Congenital and Infantile Cataract in the United Kingdom: Underlying or Associated Factors

Jugnoo S. Rahi,[1,2,3] *Carol Dezateux,*[1] *and the British Congenital Cataract Interest Group*

Purpose. Prevention of visual impairment and blindness in childhood due to congenital and infantile cataract is an important international goal. Preventive strategies require information about etiology that is currently unavailable for many regions of the world. From a national epidemiologic study, the underlying or associated factors in newly diagnosed cases of congenital or infantile cataract in the United Kingdom are reported, and the implications for future etiological research are discussed.

Methods. All children with congenital or infantile cataract newly diagnosed during 1 year in the United Kingdom were ascertained independently through two national active surveillance schemes comprising ophthalmologists and pediatricians, respectively. Detailed information about cases, including disease causes, was collected from reporting clinicians using standard questionnaires.

Results. Of 243 children with newly diagnosed congenital or infantile cataract, 160 (66%) had bilateral disease. Isolated cataract was more common in bilateral than unilateral cases (61% versus 47%, $P = 0.05$) as was cataract associated with a systemic disorder (25% versus 6%, $P < 0.001$). Conversely, cataract with associated ocular anomalies was more common in unilateral than bilateral cases (47% versus 14%, $P < 0.001$). No underlying or associated risk factors for cataract could be identified in 92% of unilateral and 38% of bilateral cases, although putative prenatal and perinatal risk factors were reported in a proportion of these idiopathic cases. Hereditary disease was associated with 56% of bilateral but only 6% of unilateral cases. Prenatal infections and other systemic factors were reported in only 6% of bilateral and 2% of unilateral cases.

Conclusions. Given the high proportion of idiopathic congenital and infantile cataract, the scope for primary prevention in the United Kingdom is currently limited. There is a need for further etiological research, to examine the roles of environmental and genetic risk factors for idiopathic cataract. (*Invest Ophthalmol Vis Sci.* 2000;41:2108–2114)

Prevention of visual impairment due to congenital and infantile cataract is an important component of the World Health Organization's international program for the elimination of avoidable blindness by 2020.[1] Although visual prognosis after treatment of congenital and infantile cataract has improved recently, especially in industrialized countries,[2] cataract in infancy is still responsible for approximately one tenth of childhood blindness in the world.[3] Thus, primary prevention of cataract in infancy is an important goal. However, information about the causes, which is necessary for planning appropriate strategies, is currently unavailable for many regions of the world and where available, has been derived mainly from studies of selected populations,[2,4–10] or from routine sources[11,12] and is often based on small numbers of cases. We report the underlying or associated factors in a nationally representative cohort of children with newly diagnosed congenital or infantile cataract in the United Kingdom, and we discuss the implications of these findings for future etiological research.

Methods

All children with congenital or infantile cataract in the United Kingdom, newly diagnosed during the 12-month period from October 1995 to September 1996 inclusive, were identified prospectively through two independent national active surveillance schemes, one comprising consultant ophthalmologists and the other consultant pediatricians. Pediatricians in the United Kingdom are responsible for the routine ocular examinations of all newborn infants (including assessment of the pupillary red reflex with a direct ophthalmoscope) that are undertaken nationally to detect cataract and other serious ocular diseases.[13] Pediatricians are also responsible for the assessment of children for the presence of associated systemic disorders, as well as for their management. There is universal and cost-free access to both ophthalmic (treatment) and pediatric (screening) services in the United Kingdom through the National Health Service. Thus, newly diagnosed cases were identified simultaneously but independently through both ophthalmologists and pediatricians.

The ophthalmic surveillance scheme was established for this study through the British Congenital Cataract Interest Group and comprised 89% of all ophthalmologists identified

From the Departments of [1]Epidemiology and [2]Ophthalmology, Institute of Child Health and Great Ormond Street Hospital, London; and the [3]Institute of Ophthalmology, London, United Kingdom.

Supported by the Medical Research Council of the UK, British Council for the Prevention of Blindness, Children Nationwide Medical Research Fund. JR was supported by a Medical Research Council Clinical Training Fellowship.

Submitted for publication October 20, 1999; revised February 4, 2000; accepted February 18, 2000.

Commercial relationships policy: N.

Corresponding author: Jugnoo S. Rahi, Department of Epidemiology and Public Health, Institute of Child Health, 30 Guilford Street, London WC1N 1EH, UK. j.rahi@ich.ucl.ac.uk

Investigative Ophthalmology & Visual Science, July 2000, Vol. 41, No. 8

through a national survey to be involved in the treatment of infants with cataract. The national scheme previously established by the British Paediatric Surveillance Unit of the Royal College of Pediatrics and Child Health[14] has facilitated the study of a number of uncommon childhood conditions and has a reporting base that is 92% complete.[15] For the duration of the study, reporting cards were sent to pediatricians monthly and ophthalmologists every 2 months with which to report all cases newly diagnosed in the preceding month or 2 months, respectively. Based on capture–recapture analysis, we estimate that 92% of eligible cases were identified through these schemes.[16]

Congenital and infantile cataract are categorized separately in standard disease classification systems with further complex subdivisions according to involvement of other organs.[17] However, in clinical practice the terms are often used interchangeably.[18] Thus, a clinical case definition encompassing both was used in this study. All children, aged 15 years or under, with newly diagnosed congenital or infantile cataract were eligible, including those with congenital cataract or cataract present from infancy or diagnosed after infancy but having salient clinical features indicating earlier onset, such as cataract morphology, an associated congenital ocular anomaly, or nystagmus.[18,19] Children with minor, visually insignificant lens opacities that did not necessitate regular follow-up or further assessment were ineligible, as were those with cataract acquired secondarily during childhood. Only children born within the United Kingdom were eligible.

After reporting a case, clinicians were asked to provide further details using a structured, mailed questionnaire. Specifically, findings of the ophthalmologic examination, other clinical assessments, and all investigations undertaken were sought. Information about cause of cataract was obtained independently from ophthalmologists and pediatricians and used to categorize cases on the basis of the cataractogenic insult(s), and, in addition, according to the presence or absence of specifically associated ocular or systemic disorders. As numerous causative factors or processes, many rare, have been implicated in congenital and infantile cataract in humans,[2,19] we collated the heterogeneous underlying or associated factors most commonly reported in published clinical studies in the taxonomy shown in Table 1. Clinicians were asked to indicate all categories of this taxonomy that applied to each child, based on the findings of the clinical assessments and investigations undertaken—for example, examination by clinical geneticists for hereditary disease or serologic investigation for prenatal infection. Thus, for example, cataract associated with ipsilateral microphthalmos and due to autosomal dominant disease was categorized in the associated ocular disease category as well as in the hereditary without systemic disorder category. Children in whom an underlying or associated risk factor for cataract could not be determined were categorized as having idiopathic disease. As appropriate, further information on cause, provided during the continued follow-up of the entire cohort, was used to supplement the initial report data.

Using this study taxonomy for analysis, and irrespective of age at diagnosis, cases were assigned to one of three clinically relevant and mutually exclusive categories: isolated cataract, cataract with a specifically associated ipsilateral ocular disorder but without systemic disease, and cataract with a specifically associated systemic disease, irrespective of any other ocular disease. Unilateral and bilateral cases were analyzed separately and within these three categories. Observed differences between unilateral and bilateral cases were examined using the test of significance for the difference in two proportions.[20]

The study conformed to the Declaration of Helsinki for research involving human subjects.

TABLE 1. Categories Used to Classify Causes of Congenital and Infantile Cataract

1. **Isolated cataract**
2. **Associated ipsilateral ocular disorder**
   Microphthalmia, persistent hyperplastic primary vitreous, aniridia, aniridia plus, anterior chamber dysgenesis syndromes, retinopathy of prematurity, ectopia lentis, posterior lenticonus, intraocular tumor
3. **Intrauterine infection/maternal infection embryopathy**
   Rubella, cytomegalovirus, varicella-herpes zoster, herpes simplex, toxoplasmosis, syphilis, Epstein–Barr virus, measles, poliomyelitis
4. **Intrauterine drug exposure**
   Chlorpromazine, corticosteroids, sulfonamides, vitamin D, vitamin A
5. **Intrauterine ionizing radiation**
6. **Prenatal/perinatal metabolic disorder**
   Galactosemia, galactokinase deficiency, hyperglycinuria, sialidosis, α-mannosidosis, sorbitol dehydrogenase deficiency, hypocalcemia (idiopathic), hypoparathyroidism or pseudohypoparathyroidism, marginal maternal galactokinase deficiency, maternal diabetes
7. **Hereditary without associated systemic disorder**
   Autosomal dominant, autosomal recessive, or X-linked recessive
8. **Hereditary with associated systemic disorder or multisystem dysmorphic syndrome**
   a. Chromosomal
      Trisomy 21, Turner's syndrome, trisomy 13–15, trisomy 16–18, deletion chromosome 5
   b. With skeletal disease
      Conradi–Hünermann syndrome, rhizomelic chondrodysplasia punctata, Stickler syndrome, Camfak syndrome
   c. With syndactyly, polydactyly, or other digital syndrome
      Rubinstein–Taybi syndrome, Ellis–van Creveld syndrome, Bardet–Biedl syndrome
   d. With central nervous system disorder
      Cereboro-oculo-facial-skeletal syndrome, Martsolf syndrome, Zellweger syndrome, Marinesco–Sjögren syndrome, Smith–Lemli–Opitz syndrome, Norrie's disease
   e. With muscle disorder
      Myotonic dystrophy, cataract, lactic acidosis and cardiomyopathy
   f. With renal disease
      Lowe's syndrome, Alport's syndrome
   g. With mandibulo-facial syndromes
      Hallerman–Streiff syndrome, Nance–Horan cataract-dental syndrome
   h. With dermatologic disorder
      Congenital icthyosis, cataract, alopecia, sclerodactyly, Schafer syndrome, Siemen's syndrome, incontinentia pigmenti
9. **Idiopathic (without a recognized cause)**

RESULTS

Two hundred forty-eight children with newly diagnosed congenital or infantile cataract were identified in 1 year in the United Kingdom, during which time there were 734,000 live births and 10.63 million children aged between 1 and 15 years.[21] Findings are reported in 243 (98%) children for whom complete data regarding underlying or associated factors were available. Of these, 160 (66%) had bilateral cataract, and 127 (52%) were boys. The median age (range) at detection of cataract was 8 weeks (birth to 15 years), with cataract in 168 children detected by the age of 1 year (Fig. 1).

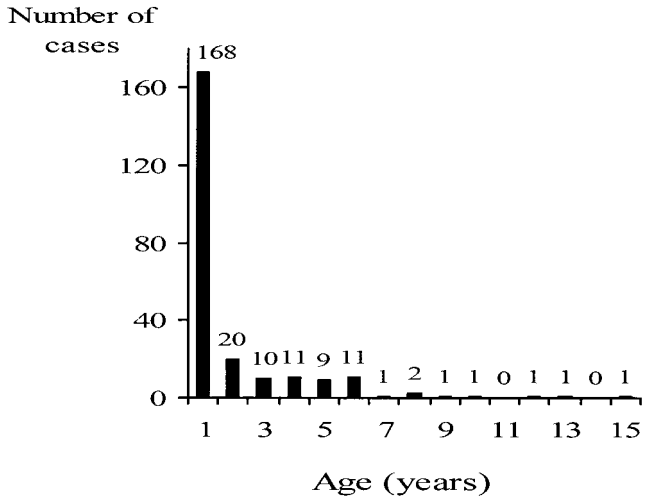

FIGURE 1. Age at detection of children with congenital and infantile cataract.

Isolated cataract was more common in bilateral than unilateral cases (61% versus 47%) as was cataract associated with a systemic disorder (25% versus 6%; Table 2). Conversely, associated ocular disorders were more common in unilateral than bilateral cases (47% versus 14%; Table 2). Microphthalmos and persistent hyperplastic primary vitreous were the most common associated ocular disorders in bilateral and unilateral cases, respectively (Table 2). There were no statistically significant differences between boys and girls in laterality or category of cataract.

No underlying or associated risk factors could be identified in 92% of unilateral and 38% of bilateral cases. Of these idiopathic cases, an associated ocular anomaly was present in 51% of those with unilateral compared with 12% of those with bilateral disease (Table 3).

In a small number of idiopathic cases, possible contributing perinatal or prenatal causative factors were reported. Fourteen (16%; 95% confidence interval [CI] 8–23) of the children with isolated idiopathic cataract were born before term (<37 weeks) and/or were of low birth weight (<2500 g) and had disease diagnosed by 1 year of age; the proportion being greater among those with bilateral (17%; 95% CI 7–27) than unilateral (13%; 95% CI 3–25) disease. By comparison, 7% of all live births nationally during the 1-year study period and 26% ($n = 12$) of children with an associated systemic disorder in the study were similarly preterm or of low birth weight.[21] Five (7%; 95% CI 4–9) of the children with unilateral idiopathic cataract, all with disease diagnosed by 3 months of age, had unaffected twins, whereas 1% of all maternities nationally during this time produced twins.[21] Severe perinatal hypoxia was also reported in one of the infants with unilateral isolated idiopathic disease who was born preterm. One child with bilateral idiopathic cataract had perinatal hypoglycemia that caused convulsions. Prolonged maternal hyperglycemia had occurred in one infant with unilateral disease. In five infants with bilateral idiopathic disease maternal ingestion of the following drugs was reported from early pregnancy: phenobarbitone ($n = 1$), sodium valproate ($n = 1$), thyroxine ($n = 2$), and atenolol ($n = 1$). In one child with unilateral cataract, maternal ingestion of fluoxetine hydrochloride (Prozac; Eli Lilly, Indianapolis, IN) was reported.

Ninety (56%) bilateral cases but only five (6%) unilateral cases were associated with hereditary disease (Table 3). There were also markedly differing patterns of inheritance according to laterality and the presence of associated disorders, as shown in Table 4. All hereditary cases of cataract associated with an ocular disorder were bilateral, most commonly by autosomal dominant inheritance. Of 13 children with cataract associated with Down syndrome, 8 had disease diagnosed in the neonatal period. Of 19 children with cataract associated with various rare autosomal recessive systemic disorders, four with bilateral disease died shortly after diagnosis.

A small number of other systemic disorders or factors were reported in 10 (6%) bilateral and 2 (2%) unilateral cases. Prenatal infections were implicated in six cases, with varying degrees of certainty. Prenatal rubella infection was associated with unilateral cataract in two children, one with microphthalmos the other with retinopathy, both of whom also had nonocular manifestations. Prenatal toxoplasma infection was implicated in one child with bilateral cataract who had a twin with chorioretinal disease. Prenatal infections were the probable underlying factor in a further three bilateral cases in which patients had salient nonocular features but in whom results of investigations remained inconclusive. Other systemic causative factors were reported in the remaining six bilateral cases. Of these, one child had severe perinatal hypoxia and died of its complications shortly after birth. In two children with cerebral

TABLE 2. Categories of Congenital and Infantile Cataract

Category	Bilateral*	Unilateral†	95% CI for Difference in Percentages
Isolated	97 (61)	39 (47)	1 to 27‡
Associated ocular disorder	22 (14)	39 (47)	−22 to −44§
Microphthalmos only	10 (6)	6 (7)	
Persistent hyperplastic primary vitreous	2 (1)	18 (22)	
Anterior segment dysgenesis	7 (4)	2 (2)	
Other‖	3 (5)	13 (16)	
Associated systemic disorder	41 (25)	5 (6)	12 to 34§

Data in Bilateral and Unilateral columns are number of cases affected with percentage in parentheses.
* $n = 160$.
† $n = 83$.
‡ $P = 0.05$.
§ $P < 0.001$.
‖ Includes three bilateral cases and nine unilateral cases due to posterior lenticonus.

TABLE 3. Underlying or Associated Risk Factors for Congenital and Infantile Cataract

Causative	Bilateral*	Unilateral†	95% CI for Difference in Percentages
Idiopathic (unknown)	60 (38)	76 (92)	−41 to −67‡
Isolated	53 (34)	37 (44)	
With associated ocular disorder	7 (4)	39 (48)	
Hereditary	90 (56)	5 (6)	38 to 62‡
Isolated	44 (28)	2 (2)	
With associated ocular disorder	15 (9)	—	
With associated systemic disorder	31 (19)	3 (4)	
Other systemic aetiological factor (all with associated systemic disorder)‖	10 (6)	2 (2)	−2 to 10§

Data in Bilateral and Unilateral columns are number of affected cases with percentage in parentheses.
* $n = 160$.
† $n = 83$.
‡ $P < 0.001$.
§ $P = 0.3$.
‖ Includes four bilateral and two unilateral cases due to prenatal infection.

palsy, underlying systemic causative factors were assumed to be responsible, and severe metabolic disturbances were implicated in three children with relevant systemic findings.

DISCUSSION

The underlying or associated factors in children with congenital and infantile cataract in the United Kingdom are diverse. Less than 1% of cases (due to prenatal rubella infection) are definitely amenable to existing specific primary preventive strategies. The scope for developing other preventive strategies is limited by a paucity of knowledge of risk factors for idiopathic disease and by limited therapeutic approaches to hereditary cataract.[22,23] This complex pattern, including the considerable differences between bilateral and unilateral disease, has implications for further etiological research.

TABLE 4. Hereditary Congenital and Infantile Cataract

Category and Hereditary Cause	Bilateral*	Unilateral†
Isolated cataract		
Autosomal dominant	40 (25)	2 (2)
Autosomal recessive	4 (2)	—
Associated ocular disorder		
Autosomal dominant (5 microphthalmos, 1 persistent hyperplastic primary vitreous, 1 posterior lenticonus, 6 anterior segment dysgenesis)	13 (8)	—
Autosomal recessive (1 persistent hyperplastic primary vitreous, 1 anterior segment dysgenesis)	2 (1)	—
Associated systemic disorder		
Chromosomal: Trisomy 21	12 (7)	1 (1)
Autosomal dominant: Marfan	1 (<1)	—
X-linked recessive: Lowe's syndrome	1 (<1)	
Autosomal recessive	17 (11)	2 (2)
Rhizomelic chondrodysplasia punctata	2	—
Atypical galactosemia	1	—
Smith–Lemli–Optiz syndrome	1	1
PEHO syndrome	1	—
Ohdo syndrome	1	—
COFS syndrome	2	—
Cockayne syndrome	1	—
Congenital icthyosis	1	—
Walker–Warburg syndrome	1	—
Other	6	1

Data are affected cases with percentages in parentheses. PEHO, progressive encephalopathy with edema, hypsarrhythmia and optic atrophy; COFS, cerebro-oculo-facial-skeletal.
* $n = 160$.
† $n = 83$.

Direct comparison with the findings of other studies[4–10,24,25] is problematic, given differences in methodology —particularly, differing case definitions and classifications of causes—and in the reporting of aggregated data for unilateral and bilateral disease in many previous studies. Although methodologically different, a meaningful comparison can be made with a recent Spanish study involving specific examination of newborn infants to ascertain congenital anomalies. In that study, 71 children with cataract were identified from more than 1 million births between 1980 and 1995.[26] Aggregated data about causes are similar to those in the present study, with idiopathic and hereditary cataract accounting for the majority of cases.[26]

There is evidence of change over time in the relative importance of different risk factors of congenital and infantile cataract in industrialized countries.[4,6,7,10,18,19,24] The implementation of specific primary preventive strategies, such as rubella immunization and avoidance of known teratogens, such as drugs or irradiation,[27] have reduced the contribution of some causative factors that continue to be important in many developing countries.[8,9] Although the pattern of underlying or associated factors in many countries currently at an intermediate level of development is similar to that seen previously in industrialized countries, this is likely to change with time, with idiopathic and hereditary disease becoming the most important categories throughout the world.

Although cataract is reported as the ocular anomaly most likely to occur in isolation, its association with microphthalmia[26] supports the critical inductive role of the normal lens in development of the globe.[23] In the present study, anomalies of the globe, without associated systemic disorders, were three times more common in unilateral than bilateral cases, and two thirds of unilateral cases had some degree of microphthalmos compared with half the bilateral cases. These findings are consistent with the occurrence of unilateral cataract associated

with microphthalmos arising more frequently as a result of a local, rather than a general, insult during embryogenesis. Extending this further, the striking differences in the causes of unilateral and bilateral disease in the present study may reflect differences in pathogenesis with local, or distal, influences predominating in unilateral disease and generalized, or proximal, factors having more impact in bilateral disease. In future etiological studies of congenital and infantile cataract, and possibly other ocular anomalies, consideration should be given to investigating and analyzing bilateral and unilateral cases separately.

Severe specific adverse perinatal events, particularly hypoglycemia, hypoxia, hypothermia, and pre-eclampsia,[4,6,7,10,24,25,28–33] as well as disorders of sugar metabolism in mothers of affected children,[25] have been reported to be associated with congenital cataract, but these factors were reported in only a small proportion of cases in the present study. Similarly, although congenital cataract has been reported after ingestion of certain drugs in pregnancy,[27] the role of drugs in six idiopathic cases in the present study is unclear. In two cases, the mothers were taking anticonvulsants that have other ocular teratogenic effects[27]; in two others, the mothers were taking thyroxine, notable in the light of animal experiments demonstrating cataract associated with hypothyroidism[24]; and in another, the mother was treated for hypertension that may have relevance, as both systemic hypertension and antihypertensive drugs have been implicated in adult cataract.[34] Further experimental work in these areas to provide clearer understanding of the mechanisms of lenticular damage may be warranted.

The overrepresentation in the present study, compared with the total population,[21] of children with isolated idiopathic cataract who were born preterm or of low birth weight, is notable in the light of population-based studies of low-birthweight and preterm children in which congenital cataract, unrelated to retinopathy of prematurity, occurs more frequently than expected.[35] An association has previously been reported between congenital ocular anomalies and both low birth weight and prematurity, but only in children with other systemic anomalies.[36,37] The observation in the present study requires confirmation in other epidemiologic studies. It will also be important to elucidate underlying mechanisms, to establish whether the effects of prematurity or low birth weight are directly cataractogenic—for example, reflecting immaturity of antioxidant enzymatic activity—or are simply markers for other events.

Although a high proportion of serious congenital anomalies in humans are of unknown origin[38] the percentage of idiopathic cases in the present study is remarkable. There has been limited study of the environmental, socioeconomic, and demographic determinants of congenital ocular anomalies,[39,40] and risk factors for idiopathic congenital and infantile cataract remain unclear.[2,4,6,18,36] In one important study in the United Kingdom[41] based on a multiple-source register of congenital anomalies, cataract was found to be associated with proximity to factory chimneys, incinerators, and gas works, suggesting a possible link with toxic combustion products. Cataract was also found to be statistically associated with deprivation, measured using composite indicators based on electoral ward, but not social class when measured using father's occupation. Given the small number of cases, however, these associations were subject to sampling error. No associations have been found with paternal age,[40] maternal age, or birth rank.[41] Although other congenital abnormalities have been reported to occur more frequently in twins than singletons,[38,42] a higher frequency of ocular anomalies has not been reported.[38,41,42] Thus, it is of interest that the proportion of twins among those with unilateral idiopathic cataract in the present study is higher than the proportion of such births nationally.[21] Should future studies confirm this observation, then population based studies of higher order births (for example, using established twin registers) may provide important insights in to the relative importance of genetic and environmental influences in pathogenesis of congenital and infantile cataract.

At present, primary prevention of hereditary cataract is restricted to preconceptional genetic counseling of couples already known to be at risk, and there are no specific therapeutic approaches.[22,23] Current work to identify the genes responsible for hereditary cataract and to elucidate the role of their products[2,23,43,44] has focused on autosomal dominant cataract which, in industrialized countries, is reported more frequently than either autosomal recessive or X-linked inheritance.[23,44] However, because autosomal recessive cataract is more commonly reported in some developing countries in populations with large average family size and high rates of consanguinity,[9] international collaboration may prove informative to primary and secondary preventive strategies against hereditary cataract.

As the clinical description by Gregg in 1941[45] of congenital cataract after rubella in pregnancy was one of the first clearly demonstrated risk factors for any congenital anomaly in humans, it is notable that an epidemic of rubella in the United Kingdom in 1996[46] accounted for the two unexpected cases of cataract in the present study. This serves as a reminder of the importance of implementing and maintaining appropriate public health measures against prenatal infections, as well as continuing public health surveillance for these potentially preventable diseases in all countries.[46] Furthermore, the findings of this study highlight the importance of liaison between pediatricians and ophthalmologists for effective initial assessment and subsequent management of all children with congenital cataract. That more than a third of bilateral cases had isolated hereditary cataract emphasizes the importance of ophthalmic examination of parents and family members of otherwise healthy children with cataract, to ensure hereditary cases are not overlooked so that genetic counseling may be provided.[2] The multisystem hereditary disorders accounting for almost a fifth of bilateral cases reflect the increasing range of such uncommon diseases and dysmorphic syndromes in which congenital cataract has been reported.[2,18,19,47] This emphasizes the importance of early evaluation by an ophthalmologist of all children with relevant systemic disorders that place them at higher risk of ocular disease[13,47] and, conversely, the value of examination of children with bilateral cataract by a dysmorphologist.

Epidemiologic studies to identify or confirm putative risk factors are needed to inform basic scientific research in this area and to develop new primary preventive strategies. One approach would be through case–control studies, to both test and generate hypotheses regarding prenatal and perinatal risk factors. Irrespective of design, given the rarity of congenital and infantile cataract and the likelihood of multiple risk factors, large collaborative studies, possibly on an international scale, are likely to be necessary. Written descriptions of the surgical

treatment of cataract, from as early as the third century BC,[48] attest to the long history of secondary prevention of visual impairment due to this disorder in adults. Attention to cataract in infancy is more recent,[2] and primary prevention remains an important goal. We suggest that the findings of this study serve to highlight an agenda for multidisciplinary research on the etiology of congenital and infantile cataract to realize this goal.

Acknowledgments

The authors are indebted to all clinicians who contributed information to the study, the Executive Committee of the British Pediatric Surveillance Unit for the opportunity to conduct the study, David Taylor and Catherine Peckham for their advice and support and for comments on an earlier draft of the manuscript, and the anonymous reviewers for their helpful comments.

References

1. Thylefors B. A global initiative for the elimination of avoidable blindness. *Am J Ophthalmol.* 1998;125:90–93.
2. Taylor D. Congenital cataract: the history, the nature and the practice. The Doyne Lecture. *Eye.* 1998;12:9–36.
3. Foster A, Gilbert C. Epidemiology of visual impairment in children. In: Taylor D, ed. *Paediatric Ophthalmology.* 2nd ed. London: Blackwell Science, 1997:3–12.
4. Pike MG, Jan JE, Wong PKH. Neurological and developmental findings in children with cataracts. *Am J Dis Child.* 1989;143:706–710.
5. Phillips CI, Levy AM, Newton M, Stokoe NL. Blindness in schoolchildren: importance of heredity, congenital cataract, and prematurity. *Br J Ophthalmol.* 1987;71:578–584.
6. Bryars JH, Archer DB. Aetiological survey of visually handicapped children in Northern Ireland. *Trans Ophthalmol Soc UK.* 1977;97:26–29.
7. Merin S, Crawford JS. The etiology of congenital cataracts. *Can J Ophthalmol.* 1971;6:178–182.
8. Angra SK. Etiology and management of congenital cataract. *Indian J Pediatr.* 1987;54:673–677.
9. Eckstein M, Vijayalakshmi P, Killedar M, Gilbert C, Foster A. Aetiology of childhood cataract in south India. *Br J Ophthalmol.* 1996;80:628–632.
10. Harley JD, Hertzberg R. Aetiology of cataracts in childhood. *Lancet.* 1965;1:1084–1086.
11. Office of Population Censuses and Surveys. Congenital malformations statistics: notifications 1991. Series MB3 No. 7. London: Her Majesty's Stationery Office; 1993.
12. Evans J. Causes of blindness and partial sight in England and Wales 1990–91: Studies on Medical and Population Subjects No 57. London: Her Majesty's Stationery Office; 1995.
13. Hall DM. *Health for All Children*. 3rd ed. Report of the Third Joint Working Party on Child Health Surveillance. Oxford, UK: Oxford University Press; 1996.
14. British Paediatric Surveillance Unit. British Paediatric Surveillance Unit 11th Annual Report 1996–1997. London: Royal College of Paediatrics and Child Health; 1997.
15. Godward S, Dezateux C. Validation of the reporting bases of the orthopaedic and paediatric surveillance schemes. *Arch Dis Child.* 1996;75:232–236.
16. Rahi JS, Dezateux C, for the British Congenital Cataract Interest Group. Capture–recapture analysis of ascertainment by active surveillance in the British Congenital Cataract Study. *Invest Ophthalmol Vis Sci.* 1999;40:236–239.
17. World Health Organisation (WHO). *International Statistical Classification of Diseases and Health Related Problems.* 10th Revision. Geneva: World Health Organisation, 1992.
18. Lambert SR, Drack AV. Infantile cataracts. *Surv Ophthalmol.* 1996;40:427–458.
19. Lloyd IC, Goss–Sampson M, Jeffrey BG, Kriss A, Russell–Eggitt I, Taylor D. Neonatal cataract: aetiology, pathogenesis and management. *Eye.* 1992;6:184–196.
20. Kirkwood BR. *Essentials of Medical Statistics*. 1st ed. Oxford, UK: Blackwell Scientific; 1988.
21. Office for National Statistics. *Birth Statistics 1996*. Series FM1 No.25. London: Her Majesty's Stationery Office; 1998.
22. Wright AF. Gene therapy for the eye. *Br J Ophthalmol.* 1997;81:620–623.
23. Francis PJ, Berry V, Moore AT, Bhattacharya S. Lens biology: development and human cataractogenesis. *Trends Genet.* 1999;15:191–196.
24. Francois J. *Congenital Cataracts*. Assen, The Netherlands: Royal Van Gorum, 1963.
25. Endres W, Shin YS. Cataract and metabolic disease. *J Inherit Metab Dis.* 1990;13:509–516.
26. Bermejo E, Martinez–Frias ML. Congenital eye malformations: clinical-epidemiological analysis of 1,124,654 consecutive births in Spain. *Am J Med Genet.* 1998;75:497–504.
27. Stromland K, Miller M, Cook C. Ocular teratology. *Surv Ophthalmol.* 1991;35:429–446.
28. Brown CA. Postnatal cataracts in premature infants. *Trans Ophthalmol Soc UK.* 1963;83:493–503.
29. Alden ER, Kalina RE, Hodson WA. Transient cataracts in low birthweight infants. *J Paediatr.* 1973;82:314–318.
30. Guy LP. Postnatal cataracts in premature infants. *Am J Ophthalmol.* 1954;38:65–68.
31. McKinna AJ. Neonatal hypoglycemia: some ophthalmic observations. *Can J Ophthalmol.* 1966;1:59.
32. Liebman SD. Postnatal development of lamellar cataracts in premature infants. *Arch Ophthalmol.* 1958;54:257–258.
33. Merin S, Crawford JS. Hypoglycemia and infantile cataract. *Arch Ophthalmol.* 1971;86:495–498.
34. Livingston PM, Carson CA, Taylor HR. The epidemiology of cataract: a review of the literature. *Ophthalmic Epidemiol.* 1995;2:151–164.
35. Alberman E, Benson J, Evans S. Visual defects in children of low birthweight. *Arch Dis Child.* 1982;57:818–822.
36. Stoll C, Alembik Y, Dott B, Roth MP. Epidemiology of congenital eye malformations in 131,760 consecutive births. *Ophthalmic Paediatr Genet.* 1992;13:179–186.
37. McGinnity FG, Bryars JH. Controlled study of ocular morbidity in school children born preterm. *Br J Ophthalmol.* 1992;76:520–524.
38. Doyle PE, Beral V, Botting B, Wale CJ. Congenital malformations in twins in England and Wales. *J Epidemiol Community Health.* 1990;45:43–48.
39. Dolk H, Busby A, Armstrong BG, Wallis PH. Geographical variation in anophthalmia and microphthalmia in England, 1988–94; *BMJ.* 1998:317: 905–910.
40. McIntosh GC, Olsham AF, Baird PA. Paternal age and the risk of birth defects in offspring. *Epidemiology.* 1995;6:282–288.
41. Knox EG, Lancashire R. Epidemiology of congenital malformations. London: Her Majesty's Stationery Office; 1991.
42. Layde PM, Erickson D, Falek A, McCarthy BJ. Congenital malformation in twins. *Am J Hum Genet.* 1980;32:69–78.
43. Scott MH, Hejtmancik JF, Wozencraft LA, Reuter LM, Parks MM, Kaiser–Kupfer M. Autosomal dominant congenital cataract. *Ophthalmology.* 1994;101:866–871.
44. Lund AM, Eiberg H, Rosenberg T, Warburg M. Autosomal dominant congenital cataract; linkage relations: clinical and genetic heterogeneity. *Clin Genet.* 1992;41:65–69.
45. Gregg NM. Congenital cataract following German measles in the mother. *Trans Ophthalmol Soc Aust.* 1941;3:35–46.
46. Tookey PA, Peckham CS. Surveillance of congenital rubella in Great Britain, 1971–96. *BMJ.* 1999:318: 769–770.
47. Cassidy L, Taylor D. Congenital cataract and multi-system disorders. *Eye.* 1999;13:464–465.
48. Sigerist HE. *A History of Medicine*: Vol. 2. *Early Greek, Hindu and Persian Medicine*. Oxford UK: Oxford University Press; 1961.

Members of the British Congenital Cataract Interest Group

Mr W. Aclimandos, Ms G. Adams, Mr S. Armstrong, Mr N. Astbury, Mr A. Assaf, Mr D. Banerjee, Miss L. Beck, Mr A. Beckingsale, Mr G. Bedford, Mr L. Benjamin, Miss B. Billington, Miss T. Blamires, Mr P. Bloom, Mr J. Brazier, Mr D. Brosnahan, Prof A. Bron, Mr I. Brown, Mr R. Brown, Mr D. Boase, Mr J. Bolger, Mr R. Bowell, Miss M. Boodhoo, Mr J. Bradbury, Mr J. Bryars, Miss P. Burgess, Mr J. Burke, Ms L. Butler, Mr D. Calver, Mr A. Casswell, Mr A. Chandna, Mr W. Church, Mr J. Clarke, Mr M. Clarke, Mr R. Condon, Mr M. Cole, Mr M. Dang, Mr S. Daya, Mr R. Darvell, Dr P.D. Davies, Mr C. Dodd, Mr R. Doran, Dr J. Dudgeon, Prof G. Dutton, Mr R. Edwards, Mr A. Evans, Mr N. Evans, Mr J. Elston, Mr H. El-Kasaby, Miss B. Enoch, Mr f.f. Fisher, Prof A. Fielder, Mr B. Fleck, Dr A. Gaskell, Miss M. Gibbens, Mr B. Greaves, Mr R. Gregson, Mr P. Gregory, Mr S. Haworth, Mr M.H. Heravi, Mr R. Holden, Mr R. Humphry, Mr C. Hutchinson, Mr J. Innes, Dr E. Johnson, Mr I.K. Jalili, Mrs N. Kayali, Mr N.C. Kaushik, Mr S. Kaye, Mr S. Kotta, Mr T. Lavy, Mr D. Laws, Miss J. Leitch, Mr C. Liu, Mr I.C. Lloyd, Miss C. MacEwen, Mr G. Mackintosh, Mr A. Mandal, Mr R. Markham, Mr G. McGinnity, Mr B. McCleod, Mr J. McConnell, Mr A. Moore, Mr A. Morrell, Mr R. Morris, Dr G. Morrice, Mr B. Moriarty, Mr A. Mushin, Mr C. Munton, Mr M. Neugebauer, Mr J. Nolan, Mr M. O'Keefe, Mr G. O'Connor, Miss R. Ohri, Mr C. Peckar, Mr S. Perry, Mr R. Phillips, Mr N. Price, Mr A. Quinn, Mr I. Quershi, Mr A. Rahman, Mr A. Rennie, Mr A. Ridgway, Mr M. Roper-Hall, Mr E. Rosen, Miss I. Russell Eggitt, Mr A. Shun Shin, Dr V. Thaller, Mr R. Taylor, Mr D. Taylor, Mr W. Tormey, Mr J. Twomey, Mr S. Verghese, Miss S. Vickers, Mr A. Vijaykumar, Mr A. Vivian, Mr H. Willshaw, Mr G. Woodruff, Mr G. Wright, Mrs J. Duvall Young, Mr B. Young, Dr J. Young, Mr A. Zaidi