Blindness in schoolchildren: importance of heredity, congenital cataract, and prematurity

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SUMMARY Of 99 children in the Royal Blind School, Edinburgh (which serves Scotland and part of N E England), 15 had optic atrophy (hydrocephalus 4, intracranial haemorrhage 2, prematurity 2, fetal distress 2, birth asphyxia 2, cerebral atrophy 1, cardiac arrest during hernia operation 1, and leukaemia 1). Fourteen had congenital cataract, 12 congenital retinal aplasia (Leber's congenital amaurosis) and 11 retinopathy of prematurity. There were small numbers in many other diagnostic categories, including three with non-accidental head injury. Mental retardation, spasticity, and nystagmus were frequent other correlates in all diagnostic categories. 'Very probably hereditary' was a conservative attribution in 36, while 'probable' seemed appropriate for 12 - that is, almost 48% were hereditary. Only about 11 cases might have been prevented through genetic counselling, which testifies to the frequency of autosomal recessive hereditary disease, although no parents were consanguineous.

The Royal Blind School (RBS), Edinburgh, is a residential school for the severely visually handicapped with a visual acuity almost invariably 3/60 or less or, occasionally, with very severe field loss. Our diagnostic survey of its 99 pupils does not include all Scottish blind children of school age, because educability is another criterion for admission, though many of the pupils are mentally retarded, some quite severely so. We have no information about blind children in other institutions for the very severely (multiply) handicapped. The only other school for the blind in Scotland is a small one in Glasgow: it has few residents, and caters for the deaf and the blind-deaf as well as some blind. The catchment area of the Edinburgh school also includes the north of England, especially the north-east, since a blind school in

Newcastle upon Tyne closed; six pupils have present home addresses in England.

This survey of the RBS is more comprehensive than our previous statistics of only hereditary cases there.¹ Another motive for the study was to compare the diagnoses in Scotland with those in 67 pupils in the Blind School of Yamanashi Prefecture, 120 km south-west of Tokyo, Japan.² One common observer in each study should make comparisons reasonably valid. The present information is also a selective update of the comprehensive survey of 776 blind children in England and Wales by Fraser and Friedmann published in 1967³ and of Sorsby's study of blindness in all age groups for 1963-8 in the same countries⁴ and of the Report of the Department of Health and Social Security for England 1969-76.⁵

Material and methods

Permission to be included in this survey was obtained from the parents of all except two pupils. Ages

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ranged from 5 to 18 years. Each pupil was fully examined and the case records at the Royal Blind School scrutinised. Binocular indirect ophthalmoscopy was often essential. Supplementary information was sometimes required from hospital records. A few patients were very difficult to examine, especially when mentally handicapped, even though the children and parents tried hard to be co-operative. In them more reliance was placed on records of previous examinations under anaesthesia and electro-diagnostic tests. The family history was obtained from parents, case records at the Royal Blind School or hospital, teachers, or our own records in our ophthalmic genetics clinic. Several children and families were already known to us in detail.⁶⁻⁹

Results

The large amount of information collected has been condensed into Table 1. The main cause of blindness has determined the classification, but some important coexistent abnormalities, ophthalmic and general, are mentioned in the last column headed 'Comments and complications.' Nystagmus was so frequent a complication that it is mentioned only in the two females in whom it was the primary cause of visual handicap.

'Optic nerve atrophy' was applied to 15 cases, but it was further divided into numerous smaller subgroups with a more fundamental diagnosis. Four cases of optic atrophy have been separately listed under injury, head, and one each under brain tumour and abscess. Of the 15 cases included under 'optic nerve atrophy' hydrocephalus accounted for four, non-traumatic intracranial haemorrhage for two (one premature and one with porencephaly,) prematurity for two, and fetal distress and birth asphyxia for two each, although at least one of the last may have had a more basic correlate, microcephaly. One each was attributed to cerebral atrophy, cardiac arrest during a hernia operation (a definitely iatrogenic disease), and leukaemia with or without virus infection or its drug treatment. Optic nerve hypoplasia (one) is not included in these 15.

There were 12 cases of congenital cataract, almost all operated upon in infancy. The mendelian dominant cases (four) seem to have fewer associated systemic diseases than the sporadic (six) or adopted (two) ones.

Another 12 cases were classified under retinal aplasia (Leber's congenital amaurosis), often with other handicaps (Table 1).

Ranking third of the single clinical entities (apart from the optic atrophy 'group' above), and closely rivalling congenital cataracts at 12 cases and retinal aplasia at 12 cases, was retinopathy of prematurity

with 11 cases. Of these, seven were mentally retarded with other serious correlates (see last column of Table 1), while three others had other serious complications but not mental retardation; Table 2 presents their birth weights, and Table 3 relates birth weights to intelligence quotient (IQ) and sex.

Only three cases of aniridia were definitely dominant. It is interesting that three of the four sporadic cases had the syndrome of a deletion of the short arm of chromosome 11 and mental retardation; one of these three also had a Wilms tumour.

Under the diagnosis 'injury, head' are a minimum of three with definitely non-accidental trauma. The possibility exists in more than one other case, but the evidence was not good enough to be certain of that cause. One patient was probably blinded indirectly by epilepsy, through head injury.

Although the numbers with other diagnoses are small (Table 1), they make up in sum a significant proportion of the pupils, of special interest because many are hereditary in origin (see 'Discussion').

Table 4 presents a classification by hereditary pattern when present. In 40 cases there was not even a suspicion of a hereditary cause. 'Very probable,' however, is a conservative description of the level of likelihood in 36; 'probable' seemed reasonable in 12; 'possible' (five) and 'suspected' (five) made up the balance of 58. (The 99th patient with cataract associated with Rh factor haemolytic disease was not classified as either genetic or non-genetic.)

Discussion

At the beginning of each session we survey new admissions to this blind school for hereditary disease. Parents may have completed their families by the time a blind child is old enough for school education, so that genetic counselling, if appropriate and not already given, is usually superfluous. Towards the end of each session we see the school leavers to offer genetic information if consent is given; it is also important for teenagers who do not have hereditary disease to be reassured on that score. Parents are also invited to attend these sessions with their teenage children, but very few do so.

We had the impression of a high prevalence of hereditary disease at various levels of probability in these children. Hence the decision to make this comprehensive survey of all pupils at the school throughout session 1984-5. We rate 36 of the 99 pupils as having 'very probable' hereditary disease, 12 as 'probable,' while another 10 are either 'possible' (five) or 'suspected' (five) (Tables 1 and 4). Accordingly heredity is responsible for between 48 and 58 of the 99 blind pupils at this school.

Mainly because so many cases are (very) probably

Table 1 Causes of blindness: diagnosis and heredity

Diagnosis	Number of cases: female/male (% almost the same since the total no. of pupils is 99)		Heredity (+) += (very) probable ± = possible -- = non- hereditary chr = chromosome abnormality	Mendelian type: AD = autosomal dominant AR = autosomal recessive X = X-linked (?) = (very) doubtful	Comments/complications MR = mentally retarded (or retardation)
	F	M			
Albinism, ocular		2	++	X-linked	Brothers
Aniridia, dominant	2	1	++	AD	1F; mother affected 1M 1F sibs; mother affected
sporadic		1	++	1M ?AR	
	2	1	chr	1M, 2F, deletion short arm chromosome 11	2F 1M have MR, 1F has nephroblastoma
Anophthalmos, sporadic		3	+	?AR ('all sporadic')	1 has MR
Behçet's disease	..	1	—	—	—
Brain tumour	..	1	—	—	1M has craniopharyngioma
abscess			—	—	1F has abscess
Cataract, congenital (12) dominant (4)	1	3	++	AD	4 have mother affected 1M has L microcornea 1F has father with retinitis pigmentosa
adopted (2)		2	?	?	1 has half-brother affected 1M has parents divorced, MR
sporadic (6)	1		+	?AR	
+ Down's syndrome		1	chr	trisomy 21	MR
+ haemolytic disease at birth	1		(±)	Rh factor	Rh — mother, child +ve
lamellar		1	?	?AR	MR, spastic, cortical blindness
+ macular degeneration		1	?	?AR	MR has ataxic diplegia
rubella, maternal	1		—	—	MR has microcornea
Coloboma	2		+	?AR (sporadic)	1 has fundus involved, 1 with microphthalmos
Cone-rod dystrophy		1	++	AR	Keratoconus and lens opacities
Cortical blindness	2	3	—	—	1F choking fit at 7/12 → anoxia, cerebral palsy, M 1M cause unknown, also optic atrophy, MR 1F had postnatal hypoxia with visual agnosia, MR 1M has MR, premature birth, seizure, gastroenteritis 1M has microcephaly, spastic quadriplegia, MR
Glaucoma, congenital	1	1	++	AR	1F bilateral enucleation
Injury, head epileptic		1	—	—	MR, subdural haematoma optic atrophy: ? after fit
non-accidental	1	2			1F, 2M have subdural haematoma, optic atrophy, MR
Keratoconus	1		+	?AR	Allergic kerato- conjunctivitis
Macular degeneration 'coloboma,' that is, foveal dysplasia with retinal aplasia	1	2	+	?AR	—
Microphthalmos		2	++	AR	1M brother affected
			+	?AR ?? X-LR (both sporadic)	1 has congenital cataract 1 has microphthalmos; has one side anophthalmos
Norrie's disease		1	++	X-linked R	Brother affected

Table 1 Causes of blindness: diagnosis and heredity (continued)

Diagnosis	Number of cases: female/male (% almost the same since the total no. of pupils is 99)		Hereditary (+) += (very) probable ± = possible – = non- hereditary chr = chromosome abnormality	Mendelian type: AD = autosomal dominant AR = autosomal recessive X = X-linked (?) = (very) doubtful	Comments/complications MR = mentally retarded (or retardation)
F	M				
Nystagmus	2		+	?AR	1F had birth asphyxia, deaf, ? albinoid fundus
?Solar burn	1		–	–	R affected (L strabismic amblyopia)
Optic nerve (see also head injury and brain tumour)					
hypoplasia	1		±	?AR	
atrophy (15)					
birth asphyxia		2	–	–	1M has cortical blindness (VER absent: ERG normal), caesarean birth after prolonged labour, microcephaly, 1M spastic, epileptic, bilat, VI nerve palsy, MR
cardiac arrest in hernia operation		1	–	–	
+ cerebral atrophy	1	2	?	?	1F MR
fetal distress			–	–	1M has MR, caesarean birth after prolonged labour
hydrocephalus	1	3	–	–	1M epileptic 1M has spina bifida, paralysis of lower limb
intracranial haemorrhage		2	–	–	1F has meningococle 1M had premature birth, diplegia and epilepsy, MR
leukaemia	1		–	–	1M has porncephaly, MR
± virus encephalitis					?Treatment of leukaemia caused optic atrophy
prematurity	1	1	–	–	1M weighed 1134 g at birth; EEG abnormal, MR 1F has spastic diplegia, ?MR
Retina					
aplasia (Leber's congenital amaurosis)	5	7	++	AR	2F and 3M have MR (incl. 1M hypothyroid and 1M cerebral palsy) 1M myopic 1F has sister affected
Bardet-Biedl syndrome		1	++	AR	Polydactyly, myopia
fold, retinal		1	++	AR	L total detachment, enucleation
non-attachment, bilateral		1	++	AR	Not premature
retinoschisis		1	++	X-linked	2 Brothers affected; typical family history
retinitis pigmentosa	1		++	X-linked	Affected carrier; typical family history
	1		++	AR	Sister affected
		1	++	AR	Deaf; Usher's syndrome
retinoblastoma		1	++	AR	Osteosarcoma of leg; amputated
retinopathy of prematurity	2	9	–	–	4M have MR (incl. 1 diplegic, 1 ataxic and 1 cataract) 1 cataract, 1 twin died, 1 ataxia diplegia, 1 patent ductus
Septo-optic dysplasia		1	–	–	Birthweights 709–1503 g MR

Table 2 *Retinopathy of prematurity*

<i>Year of birth</i>	<i>Number</i>	<i>Birth weight in g</i>
1966	1	1304
1967-70	0	—
1971	3	1304, 1474, 1503
1972	2	709, 1361
1973 and 74	0	—
1975	1	907
1976 and 77	0	—
1978	1	998
1979	2	<907, 992
1980	1	1247

Table 3 *Birthweight and IQ*

<i>Birth weight</i>	<i>Total</i>		<i>Low IQ</i>		<i>Normal IQ</i>	
	<i>F</i>	<i>M</i>	<i>F</i>	<i>M</i>	<i>F</i>	<i>M</i>
<2.5 kg	7	15	3	12	4	3
≥2.5 kg	26	45	7	16	19	29
Not known	1	5	—	4	1	1
Totals	34	65	10	32	24	33

autosomal recessive in causation (42), few could be said to be preventable by the parents' refraining from having children. Only the seven dominant cases, and possibly one of the two with X-linked ocular albinism, the X-linked retinoschisis, the X-linked retinitis pigmentosa, and the case of autosomal recessive retinitis pigmentosa might have been avoidable through genetic counselling. The boy with Norrie's disease and his younger brother, also affected but not yet at school, probably had inherited a mutation from his mother.⁶ The girl from a family with definite X-linked retinitis pigmentosa¹ may be showing a surprisingly severe manifestation of the carrier

state. Her mother is a carrier, but the girl's electroretinogram (ERG) is not typical, and high myopia is a factor in her 'blindness'; she has no chromosome abnormalities which might have offered an explanation for this anomaly.

Consanguinity of parents was totally absent, which eliminated one support for a diagnosis of recessive disease. In contrast, in Yamanashi, Japan, 12% of the non-environmental cases had some consanguinity of parents, the majority being full cousins.² However, that cultural difference is probably diminishing with a fall in the rate of consanguineous marriage in Japan, once the highest in the world.¹⁰

All but one of the 12 cases of the remarkably common retinal aplasia was sporadic, as would be expected in autosomal recessive disease. The one exception had an elder sister affected, but no counselling was given to the parents after the first child was diagnosed – which also applied to the family of the girl with autosomal recessive retinitis pigmentosa. It is interesting that no cases of retinal aplasia (Leber's congenital amaurosis) were seen in Yamanashi, Japan.²

Many diseases may be difficult for a non-geneticist to attribute to an autosomal recessive cause.⁷ The diagnosis will be very difficult in very rare diseases, as in at least one of the males with macular 'coloboma' (foveal dysplasia) plus retinal aplasia – an affected elder brother makes a recessive cause likely* – and in bilateral non-attachment of retina.¹¹ Indeed there may well be other cases in Table 1 with unsuspected recessive disease, and it is very likely that the catalogue of such diseases in general is still incomplete.

Although bilateral congenital cataract is generally thought to have a good prognosis, there are 12 out of 99 cases in this blind school. The proportion that

Table 4 *Probability of heredity as a cause of blindness*

<i>Likelihood of being hereditary</i>	<i>Auto-somal dominant</i>	<i>Auto-somal recessive</i>	<i>X-linked</i>	<i>Chromosome</i>	<i>Total</i>
++ (Very probable)	7	24	5		36
+ (Probable)	0	12	0	0	12
± (Possible)	0	1	0	1 Down's syndrome 3 deletion in short arm chr 11	5
? (Suspected)	0	5	0	0	5
None	—	—	—	—	40
Subtotal					98
+1 Haemolytic disease					1
Total					99

these 12 constitute of all cases of congenital cataract, presumably most coping adequately enough after operation, is unknown. The apparently unrelated systemic diseases in the sporadic cases may be interpreted as suggesting they are not hereditary in origin, although recessive inheritance is possible. There were twice as many males (eight) as females (four), an inexplicable inequality also noted in childhood cataract blindness in 1967.¹² The proportion of cases of blindness due to congenital cataract was even higher in Yamanashi (16/67) than in Edinburgh (12/99), the latter figure being very similar to that for England in the age group 5-15 in 1969-76.¹³

In general, males (65) considerably outnumber females (34), yet only five cases have X-linked recessive disease (of which one is actually a female). The female:male ratio, in the very probably and probably hereditary group, excluding the five cases with X-linked disease was, very surprisingly, 19:27. Perhaps even more surprising was the ratio in the definitely non-hereditary group, namely 11:29. In the Yamanashi Blind School survey a similar under-representation of females compared with males was found both in the hereditary group (12 F to 21 M in the dominant and (very) probably autosomal recessive) and the non-hereditary group (5 F to 13 M). Overall in Japan there were 20 F to 28 M in the ≤ 18 years age group, which excludes the 3 F and 16 M in the ≥ 19 years group, in whom 'retraining' may have been more favoured by, or for, males. The 5 F:7 M ratio in our retinal aplasia cases may easily be due to chance or to lack of differentiation within a heterogeneous group. The 2 F:9 M ratio in retinopathy of prematurity is difficult to explain. Neither Sorsby's statistics¹⁴ nor those of Fraser and Friedmann¹⁵ show a male excess in retrolental fibroplasia as it was then called, but two other reports have recorded a preponderance of males,^{16,17} attributed to their greater immaturity than girls for a given birthweight.

In the group with low birthweight (< 2.5 kg) and low IQ there is a preponderance of males, 3 F to 12 M, but in the small group with a low birthweight but normal IQ there is no significant difference, 4 F to 3 M (Table 3). An excess of males is also seen in those with normal IQ and normal birthweight, 19 F to 29 M, and even more so in those with low IQ and normal birthweight, 7 F to 16 M. In six children, 1 F and 5 M, the birthweight was not known; 4 M had low IQ, and 1 F and 1 M were mentally normal.

The excess of males is difficult to understand. More male babies destined to be blind may survive for some reason. However, the parents of male blind children may feel that these boys should have every educational advantage available, even if this means residential schooling far from home. They may prefer

to keep blind girls at home, regarding them as ineducable, or send them to homes for the multiply handicapped, perhaps feeling that education may not be so important for them and also perhaps being unwilling to allow their daughters to live away from home at an early age. Table 3 shows that the excess of males is marked in the low IQ group, which is consistent with these explanations.

The much greater apparent prevalence of optic atrophy (38% of blind males and the same proportion of blind females) aged 5-15 in England 1969-76¹³ than in our series (15/99) and in the Japanese series (1/67) may be at least in part due to the use of that diagnosis as a broader category in the English series.¹³ Indeed, optic atrophy is a very imprecise diagnosis.

In Yamanashi 14.5% of the school age children had retinopathy of prematurity. However, the youngest was 11 years old, which may indicate the disappearance in Japan of this disease, which has been described as iatrogenic. Fraser and Friedmann record figures which clearly show the epidemic in England and Wales between 1946 and 1956.¹⁸ Our Table 2 may be interpreted as supporting the view sometimes expressed that the disease in Britain, having almost disappeared around the mid-1970s, has recrudesced in the last decade. This has been explained by a recent trend towards high-technology rescue of ever smaller weight premature babies who would not previously have survived. Evidence in Table 2 may support that. Of those with births between 1966 and 1972, only one weighed *less* than 1000 g, whereas during 1975-80 only one weighed *more* than 1000 g. Similarly, the latter evidence would support a paediatrician's claim that measures to prevent this disease have been successful in premature babies with a weight of 1000 g or more. Our preoccupation with sight, however, should not blind us to the multiple handicaps both in this important subgroup and in all the other pupils. Ophthalmic morbidity from prematurity is presumably more common than frank ophthalmic mortality (that is, blindness), so that blindness statistics underestimate the penalty from prematurity. Furthermore, prematurity is a cause of many non-ocular defects in the visual system (Table 1) and of course in many other systems.

Ophthalmologists, having chosen a specialty which absolves them almost entirely from dealing with the problems of general disabling chronic disease and dysthanasia²¹ (unpleasant or painful death, compare euthanasia), may be oversensitive to the multiple handicaps in some unfortunate patients. Paediatricians (and geriatricians, among others) have chosen specialties which demand involvement with patients on many difficult risk-taking occasions, including resuscitation and survival. Vicarious responsibility

by parents (or other relatives) and doctors for decision making on behalf of premature and predictably multihandicapped, mentally retarded, sightless, and insightless babies (or others) has attracted more critical discussion recently.^{19, 20}

There were three victims of injury euphemistically called non-accidental, all being mentally retarded. No such diagnoses were made in the Yamanashi Japan, survey.²

Scotland produced only one case in which high myopia may have been a contributory factor (the female probable carrier of X-linked retinitis pigmentosa), whereas 5/67 were found in Yamanashi.² It is surprising that one case of Behçet's disease, with a very well justified diagnosis, was found in Scotland. Only one was also found in Yamanashi Blind School, but the disease is far more prevalent in Japan – 10/100 000 compared with 0.6/100 000 in Britain.²²

The staff at the Royal Blind School have a clear impression of an increase in multiple handicap among the pupils, but that may well result from a reduction in the prevalence of 'pure' blindness, so that more places are available for the multiply handicapped who previously had to go to other institutions. As in Yamanashi, Japan, we have been impressed by the happy atmosphere among the pupils in the Blind School and the very high standard of care and education provided by the very concerned teachers and other staff. The staff:pupil ratio is necessarily high. Their very sheltered environment and the sharing of their affliction with many blind peers help the blind children to minimise their great misfortune, albeit at high economic cost. It is probably easier to become reconciled to blindness or other handicap starting from birth or early childhood than to later blindness. However, at the end of their school days, their problems increase considerably, as they compete in the sighted world for training and employment. We may be guilty of overvaluing sight, as sighted individuals with a professional concern with alleviating defects in vision. The information we provide on hereditary risks (we never volunteer advice) in our ophthalmic genetics clinic probably has less effect than we originally hoped and expected, but does probably make some contribution to the prevention of blindness, often of a lifetime's duration.

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