<td>10</td>
<td>7</td>
<td>12</td>
</tr>
<tr>
<td>South Asia</td>
<td>33</td>
<td>7</td>
<td>1</td>
<td>20</td>
<td>5</td>
<td>5</td>
<td>29</td>
</tr>
<tr>
<td>Latin America</td>
<td>8</td>
<td>20</td>
<td>1</td>
<td>26</td>
<td>10</td>
<td>10</td>
<td>25</td>
</tr>
<tr>
<td>Europe, USA</td>
<td>1</td>
<td>8</td>
<td>1</td>
<td>30</td>
<td>2</td>
<td>23</td>
<td>35</td>
</tr>
</tbody>
</table>

1.1.3 Childhood Blindness in South India

There is no good survey data on the prevalence of childhood blindness in India. The prevalence is likely to be somewhere between the figures from European countries (0.3 per thousand) (Stoll et al. 1992) and countries such as Nepal (1.1 per thousand). A conservative estimate would therefore be 0.5 per thousand children or approximately 200 blind children per million total population. Based on these estimates, there are 200,000 (+/- 50,000) blind children in India. The incidence of childhood blindness is unknown, but is probably in the range of 20-100 new blind children per year per million total population.
Blind school surveys in south India have shown that the major cause of childhood blindness is corneal scarring due to Vitamin A deficiency and measles (19-31%). Cataract accounts for 10-24% (Gilbert et al. 1993a; Rahi et al. 1995), and of those children, approximately 40% are blind due to late surgery and/or uncorrected aphakia, 40% due to unoperated cataract and 20% due to the complications of surgery. The other causes of blindness are retinal disease (21%) and microphthalmos/anophthalmos (25%). Hereditary factors accounted for 23% of the causes of childhood blindness and post-natal factors for 28%. The WHO form has now been used in a number of blind school surveys in other developing countries and has shown that 10-40% of childhood blindness may be due to cataract (Table 7)

Table 7 Proportion of childhood blindness due to cataract in recent blindness surveys in developing countries

<table>
<thead>
<tr>
<th>Country, Author, Year of study</th>
<th>Number Examined</th>
<th>Number with cataract</th>
<th>% of blindness due to cataract</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jamaica, (Moriarty, 1988)</td>
<td>108</td>
<td>42</td>
<td>39</td>
</tr>
<tr>
<td>West Africa (Gilbert et al. 1993a)</td>
<td>284</td>
<td>28</td>
<td>10</td>
</tr>
<tr>
<td>India, (Rahi et al. 1995)</td>
<td>1411</td>
<td>162</td>
<td>12</td>
</tr>
<tr>
<td>Philippines, (Gilbert and Foster, 1993)</td>
<td>190</td>
<td>26</td>
<td>14</td>
</tr>
<tr>
<td>Chile, (Gilbert et al. 1994)</td>
<td>217</td>
<td>20</td>
<td>9</td>
</tr>
<tr>
<td>Sri Lanka, (Eckstein et al. 1995)</td>
<td>226</td>
<td>39</td>
<td>17</td>
</tr>
<tr>
<td>Malawi (Gilbert et al. 1993a)</td>
<td>137</td>
<td>18</td>
<td>13</td>
</tr>
<tr>
<td>Kenya (Gilbert et al. 1993a)</td>
<td>77</td>
<td>7</td>
<td>9</td>
</tr>
</tbody>
</table>

It is estimated that globally there are over 200,000 children blind from cataract. The prevalence of infantile cataract has been reported to be as high as 6 to as low as 1.2 cases per 10,000 births (Stewart-Brown and Halsum, 1988; Stoll et al. 1992; Stayte et al. 1993). These differences may reflect ethnic and racial diversity of the populations studied but are most likely due to the different methodologies used in acquiring the data. The lowest prevalences have been
reported in two population based studies from the USA which have relied primarily on hospital discharge diagnoses. The highest prevalence documented is from European studies surveying cohorts of older children.

The birth defects monitoring program is a national surveillance system in the US which monitors hospital discharge data for birth defects and other conditions of the new-born (Edmonds et al. 1981). The prevalence of cataract recorded in neonatal discharge records from 1988 to 1991 was 1.2 per 10,000 births (Myrianthopoulos, 1985). In another American study (Collaborative Perinatal Project) (Remaley et al. 1995), pregnant women were enrolled and the 53,724 children born were carefully followed up. Congenital cataract developed in 1.6 per 10,000 infants within the first year of life. In contrast European population-based studies have found a 3-5 times higher prevalence of infantile cataracts. The Birth Cohort Study evaluated 87% of all children born in the UK over four days in 1970 when they were 10 years of age (Stewart-Brown and Halsum, 1988). Of the 12,853 children evaluated, four had bilateral cataracts (3.3/10,000) and three had unilateral cataracts (2.3/10,000) for a combined prevalence rate of 5.6/10,000. A similar study in Oxford found four children with cataracts out of a birth cohort of 6687 children (6/10,000) (Stayte et al. 1993). While the cataracts in two of these children were diagnosed during infancy, the cataracts in the other two children were not as visually significant and were not diagnosed until the children were 2-5 years of age. A French study reported the incidence of congenital cataract as 2.3 per 10,000 live births, examining 131,760 consecutive births during the first year of life (Stoll et al. 1992; Eurocat working group, 1991).

In general the British studies probably provide a closer approximation of the true prevalence of cataracts during early childhood than the American studies, but they are flawed by their reliance on medical records rather than clinical examination. It is likely that many visually insignificant cataracts were missed in these studies. In addition, some of the cataracts may have wrongly
been assumed as infantile when in fact they may have been acquired later in childhood. The methodologies used in several of the American studies were flawed by their reliance on hospital discharge summaries. Since most infantile cataracts are not diagnosed during the neonatal period, these studies will tend to underestimate the true prevalence. In the American collaborative study (Myrianthopoulos, 1985) fifty-four new cases of cataract were recognised during the follow up period of seven years which had not been noted at the initial examination. The total prevalence of cataract at seven years in this study was 16.3 per 10,000 children.

While infantile cataracts continue to be one of the most common causes of blindness in developing countries, they are becoming a less common cause of blindness in developed countries. For example, while in 1971, 10% of the children enrolled in a North American blind school had infantile cataracts, the percentage had dropped to 1% by 1991 (Biglan, 1992). In the United Kingdom blindness due to congenital cataract has recently shown a decrease in prevalence (Statistical Bulletin 1991). This improvement can be at least partially attributed to the earlier diagnosis and treatment of infantile cataracts as well as to improved visual rehabilitation. The incidence may also have gone down because of improved ante-natal screening for systemic abnormalities such as Down's syndrome and vaccination against rubella.
1.2 India

1.2.1 The Demography of India and Tamil Nadu

India has a population (1995 estimate) of approximately 1.1 billion, this represents an increase of about 220 million, over the 1981 census total. The overall population density in 1993 was about 275 persons per sq. km. More than 70 percent of India's population lives in rural areas.

India consists geographically of the entire Indian Peninsula and portions of the Asian mainland. It is bounded on the north by Afghanistan, China, Nepal, and Bhutan; on the east by Bangladesh, Burma (Myanmar), and the Bay of Bengal; on the south by Palk Strait and the Gulf of Mannar (which separate it from Sri Lanka) and the Indian Ocean; and on the west by the Arabian Sea and Pakistan. With Jammu and Kashmir (the definitive status of which has not been determined), India has an area of 1,270,000 square miles.

Successive five-year plans, in force since 1951, have achieved a steady rate of economic growth, except for periods of severe drought, such as in 1979 and 1987. In 1992 India's gross domestic product was estimated at $269.7 billion. More than 60 percent of the workers of India are engaged in farming, which generates about one-third of the value of the country's annual domestic product. Overall life expectancy at birth was 58 years in the late 1980s, compared with 32 years in 1941. The infant mortality rate declined from 151 to 91 per 1000 live births between 1965 and 1989. In 1990 about 365,000 doctors were practising in addition to "herb doctors" and unregistered practitioners. The country was served by 650,000 hospital beds.
Figure 6 The Indian Sub-Continent
Figure 7 Map of South India
The clinical work for this thesis was undertaken at the Aravind Eye Hospital. The hospital is situated in the ancient south Indian city of Madurai in the state of Tamil Nadu approximately 400 miles south of Madras. The state of Tamil Nadu has a population of nearly 60 million of which a third live in the towns and cities and two thirds in rural areas. Madurai has a population of just over 1 million and is situated in the southern half of the state. In this region of India 32% of the population is less than 15 years old and 14% less than 6 years old (1993 census). About 63% of the population is literate and economically Tamil Nadu is in the middle tier of Indian states with a moderately well developed infrastructure.
Figure 8 State of Tamil Nadu
Figure 9 Madurai city centre
1.2.2 The Aravind Eye Hospital

Aravind hospital is presently (1997) the largest eye hospital in the world with 1400 beds. In 1994 the hospital carried out 72,000 surgical operations of which 29,000 were intracapsular cataract extractions and 25,000 were extracapsular cataract extractions with IOL's. The number of outpatients examined and treated in the same year exceeded 650,000. The hospital employs 77 ophthalmologists including 'residents', over 300 other clinical staff, mostly nurses and 304 non clinical staff.

Aravind hospital is split into two sections; there is a paying section of 500 beds and a free section of about 900 beds. The revenue generated through the paying section pays entirely for the maintenance and running expenses of the free section as well as providing free medical care for those patients who cannot afford it.

The paediatric ophthalmic department is staffed by one Consultant Ophthalmologist (Dr Vijayalakshmi) and four residents in training. The department examines all children who attend the hospital whether they are able to pay for treatment or not. In 1995, over 27,000 children were examined by the paediatric ophthalmology department and 1,800 operations were performed.

Table 8 Type of surgery performed on children in 1995 at the Aravind hospital

<table>
<thead>
<tr>
<th>Type of surgery</th>
<th>Paying patients</th>
<th>Free patients</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cataract</td>
<td>483</td>
<td>556</td>
<td>1039</td>
</tr>
<tr>
<td>Strabismus</td>
<td>201</td>
<td>112</td>
<td>313</td>
</tr>
<tr>
<td>Other</td>
<td>210</td>
<td>231</td>
<td>441</td>
</tr>
</tbody>
</table>
Figure 10 Aravind Eye Hospital. Paying section above. Free section below.
The catchment population for the hospital is approximately 15 million people but it is increasing all the time as more people become aware of its services and reputation.

**Barriers to access**

**Logistics**

In India, the majority of the population (70%) live in rural areas whilst the eye care facilities are predominantly concentrated in the urban areas. This presents problems in logistics with economic implications. The roads flood easily and are often impassable in the rainy season. Public transport is relatively expensive for rural Indians and journeys are often long and arduous. This is especially true in the mountainous areas when many hours of trekking are required to reach the nearest road.

**Socio-economic**

In India, eye care and cataract surgery is provided free or at a nominal charge in the Government and non-profit hospitals. Although the eye care services are free, the patient incurs substantial expenses to access this free eye care. There is the cost of travel to hospital, the child has to be accompanied by at least one adult. For the parents, in addition to the travel costs there is loss of salary for the time away from work. The children’s parents will need to buy food, medications and spectacles. The average family has 4 children and the arrangements to ensure the others are looked after can be difficult. The sum total of these costs can be substantial for a family and this inhibits the number of
parents who are willing to bring their children for cataract surgery.

**Information**

Brilliant et al (1991) showed awareness regarding surgical intervention for age related cataract in a typical Asian population was less than 8%. While there is an increasing awareness with the advent of national programs to control blindness and the use of television, there is still likely to be a significant portion of the population unaware about adult and childhood cataract and its treatment.

There are many misconceptions amongst those who know about cataract. Some believe that it is necessary to wait for the cataract to mature and others believe that they should only be operated in the summer months or monsoon season. These misconceptions and lack of information leads to delay in accessing surgery and often not accessing the service at all. This applies to children as well as adults.

**Health Behaviour**

Traditional practices, beliefs and a fatalistic attitude towards blindness, lack of faith in the intervention and fear about the surgical procedures influence the behaviour of the parents and children leading to lower levels of acceptance.
1.3 The Lens

1.3.1 Definition Of Childhood Cataract

There are a variety of definitions used when discussing childhood cataract. The terms congenital, infantile, developmental and early onset are often used interchangeably and this makes comparisons between different studies difficult. As early history is often not available particularly in countries with limited health care facilities and it is usually not possible to know whether a cataract was truly congenital or whether it developed during the first few months of life. In contrast to congenital cataract, infantile and developmental cataracts are not necessarily present at birth. In this thesis the term infantile cataract is used when there is reasonable evidence that the cataract was present at birth or within the first few months of life.

1.3.2 Embryology

An understanding of the embryology of the lens is helpful when classifying infantile cataracts. The lens forms from surface ectodermal cells that respond to lens inducers which emanate from the anterior neural plate, optic vesicle and neural crest (Grainger, 1992). Beginning on the 28th day of gestation, this single layer of ectodermal cells thickens and becomes the lens placode (Zwaan, 1975). As the lens develops it forms "zones of discontinuity" which are identifiable demarcated areas. These areas can be useful as they sometimes make it possible to distinguish between the occurrence of a prenatal toxic insult from an insult occurring during the postnatal period. On the 33rd day of gestation the lens placode invaginates to form the lens cup. When the lens cup separates from the overlying ectoderm it is referred to as the lens vesicle (Smelser, 1965).
The lens vesicle initially consists of a single layer of epithelial cells covered by a basal lamina. The basal lamina thickens to become the lens capsule. Primary lens fibres are laid down to fill the lens vesicle by 45 days of gestation and these form the clear embryonic nucleus. The epithelial cells on the anterior surface of the lens vesicle then migrate laterally to the equatorial region and form the lens bow. The cells in the bow region are laid down between the third and eighth month of gestation and form secondary fetal nuclear fibres which elongate and encapsulate the embryonic nucleus. The interface at which they meet forms the lens sutures. The anterior lens suture has an upright Y configuration while the posterior suture has an inverted Y configuration. The sutures at birth are located just beneath the lens capsule. Other sutures are formed as additional fibres continue to be laid down creating the cortex of childhood. Throughout life new lens fibres replicate at the lens equator and their nuclei migrate to the area beneath the anterior capsule. Young lens cells occupy a thin layer, contain nuclei and attach to their basement membrane the capsule. Mature lens fibres, now without nuclei occupy the remainder of the lens. The removal of the lens during embryogenesis may result in flattening of the cornea, arrested development of the vitreous and a slowing of axial elongation (Coulombre, 1964).
Figure 11  Bilateral cataract in 4 year old girl (study no.513)
1.3.3 Cataract Morphology

Infantile cataracts are usually subdivided on the basis of their morphology (Table 9) (Merin, 1986; Lambert, S.R. and Drack, A.V. 1996). The classification can be helpful in suggesting an aetiology but can also be misleading as there can be great variability in the cataract morphology even within the same pedigree (Gottrau et al. 1993; Harrod and Friedman, 1991; Rubin et al. 1994; Scott et al. 1994). The morphological appearance of cataracts can also be helpful in predicting the visual prognosis (Parks et al. 1993; Parks, 1982).

Table 9 Morphological types of congenital cataracts

<table>
<thead>
<tr>
<th>1</th>
<th>Zonular</th>
</tr>
</thead>
<tbody>
<tr>
<td>a.</td>
<td>Nuclear</td>
</tr>
<tr>
<td>b.</td>
<td>Lamellar</td>
</tr>
<tr>
<td>c.</td>
<td>Sutural</td>
</tr>
<tr>
<td>d.</td>
<td>Capsular</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>2</th>
<th>Polar</th>
</tr>
</thead>
<tbody>
<tr>
<td>a.</td>
<td>Anterior</td>
</tr>
<tr>
<td>b.</td>
<td>Posterior</td>
</tr>
<tr>
<td>i.</td>
<td>posterior lentiglobus</td>
</tr>
</tbody>
</table>

3 Total

4 Membranous

5 PHPV

1. Zonular cataracts

These are the most common type of infantile cataract and are so called because they are confined to specific zones of the developing lens (Falls, 1943). A nuclear cataract refers to opacification of the central zone of the lens,
specifically the region between the anterior and posterior Y sutures. The cataract is usually 3-4mm in diameter and often has opacified cortical fibres (riders) encircling the nuclear opacity (Hiles and Carter, 1979). They are usually bilateral (>60%) and are associated with microphthalmos and microcornea (Johnson and Parks, 1991). The density of nuclear cataracts is very variable and they are often transmitted as an autosomal dominant defect (Marner, 1949). If the disturbance occurs during the first 3 months of life, the opacity is limited to the inner part of the nucleus of the lens and has been termed a central pulverulent cataract or Coppock cataract (Hegab, 1991; Renwick and Lawler, 1963).

Lamellar cataracts are characterised by a lamella of lenticular opacification sandwiched between a clear nucleus and cortex. They occur as a result of a transient insult to the lens during its development; the earlier the lens insult, the deeper the opacity within the lens. They are usually bilateral but frequently an interocular difference in the degree of lenticular opacification is present.

Sutural cataracts are congenital and often hereditary and occur along the anterior and posterior Y sutures. They can be associated with nuclear cataracts but when they occur as an isolated finding they seldom impair vision.

Capsular cataracts are lens opacities which involve either the anterior or posterior lens capsule, sparing the lens cortex. Anterior capsular opacities are usually visually insignificant.

2. **Polar cataracts**

Polar cataracts are opacities of the subcapsular cortex which occur in either the anterior or posterior pole of the lens and affect both the capsule and underlying lens. Anterior polar cataracts are typically 0.5-2mm in diameter and are usually visually insignificant. Over 90% are unilateral and when bilateral are asymmetrical (Jaafar and Robb, 1984). They are easily visible and often diagnosed at birth. They do not usually progress over time. Posterior polar
cataracts are often small but impair vision because of their proximity to the nodal point of the eye. Posterior lentiglobus is a distinctive type of posterior polar cataract usually 1-5 mm in size. They are usually centered on the posterior pole of the lens (Cheng et al. 1991) and often develop in infancy and early childhood. They probably form because of a congenital weakness in the posterior lens capsule allowing posterior cortical lamellae to prolapse through the capsular defect (Johnson and Parks, 1991). These prolapsed lamellae then opacify.

3. **Total cataracts**

   Total cataracts involve the entire lens and may develop in infants. In some cases they can form from partial cataracts while in other cases the lens is completely opacified when the cataract is first diagnosed. Any type of cataract can ultimately progress to this, but they often begin as lamellar or nuclear cataracts (Francois, 1961; Merin, 1986).

4. **Membranous cataract**

   These occur when the lens cortex and nucleus are partially or completely reabsorbed. The anterior and posterior capsules then fuse to form a dense white membrane with a small quantity of lens material sandwiched between them (Smith et al. 1990).

5. **Persistent hyperplastic primary vitreous (PHPV)**

   PHPV is usually a unilateral condition associated with a retrolenticular fibrovascular membrane. The lens is often clear at birth but opacifies over time (Pollard, 1991). The lens may be pushed forward by the membrane causing the anterior chamber to shallow. More than two-thirds of the affected eyes are microphthalmic and often have rubeosis of the iris and secondary glaucoma (Scott et al. 1989).
1.3.4 Aetiology Of Childhood Cataract

There are many known causes of childhood cataract (Figure 12 and Table 10). Previous studies of cataract aetiology have established a definite causative factor in 30-70% of cases (Hing et al. 1990; Kohn, 1976; Merin and Crawford, 1971; Jain et al. 1983; Francois, 1961; Harley and Hertzberg, 1965).

Figure 12 Aetiology of childhood cataract split into major groups

Galactokinase deficiency (AR)  
Galactosaemia (AR)  
Hypoparathyroidism  
Diabetes/hypoglycaemia  
New mutation (50%)  
Familial (8-23%)  
Chromosomal  
With systemic disease e.g. Lowe's, metabolic  

dereditary

Secondary embryodysgenesis  
Microphthalmos, aniridia  
Coloboma, PHPV  
Neural crest abnormality  
Post lenticusus  
Persistent pupillary membrane  
Intraocular tumour  
Trauma  
Uveitis  
Steroid treatment  
Prematurity  
Maternal illness - measles, CMV, zoster  
Simplex, toxo, rubella  
Maternal drugs  
Maternal nutrition  
Other medical practices

Infantile cataracts most commonly occur secondary to genetic or metabolic diseases, intrauterine infections or trauma. Less commonly they may occur as a side effect of treatment with certain medications or radiation therapy. The relative frequency of the different causes varies depending on the geographic area studied but in those studies performed in the developed world, the majority of cataracts are hereditary (autosomal dominant) or are associated with other ocular or systemic disease (Merin and Crawford, 1971; Francois, 1961). Although information is limited, the same is unlikely to be true in the
developing world where the congenital rubella syndrome probably remains an important aetiological factor.

**Genetic**

Infantile cataracts can be inherited as autosomal dominant, autosomal recessive or X-linked recessive traits (Krill et al. 1969; Lewis et al. 1990; Warburg et al. 1993; Lund et al. 1992). The first human disease to be assigned to an autosome was the Coppock cataract.

Renwick and Lawler (1963) employed pedigree studies for linkage analysis. They analysed blood and saliva samples from members of the Coppock family for common markers and found a strong indication of close linkage with the Duffy blood group locus. This was subsequently assigned to chromosome 1 by linkage to a cytogenetic marker.

Autosomal dominant congenital cataracts (ADCC) are most commonly bilateral nuclear opacities, but there is marked variability within pedigrees (Salmon et al. 1988). In an extended pedigree of 28 patients with autosomal dominant nuclear cataracts, nineteen affected members had unilateral cataracts while nine had bilateral cataracts (Scott et al. 1994). Less commonly, anterior polar and posterior polar cataracts can be dominantly inherited (Gibbs et al. 1993; Rubin et al. 1994). In the Western world the majority of inherited cataracts are inherited as autosomal dominant traits (Jaafar and Robb, 1984). In other countries where there is a high prevalence of parental consanguinity several studies have shown high rates of autosomal recessive inheritance (Baghdassarian and Tabbara, 1975; Mostafa et al. 1981)
Table 10 Classification of childhood cataracts based on aetiology

**Isolated finding**

**Hereditary**
- Autosomal dominant
- Autosomal recessive
- X-linked

**Sporadic**

**Part of syndrome or systemic disease**

**Hereditary**
- With renal disease
  - Lowe’s syndrome
  - Alport’s syndrome
- With CNS disease
  - Laurence-Moon-Bardet-Biedl syndrome
  - Sjogren’s syndrome
  - Norries disease
  - Smith-Lemli-Opitz syndrome
- With skeletal disease
  - Conradi’s syndrome
  - Stickler’s syndrome
- With abnormalities of head and face
  - Hallermann-Streiff syndrome
  - Francois dysphalic syndrome
  - Pierre Robin syndrome
  - Oxycephaly
  - Crouzon’s disease
  - Apert’s syndrome
- With polydactyly
  - Rubinstein-Taybi syndrome

**With skin disease**
- Rothmund-Thompson syndrome
- Bloch-Sulzberger syndrome
- Cockayne’s syndrome
- Incontinentia pigmenti
- Siemens syndrome
- Ectodermal dysplasia

**With Chromosomal disorders**
- Trisomy 13
- Trisomy 18
- Trisomy 21
- Turner’s syndrome
- Patau’s syndrome

**With metabolic disease**
- Galactosaemia
- Galactokinase deficiency
- Fabry’s disease
- Refsum’s disease
- Mannosidosis
- Sialidosis
- Hypocalcaemia

**Nonhereditary**

**Prenatal**
- Rubella
- CMV
- Varicella Zoster
- Herpes Simplex
- Toxoplasma

**Postnatal**
- PHPV
- Aniridia
- Retinopathy of prematurity
- Anterior chamber cleavage syndromes
- Intraocular tumour
- Congenital retinal detachment
Advanced molecular biologic techniques are being used in combination with more classical linkage and chromosomal studies to pinpoint the genetic loci for a variety of congenital cataracts (Lund et al. 1992) (Table 11). With the availability of DNA markers, restriction fragment length polymorphism (RFLP) analysis, and several generations of affected individuals, researchers have recently mapped the gene for an X-linked cataract associated with dental abnormalities (Nance-Horan syndrome) (Toutain et al. 1997). With use of more classical linkage analysis and various DNA markers, the locus of another ADCC was found on chromosome 16 (Eiberg et al. 1988). Another ADCC was linked to the G crystallin gene cluster on chromosome 2 (Lubsen et al. 1987), and yet another to a translocation between chromosomes 3 and 4 (Reese et al. 1987). These studies support the concept of genetic heterogeneity in autosomal dominant congenital cataract.

There is now experimental evidence that certain inherited cataracts are due to gene defects that cause incorrect folding of proteins (Chambers and Russell, 1991). The Philly cataract in mice which results in a dense nuclear opacity is due to a defect in the gene (loss of 12 nucleotides) for one of the Beta crystallins. The resulting absence of amino acids prevents correct folding of the protein. Studies conducted by Lubsen and colleagues (Lubsen et al. 1987) have shown that the Coppock cataract appears to be associated with a defect in one of the high phase separation temperature g-crystallin genes. A mutant gene may produce a protein whose phase separation temperature is so elevated above that of the normal protein that phase separation occurs at body temperature.
Table 11 Genetic location of inherited cataracts

<table>
<thead>
<tr>
<th>Type</th>
<th>Chromosome/Locus</th>
<th>Gene</th>
<th>Authors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Coppock</td>
<td>1q21-q25</td>
<td>unknown</td>
<td>Renwick and Lawler, 1963</td>
</tr>
<tr>
<td>Coppock-like</td>
<td>2q33-q36</td>
<td>gamma E crystallin</td>
<td>Lubsen et al. 1987</td>
</tr>
<tr>
<td>Marner</td>
<td>16q22.1</td>
<td>unknown</td>
<td>Eiberg et al. 1988</td>
</tr>
<tr>
<td>Posterior polar</td>
<td>16q22.1</td>
<td>unknown</td>
<td>Maumenee, 1979</td>
</tr>
<tr>
<td>Cerulean</td>
<td>17q24</td>
<td>unknown</td>
<td>Armitage et al. 1995</td>
</tr>
<tr>
<td>Nance-Horan</td>
<td>Xp22.31-p22.13</td>
<td>unknown</td>
<td>Lewis et al. 1990</td>
</tr>
<tr>
<td>Anterior polar</td>
<td>17p13</td>
<td>unknown</td>
<td>Toutain et al. 1997</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Berry et al. 1996</td>
</tr>
</tbody>
</table>

Metabolic Disorders

Galactosaemia is the most common metabolic disturbance causing cataracts. It is inherited as an autosomal recessive trait and causes hepatosplenomegaly and mental retardation unless treated by dietary restriction. It can be diagnosed by testing for reducing substances in the urine. Galactokinase deficiency is more common and does not cause any systemic illness apart from cataract. It may also be detected by looking for urinary reducing substances and can be differentiated from galactosaemia by other enzymatic assays.

Galactosaemia may be caused by a transferase, galactokinase or epimerase deficiency (Stambolian, 1988). Galactosaemia due to galactose-1-phosphate uridyl transferase (GALT) deficiency occurs in approximately 1:40,000 newborns in the UK and 1:23,000 newborns in Ireland (Beigi et al. 1993). A homozygous mutation on exon 6 of the GALT gene on chromosome 9 13p is found in two thirds of children with transferase deficiency (Elsas and Leslie, 1993). This results in the accumulation of galactose-1 phosphate in the blood. Galactose is converted to galactitol in the lens and the raised concentration of galactitol may cause osmotically induced lens fibre swelling and
opacification (Endres and Shin, 1990; Harding, 1992). Early on, the lens appears to have an oil droplet in the centre. This is reversible with the elimination of galactose from the diet. If left untreated the cataract will progress to a total cataract and the child will fail to thrive and be developmentally delayed.

Galaktokinase deficiency may cause cataracts with few or no systemic abnormalities. The galaktokinase gene is on chromosome 17 and heterozygotes for the gene have half normal values on blood tests. Partial loss of enzyme activity may lead to cataracts in later life (Stambolian et al. 1995).

Metabolic disorders of glycoprotein degradation such alpha mannosidosis result in an accumulation of abnormal oligosaccharides which cause opacification of the posterior lens capsule (Letson and Desnick, 1978).

Lowe's syndrome is a rare X linked recessive condition manifested in infancy by dysmorphic facies, mental retardation, failure to thrive, aminoaciduria, vitamin D resistant rickets and cataracts. The lens tends to be abnormally shaped and the lenses of female carriers of the syndrome may also be abnormal (Fagerholm et al. 1991).

Hypocalcaemia in the neonate causes typical cataracts which are lamellar with cortical dots. Children suffer from fits and fail to thrive. Lamellar cataracts may also develop in low birth weight infants with hypoglycaemia (Merin, 1986).

Infectious

Although a number of viruses have been implicated in congenital cataract formation, the mechanisms whereby they cause lens damage is not clear. Zimmerman (1968) examined a series of eyes with cataract due to congenitally acquired rubella (CAR) and was interested to note the relatively normal appearance of the lens epithelium and capsule. The central lens fibres however were abnormal as they still contained nuclei. Virus could be isolated directly from the cells and it seemed likely that the pathology was due to a direct viral effect.
This was supported by tissue preparations of lens cells infected with rubella virus. These showed that there was retarded cell division as well as associated tissue necrosis.

Infantile cataracts have also been reported to occur in children after intrauterine Varicella (Shrivastva et al. 1988; Lambert et al. 1989), toxoplasmosis and herpes simplex infections (Ourth, 1971; Siegel, 1973).

**Oxidative damage**

There has been interest recently concerning the effects of oxidation on the developing lens by oxygen derived free radicals (Harding, 1993). These free radicals can oxidise lipids and proteins causing the cell membranes to be damaged. If for some reason the concentration of these free radicals becomes too high in the region of the lens or if the concentration of free radical scavengers too low, opacification may result. Electron microscopic examination of congenital zonular cataracts shows that normal lens fibre membranes are broken down resulting in secondary degeneration of the fibre contents (Gottrau et al. 1993). There is also some evidence that children with Down's syndrome have increased free radical activity and that this may be a factor in the associated cataract (Bras et al. 1989).

**Teratogens**

Abortifacients have been cited as a cause of cataract in India (Angra, 1987) but there was no control group in this retrospective study and recall data can be unreliable. Data from the Collaborative Perinatal Project (Heinonan et al. 1977) was used to identify risk factors for congenital cataract but found no association with maternal drug ingestion during pregnancy. They prospectively reviewed more than 50,000 pregnancies for relative risk of malformation production after exposure to various agents during pregnancy.
**Prematurity**

Low birth weight premature infants were noted in one study to have an incidence of transient cataracts of 2.7% (Alden et al. 1973). These usually had resolved completely after four months. All of the infants with transient cataracts were septic and had been treated with Kanamycin; 80% of these infants also had an unexplained metabolic acidosis. Pike (1989) has pointed out that prematurity and low birth weight by themselves are unlikely to be a cause of cataract but are more likely to be related to other events in pregnancy or to fetal abnormalities and it is these that predispose to the cataract.

**Laser Photocoagulation**

Christiansen and colleagues (1995) recently reported total cataracts in six eyes following argon laser photoablation of the avascular retina in four infants with threshold retinopathy of prematurity. They proposed that the vasculature on the anterior lens surface absorbed the laser energy causing thermal injury to the lens.
1.3.5 Aetiology of Childhood Cataract in India

There have only been two published studies from India. Angra (1987) in North India looked at 200 cases of 'congenital' cataract and found that 31% were idiopathic, 14% were hereditary and 21% may have been due to rubella. This study was retrospective and methods of patient selection were not described. Parents were not examined and rubella diagnosis was made only on clinical grounds. Jain (1983) prospectively enrolled 76 children with cataract from the general clinic over one and a half years and noted that 20% of the cataracts were hereditary, 9% were due to metabolic diseases and 5% had an associated syndrome. Nearly 8% had a positive rubella titre but the disease may have been acquired after birth and the significance is questionable.
1.4 Congenitally Acquired Rubella

1.4.1 Historical Background

In 1941 N. McAllister Gregg an Australian ophthalmologist, published his now famous retrospective study "Congenital cataract following German measles in the mother", in which he showed that, if acquired in early pregnancy, rubella could cause congenital malformation. Seventy-eight babies, all with a similar type of congenital cataract, were born in New South Wales after a large rubella epidemic in 1940. All but ten of the mothers had a clinical history of rubella, usually in the first or second month of pregnancy. Congenital defects of the heart were recorded in 44 of the 67 cases whose cardiac condition was documented. These findings were confirmed by Swan(1943) who in addition to reporting cataracts and heart defects, noted that many congenitally infected infants were deaf and some also had microcephaly. Deafness occurred in children whose mothers had noticed a rash about 2 months into the pregnancy. Mothers of children with cataract but who were not deaf reported their rash at a slightly earlier gestational age (1.5 months). Congenital deafness was also reported by Gregg(1946), who in addition had observed dental defects and low birth weight.

In order to obtain a more accurate assessment of the risks of maternal rubella, prospective studies were carried out during the 1950’s, in which the outcome of pregnancy of women having a history of rubella at different stages of their pregnancy was assessed. These showed that the incidence of congenital malformations following maternal rubella was much less than in the previously conducted retrospective studies. The risks of major malformation after maternal
infection in the first trimester varying from 10.4% to 54.2% (Johnson and Whitehead, 1989; Cooper and Krugman, 1967; Dudgeon, 1985). However these studies might have underestimated the incidence of congenital malformation, as they were conducted before laboratory diagnosis was available.

Another epidemic in the USA in 1963 resulted in an estimated 20-30,000 rubella damaged babies being born (Cooper, 1969). Vaccine development was spurred on in the wake of this epidemic and was produced for the first time in 1965 (Plotkin and Oski, 1965). Immunisation was widely introduced in the USA and Europe in 1969 and since then the disease has been potentially preventable.

1.4.2 Epidemiology of Rubella

Clinical diagnosis of rubella is unreliable because: a) many viruses such as enteroviruses produce the same symptoms as rubella virus and b) many children (25%) are completely asymptomatic with no rash. For these reasons rubella is not a notifiable disease in most countries and its surveillance is particularly difficult (Banatvala and Best, 1990).

There is limited data from the developing world about the incidence of rubella infection and congenitally acquired rubella (CAR). The WHO has been unable to provide advice on the use of rubella vaccines in many countries because adequate sero-prevalence data is not readily available (Miller, 1991).

In the absence of immunisation, rubella is endemic. Outbreaks occur at irregular intervals, usually in spring and early summer in temperate climates. The size of the outbreak depends on the number of susceptible individuals in the
population. Introduction of the virus into isolated communities results in the infection of virtually every susceptible individual in contact with the virus. For this reason island populations are particularly susceptible to rubella epidemics leading to large numbers of children with CAR (Moriarty, 1988).

Since surveillance of clinical rubella in developing countries is almost impossible, data can only be gathered from serological surveys. Comparison between surveys is difficult because different methodologies are used. Surveillance of CAR cases is made more difficult because these children are seen by many different types of medical specialist and often die young (Miller, 1989).

1.4.3 Susceptibility Of Women Of Child Bearing Age To Rubella Infection

Susceptibility depends on two factors:

1) the number of women of childbearing age who are not immune.

2) rubella transmission amongst children.

In the UK over 96% of women of childbearing age are immune to rubella either because of natural immunity after infection or because of active vaccination. It is not therefore surprising that there were only 2 notified cases of pregnant women contracting rubella in 1992. Because few developing countries have rubella immunisation programmes the situation there is likely to be very different. The number of women of childbearing age who are susceptible to rubella infection is shown in Table 12.
Table 12  Susceptibility of women of child bearing age to rubella infection (Miller, 1991; Seth et al. 1985; Global advisory group, 1991; Takahashi et al. 1990)

<table>
<thead>
<tr>
<th>Region</th>
<th>Country</th>
<th>Women susceptible</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>Nigeria</td>
<td>34%</td>
</tr>
<tr>
<td></td>
<td>South Africa</td>
<td>8%</td>
</tr>
<tr>
<td></td>
<td>Gambia</td>
<td>7%</td>
</tr>
<tr>
<td></td>
<td>Togo</td>
<td>36-67%</td>
</tr>
<tr>
<td></td>
<td>Kenya</td>
<td>25%</td>
</tr>
<tr>
<td>South America</td>
<td>Brazil</td>
<td>18%</td>
</tr>
<tr>
<td></td>
<td>Panama(rural)</td>
<td>65%</td>
</tr>
<tr>
<td></td>
<td>Panama (cities)</td>
<td>30%</td>
</tr>
<tr>
<td></td>
<td>Trinidad</td>
<td>47%</td>
</tr>
<tr>
<td></td>
<td>Jamaica</td>
<td>47%</td>
</tr>
<tr>
<td></td>
<td>Hawaii</td>
<td>58%</td>
</tr>
<tr>
<td></td>
<td>(USA)</td>
<td>(3%)</td>
</tr>
<tr>
<td>South East Asia</td>
<td>North India(rural)</td>
<td>57%</td>
</tr>
<tr>
<td></td>
<td>Sri Lanka</td>
<td>43%</td>
</tr>
<tr>
<td></td>
<td>China</td>
<td>3-30%</td>
</tr>
<tr>
<td></td>
<td>Singapore</td>
<td>50%</td>
</tr>
<tr>
<td></td>
<td>Thailand</td>
<td>25%</td>
</tr>
<tr>
<td></td>
<td>Taiwan</td>
<td>32%</td>
</tr>
<tr>
<td>Eastern Mediterranean</td>
<td>Egypt</td>
<td>19%</td>
</tr>
<tr>
<td></td>
<td>Lebanon</td>
<td>12%</td>
</tr>
<tr>
<td></td>
<td>Iran</td>
<td>11%</td>
</tr>
<tr>
<td></td>
<td>Israel</td>
<td>5%</td>
</tr>
<tr>
<td>Western Europe</td>
<td>UK</td>
<td>3%</td>
</tr>
</tbody>
</table>

Results of serological surveys can be difficult to interpret, however they do show that rubella infection is widespread and endemic in most developing countries. The proportion of susceptible women varies from country to country and even within countries. Very high rates of susceptibility were found in island populations such as Jamaica, Trinidad and Taiwan (Lin and Chen, 1994). African countries varied widely 3% in South Africa to almost 30% in Nigeria and Kenya. In Panama it was shown that women migrating from rural areas to cities...
were at high risk compared to those settled in cities; 65% of rural population non
immune, compared to 30% of town people (Saad de Owens and Tristan de
Espino, 1989).

1.4.4 Seroepidemiology of Rubella in India

In India there is little data on the incidence of CAR or on the
seroepidemiology of rubella in the female population. The first
seroepidemiological study was performed around New Delhi in 1968 (Seth et al.
1971) and showed that women in urban areas (88%) were more likely to be
immune to rubella than those in the rural areas (72%). This is probably because
the chance of exposure is less in the lower populated rural areas. In subsequent
years similar studies were performed at Chandigarh in northern India (Pal et al.
1974) and at Calcutta in eastern India (Chakrabarty et al. 1973). The areas in
the north had a similar profile to New Delhi, but in the east around Calcutta only
55% of women of childbearing age were immune to rubella infection. This is
interesting as the population density in this area is very high and it may be
supposed that epidemics would be common. It has been suggested that these
variations could be due to marked differences in the distribution of HLA antigens
among some ethnic groups (Honeyman and Menser, 1974) and that ethnicity
may be a significant factor in the epidemiology of rubella. Satpathy (1989)
showed that in and around New Delhi there has been a 20% drop in immunity in
the young female population over the last 20 years. The reasons for this are
unclear but may be because some of the population is now immunised thus
making herd immunity less likely.
In south India there is no published seroepidemiological data on rubella susceptibility or on the incidence of CAR. Evidence that there may be a problem in this area comes from a report by Gray (1989) who noted that up to 29% of children at a deaf school in Madras had ophthalmic signs of CAR. John and Ponnuraj (1994) have also reported localised outbreaks of rubella and CAR around Vellore.

1.4.5 Clinical Manifestations of Congenitally Acquired Rubella Related to Gestational Age at Time of Maternal Infection.

Rubella is generally a mild disease with few complications. However, when acquired in the first 12 weeks of pregnancy, it results in congenital infection associated with one or more severe defects in 80-90% of cases. When maternal infection occurs between 13 and 20 weeks, the risk of congenital anomalies declines to about 17%; in some cases, there is serological evidence of infection, but no virus is excreted and no anomalies occur.

The virus passes through the placenta to infect the foetus at the viraemia stage of the disease just before the mother develops a rash. The foetus is infected before its immune system has developed and so there is no inflammatory response mounted to the infection. The virus firstly inhibits cell growth of all living cells, and secondly it causes tissue necrosis. It is the virus and not the immune system that damages the body tissues.
The severity of the infection is determined by the stage of development that the foetus has reached at the time the mother contracts the disease. If the foetus is affected in the first trimester there is a 75% chance that it will have severe anomalies, a 20% chance that it will naturally abort and a 20% chance that it will die within the first four weeks of life (Banatvala and Best, 1990). If the mother contracts rubella after the first trimester the risk of serious harm to the foetus greatly diminishes although up to 70% may have some degree of deafness if infection occurs before 16 weeks (Ueda et al. 1979). After 20 weeks gestation the foetus is protected from the effects of the virus by its own immune system.
1.4.6 Clinical Manifestations Of Congenitally Acquired Rubella

In the first eight weeks during the critical phase of organogenesis, cardiac and eye defects are likely (Givens et al. 1993; Kaplan et al. 1990; Romano et al. 1979; Geltzer et al. 1967).

Ocular manifestations

The eye can be affected in a number of ways:

- **Cataract** The cataract is typically nuclear and pearly white with indistinct margins. There is an equatorial rim of normal cortical fibres which is of variable size and the lens is spherophakic. The lens capsule appears completely normal (Zimmerman, 1965). The majority of cataracts are bilateral (5:1) and are usually present at birth but may develop in the first few weeks.

- **Cornea** The cornea is often hazy at birth which may be due to raised intraocular pressure or to decompensation of the corneal endothelium from a direct viral effect (Zimmerman, 1968).

- **Microphthalmos** This is associated with cataract and only rarely occurs on its own.

- **Glaucoma** Congenital glaucoma may occur in up to 25% of cases of CAR. Sears (1967) reviewed 150 neonates with CAR and glaucoma. He concluded that glaucoma may be related to abnormal anterior segment development, necrosis of the angle structures or to deposition of cellular debris over the trabecular endothelium.

- **Uveitis** Uveitis is nearly always present (Zimmerman, 1968) and there is sector atrophy and necrosis of the iris stroma. The pupil does not dilate because the iris muscles atrophy.
Retinopathy. Pigmentary retinopathy occurs in up to 60% of cases of CAR (Collis and Cohen, 1970; Menser et al. 1967a). It is not by itself a cause of visual failure but can be associated with development of sub-retinal neovascular membranes which may begin to appear after 10 years or more (Arnold et al. 1994; Deutman and Grizzard, 1978; Frank and Purnell, 1978). Gregg (1946) provided a colourful description of rubella retinitis: "It was like a piece of coarse Scotch tweed used for a sports coat over which pepper had been thrown." A typical finding is widespread pigment deposits, usually of greatest density in the macula. Sometimes the pigment has a spicule like form similar to that found in retinitis pigmentosa.

Diabetic retinopathy. More than 30% of children with CAR develop diabetes mellitus and they appear to be at greater risk of developing diabetic retinopathy than the normal diabetic population (Givens et al. 1993).
Figure 14 Ocular manifestations of rubella.

Rubella cataract (nuclear, pearly white with indistinct margins)  (Study no 323)
Figure 14  Ocular manifestations of rubella.
Cloudy cornea, cataract, microphthalmos  (Study no 215)
Non ocular manifestations

Cardiac

The cardiac defects that commonly occur are; patent ductus arteriosus (PDA), proximal valvular or peripheral pulmonary artery stenosis (PAS), and ventricular septal defect (VSD) (Cooper and Krugman, 1967). Other rarer manifestations include neonatal myocarditis and damage to the intima of renal and pulmonary arteries.

Deafness

Hearing loss follows destruction of the organ of Corti (Seller et al. 1981). Central auditory impairment may also occur. Hearing loss, which can be unilateral or bilateral may sometimes be the only rubella induced congenital anomaly (Cooper, 1969).

Other

The characteristic morbilliform rash observed in adults is seen in 15% of infants, and there may be hepatosplenomegaly, jaundice, anaemia, thrombocytopenia, pneumonitis, and genitourinary defects. Rubella panencephalitis is rare and tends to occur between the ages of 8-20 years. It is postulated to be immune complex mediated or by virus mediated autoreactivity to brain antigens (Martin et al. 1989).
Table 13 Clinical features associated with congenitally acquired rubella

<table>
<thead>
<tr>
<th>Transient</th>
<th>Common</th>
<th>Uncommon</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low birth weight</td>
<td>Cloudy cornea</td>
</tr>
<tr>
<td></td>
<td>Thrombocytopenia</td>
<td>Hepatitis</td>
</tr>
<tr>
<td></td>
<td>Hepatosplenomegaly</td>
<td>Generalised lymphadenopathy</td>
</tr>
<tr>
<td></td>
<td>Bone lesions</td>
<td>Haemolytic anaemia</td>
</tr>
<tr>
<td></td>
<td>Meningoencephalitis</td>
<td>Pneumonitis</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Developmental</td>
<td>Sensorineural deafness</td>
<td>Myopia</td>
</tr>
<tr>
<td></td>
<td>Pulmonary stenosis</td>
<td>Thyroiditis</td>
</tr>
<tr>
<td></td>
<td>Mental retardation</td>
<td>Hypothyroidism</td>
</tr>
<tr>
<td></td>
<td>Diabetes mellitus</td>
<td>Growth hormone deficiency</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Permanent</td>
<td>Sensorineural deafness</td>
<td>Glaucoma</td>
</tr>
<tr>
<td></td>
<td>Pulmonary stenosis</td>
<td>Thyroid disease</td>
</tr>
<tr>
<td></td>
<td>Patent ductus arteriosus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ventricular septal defect</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cataract</td>
<td>Myocarditis</td>
</tr>
<tr>
<td></td>
<td>Retinopathy</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Microphthalmia</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Microcephaly</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Psychomotor retardation</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Diabetes mellitus</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Inguinal hernia</td>
<td></td>
</tr>
</tbody>
</table>

1.4.7 Virological Diagnosis Of Congenitally Acquired Rubella

In India and other developing countries there is a need to determine;

i. the incidence of CAR and

ii. the potential risk to pregnant mothers of becoming infected with rubella.

Without this information it is not possible to undertake cost-benefit analysis of a rubella vaccination strategy. Part of the reason for the paucity of epidemiological data on rubella infection and CAR from the developing world has been the limited access to reliable and simple diagnostic tests.
A diagnosis of congenitally acquired rubella can be established by:

i. detection of rubella specific IgM in serum samples obtained in early infancy (Cradock-Watson, 1991).

ii. detection of persistent rubella IgG antibody in the infant, i.e. the presence of antibodies at a time beyond which maternal antibodies are usually no longer detected (approximately 6 months of age).

iii. isolation of rubella virus from the infant during early infancy (e.g. cataractous lens) (Cotlier et al. 1966).

Figure 15 illustrates the pattern of antibody responses in infancy in congenitally acquired rubella.

*Figure 15 Immune responses in congenitally acquired rubella*
(From Hermann (1979))
At birth, both maternally derived specific IgG antibodies and specific IgM and IgG synthesised in utero by the fetus are present. The detection of rubella specific IgM in cord, neonatal or infant sera by an IgM antibody capture assay has been the method of choice for the diagnosis of congenitally acquired rubella (Thomas et al. 1993). If other IgM assays are used, rubella specific IgM may not always be detected at birth. Specific IgM has been detected in all symptomatic babies up to the age of 3 months, in 90% of infants aged 3-6 months, but in fewer than 50% of infants aged 6-12 months and only occasionally in children over one year old (Cradock-Watson, 1991). The absence of specific IgM by IgM antibody capture assays in the neonatal period virtually excludes CAR.

The detection of specific IgG may be of value for the diagnosis of congenital infection when tests for specific IgM have not been conducted in early infancy. Since rubella is uncommon under the age of 1 year, specific IgG detected between the ages of 6-18 months may be indicative of congenital infection. Thomas et al (1993) have demonstrated that the maturation of the immune response to the rubella virus is abnormally slow in congenital rubella cases especially the development of high avidity specific IgG. They conclude that avidity studies may permit serological confirmation of CAR for longer than is present with other tests and this may prove useful in future retrospective studies.

Isolation of rubella virus from the cataractous lens of infants with CAR was first reported by Cotlier et al (1966). Although virus isolation attempts have not always been successful (Murphy et al. 1967; Scheie et al. 1967; Kanra and Firat, 1979), rubella virus has been isolated from lens material obtained from children up to three years of age (Menser et al. 1967b). Rubella virus isolation is
time consuming, technically demanding and therefore available in few laboratories world-wide. An additional problem is that rubella is a labile virus and there is little chance of isolating virus from specimens which have been in transit at ambient temperatures for more than 72 hours (Bosma et al. 1995).

1.4.8 Prevention of Congenitally Acquired Rubella

If the introduction of rubella vaccine is contemplated, the local seroepidemiology must be known. There are two alternative immunisation strategies:

1. Immunise females with rubella vaccine before child-bearing age. The aim is to protect at risk individuals who may not have acquired natural immunity through rubella infection in childhood.

2. Immunise all children at 9 months of age in order to obtain “herd immunity” and so eliminate epidemics of the disease. A coverage rate of at least 90% must be attained every year to prevent an epidemic. If the coverage rate is not maintained and an epidemic occurs the large number of susceptible child-bearing women in the community would then be at risk of acquiring rubella while pregnant with a resultant epidemic of cases of CAR.

In India at the present time there is no official program of rubella vaccination (Ponnuraj et al, 1991; Samuel and John, 1996), although measles immunisation is now routinely given at nine months of age with an estimated uptake of more than 60% of the target population. Rubella is a relatively labile virus and failure to follow the manufacturer’s storage instructions may result in its inactivation. A small proportion of vaccinees, about 5% who fail to sero-convert after vaccination usually respond satisfactorily when revaccinated.
1.5 The Management Of Bilateral Infantile Cataracts

1.5.1 Introduction

The timing and techniques for removing cataracts in infants has greatly changed over the last twenty years. The work by Wiesel and Hubel (1963) and later by Von Noorden (1979) made ophthalmologists aware of the importance of amblyopia in the management of visual disorders in childhood. Amblyopia implies a loss of vision that occurs as a result of visual deprivation during a sensitive period of development of the visual system. Ikeda and Wright (1974) showed that even a small amount of defocusing was sufficient to cause profound neurophysiological effects leading to amblyopia. If an infant does not have a focused image on the retina throughout much of the waking day due to inadequately corrected aphakia or to a lens opacity it is likely that the vision will be permanently reduced by the ensuing amblyopia. Elston and Timms (1992) suggest that there may be a latent period of up to 6 weeks after the child is born when it is relatively resistant to amblyopia. Greater understanding of the important role of amblyopia in the visual outcome after childhood cataract removal has meant that surgical intervention is now recommended earlier. As recently as the 1970's, it was recommended that surgery be deferred until an infant was 3-6 months of age (Sheppard and Crawford, 1973). If a child develops bilateral deprivation amblyopia, nystagmus will usually appear between 2 and 3 months of age. The nystagmus indicates that the opportunity for developing the fixation reflex has probably passed. The key to comprehending the appropriate timing of treatment for congenital cataracts is knowledge of the
development of the fixation reflex. It is not present at birth. The cellular, axonal and synaptic connections between the retina, geniculate bodies and cortex that serve this reflex become established during the first three months of life. If the reflex is not established during this critical period, it never will be and the child will have profound deprivation amblyopia. Taylor et al (1979) observing patients with congenital or acquired cataracts, deduced that susceptibility to deprivation amblyopia decreased logarithmically with age. They also noted that provided optical correction was started early, deprivation from birth was more readily reversed in infants treated before they were 4 months old. Intervention after the infants were 6 months of age produced uniformly poor results. In summary the combined work of Taylor and later Elston suggested that the critical period was between 6 weeks and 4 months, the first six weeks of life representing a latent period for binocular development. Therefore surgery and aphakic correction should ideally be accomplished between 4-8 weeks, with little likely benefit gained by earlier intervention.

1.5.2 Pre Operative Assessment

Most children with cataract can be categorised into those who are obviously candidates for surgery and subsequent treatment and those who are not. Children who are borderline must be assessed by a variety of techniques. Observation of the child’s fixation behaviour and in particular the presence of unsteady fixation and frank nystagmus are indications that a child is unable to see clearly. When possible behavioural observation can be backed up with preferential looking tests and visually evoked cortical responses. The traditional
technique of assessing the clarity with which the fundus can be viewed by ophthalmoscopy is notoriously unreliable.

1.5.3 Surgical Technique

Different surgical techniques have been advocated in the past. Because of the high complication rates many are of historic interest only. Optical iridectomy is probably the oldest technique and was useful if the cataract was centrally placed. Needling, linear extraction and intracapsular extraction are commonly associated with serious intra and post-operative complications. Scheie (1960) reintroduced the aspiration technique using an operating microscope and the complication rate fell dramatically. For complete cataracts he recommended aspirating the lens cortex as a single procedure. One or more further procedures were often required to remove the opacified posterior capsule (Parks and Hiles, 1967). For partial cataracts he recommended a two stage procedure, an initial needling of the anterior capsule followed by aspiration of the cortex several days later.

Today there are two basic choices of surgical technique with a number of possible variations.

1. Extracapsular cataract extraction (aspiration) or phakoemulsification

The technique involves removing part of the anterior capsule and aspirating the lens material with a specialised suction cannula or a phakoemulsification machine. Aspiration is a relatively safe and simple technique but leaves behind the posterior capsule. In children the posterior capsule tends to rapidly opacify either by renewed growth of lens fibres or from fibroblasts that originate in and around the equator of the capsule. A further
procedure to clear this area is necessary to prevent amblyopia developing. The opaque posterior capsule also makes accurate refraction difficult. Methods to remove at least some of the posterior capsule at surgery include:

a) performing a primary posterior capsulotomy by using a bent needle to create a linear or circular tear in the capsule while the anterior chamber remains filled with air.

b) doing a posterior capsulorrhexis which may be combined with a partial anterior vitrectomy (Gimbel, 1994)

c) doing a limited anterior vitrectomy and posterior capsulectomy with a lensectomy probe after completing aspiration. (Douvas, 1981)

d) doing a YAG capsulotomy at the end of the aspiration while the child remains anaesthetised.

2. Lensectomy

By this method a vitrectomy machine is used to remove the entire lens including most of the anterior and posterior capsule. Since the vitreous body is attached to the posterior capsule in childhood, it is inevitable that the anterior vitreous is damaged and an anterior vitrectomy is necessary. The approach to the lens can be made through the pars plana, pars plicata or limbus (Peyman et al. 1981). An anterior approach is less likely to damage the retina but makes cutting the lens material under the point of entry more difficult. If the lensectomy probe is introduced through a peripheral iridectomy, this area of lens becomes more accessible. A key advantage of lensectomy is that it immediately produces a clear pupillary area and makes secondary opacification unlikely. Taylor (1981)
did not have to perform any discissions in 23 eyes following lensectomy, whereas 32 reoperations were required in 28 eyes following lens aspiration alone. Retinoscopy and accurate refraction are made easy and optimum optical correction may mean that amblyopia is less likely to develop. Lensectomy equipment is necessarily expensive and requires skill and experience to use it correctly.

The problem of amblyopia developing in the unoperated eye and complications associated with anaesthesia have prompted suggestions that both eyes could be operated on at the same time (Guo et al. 1990). Others caution against simultaneous surgery after reports of endophthalmitis following cataract removal (Good et al. 1990). There have been no reports from the developing world on the relative merits of simultaneous surgery. In particular the risk of paediatric anaesthesia, often with few facilities for monitoring vital function must be balanced against the risk of blinding endophthalmitis.

1.5.4 Complications Of Surgery

The risk of complications developing in infant eyes after cataract surgery is higher than that in adult eyes.

Per-operative Complications

Insufficient removal of cortical material This is a problem particularly with aspiration techniques and makes posterior capsule opacification more likely as well as post operative inflammation.

Iris damage May be a problem with the lensectomy procedure, which occurs when the probe catches the iris.
Loss of lens material into vitreous. This can occur during lensectomy when the posterior capsule is broken before the cortex has been totally cleared.

Vitreous attachments to entry site. This may be a problem in any procedure after the vitreous has been disturbed and makes epithelial downgrowth and infection more likely.

Post operative Complications

1. Amblyopia

Amblyopia is the greatest threat to vision following infantile cataract surgery. It occurs because the retina receives a defocused image during the critical period of visual development, and is associated with neuroanatomical changes in the lateral geniculate nucleus (Lambert and Boothe, 1994).

2. Glaucoma

Glaucoma is one of the most common complications of infantile cataract surgery, with a prevalence as high as 24%. This may be due to angle closure in which case it occurs soon after surgery, or if it is open angle it may develop insidiously, often many years after surgery.

Most of the early descriptions implicated pupil block with angle closure as the basic mechanism (Fox, 1936). This can occur after a lensectomy if the anterior vitrectomy is insufficient, or following an aspiration if the posterior capsule is ruptured. In both situations the vitreous moves forward into the anterior chamber blocking the pupil as it does so. Fibrin covering the pupil in the immediate post operative period may also cause pupil block glaucoma. Chronic
angle closure glaucoma has been noted to occur less frequently after a lensectomy than after a lens aspiration (Asrani and Wilensky, 1995).

Chandler (1965) described several “quite exceptional cases” of open angle glaucoma following multiple surgical procedures on eyes with congenital cataract. Later Phelps and Arafat (1977) described eighteen patients who developed open angle glaucoma between 2 and 45 years after cataract surgery performed during infancy. They suggested that cataract and glaucoma might either be a manifestation of a single ocular syndrome or that the glaucoma developed as a result of the surgery. More recently Simon et al (1991) described a series in which 8 of 34 eyes (24%) developed open angle glaucoma over a follow up period of 69-105 months (mean interval 6.8 years). The study was retrospective and only half the children asked to attend follow up did so. No efforts were made to trace children that failed to attend. A single surgeon and single operative technique were used (limbal lensectomy with anterior vitrectomy) but no standardised preoperative assessment details were available. They concluded that open angle glaucoma was a significant complication and that the risk increased 5 years or more after surgery.

Chrousos et al (1984) looked retrospectively over 15 years and reported that 24 of 338 (6%) eyes developed glaucoma after a mean follow up of 41

<table>
<thead>
<tr>
<th>Author</th>
<th>Open angle (%)</th>
<th>Closed angle (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keech (1989)</td>
<td>62</td>
<td>38</td>
</tr>
<tr>
<td>Robb (1992b)</td>
<td>80</td>
<td>20</td>
</tr>
<tr>
<td>Mills (1994)</td>
<td>74</td>
<td>26</td>
</tr>
<tr>
<td>Simon (1991)</td>
<td>94</td>
<td>6</td>
</tr>
<tr>
<td>Asrani (1995)</td>
<td>80</td>
<td>20</td>
</tr>
</tbody>
</table>
months. The operations had been performed by different surgeons using different techniques and in all cases the eye had undergone "at least one or more secondary membrane procedure". Munoz (1995) reported a single case of bilateral open angle glaucoma developing in a child with bilateral hereditary cataract soon after pars plicata lensectomies. They compared the outcome with the child's mother who had bilateral aspirations for similar morphological cataracts when she was 18 months old but did not develop glaucoma. It was concluded that the difference was because certain cataracts are predisposed to develop glaucoma. They did not consider whether the age at the time of surgery or the type of procedure may be significant factors.

There is no doubt that open angle glaucoma is a significant cause of visual morbidity following congenital cataract extraction and that it may develop many years after surgery. However the mechanism for it is unknown as are the factors which may influence it. Gonioscopy of these eyes generally reveals a deep anterior chamber, increased pigmentation of the trabecular meshwork, and the iris inserting into the posterior aspect of the trabecular meshwork (Asrani and Wilensky, 1995; Walton, 1995; Phelps and Arafat, 1977). Peripheral anterior synechiae are usually confined to the area of the surgical incision.

In support of a causal relationship for infantile cataract surgery and the development of open angle glaucoma, Simon (1991) noted that glaucoma developed only in the eye that underwent cataract surgery in a child with bilateral cataracts. Open angle glaucoma appears to occur with equal frequency after lens aspiration or lensectomy (Mills and Robb, 1994; Chrousos et al. 1984). Possible risk factors for open angle glaucoma are microcornea and surgery at an early age (Egbert et al. 1995; Keech et al. 1989; Parks et al. 1993). So far no
randomised clinical trials comparing surgical techniques and age at surgery on the incidence of open angle glaucoma have been undertaken. The randomised clinical trial described in this thesis was partly designed with this in mind.

Table 15 Open angle glaucoma complicating congenital cataract surgery

<table>
<thead>
<tr>
<th>Type of surgery</th>
<th>First Author</th>
<th>No. eyes in series</th>
<th>No. eyes developing glaucoma</th>
<th>Mean follow up (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspiration</td>
<td>Chrousos (1984)</td>
<td>338</td>
<td>24 (6%)</td>
<td>5.5</td>
</tr>
<tr>
<td></td>
<td>Keech (1989)</td>
<td>20</td>
<td>3 (15%)</td>
<td>3.6</td>
</tr>
<tr>
<td></td>
<td>Robb (1992b)</td>
<td>58</td>
<td>11 (19%)</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>Mills (1994)</td>
<td>125</td>
<td>14 (11%)</td>
<td>7.4</td>
</tr>
<tr>
<td>Lensectomy</td>
<td>Chrousos (1984)</td>
<td>54</td>
<td>0</td>
<td>2.1</td>
</tr>
<tr>
<td></td>
<td>Simon (1991)</td>
<td>34</td>
<td>8 (24%)</td>
<td>6.8</td>
</tr>
<tr>
<td></td>
<td>Keech (1989)</td>
<td>105</td>
<td>5 (5%)</td>
<td>3.6</td>
</tr>
<tr>
<td></td>
<td>Egbert (1995)</td>
<td>84</td>
<td>6 (7%)</td>
<td>-</td>
</tr>
</tbody>
</table>

The diagnosis of glaucoma in a child may be difficult to establish as they lack the clinical signs of congenital glaucoma such as buphthalmos and the IOP is often difficult to measure. Egbert (1995) noted that an excessive loss of hyperopia was often a sign of glaucoma in children following cataract surgery. It can be notoriously difficult to control the IOP topically or with surgery (Munoz et al. 1995).

3. Posterior Capsule Opacification and Secondary Membranes

Posterior capsule opacification following extracapsular cataract surgery is nearly universal in infantile eyes if the posterior capsule is left intact. It is a manifestation of migration of lens epithelial cells onto the posterior capsule and
often occurs within a few months of surgery. Collagen production by these epithelial cells produces a white fibrotic opacity (McDonnell et al. 1984). In children the rate of opacification is much higher than in adults presumably because the rate of cell turnover is higher. Aspiration techniques that leave the posterior capsule intact lead to an extremely high incidence of secondary membranes (France, 1984). In addition to requiring further general anaesthetics and repeated operations, the delay in anti-amblyopia therapy contributes to the poor visual outcome.

Table 16 summarises the results from a number of operative series. The aspiration technique leaving behind the posterior capsule results in the highest rate of secondary membranes (40-75%). However Chrousos (1984) analysed 392 consecutive childhood cataract aspiration procedures with a mean follow up of 5.5 years and showed that even after a small posterior capsulotomy that leaves the vitreous intact up to 11% may re-opacify. Caputo (1990) noted that 3 of 76 eyes which had a small posterior capsulotomy had significant central opacification within 12 months. Morgan and Karciglu (1987) reported that 3 out of 4 eyes that had a lensectomy and limited anterior vitrectomy developed membrane opacification over the vitreous face within six months of surgery.
Table 16 Secondary membranes complicating infantile cataract surgery

<table>
<thead>
<tr>
<th>Type of surgery</th>
<th>First author</th>
<th>No. eyes in series</th>
<th>No. eyes developing secondary membranes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Aspiration alone</strong></td>
<td>Chrousos (1984)</td>
<td>304</td>
<td>189 (62%)</td>
</tr>
<tr>
<td></td>
<td>France (1984)</td>
<td>77</td>
<td>29 (47%)</td>
</tr>
<tr>
<td></td>
<td>Taylor (1981)</td>
<td>28</td>
<td>19 (68%)</td>
</tr>
<tr>
<td></td>
<td>Parks (1967)</td>
<td>52</td>
<td>38 (73%)</td>
</tr>
<tr>
<td></td>
<td>Keech (1989)</td>
<td>20</td>
<td>15 (75%)</td>
</tr>
<tr>
<td><strong>Aspiration and primary capsulotomy</strong></td>
<td>Chrousos (1984)</td>
<td>34</td>
<td>4 (11.7%)</td>
</tr>
<tr>
<td></td>
<td>Caputo (1990)</td>
<td>76</td>
<td>3 (4%)</td>
</tr>
<tr>
<td><strong>Lensectomy</strong></td>
<td>Chrousos (1984)</td>
<td>54</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Taylor (1981)</td>
<td>23</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Green (1990)</td>
<td>52</td>
<td>6 (11%)</td>
</tr>
<tr>
<td></td>
<td>Keech (1989)</td>
<td>105</td>
<td>10 (11%)</td>
</tr>
</tbody>
</table>

4. Retinal Detachment

Retinal detachment is a well recognised and usually a late complication of infantile cataract surgery. Occasionally detachments occur within a few months of surgery presumably related to vitreous traction exerted during the procedure. However most detachments occur many years after surgery with an average delay of 20 to 30 years (Toyofuku et al. 1980; Jagger et al. 1983). Because of this delay, the overall incidence of this complication is probably an underestimate given the relatively short term follow up of children (Kanski et al. 1974)(Table 17). Shapland (1934) estimated that the real incidence may be closer to 10%.
Table 17 Retinal detachment complicating congenital cataract surgery

<table>
<thead>
<tr>
<th>Type of surgery</th>
<th>First Author</th>
<th>No. eyes in series</th>
<th>No. eyes developing retinal detachment</th>
<th>Mean follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspiration</td>
<td>Keech (1989)</td>
<td>20</td>
<td>1 (5%)</td>
<td>3 years</td>
</tr>
<tr>
<td></td>
<td>Chrousos (1984)</td>
<td>338</td>
<td>5 (1.5%)</td>
<td>6 years</td>
</tr>
<tr>
<td>Lensectomy</td>
<td>Chrousos (1984)</td>
<td>54</td>
<td>1 (1.8%)</td>
<td>2 years</td>
</tr>
<tr>
<td></td>
<td>Keech (1989)</td>
<td>105</td>
<td>1 (1%)</td>
<td>3 years</td>
</tr>
</tbody>
</table>

The retinal detachments are usually rhegmatogenous secondary to round holes along the posterior vitreous base. Many eyes also have vitreoretinal changes indicative of traction on the peripheral retina which probably contributes to hole formation. High myopia (>6 Dioptres) and reoperations have been reported to increase the risk of retinal detachment (Robb and Petersen, 1992b; Keech et al. 1989).

The question that will remain unanswered for some years is whether lensectomy with anterior vitrectomy will result in a higher or lower incidence of retinal detachment (Taylor, 1981). While a lensectomy is associated with a lower incidence of re-operations (Chrousos et al. 1984), the addition of an anterior vitrectomy hastens the development of a posterior vitreous detachment, which may increase the risk of a retinal detachment.

Treatment of retinal detachments following childhood cataract surgery is particularly difficult because there are often multiple breaks, and the lens remnants and miosed pupil interfere with the view (Jagger et al. 1983).
5. Cystoid Macular Oedema

Cystoid macular oedema is probably a rare complication following cataract surgery in infancy but because of the difficulty of performing fluorescein angiography at this age, it is rarely evaluated.

Table 18  Cystoid Macular Oedema complicating congenital cataract surgery

<table>
<thead>
<tr>
<th>Type of Surgery</th>
<th>First Author</th>
<th>No. of eyes in series</th>
<th>No. of eyes developing CMO</th>
<th>Age at surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspiration</td>
<td>Hoyt (1982)</td>
<td>27</td>
<td>1(3.7%)</td>
<td>3/52-20/12</td>
</tr>
<tr>
<td></td>
<td>Poer (1981)</td>
<td>25</td>
<td>0</td>
<td>7/12-14 years</td>
</tr>
<tr>
<td>Lensectomy</td>
<td>Hoyt (1982)</td>
<td>27</td>
<td>10(37%)</td>
<td>3/52-20/12</td>
</tr>
<tr>
<td></td>
<td>Peyman (1981)</td>
<td>32</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>Morgan (1984)</td>
<td>10</td>
<td>0</td>
<td>5/12-7 years</td>
</tr>
<tr>
<td></td>
<td>Pinchoff (1988)</td>
<td>12</td>
<td>0</td>
<td>8/52-36/52</td>
</tr>
<tr>
<td></td>
<td>Gilbard (1983)</td>
<td>25</td>
<td>1(4%)</td>
<td>-</td>
</tr>
</tbody>
</table>

Hoyt et al (1982) observed that cystoid macular oedema (CMO) occurred in 10 of 27 eyes undergoing lensectomy/vitrectomy procedures and in 1 of 27 eyes undergoing aspiration. Unfortunately the presence of CMO was not documented photographically and its appearance was atypical. This report contradicted the work of Poer et al (1981) who found no definite case of CMO amongst 25 eyes of 18 children. Others (Pinchoff et al. 1988; Gilbard et al. 1983) have also failed to find evidence of CMO using similar diagnostic criteria and the same surgical technique as Hoyt. Pinchoff (1988) concluded that CMO was no more likely to occur with one method than another, and Parks (1984)
wrote that even if CMO did occur “the best visual acuity in patients with intractable amblyopia is usually far worse than the best acuity in recovered clinically significant CMO”.

Table 19 Summary of Advantages and Disadvantages of Surgical Techniques

<table>
<thead>
<tr>
<th></th>
<th>Lensectomy</th>
<th>Aspiration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Advantages</strong></td>
<td>No capsule opacification</td>
<td>Cheap</td>
</tr>
<tr>
<td></td>
<td>Accurate refraction possible</td>
<td>Relatively simple technique</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Vitreous need not be disturbed</td>
</tr>
<tr>
<td><strong>Disadvantages</strong></td>
<td>Expensive</td>
<td>Posterior capsule opacification</td>
</tr>
<tr>
<td></td>
<td>Technically difficult</td>
<td></td>
</tr>
<tr>
<td></td>
<td>? Increased risk of retinal detachment, glaucoma, cystoid macular oedema</td>
<td></td>
</tr>
</tbody>
</table>

1.5.5 Visual Rehabilitation

In order to visually rehabilitate an infantile eye after cataract extraction, the eye must be focused optically and amblyopia treated.

**Optical correction**

Correction of paediatric aphakia can be accomplished with spectacles, contact lenses (Levin et al. 1988; Amaya et al. 1990), IOL implants or epikeratophakia (Kelley et al. 1986). A recent review by Morgan (1993) stated that “most clinicians agree that contact lenses and aphakic spectacles are the first and second choices, respectively for children who have bilateral cataracts and that contact lenses are the best option for unilateral aphakia; however disagreement arises when considering a patient who is contact lens non compliant or is a poor candidate because of socio-economic conditions.”
In infants whichever method is chosen, it is important to ensure a well focused image on the retina as soon as possible. Aphakic children younger than 3 years may be provided with approximately 2 Dioptres of overcorrection to focus on near objects. The hypermetropia decreases rapidly in the first few years of life and needs regular refraction and repeat prescribing. When the child reaches school age, either bifocals (if spectacles are worn) or reading glasses over contact lenses will be necessary.

In India and other developing countries, contact lenses are not commonly used. The expense of replacing lenses together with the risks of infection, poor compliance and limited follow up restrict their use to children from well motivated and “wealthy” families in large cities. Epikeratophakia is not an option because the donor material is not available and as yet the equipment and infrastructure to create the lenticules are not available.

The choice in India is between spectacles and IOL’s. Both have advantages and disadvantages. For unilateral aphakia, spectacle correction is not possible because of the marked retinal image disparity (approx. 30%) that would result between the two eyes (Elsas, 1990). For bilateral aphakia, anisokonia is not a problem, however spectacles are an imperfect solution because of alterations in the peripheral field of vision, induced distortion and prismatic effects. In addition, obtaining stable centration with heavy glasses is difficult and the optical centre of the lens does not move with the eye.

The additional problem of compliance with aphakic glasses in the developing world is highlighted by Shrivasta (1988) who noted that 52% of patients in central India who could be traced following surgery were not wearing
aphakic spectacles either because they had never been prescribed (21%) or were lost or broken (79%).

**Intraocular lenses**

IOL implantation has increased in recent years and is rapidly becoming the preferred means of optical correction in older children (Wilson et al. 1994). There are four main reasons why IOL implantation in children has been viewed with considerable caution in the past (Hing et al. 1990; Masket, 1991).

1. The surgical technique is more difficult in children than in adults.

2. Infants have a higher proportion of post-operative complications as a result of the inflammatory and fibrotic responses. Wilson-Holt (1991) described a case of possible sympathetic ophthalmitis developing in a child after a secondary implant and Vajapee (1991) reported on 16 children who developed inflammatory pupil block glaucoma following posterior chamber IOL implantation.

3. The long term effects of PMMA (polymethylmetacrylate) in children’s eyes is not established.

4. Hypermetropia decreases markedly over the first 2 years of life, in most children and therefore the required full correction for aphakia at 3 months of age is likely to become markedly over-corrected 2 years later.

IOL’s are now being used in India. Gupta et al(1992) reported on complications and visual outcome on 22 eyes with IOL’s and recommended use of IOL’s despite the high complication rate; 18 eyes developed pupillary membranes and 2 developed pupil capture of the IOL. Vats (1993) claimed that 70% of eyes showed good visual recovery. Vasavada (1994) implanted IOL’s in 21 eyes of infants aged 2-8 months with unilateral and bilateral cataracts.
Although 20 eyes had stable IOL fixation, all except one child required further surgery to break synechiae or remove the posterior capsule.

Table 20 shows the complication rate from various series using IOL's in children. Visual acuity data has not been included because there is so much variation in the ages of children at surgery and the types of cataract included.

<table>
<thead>
<tr>
<th>First Author</th>
<th>No. eyes in series</th>
<th>Severe uveitis (%)</th>
<th>Pupil capture (%)</th>
<th>Post capsule Opacification (%)</th>
<th>Age at surgery (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gupta (1992)</td>
<td>22</td>
<td>22</td>
<td>9</td>
<td>27</td>
<td>3 - 11</td>
</tr>
<tr>
<td>Menezo (1994)</td>
<td>178</td>
<td>9</td>
<td>8</td>
<td>49</td>
<td>0.3 - 18</td>
</tr>
<tr>
<td>Vats (1993)</td>
<td>40</td>
<td>25</td>
<td>37</td>
<td>?</td>
<td>0.5 - 12</td>
</tr>
<tr>
<td>Markham (1992)</td>
<td>16</td>
<td>12</td>
<td>?</td>
<td>56</td>
<td>0.4 - 8</td>
</tr>
<tr>
<td>Koenig (1993)</td>
<td>8</td>
<td>?</td>
<td>?</td>
<td>37</td>
<td>4 - 17</td>
</tr>
<tr>
<td>Bienfait (1990)</td>
<td>23</td>
<td>0</td>
<td>9</td>
<td>83</td>
<td>0.4 - 11</td>
</tr>
<tr>
<td>Hiles (1984)</td>
<td>225</td>
<td>4</td>
<td>7</td>
<td>13</td>
<td>0.5 - 19</td>
</tr>
</tbody>
</table>

The clinical trial described in this thesis was limited to children with bilateral cataracts. Because both eyes are rendered aphakic image disparity is not a problem and therefore aphakic spectacles are an acceptable alternative to IOL's.

1.5.6 Visual Outcome

The visual outcome of eyes with infantile onset cataracts is dependent on many factors. These include:

Factors related to the patient -

- Age of onset
- Age at surgery
- Duration of opacity
Age at which the optical correction is initiated

Compliance with optical rehabilitation and occlusion

Other systemic anomalies

Factors related to the eye -

Laterality

Density

Other ocular anomalies

Complications of management

Although there are many papers on the visual outcome following surgery, it is difficult to compare results as many sources of bias exist. The management of cases varies greatly between studies; different occlusion protocols, variation of timing between surgery, different methods of acuity assessment (in particular using methods which underestimate amblyopia), different ways of presenting acuity data (e.g. best uniocular vision versus binocular vision), different managements of aphakia and varying inclusion and exclusion criteria. Table 21 and Table 22 show visual acuity results after surgery for bilateral cataracts for both complete and partial types of cataract. Unilateral cataract results are not discussed because of the profound effects of deprivation amblyopia on the affected eye if not managed within the first few weeks of life (Lloyd et al. 1995). Parks et al (1993) showed that cataract type was a good predictor of visual outcome but failed to indicate whether this was because of a close relationship between covariables since cataract type is linked to age at onset of opacity and age at surgery. He noted that lamellar and posterior lentiglobus cataracts were
associated with the best visual outcomes. Microphthalmos and nystagmus have been reported to be poor prognostic signs (Migdal, 1981; Gelbart et al. 1982).

Table 21 Visual outcome in incomplete bilateral congenital cataract

<table>
<thead>
<tr>
<th>First Author</th>
<th>No. eyes in study</th>
<th>Binocular Vision better than 6/18</th>
<th>Binocular Vision less than 6/60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Francois (1979)</td>
<td>167</td>
<td>70%</td>
<td>17%</td>
</tr>
<tr>
<td>Gelbart (1982)</td>
<td>48</td>
<td>60%</td>
<td>27%</td>
</tr>
<tr>
<td>Parks (1982)</td>
<td>32</td>
<td>100%</td>
<td>0%</td>
</tr>
<tr>
<td>Wright (1992)</td>
<td>44</td>
<td>73%</td>
<td>2%</td>
</tr>
<tr>
<td>Robb (1992a)</td>
<td>38</td>
<td>73%</td>
<td>18%</td>
</tr>
</tbody>
</table>

**Strabismus**

Strabismus occurs in a high percentage of children with either unilateral or bilateral cataracts. France and Frank (1984) reported that 40% of all children with cataract have strabismus preoperatively, whereas 71% have strabismus postoperatively. He noted that 83% of the children with congenital cataracts have an esotropia, whereas 69% of children with acquired cataracts have an exotropia. The timing of strabismus surgery remains controversial, Hiles and Sheridan (1977), recommended postponing strabismus surgery until there is a stable angle of alignment, whereas others have advocated early strabismus surgery to reduce the need for occlusion therapy.

**Nystagmus**

Nystagmus develops commonly in children with dense bilateral cataracts if treatment is delayed. If cataract surgery is performed within a month of the onset of nystagmus, the nystagmus will frequently resolve (Yagasaki et al. 1993). Nystagmus may occur after surgery for bilateral cataracts but immediate optical correction reduces the likelihood (Bradford et al. 1994).
In summary, those children operated on prior to eight weeks of age have the best visual results (Rogers et al. 1981; Lewis et al. 1995). Unfortunately as Jain (1983) reported, in India most children with infantile cataracts do not undergo surgery until they are one to five years of age, primarily due to a delay in diagnosis. They are therefore ultimately likely do worse. As many as one-quarter of children with bilateral infantile onset cataracts are legally blind even after treatment (Table 22).

Table 22 Visual outcome in total bilateral congenital cataract

<table>
<thead>
<tr>
<th>First Author</th>
<th>No. eyes in study</th>
<th>Binocular Vision better than 6/18</th>
<th>Binocular Vision less than 6/60</th>
</tr>
</thead>
<tbody>
<tr>
<td>Francois (1979)</td>
<td>100</td>
<td>25%</td>
<td>50%</td>
</tr>
<tr>
<td>Neumann (1993)</td>
<td>28</td>
<td>78%</td>
<td>0%</td>
</tr>
<tr>
<td>Bradford (1994)</td>
<td>46</td>
<td>43%</td>
<td>14%</td>
</tr>
<tr>
<td>Robb (1992a)</td>
<td>26</td>
<td>19%</td>
<td>11%</td>
</tr>
<tr>
<td>Lorenz (1991)</td>
<td>58</td>
<td>33%</td>
<td>25%</td>
</tr>
</tbody>
</table>

1.5.7 Summary

This introduction has aimed to describe the relevance of childhood blindness in the wider perspective of global blindness and to show that cataract remains an important cause. The aetiology of cataract has been reviewed and has highlighted the fact that causes vary between different population groups and in different geographic areas. The management of childhood cataract is not straightforward and surgery is only one stage in the child’s visual rehabilitation. This must be followed by adequate correction of aphakia, treatment of amblyopia and clinical follow up to pick up glaucoma and other complications. In India there is only limited available data on the causes, visual outcome and most appropriate management for childhood cataract.
CHAPTER TWO
The Aetiology of Childhood Cataract in South India

2.1 Introduction

2.2 Study Objectives

2.3 Patients and Methods

2.4 Results

2.4.1 Non-Traumatic Cataract
2.4.2 Hereditary Cataract
2.4.3 Secondary Cataract
2.4.4 Rubella Cataract
2.4.5 Cataract of Undetermined Cause
2.4.6 Traumatic Cataract
2.4.7 Reasons for Late Presentation
2.4.8 Advice by Health Professional

2.5 Discussion
2. CHAPTER TWO

The Aetiology of Childhood Cataract in South India

2.1 Introduction

In order to determine the principle aetiology and demography of childhood cataract in south India, an observational study with a case control element was carried out over a period of nine months at the Aravind Eye Hospital in 1993-4.

2.2 Study Objectives

1. To ascertain the aetiology of childhood cataract seen at the Aravind Eye Hospital.
2. To determine the proportion of causes of childhood cataract that might be potentially preventable.
3. To determine how long children with cataract delay their presentation to hospital and to ascertain the reasons why this may be so.
4. To document local beliefs and traditional practices with regard to childhood cataract and to determine whether these caused undue harm.

2.3 Patients and Methods

A total of 514 consecutive children aged 0-15 years with traumatic and non-traumatic cataract (sufficient to cause visual loss) presented to the paediatric eye clinic at the Aravind Eye Hospital over a nine month period in
1993-4. All of the children had a full ocular examination performed by one ophthalmologist (the author).

All parents were interviewed by a single trained interviewer using a standardised questionnaire in the local language.

Children in the non traumatic group and who were less than 1 year old had blood and saliva taken for determination of rubella specific IgM.

Other tests such as serum calcium, urinary reducing sugars and blood glucose were performed when clinically indicated.

**Entry criteria**

1. Age 0-15 years.
2. Cataract in one or both eyes affecting visual acuity (traumatic or non-traumatic).
3. First attendance at Aravind Hospital having had no previous hospital treatment for cataract.

**Interview and questionnaire**

Parents were interviewed by a single trained female Tamil interviewer using a standardised questionnaire translated into the two local languages, Tamil and Malayalam. The interviews took place in a quiet area away from the main clinic. Responses were recorded on the questionnaire and this was then handed on to the doctor performing the clinical examination. The interviewer spoke fluent Tamil and Malayalam and had been involved with other clinical studies previously. Interviewer bias was possible but was reduced by using a standardised interview form and using an interviewer who had been well trained and had previous experience.
Parents were asked questions about the child's ocular history, as well as about maternal illness during pregnancy, maternal drug ingestion, family history of cataract, and socio-economic and demographic information. This included questions about reasons for delayed attendance and whether other health professionals or village healers had been involved in the management. If parents where unavailable they were requested to attend at the next visit so that the questionnaire could be repeated. (Appendices)

The questionnaire was piloted before the study began on 30 children and their parents. Three of the questions about previous treatment by eye doctors and local healers were rephrased and four questions relating to social class were omitted from the questionnaire after the pilot study.

2.3.1 Clinical Examination

All of the children had a full ocular examination performed by one ophthalmologist (the author). Whenever possible children were examined on the slit lamp microscope and by direct and indirect ophthalmoscopy after pupil dilatation. Intraocular pressures were measured using the Keeler 2000 Pulsair Tonometer. Those children who appeared systemically unwell or who had any physical abnormalities were also examined by a paediatrician.

Parents and siblings of children with non traumatic cataract were examined on the slit lamp to assess them for evidence of hereditary cataract.

Children less than one year old with non-traumatic cataract had saliva samples collected to test for evidence of rubella specific IgM in the manner documented in Chapter 3. Blood samples to determine the levels of calcium
and glucose and urine for reducing sugars after a milk meal were taken and analysed only when clinically appropriate. B-scan ultrasonography was performed whenever it could help to determine the aetiology.

### 2.4 Results

Over nine months, a total of 514 consecutive children attending the paediatric eye clinic with cataract were enrolled into the study. Of the 514 children with cataract, 366 cataracts (71%) were non-traumatic (infantile) and 148 (29%) were caused by trauma. There were 326 boys and 188 girls. In this part of India for a number of cultural and social reasons boys are brought to hospital more readily than girls. This almost certainly reflects their position in society (gender selection bias) rather than the fact that cataract is commoner in boys (Brilliant et al. 1991).

Wherever possible parents were interviewed and if the cataract was non-traumatic they were examined on the slit lamp. Table 23 shows the number of parents, grandparents and other relatives interviewed.

*Table 23 Person interviewed with questionnaire*

<table>
<thead>
<tr>
<th>Person interviewed</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mother alone</td>
<td>44.5%</td>
</tr>
<tr>
<td>Both parents</td>
<td>33.1%</td>
</tr>
<tr>
<td>Father alone</td>
<td>11%</td>
</tr>
<tr>
<td>Grandparents only</td>
<td>3.9%</td>
</tr>
<tr>
<td>Uncle/ Aunt no parent</td>
<td>5.8%</td>
</tr>
<tr>
<td>No close relative</td>
<td>1.7%</td>
</tr>
</tbody>
</table>

In the analysis of pre-natal and perinatal events during pregnancy, the questionnaire data was excluded if the mother had not been interviewed.
Most children lived in Tamil Nadu but children also came from the neighbouring states of Kerala and Andra Pradesh (Figure 17).

The age of all children at the time of their first presentation is shown in Figure 18.
Table 24 compares these ages by cataract aetiology and shows that children with traumatic cataract tended to present later (80% after the age of 6 years) than those with non-traumatic cataract (45% after age 6 years). There was no significant difference in the age at presentation between the sexes.

**Table 24 Cataract aetiology by age of presentation**

<table>
<thead>
<tr>
<th>Age at presentation</th>
<th>Hereditary</th>
<th>Rubella</th>
<th>Trauma</th>
<th>Other/Unknown</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-12 months</td>
<td>18 (19%)</td>
<td>25 (50%)</td>
<td>1 (1%)</td>
<td>57 (26%)</td>
<td>101 (20%)</td>
</tr>
<tr>
<td>1- 5 years</td>
<td>28 (30%)</td>
<td>14 (28%)</td>
<td>29 (20%)</td>
<td>58 (26%)</td>
<td>129 (25%)</td>
</tr>
<tr>
<td>6- 15 years</td>
<td>47 (51%)</td>
<td>11 (22%)</td>
<td>118 (79%)</td>
<td>108 (48%)</td>
<td>284 (55%)</td>
</tr>
<tr>
<td>Total</td>
<td>93</td>
<td>50</td>
<td>148</td>
<td>223</td>
<td>514 (100%)</td>
</tr>
</tbody>
</table>
2.4.1 Non-Traumatic Cataract

In the group of children with non-traumatic cataract there was a predominance of males, 215 boys to 151 girls (3:2). There were nearly four times as many children with bilateral cataract as unilateral cataract (286:80) and of the 286 children with bilateral cataract at least 110 (38%) were truly congenital (from parent interview). Of the definite bilateral congenital cataracts, 21% presented before they were 3 months old, and 68% before the age of 1 year. The causes of all non-traumatic cataract both unilateral and bilateral are indicated in Table 25.

Table 25 Aetiology of non-traumatic cataract in 366 children in S. India by eye involvement

<table>
<thead>
<tr>
<th>Cause</th>
<th>Unilateral</th>
<th></th>
<th>Bilateral</th>
<th></th>
<th>Total</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Hereditary</td>
<td>6</td>
<td>1.6</td>
<td>87</td>
<td>23.8</td>
<td>93</td>
<td>25.4</td>
</tr>
<tr>
<td>Embryodysgenesis</td>
<td>10</td>
<td>2.7</td>
<td>44</td>
<td>12</td>
<td>54</td>
<td>14.8</td>
</tr>
<tr>
<td>Secondary</td>
<td>19</td>
<td>5.2</td>
<td>9</td>
<td>2.5</td>
<td>28</td>
<td>7.7</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
<td>0.5</td>
<td>1</td>
<td>0.3</td>
<td>3</td>
<td>0.8</td>
</tr>
<tr>
<td>Undetermined</td>
<td>43</td>
<td>11.7</td>
<td>145</td>
<td>39.6</td>
<td>188</td>
<td>51.4</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>80</strong></td>
<td></td>
<td><strong>286</strong></td>
<td></td>
<td><strong>366</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

The causes of bilateral cataract are shown in Figure 19. Over half the children (51%) had no cause determined after examination and investigations, 25% had hereditary cataract and a further 15% had a presumptive diagnosis of congenitally acquired rubella (CAR) based on clinical features, maternal history and serology where appropriate.
2.4.2 Hereditary Cataract

Autosomal dominant inheritance was diagnosed when there was a positive family history from interview or one of the parents was demonstrated to have congenital cataract on slit lamp examination or was aphakic from surgery performed during childhood. Of those parents who were examined and had evidence of congenital cataract, 50 (68%) had been previously unaware of the condition. A total of 80 children (22%) had autosomal dominant hereditary cataract and 92% of these were bilateral. The morphology of autosomal dominant cataract was variable; 40% were zonular (lamellar), 16% total, and 5% nuclear. The remainder were difficult to categorise with multiple but discrete areas of the lens being affected.
There was no case of unilateral lamellar cataract. Associated microphthalmos was present in seven (9%) of the children (14 eyes). Different morphological types of cataract were observed in the siblings of affected parents. In one case of a mother and dizygotic twins, the mother and one twin had bilateral lamellar cataracts and the other twin a unilateral total cataract.

Eight children (2%) had definite recessively inherited cataract, but recessive disease in general was difficult to diagnose because family history was often incomplete and siblings did not routinely attend the clinic. There was no significant difference (p=0.6) in the rates of consanguineous marriage between the parents of children who developed hereditary cataract (33%) and those that had cataract for some other reason (29%).

2.4.3 Secondary Cataract

Cataract due to other eye disease such as uveitis (8), PHPV(5), aniridia (3), posterior lenticus (3), and others (5) accounted for 7.7% of non-traumatic cataract. The syndromes of Hallermann-Streiff (2), Marfans (2), Down’s (2) were associated with cataract in 6 children (1.6%). One child had oculocutaneous albinism and there were 22 children (6%) who had CNS abnormalities manifesting as grossly delayed milestones or epilepsy. None of these children had evidence of congenital toxoplasmosis or viral disease.

2.4.4 Rubella Cataract

The cause of cataract in children less than one year old is shown in Table 26. The proportion of cataract of unknown origin remains similar but a greater proportion of children have congenitally acquired rubella.
Table 26 Aetiology of cataract in 101 infants (aged 0-12 months) in S. India by eye involvement

<table>
<thead>
<tr>
<th>Cause</th>
<th>Unilateral</th>
<th>Bilateral</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-traumatic</td>
<td>n</td>
<td>n</td>
<td>n</td>
</tr>
<tr>
<td>Hereditary</td>
<td>2</td>
<td>16</td>
<td>18</td>
</tr>
<tr>
<td>Congenitally acquired rubella</td>
<td>4</td>
<td>21</td>
<td>25</td>
</tr>
<tr>
<td>Embryodysgenesis (not CAR)</td>
<td>3</td>
<td>1</td>
<td>4</td>
</tr>
<tr>
<td>Secondary</td>
<td>4</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Undetermined</td>
<td>11</td>
<td>36</td>
<td>47</td>
</tr>
<tr>
<td>Traumatic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Trauma</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>25</strong></td>
<td><strong>76</strong></td>
<td><strong>101</strong></td>
</tr>
</tbody>
</table>

Table 27 Morphological characteristics of non-traumatic cataract in 100 infants under 1 year old

<table>
<thead>
<tr>
<th>Morphology</th>
<th>Rubella</th>
<th>Non rubella</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamellar</td>
<td>0</td>
<td>11</td>
<td>11</td>
</tr>
<tr>
<td>Total</td>
<td>0</td>
<td>39</td>
<td>39</td>
</tr>
<tr>
<td>Nuclear</td>
<td>25</td>
<td>5</td>
<td>30</td>
</tr>
<tr>
<td>Post Polar</td>
<td>0</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Mixed</td>
<td>0</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>25</strong></td>
<td><strong>75</strong></td>
<td><strong>100</strong></td>
</tr>
</tbody>
</table>

The morphological characteristics of cataracts in children under 1 year old with and without rubella are given in Table 27. In all cases of confirmed CAR the cataract appeared as a dense central nuclear opacity surrounded by a less dense cortical opacity with variable extension towards the periphery. Nuclear cataract in this group of children had a positive predictive value for CAR of 83%. Nuclear cataracts were much less common in the non rubella group (6.7%).
The causes of bilateral non-traumatic cataract in children less than 1 year old are illustrated graphically in Figure 20.

*Figure 20 Aetiology of bilateral non-traumatic cataract in 76 children under 1 year old*

2.4.5 Cataract of Undetermined Cause

The study was initially designed so that the children with traumatic cataract would act as the control group for all children with cataract of unknown aetiology. It was evident from the pilot study and reviewing old patient records that children with traumatic cataracts tended to be older than children with non-traumatic cataract. Preliminary analysis of the data from the pilot study revealed that all events in pregnancy were reported more in the unknown group and the hereditary group than in the traumatic group. The study was redesigned so that the control group was made up of children with infantile/congenital cataracts that were known to be hereditary.
In case-control studies interviews with patients or their relatives are often the major source of information on past exposure. Biased recall and poor memory may lead to inaccurate data. Some of the questions asked required a clear recall of events during pregnancy and for some mothers this was many pregnancies and many years ago. We were aware that this could be a source of recall bias with the older mothers having forgotten more episodes than the younger ones and therefore reporting all events in pregnancy less, and we tried to reduce this bias by using a control group of children of similar age. In this study it is quite possible that a mother who has a child with a congenital disorder (cataract of unknown aetiology) and is trying to recall past exposures to X-ray or drug ingestion may tend to over-estimate her exposure as compared with a woman who has given birth to a normal child. The occurrence of a congenital cataract may stimulate other family members to provide information to the mother regarding a family history of illness and exposure believed to be associated with the disease. In south India there is great stigma attached to the birth of a child with a physical defect, particularly a boy and the parents and relatives may try hard to find some external cause that may be responsible. Using hereditary cataract as the control group may reduce this type of error but these families are likely to be aware of the condition which contrasts with cataract of unknown origin. The ideal control group would have been children from the same village as the affected child. Unfortunately this was difficult to organise as the catchment area for children attending the clinic was too great and the study resources inadequate.

In the group of children with cataract of undetermined origin, insults to the fetus during pregnancy, either toxins or infections may be important. Seventy
four per cent of mothers of children under 1 year old with idiopathic cataract admitted taking some type of medicine during the pregnancy apart from iron supplements and vitamins but similarly 73% of mothers of the control group (children with hereditary cataract) also gave a positive history of medicine use.

In Table 28 odds ratios are presented comparing children with known hereditary cataract against those with cataract of unknown origin searching for possible aetiological factors. The limitations of this comparison have been discussed.

Mothers using abortifacients during pregnancy and the child being premature were associated with a slightly increased risk of having a cataract of unknown aetiology compared to children with hereditary cataract. Maternal illness at any time during pregnancy and the mother having severe diarrhoea during pregnancy did not appear to be risk factors for cataract in this analysis.

Table 28. Odds ratios for children with cataract of unknown aetiology compared with children with known hereditary cataract.

<table>
<thead>
<tr>
<th></th>
<th>Children with cataract of unknown aetiology (n=188)</th>
<th>Children with hereditary cataract (n=93)</th>
<th>Odds ratio</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mother used abortifacient in early pregnancy</td>
<td>11</td>
<td>2</td>
<td>2.83</td>
<td>0.6-18.9</td>
<td>0.17</td>
</tr>
<tr>
<td>Premature infant</td>
<td>18</td>
<td>4</td>
<td>2.36</td>
<td>0.72-8.51</td>
<td>0.12</td>
</tr>
<tr>
<td>Maternal fever during pregnancy</td>
<td>19</td>
<td>15</td>
<td>0.58</td>
<td>0.27-1.29</td>
<td>0.14</td>
</tr>
<tr>
<td>Any maternal illness during pregnancy</td>
<td>20</td>
<td>11</td>
<td>0.89</td>
<td>0.38-2.08</td>
<td>0.76</td>
</tr>
<tr>
<td>Mother having severe diarrhoea during pregnancy</td>
<td>11</td>
<td>6</td>
<td>0.9</td>
<td>0.3-2.84</td>
<td>0.84</td>
</tr>
</tbody>
</table>
2.4.6 Traumatic Cataract

The majority of children with traumatic cataract were boys (75%) and were from rural areas (75%). Penetrating injury was four times as common as blunt injury (121:27).

Trauma occurred most commonly while children were playing (91%), work related injuries were unusual (5%). Eighty per cent of traumatic cases of cataract occurred in children over the age of 5 years.

Figure 21 illustrates the different types of injury against the age of the child; injuries from thorn bushes increase with age and injuries from sharpened sticks, often from makeshift bow and arrows occurred more commonly after the age of 3 years.

![Figure 21 Aetiology of traumatic cataract by age](image)

<table>
<thead>
<tr>
<th>Age of children</th>
<th>Stick 0-20</th>
<th>Thorn 0-20</th>
<th>Firecracker 0-20</th>
<th>Other 0-20</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-3 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>12 (8)</td>
</tr>
<tr>
<td>4-6 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>28 (19)</td>
</tr>
<tr>
<td>7-9 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>44 (30)</td>
</tr>
<tr>
<td>10-12 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>44 (30)</td>
</tr>
<tr>
<td>13-15 years</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>20 (13)</td>
</tr>
<tr>
<td>Total</td>
<td>42 (28%)</td>
<td>31 (21%)</td>
<td>8 (5%)</td>
<td>67 (46%)</td>
<td>148</td>
</tr>
</tbody>
</table>
2.4.7 Reasons For Late Presentation

Parents of all children (traumatic and non-traumatic) were asked a series of questions about the timing of their visit to hospital and if it had been delayed what were the reasons for this.

The age at presentation for children with bilateral cataract was associated with the type of cataract, its severity and time of onset. The median age of first hospital visit for children with bilateral total or nuclear cataract was 24 months compared with 72 months for children with lamellar cataract.

*Figure 22. Age at presentation by type of cataract (Bilateral)*

The delay in attendance (time between parents noticing child’s visual problem and first hospital visit) for cataract was associated with the time taken to
reach hospital (>4 hours) p=0.032 but was not significantly related to whether they lived in the city or in rural areas (p=0.18). (Table 29, Table 30)

Table 29 Children with cataracts: delay in attendance against travel time

<table>
<thead>
<tr>
<th>Time required to travel to hospital</th>
<th>Early delay ≤ 3 months</th>
<th>Late delay &gt; 3 months</th>
<th>χ²</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 4 hours</td>
<td>44</td>
<td>61</td>
<td>4.61</td>
<td>0.03</td>
</tr>
<tr>
<td>&gt; 4 hours</td>
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Table 30 Children with cataracts: delay in attendance against urban / rural domicile

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Figure 23 shows the reasons for delayed presentation given by the parents of children with non-traumatic cataract. About one third said that they had been advised to delay attending and another third had insufficient money or time. Fifteen per cent said that they were unaware that any treatment was possible.
2.4.8 Advice By Health Professional

Thirty percent of parents said that they had been told to delay their journey to hospital by a health professional or village healer (Figure 23). Parents were asked whether they had already been to see another ophthalmologist or health professional prior to the first hospital visit and if so, what advice they had been given.

Over 80% of parents had seen a health professional before coming to hospital and in half of the cases they had been advised to delay treatment for more than a few months. This may have been in the mistaken belief that a delay
would make no difference to the final visual outcome. Parents of children under
the age of 3 months were often told to delay until they were old enough for a
general anaesthetic.

*Figure 24 Graph showing advice given to parents of children with non-traumatic cataract by health professionals (n=290)*

Only 6% of parents and their children had been to see a local healer and
few of these were given any treatment. There was no evidence of serious harm
from traditional eye practices amongst the study population.

### 2.5 Discussion

Previous studies of childhood cataract aetiology have established a
definite causative factor in 30-70% of cases (Francois, 1961; Kohn, 1976; Tytla
et al. 1993; Jain et al. 1983; Harley and Hertzberg, 1965). The causes vary between studies but in those studies performed in the developed world the majority of cataracts are hereditary (autosomal dominant) or are associated with other ocular or systemic disease. The same is unlikely to be true in the developing world where rubella remains an important aetiological factor.

Blind school surveys performed in south India have shown that childhood cataract is a significant cause of blindness and severe visual impairment (Gilbert et al. 1993a; Rahi et al. 1995), accounting for up to 20% of all childhood blindness. There have been only two published studies from India. Angra (1987) in North India looked at 200 cases of 'congenital' cataract and found that 31% were idiopathic, 14% were hereditary and 21% may have been due to rubella. Parents were not examined and rubella diagnosis was made only on clinical grounds. Jain (1983) prospectively enrolled 76 children with cataract from the general clinic over one and a half years and noted that 20% of the cataracts were hereditary, 9% were due to metabolic diseases and 5% had an associated syndrome. Nearly 8% had a positive rubella titre but the disease may have been acquired after birth and the significance is questionable.

A number of studies have implicated teratogens as a cause of cataract and many preparations in this population were taken during pregnancy. Abortifacients are occasionally used and have been cited as a cause of congenital cataract in India (Angra, 1987). We did not however detect a statistically significant correlation between any particular ante-partum medicine and cataract. It is difficult to obtain an accurate history of drug ingestion and drug preparations are so variable and freely available that an epidemiological study would be difficult to conduct.
Mothers who had severe diarrhoea (requiring intravenous rehydration) during pregnancy were not at increased risk of having a child with cataract although there is some evidence that adult cataract may be induced by severe life threatening diarrhoeal disease or heatstroke (Minassian et al. 1989).

Merin and Crawford reported on 386 cases from Canada (1971); the majority of cases were not isolated findings but rather part of a more generalised disorder with 60% of children having other ocular or systemic abnormalities. The population seen in the present study appears quite different. Firstly apart from those with CAR, most children were generally healthy. It is likely that children with associated severe systemic disease may have died before being seen or been too unwell to make the arduous journey to hospital.

Children with hereditary cataract tended to present later, over 51% attended hospital for the first time after the age of 5 years whereas children with CAR were more likely to present before they were one year old (54%). Hereditary cataract accounted for 25% of all the infantile cataracts seen. Previous studies have reported 8 - 23% of cases being hereditary (Hiles and Kilty, 1994). The lower figure may be because cases had been missed by not having the opportunity to examine parents and siblings. In this study approximately half the parents who had congenital cataract diagnosed on slit lamp examination were previously unaware that they had any visual problem. While recessively inherited cataract is rare in Europe and USA (Saebo, 1949) other communities where consanguineous marriages occur may have a higher incidence of cataract (Elder and De Cock, 1993; Gilbert et al. 1995; Baghdassarian and Tabbara, 1975; Mostafa et al. 1981). In this study autosomal recessive inheritance was very unusual despite a high degree of
consanguinity. Microphthalmos was not commonly associated with inherited cataract (9%) which is contrary to the findings of others (Lloyd et al. 1992) and it is possible that both the incidence of recessive cataract and the low incidence of microphthalmos associated with hereditary cataract are because the genetic abnormalities in the Indian population are different.

This study has shown that congenitally acquired rubella is a common cause of cataract in south India, accounting for over a quarter of all new cases of congenital cataract. The observation of a nuclear cataract in children aged under 1 year had a positive predictive value of 83% in identifying children with cataract due to rubella. The morphology (a central dense opacity with clear surrounding cortex) is similar to what Gregg described in his initial report associating cataract and CAR (1941). A deaf school survey performed in south India (Gray, 1989) concluded that up to 29% of children had retinal pigmentation consistent with CAR and is further evidence that rubella may be a significant cause of childhood disability.

This study has shown that nearly half of non-traumatic bilateral cataract in children in south India is due to potentially preventable causes i.e. CAR and hereditary disease. Health education of women of childbearing age concerning the use of drugs and medication during pregnancy may also have a positive impact. Education of health professionals highlighting the importance of early referral and treatment available may also be appropriate.
CHAPTER THREE
Diagnosis Of Congenitally Acquired Rubella Using Saliva

3.1 Introduction

3.2 Study Objectives

3.3 Detection Of Antibodies From Saliva

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3.4.1 Sample Collection And Storage

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3. CHAPTER THREE

Diagnosis of Congenitally Acquired Rubella using Saliva

3.1 Introduction

Gregg (1941) first described the association between rubella infection in pregnancy and congenital cataract, deafness and heart defects in the new-born, now known as the Congenital Rubella Syndrome (CRS). Subsequently large numbers of affected babies were identified in the USA, Europe and Australia (Banatvala and Best, 1990).

An effective vaccine against rubella was introduced in 1969 and since then the disease has been potentially preventable. Immunisation has led to the virtual eradication of congenitally acquired rubella (CAR) in the developed world. There is little information however on rubella infection and on the incidence of congenital rubella syndrome in the developing world (Global advisory group, 1991). Serological surveys in India have indicated that up to 45% of women of childbearing age are susceptible to rubella and so potentially at risk of acquiring infection during pregnancy (Seth et al. 1985). In India at the present time there is no official program of rubella vaccination (Ponnuraj et al, 1991; Samuel and John, 1996), although measles immunisation is now routinely given at nine months of age with an estimated uptake of more than 60% of the target population.

Epidemics of rubella and cases of CAR in the developing world are rarely reported. There is likely to be under reporting since surveillance is weak
and facilities to confirm the diagnosis are often inadequate. A high mortality in babies with multiple congenital defects means that deafness and blindness surveys are likely to reveal only those CAR affected infants at the milder end of the spectrum of abnormalities.

A diagnosis of congenitally acquired rubella can be established by:

1. Detection of rubella specific IgM in serum samples obtained in early infancy.

2. Detection of persistent rubella IgG antibody in the infant, i.e. the presence of antibodies at a time beyond which maternal antibodies are usually no longer detected - approximately 6 months of age.

3. Isolation of rubella virus from the infant during early infancy (cataractous lens).

Obtaining serum samples from young sick children for detection of rubella specific IgM can be especially difficult, particularly in rural areas where there is no facility for storage or transportation of blood products. These factors limit the amount of data available on the incidence of congenital rubella infection. This makes planning of immunisation strategies difficult as there is likely to be a substantial under-diagnosis of rubella infection and to a false impression of the epidemiology of CAR.

Identification of current or recent infections and of immune and susceptible individuals by testing body fluids that are more easily collected than blood would greatly facilitate the investigation of rubella and CAR epidemiology.
3.2 Study Objectives

This study was performed in order to answer two questions:

1. To determine whether the congenital rubella syndrome was an important cause of infantile cataract in south India.

2. To determine whether examination of saliva for rubella specific IgM would be an equally reliable but less invasive and more practical test for confirming the diagnosis than examination of serum.

3.3 Detection of Antibodies from Saliva

Despite salivary immunoglobulin concentration being about 800-fold lower than that in plasma, it has been demonstrated that immune status to several viruses can be accurately determined by testing saliva for the presence of virus specific IgG. Figure 26 illustrates the sources of immunoglobulin in whole saliva and compares the immunoglobulin concentrations in serum and saliva.

The accurate detection of virus specific IgG in human saliva was first described for human immunodeficiency virus (HIV), hepatitis A virus and the core antigen of hepatitis B virus (Parry et al. 1987). Subsequently, virus specific IgM detection in saliva was reported in patients with recent hepatitis B (Parry et al. 1989). Detection of class specific antibodies was achieved using assays based on the antibody capture principle (Duermeyer et al. 1979).

Salivary detection of rubella specific IgM and IgG has not previously been described in infants or young children and has not been used in a developing country. This study was designed to investigate the salivary diagnosis for
congenital rubella syndrome and to determine whether saliva could be
adequately stored in remote and hot environments.

Specimens were collected from infants with cataract and from a control
group and tested by antibody capture assays for virus specific IgM. Sensitivity
and specificity data are presented as well as sequential sampling data.
Sources of Immunoglobulin in whole saliva

1. Major salivary glands
   - IgA, G, M

2. Minor salivary glands
   - IgA, G, M

3. Gingival crevicular fluid
   - IgA, G, M

4. Mucosal lymphoid cells

Immunoglobulin concentrations (mg/100ml) in serum & saliva

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<td>parotid saliva</td>
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<td>Serum: saliva ratio</td>
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3.4 Materials and Methods

Over a nine month period during 1993-4, ninety-five consecutive children less than 1 year old with unilateral or bilateral non-traumatic infantile cataract presenting to the paediatric ophthalmic department of the Aravind eye hospital were studied. Informed consent and a detailed history was obtained from the parents. All the children underwent an ophthalmic examination by the author including direct and indirect ophthalmoscopy and IOP assessment. Those infants that were systemically unwell were also examined by a paediatrician at the local children's hospital.

Thirty six children under 1 year old attending the same paediatric eye clinic over the same period with a diagnosis of epiphora due to blocked naso-lacrimal ducts but who were otherwise fit and well were used as a control group. These children had saliva samples taken but no blood.

Paired serum and saliva samples were taken from the children with cataract in order to evaluate the specificity and sensitivity of the saliva test, against the gold standard of the serum antibody assay.

3.4.1 Sample Collection And Storage

Blood samples were collected by finger or heel prick onto a filter paper strip and saliva samples were collected using the Orasure device (Epitope Inc, Beaverton). The collection of saliva was simple and did not distress the infant or parents.
Figure 26 Photographs contrasting the collection of blood and saliva from infants used to detect rubella specific IgM.
The saliva collection device is a sterile absorbent pad on the end of a stick. It tastes sweet and infants will often put it in their mouth and suck it. The pad is wiped gently over the gums (gingival crevicuiar margin) where the maximum dose of immunoglobulin rich crevicular fluid is found. Once there is adequate saliva the pad is placed in an individual tightly sealed plastic tube containing preservatives.

In this study the blood spots were kept in a refrigerator at 4 degrees centigrade and the pads were stored in their tube at room temperature for up to eight weeks before being transported by air to the Central Public Health Laboratory, London. No other special transport or storage facilities were required.

3.5 Laboratory Assays

3.5.1 Saliva Extraction

Saliva was extracted from the Orasure device by centrifuging the tube and pad. The saliva was then stored at -30°C before testing. Serum was extracted from a measured area of filter paper into 200μl phosphate buffered saline (Faraclegan et al. 1987).

3.5.2 IgM Antibody Capture Radioimmunoassay (MACRIA) (Figure 27)

Polystyrene beads were coated with rabbit antibody to human IgM (μ-chain specific, code no.A426, Dakopatts Ltd, Copenhagen, Denmark,
concentration 3.1 mg/litre). The coated beads were incubated in 200µl undiluted crevicular swab fluid for 3 hours at 37°C, then washed four times with phosphate buffered saline (PBS) and 0.1% Tween.

The rubella viral antigen was then added. Rubella haemagglutinin (Judith strain) prepared by the Division of Microbiological reagents, Central Public Health Laboratory was used at a dilution of 1/12. The antigen was diluted in PBS containing 10% fetal calf serum (FCS) and 0.1% Tween and incubated at room temperature overnight.

Binding of the antigen was demonstrated by addition of a dilution of murine monoclonal antibody; 1/50,000 anti rubella, followed by ¹²⁵I-labelled anti-mouse IgG (Amersham International, Aylesbury, UK, code IM131, 100,000 counts per minute). The ¹²⁵I anti-mouse label was diluted in PBS with 10% fetal calf serum, 2% human serum and 5% rabbit serum and incubated for 2 hours at 37°C. The beads were washed in PBS and Tween and the bound ¹²⁵I was measured in a gamma counter.

In each assay run four wells of serum unreactive for the homologous antibody (dilute 1/50) and two each of a strong and a weakly IgM reactive serum and an unreactive saliva control were included. Test results were calculated as the total bound radioactivity of each specimen divided by the mean radioactivity bound of the 4 negative serum controls and expressed as Test : Negative (T:N) ratios. Saliva and serum specimens were considered positive for rubella specific IgM if the Test : Negative ratio was equal or greater than 3.
Rubella specific IgM detection by MACRIA

1. Anti IgM + specimen
2. Captured antibody + rubella antigen
3. Add anti rubella monoclonal antibody
4. Add I^{125} labelled sheep anti mouse antibody
5. Count in Gamma-counter

High count: POSITIVE
Low count: NEGATIVE
3.5.3 Samples For Sequential Testing

Infants in the study with confirmed congenital rubella syndrome at their first visit (elevated rubella specific IgM, T:N ratio ≥3) who were able to reattend the hospital, had sequential saliva and serum samples taken at each successive visit. This was done to determine the suitability of saliva testing for children of different ages and to provide information on the amount of IgM secreted by children with the disease as they became older.

3.6 Results

The mean age of the 95 cases was 6.2 months (range 1-11 months, SD 3.7) and the 36 controls 7.3 months (range 1-11 months, SD 3.4). The male to female ratio was 1.1:1 in cases and 1.3:1 in controls.

Twenty five out of 95 cases (26.3%) had congenital rubella infection confirmed by detection of rubella specific IgM from both saliva and serum. There was no case of raised rubella specific IgM in the 36 controls ($p<0.005$). (Rubella virus RNA was detected in 8 (53.3%) of 15 samples of lens tissue from infants with confirmed rubella specific IgM (Bosma et al. 1995)).
Table 31 Results of serum and saliva samples from 95 children under 1 year old at first presentation. Positive results in bold.

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<th>Macria units saliva</th>
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<td>282</td>
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<td>130</td>
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<td>89.3</td>
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</tr>
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</tr>
<tr>
<td>323</td>
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<td>151.2</td>
<td>&gt;100</td>
<td>&gt;100</td>
</tr>
<tr>
<td>331</td>
<td>5/12</td>
<td>1.6</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>337</td>
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<td>1.6</td>
<td>1</td>
<td>1.4</td>
</tr>
<tr>
<td>347</td>
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<td>1</td>
<td>1</td>
</tr>
<tr>
<td>362</td>
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<td>&lt;1</td>
<td>1.2</td>
</tr>
<tr>
<td>364</td>
<td>11/12</td>
<td>0.8</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>365</td>
<td>7/12</td>
<td>1.5</td>
<td>1</td>
<td>1.3</td>
</tr>
<tr>
<td>367</td>
<td>3/12</td>
<td>112</td>
<td>&gt;100</td>
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<tr>
<td>393</td>
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</tr>
<tr>
<td>395</td>
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<td>142.7</td>
<td>&gt;100</td>
<td>122.1</td>
</tr>
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<td>10</td>
<td>3.5</td>
</tr>
<tr>
<td>414</td>
<td>11/12</td>
<td>13.7</td>
<td>9.3</td>
<td>68.4</td>
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<tr>
<td>421</td>
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<td>2.6</td>
<td>0.8</td>
</tr>
<tr>
<td>422</td>
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<td>0.8</td>
<td>1</td>
<td>1.1</td>
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<td>428</td>
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<tr>
<td>430</td>
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<td>1.7</td>
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</tr>
<tr>
<td>431</td>
<td>6/12</td>
<td>1.1</td>
<td>1</td>
<td>0.7</td>
</tr>
<tr>
<td>Study No.</td>
<td>AGE</td>
<td>Macria T/N saliva</td>
<td>Macria units saliva</td>
<td>Macria blood</td>
</tr>
<tr>
<td>----------</td>
<td>-----</td>
<td>------------------</td>
<td>---------------------</td>
<td>--------------</td>
</tr>
<tr>
<td>434</td>
<td>10/12</td>
<td>1.5</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>439</td>
<td>7/12</td>
<td>18.5</td>
<td>17</td>
<td>5.9</td>
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<tr>
<td>448</td>
<td>10/12</td>
<td>1.2</td>
<td>1</td>
<td>1.2</td>
</tr>
<tr>
<td>450</td>
<td>8/12</td>
<td>7.6</td>
<td>5.2</td>
<td>52.5</td>
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<td>456</td>
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<td>1.8</td>
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<td>467</td>
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<td>1</td>
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<td>473</td>
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<td>1.8</td>
<td>1.2</td>
</tr>
<tr>
<td>488</td>
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<td>100</td>
<td>24.8</td>
</tr>
<tr>
<td>492</td>
<td>11/12</td>
<td>5.7</td>
<td>3.8</td>
<td>1.4</td>
</tr>
<tr>
<td>507</td>
<td>11/12</td>
<td>0.9</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>514</td>
<td>5/12</td>
<td>25.5</td>
<td>31</td>
<td>5.6</td>
</tr>
</tbody>
</table>

3.6.1 Paired Samples

Rubella specific IgM was detected in saliva and serum in 17 paired samples and was absent in 44 paired samples (sensitivity 100%; 95% confidence interval 80.5 to 100%. Specificity 100%; 95% confidence interval 92-100%). Saliva testing gave no false positive and no false negative results compared with serum.

The results of the 17 paired serum and saliva samples positive for rubella specific IgM are shown in Figure 28. The mean Test : Negative (T:N) ratios were 56 (SD 38) in serum and 61 (SD 43) in saliva samples.

All 131 saliva samples from cases and controls were shown to contain IgG indicating that there was adequate antibody for testing. In 122 samples total IgG levels were >2mg/l. In the remaining 9 samples IgG levels ranged from 0.36-1.99 mg/l.
3.6.2 Sequential Testing

Seven children who had confirmed CAR had repeat saliva samples taken at each follow up visit (Table 32). The Test : Negative control (T:N) ratios are plotted against the age of the child at the time when the samples were taken. The result is considered positive if the T:N ratio is ≥3. (Figure 29)

Rubella specific IgM persisted in all children until they were 6 months old. One child became negative after nine months but five of the seven children remained positive up to the age of 14 months. One child with persistent fever and failure to thrive had high levels of rubella specific IgM until 19 months of age.
Figure 29. Sequential T:N ratios from 7 infants with confirmed CAR
Table 32. Macria Results from sequential samples taken from 7 infants with confirmed CAR

<table>
<thead>
<tr>
<th>Study No.</th>
<th>AGE</th>
<th>Macria T/N saliva</th>
<th>Macria units saliva</th>
<th>Macria blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>117</td>
<td>2/12</td>
<td>65.1</td>
<td>100</td>
<td>-</td>
</tr>
<tr>
<td>117</td>
<td>6/12</td>
<td>3.3</td>
<td>1.9</td>
<td>9.4</td>
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<tr>
<td>117</td>
<td>12/12</td>
<td>6.2</td>
<td>3.5</td>
<td>5.2</td>
</tr>
<tr>
<td>170</td>
<td>6/12</td>
<td>53.2</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>170</td>
<td>9/12</td>
<td>20.9</td>
<td>21</td>
<td>7.5</td>
</tr>
<tr>
<td>170</td>
<td>18/12</td>
<td>18.9</td>
<td>17</td>
<td>-</td>
</tr>
<tr>
<td>178</td>
<td>1/12</td>
<td>83.6</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>178</td>
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<td>100</td>
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<tr>
<td>178</td>
<td>6/12</td>
<td>116.9</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>178</td>
<td>9/12</td>
<td>114.7</td>
<td>100</td>
<td>86.6</td>
</tr>
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<td>178</td>
<td>13/12</td>
<td>39.4</td>
<td>68</td>
<td>-</td>
</tr>
<tr>
<td>202</td>
<td>2/12</td>
<td>83</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>202</td>
<td>8/12</td>
<td>8.8</td>
<td>5.2</td>
<td>6</td>
</tr>
<tr>
<td>202</td>
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<td>4</td>
<td>-</td>
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<tr>
<td>202</td>
<td>14/12</td>
<td>6.5</td>
<td>4.6</td>
<td>-</td>
</tr>
<tr>
<td>215</td>
<td>3/12</td>
<td>16.9</td>
<td>22</td>
<td>30</td>
</tr>
<tr>
<td>215</td>
<td>9/12</td>
<td>1.6</td>
<td>&lt;1</td>
<td>-</td>
</tr>
<tr>
<td>403</td>
<td>6/12</td>
<td>14.6</td>
<td>10</td>
<td>3.5</td>
</tr>
<tr>
<td>403</td>
<td>11/12</td>
<td>2.6</td>
<td>1.4</td>
<td>2.7</td>
</tr>
<tr>
<td>439</td>
<td>7/12</td>
<td>18.5</td>
<td>17</td>
<td>5.9</td>
</tr>
<tr>
<td>439</td>
<td>13/12</td>
<td>7.4</td>
<td>4.3</td>
<td>5</td>
</tr>
<tr>
<td>439</td>
<td>19/12</td>
<td>4.3</td>
<td>2.9</td>
<td>-</td>
</tr>
</tbody>
</table>
3.7 Clinical Features Of Children With Congenital Rubella Syndrome

Congenital rubella syndrome was suspected clinically in 19 of the 25 cases of congenital cataract in which rubella specific IgM was detected. The other six children had clinical features compatible with congenital rubella syndrome although the diagnosis had not been made prior to laboratory confirmation. Clinical diagnosis had a sensitivity of 76% (19/25) and specificity of 100% compared to serological confirmation using either blood or saliva samples.

![Figure 30: Clinical diagnosis versus IgM rubella specific antibodies]

<table>
<thead>
<tr>
<th>Rubella specific IgM Antibody detected</th>
<th>+</th>
<th>-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical diagnosis of CRS</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>+</td>
<td>19</td>
<td>0</td>
</tr>
<tr>
<td>-</td>
<td>6</td>
<td>70</td>
</tr>
</tbody>
</table>

25    70

Sensitivity 76% (19/25)
Specificity 100%
Table 33 Clinical and ocular features of the 25 cases of confirmed CAR.

<table>
<thead>
<tr>
<th>Study No.</th>
<th>Ocular Features</th>
<th>Non ocular features</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>Unilateral corneal opacity. Bilateral nuclear cataracts. Bilateral microphthalmos</td>
<td>none</td>
</tr>
<tr>
<td>5</td>
<td>Unilateral nuclear cataract and microcornea</td>
<td>none</td>
</tr>
<tr>
<td>32</td>
<td>Bilateral nuclear cataracts</td>
<td>Deaf, PDA</td>
</tr>
<tr>
<td>117</td>
<td>Bilateral nuclear cataracts. Atrophic iris. Bilateral Microphthalmos</td>
<td>Deaf, VSD</td>
</tr>
<tr>
<td>170</td>
<td>Bilateral nuclear cataracts. Bilateral microphthalmos. Small unreactive pupils. Atrophic iris</td>
<td>deaf, scaly skin</td>
</tr>
<tr>
<td>178</td>
<td>Bilateral nuclear cataracts. Bilateral microphthalmos. Corneal opacities. Retinopathy</td>
<td>PDA, pulmonary stenosis, constant fever, low weight</td>
</tr>
<tr>
<td>193</td>
<td>Bilateral nuclear cataracts. Bilateral microphthalmos. Small unreactive pupils</td>
<td>PDA</td>
</tr>
<tr>
<td>202</td>
<td>Bilateral nuclear cataracts. Bilateral microphthalmos. Corneal opacities</td>
<td>none</td>
</tr>
<tr>
<td>203</td>
<td>Bilateral nuclear cataracts. Unilateral Corneal opacity. Bilateral microphthalmos</td>
<td>died after 6/12</td>
</tr>
<tr>
<td>207</td>
<td>Bilateral nuclear cataracts. Bilateral microcornea. Corneal opacities</td>
<td>deaf</td>
</tr>
<tr>
<td>210</td>
<td>Bilateral nuclear cataracts. Bilateral microphthalmos</td>
<td>VSD</td>
</tr>
<tr>
<td>211</td>
<td>Unilateral nuclear cataract. Microcornea</td>
<td>VSD</td>
</tr>
<tr>
<td>215</td>
<td>Bilateral nuclear cataracts. Cloudy Corneas. Left leucoma. Bilateral microphthalmos</td>
<td>VSD, PDA, Deaf, severely delayed milestones</td>
</tr>
<tr>
<td>288</td>
<td>Bilateral nuclear cataracts</td>
<td>nil</td>
</tr>
<tr>
<td>300</td>
<td>Bilateral nuclear cataracts. Bilateral microphthalmos</td>
<td>PDA</td>
</tr>
<tr>
<td>310</td>
<td>Bilateral nuclear cataracts. Rotatory nystagmus. Bilateral microphthalmos</td>
<td>small, failure to thrive</td>
</tr>
<tr>
<td>323</td>
<td>Bilateral nuclear cataracts</td>
<td>small, delayed milestones</td>
</tr>
<tr>
<td>367</td>
<td>Bilateral nuclear cataracts. Bilateral microphthalmos</td>
<td>ASD</td>
</tr>
<tr>
<td>395</td>
<td>Bilateral nuclear cataracts. Bilateral microphthalmos</td>
<td>PDA, hepatosplenomegaly, deaf</td>
</tr>
<tr>
<td>403</td>
<td>Bilateral nuclear cataracts. Miosis. Bilateral microphthalmos, Retinopathy</td>
<td>VSD, low weight, very delayed milestones, deaf</td>
</tr>
<tr>
<td>414</td>
<td>Unilateral nuclear cataract. Rigid small pupil. Unilateral microphthalmos</td>
<td>nil</td>
</tr>
<tr>
<td>439</td>
<td>Bilateral nuclear cataracts. Right microcornea</td>
<td>no maternal history, no deafness, normal milestones</td>
</tr>
<tr>
<td>450</td>
<td>Unilateral nuclear cataract. Rigid pupil</td>
<td>delayed milestones</td>
</tr>
<tr>
<td>488</td>
<td>Bilateral nuclear cataracts. Bilateral microphthalmos</td>
<td>PDA, deaf</td>
</tr>
<tr>
<td>514</td>
<td>Bilateral nuclear cataracts. Bilateral microphthalmos. Iris atrophy. Bilateral corneal haze</td>
<td>ASD</td>
</tr>
</tbody>
</table>
3.8 Maternal symptoms

There was a positive maternal history of fever and rash during the first half of pregnancy in 12/25 (48%) confirmed cases. Another two mothers had a fever but no rash (8%). No mothers had a rash without fever. Of the 70 infants with cataract but who did not have CAR, 13 (19%) of the mothers had a fever during the first half of pregnancy and 2 (3%) mothers had a rash. There were no cases of maternal rash and fever in the 70 cases of infantile cataract where rubella IgM was not detected. There were 6 babies with CAR who were born at least one month premature compared with 5 of the 70 children who did not have rubella infection (p=0.02).(Table 34)

Table 34. Comparison of maternal symptoms and prematurity of infants in cases of CAR against other causes of cataract in children under 1 year.

<table>
<thead>
<tr>
<th>Maternal Symptom</th>
<th>CAR (n=25)</th>
<th>Non CAR (n=70)</th>
<th>Odds Ratio</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever only</td>
<td>14</td>
<td>13</td>
<td>5.6</td>
<td>=0.003</td>
</tr>
<tr>
<td>Rash only</td>
<td>12</td>
<td>2</td>
<td>31.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fever and rash</td>
<td>12</td>
<td>0</td>
<td>undefined</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Premature delivery</td>
<td>6</td>
<td>5</td>
<td>4.1</td>
<td>=0.02</td>
</tr>
</tbody>
</table>

3.9 Ocular features

3.9.1 Cataract Morphology

Of the 25 children who had CAR, 21 (84%) had bilateral cataract and 4 (16%) had unilateral cataract (ratio 5.3:1). The morphological characteristics of
cataracts in the rubella and non rubella children under one year old are presented in Table 35.

Table 35  Cataract morphology in children with congenitally acquired rubella (CAR) compared to those with cataract from other causes.

<table>
<thead>
<tr>
<th>Morphology</th>
<th>CAR</th>
<th>Non CAR</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamellar</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>0</td>
<td>34</td>
<td>34</td>
</tr>
<tr>
<td>Nuclear</td>
<td>25</td>
<td>5</td>
<td>30</td>
</tr>
<tr>
<td>Post Polar</td>
<td>0</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Mixed</td>
<td>0</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>Total (children)</td>
<td>25</td>
<td>70</td>
<td>95</td>
</tr>
</tbody>
</table>

In all cases of confirmed CAR the cataract appeared as a dense central nuclear opacity surrounded by a less dense cortical opacity with variable extension towards the periphery. Nuclear cataracts were only seen in 6.7% of the non rubella group. Nuclear cataract in this group of children had a positive predictive value for CAR of 83%.

3.9.2 Other Features

Associated eye disease was common in CAR cases;

**Microphthalmos**

38/50 (76%) eyes of infants with CAR were microphthalmic. The mean corneal diameter of these eyes was 9.9mm (range 7.5-11.5mm). There were no cases of microphthalmos in eyes which did not have cataracts. In three children with bilateral cataract the microphthalmos was unilateral.
Corneal opacity

10/50 (20%) eyes from infants with CAR had cloudy corneas. In two cases this was definitely associated with glaucoma but in the remainder the IOP as measured by the Keeler 2000 Pulsair tonometer was within normal limits (<21mmHg).

Figure 31 Graph showing other ocular abnormalities in children with CAR
Glaucoma

2/50 (4%) cataract eyes in 2 infants with CAR had glaucoma at the time of presentation. This was diagnosed by IOP over 21mmHg and optic disc cupping. Both eyes had corneal oedema and were microphthalmic.

3.10 Systemic Non Ocular Features

Of those infants with CAR, 64% of children had some non ocular abnormality at first presentation.

Cardiac disease

13/25 (52%) children had cardiac disease determined by physical examination and echocardiography where necessary. Three of the affected children had already had cardiac surgery before presenting with cataract. The various types of cardiac abnormality are shown in Table 36.

Table 36. Type of cardiac abnormality affecting children with CAR

<table>
<thead>
<tr>
<th>Cardiac Abnormality</th>
<th>Number of children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patent ductus arteriosus (PDA)</td>
<td>7</td>
</tr>
<tr>
<td>Ventriculo-septal defect (VSD)</td>
<td>5</td>
</tr>
<tr>
<td>Pulmonary stenosis (PS)</td>
<td>1</td>
</tr>
<tr>
<td>Atrial septal defect</td>
<td>2</td>
</tr>
</tbody>
</table>

Deafness

8/25 (32%) infants were profoundly deaf on examination in the clinic. The parents of a further 7(28%) infants thought that their children had hearing difficulties but this could not be confirmed by examination in the clinic.
No systemic abnormality or maternal history

There were a total of 5 infants (20%) who did not have any other feature of CAR apart from nuclear cataract and had no maternal history of fever or rash during early pregnancy.

Figure 32 Graph showing number of children with CAR who also had non ocular disease at first presentation.
3.11 Discussion

3.11.1 Diagnosis Of Rubella Specific IgM From Saliva

1. This study demonstrates excellent agreement between test results in saliva and serum in the 61 paired samples suggesting that saliva is as reliable as serum in detecting rubella specific IgM in infants.

2. Despite the fact that the infants tested were all less than one year old, had few teeth and therefore produced little crevicular fluid, adequate saliva samples were collected from all cases.

3. The storage and transport of samples was not ideal, but this study indicates the potential of the Orasure device for undertaking studies remote from testing centres.

4. Sequential testing has shown that rubella specific IgM can be detected in saliva up to the age of 19 months and is almost always present for the first 9 months.

5. Detection of rubella specific IgM aided the diagnosis in 6/25 cases where clinical features and history alone were insufficient.

3.11.2 Congenital Rubella Syndrome In South India

1. The study shows that a quarter of infants under 1 year old attending the Aravind Eye Hospital with non-traumatic cataract have congenital rubella syndrome.
2. A cataract of nuclear morphology in this group of infants had a positive predictive value for CAR of 83%.

3.12 Conclusions

Improved surveillance is required for congenitally acquired rubella in the developing world. The identification of rubella specific IgM in saliva has been shown in this study to offer a simple, accurate, non-invasive test to be used on infants. This can enhance surveillance based on clinical case finding.

The study suggests that congenitally acquired rubella is an important cause of congenital cataract in Tamil Nadu, south India. However this group of hospitalised children may not be representative of all children with congenital cataract in the community and therefore more extensive studies are needed to establish the true scale of the problem.

Salivary diagnosis of rubella specific IgG can be used to determine the seroprevalence of rubella infection amongst girls of childbearing age. This will aid planning of effective immunisation programs.

A community based study of young women using salivary diagnosis of rubella specific IgG is now underway in Vellore, Tamil Nadu.

India has an effective immunisation program against measles and it would be potentially feasible to change from measles only to a combined vaccination of measles, mumps and rubella (MMR). Figure 33 shows a mother who gave birth to a child with CAR, the scars on the mother’s arm show that she had been immunised against measles and tuberculosis.
Figure 33  Mother who was successfully immunised against measles and tuberculosis (scars) but gave birth to a child with congenitally acquired rubella. (Study no. 170)
CHAPTER 4

A Randomised Clinical Trial Of Lensectomy Versus Lens Aspiration And Primary Capsulotomy For Children With Bilateral Cataracts.

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4. CHAPTER 4

A Randomised Clinical Trial Of Lensectomy Versus Lens Aspiration And Primary Capsulotomy For Children With Bilateral Cataracts.

4.1 Introduction

In general children in south India with bilateral cataract have a poor visual prognosis (Rahi et al. 1995). The reasons for this may be separated into family (consumer) and surgical (provider) constraints;

Family constraints

1. The child's attendance at clinic is often delayed (see Chapter 2) and they have developed significant amblyopia before surgery can be performed to clear the visual axis.

2. Children and their parents often fail to attend follow up appointments because of the large distances and expenses involved in getting to hospital.

3. Parents and children fail to attend for secondary surgical procedures such as capsulotomies and membranectomies.

4. Topical medication is expensive for many families and compliance with treatment is low.

5. Accurate aphakic correction requires continued follow up as well as replacement glasses. Many families cannot afford this and fail to attend.

6. Children and parents fail to manage occlusion therapy.
Medical Constraints

1. Appropriate surgical techniques have not been defined in this region.
2. Equipment such as operating microscopes and vitrectomy equipment are expensive to purchase and to maintain and are available in only a few centres.
3. Surgical skill and experience is spread unevenly throughout the country and often limited to major centres.
4. Facilities for managing aphakia and amblyopia are often lacking.

4.1.1 Background To The Clinical Trial

As listed above there are many constraints in this region not present in the developed world. The aim of this clinical trial was to determine the most appropriate surgical technique for children in south India. In particular the type of surgery and the follow up should not be excessively expensive or require levels of skill and equipment not easily available. It should be equally acceptable to children and parents in terms of post operative pain and considering the difficulties of getting children to return for follow up should require the least number of interventions.

4.1.2 Hypothesis

There are two principle procedures used in the management of childhood cataract. Both have specific advantages and disadvantages. (See Chapter 1) In
south India almost all cataracts are removed by aspiration of the lens contents with or without a primary capsulotomy. Because the posterior capsule opacifies, accurate refraction is made more difficult and vision deteriorates as the opacity increases. Lensectomy may be the better choice as the posterior capsule is removed at the time of surgery. The hypothesis is that lensectomy is a better treatment option for young children with bilateral cataract in the context of a developing world situation.

4.1.3 Summary Of The Trial Design

Children aged between 0-10 years with bilateral symmetrical cataracts significantly affecting vision and who required surgery in both eyes had one eye randomised to undergo either a lensectomy procedure or an ECCE with a primary capsulotomy. The second eye automatically had the alternate procedure. Each child therefore had a different procedure on each eye and the procedures were therefore matched for personal factors.

4.1.4 Objectives And Main Outcome Measures

1. To determine the frequency and cause of operative, early post operative and late complications (initially up to 1 year follow up) between the two techniques.
2. To compare visual acuity results between the two surgical techniques at follow up one year after surgery.
3. To compare secondary intervention rates within 1 year of the initial surgery between the two surgical techniques.
4. Using the results of 1, 2 and 3, to determine which method of treatment, lensectomy or ECCE may be the most suitable treatment for young children in south India.

4.2 Methods

4.2.1 Recruitment Of Subjects

Children were recruited from the Aravind Hospital paediatric eye clinic. All children with cataracts attend this clinic and are assessed by the Consultant in charge (Dr Vijayalakshmi).

Every child with a cataract that presented to the clinic was recruited into the aetiology study (Chapter 2) and of these, a subset of children with bilateral cataract who required bilateral surgery were enrolled into the randomised clinical trial.

4.2.2 Inclusion Criteria

1. Age 0-10 years inclusive.
2. Either sex.
3. Current residence in state of Tamil Nadu or Kerala
4. Bilateral symmetrical cataracts, with both eyes requiring surgery.
5. If visual acuity measurable then the acuity in each eye to be within 0.3 log MAR units of the other.
6. Both eyes suitable for either a lensectomy or ECCE with primary capsulotomy.
The restriction of inclusion age to under 10 years was made because cataracts in children above this age behave more like adult cataracts and there is general agreement that extracapsular techniques often with intraocular lenses are appropriate. Because of the difficulties of asking parents to travel long distances with their children for follow up, recruitment was limited to Tamil Nadu and the neighbouring state of Kerala.

4.2.3 Exclusion Criteria

1. Sick or underweight children where they may be at increased risk from general anaesthesia.

2. Systemic illness including mental retardation where acuity testing might be difficult.

3. Parents unwilling or unable to bring children for follow up.

4. Pre-existing ocular diseases including glaucoma, corneal opacification and retinal detachment.

5. Previous intraocular surgery.
Figure 34 Map of India showing the catchment area for the clinical trial
### 4.2.4 Intervention and Follow up Schedule

Children enrolled into the study had surgery performed on one eye on the first working day after the clinic visit. Second eye surgery was performed within five days of the first operation. The treatment and follow up schedule was as outlined below:

<table>
<thead>
<tr>
<th>Day</th>
<th>Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td>-1</td>
<td>Preoperative examination, including visual acuity assessment and entry into aetiology study. Decision making on eligibility for studies. Randomisation if appropriate.</td>
</tr>
<tr>
<td>0</td>
<td>Surgery, fill out surgical report.</td>
</tr>
<tr>
<td>1</td>
<td>Examination, fill out form</td>
</tr>
<tr>
<td>3</td>
<td>Examination, fill out form</td>
</tr>
<tr>
<td>5</td>
<td>Examination, fill out form</td>
</tr>
</tbody>
</table>

| Day 0 | Second eye Surgery, fill out surgical report. |
| Day 1 | Examination, fill out form. |
| Day 3 | Examination, fill out form. |
| Day 5 | Examination, data entry. Refraction and aphakic spectacles. Discharge. |

- Week 4: Examination, IOP, visual acuity assessment, refraction, fill out form
- Month 3: Examination, IOP, visual acuity assessment, refraction, fill out form
- Month 6: Examination, IOP, visual acuity assessment, refraction, fill out form
- Year 1: Examination, IOP, visual acuity assessment, refraction, **End Point 1**
- Year 2,3,4,5: Annual Review, acuity, refraction, IOP.
- Year 5: Final end point.
4.2.5 Randomisation

Each child enrolled into the clinical trial was randomised. A sealed envelope contained a printed card which had details of both the side to be operated on and the type of procedure to be performed (ECCE or lensectomy). The randomisation list was generated by computer (D-Base random test program) and the pattern was tested for randomness.

The envelope was opened in the clinic the day before surgery so that the operating list could be completed accurately and the card attached to the patient notes.

The second eye automatically had the alternate procedure. Each child therefore had one cataract removed by lensectomy and one removed by aspiration with a primary capsulotomy.
4.2.6 Decision Making Tree

Has child entered aetiology study?

Does child have bilateral operable cataracts?

Is the child aged between 0-10 years?

Are parents and child able to attend follow up examination?

If the answer to all these questions is yes then child may enter studies

Can child undergo either lensctomy or ECCE in both eyes?

Is child suitable for randomisation?

Do parents agree consent and sign form?

Child enters randomised trial

Attach sealed randomisation envelope to notes
4.2.7 Informed Consent And Ethical Approval

Informed consent was always obtained from parents before children were enrolled into the trial. Parents were given a form written in their local language, either Tamil or Malayalam outlining the reasons for the trial and they had the trial explained to them by the study co-ordinator. Those parents unable to read had the form explained to them and the signed copies kept with the study booklet.

The trial was approved by the ethical committee of the Aravind Eye Hospital and the Government of India Medical Research Council.

4.2.8 Study Forms

The study forms were designed by the author. There were separate forms for the first visit and follow up visits. (Appendices page 254) The forms were printed locally and were kept with the hospital notes in a separate cabinet in the clinic. All children had a card with their study number and this enabled the hospital reception to direct study children to the correct clinic for follow up. The card had the follow up dates clearly written.

4.2.9 Pre operative Examination

All of the children had a full ocular examination performed by one ophthalmologist (author). Whenever possible children were examined on the slit lamp microscope and by direct and indirect ophthalmoscopy after pupil dilatation. Intraocular pressures were measured using the Keeler Pulsair Tonometer or a Goldman Tonometer. Those children who appeared systemically unwell or who had other physical abnormalities were examined by a paediatrician and an anaesthetist.
4.2.10 Documentation

Each cataract was documented photographically at the beginning of surgery using the camera attachment on the operating theatre microscope. The camera used was a Nikon F90 with Kodak tungsten transparency film (ASA 360). No external flash system was required. Films were processed locally and stored in an air conditioned environment.
4.2.11 Visual Acuity Assessment

Visual function was a key outcome measure in this study and accurate assessment of vision was a priority. Visual acuity was measured using a number of techniques which depended on the child’s age, vision and ability. Keeler acuity cards, Cardiff cards, Cambridge crowding cards and Snellen acuity were all used. A visual function battery (Droste et al. 1991) was used in infants with very poor vision. Visual acuity measurements were made using the most appropriate tests for the individual children. The goal was to be able to record a Snellen acuity for distance and for reading on each child before the end of the study. Preferential looking tests were used for children whenever Snellen acuity was not possible. All acuities from the various tests were recorded on the examination forms. (Appendix, page 254)

Vision testing was always performed in the same room which was situated adjacent to the paediatric clinic and was relatively quiet. There were no windows and constant illumination was provided by six fluorescent tube lights on the ceiling.

Grating card visual acuities were recorded in cycles per degree (cy/deg) and optotype acuities recorded in logMAR units. All acuity measurements were converted to log MAR units for analysis.

4.2.11.1 Visual Acuity Examiner

A single trained Indian examiner performed all visual acuity tests throughout the period of the study (Up to year 1 endpoint). Before the study
commenced the examiner underwent one week of training using the different techniques. At the end of the week interobserver reliability tests were performed using the Kappa statistic ($\kappa$) between the examiner and the author (Table 37). Kappa is defined as the agreement beyond chance divided by the amount of agreement possible beyond chance. Agreement of the two estimates was recorded as good if they were within +/- 1.0 octave where 1 octave is a doubling or halving of spatial frequency and is equivalent to 0.3 log MAR units. Kappa values above 0.6 were deemed acceptable for this study.

Table 37 Inter-observer reliability testing between author and examiner for acuity tests after one week of examiner training.

<table>
<thead>
<tr>
<th>Visual acuity test</th>
<th>Kappa ($\kappa$) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keeler cards</td>
<td>0.72</td>
</tr>
<tr>
<td>Cardiff cards</td>
<td>0.88</td>
</tr>
<tr>
<td>Cambridge cards</td>
<td>0.91</td>
</tr>
<tr>
<td>Snellen acuity</td>
<td>0.88</td>
</tr>
</tbody>
</table>

4.2.11.2 Visual Assessment Using Behavioural Tests

Visual Function Battery

For those children who were unable to perform the Cardiff or Keeler acuity tests due to age, lack of co-operation or poor vision, visual assessment was made using a “visual function battery”. This is a behavioural test based on the work of Droste (1991).

The test was designed to be able to characterise children with severe visual impairment and to standardise acuity results. Outcome groups could then
be compared in controlled studies of therapeutic interventions in children with severe visual impairment.

With the visual function battery, a quotient of relative visual function is determined based on a variety of gross behavioural indicators of visual function. The visual function battery used in this trial involved six categories of testing. Besides testing for bare light perception, the tests were selected to give the child multiple opportunities to demonstrate some degree of light projection, mostly by fixation and orientation behaviour.

Three trials were made in each category. The final "visual function quotient" was computed as the number of successful trials divided by the total number of trials. The categories used were as follows:

1. **Light perception** - reaction to a high intensity light source (indirect ophthalmoscope) manifested by gaze avoidance, squinting, or head movement.
2. **Fixation** - ability to reliably orient towards a penlight, face, or familiar large object.
3. **Following** - ability to track a large object in horizontal or vertical directions by smooth pursuit, a series of saccades, or head reorientation.
4. **Fix and Follow** - ability to follow a red Maddox rod in horizontal or vertical directions when retro-illuminated by a penlight.
5. **Optokinetic Nystagmus** - development of grossly observable optokinetic nystagmus in response to a cloth tape with 5cm stripes hand-moved horizontally 15-20cm from the subject.
6. **Grab large object** - ability to successfully grab a large familiar object placed in front of the child. In this study a red teddy bear was used.
Figure 35 Visual acuity testing using visual function battery.
Assessment of optokinetic nystagmus (above) and ability to follow large object (below)
4.2.11.3 Visual Assessment Using Preferential Looking Tests

Cardiff Cards

The vanishing optotype acuity test (Cardiff test) is a new type of visual acuity test which was developed primarily for children between one and three years of age. (Woodhouse et al. 1992) Although a number of tests are available to assess the vision of small children they may be unsuitable for a subgroup of children who lack adequate cognitive and motor abilities to perform pattern recognition tests or who become easily bored and restless when faced with a grating acuity test (Fielder et al. 1992).

The Cardiff test is easy to use and requires little or no explanation. The test has been validated against a grating acuity test in children with normal vision (Adoh et al. 1992) but when this clinical trial started it had yet to be validated for small children with visual impairment.

The test uses the combined principles of preferential looking and of the "vanishing optotype". Vanishing optotypes were first described in 1977 (Howland et al. 1978) and are constructed such that their detection and recognition thresholds are almost identical. They consist of black and white stripes on a neutral grey background, the average luminance being equal to the background. The optotype (which is in the form of pictures) fades completely into the background when the retinal image is not resolved making it invisible rather than blurred.

The Cardiff acuity test has many potential advantages over grating preferential looking tests in the clinic. It is quicker, more user friendly and is
generally liked by children. The end point is often very clear cut, the child suddenly losing interest when no picture is perceived. It was particularly useful in the setting of this trial as it does not rely on letter recognition but instead uses pictures that are universally understood. Children who were often very anxious at finding themselves in a hospital environment in a large city enjoyed doing the test as a game. The cards are more robust than grating cards because dirty finger prints do not significantly reduce the child's ability to discriminate the position of the shape on the card. Finger marks on grating cards usually make the card unusable. This is particularly important in environments were the cost of replacing cards is prohibitively expensive. One problem with the Cardiff test is that it is only possible to test acuities down to the 20/400 level which is a much narrower range than the grating tests. This means that at present it is not a useful tool for children with severe visual impairment. However it should be possible to create optotypes to test acuities in this range which will be a significant benefit.

Because the test had not been validated for children with visual impairment when the clinical trial began, a separate study was undertaken to investigate the validity of the Cardiff (optotype) test compared to an established and validated grating acuity card test (Keeler cards)(Preston et al. 1987; Teller et al. 1986) for a specific group of children with visual impairment. This was carried out before the clinical trial commenced (Eckstein et al. 1994).

4.2.11.4 Validation Of The Cardiff Card Test For Children With Visual Impairment

The optotype test uses computer generated shapes which consist of a white band surrounded by a black band of half the width on a neutral grey
background. The overall size of the shape remains identical but the width of the white and black bands is varied. The cards are calibrated in minutes of arc and the range of acuities is equivalent to 20/20 to 20/200 at 1 metre viewing distance. Each successive card varies by 0.1 log step. Usage of the logarithm of the minimum angle of resolution (log MAR) means that the working distance can be varied to increase the range of acuities such that at 0.5 meters, acuities between 20/40 to 20/400 can be measured. (Table 38)

Table 38   Key to Cardiff Cards with Snellen Equivalents

<table>
<thead>
<tr>
<th>Snellen</th>
<th>logMAR</th>
<th>CARD</th>
<th>Snellen</th>
<th>logMAR</th>
</tr>
</thead>
<tbody>
<tr>
<td>6/60</td>
<td>1.0</td>
<td>A</td>
<td>6/120</td>
<td>1.3</td>
</tr>
<tr>
<td>6/48</td>
<td>0.9</td>
<td>B</td>
<td>6/96</td>
<td>1.2</td>
</tr>
<tr>
<td>6/38</td>
<td>0.8</td>
<td>C</td>
<td>6/76</td>
<td>1.1</td>
</tr>
<tr>
<td>6/30</td>
<td>0.7</td>
<td>D</td>
<td>6/60</td>
<td>1.0</td>
</tr>
<tr>
<td>6/24</td>
<td>0.6</td>
<td>E</td>
<td>6/48</td>
<td>0.9</td>
</tr>
<tr>
<td>6/19</td>
<td>0.5</td>
<td>F</td>
<td>6/38</td>
<td>0.8</td>
</tr>
<tr>
<td>6/15</td>
<td>0.4</td>
<td>G</td>
<td>6/30</td>
<td>0.7</td>
</tr>
<tr>
<td>6/12</td>
<td>0.3</td>
<td>H</td>
<td>6/24</td>
<td>0.6</td>
</tr>
<tr>
<td>6/9.5</td>
<td>0.2</td>
<td>I</td>
<td>6/19</td>
<td>0.5</td>
</tr>
<tr>
<td>6/7.5</td>
<td>0.1</td>
<td>J</td>
<td>6/15</td>
<td>0.4</td>
</tr>
<tr>
<td>6/6</td>
<td>0.0</td>
<td>K</td>
<td>6/12</td>
<td>0.3</td>
</tr>
</tbody>
</table>

Forty eight children fulfilling the entry criteria of being aged between one and four years and with visual impairment (best VA <6/18-6/60) or severe visual impairment (best VA <6/60-3/60) were entered into the study. Children who were developmentally delayed or who had severe physical handicap were excluded.
Each child was tested using optotype cards and Keeler acuity cards in the same brightly lit room. The examiners were not informed of the clinical diagnosis or of each other's results. The scores were noted down by a third examiner who was not involved in vision testing. Children were randomly assigned to undergo the optotype test either first or second. Binocular testing was always performed before monocular testing and best refractive correction was used whenever possible.

**Cardiff card procedure**

Once the child was comfortably seated the first card was presented at eye level at a distance of 1 metre. The examiner watched the child's eye movement, whether up or down and made a choice as to the direction of gaze, being unaware of the position of the shape. The card was then checked to see if the choice was correct and a second similar card presented. If both choices were correct the examiner would move onto the next group of cards descending in 0.1 log increments. The procedure was continued until a false choice of shape position or no definite fixation was observed in one of the cards. At this point the examiner went back to the previous acuity level and showed all three cards. The endpoint was taken as the highest level that two out of the three cards were definitely seen correctly. The test was always performed at 1 metre initially but altered to half a metre if the child began to lose attention or was unable to visualise any of the cards.
Keeler acuity card procedure (Chandna et al. 1988; Teller et al. 1986)

The cards were placed face down in two stacks. On top of one stack was a card containing a low spatial frequency grating. Beneath this card were acuity cards containing gratings of higher spatial frequencies. The gratings in this stack were arranged sequentially with the highest spatial frequency grating on the bottom. The second stack of cards contained cards with spatial frequencies lower than those of the first stack, arranged sequentially with the highest spatial frequency grating on top and the lowest spatial frequency grating on the bottom. This provided a continuous series of gratings in the two stacks, so that to proceed sequentially to higher or lower spatial frequency the tester had only to move the top card in one stack to the top of the other stack and pick up the next card in the first stack.

Testing began by showing the child a coarse grating, likely to be visible (<0.64 cycles/cm) followed by a blank card. The test distance was set at 38 cm initially. The cards were presented in descending order with at least two presentations per card, beginning with a coarse grating and moving down sequentially in octave steps toward finer gratings. For each card shown a tentative decision was made as to whether the child was able to see the grating.

Each card was presented at least twice once with the grating on one side then with the card turned 180 degrees so that the grating was on the opposite side.

Any consistent cue from the child was used to arrive at an acuity estimate. This included, verbal responses, pointing, eye movements, or a dampening or change in the quality of nystagmus.
Results

Grating card visual acuities were recorded in cycles per degree (cy/deg) and optotype acuities recorded in logMAR units and converted where necessary, for analysis. A plot of binocular acuity results of the two tests in cycles per degree is presented in Figure 36. The line of equality shows where all the points would be if the two tests gave identical acuities each time. The outer dotted lines represent agreement of the two estimates to within +/- 1.0 octave. (1 octave is a doubling or halving of spatial frequency and is equivalent to 0.3 log MAR units). The simple plot of the results of the grating test against the optotype test shows clustering close to the line of perfect agreement but this method does not enable a statistical assessment to be made between the two tests.
Figure 36. Plot of the grating test (Keeler Cards) against the optotype test (Cardiff Cards). The solid line represents perfect agreement and the dashed lines represent agreement of the two estimates to within +/- 1.0 octave, where 1 octave is a doubling or halving of spatial frequency (cycles/degree) and is equivalent to 0.3 log MAR. (Numbers in parentheses equal number of overlapping points)
The difference between the two test acuity scores in log MAR units (grating-optotype) plotted against the corresponding mean acuity score for each child ((grating + optotype)/2) is presented in Figure 37. The differences between the two tests lie between plus 0.3 and minus 0.2 logMAR units, with a tendency for the optotype test to record a better visual acuity (lower logMAR score, i.e. greater number of points above the line) than the grating test. Figure 37 gives a representation of the level of variability and also enables an assessment of the magnitude of the discrepancies to be made (Bland and Altman, 1986). The dotted lines represent the mean difference plus or minus two Standard Deviations which are the acceptable limits of agreement. All of the acuity readings fall between the two lines and are within one octave of each other. The intraclass correlation coefficient which is equivalent to the Kappa statistic and is an alternative means of comparing the two tests is 0.81 (p<0.01) again demonstrating good agreement between the two measurements of visual acuity.
Figure 37 Plot of the difference between the two tests against their mean, giving a representation of the level of variability. Mean difference = 0.08 min arc, standard deviation of difference = 0.14 min arc. Mean + 2SD = 0.36 min arc, mean - 2SD = -0.2 min arc. (Numbers in parentheses equal number of overlapping points)
**Discussion of validation testing**

These results demonstrate that in children with visual impairment the optotype test acuities are also comparable with an established grating acuity test (Keeler cards) and this finding has now been substantiated by others (Mackie et al. 1995).

The Cardiff test is not a recognition test despite the shapes on the cards. The examiner is judging eye movement primarily (pattern detection) and not requiring the child's visual system to perform the more complex task of discriminating the pattern. It is likely therefore that this test will overestimate visual acuity when comparing results with recognition tests. (Kushner, 1994; Lamkin, 1992)

The Cardiff test has not been shown to be any better at identifying amblyopia than a grating acuity test (Mayer et al. 1984; Moseley et al. 1988) and in one study was shown to significantly underestimate the degree of amblyopia (Horwood, 1994).
Figure 38 Cardiff acuity test being performed
4.2.11.5 Other Acuity Tests

Snellen Acuity

Standard Snellen acuity was measured at 6 metres using a backlit Snellen chart with Tamil letters or numbers whenever children were old enough or had good enough vision to be able to co-operate. Single letter acuity was tested with the Sheridan-Gardiner test.

Cambridge Crowding Cards

Children with amblyopia have increased difficulty identifying test letters when they are presented in a linear or two-dimensional array rather than as isolated characters. This observation, sometimes described as the "crowding phenomenon" is an example of the effect of contour interaction on visual acuity.

Because the Sheridan-Gardiner test is a single letter test, children with poor vision due to amblyopia will do better than on a Snellen chart. The Cambridge crowding test asks the child to identify a letter surrounded by 4 others and is designed specifically to detect amblyopia (Atkinson, 1985). This test was used for all children that were old enough and had good enough vision to see the letters.

Reading vision

Snellen near vision charts were used to assess reading vision when acuity was adequate.

Stereopsis

Assessment of stereopsis was made whenever possible using the Titmus fly and Lang stereo test.
Figure 39  Assessment of near vision and Cambridge crowding acuity test
4.2.11.6 Recording Of Visual Acuity

Visual acuity was recorded on the forms in the standard units for each test performed. The Keeler cards are calibrated in cycles per degree at 38cm whereas the Cardiff cards are calibrated in log MAR units. All visual acuities were converted to log MAR (logarithm of the minimum angle of resolution) units for analysis. (Conversion chart, Table 39) (Bailey and Lovie, 1976). A typical child had acuity measured with both Cardiff and Keeler cards and then as it developed, Snellen acuity would also be tested. More than one acuity test was performed whenever possible.
Table 39 Conversion table between Snellen, Cardiff and Keeler acuities (Bailey and Lovie, 1976)

<table>
<thead>
<tr>
<th>Snellen</th>
<th>log MAR</th>
<th>Cycles/degree</th>
</tr>
</thead>
<tbody>
<tr>
<td>6/1000</td>
<td>2.2</td>
<td>0.18</td>
</tr>
<tr>
<td>6/620</td>
<td>2.0</td>
<td>0.29</td>
</tr>
<tr>
<td>6/500</td>
<td>1.9</td>
<td>0.36</td>
</tr>
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<td>6/250</td>
<td>1.6</td>
<td>0.72</td>
</tr>
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<td>6/190</td>
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<td>0.96</td>
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<td>6/120</td>
<td>1.3</td>
<td>1.5</td>
</tr>
<tr>
<td>6/96</td>
<td>1.2</td>
<td>2.0</td>
</tr>
<tr>
<td>6/76</td>
<td>1.1</td>
<td>2.5</td>
</tr>
<tr>
<td>6/60</td>
<td>1.0</td>
<td>3.0</td>
</tr>
<tr>
<td>6/48</td>
<td>0.9</td>
<td>3.8</td>
</tr>
<tr>
<td>6/38</td>
<td>0.8</td>
<td>5.0</td>
</tr>
<tr>
<td>6/30</td>
<td>0.7</td>
<td>6.5</td>
</tr>
<tr>
<td>6/24</td>
<td>0.6</td>
<td>7.5</td>
</tr>
<tr>
<td>6/19</td>
<td>0.5</td>
<td>9.6</td>
</tr>
<tr>
<td>6/15</td>
<td>0.4</td>
<td>12.5</td>
</tr>
<tr>
<td>6/12</td>
<td>0.3</td>
<td>15.0</td>
</tr>
<tr>
<td>6/9.5</td>
<td>0.2</td>
<td>21.6</td>
</tr>
<tr>
<td>6/7.5</td>
<td>0.1</td>
<td>25.5</td>
</tr>
<tr>
<td>6/6</td>
<td>0.0</td>
<td>30.0</td>
</tr>
</tbody>
</table>

4.2.12 Refraction and Aphakic Correction

Children were refracted by a trained optometrist before discharge and at every out patient follow-up appointment. Spectacles were provided free for all children prior to discharge and changed whenever clinically necessary. Special small frames for babies and infants were used when necessary. Parents were instructed to encourage children to use them as much as possible.
Figure 40 Spectacles with small frames kept in place with ingenuity
4.2.13 Surgical Procedure

**Preoperative preparation**

All children were assessed to determine fitness to undergo a general anaesthetic by the Consultant anaesthetist. Atropine and vallergan were used as the pre-medication in quantities determined by the weight of the child.

**Anaesthetic**

General anaesthesia was used throughout. Muscle relaxants were used for intubation but not during the surgery. Anaesthesia was monitored using a pulse oximeter.

**Surgeon**

A single highly experienced Consultant paediatric ophthalmologist Dr P. Vijayalakshmi who had performed over 4000 paediatric cataract extractions undertook all of the surgical procedures including secondary membranectomies. This was done in order to avoid the problems of operator bias in the analysis.

**Quality Control**

All procedures were observed by the author and photographic records kept of each case. Study forms were filled in at the end of each procedure and returned to the study co-ordinator.
Figure 41 Eye Theatres at the Aravind eye hospital
4.2.13.1 Surgical Procedure For Lensectomy

The ocular adnexa and skin surrounding the eye were cleaned with povidone iodine and the surgical field draped with sterile towels. The eye was then irrigated with sterile saline solution. A lid speculum was inserted and a superior rectus suture attached. After a small conjunctival flap was produced, a 3mm limbal incision was made. A peripheral iridectomy was performed and an MVR blade put through the iridectomy, cutting the capsule and mobilising the lens material (Figure 42 a&b). The lensectomy cutter (Peyman Vitreophage) was inserted and the entire lens contents removed along with a portion of the anterior vitreous (Figure 42 c&d). The section was closed with two 10-O nylon sutures. The anterior chamber was maintained with Ringers solution and air and a bubble of air remained in the AC at the end of the procedure. After the superior rectus suture was removed, 5mg of gentamicin was injected subconjunctivally into the lower fornix. The eye was padded until the first post-operative examination.
Figure 42. Lensctomy procedure. A) Limbal section and creation of iridectomy. B) MVR blade passing through the iridectomy, capsule and mobilising lens material. (Study no. 470)
Figure 42 C&D Lensectomy procedure. Peyman vitreophage removing entire lens, capsule and anterior vitreous.
4.2.13.2 Surgical Procedure For Aspiration With Primary Capsulotomy

The ocular adnexa and skin surrounding the eye were cleaned with povidone iodine, the surgical field draped with sterile towels and the eye irrigated with sterile saline solution. A lid speculum was inserted and a superior rectus suture attached. A 3mm limbal incision was made and an irrigating cystitome inserted into the anterior chamber and a circular “can opener” type capsulotomy produced. A Storz irrigation aspiration cannula was used to remove the lens material (Figure 43 a&b). Air maintained the depth of the anterior chamber and the section closed with two 10-O nylon sutures. The cystitome on the end of a syringe of air was re-inserted into the eye through the same incision between the sutures and after filling the chamber with air, a small perforation in the posterior capsule at the six o'clock position was made. The tip was turned slightly to one side and the posterior capsule drawn up leaving a central gap (Figure 43 c&d). The anterior chamber was again filled with air to keep the vitreous face back. After the superior rectus suture was removed 5mg of gentamicin was injected subconjunctively into the lower fornix. The eye remained padded until the first post-operative examination.
Figure 43 a&b  ECCE procedure. Anterior can opener style capsulotomy (above). Aspiration of lens material (below).
Figure 43 c&d  ECCE procedure. Primary posterior capsulotomy. (Study no. 121 and 201)
4.2.13.3 Between Operations

Children normally had surgery to the second eye within five days of the first operation. The time between operations was recorded on the appropriate form. (Appendix) The unoperated eye was not patched following first eye surgery.

4.2.14 Immediate Post-Operative Follow Up

The children were assessed daily by a single observer (author). On day 1, 3 and 5 following surgery for each eye the details were entered onto the standardised form. A combination of gentamicin 0.3% and betnesol 1.5% were normally given four times a day to the operated eye(s) after the first examination on day 1. If the clinical situation warranted more frequent drop application or different drops, this was recorded on the appropriate form.

Children were refracted and given aphakic spectacles after surgery had been completed to both eyes. This was done before the child left hospital and the parents were told the importance of using the glasses continually.

4.2.15 Longer Term Follow Up.

Children were reviewed after 4 weeks, 3 months, 6 months, 1 year and then annually. They could be reviewed more often if clinically necessary. All children were reviewed at year one and two by the author. Examinations on
other occasions were performed whenever possible by the same examiner. All visual acuity testing was performed by a single examiner (N. Poornima).

4.2.16 Recording of Complications

The following is an outline of the definition of specific complications:

1. **Iritis** If possible all children who had an inflamed eye post-operatively were examined on the slit lamp. Some degree of inflammation was common but it was only recorded if severe. (greater than 50 cells visible in a 2 x 1mm slit beam at 45 degrees of oblique illumination).

2. **Residual cortex** This was recorded as positive if associated with iritis or if the cortex involved the pupillary area.

3. **Special treatment** If more frequent drops were required than the standard protocol permitted, this was recorded under “special treatment”.

4. **Opacification of the posterior capsule** (PCO) This was relevant to those cases where a part of the posterior capsule remained. Opacification was classified into 3 types:

   - **Type 1** - PCO not seen in the central visual axis, seen only when the pupil is dilated and direct ophthalmoscopy gives a clear view of the fundus.
   - **Type 2** - PCO seen in the central visual axis in an undilated pupil. The fundus details are only minimally obscured.
   - **Type 3** - PCO is seen in the central visual axis in an undilated pupil. The fundus details cannot be clearly made out.

5. **Gleaucoma** Intraocular pressure was measured using the Keeler Pulsair 2000 pneumotonometer at all post operative visits. Goldman tonometry was
used for older children. Pupils were dilated at the six month, one and two year visit and an assessment of the optic disc was made. A diagnosis of glaucoma was made if the IOP was >21mmHg and the optic disc showed signs of increased cupping or if the IOP was consistently higher than 26mmHg.
4.2.17 Protocol Deviations, Withdrawals And Patients Lost To Follow Up.

If the operative technique to which the child had been randomised became impossible to perform once the operation was underway, the child remained in the study and the reasons for failure recorded. If the other eye had not already had surgery, it remained randomised to the alternative treatment to the first eye. In the event of a serious complication either surgical or anaesthetic when operating on the first eye the Consultant with overall clinical responsibility had to decide whether the child should be withdrawn from the randomised arm of the study.

Children were considered lost to follow up only when all of the following events were encountered:

a) The child/parents failed to return on two consecutive visits.
b) No answer was received when the child was summoned by letter on two occasions.
c) A home visit failed to trace the child.

For the follow up visits after discharge, the time-window within which a visit (spontaneous or following a reminder letter) was accepted as providing the necessary data was:

- Four week visit: attendance +/- two weeks (2-6 weeks)
- Three month visit: attendance +/- four weeks (8-12 weeks)
- Six month visit: attendance +/- six weeks (20-32 weeks)
- One year visit: attendance +/- twelve weeks (40-64 weeks)
- Two year visit: attendance +/- twelve weeks (92-116 weeks)
Patient Contact

Each parent was issued with a follow up card that listed the dates of the five follow up visits.

Patients were contacted by post two weeks before each visit became due. If they failed to turn up a second letter was sent. Children who failed to turn up after the second letter was sent were traced by a trained "social worker" who went to the town or village and personally asked them to return.

If parents and children were unwilling or unable to return they were asked to see a local ophthalmologist and a report sent on.

4.2.18 Economic Incentives

One of the reasons for not seeking health care in most developing countries is the economic barrier associated with the cost of treatment and access costs. Previous studies done at Aravind Hospital have demonstrated that removing economic barriers improves acceptance of treatment and follow up attendance (Brilliant et al. 1991). With this in mind the following economic incentives were provided if required:

Surgery:  
Anaesthetic costs
Food during hospital stay for child and one parent

At discharge:  
Medicines for all children for a four week period.
Return bus fare for all patients (Child and one parent)
Aphakic glasses for all children
At four week follow up: Medicine to all patients
Return bus fare for all patients (Child and one parent)
Reimbursement of lost earnings to one parent
Aphakic spectacles if necessary

At three month follow up: Return bus fare for all patients (Child and one parent)
Reimbursement of lost earnings to one parent
Aphakic spectacles if necessary

At six month follow up: Return bus fare for all patients (Child and one parent)
Reimbursement of lost earnings to one parent
Aphakic spectacles if necessary

At one year follow up: Return bus fare for all patients (Child and one parent)
Reimbursement of lost earnings to one parent
Aphakic spectacles if necessary

4.2.19 Data Recording and Analysis

Data Entry

Data was entered onto a database (dBase IV (DOS Version), Ashton-Tate) specifically designed by the author. The program enabled easy data entry by displaying the study proforma on the computer screen and had built in range checks and validation components. All data was double entered before being
"cleaned". Data was later transferred to Microsoft Access, Borland Paradox and Epi Info Version 5 and 6.

Stages of Data Entry

Data entry for each child was completed in six stages.
1. At the time of discharge: pre-operative exam, surgical report and first week post operative data.
2. After the four week visit: four week follow up data.
3. After the three month visit: three month follow up data.
4. After the six month visit: six month follow up data.
5. After the one year visit: one year follow up data.
6. After the two year visit: two year follow up data

4.2.20 Study End Point And Sample Size Considerations

The end point used for sample size projections was a difference in visual acuity (clinical gain) of 0.3 log MAR units or more at 1 year following surgery using a series of visual acuity tests. To estimate the percentage of eyes expected to improve following surgery, data from several earlier retrospective studies were used (Francois, 1979; Bradford et al. 1994; Parks, 1982; Neumann et al. 1993; Robb and Petersen, 1992a). Setting the significance level at 0.05 and the power at 0.90, it was determined that a sample size of 55 children was required to detect these differences (Epi-Info 6). Assuming a 15% dropout rate within one year of follow up and the fact that each child had both procedures, the requisite sample size was 63 (i.e. 126 eyes in total). The results from a total of 65 children were analysed.
4.2.21 Statistical Analyses

The study was designed with matched pairs so that if a substantial number of children were lost to follow up, there would still be equal numbers having had each procedure and meaningful analysis would still be possible. Children were matched for personal factors and exposures because results were compared between eyes of the same child. Confounders such as age, sex and race were therefore eliminated. Because interventions were performed on both eyes, the outcome data cannot be regarded entirely as that from two distinct observations because the two outcomes are not strictly independent of each other (Thompson, 1993; Morris, 1993).

The Chi-squared test was used to compare binary aspects of patient data. The significance level was set at P<0.05. McNemars Chi squared test was used to analyse all matched pair data (Thompson, 1993). Two way analysis of variance (ANOVA related sample comparison) was performed to compare visual acuity expressed as log scale scores between the two eyes at baseline, six months and one year after randomisation as well as to assess acuity change over time. Univariate and multivariate logistic regression was used to analyse risk factors for good and bad outcome on individual children rather than on eyes.

4.2.22 Specific Personnel and Roles

Dr P Vijayalakshmi Consultant Ophthalmologist; overall clinical responsibility for the study, obtain informed parental consent, surgeon for all cases.

Dr M Eckstein (Author) - overall co-ordinator of study; quality control,
adverse affects monitoring, reporting, data entry, budget control.

Miss N Poornima - local study co-ordinator; fill in front data sheet of proforma, allocate study number, arrange follow up dates, arrange incentive payments for aphakic spectacles, travel and treatment costs. Visual acuity testing.
4.3 Results

4.3.1 Baseline Characteristics

4.3.1.1 Description of Sample

Over a nine month period in 1993-4, 127 children aged between 0-10 years with bilateral cataract attended the paediatric eye clinic for the first time. Of these children, 65 fulfilled all of the entry criteria and were enrolled into the clinical trial. No child that was eligible to enter the trial failed to enrol. The 62 children who had bilateral cataract that required surgery but who did not fulfil the entry criteria were followed up using a similar protocol to the children who were in the trial.

| Target sample (children with non-traumatic cataract age 0-15 years) | 366 |
| Selected sample (children <10 years with bilateral cataract) | 127 |
| Entered randomised study | 65 |
| Sample seen at 1 year post op | 60 (3 died and 2 lost to follow up) |
| Did not fulfil entry criteria | 62 |
4.3.1.2 Ineligibility

A total of 62 children were ineligible to enter the trial and the reasons are shown in Table 40. Three children lived in states other than Tamil Nadu or Kerala and the distances were too great for continued long term follow up. Thirty three children had cataracts which were not symmetrical such that one was obviously more dense than the other or had other associated ocular disease.

<table>
<thead>
<tr>
<th>Reason for ineligibility</th>
<th>No. of children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Live too far away</td>
<td>3</td>
</tr>
<tr>
<td>Cataracts not symmetrical</td>
<td>24</td>
</tr>
<tr>
<td>Other associated ocular disease</td>
<td>9</td>
</tr>
<tr>
<td>Child unfit for anaesthetic</td>
<td>4</td>
</tr>
<tr>
<td>Lensectomy preferable in both eyes</td>
<td>4</td>
</tr>
<tr>
<td>ECCE /IOL preferable in both eyes</td>
<td>18</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>62</strong></td>
</tr>
</tbody>
</table>

There were 22 children who were excluded because either a lensectomy or aspiration with or without an intraocular lens were felt to be more appropriate treatments by the clinician with overall responsibility for the study. The reasons for these decisions is shown in Table 41 and Table 42. The anaesthetist felt that four of the children were too young or too small for safe general anaesthesia and surgery was deferred until a later date.
Table 41 Reason for bilateral lensectomy to be performed

<table>
<thead>
<tr>
<th>Study No</th>
<th>Age (months)</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>53</td>
<td>36</td>
<td>bilateral dense membranous cataracts with opacified posterior capsule</td>
</tr>
<tr>
<td>331</td>
<td>5</td>
<td>membranous cataract with opacified posterior capsule</td>
</tr>
<tr>
<td>439</td>
<td>7</td>
<td>congenital rubella with dense nuclear cataracts</td>
</tr>
<tr>
<td>470</td>
<td>48</td>
<td>congenital rubella with dense nuclear cataracts</td>
</tr>
</tbody>
</table>

Table 42 Reason for bilateral lens aspiration / ECCE to be performed

<table>
<thead>
<tr>
<th>Study No</th>
<th>Age (months)</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>34</td>
<td>72</td>
<td>bilateral intraocular lens implant</td>
</tr>
<tr>
<td>37</td>
<td>120</td>
<td>bilateral intraocular lens implant</td>
</tr>
<tr>
<td>71</td>
<td>80</td>
<td>bilateral intraocular lens implant</td>
</tr>
<tr>
<td>88</td>
<td>92</td>
<td>bilateral intraocular lens implant</td>
</tr>
<tr>
<td>168</td>
<td>72</td>
<td>bilateral intraocular lens implant</td>
</tr>
<tr>
<td>182</td>
<td>84</td>
<td>cataract too hard for probe</td>
</tr>
<tr>
<td>246</td>
<td>72</td>
<td>bilateral intraocular lens implant</td>
</tr>
<tr>
<td>250</td>
<td>72</td>
<td>bilateral intraocular lens implant</td>
</tr>
<tr>
<td>271</td>
<td>120</td>
<td>bilateral intraocular lens implant</td>
</tr>
<tr>
<td>289</td>
<td>84</td>
<td>bilateral intraocular lens implant</td>
</tr>
<tr>
<td>298</td>
<td>120</td>
<td>bilateral intraocular lens implant</td>
</tr>
<tr>
<td>316</td>
<td>96</td>
<td>cataract too hard for probe</td>
</tr>
<tr>
<td>322</td>
<td>84</td>
<td>cataract too hard for probe</td>
</tr>
<tr>
<td>419</td>
<td>72</td>
<td>bilateral intraocular lens implant</td>
</tr>
<tr>
<td>435</td>
<td>108</td>
<td>bilateral intraocular lens implant</td>
</tr>
<tr>
<td>458</td>
<td>120</td>
<td>bilateral intraocular lens implant</td>
</tr>
<tr>
<td>463</td>
<td>120</td>
<td>bilateral intraocular lens implant</td>
</tr>
<tr>
<td>479</td>
<td>84</td>
<td>bilateral intraocular lens implant</td>
</tr>
</tbody>
</table>

4.3.2 Demography

Children entering the trial came from the states of Tamil Nadu (84%) and Kerala (16%). The majority (74%) came from rural areas which is in keeping with the census data from the two states. The most recent census (1993) shows that three quarters of Indian people still live in rural areas. The mean travelling time to hospital from home was 6.1 hours (range 1-22 hours).
Of the 65 children who entered the randomised trial, there were 31 boys and 34 girls. They had a mean age of 53 months (Range: 3 months-10 years).

Figure 4.4 Age at first presentation of children enrolled into clinical trial

Graph indicating age at first presentation of children entering clinical trial

4.3.2.1 Ocular characteristics

At first presentation, 35 children (54%) had nystagmus (mean age 48 months, SD =43 months, range 3-120 months). Children with nystagmus were more likely to have total cataracts rather than lamellar cataracts (p= 0.02) and were also likely to be younger (p=0.07).

There were 40 children (62%) who had a manifest strabismus at first presentation (mean age 57 months, SD = 38 months, range 3-120 months). Twenty children had an exotropia and twenty had an esotropia.
4.3.2.2 Aetiology

The aetiology of cataracts in the sample of children who were eligible to enter the clinical trial is illustrated in Table 43 and this is compared with children who had bilateral cataracts but who were ineligible to enter the trial.

Table 43 Aetiology of cataracts in children both ineligible and eligible to enter the clinical trial

<table>
<thead>
<tr>
<th>Aetiology of cataract</th>
<th>Children entered into clinical trial</th>
<th>Ineligible children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autosomal dominant</td>
<td>18</td>
<td>20</td>
</tr>
<tr>
<td>Autosomal recessive</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Secondary</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Congenital rubella</td>
<td>4</td>
<td>11</td>
</tr>
<tr>
<td>Unknown</td>
<td>41</td>
<td>26</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>65</strong></td>
<td><strong>62</strong></td>
</tr>
</tbody>
</table>

The majority of children with congenital rubella were either too unfit for general anaesthesia or had other associated ocular disorders which prevented their inclusion. There were no significant differences between the other groups.

4.3.2.3 Follow up

Of the 65 children enrolled, 60 children (92%) attended follow up at 1 year. Of the five children who did not attend, 3 had died during the study period. One child failed to attend any follow up visits after the one month review following surgery and could not be traced and one child left hospital after the first operation and failed to return for second eye surgery or any further follow up. This child could not be traced. (Table 44)
Table 44  Reasons for follow up failure

<table>
<thead>
<tr>
<th>Study Number</th>
<th>Age of child</th>
<th>Reason for failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>147</td>
<td>7 months</td>
<td>died of meningitis 3 months after surgery</td>
</tr>
<tr>
<td>203</td>
<td>7 months</td>
<td>died of pneumonia four weeks after surgery</td>
</tr>
<tr>
<td>204</td>
<td>7 years</td>
<td>died of pneumonia six months after surgery</td>
</tr>
<tr>
<td>295</td>
<td>6 months</td>
<td>failed all reviews after 1/12, unable to trace</td>
</tr>
<tr>
<td>306</td>
<td>10 years</td>
<td>only one eye operated, unable to trace</td>
</tr>
</tbody>
</table>

Of those children who were seen at the one year follow up visit, 50 (83%) had completed all visits successfully (1,3,6 months) and 8 (13%) had missed only one visit. One child (2%) had missed 2 visits but re-attended at 1 year without tracing and one child (2%) required tracing and collecting.

4.3.3 Baseline Ophthalmic Data

Morphology

The morphology of the cataracts are described in Table 45. In all cases the cataract had similar morphology in each pair of eyes.

Table 45  Cataract type (both eyes) in 65 children enrolled into clinical trial

<table>
<thead>
<tr>
<th>Type of cataract</th>
<th>No of children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>27 (41.5%)</td>
</tr>
<tr>
<td>Nuclear</td>
<td>4 (6.2%)</td>
</tr>
<tr>
<td>Lamellar</td>
<td>22 (33.8%)</td>
</tr>
<tr>
<td>Posterior Polar</td>
<td>2 (3.1%)</td>
</tr>
<tr>
<td>Mixed</td>
<td>10 (15.4%)</td>
</tr>
</tbody>
</table>
Corneal Diameter

There were 3 children who had corneal diameters of less than 10mm in the vertical and horizontal plane in both eyes. The corneal diameters in all 130 eyes are indicated in the graphs. The mean vertical corneal diameter was 10.64mm and mean horizontal diameter was 10.93mm.

Figure 45 Graph of vertical corneal diameter, mean=10.64mm SD=0.91mm

Figure 46 Graph of horizontal corneal diameter, mean=10.93mm SD=0.97mm
4.3.4 Time Between Surgical Procedures

Whenever possible operations on the second eye of individual children were performed within a few days of the first operation. In some cases because the child was unwell and could not have safely tolerated a second anaesthetic, surgery was delayed for a few weeks. One child went home after surgery to the first eye had been completed but failed to return for surgery on the second eye. The graph (Figure 47) shows the time between surgical procedures for the 64 children who had surgery to both eyes.

*Figure 47 Time in days between surgery for the two eyes (64 children)*

![Graph showing time between surgery for the two eyes.]

The majority of children (86%) had surgery to both eyes completed within 7 days but there were 6 children (9%) who waited for between 14 and 21 days for the second procedure. Neither the operated or unoperated eyes were occluded between procedures. For the 9 procedures that were delayed by more than 7 days there were 5 children who had the lensectomy first and 4 who had the ECCE first. In the analysis these children have been included with the
others as there was no significant overall bias between techniques performed before the delay.

4.3.5 Surgical Complications

a) *Failure to complete randomisation as planned*

There were no cases where the procedure had to be altered after randomisation but before surgery was begun. In five cases it was not possible to complete the randomised procedure and either the procedure had to be substantially modified or converted. Table 46 shows the reasons for the alteration in procedure. These eyes were analysed on an intention to treat basis and so even if the procedure was converted from an ECCE to a lensectomy during the procedure the eye remained in the ECCE group.

*Table 46 Reasons for conversion from one procedure to another after randomisation*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Reason for failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>79</td>
<td>Large central defect in posterior capsule</td>
</tr>
<tr>
<td>195</td>
<td>Vitreous pressure too high to allow anterior capsulotomy</td>
</tr>
<tr>
<td>198</td>
<td>Posterior capsulotomy not possible</td>
</tr>
<tr>
<td>294</td>
<td>Central defect in posterior capsule</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Reason for failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>204</td>
<td>Nucleus too hard for probe to cut</td>
</tr>
</tbody>
</table>
b) *Intra-operative complications*

The complications during surgery are indicated in Table 47. Analysis has been performed using McNemars $\chi^2$ for matched pairs.

Lensectomy was significantly associated with failure to remove all of the lens cortex, with iris trauma and with loss of some lens material into the vitreous. In only one case however was it necessary to refer the child for a pars plana vitrectomy for removal of the lens nucleus from the vitreous. The other 4 eyes which had cortical lens material in the vitreous had no post operative problems. Machine failure (Peyman Vitreophage) was a significant problem in the lensectomy group and a backup machine or a technician were required in 8 cases.

Extracapsular cataract surgery was much more likely to result in vitreous in the anterior chamber at the end of the procedure following the primary posterior capsulotomy. There were no cases of corneal decompensation or raised IOP due to vitreous in the anterior chamber.

*Table 47 Complications during surgery of the two techniques*

<table>
<thead>
<tr>
<th></th>
<th>Lensectomy</th>
<th>ECCE</th>
<th>$\chi^2$</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remnants of cortex</td>
<td>13</td>
<td>1</td>
<td>8.6</td>
<td>0.003</td>
</tr>
<tr>
<td>Iris atrophy</td>
<td>27</td>
<td>0</td>
<td>25</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Iris haemorrhage</td>
<td>5</td>
<td>0</td>
<td>3.2</td>
<td>0.07</td>
</tr>
<tr>
<td>Vitreous in anterior chamber</td>
<td>0</td>
<td>13</td>
<td>11.1</td>
<td>0.009</td>
</tr>
<tr>
<td>Machine fault</td>
<td>8</td>
<td>0</td>
<td>6.1</td>
<td>0.013</td>
</tr>
<tr>
<td>Lens material falling into vitreous</td>
<td>5</td>
<td>0</td>
<td>3.2</td>
<td>0.07</td>
</tr>
</tbody>
</table>
Figure 48 Immediate complications; vitreous in wound following primary capsulotomy. (Study no. 312)
c) **Complications during the first week**

The complications of the two techniques during the first week following surgery are shown in Table 48. In general the complication rate was low and there was no significant difference between the two techniques when analysed as matched pairs. There were no cases of endophthalmitis, choroidal haemorrhage or iris prolapse. There were 2 children who required extra topical steroid during the first week in each eye, seemingly a function of the child rather than the surgical technique. In the other children, 3 ECCE and 2 lensectomy eyes required extra steroid.

<table>
<thead>
<tr>
<th>Complication</th>
<th>Lensectomy</th>
<th>ECCE</th>
<th>(\chi^2) (McNemars)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corneal oedema</td>
<td>2</td>
<td>2</td>
<td>0.5</td>
<td>=0.5</td>
</tr>
<tr>
<td>Hyphaema</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>=1</td>
</tr>
<tr>
<td>Iritis</td>
<td>3</td>
<td>2</td>
<td>0</td>
<td>=1</td>
</tr>
<tr>
<td>Extra topical steroid treatment</td>
<td>4</td>
<td>5</td>
<td>0</td>
<td>=1</td>
</tr>
</tbody>
</table>

**Table 48 Complications during the first week after surgery of the two techniques**

**d) Secondary procedures required**

Table 49 shows the number and type of secondary procedure performed over the 12 months following the initial surgery. The ECCE group required significantly more secondary interventions than the lensectomy group (P<0.05). These were either YAG capsulotomies or surgical membranectomies.
Table 49 Secondary procedures required during the 12 months following initial surgery

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Lensectomy</th>
<th>ECCE</th>
<th>$\chi^2$ (McNemars)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>YAG capsulotomy</td>
<td>0</td>
<td>9</td>
<td>7.1</td>
<td>&lt;0.008</td>
</tr>
<tr>
<td>Membranectomy</td>
<td>1</td>
<td>5</td>
<td>1.5</td>
<td>&lt;0.22</td>
</tr>
<tr>
<td>Vitrectomy to remove lens from vitreous</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Retinal detachment repair</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Any secondary surgical procedure</td>
<td>2</td>
<td>14</td>
<td>7.6</td>
<td>&lt;0.008</td>
</tr>
</tbody>
</table>

e) Complications up to and including one year follow up

Table 50 describes the complications that have occurred at any time between surgery up to and including the one year follow up examination. The only significant difference between techniques was the amount of capsule opacification which affected visual acuity (Type 2 and 3).

There was one retinal detachment which occurred in a lensectomy eye and was noted at the 3 month follow up examination. This was treated by a pars plana vitrectomy and gas but developed PVR and the eye became phthisical and blind. One eye which had a lensectomy, developed localised epithelial ingrowth from the wound site. This eye maintained good vision at the one year follow up. No eyes developed glaucoma during the first year of follow up.

Table 50 Complications up to and including one year follow up

<table>
<thead>
<tr>
<th>Complication</th>
<th>Lensectomy</th>
<th>ECCE</th>
<th>$\chi^2$ (McNemars)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Capsule opacification affecting vision (type 2 and 3)</td>
<td>1</td>
<td>28</td>
<td>20</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pupil decentration affecting vision</td>
<td>2</td>
<td>1</td>
<td>0.5</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>Retinal detachment</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Epithelial ingrowth</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>
4.3.5.1 Posterior Capsule Opacification

Type 2 or type 3 capsule opacification occurred in 28 (43%) eyes which had an ECCE and in one (1.6%) eye which had a lensectomy when the anterior capsule was inadvertently not removed. There were 14 eyes (21%) which had an ECCE where the primary capsulotomy was noted to be inadequate within the first month following surgery. The capsulotomy was either too small or was not in the visual axis. Table 51 describes the secondary procedures performed on eyes with type 3 capsule opacification within one year of initial surgery.

In Figure 49, a Kaplan-Meier curve has been used to illustrate the failure of the primary capsulotomy in ECCE eyes against time of follow up. It shows the time taken to develop type 2 and type 3 capsule opacification. In half of the cases the initial surgical capsulotomy during the procedure was noted to be inadequate but the other half had photographically documented adequate
primary capsulotomies. In those capsulotomies that appeared adequate initially, the capsular rim seemed to contract over the following twelve months so that at some stage it occluded the visual axis. The curve shows that by the 6 month follow up appointment, nearly 40% of ECCE/primary capsulotomy eyes have significant capsule opacification and that the number of new cases developing opacification appears to slow down.

Figure 49 Kaplan-Meier survival analysis following primary capsulotomy showing failure, i.e. development of type 2 or type 3 opacification against follow up time.
Figure 50  YAG capsulotomy (Study no.301) and membranectomy (Study no.365) following closure of primary capsulotomy.
Figure 51 Posterior capsulotomies contracting and closing (Study no. 503 and 365).
4.3.6 Aphakic Correction And Treatment Of Amblyopia

In the trial all aphakia was corrected with spectacles. In general children coped well and managed to adapt to the visual aberrations from aphakic spectacles. Table 52 summarises spectacle use and associated problems.

Table 52 Spectacle use and problems at each follow up examination

<table>
<thead>
<tr>
<th></th>
<th>Month 1</th>
<th>Month 3</th>
<th>Month 6</th>
<th>Year 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children refusing to use spectacles</td>
<td>9</td>
<td>10</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>Lost spectacles</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Broken spectacles</td>
<td>2</td>
<td>3</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Bifocal spectacles used</td>
<td>0</td>
<td>0</td>
<td>9</td>
<td>13</td>
</tr>
</tbody>
</table>

Despite the spectacles being provided free, parents and children looked after them well. Four children had lost the glasses and 14 pairs had been broken during the year. There were 9 children who would not wear spectacles at the one year review and the majority of these had very poor vision and spectacles were of questionable benefit. Bifocal spectacles were prescribed whenever it was felt that they would assist with close vision and were being used by 13 children at the 1 year follow up examination.

Treatment for amblyopia with patching was not commonly used because compliance was generally poor. Five children however were asked to patch one eye when amblyopia appeared to be progressing over the course of the follow up period. Two of these were at month 3 and three at month 6.

Parents were asked at the one year follow up examination how many hours a day the children used their spectacles. This ranged from none to 12 hours, mean 8.5 (SE= 0.63).
4.3.7 Visual Outcome

4.3.7.1 Visual acuity measurements

The visual acuities (converted into log MAR units, Table 53) of the study children at baseline, months 1, 3, 6 and 12 are recorded in Table 55. Missing values due to missed follow up are indicated by a space. Children who were unable to co-operate adequately for uniocular testing, had only their binocular acuity recorded and this is shown in italics.

Table 53 Snellen equivalents of log MAR acuity (Bailey and Lovie 1976)

<table>
<thead>
<tr>
<th>Snellen</th>
<th>log MAR</th>
<th>Snellen</th>
<th>log MAR</th>
</tr>
</thead>
<tbody>
<tr>
<td>6/1000</td>
<td>2.2</td>
<td>6/38</td>
<td>0.8</td>
</tr>
<tr>
<td>6/620</td>
<td>2.0</td>
<td>6/30</td>
<td>0.7</td>
</tr>
<tr>
<td>6/500</td>
<td>1.9</td>
<td>6/24</td>
<td>0.6</td>
</tr>
<tr>
<td>6/250</td>
<td>1.6</td>
<td>6/19</td>
<td>0.5</td>
</tr>
<tr>
<td>6/190</td>
<td>1.4</td>
<td>6/15</td>
<td>0.4</td>
</tr>
<tr>
<td>6/120</td>
<td>1.3</td>
<td>6/12</td>
<td>0.3</td>
</tr>
<tr>
<td>6/96</td>
<td>1.2</td>
<td>6/9.5</td>
<td>0.2</td>
</tr>
<tr>
<td>6/76</td>
<td>1.1</td>
<td>6/7.5</td>
<td>0.1</td>
</tr>
<tr>
<td>6/60</td>
<td>1.0</td>
<td>6/6</td>
<td>0.0</td>
</tr>
<tr>
<td>6/48</td>
<td>0.9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 54 shows the number of children unable to have uniocular vision assessed at each follow up visit. At the one year follow up visit, 92% of children had uniocular acuity recorded compared with only 46% of children at their first visit (baseline). As children were seen repeatedly during the year they became more confident of their surroundings and were more relaxed during the vision testing. Also as their vision improved they became more tolerant of patching for the uniocular acuity test and became more compliant.
Figure 52 The problem of uniocular visual acuity assessment.
Table 54  

<table>
<thead>
<tr>
<th>Follow up examination</th>
<th>Number of children unable to co-operate for uniocular testing. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>35/65 (54%)</td>
</tr>
<tr>
<td>1 Month</td>
<td>18/64 (28%)</td>
</tr>
<tr>
<td>3 Months</td>
<td>12/55 (22%)</td>
</tr>
<tr>
<td>6 Months</td>
<td>8/58 (14%)</td>
</tr>
<tr>
<td>1 Year</td>
<td>5/60 (8%)</td>
</tr>
</tbody>
</table>

Figure 53 Graph showing the difference in acuity in log MAR units between eyes which had uniocular acuity recorded at baseline examination.

Although less than 50% of children complied with uniocular testing at the baseline examination, the majority that did had similar acuities in both eyes (Figure 53). Children who had more than a 0.3 log MAR difference in acuity were excluded from the trial (see inclusion criteria, page 142). For some of the analysis when comparing baseline acuities to one year acuity we have assumed that the uniocular acuities were close to the binocular acuity. This has been clearly stated in the analysis whenever the assumption has been made.
Table 55 Visual acuity data of all eyes at baseline and at follow up appointments (logMAR).
Binocular acuity in italics.
,
s tu d y No.
9
20
30
31
35
36
38
39
43
47
56
59
60
61
65
70
72
78
79
86
97
100
103
112
121
127

2.2
2.2
2.2
0.6
1.3
2.2
2.2
1.2
2.2
2.2
1.3
0.9
2.2
1
1
1.2
1.9
2.2
2.2
1.3
2.2
2.2
1.6
1.6
0.8
0.7

147

2.2

171
174
189
190
192
194
195
198
201

206
226
258
266
270
272
290
293
294

0.8
2.2
2.2
2.2
2.2
2.2
2.2
2.2
0.7
2.2
2.2
2.2
1.2
2.2
2.2
2.2
0.6
2.2
2.2
2.2

1.3
2.2
2.2
0.4
0.3
2.2
1
0.4
1
2.2
1
0.9
2.2
1
0.7
1.2
1
2.2
2.2
1.2
0.7
1.1
0.7
0.4
0.4
0.4
2.2
0.3
1.1
1.3
0.4
1
2.2
2.2
2.2
0.4
2.2
1.1
2.2
0.7
2.2
2.2
1
0.4
1
2.2
1.1

295

2.2

2.2

tost to FU

-

301
305

2.2
2.2

1
2.2

m

2.2

tost to FU

1
1.2
-

1
1.1
je

0.7
1.2
-

312
321
336
337
365
370
378
384
406
409
441
461
503
513

0.7
1
1.9
2.2
2.2
2.2
2.2
2.2
2.2
0.8
2.1
2.2
0.8
2.2

0.1
0.3
0.6
2.2
2.2
0.8
0.9
0.3
0.3
0.8
1.2
1.2
0.5
1.6

0.1
0.1
0.3
2.2
2.2
0.6
0.7
0.4

0.2

0.2
0.2
0.2
2.2
1.4
0.6
0.6
0.3
0.3
0.3
0.7
0.7
0.2
1.4

203
204

1.3
1.4
0.1
0.3
2.2
1
0.6
2.2
0.7
0.3
1.1
0.9
0.2
0.4
1
1
1.1
0.3
1.2
0.9
0.2
0.2
0.2
2 .2
0.2
1
0.9
0.7
1.2
1.3
0.9
0.3
died
1
1.1
2.2
2.2
0.5
0.2
1
2.2

0.6
0.7
0.9
0.6
0.9

1.3
2.2
1.4
0.1
0.2
2.2
0.9
0.3
0.5
2.2
0.5
0.2
1.9
0.9
0.2
0.3
2.2
1
1
0.6
1
0.7
0.3
0.2
0.1
died
0.2
1
0.9
0.5
0.9
1.3
1.9
0.9
0.3

1
1
0.7
1.2
2.2
0.3
0.2
1
2.2
0.9

0.2
2.2
1.3
0.6
0.3
0.2
0.3
0.6
0.9
0.3
1

ECCE

1
2.2
1
0.1
0.3
1.6
0.6
0.3
0.6
1.3
0.6
0.3
1
0.9
0.1
0.6
2.2
1
1
0.2
0.6
1.1
0.9
0.2
0.2
0.1

2.2
2.2
2.2
0.6
1.3
2.2
2.2
1
2.2
2.2
1.3
1
2.2
1
1
1.3
1.6
2.2
2.2
1
2.2
2.2
1.6
1.9
0.8
0.7

1.6
2.2
2.2
0.3
0.3
2.2
1
0.6
0.7
2.2
1.3
1
2.2
1
0.8
1.2
1
2.2
2.2
1.2
0.7
1.4
0.7
0.4
0.4
0.4

-

2.2

2.2

0.4
0.6
0.9
0.3
1.1
0.7
0.7
0.8
0.6

0.7
2.2
2.2
2.2
2.2
2.2
2.2
2.2
0.7

0.3
1.1
0.7
0.4
1.1
2.2
2.2
2.2
0.4

-

2.2
2.2

2.2

died
0.5
1
1.3
1.2
0.3
0.2
1.3
1.1
0.7

2.2
0.9
2.2
2.2
2.2
0.7
2.2
2.2
2.2

1
2.2
0.6
2.2
2.2
1
0.3
1
2.2
1.1

1.3
1.4
0.1
0.7
2.2
1
0.4
2.2
0.6
0.4
1.3
0.7
0.6
0.6
1
1
1.1

0.7
1.4
1.3
0.9
0.7
died

0.4
1.9
0.7
0.3
0.2
0.1
died
0.2
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0.3
0.5
0.9
1.3
1.4
0.9
0.3
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0.7

0.6

1.1

1.6
0.7
1.2
2.2
0.3
0.5
1
2.2
0.9
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1
1.3
1.1

0.3
1.6
0.9
0.4
0.3
0.2
2 .2
0.2
1
0.3

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2.2
2.2
0.6
0.3
1
2.2

tost to FU

208

2.2
2.2
2.2
1
1.2
1.9
2.2
2.2
2.2
2.2
2.2
2.2
1
1.9
2.2
0.8
2.2

1
2.2

1
1.4

tost to FU
2.2
0.3
0.6
2.2
2.2
0.8
0.9
0.3
0.6
0.8
1
1.2
0.5
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1.3
2.2
1.4
0.1
1
2.2
0.9
0.3
0.4
2.2
0.7
0.4
1.2
0.6
0.6
0.4
1
1
1

1
0.2
0.3
2.2
2.2
0.6
0.7
0.3
1.1
1
1.1
0.6
0.9

0.2
2.2
1.3
0.6
0.3
0.3
1.1
1
1.1
0.9
1

1
2.2
1
0.2
1
1.4
0.7
0.3
0.6
1.3
0.6
0.9
1
0.6
0.2
0.6
0.6
1
1
0.2
0.5
1
1
0.4
0.3
0.3
0.4
0.6
0.4
0.3
1.1
1
1.6
0.9
0.6
died
1.4
0.3
1.3
1.1
0.3
0.5
0.9
1.1
1

- %
0.9
1
1
0.2
0.2
2.2
1.2
0.9
0.7
0.2
0.4
1.1
1.2
0.9
0.7
0.7

:


4.3.7.2 Visual Acuity At Baseline Examination

The mean binocular acuity (log MAR) for all children at baseline was 1.8 (SE= 0.052). The mean acuity from uniocular vision testing when possible in 60 eyes from 30 children was 1.8 (SE= 0.073) in eyes that were randomised for lensectomy and 1.8 (SE= 0.072) in eyes randomised for ECCE. However baseline acuity was often difficult to record accurately because of poor compliance and indistinct endpoints in the preferential looking tests. Many children had binocular acuity recorded as 6/1000 (2.2 log MAR) but it is likely that a proportion of these had much better acuity than this. Children who could only be assessed with the visual function battery and who could not be assessed even binocularly with the Keeler cards had a vision of log MAR 2.2 recorded.

Figure 54 Histogram showing binocular visual acuity (log MAR) with Snellen equivalents at baseline for 65 children.
There were 48 children (74%) who were blind or severely visually impaired at baseline (Table 60). No children had acuity better than 6/18 (0.5 log MAR) but 14 (22%) children had binocular acuity better than 6/60. (Figure 54)

### 4.3.7.3 Functional Visual Outcome One Year After Surgery

Table 56 and the graph in Figure 55 shows the visual acuity in log MAR units with Snellen equivalents for all 120 eyes at the one year follow up examination.

<table>
<thead>
<tr>
<th>Log MAR Acuity (Snellen Equivalent)</th>
<th>Lensectomy</th>
<th></th>
<th></th>
<th>ECCE</th>
<th></th>
<th></th>
<th>TOTAL</th>
<th>cumulative %</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1 (6/7.5)</td>
<td>3</td>
<td>5</td>
<td></td>
<td>0</td>
<td>0</td>
<td></td>
<td>3</td>
<td>2.5</td>
</tr>
<tr>
<td>0.2 (6/9.5)</td>
<td>8</td>
<td>13.3</td>
<td>6</td>
<td>10</td>
<td>14</td>
<td>11.7</td>
<td>14.2</td>
<td></td>
</tr>
<tr>
<td>0.3 (6/12)</td>
<td>8</td>
<td>13.3</td>
<td>6</td>
<td>10</td>
<td>14</td>
<td>11.7</td>
<td>25.9</td>
<td></td>
</tr>
<tr>
<td>0.4 (6/15)</td>
<td>1</td>
<td>1.7</td>
<td>4</td>
<td>6.7</td>
<td>5</td>
<td>4.2</td>
<td>30.1</td>
<td></td>
</tr>
<tr>
<td>0.5 (6/19)</td>
<td>1</td>
<td>1.7</td>
<td>2</td>
<td>3.3</td>
<td>3</td>
<td>2.5</td>
<td>32.6</td>
<td></td>
</tr>
<tr>
<td>0.6 (6/24)</td>
<td>9</td>
<td>15</td>
<td>7</td>
<td>11.7</td>
<td>16</td>
<td>13.3</td>
<td>45.9</td>
<td></td>
</tr>
<tr>
<td>0.7 (6/30)</td>
<td>6</td>
<td>10</td>
<td>4</td>
<td>6.7</td>
<td>10</td>
<td>8.3</td>
<td>54.2</td>
<td></td>
</tr>
<tr>
<td>0.8 (6/38)</td>
<td>1</td>
<td>1.7</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0.8</td>
<td>55.0</td>
<td></td>
</tr>
<tr>
<td>0.9 (6/48)</td>
<td>3</td>
<td>5</td>
<td>6</td>
<td>10</td>
<td>9</td>
<td>7.5</td>
<td>62.5</td>
<td></td>
</tr>
<tr>
<td>1.0 (6/60)</td>
<td>6</td>
<td>10</td>
<td>12</td>
<td>20</td>
<td>18</td>
<td>15</td>
<td>77.5</td>
<td></td>
</tr>
<tr>
<td>1.1 (6/75)</td>
<td>3</td>
<td>5</td>
<td>4</td>
<td>6.7</td>
<td>3</td>
<td>3.3</td>
<td>83.3</td>
<td></td>
</tr>
<tr>
<td>1.2 (6/96)</td>
<td>2</td>
<td>3.3</td>
<td>2</td>
<td>3.3</td>
<td>4</td>
<td>3.3</td>
<td>86.6</td>
<td></td>
</tr>
<tr>
<td>1.3 (6/120)</td>
<td>3</td>
<td>5</td>
<td>2</td>
<td>3.3</td>
<td>5</td>
<td>4.2</td>
<td>90.8</td>
<td></td>
</tr>
<tr>
<td>1.4 (6/190)</td>
<td>2</td>
<td>3.3</td>
<td>2</td>
<td>3.3</td>
<td>4</td>
<td>3.3</td>
<td>94.1</td>
<td></td>
</tr>
<tr>
<td>1.6 (6/250)</td>
<td>1</td>
<td>1.7</td>
<td>1</td>
<td>1.7</td>
<td>2</td>
<td>1.7</td>
<td>95.8</td>
<td></td>
</tr>
<tr>
<td>2.2 (6/1000)</td>
<td>3</td>
<td>5</td>
<td>2</td>
<td>3.3</td>
<td>5</td>
<td>4.2</td>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>
In tables 57 and 58 the Snellen equivalents are given of those eyes that had accurate uniocular visual assessment pre operatively and at the one year review. The tables have been separated by randomised surgical procedure and show that there is little difference between the two groups after one year for eyes seeing better than 6/60. More lensectomy than ECCE eyes had acuity better than 6/18 but this was not significant.

Table 59 gives the Snellen equivalents for binocular acuity for all children and shows that 87% of children had acuity better than 6/60 after one year and 40% had acuity better than 6/18. Only 23% of children could see 6/60 or better before surgery.
Table 57 Snellen equivalents of pre-operative and one year post operative acuity for eyes which had a lensectomy and had uniocular acuity measured.

<table>
<thead>
<tr>
<th>Snellen Acuity</th>
<th>Pre-Op</th>
<th>One year post-op</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>6/6-6/18</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>&lt;6/18-6/60</td>
<td>13</td>
<td>43</td>
</tr>
<tr>
<td>&lt;6/60-3/60</td>
<td>6</td>
<td>20</td>
</tr>
<tr>
<td>&lt;3/60</td>
<td>11</td>
<td>37</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>30</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 58 Snellen equivalents of pre-operative and one year post operative acuity for eyes which had an ECCE and had uniocular acuity measured.

<table>
<thead>
<tr>
<th>Snellen acuity</th>
<th>Pre-Op</th>
<th>One year post-op</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>6/6-6/18</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>&lt;6/18-6/60</td>
<td>15</td>
<td>50</td>
</tr>
<tr>
<td>&lt;6/60-3/60</td>
<td>4</td>
<td>13</td>
</tr>
<tr>
<td>&lt;3/60</td>
<td>11</td>
<td>37</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>30</td>
<td>100</td>
</tr>
</tbody>
</table>

Table 59 Snellen equivalents of pre-operative and one year post operative binocular acuity for all children.

<table>
<thead>
<tr>
<th>Snellen acuity</th>
<th>Pre-Op</th>
<th>One year post-op</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>6/6-6/18</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>&lt;6/18-6/60</td>
<td>15</td>
<td>23</td>
</tr>
<tr>
<td>&lt;6/60-3/60</td>
<td>6</td>
<td>9</td>
</tr>
<tr>
<td>&lt;3/60</td>
<td>44</td>
<td>68</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>65</td>
<td>100</td>
</tr>
</tbody>
</table>

212
There were 36 children who were blind or severely visually impaired (<6/60) at the baseline examination but who had normal vision or were only visually impaired (WHO definition) at the one year follow up examination. Eight children remained blind or severely visually impaired following surgery (Table 61). There were no children who became severely visually impaired as a result of surgery although one child did lose significant vision in one eye following a retinal detachment.

Table 60 WHO definitions of visual loss

<table>
<thead>
<tr>
<th>Category of visual loss</th>
<th>Visual acuity in the better eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>≥6/18</td>
</tr>
<tr>
<td>Visual impairment</td>
<td>&lt;6/18-6/60</td>
</tr>
<tr>
<td>Severe visual impairment</td>
<td>&lt;6/60-3/60</td>
</tr>
<tr>
<td>Blind</td>
<td>&lt;3/60-NPL</td>
</tr>
</tbody>
</table>

Table 61 Change in functional vision after surgery (WHO criteria)

<table>
<thead>
<tr>
<th>Number of children who were blind or had severe visual impairment prior to surgery but who had normal vision or only visual impairment one year after surgery.</th>
<th>36/44</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of children who did not improve following surgery and remain blind or severely visually impaired at one year follow up</td>
<td>8/44</td>
</tr>
</tbody>
</table>

4.3.7.4 Reading vision

There were 17 children who could be assessed for near vision at the one year examination. No significant difference existed between the surgical techniques with uniocular testing.
Table 62 Binocular reading vision at year one in 17 children

<table>
<thead>
<tr>
<th>Binocular reading vision</th>
<th>Number of children</th>
</tr>
</thead>
<tbody>
<tr>
<td>n5</td>
<td>9</td>
</tr>
<tr>
<td>n6</td>
<td>4</td>
</tr>
<tr>
<td>n8</td>
<td>1</td>
</tr>
<tr>
<td>n12</td>
<td>1</td>
</tr>
<tr>
<td>n18</td>
<td>2</td>
</tr>
</tbody>
</table>

4.3.7.5 **Stereopsis**

Stereopsis was routinely tested for at every post operative visit. Twelve children (20%) exhibited some form of gross stereopsis one year after surgery with the Titmus fly test or Lang stereotest.

4.3.7.6 **Visual outcome analysed by surgical technique (matched pairs)**

The proportion of eyes which had a lensectomy and an ECCE achieving the study end point, a change in visual acuity of 0.3 log MAR units was not significantly different between the matched pairs using McNemars $\chi^2$ test. ($\chi^2=0.32 \, p=0.57$). (Table 63) *(uniocular acuity estimated from binocular acuity)*

Table 63 Comparison of change in log MAR acuity stratified by randomised treatment at baseline and one year following surgery. McNemar $\chi^2 =0.32 \, p=0.57$

<table>
<thead>
<tr>
<th>Change in log MAR acuity</th>
<th>Lensectomy eyes (%)</th>
<th>ECCE eyes (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥ 0.3 (improved)</td>
<td>54 (90)</td>
<td>52 (87)</td>
</tr>
<tr>
<td>within 0.3 (unchanged)</td>
<td>5 (8)</td>
<td>8 (13)</td>
</tr>
<tr>
<td>≤ 0.3 (worse)</td>
<td>1 (2)</td>
<td>0</td>
</tr>
<tr>
<td><strong>Total no eyes</strong></td>
<td><strong>60</strong></td>
<td><strong>60</strong></td>
</tr>
</tbody>
</table>
If the same analysis for matched pairs is undertaken for the 54% of eyes where uniocular acuities were recorded successfully in both eyes at baseline (Table 64) the difference remains very similar and is not significant (p=0.61).

Table 64  Comparison of change in log MAR acuity stratified by randomised treatment at baseline and one year following surgery for those children who had uniocular acuity measured successfully at baseline. McNemar $\chi^2 = 0.25$ p=0.61

<table>
<thead>
<tr>
<th>Change in log MAR acuity</th>
<th>Lenscetomy eyes (%)</th>
<th>ECCE eyes (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\geq 0.3$ (improved)</td>
<td>26 (87)</td>
<td>23 (77)</td>
</tr>
<tr>
<td>within 0.3 (unchanged)</td>
<td>3 (10)</td>
<td>7 (23)</td>
</tr>
<tr>
<td>$\leq 0.3$ (worse)</td>
<td>1 (3)</td>
<td>0</td>
</tr>
<tr>
<td>Total no eyes</td>
<td>30</td>
<td>30</td>
</tr>
</tbody>
</table>

The visual acuity in most eyes improved and this is shown graphically in Figure 56 where the change in acuity between baseline and one year follow up examination are plotted for eyes randomised to lenscetomy and ECCE.
Figure 56 Histogram of change in acuity in lensectomy and ECCE eyes one year after surgery compared with baseline. Negative values indicate a worsening of vision.

The mean visual acuity of eyes at baseline examination and at follow up appointments where uniocular acuity could be tested satisfactorily are shown in Table 65.

Table 65 Mean acuity of lensectomy and ECCE eyes compared over time for children co­operating with uniocular acuity assessment.

<table>
<thead>
<tr>
<th>Examination time (number children)</th>
<th>Lensectomy</th>
<th></th>
<th></th>
<th></th>
<th>ECCE</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean acuity (log MAR)</td>
<td>SD</td>
<td>Standard error</td>
<td>Mean acuity (log MAR)</td>
<td>SD</td>
<td>Standard error</td>
<td></td>
</tr>
<tr>
<td>Baseline (30)</td>
<td>1.80</td>
<td>.59</td>
<td>.073</td>
<td>1.80</td>
<td>.58</td>
<td>.072</td>
<td></td>
</tr>
<tr>
<td>1 month (46)</td>
<td>1.20</td>
<td>.73</td>
<td>.091</td>
<td>1.26</td>
<td>.72</td>
<td>.091</td>
<td></td>
</tr>
<tr>
<td>3 months (43)</td>
<td>0.92</td>
<td>.64</td>
<td>.087</td>
<td>0.98</td>
<td>.62</td>
<td>.084</td>
<td></td>
</tr>
<tr>
<td>6 months (50)</td>
<td>0.88</td>
<td>.65</td>
<td>.085</td>
<td>0.93</td>
<td>.60</td>
<td>.078</td>
<td></td>
</tr>
<tr>
<td>12 months (55)</td>
<td>0.75</td>
<td>.52</td>
<td>.067</td>
<td>0.80</td>
<td>.45</td>
<td>.058</td>
<td></td>
</tr>
</tbody>
</table>
The scatterplots in Figure 57 graphically represent the change in acuity following surgery in the two groups. Points above the line of equality represent improved acuity. The lines either side of the line of equality represent a change of 0.3 log MAR units (study end point). For these scatterplots the uniocular acuitities have been estimated from binocular acuity where no uniocular measurements were possible.
Figure 57 Scatterplot of visual acuity at 1 year versus baseline for eyes randomised to ECCE above and lensectomy below. Points above the line of equality represent improved acuity. The lines either side of the line of equality represent a change of 0.3 log MAR units.
The graph in Figure 58 shows how the visual acuity of the two surgical techniques varied with time in those eyes which had uniocular acuity recorded. The mean acuity for lensectomy and ECCE eyes are represented by the bar chart plotted for each follow up visit. Children who did not co-operate with uniocular acuity testing have not been included.

*Figure 58 Mean visual acuity (logMAR) of lensectomy and ECCE eyes compared at baseline and over the first 12 months following surgery (error bars = standard error of mean)*

While both procedures appeared to produce an improvement in vision over time, the lensectomy group did slightly better than the ECCE group at every examination following surgery.
4.3.7.7 Visual outcome in individual children comparing matched pair data over time.

Because the study was designed so that each eye was matched for personal factors with the other (same child) and because the cataracts were symmetrical and the baseline acuities similar in both eyes, it is possible to analyse the results comparing one technique directly with the other in each individual child (matched pair data). The paired design is more powerful in detecting differences between the two techniques as extraneous variation among the observations is controlled.

The mean of the difference in acuity between techniques for matched pairs is shown in Table 66. This table shows that there was a significant difference in acuity only at the 3 month visit and that at all other times including the one year follow up, the difference in acuity was not significant.

The visual acuity for matched pairs are shown and compared in Table 67. The graph in Figure 59 shows a plot of these log MAR acuities of the lensectomy and ECCE eyes for each child.

Table 66 Paired comparison of log MAR acuity following surgery. $T = \text{paired t distribution}, \ SE = \text{standard error of mean}.$

<table>
<thead>
<tr>
<th>Examination time following surgery (number of children)</th>
<th>Mean of difference (log MAR) between matched pairs</th>
<th>SE</th>
<th>95% CI</th>
<th>T</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month (64)</td>
<td>0.036</td>
<td>0.036</td>
<td>-0.11 to 0.04</td>
<td>0.99</td>
<td>0.32</td>
</tr>
<tr>
<td>3 months (55)</td>
<td>0.064</td>
<td>0.028</td>
<td>-0.11 to 0.05</td>
<td>2.24</td>
<td>0.03</td>
</tr>
<tr>
<td>6 months (58)</td>
<td>0.047</td>
<td>0.046</td>
<td>-0.14 to 0.09</td>
<td>1.02</td>
<td>0.31</td>
</tr>
<tr>
<td>12 months (60)</td>
<td>0.055</td>
<td>0.05</td>
<td>-0.15 to 0.09</td>
<td>1.10</td>
<td>0.28</td>
</tr>
</tbody>
</table>
Table 67  log MAR acuity in ECCE and lensectomy eyes compared at one year follow up (binocular acuity in italics). A negative difference indicates lensectomy acuity better than ECCE acuity.

<table>
<thead>
<tr>
<th>Study no</th>
<th>Acuity in lensectomy eye one year post op</th>
<th>Acuity in ECCE eye one year post op</th>
<th>Difference between techniques after one year (log MAR units)</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>20</td>
<td>2.2</td>
<td>2.2</td>
<td>-</td>
</tr>
<tr>
<td>30</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>31</td>
<td>0.1</td>
<td>0.2</td>
<td>0.1</td>
</tr>
<tr>
<td>35</td>
<td>0.3</td>
<td>1</td>
<td>-0.7</td>
</tr>
<tr>
<td>36</td>
<td>1.6</td>
<td>1.4</td>
<td>0.2</td>
</tr>
<tr>
<td>38</td>
<td>0.6</td>
<td>0.7</td>
<td>-0.1</td>
</tr>
<tr>
<td>39</td>
<td>0.3</td>
<td>0.3</td>
<td>0</td>
</tr>
<tr>
<td>43</td>
<td>0.6</td>
<td>0.6</td>
<td>0</td>
</tr>
<tr>
<td>47</td>
<td>1.3</td>
<td>1.3</td>
<td>0</td>
</tr>
<tr>
<td>56</td>
<td>0.6</td>
<td>0.6</td>
<td>0</td>
</tr>
<tr>
<td>59</td>
<td>0.3</td>
<td>0.9</td>
<td>-0.6</td>
</tr>
<tr>
<td>60</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>61</td>
<td>0.9</td>
<td>0.6</td>
<td>0.3</td>
</tr>
<tr>
<td>65</td>
<td>0.1</td>
<td>0.2</td>
<td>-0.1</td>
</tr>
<tr>
<td>70</td>
<td>0.6</td>
<td>0.6</td>
<td>1.6</td>
</tr>
<tr>
<td>72</td>
<td>2.2</td>
<td>0.6</td>
<td>1.6</td>
</tr>
<tr>
<td>78</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>79</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>86</td>
<td>0.2</td>
<td>0.2</td>
<td>0</td>
</tr>
<tr>
<td>97</td>
<td>0.6</td>
<td>0.5</td>
<td>0.1</td>
</tr>
<tr>
<td>100</td>
<td>1.1</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>103</td>
<td>0.9</td>
<td>1</td>
<td>-0.1</td>
</tr>
<tr>
<td>112</td>
<td>0.2</td>
<td>0.4</td>
<td>-0.2</td>
</tr>
<tr>
<td>121</td>
<td>0.2</td>
<td>0.3</td>
<td>-0.1</td>
</tr>
<tr>
<td>127</td>
<td>0.1</td>
<td>0.3</td>
<td>-0.2</td>
</tr>
<tr>
<td>171</td>
<td>0.4</td>
<td>0.4</td>
<td>0</td>
</tr>
<tr>
<td>174</td>
<td>0.6</td>
<td>0.6</td>
<td>0</td>
</tr>
<tr>
<td>189</td>
<td>0.9</td>
<td>0.4</td>
<td>0.5</td>
</tr>
<tr>
<td>190</td>
<td>0.3</td>
<td>0.3</td>
<td>0</td>
</tr>
<tr>
<td>192</td>
<td>1.1</td>
<td>1.1</td>
<td>-</td>
</tr>
<tr>
<td>194</td>
<td>0.7</td>
<td>1</td>
<td>-0.3</td>
</tr>
<tr>
<td>195</td>
<td>0.7</td>
<td>1.6</td>
<td>-0.9</td>
</tr>
<tr>
<td>198</td>
<td>0.8</td>
<td>0.9</td>
<td>-0.1</td>
</tr>
<tr>
<td>201</td>
<td>0.6</td>
<td>0.6</td>
<td>0</td>
</tr>
<tr>
<td>206</td>
<td>0.5</td>
<td>1.4</td>
<td>-0.9</td>
</tr>
<tr>
<td>226</td>
<td>1</td>
<td>0.3</td>
<td>0.7</td>
</tr>
<tr>
<td>258</td>
<td>1.3</td>
<td>1.3</td>
<td>-</td>
</tr>
<tr>
<td>266</td>
<td>1.2</td>
<td>1.1</td>
<td>0.1</td>
</tr>
<tr>
<td>270</td>
<td>0.3</td>
<td>0.3</td>
<td>0</td>
</tr>
<tr>
<td>272</td>
<td>0.2</td>
<td>0.5</td>
<td>-0.3</td>
</tr>
<tr>
<td>290</td>
<td>1.3</td>
<td>0.9</td>
<td>0.4</td>
</tr>
<tr>
<td>293</td>
<td>1.1</td>
<td>1.1</td>
<td>-</td>
</tr>
<tr>
<td>294</td>
<td>0.7</td>
<td>1</td>
<td>-0.3</td>
</tr>
<tr>
<td>301</td>
<td>0.7</td>
<td>0.9</td>
<td>-0.2</td>
</tr>
<tr>
<td>305</td>
<td>1.2</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>312</td>
<td>0.2</td>
<td>1</td>
<td>-0.8</td>
</tr>
<tr>
<td>321</td>
<td>0.2</td>
<td>0.2</td>
<td>0</td>
</tr>
<tr>
<td>336</td>
<td>0.2</td>
<td>0.2</td>
<td>0</td>
</tr>
<tr>
<td>337</td>
<td>2.2</td>
<td>2.2</td>
<td>-</td>
</tr>
<tr>
<td>365</td>
<td>1.4</td>
<td>1.2</td>
<td>0.2</td>
</tr>
<tr>
<td>370</td>
<td>0.6</td>
<td>0.9</td>
<td>-0.3</td>
</tr>
<tr>
<td>378</td>
<td>0.6</td>
<td>0.7</td>
<td>-0.1</td>
</tr>
<tr>
<td>384</td>
<td>0.3</td>
<td>0.2</td>
<td>0.1</td>
</tr>
<tr>
<td>406</td>
<td>0.3</td>
<td>0.4</td>
<td>-0.1</td>
</tr>
<tr>
<td>409</td>
<td>0.3</td>
<td>1.1</td>
<td>-0.8</td>
</tr>
<tr>
<td>441</td>
<td>0.7</td>
<td>1.2</td>
<td>-0.5</td>
</tr>
<tr>
<td>461</td>
<td>0.7</td>
<td>0.9</td>
<td>-0.2</td>
</tr>
<tr>
<td>503</td>
<td>0.2</td>
<td>0.7</td>
<td>-0.5</td>
</tr>
<tr>
<td>513</td>
<td>1.4</td>
<td>0.7</td>
<td>0.7</td>
</tr>
</tbody>
</table>
Figure 59 Graph of uniocular log MAR acuity comparing vision in lensectomy and ECCE eyes in the same child one year following surgery (matched pair data). Points above the line of equality have better acuity in lensectomy eye compared with ECCE eye. (55 children) P=0.09

The points that lie above the line of equality are children who have better acuity in the lensectomy eye compared to the ECCE eye and points below the line have better acuity in the ECCE eye. Although the scatter is close to the line, the majority of points are above. The lines either side of the line of equality indicate a change of +/- 0.3 log MAR units. If a reliable difference in outcome...
between the procedures is taken as 0.3 log MAR units then 12 children did significantly better in their lensectomy eye and 6 children in their ECCE eye. This difference was not statistically significant; McNemars $\chi^2 = 2.81$ p=0.09.

4.3.7.8 Visual acuity by time assuming no secondary procedures on posterior capsule were performed

Because the ability to perform secondary procedures such as a YAG capsulotomy or membranectomy are very limited in south India, and because many children would not normally attend for further follow up, the acuity data comparing surgical procedures has also been analysed by artificially assuming that no resources for secondary removal of the opacified capsule were available.

If visual acuity improvement following secondary procedures to the posterior capsule (YAG and membranectomy) are ignored then the graph in Figure 59 would appear as shown in Figure 60. In this graph the final recorded vision prior to any secondary procedure to the posterior capsule is used. In all previous analysis the vision after the capsule has been removed from the visual axis has been used. Again points above the line of equality represent better vision in the lensectomy eye compared to the ECCE eye for individual children (Data in Table 68). There are now many more points above the line, showing that lensectomy eyes appear to be doing relatively better. The lines either side of the line of equality indicate a change of +/- 0.3 log MAR units.

If a reliable difference in outcome between the procedures is taken as 0.3 log MAR units then 19 children did significantly better in their lensectomy eye and 5 children in their ECCE eye. This difference was statistically significant; McNemars $\chi^2 = 13.38$ p< 0.05.
Table 68 Log MAR acuity compared at one year follow up in matched pair lensectomy and ECCE eyes prior to secondary intervention.

<table>
<thead>
<tr>
<th>Study no.</th>
<th>Acuity in lensectomy eye one year post op, prior to any secondary intervention</th>
<th>Acuity in ECCE eye one year post op, prior to any secondary intervention</th>
<th>Difference in acuity</th>
</tr>
</thead>
<tbody>
<tr>
<td>9</td>
<td>1</td>
<td>1.9</td>
<td>0.9</td>
</tr>
<tr>
<td>30</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>31</td>
<td>0.1</td>
<td>0.2</td>
<td>0.1</td>
</tr>
<tr>
<td>35</td>
<td>0.3</td>
<td>1</td>
<td>0.7</td>
</tr>
<tr>
<td>36</td>
<td>1.6</td>
<td>1.4</td>
<td>-0.2</td>
</tr>
<tr>
<td>38</td>
<td>0.6</td>
<td>0.7</td>
<td>0.1</td>
</tr>
<tr>
<td>39</td>
<td>0.3</td>
<td>0.3</td>
<td>0</td>
</tr>
<tr>
<td>43</td>
<td>0.6</td>
<td>0.6</td>
<td>0</td>
</tr>
<tr>
<td>47</td>
<td>1.3</td>
<td>1.3</td>
<td>0</td>
</tr>
<tr>
<td>56</td>
<td>0.6</td>
<td>1.9</td>
<td>1.3</td>
</tr>
<tr>
<td>59</td>
<td>0.3</td>
<td>0.9</td>
<td>0.6</td>
</tr>
<tr>
<td>60</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>61</td>
<td>0.9</td>
<td>0.6</td>
<td>-0.3</td>
</tr>
<tr>
<td>65</td>
<td>0.1</td>
<td>0.6</td>
<td>0.5</td>
</tr>
<tr>
<td>70</td>
<td>0.6</td>
<td>0.6</td>
<td>0</td>
</tr>
<tr>
<td>72</td>
<td>2.2</td>
<td>0.6</td>
<td>-1.6</td>
</tr>
<tr>
<td>78</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>79</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>86</td>
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<td>0.2</td>
<td>0</td>
</tr>
<tr>
<td>97</td>
<td>0.6</td>
<td>0.5</td>
<td>-0.1</td>
</tr>
<tr>
<td>100</td>
<td>1.1</td>
<td>1</td>
<td>-0.1</td>
</tr>
<tr>
<td>103</td>
<td>0.9</td>
<td>1</td>
<td>0.1</td>
</tr>
<tr>
<td>112</td>
<td>0.2</td>
<td>0.4</td>
<td>0.2</td>
</tr>
<tr>
<td>121</td>
<td>0.2</td>
<td>0.3</td>
<td>0.1</td>
</tr>
<tr>
<td>127</td>
<td>0.1</td>
<td>0.3</td>
<td>0.2</td>
</tr>
<tr>
<td>171</td>
<td>0.4</td>
<td>0.4</td>
<td>0</td>
</tr>
<tr>
<td>174</td>
<td>0.6</td>
<td>0.6</td>
<td>0</td>
</tr>
<tr>
<td>189</td>
<td>0.9</td>
<td>0.4</td>
<td>-0.5</td>
</tr>
<tr>
<td>190</td>
<td>0.3</td>
<td>0.3</td>
<td>0</td>
</tr>
<tr>
<td>194</td>
<td>0.7</td>
<td>2</td>
<td>1.3</td>
</tr>
<tr>
<td>195</td>
<td>0.7</td>
<td>1.6</td>
<td>0.9</td>
</tr>
<tr>
<td>198</td>
<td>0.8</td>
<td>0.9</td>
<td>0.1</td>
</tr>
<tr>
<td>201</td>
<td>0.6</td>
<td>0.9</td>
<td>0.3</td>
</tr>
<tr>
<td>206</td>
<td>0.5</td>
<td>1.4</td>
<td>0.9</td>
</tr>
<tr>
<td>226</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>266</td>
<td>1.2</td>
<td>1.1</td>
<td>-0.1</td>
</tr>
<tr>
<td>270</td>
<td>0.3</td>
<td>0.3</td>
<td>0</td>
</tr>
<tr>
<td>272</td>
<td>0.2</td>
<td>0.7</td>
<td>0.5</td>
</tr>
<tr>
<td>290</td>
<td>1.3</td>
<td>0.9</td>
<td>-0.4</td>
</tr>
<tr>
<td>294</td>
<td>0.7</td>
<td>1</td>
<td>0.3</td>
</tr>
<tr>
<td>301</td>
<td>0.7</td>
<td>1</td>
<td>0.3</td>
</tr>
<tr>
<td>305</td>
<td>1.2</td>
<td>1.4</td>
<td>0.2</td>
</tr>
<tr>
<td>312</td>
<td>0.2</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>321</td>
<td>0.2</td>
<td>0.2</td>
<td>0</td>
</tr>
<tr>
<td>336</td>
<td>0.2</td>
<td>0.2</td>
<td>0</td>
</tr>
<tr>
<td>365</td>
<td>1.4</td>
<td>1.9</td>
<td>0.5</td>
</tr>
<tr>
<td>370</td>
<td>0.6</td>
<td>1</td>
<td>0.4</td>
</tr>
<tr>
<td>378</td>
<td>0.6</td>
<td>0.7</td>
<td>0.1</td>
</tr>
<tr>
<td>384</td>
<td>0.3</td>
<td>0.2</td>
<td>-0.1</td>
</tr>
<tr>
<td>406</td>
<td>0.3</td>
<td>0.6</td>
<td>0.3</td>
</tr>
<tr>
<td>409</td>
<td>0.3</td>
<td>1.1</td>
<td>0.8</td>
</tr>
<tr>
<td>441</td>
<td>0.7</td>
<td>1.2</td>
<td>0.5</td>
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<tr>
<td>461</td>
<td>0.7</td>
<td>0.9</td>
<td>0.2</td>
</tr>
<tr>
<td>503</td>
<td>0.2</td>
<td>0.9</td>
<td>0.7</td>
</tr>
<tr>
<td>513</td>
<td>1.4</td>
<td>0.7</td>
<td>-0.7</td>
</tr>
</tbody>
</table>
Table 69 Paired comparison of log MAR acuity 1 year following surgery assuming no secondary intervention. \( T = \) paired \( t \) distribution, \( SE = \) standard error of mean

<table>
<thead>
<tr>
<th>Examination time following surgery (number of children)</th>
<th>Mean of difference (log MAR) between matched pairs</th>
<th>SE</th>
<th>95% CI</th>
<th>T</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 year (60)</td>
<td>-0.15</td>
<td>0.06</td>
<td>-0.27 to 0.12</td>
<td>2.42</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Table 69 compares the mean acuity of matched pair lensectomy and ECCE eyes prior to secondary intervention. The difference between the means
is significant one year following surgery, the lensectomy eyes being better than the ECCE eyes.

4.3.8 Prognostic Factors for Good Outcome Following Surgery

4.3.8.1 Reason For Visual Failure At Year One

The reasons suggested for visual failure taken as a log MAR score of greater than 0.6 (6/24) one year after surgery are described in Table 70. There is no significant difference between the two procedures analysed as matched pairs but posterior capsule thickening is as might be expected highly associated with surgery which does not clear the posterior capsule completely. The three children which had poor acuity due to posterior capsule thickening were awaiting further surgery to clear the visual axis at the year one review.

There were no cases of glaucoma diagnosed up to and including the year one review. Amblyopia with or without nystagmus was by far the most common cause of visual failure recorded. One child had a retinal detachment following lensectomy noted at the month 3 review.

<table>
<thead>
<tr>
<th></th>
<th>Lensectomy</th>
<th>ECCE</th>
<th>$\chi^2$ (McNemars)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amblyopia +/- nystagmus</td>
<td>37</td>
<td>40</td>
<td>0.29</td>
<td>=0.529</td>
</tr>
<tr>
<td>Posterior capsule thickening</td>
<td>0</td>
<td>3</td>
<td>3.07</td>
<td>=0.079</td>
</tr>
<tr>
<td>Retinal detachment</td>
<td>1</td>
<td>0</td>
<td>1.01</td>
<td>=0.315</td>
</tr>
<tr>
<td>Glaucoma</td>
<td>0</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Table 70 Visual failure (VA less than 6/24, log MAR >0.6) in matched pairs one year after surgery
Figure 61 Glaucoma assessment at review using Keeler pulsair tonometer
The scatterplot in Figure 62 graphically represents the final visual outcome compared to the age of the child at initial presentation. There is no significant difference between the two techniques for any particular age group. The trend however is for the vision to be better in older children in both groups (lensectomy and ECCE), but older children tend to perform acuity tests better and this may act as a source of bias.

Figure 62 Scatterplot of age at presentation versus final acuity for lensectomy and ECCE (120 eyes)
4.3.8.2 Predictors Of Good Visual Outcome For Each Child At Year One

The data has been analysed by child (rather than by eye) to detect predictors of good and bad outcome. Univariate and multivariate analysis using logistic regression has been used (SAS program). Good outcome has been taken as a binocular acuity of 0.6 log MAR or better (6/24 Snellen equivalent).

Univariate Logistic Regression Analysis

Table 71 presents the results of the univariate logistic regression analysis of potential predictors of good and bad outcome (modelling performed by Dr Ben Shlomo). This analysis which does not take account of confounding factors indicates that presentation after the age of 3 years, a cataract which is lamellar and the absence of nystagmus are associated with a good outcome.

Table 71 Univariate analysis; predictors of good outcome

<table>
<thead>
<tr>
<th>Variable</th>
<th>n</th>
<th>Odds ratio (95%CI’s)</th>
<th>$\chi^2$ Value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at presentation</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;3-10 years</td>
<td>36</td>
<td>9.0 (2.73-29.7)</td>
<td>14.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>0-3 years</td>
<td>24</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Type of cataract</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lamellar</td>
<td>20</td>
<td>3.7 (1.1-12.03)</td>
<td>4.6</td>
<td>0.032</td>
</tr>
<tr>
<td>Other</td>
<td>40</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aetiology</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hereditary</td>
<td>18</td>
<td>1.4 (0.46-4.40)</td>
<td>0.38</td>
<td>0.53</td>
</tr>
<tr>
<td>Non-hereditary</td>
<td>42</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>28</td>
<td>0.90 (0.28-2.84)</td>
<td>0.04</td>
<td>0.84</td>
</tr>
<tr>
<td>Female</td>
<td>32</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nystagmus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>29</td>
<td>5.7 (1.85-17.59)</td>
<td>9.87</td>
<td>0.002</td>
</tr>
<tr>
<td>Yes</td>
<td>31</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Squint</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>22</td>
<td>2.4 (0.79-7.15)</td>
<td>2.38</td>
<td>0.12</td>
</tr>
<tr>
<td>Yes</td>
<td>38</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Multivariate Logistic Regression Analysis

Using a multivariate model (modelling performed by Dr Ben Shlomo), the number of factors associated with good outcome are limited (Tables 72-74) to the absence of nystagmus and age of presentation greater than 3 years.

Table 72 Multivariate logistic regression analysis of relationship between good outcome and cataract type controlling for age.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Multivariate Odds Ratio (95% CI's)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cataract type (Lamellar)</td>
<td>1.8 (0.40, 8.12)</td>
</tr>
</tbody>
</table>

Table 73 Multivariate logistic regression analysis of relationship between age and nystagmus for good outcome.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Multivariate Odds Ratio (95% CI's)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (&gt;3 years)</td>
<td>9.6 (2.54-36.2)</td>
</tr>
<tr>
<td>Nystagmus (no)</td>
<td>6.2 (1.65-22.89)</td>
</tr>
</tbody>
</table>

Table 74 Multivariate logistic regression analysis of relationship between good outcome and cataract type, age, aetiology, sex, nystagmus and squint.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Multivariate Odds Ratio (95% CI's)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (&gt;3 years)</td>
<td>8.2 (2.04-32.74)</td>
<td>=0.003</td>
</tr>
<tr>
<td>Cataract type (Lamellar)</td>
<td>1.8 (0.40-8.12)</td>
<td>=0.45</td>
</tr>
<tr>
<td>Aetiology (hereditary)</td>
<td>0.89 (0.19-4.21)</td>
<td>=0.88</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>0.8 (0.22-3.20)</td>
<td>=0.80</td>
</tr>
<tr>
<td>Nystagmus (no)</td>
<td>5.6 (1.3-24.25)</td>
<td>=0.02</td>
</tr>
<tr>
<td>Squint (no)</td>
<td>1.2 (0.25-5.91)</td>
<td>=0.81</td>
</tr>
</tbody>
</table>
4.4 Discussion

4.4.1 General Comments

The trial was designed to determine the most suitable surgical treatment for young children with bilateral cataract in south India.

Randomised allocation of surgery to the first eye of each child was successful in ensuring comparability between the two groups and the difference in outcome between the two groups was entirely related to the surgery. Because a single surgeon undertook all of the procedures bias due to technique was minimised.

Follow up rates were extremely high and because each child was in effect its own control, losses were comparable between groups. Analysis by intention to treat (by operation allocated) was indistinguishable from analysis by operation performed. There was no bias from losses at follow up.

The data shows that eyes that had a lensectomy required fewer secondary procedures than those that had an ECCE and primary capsulotomy (P<0.05) and that this was because many of the capsulotomy openings either contracted to involve the visual axis or the vitreous face became opaque.

Machine failure was a problem in the lensectomy group and in 8/65 (12%) procedures conversion to an extracapsular technique would have been required if backup machines and technicians were not readily available.

There were few complications related to the surgery from either group and up to one year there has been only one retinal detachment and no case of
glaucoma detected. There was no significant difference in rates of complication between the techniques.

Visual acuity improved in almost all eyes following surgery and 82% of children who were blind or severely visually impaired prior to surgery improved to a binocular vision of at least 6/60.

There was no significant difference in visual outcome between the two techniques at the end point. However a difference would have occurred if the posterior capsules had not been dealt with by YAG laser or surgical membranectomy and this has relevance to the local population where such treatment may not always be available or affordable.

Although the main objectives have been addressed successfully there are possible sources of bias.

4.4.2 Possibility Of Bias In Assessment Of Visual Outcome

a) Observer bias in acuity testing

Although acuity testing was performed after a suitable length of examiner training, there is always the possibility of observer bias due to the tester influencing the acuity result (Quinn et al. 1993). The tester was intentionally blind to the treatment and this should have minimised observer bias.

b) Time of onset of cataract

Although children were only randomised if the cataracts were approximately symmetrical, the onset of the cataract in each eye could not be accurately determined. If the cataract in one eye developed earlier and more rapidly than the other, amblyopia is more likely to be present in the first eye
affected. Overall, this bias should be small because of the large numbers of children enrolled, and the randomisation procedure.

c) Delay in second eye surgery

There were a number of cases where surgery to the second eye had to be delayed. It is possible that this made the development of amblyopia more likely in the unoperated eye which was not patched between procedures. This is unlikely to be a significant cause of bias because most children were more than 3 years old and the risk of developing amblyopia small. The randomisation process meant that both procedures were equally likely to be delayed.

4.4.3 Possibility Of Bias in Univariate And Multivariate Analysis

Although age above 3 years at first presentation was a significant predictor of good outcome in both univariate and multivariate analysis, it is likely that older children tend to perform the visual acuity tests better and young children may have better acuity than we were able to record. Older children were more likely to have lamellar cataracts and these tend to occur later on and produce less amblyopia than other types of cataract.

The worst affected children who have very poor functional vision are more likely to be brought to hospital by their parents at a younger age. These children have almost always developed nystagmus and severe amblyopia by the time they are first examined and have a poor visual prognosis.
The situation in the developed world is very different. In general infants with bilateral cataract who present within the first few weeks after birth do better than children presenting later. In this case children have surgery and aphakic correction before the development of nystagmus and amblyopia and are in a good prognostic group.

4.4.4 Tolerance of Aphakic Glasses

We were impressed with the number of infants and their parents who managed to look after the spectacles and use them regularly. Contact lenses are not an option in this population and use of IOL's in infants remains controversial. It is likely that in the future more infants will have lens implants but in the those infants less than a year old, other forms of aphakic correction will probably remain more suitable.

4.4.5 Glaucoma and Retinal Detachment

The incidence of open angle glaucoma following cataract surgery in infants is anywhere between 5-24% (see Chapter one). This trial was designed so that glaucoma assessment was made at each visit. Because glaucoma tends not to occur for several years following surgery the trial is set to run for at least five years and possibly ten. We expect to see cases developing over the next few years but the incidence may be lower in this group because they are older at initial presentation than other groups studied. We will be able to compare glaucoma incidence between the surgical groups and correlate it with age at surgery.
Retinal detachment may occur at any time after surgery and the chances of observing any statistical difference between the groups is very small.

4.4.6 Relevance To Other Populations

The results from this trial are likely to be relevant to many parts of India where the population and health care resources are similar. However if adequate general anaesthesia with muscle relaxant is not available, for instance using intravenous ketamine, surgical outcomes are likely to be different as positive pressure from the vitreous may make ECCE and primary capsulotomy a more difficult procedure.

We are aware that the surgeon operating on the study children was highly experienced and complication rates were probably lower than they might have been in many other less specialised units. In particular the complications following lensectomy which is a technically more demanding procedure may be significantly higher and lead to a different outcome.
4.5 Conclusions

1. There was no significant difference in the rate of surgical complications between the two groups.

2. There was no significant difference in visual outcome between procedures at the end of the first year.

3. Although there have been no cases of glaucoma, the trial has been designed to continue for up to ten years and may help to determine the importance of surgical technique on the incidence of glaucoma.

4. Both groups did well and 87% of children had a binocular acuity of more than 6/60, one year after surgery. No children had a decrease in binocular acuity following surgery. Nearly 90% of eyes had an improved acuity of at least 0.3 log MAR units (doubling of Snellen acuity) after surgery.

5. The ECCE/primary capsulotomy group required more secondary interventions and if these had been denied, the lensectomy group would have done significantly better visually (≥0.3 log MAR units).
Summary of Thesis

This studies in this thesis were designed to determine the aetiology of childhood cataract in south India, with particular regard to potentially preventable causes and to investigate appropriate surgical management of bilateral cataract.

Salivary detection of rubella specific IgM in infants proved to be a very useful tool with specificity and sensitivity equal to the gold standard (serum). The saliva collection devices successfully stored the samples in hot and humid conditions for up to five months prior to testing. We have shown that saliva collection is a less invasive and more practical test for confirming the diagnosis than examination of serum.

Congenitally acquired rubella (CAR) was found to be an important cause of infantile cataract accounting for up to 25% of cases in children less than one year old. In the aftermath of these results a large seroepidemiological study was designed and is now underway in Tamil Nadu. This new study aims to determine the seroprevalence of rubella antibodies in women of childbearing age and the results will be used to formulate future immunisation strategies in India.

We successfully showed that cataract morphology could be used to aid diagnosis of CAR since a nuclear cataract with a less dense cortical opacity extending to the periphery had a positive predictive value of 83% for CAR.

The quality of the data from the aetiology questionnaire was unfortunately affected by recall bias of the respondents and by the large number of mothers unable to attend hospital with their children and therefore unavailable to participate. The reliability of responses that inquired about medications particularly abortifacients taken during pregnancy was poor due to strong cultural taboos. Data quality was also affected because the control group in the case control study had to be changed after the study commenced. The original control group chosen were discovered to be inadequately age matched. The ideal control group would have been children from the same village as the affected child. This was impossible to organise as the catchment area for children attending the clinic was too great and the study resources inadequate.

The questionnaire showed that children with cataract often had referral to hospital delayed because health professionals had inadequate knowledge of the condition and its treatment. Education of health professionals highlighting the importance of early referral and treatment available is likely to be appropriate and may improve functional visual outcome following surgery.

The clinical trial was designed to determine the most appropriate surgical treatment for children with bilateral cataract in south India. Although the follow up was better than expected, a significant amount of baseline data was lost because we were unable to record accurate unioocular acuities on the younger children at their first examination. Despite this the trial has shown that both lensectomy and lens aspiration with primary capsulotomy can be effective surgical treatments for bilateral cataract in this population with nearly 90% of eyes improving by at least 0.3 log MAR units of acuity. No significant difference has been demonstrated so far between the two surgical groups in rates of complication or of visual outcome. If secondary procedures to clear the visual axis had been hypothetically unavailable then the lensectomy group would have done better one year after surgery. The trial is continuing and we hope to be able to maintain the good follow up and be in a position to determine significant associations for eyes which develop glaucoma and other late complications over the next ten years.
5. References


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6. Appendices

Data Entry Forms
CHILDHOOD CATARACT AETIOLOGY
STUDY
1993-1994

Child Study Number: 
Name of Child: 
Medical record number: 

Are blood and saliva samples required from this child? [ ]

no=1
yes=2

If yes please make sure that the doctor is informed and that the samples are taken, labelled and stored.

Aravind Eye Hospital, Madurai, S. India and ICEH, London, England
<table>
<thead>
<tr>
<th><strong>date</strong></th>
<th>Todays Date: [....../....../.........]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>inter</strong></td>
<td>Interviewer MM=1, MBE=2, other=3 initials here</td>
</tr>
<tr>
<td><strong>respond</strong></td>
<td>Who interviewed mother=1, father=2, mother and father=3, uncle/aunt=4, grandparent=5, no relation=6, other relation=7</td>
</tr>
<tr>
<td><strong>tongue</strong></td>
<td>Language of Interview Tamil=1, Malayalam=2, Telugu=3, none of these=9</td>
</tr>
<tr>
<td><strong>money</strong></td>
<td>Is Child Paying or Free? pay=1, free=2</td>
</tr>
<tr>
<td><strong>sex</strong></td>
<td>Is the child male or female? male=1, female=2</td>
</tr>
<tr>
<td><strong>age</strong></td>
<td>Approximate age of child? fill in one box only</td>
</tr>
<tr>
<td><strong>travel</strong></td>
<td>Approximate hours of travel from home to this hospital</td>
</tr>
<tr>
<td><strong>trauma</strong></td>
<td>Has this cataract been caused by trauma? yes=1, no=2, unknown=9</td>
</tr>
<tr>
<td><strong>side</strong></td>
<td>Is the cataract unilateral or bilateral? (from notes) unilateral=1, bilateral=2</td>
</tr>
</tbody>
</table>

**Child and cataract details (From Interview)**

<table>
<thead>
<tr>
<th><strong>dob</strong></th>
<th>Date of birth [dd mm yy]</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>state</strong></td>
<td>In which state was your child born? Tamil nadu=1, Kerala=2, Andra Pradesh=3, other=5, don't know=9</td>
</tr>
<tr>
<td><strong>urban</strong></td>
<td>Do you live in a town or in the country? urban=1, rural=2</td>
</tr>
</tbody>
</table>
child study number __

How were you referred to this hospital?

self referral=1
from an eye camp=2
by an ophthalmologist=3
by a general doctor=4
other=5 specify ___________

How old was your child when you first thought it had a problem with its eyesight?

fill in one box only
leave blank for traumatic cataract

days [ ]
months [ ]
years [ ]

Did you delay coming to this hospital because

thought child was too young=1
did not think anything could be done for child=2
did not have enough money=3
were advised to delay coming=4
other reason=5 specify ___________
did not delay coming=6

As far as you know did any other member of your family have a cataract in childhood?

no=1
yes=2
don’t know=9

If yes was it

brother or sister of child=1
mother or father of child=2
uncle or aunt of child=3
grandparent of child=4
mother and sibling of child=5
father and sibling of child=6
other combination=7 specify _____________________
fill in 9 if nobody has childhood cataract

Have you already seen an eye doctor somewhere else?

yes=1
no=2
don’t know/not relevant=9

If you have seen an eye doctor what advice were you given

told to go to a hospital immediately=1
told to delay attendance at hospital for a few months=2
told to delay attendance at hospital for a few years=3
not told to seek further help=4
other=6 specify _____________________
don’t know/not relevant=9

Have you been given any treatment for the eye problem by any other doctor who is not an eye doctor?

have not seen any other doctor=1
given eye drops/ointments/tablets=2
other=6 specify ____________________________
don’t know=9

Have you been given any treatment for the eye problem by a local healer who is not a doctor?

have not seen a local healer=1
given eye drops/ointments=2
given tablets or syrup=3
given other treatment=4 specify ____________________________
don’t know=9
Questions for the mother of child

**fever**
Did you have a fever at any stage of your pregnancy? [ ]
- no=1
- yes=2
- don't know=9

**rash**
Did you have a rash at any stage of your pregnancy? [ ]
- no=1
- yes=2
- don't know=9

**prem**
Was your child born prematurely?
- no=1
- it was born between one and four weeks early=2
- it was born more than four weeks early=3
- don't know=9

**illness**
Did you have any other illness during your pregnancy? [ ]
- no=1
- yes=2 Specify ____________________________
- don't know=9

**pregtab**
What medication did you take during or shortly before pregnancy? [ ]
- none=1
- fertility medicine=2
- antibiotic medicine=3
- vitamin or iron supplements=4
- medicine to cause an abortion=5
- medicine to prevent an abortion=6
- medicine for dehydration=7
- some medicine but don't know what=8
- don't know=9

**dehydro**
Did you have an episode of severe diarrhoea or vomiting during your pregnancy that required a visit to the doctor, or at least three days in bed? [ ]
- no=1
- yes=2
- don't know=9

**xray**
Did you have an X-ray during pregnancy? [ ]
- none=1
- chest X-ray=2
- stomach X-ray=3
- unknown=9

**school**
Does your child go to school at the moment?
- It is not old enough to go to school =1
- It is in the appropriate grade for its age=2
- It goes to school but has failed in a class=3
- It was not able to manage at school and has left school=4
- It has never been sent to school =5
- It goes to a special school for the blind=6
- other=7 Specify ____________________________

**consang**
Are the parents of the child related?
- not related=1
- first cousins=2
- second cousins=3
- uncle/niece=4
- other relationship=5 Specify ____________________________
- don't know=9
EXAMINATION

docexam Name of examining doctor
MBE=1 ANA=2 other=3

Parent Examination

Examine mother and father if present (NOT for traumatic cataracts)

pacat Has father got a cataract?
no cataract=1
bilateral congenital cataract=2
has had cataract extraction=3
unilateral cataract=4
other type of cataract=5 Specify ______________________
not examined/not relevant=9

macat Has mother got a cataract?
no cataract=1
bilateral congenital cataract=2
has had cataract extraction=3
unilateral cataract=4
other type of cataract=5 Specify ______________________
not examined/not relevant=9

Child Examination

wobble Is Nystagmus present?
no nystagmus=1
horizontal nystagmus=2
other type of nystagmus=3 ______________________

squint Has the child any manifest strabismus?
no evidence of strabismus=1 esotropia=2
exotropia=3 other deviation=4

RAPD Is there an RAPD?
right eye [ ]
left eye [ ]

global Eye structure
right eye [ ]
left eye [ ]

Cornea
right eye [ ]
left eye [ ]

central scar=2

general corneal haze=3

peripheral scar=4
other=5
not examined=9

catsort Cataract Description
right eye [ ]
left eye [ ]

no cataract=1

total cataract=2

nuclear cataract=3

lamellar cataract=4

posterior polar=5

anterior polar=6

suture cataract=7

other type of cataract=9 specify ______________________
child study number __

**cattide**

Is the cataract:  
- unilateral = 1  
- bilateral but asymmetrical = 2  
- bilateral and symmetrical = 3

**Draw cataract:** (Leave blank if no cataract) (do not code)

- front  
- back  
- front  
- back  
- right eye  
- left eye

**deform**

Has the child any other gross physical abnormalities?  
- none = 1  
- small for age = 2  
- multiple congenital malformations = 3  
- deafness = 4  
- other = 6 Specify __________________________

**aetiol**

If the aetiology of cataract is known, is it?  
- traumatic = 1  
- Autosomal dominant inheritance = 2  
- Autosomal recessive inheritance = 3  
- other inheritance = 4  
- secondary = 5 Specify __________________________  
- metabolic = 6 Specify __________________________  
- embryodyogenesis = 7  
- other = 8 Specify __________________________  
- unknown = 9

---

**For Traumatic Cataracts**

**How long ago was injury?**

- days [ ]  
- months [ ]

**Time between injury and first attendance at an eye clinic**

- days [ ]  
- months [ ]

Mark one box only

**Type of Injury**

- penetrating = 1  
- blunt = 2 (unknown = 9)

**Object**

- Thorn = 1  
- bow and arrow = 5  
- Other vegetable material = 2  
- other = 8 Specify __________________________  
- Stick = 3  
- unknown = 9  
- Metal object = 4

**Cause**

- Accident at home = 1  
- Violent injury = 4  
- Accident at work = 2  
- unknown = 9  
- Play injury = 3

Brief description (all cases) ____________________________________________
### CHILDHOOD CATARACT OUTCOME STUDIES
#### 1993-1994

**Study Number:** ____  
**Age:** ____

**Name of Child:** ____________________________

**Outpatient Number:** ____________

### Check Sheet

<table>
<thead>
<tr>
<th>Form</th>
<th>Completed</th>
<th>Data Entry</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aetiology form</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td>Pre-op examination form</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td>Surgery 1 form</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td>Surgery 2 form</td>
<td>[ ]</td>
<td></td>
</tr>
<tr>
<td>Post op form</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Week 4 form</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Month 3 form</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Month 6 form</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Year 1 form</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
</tbody>
</table>
Child Study Number ______

Child/ Parent Address:

Name and address of close relative or friend:

Follow up visit schedule

<table>
<thead>
<tr>
<th></th>
<th>Expected Week beginning</th>
<th>Actual</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 4</td>
<td>[ / / ]</td>
<td>[ / / ]</td>
</tr>
<tr>
<td>Month 3</td>
<td>[ / / ]</td>
<td>[ / / ]</td>
</tr>
<tr>
<td>Month 6</td>
<td>[ / / ]</td>
<td>[ / / ]</td>
</tr>
<tr>
<td>Year 1</td>
<td>[ / / ]</td>
<td>[ / / ]</td>
</tr>
</tbody>
</table>
Decision Making Tree

Has child entered aetiology study?  
Does child have bilateral operable cataracts?  
Is the child aged between 0-10 years?  
Are parents and child able to attend follow up examination?  

If the answer to all these questions is yes then child may enter studies

Can child undergo either lensectomy or ECCE in both eyes?

Is child suitable for randomisation?

Do parents agree consent and sign form?

Child enters follow up survey

Child enters randomised trial

Attach sealed randomisation envelope to notes

If child has entered the randomised trial collect and attach the sealed envelope containing treatment assignment and eye to be operated.
PRE-OPERATIVE EXAMINATION

<table>
<thead>
<tr>
<th>Visual Acuity</th>
<th>Refn Right</th>
<th>Refn Left</th>
<th>Right eye</th>
<th>Left eye</th>
<th>Both eyes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Keeler (cycles per degree)</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Cardiff (LogMAR)</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>VFQ</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Snellen</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
</tbody>
</table>

**VFQ**

Mark number of correct responses out of three trials

<table>
<thead>
<tr>
<th>Test</th>
<th>Right eye</th>
<th>Left eye</th>
<th>Both eyes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Light Perception</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fixation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Following</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maddox Rod</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Optokinetic Nystagmus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grabbing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>VFQ: No of correct responses</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>No of total trials</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Which study is child in?  [ ]

outcome survey=1
randomised trial=2

Has an A-Scan been performed?  [ ]

yes=1
no=8

If yes, what is axial length

<table>
<thead>
<tr>
<th>Right eye</th>
<th>Left eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>[ ]</td>
<td>[ ]</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Right eye</th>
<th>Left eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>[ ]</td>
<td>[ ]</td>
</tr>
</tbody>
</table>

Has a B-Scan been performed?  [ ]

yes=1
no=8
SURGICAL RECORD (ONE) FIRST EYE

Date of surgery: [ / / ]

Laterality:
right eye=1
left eye=2

Corneal Diameter
vertical [ ]
horizontal [ ]

Anaesthetic complications:
yes=1
no=8
specify complication

Pupil Diameter:
good mydriasis=1
moderate mydriasis=2
poor mydriasis=3

Surgical Procedure:
randomised lensectomy=1
randomised ECCE and Primary capsulotomy=2
randomised ECCE, primary capsulotomy not possible=3
non randomised lensectomy=4
non randomised ECCE and primary capsulotomy=5
non randomised ECCE=6
non randomised ECCE and IOL=7
non randomised lensectomy and IOL=8

Regarding Planned Surgical Procedure:
completed successfully as planned=1
modified=2
aborted/converted=3 Reasons

Intraoperative Complications:
yes=1, no=8, not relevant=9
Descemets tear >1/4 of cornea
bleeding into AC
shallowing of AC due to vitreous pressure
iris prolapse
iris sphincter tear
corneal endothelial cell damage
remnants of cortex
other, specify

specific to all lensectomy procedures:
iris damage
iris haemorrhage
loss of lens material into vitreous
remnants of lens material
machine fault

specific to all ECCE procedures:
good posterior capsulotomy
vitreous disruption
unplanned posterior capsule rupture
vitreous in AC
vitreous loss to section
zonular dialysis
SURGICAL RECORD (TWO) SECOND EYE

Date of surgery:
[ / / ]
dd mn yy

Laterality:
right eye=1
left eye=2

Corneal Diameter
vertical mm
horizontal mm

Anaesthetic complications:
yes=1
no=8
specify complication _________________________________

Pupil Diameter:
good mydriasis=1
moderate mydriasis=2
poor mydriasis=3

Surgical Procedure:
randomised lensectomy=1
randomised ECCE and Primary capsulotomy=2
randomised ECCE, primary capsulotomy not possible=3
non randomised lensectomy=4
non randomised ECCE and primary capsulotomy=5
non randomised ECCE=6
non randomised ECCE and IOL=7
non randomised lensectomy and IOL=8

Regarding Planned Surgical Procedure:
completed successfully as planned=1
modified=2
aborted/converted=3 Reasons _________________________________

Intraoperative Complications:
yes=1, no=8, not relevant=9
Descemets tear >1/4 of cornea
bleeding into AC
shallowing of AC due to vitreous pressure
iris prolapse
iris sphincter tear
corneal endothelial cell damage
remnants of cortex
other, specify _________________________________

specific to all lensectomy procedures:
iris damage
iris haemorrhage
loss of lens material into vitreous
remnants of lens material
machine fault Specify ________________

specific to all ECCE procedures:
good posterior capsulotomy
vitreous disruption
unplanned posterior capsule rupture
vitreous in AC
vitreous loss to section
FIRST WEEK POST-OPERATIVE EXAMINATION

<table>
<thead>
<tr>
<th></th>
<th><strong>Right Eye</strong></th>
<th><strong>Left Eye</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day1 Day2 Dis</td>
<td>Day1 Day2 Dis</td>
</tr>
<tr>
<td>If after completing examination, no listed complications have been found, mark box with a 1.</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ] [ ]</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ] [ ]</td>
</tr>
<tr>
<td>Considerable discomfort / agitation</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
</tr>
<tr>
<td>Eyelid swelling</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
</tr>
<tr>
<td>Chemosis</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
</tr>
<tr>
<td>Severe conjunctival inflammation</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
</tr>
<tr>
<td>Corneal oedema</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
</tr>
<tr>
<td>Shallow AC</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
</tr>
<tr>
<td>Hyphaema</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
</tr>
<tr>
<td>Leaking wound</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
</tr>
<tr>
<td>Iritis</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
</tr>
<tr>
<td>Hypopyon</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
</tr>
<tr>
<td>Iris incarceration in wound</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
</tr>
<tr>
<td>Iris prolapse</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
</tr>
<tr>
<td>Decentered pupil</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
</tr>
<tr>
<td>Residual cortex</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
</tr>
<tr>
<td>Vitreous knuckle</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
</tr>
<tr>
<td>Vitreous in AC</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
</tr>
<tr>
<td>Vitreous to section</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
</tr>
<tr>
<td>Pupil block glaucoma</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
</tr>
<tr>
<td>Endophthalmitis</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
</tr>
<tr>
<td>Choroidal Detachment</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
</tr>
<tr>
<td>Retinal Detachment</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
</tr>
<tr>
<td>Special treatment required</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
<td>[ ] [ ] [ ] [ ] [ ] [ ]</td>
</tr>
</tbody>
</table>

**Specific to ECCE with no IOL with or without primary capsulotomy**

| Posterior capsule opacification | [ ] [ ] [ ] [ ] [ ] [ ] |
| Type1=1, Type2=2, Type3=3 |

**Specific to ECCE with IOL**

| Posterior capsule opacification | [ ] [ ] [ ] [ ] [ ] [ ] |
| (Type1=1, Type2=2, Type3=3) |
| Pupil capture | [ ] [ ] [ ] [ ] [ ] [ ] |
| Malposition of haptic | [ ] [ ] [ ] [ ] [ ] [ ] |
| Dislocated lens | [ ] [ ] [ ] [ ] [ ] [ ] |
| Deposits on implant | [ ] [ ] [ ] [ ] [ ] [ ] |
| Fibrin over implant | [ ] [ ] [ ] [ ] [ ] [ ] |
| Posterior synechiae(>3) | [ ] [ ] [ ] [ ] [ ] [ ] |

Comments
### Four Week Post-Operative Exam

**Date of examination**

[ / / ]

**Has any extra treatment been required since discharge?**

- yes=1
- no=2

**If yes what was the treatment?**

- Other surgical intervention=1 specify ____________________________
- Other non surgical intervention=2 specify ____________________________

**Is child wearing spectacle correction?**

- yes=1
- no=2

**If NO why not?**

- Not required=1
- Has not been given glasses=4
- Lost glasses=2
- Child will not wear glasses=5
- Broken glasses=3
- Other=8 Specify ____________________________

**Approx How long does child wear glasses per day?**

--- Hours

**Has the child any manifest strabismus?**

- No evidence of strabismus=1
- Esotropia=2
- Exotropia=3
- Other deviation=4

### Visual Acuity

<table>
<thead>
<tr>
<th></th>
<th>Refn Right:</th>
<th>Refn Left:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Right eye</td>
<td>Left eye</td>
</tr>
<tr>
<td>Keeler  (cycles per degree)</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Cardiff (LogMAR)</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>VFQ</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Snellen</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
</tbody>
</table>

### VFB

Mark number of correct responses out of three trials

<table>
<thead>
<tr>
<th>VFB</th>
<th>Right eye</th>
<th>Left eye</th>
<th>Both eyes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Light Perception</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fixation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Following</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maddox Rod</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Optokinetic Nystagmus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grabbing</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

VFQ= No of correct responses

No of total trials

---
Eye Examination

YES=1, NO=8, Not Examined / not relevant =9

<table>
<thead>
<tr>
<th>If after completing examination, no listed complications have been found, mark box with a 1.</th>
<th>Right Eye</th>
<th>Left Eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nystagmus</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Severe conjunctival inflammation</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Corneal oedema</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Shallow AC</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Hyphaema</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Mild Iritis</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Mod Iritis</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
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<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
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<td>Endophthalmitis</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Retinal detachment</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Other Specify</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
</tbody>
</table>

Specific to ECCE with no IOL with or without primary capsulotomy

Posterior capsule opacification
Type1=1, Type2=2, Type3=3

Specific to ECCE with IOL

Posterior capsule opacification
Type1=1, Type2=2, Type3=3
Pupil capture
Malposition of haptic
Dislocated lens
Deposits on implant
Fibrin over implant
Posterior synechiae(>3)

Administrators/Doctors comments
Include reasons for non attendance, extra complications, extra visits:
THREE MONTH POST-OPERATIVE EXAM

Date of examination [ / / ]

Has any extra treatment been required since discharge?
none=1
surgical membranectomy/capsulotomy=2
yag capsulotomy=3
other surgical intervention=4 specify
non surgical intervention=5 specify

Has child wearing spectacle correction?
yes=1
no=2

If NO why not?
not required=1  has not been given glasses=4
lost glasses=2  child will not wear glasses=5
broken glasses=3  other=8 Specify

Approx How long does child wear glasses per day? ___ Hrs

Has the child any manifest strabismus?
no evidence of strabismus=1
esotropia=2
exotropia=3
other deviation=4

Visual Acuity

<table>
<thead>
<tr>
<th>Visual Acuity</th>
<th>Refn Right:</th>
<th>Refn Left:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<tr>
<td>Keeler (cycles per degree)</td>
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<tr>
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</tbody>
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VFB

Mark number of correct responses out of three trials

<table>
<thead>
<tr>
<th>VFB</th>
<th>Right eye</th>
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<tbody>
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<td>Light Perception</td>
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<tr>
<td>VFQ</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No of correct responses</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No of total trials</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Eye Examination

YES=1, NO=8, Not Examined / not relevant = 9

If after completing examination, no listed complications have been found, mark box with a 1.

<table>
<thead>
<tr>
<th>Right Eye</th>
<th>Left Eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>[ ]</td>
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</tbody>
</table>

Nystagmus
Corneal oedema
Shallow AC
Hyphaema
Mild Iritis
Mod Iritis
Severe Iritis
Hypopyon
Iris prolapse
Decentered pupil
Residual cortex
Vitreous in AC
Vitreous to section
Pupil block glaucoma
Endophthalmitis
Retinal detachment

Specific to ECCE with no IOL with or without primary capsulotomy

Posterior capsule opacification [ ] [ ]
Type 1=1, Type 2=2, Type 3=3

Specific to ECCE with IOL

Posterior capsule opacification [ ] [ ]
(Type 1=1, Type 2=2, Type 3=3)
Pupil capture [ ] [ ]
Malposition of haptic [ ] [ ]
Dislocated lens [ ] [ ]
Deposits on implant [ ] [ ]
Fibrin over implant [ ] [ ]
Posterior synechiae (>3) [ ] [ ]

Administrators/Doctors comments
Include reasons for non attendance, extra complications, extra visits:
SIX MONTH POST-OPERATIVE EXAM

Date of examination [ / / ]

Has any extra treatment been required since discharge? [ ]
- none=1
- surgical membranectomy/capsulotomy=2
- yag capsulotomy=3
- other surgical intervention=4 specify ____________________
- non surgical intervention=5 specify ____________________

Is child wearing spectacle correction? [ ]
- yes=1
- no=2

If NO why not? [ ]
- not required=1
- has not been given glasses=4
- lost glasses=2
- child will not wear glasses=5
- broken glasses=3
- other=8 specify ____________________

Approx How long does child wear glasses per day? _____ Hrs

Has the child any manifest strabismus? [ ]
- no evidence of strabismus=1
- esotropia=2
- exotropia=3
- other deviation=4

**Visual Acuity**

<table>
<thead>
<tr>
<th></th>
<th>Right eye</th>
<th>Left eye</th>
<th>Both eyes</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Keeler</strong> (cycles per degree)</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td><strong>Cardiff</strong> (LogMAR)</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td><strong>VFQ</strong></td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td><strong>Snellen</strong></td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
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</table>

**VFQ**

Mark number of correct responses out of three trials

<table>
<thead>
<tr>
<th></th>
<th>Right eye</th>
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<td>Grabbing</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td><strong>VFQ</strong> No of correct responses</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>No of total trials</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
</tbody>
</table>

12
Eye Examination

YES=1, NO=8, Not Examined / not relevant =9

| If after completing examination, no listed complications have been found, mark box with a L. |
|--------------------------------------------------|--------------------------------------------------|
| Right Eye                                       | Left Eye                                         |
| Nystagmus                                       | [ ]                                              |
| Corneal oedema                                  | [ ]                                              |
| Shallow AC                                      | [ ]                                              |
| Chronic Iritis                                  | [ ]                                              |
| Decentered pupil                                | [ ]                                              |
| Vitreous in AC                                  | [ ]                                              |
| Vitreous to section                             | [ ]                                              |
| Open angle glaucoma                             | [ ]                                              |
| Endophthalmitis                                 | [ ]                                              |
| Retinal detachment                              | [ ]                                              |
| Special treatment required                      | [ ]                                              |
| Other Specify                                    | [ ]                                              |

Specific to ECCE with no IOL with or without primary capsulotomy

Posterior capsule opacification [ ]

Specific to ECCE with IOL

Posterior capsule opacification [ ]

Pupil capture [ ]

Malposition of haptic [ ]

Dislocated lens [ ]

Deposits on implant [ ]

Fibrin over implant [ ]

Posterior synechiae(>3) [ ]

Administrators / Doctors comments

Include reasons for non attendance, extra complications, extra visits:
Child Study Number ______

**ONE YEAR POST-OPERATIVE EXAM** *(End Point)*

Date of examination [ / / ]

<table>
<thead>
<tr>
<th>Visual Acuity</th>
<th>Refn Right</th>
<th>Refn Left</th>
<th>Correction used (Dioptres)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Keeler</strong> (cycles per degree)</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td><strong>Cardiff</strong> (LogMAR)</td>
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</tr>
<tr>
<td><strong>VFQ</strong></td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td><strong>Snellen/SG</strong></td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Jaeger near</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Snellen near</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
</tbody>
</table>

**Is child routinely wearing spectacle correction?**
- ordinary glasses=1
- bifocals=2
- has not been given glasses=4
- child will not wear glasses=6
- other=8 Specify ___________________

**Approx How long does child wear glasses per day?**
_______ Hrs

**Is there evidence of binocularity?**
- yes=1
- no=2

**Does the child have nystagmus?**
- yes=1
- no=2

**Does the child have a manifest strabismus?**
- no evidence of strabismus=1
- esotropia=2
- exotropia=3
- other deviation=4 ___________________

**Has any extra treatment been required at any stage since discharge?**
- State eye, time after surgery, any complications
- none=1
- surgical membranectomy/capsulotomy=5 _______________
- yag capsulotomy=2 _______________
- other surgical intervention=3 specify ___________________
- non surgical intervention=4 specify ___________________
Child Study Number ______

**IOP Measurement**

State method ______

**Eye Examination**

YES=1, NO=8, Not Visualised =7, Not Examined / not relevant =9

<table>
<thead>
<tr>
<th>Eye</th>
<th>Right</th>
<th>Left</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corneal Opacity/Oedema</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Pupil irregular</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Pupil Decentered</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Post Capsule Opacified (grade 1-3)</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Inadequate Primary Capsulotomy</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Glaucomatous optic disc cup</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Macula Pathology (outline)</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Retinal detachment (outline)</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Other (outline)</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
</tbody>
</table>

**Vision at 1 year compared to preop Vision in +/- LogMAR**

| [ ] | [ ] |

**Reasons For Visual Impairment**

<table>
<thead>
<tr>
<th>Reason</th>
<th>Right Eye</th>
<th>Left Eye</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nystagmus=1</td>
<td>Major [ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Minor [ ]</td>
<td></td>
<td>[ ]</td>
</tr>
<tr>
<td>Stimulus deprivation amblyopia=2</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Corneal Opacity=3</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Capsule Opacification=4</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Vitreous Opacification=5</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Macula pathology (Comment)=6</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Retinal pathology (Comment)=7</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Other Reason (Comment)=8</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>no impairment=9</td>
<td></td>
<td>[ ]</td>
</tr>
</tbody>
</table>

**Follow Up**

Completed all visits successfully =1
Missed 1 visit only =2
Missed >1 visit but attended 1 year follow up without tracing=3
Required tracing and collecting=4 why did child not attend? ____________________
Traced but unable to come=5 why? ____________________
Unable to trace=6 why? ____________________

**Comments**

Month for annual review: ____________
CHILDHOOD CATARACT OUTCOME STUDY

YEARLY POST-OPERATIVE EXAM  2 3 4 5  Other ______

Date of examination  [ / / ]

<table>
<thead>
<tr>
<th>Visual Acuity</th>
<th>Refn Right:</th>
<th>Refn Left:</th>
</tr>
</thead>
</table>

Present glasses prescription (Dioptries):

<table>
<thead>
<tr>
<th></th>
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</tr>
<tr>
<td>Snellen/SG/Cambridge</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>Near vision</td>
<td>[ ]</td>
<td>[ ]</td>
<td>[ ]</td>
</tr>
<tr>
<td>BSV yes=1 no=2</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Is child routinely wearing glasses? yes=1, broken=2, other=3 [ ]

Does the child have nystagmus? yes=1 no=2 [ ]

Does the child have a manifest strabismus? yes=1 no=2 [ ]

Any treatment required this visit? none=1 yag capsulotomy=2 other=3 [ ]

EXAMINATION

IOP Measurement [ ] mmHg Right [ ] mmHg Left

YES=1, NO=8, Not Visualised =7, Not Examined / not relevant =9

Post capsule opacity reducing vision [ ] [ ]
Glaucomatous optic disc cup [ ] [ ]
Other (describe) [ ] [ ]

Vision since last visit? better=1, same=2, worse=3 [ ]
If worse why? [ ]

If failure to attend, why? [ ]