Genetic counselling for handicapped school leavers

M VOWLES

From the Department of Paediatrics, Royal Devon and Exeter Hospital (Heavitree), Exeter

SUMMARY A total of 287 school leavers with 299 unassociated handicaps from seven special schools for physically handicapped, visually handicapped, and deaf children were given genetic counselling from 1973 to 1979. The practical aspects of running this project are described. The risk needed were those of having an affected child: 54 (18.8%) were given a high risk (greater than 1 in 10), 89 (31.0%) were given a moderate risk (1 in 10 to 1 in 40), 69 (24.0%) were given a low risk (less than 1 in 40), and 83 (28.5%) were told that their risk was the same as that of the general population. Of the 299 total handicaps, 25 (8.4%) were thought to be autosomal dominant conditions, 38 (12.7%) to be autosomal recessive conditions, and 8 (2.7%) to be X linked conditions. Empirical risks were given for 145 (48.5%) diagnoses, and general population risks for the remaining 83 (27.7%).

Genetic screening seeks to identify in a population those persons with a genotype associated with incipient or established disease or which may lead to specific genetic disease in their offspring. Not only is there mass screening in the UK and some other countries for phenylketonuria in the newborn and Rhesus negativity in pregnant women, but also during the last decade there have been some notable programmes for selective screening of adult sub-populations known to be at risk of having a child with a genetic disorder; for example, the detection of Down syndrome in the fetuses of older mothers, the identification of carriers of the Tay Sachs allele in high school students in Montreal,¹ and of carriers of the thalassaemia allele in intermediate schools in Latium.^{2,3}

Just as some of the participants in these programmes may run the risk of having an affected child, so may a proportion of pupils in special schools for the handicapped. Moreover they will eventually disperse into a society where they will not automatically receive genetic advice. A service offering genetic counselling to handicapped school leavers was accordingly started in Exeter in 1973, some five years after the institution of a genetic advisory service in the area when medical personnel in both hospital and community practice were already aware of the benefits provided by the service.

Probands

The index patients came initially from St Loye's residential college for further education and training

of the disabled and from the residential West of England School for the Visually Handicapped, both situated in Exeter. In 1974, school leavers from the Royal West of England School for the Deaf, also residential, were included. In 1975 a similar service was started at two non-residential schools in Plymouth, one for physically handicapped (Woodedlands) and the other for deaf children (Hartley House), and in 1977 a further non-residential school for the physically handicapped in Torquay (Steps Cross) was included. Finally, Dame Hannah Rogers residential school for the handicapped at Ivybridge has been included since 1978. The numbers and distribution of the consultands are shown in table 1.

Approach and methods

This project would have been difficult without the enthusiastic support of the headmasters and medical officers of the schools concerned, which has been maintained throughout the seven years since it

TABLE 1 *Handicapped school leavers counselled*

	1973	1974	1975	1976	1977	1978	1979	Total
Physical handicap (Exeter)	2	8	12	11	11	17	4	65
Partially sighted (Exeter)	9	12	14	11	8	6	16	76
Deaf (Exeter)		3	6	16	12	15	27	79
Deaf (Plymouth)			3	3	1	4	5	16
Physical handicap (Plymouth)			4	3	1	5	4	17
Physical handicap (Torquay)					6	11	11	28
Physical handicap (Ivybridge)						1	5	6
Total	11	23	39	44	39	59	72	287

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started. At four of the schools, the Royal West of England School for the Deaf (Exeter), the West of England School for the Visually Handicapped (Exeter), Hartley House School for the Deaf (Plymouth), and Steps Cross School for the Physically Handicapped (Torquay), all school leavers are offered an appointment irrespective of whether their handicap is congenital or acquired. At St Loye's College for the Disabled (Exeter) the problems are assessed by an experienced medical officer who then refers only those who have disorders or defects with possible genetic implications, while the others are reassured as part of their routine care. A similar course of action is followed both at Woodlands School for the Physically Handicapped (Plymouth) and Dame Hannah Rogers School for the Physically Handicapped (Ivybridge) after the diagnoses and records have been checked.

A few weeks before counselling takes place the headmaster in each school writes to the parents of the pupils concerned to explain the purpose of genetic counselling, request their permission for the consultation, and invite them to attend. Out of 287 pupils the parents of only four have withheld permission. Attendance rate by the parents is low, especially at the residential schools where they may have to travel up to 200 miles, well beyond the Devon county boundary.

A short proforma is enclosed with this letter requesting details of family history and consanguinity in first and second degree relatives of the child. Although this information is not relied upon, it may supplement and corroborate that provided by the Local Education Authority, the school, and hospital medical records all of which are studied before consultation. The next and very important step is for the medical officers or headmasters to discuss genetic counselling with the pupils concerned either in a group situation or with separate individuals or sometimes both, a few days before the consultation.

The first consultands in 1973 were seen in a small paediatric research unit attached to the Royal Devon and Exeter Hospital (Heavitree). Difficulties in communication were soon experienced with the deaf school leavers and it seemed unlikely that the odds were being understood in every case. All counselling sessions were therefore moved to the various school premises where, if the parents were not present, a teacher attended and, if necessary in the schools for the deaf, acted as an interpreter. This had a further advantage in that discussions subsequently took place between teachers and consultands and although a further interview has always been offered this has not yet been taken up.

Counselling given

The risks that were needed for the 287 school leavers seen (appendix) were those of having an affected child. Fifty-four (18.8%) were given a high risk (greater than 1 in 10), 89 (31.0%) were given a moderate risk (1 in 10 to 1 in 40), 69 (24.0%) were given a low risk (less than 1 in 40), and 83 (28.5%) were told that their risk was the same as that of the general population. These figures include six consultands considered to have two unassociated conditions in different risk categories (Nos 26, 53, 124, 168, 203, 139), and two where the consultand was at risk of developing and subsequently passing on a heritable condition (Nos 1 and 28). Furthermore, there were four consultands considered to have two unassociated conditions in the same risk category (Nos 54, 81, 89, 103) (appendix).

Twenty-five (8.4%) school leavers (Nos 1, 2, 3, 5, 6, 20-25, 28-30, 32-38, 40, 53, 54) were thought to have an autosomal dominant condition with up to a 1 in 2 risk of having an affected child. One of these (No 54) had two unassociated conditions each having up to a 1 in 2 risk, and two more (Nos 23 and 28) were at risk of developing an autosomal dominant condition in later life. Modifications of risk were discussed for those conditions where manifestation is variable or penetrance incomplete.

Thirty-eight (12.7%) consultands were considered likely to have an autosomal recessive condition. Of these, seven (0.2%) were thought to have only a moderate risk for their children unless they married a relative or a person who was either heterozygous or homozygous for the same abnormal gene (Nos 113-116, 118, 122, 139). The remaining 31 (10.8%) were given a low risk with the same proviso regarding marriage partners (Nos 124, 141, 168-172, 174-186, 189-192, 194-196, 199, 201, 204, 205). Three (Nos 124, 168, 203) had a further handicap for which they were given the appropriate risks; 'moderate' for case No 124 and 'as for the general population' in Nos 168 and 203. Also in this cohort of 38 consultands, one (No 172) is likely to be infertile and thus there would be no risk to his offspring. It was not deemed a psychologically opportune age at which to discuss this problem and he was advised to seek further counselling before marriage.

X linked genes were considered to be the cause of the handicap in eight (2.7%) cases. Three of these (Nos 117, 120, 121) were classified in the moderate risk group and five (Nos 140, 173, 180, 187, 200) were given a low risk for their offspring to be affected, although they were told that their daughters would all be carriers of the abnormal gene.

Empirical risks were the basis of genetic counselling

in a further 145 (48.5%) probands. Thirty (10.5%) were given a high risk (Nos 4, 7-19, 26, 27, 31, 39, 41-52) and 79 (27.5%) were given a moderate risk (Nos 23, 26, 28, 53, 55-112, 119, 123-138). Three of these (Nos 81, 89, 103) had two unassociated conditions each with a moderate risk.

The handicaps affecting the remaining 83 (27.7%) probands (Nos 139, 168, 203, 208-287) were thought to be acquired and they were reassured that the risks for their progeny were the same as for the general population. However, a further eight not only had a handicap in this category but also an unassociated one which was not acquired. Four (Nos 23, 26, 28, 53) have already been included in the list of autosomal dominant conditions, three (Nos 124, 139, 168) in that of autosomal recessive conditions, and one (No 203) was given an empirical risk (table 2).

The many different handicaps affecting the consultands from the seven schools and the even greater diversity of aetiological factors have been reduced to three major groups: physically handicapped, deaf, and visually handicapped. One hundred and nine consultands in the 'physically handicapped' group were given the following risks: 20 (18.3%) were given a high risk, 43 (39.4%) were given a moderate risk, and 31 (28.5%) a low risk. The remaining 15 (13.8%) were reassured that the risks for their children are the same as for the general population (table 3). The 97 consultands in the 'deaf' group were given the following risks: nine (9.2%) were given a high risk, 35 (36.1%) were given a moderate risk, and two (2.1%) a low risk, while 51 (52.6%) consultands were reassured that their children would have no added risk (table 4). The third group, 'visually handicapped', consisted of 81 consultands of whom 25 (30.9%) were given a high risk, seven (8.6%) a moderate risk, and 35 (43.2%) a low risk. The remaining 14 (17.3%) were reassured that their offspring are unlikely to be similarly affected (table 5).

It became apparent at an early stage in this project that the youngsters were unable to evaluate risk figures at the age of 16 years. For this reason terms of 'high', 'moderate', or 'low' chances of their having

TABLE 3 *Risk groups, physically handicapped*

High	
>1 in 10	20 (18.3%)
Moderate	
1 in 10 to 1 in 40	43 (39.4%)
Low	
<1 in 40	31 (28.5%)
General population	15 (13.8%)
Total	109 (100.0%)

TABLE 4 *Risk groups, deaf*

High	
>1 in 10	9 (9.2%)
Moderate	
1 in 10 to 1 in 40	35 (36.1%)
Low	
<1 in 40	2 (2.1%)
General population	51 (52.6%)
Total	97 (100.0%)

TABLE 5 *Risk groups, visually handicapped*

High	
>1 in 10	25 (30.9%)
Moderate	
1 in 10 to 1 in 40	7 (8.6%)
Low	
<1 in 40	35 (43.2%)
General population	14 (17.3%)
Total	81 (100.0%)

affected offspring were used. The actual odds, if known, were occasionally given to a consultand where it seemed helpful and were quoted in the reports sent to the School Medical Officers and the family doctors for inclusion in school and NHS medical records.

The possibility that one handicapped person might marry another similarly affected or with a handicap of a different nature was raised at each interview and the consultands were strongly advised to seek further counselling if such a situation should arise. A further consultation before marriage was also recommended if the handicap was such that it was difficult to give an accurate diagnosis at the time of leaving school.

Finally contraception and the possibilities of

TABLE 2 *Genetic basis of risk estimation (287 probands; 299 unrelated diagnoses)*

Risk	Autosomal dominant	Autosomal recessive	X linked recessive	Empirical	Acquired	Total
High						
> 1 in 10	25	—	—	30	—	55 (18.4%)
Moderate						
1 in 10 to 1 in 40	—	7	3	82	—	92 (30.8%)
Low						
< 1 in 40	—	31	5	33	—	69 (23.1%)
General population	—	—	—	—	83	83 (27.7%)
Total	25 (8.4%)	38 (12.7%)	8 (2.7%)	145 (48.5%)	3 83 (27.7%)	299 (100.0%)

antenatal diagnosis were discussed briefly when pertinent, but options such as adoption and AID were not introduced.

Discussion

In assessing the correct risks there were two problem areas. Firstly, how should one advise the isolated cases of conditions thought to be the result of autosomal dominant, autosomal recessive, or X linked recessive genes? Nine (Nos 1-4, 32, 33, 35-37) of the 23 autosomal dominant group were isolated cases although factors such as illegitimacy or 'formes frustes' could not be ruled out as the parents were not interviewed or examined. Two (Nos 183, 184) of the 38 assessed as being homozygous for autosomal recessive genes could be heterozygous for X linked recessive genes, but in this event a low risk for their children is also appropriate, with the proviso that their daughters would be obligate carriers and so further genetic counselling was advised both for them and their female offspring. Myopia affecting case No 201 could be polygenic/multifactorial instead of autosomal recessive but once again a similar risk, this time 'low', would apply. Secondly, the group of 142 probands given empirical risk figures comprises conditions such as spina bifida where family studies have been done, conditions such as arthrogryposis where no such studies exist, and some cases where, although the clinical findings were described, a precise diagnosis was not made in terms of aetiology, for example, optic atrophy (No 31). Heterogeneity led to some consultands being given an empirical risk figure when in fact their handicap could have been the result of a single gene. One feels uneasy that such a large proportion (48.57%) of these handicapped young people were given empirical risk figures, although those in the high risk group (10%) were based on family studies.

None of the 287 probands had been given any previous genetic counselling. There was no evidence in any of the records examined, whether NHS file, Local Authority, school or hospital records, that any assessment had been made of the genetic component of the various handicaps. Most of those whose handicap was the result of a non-genetic cause, for example, rubella or meningitis, were aware of the aetiology, but even some of these were unsure whether their children might or might not be affected. In the 14 cases where there was a family history of a dominant condition only two had been made aware by their families of a high risk to their offspring. One of these repeated throughout the interview "My mother says I must not get married"!

Overall, it was difficult to assess how many had been previously concerned about the possible risks

to their offspring, as attention had been drawn to this by the teaching of elementary genetics in biology lessons and by the preparatory talks by the head-teachers shortly before the genetic counselling interview, but a number were obviously glad of the opportunity to discuss the matter. Moreover, they were made aware that genetic counselling is available for themselves, their relatives, and for other handicapped persons with whom they may well come in contact. Indeed, this was initiated immediately for the sibs of consultands with autosomal dominant and recessive conditions and for both male and female first degree relatives of those who had an X linked condition.

Out of 287 school leavers approached, the parents of only four withheld permission, a 99% acceptance rate. This high uptake reflects not only the tactful approach made by the head teachers to both parents and pupils, but also the desire on the part of the parents for their affected child to discuss the problem with a genetic counsellor. It compares favourably with the 75% participation rate reported in both 'A Study of Tay-Sachs Screening Among High School Students' by Clow and Scriver¹ and that of 70% reported in 'First Premarital Screening of Thalassaemia Carriers in Intermediate Schools in Latium' by Silvestroni *et al.*,² which increased to 76% four years later,³ although the genetic problems and implications are so different that perhaps a comparison is invidious. All three projects, however, share the importance of offering genetic advice premaritally and at a time when the subjects still have the support of an understanding school staff should they be distressed by the advice given. Furthermore, in the case of the UK, the advice is incorporated in their NHS general practitioner and hospital records for future reference.

From table 6 it can be deduced that in 1978 over 3000 pupils known to be handicapped, physically or visually or in their hearing or a combination of these, were in their final school year at special schools. They formed a 'captive' group where genetic counselling might have been of benefit not only to the subjects concerned but also in a few instances to their relatives. Moreover, by improving the awareness of genetic risks before reproduction takes place there is a real possibility that the incidence of certain

TABLE 6 *Handicapped pupils in England and Wales (1978) aged 5 to 16 years*

Physically handicapped	17 000
Deaf and partially hearing	11 600
Blind and partially sighted	4 000
Total	32 600
Number of school leavers (approx)	3 200

severe genetic disorders in the population might be reduced. Such long term effects will not be evident for many years; however, a follow-up has been started of those probands seen in 1973, now aged 22, similar to those of Carter *et al*⁴ and Emery *et al*.⁵ At follow-up probands are asked whether they understood the risk assessment given to them, whether it affected their feelings about having children, and whether their feelings have changed in the last seven years. At the same time pedigrees are updated and, where necessary, previous genetic advice is amended in the light of recent advances.

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Requests for reprints to Dr M Vowles, Department of Paediatrics, Royal Devon and Exeter Hospital (Heavitree), Gladstone Road, Exeter EX1 2ED.

APPENDIX *The risks quoted are those which related to particular families and which were considered appropriate at the time of counselling. They should not be regarded as applicable to all families with similar diagnoses.*

Name	Sex	Handicap	Cause	Family history	Sibs
HIGH RISK (GREATER THAN 1 IN 10)					
1 RB	M	Ectrodactyly (R)	—	—	6 ☐ 2 ☐
2 EF	F	Achondroplasia	—	—	1 ☐ 8 ☐
3 JD	F	Achondroplasia	—	—	2 ☐
4 MB	F	Dystonia musculorum deformans	—	Unknown (adopted)	Unknown
5 AF	M	Dejerine-Sottas disease	—	—	1 ☐
6 KP	M	Atypical muscular dystrophy	—	F	1 ☐ 2 ☐
7 JH	M	Manic depressive disorder	—	F; pat g/f	1 ☐ 1 ☐
8 PW	M	Asthma, eczema	—	F	1 ☐
9 MP	M	Asthma, eczema	—	M	2 ☐ 2½ ☐
10 NH	M	Asthma, eczema	—	—	3 ☐
11 AW	F	Asthma, eczema	—	F	1 ☐
12 GR	F	Asthma, eczema	—	—	1 ☐
13 CE	F	Asthma, eczema	—	—	1 ☐
14 SA	F	Asthma	—	M; mat g/f	1 ☐ 2 ☐
15 KC	M	Asthma, eczema	—	M; mother's sister's 2 daughters	1 ☐ 2 ☐
16 MJ	M	Asthma, eczema	—	M	1 ☐ 2 ☐
17 DB	F	Asthma, hay fever	—	M	1 ☐ 1 ☐
18 AW	M	Asthma, hay fever	—	—	2 ☐
19 KW	M	Asthma	—	Unknown (adopted)	Unknown
20 CB	F	Treacher-Collins syndrome	—	F; father's brother	1 ☐
21 SC	F	Sensorineural deafness (bil)	—	F; pat g/m; father's sister	1 ☐
22 JM	M	Waardenburg syndrome	—	F; M; mat g/m	1 ☐
23 *LH	F	Sensorineural deafness (bil)	—	M; otosclerosis	—
24 KL	F	Sensorineural deafness (bil)	—	F; pat g/f; father's brother; father's brother's 2 sons	1 ☐
25 JR	F	Sensorineural deafness (bil)	—	M; mat g/m; mother's sister	—
26 *NB	M	Sensorineural deafness (bil), Meniere's disease	—	M; Meniere's disease	1 ☐
27 MW	F	Sensorineural deafness (bil)	—	Mother's sister	3 ☐ 1 ☐
28 *DD	F	Sensorineural deafness (bil)	—	F; otosclerosis	—
29 KJ	M	Sensorineural deafness (bil)	—	M; mat g/m; mat g/g/m	1 ☐ 1 ☐
30 SR	F	Cataracts (bil)	—	F	2 ☐ 1 ☐
31 JK	M	Optic atrophy and nystagmus	—	—	—
32 DB	M	Marfan syndrome	—	—	3 ☐ 1 ☐
33 BC	M	Aniridia and nystagmus	—	—	2 ☐ 1 ☐
34 KD	M	Colobomata of lens and iris (bil)	—	—	1 ☐
35 RD	M	1st arch syndrome	—	F (forme fruste)	1 ☐ 1 ☐
36 RD	F	Aniridia, glaucoma	—	—	1 ☐ 1 ☐

APPENDIX—continued

Name	Sex	Handicap	Cause	Family history	Sibs
37 SH	M	Craniofacial dysostosis	—	—	1 ☐
38 JH	M	Cataracts (bil)	—	M; mat g/m	1 ☐ 2 ☐
39 GR	F	Retinitis pigmentosa	—	—	1 ☐ 1 ☐
40 DD	M	Hypermetropia, amblyopia	—	M; mother's sister, cyclopegia	1 ☐
41 BB	M	Nystagmus	—	—	3 ☐
42 WW	F	Cataracts (bil)	—	—	1 ☐
43 JK	F	Cataracts (bil)	—	—	2 ☐
44 SS	F	Cataracts (bil)	—	—	2 ☐
45 RO'N	M	Cataracts (bil)	—	—	2 ☐
46 JT	M	Cataracts (bil)	—	—	2 ☐ 1 ☐
47 MB	F	Cataracts (bil)	—	—	—
48 CC	F	Cataracts (bil)	—	—	1 ☐
49 JH	F	Cataracts (bil)	—	—	1 ☐ ☐ twin of JH
50 JI	F	Cataracts (bil)	—	—	1 ☐
51 KW	F	Cataracts (bil)	—	—	—
52 HT	F	Cataract (R)	—	—	1 ☐ 1 ☐
53 *TC	M	Myopia, blepharophimosis	—	F; father's sister's son and daughter, blepharophimosis	1 ☐ ☐ phimosis
54 *SM	F	Craniofacial dysostosis	—	M; mat g/m; mother's sister and brother, craniofacial dysostosis	1 ☐
MODERATE RISK (1 IN 10 TO 1 IN 40)					
55 LW	F	Spina bifida	—	—	2 ☐
56 WT	F	Spina bifida	—	—	3 ☐ 4 ☐
57 LH	M	Spina bifida	—	—	1 ☐
58 PC	F	Spina bifida	—	—	—
59 AF	F	Spina bifida	—	—	1 ☐ 1 ☐
60 NS	F	Spina bifida	—	—	1 ☐ 1 ☐
61 JB	F	Spina bifida	—	—	1 ☐ 1 ☐
62 LP	M	Spina bifida	—	—	—
63 JS	M	Spina bifida	—	—	2 ☐
64 JP	F	Spina bifida	—	—	1 ☐
65 TS	M	Spina bifida	—	—	2 ☐ 2 ☐
66 PC	M	Spina bifida	—	—	3 ☐ 3 ☐
67 SS	M	Spina bifida	—	—	2 ☐ 2 ☐
68 CL	M	Spina bifida	—	—	1 ☐
69 SC	M	Spina bifida	—	—	3 ☐ 1 ☐
70 SC	M	Spina bifida	—	—	1 ☐ 1 ☐
71 TP	F	Spina bifida	—	—	3 ☐ 1 ☐
72 SW	M	Encephalocele	—	—	1 ☐
73 PA	F	Eisenmenger's complex	—	—	1 ☐ 1 ☐
74 CR	M	Falot's tetralogy	—	—	3 ☐ 1 ☐
75 HC	F	Transposition of great vessels, VSD	—	—	1 ☐ 2 ☐
76 AW	M	Transposition of great vessels	—	—	2 ☐ 2 ☐
77 GC	M	Transposition of great vessels	—	—	3 ☐ 2 ☐
78 HD	F	Transposition of great vessels	—	—	3 ☐
79 MM	M	Transposition of great vessels, tricuspid atresia	—	—	2 ☐ 2 ☐
80 AS	M	Diabetes (juvenile onset)	—	M; adult onset	2 ☐
81 *AD	M	Diabetes (juvenile onset), epilepsy	—	—	1 ☐
82 SG	F	Diabetes (juvenile onset)	—	—	—
83 KF	M	Diabetes (juvenile onset)	—	—	3 ☐ 1 ☐
84 CT	M	Epilepsy	—	—	3 ☐
85 GT	M	Epilepsy	—	—	3 ☐
86 KT	M	Epilepsy	—	—	1 ☐
87 KL	F	Epilepsy	—	—	—
88 GG	M	Epilepsy	—	—	1 ☐
89 *GM	M	Epilepsy, asthma	—	—	1 ☐
90 PC	M	Epilepsy	—	—	2 ☐
91 DW	F	Epilepsy	—	—	1 ☐
92 DH	M	Epilepsy	—	Father's brothers; father's brother's daughter	—
93 CC	F	Epilepsy (mid-temporal)	—	—	1 ☐ 3 ☐
94 RS	M	Epilepsy	—	—	2 ☐ 2 ☐
95 JM	M	Epilepsy	—	—	—
96 KT	M	Sensorineural deafness (bil)	—	—	1 ☐ 1 ☐
97 EC	F	Sensorineural deafness (bil)	—	—	1 ☐ 2 ☐
98 JB	F	Sensorineural deafness (bil)	—	—	1 ☐
99 AH	F	Sensorineural deafness (bil)	—	—	—
100 TC	M	Sensorineural deafness (bil)	—	—	2 ☐ 2 ☐
101 SD	M	Sensorineural deafness (bil)	—	—	1 ☐ 1 ☐
102 TD	M	Sensorineural deafness (bil)	—	—	2 ☐
103 *PC	M	Sensorineural deafness (bil), Hirschsprung's disease	—	—	2 ☐ 1 ☐

APPENDIX—continued

Name	Sex	Handicap	Cause	Family history	Sibs
104 PK	M	Sensorineural deafness (bil)	—	—	1 ☐ 1 ☐
105 NS	M	Sensorineural deafness (bil)	—	—	1 ☐ 1 ☐
106 LA	F	Sensorineural deafness (bil)	—	—	2 ☐ 2 ☐
107 CT	M	Sensorineural deafness (bil)	—	—	2 ☐ 2 ☐
108 TW	M	Sensorineural deafness (bil)	—	—	1 ☐ 1 ☐
109 RR	M	Sensorineural deafness (bil)	—	—	1 ☐ 1 ☐
110 GH	M	Sensorineural deafness (bil)	—	—	1 ☐ 1 ☐
111 MMcG	F	Sensorineural deafness (bil)	—	—	1 ☐ 1 ☐
112 SD	M	Sensorineural deafness (bil)	—	—	1 ☐ 1 ☐
113 VA	M	Sensorineural deafness (bil)	—	Parents second cousins	1 ☐ 1 ☐
114 PC	M	Sensorineural deafness (bil)	—	—	2 ☐ 2 ☐
115 AC	F	Sensorineural deafness (bil)	—	—	1 ☐ 1 ☐
116 NJ	M	Sensorineural deafness (bil)	—	—	1 ☐ 1 ☐
117 AR	M	Sensorineural deafness (bil)	—	Mother's sister's 2 sons	1 ☐ 1 ☐
118 BR	M	Sensorineural deafness (bil)	—	—	1 ☐ 1 ☐
119 AT	F	Sensorineural deafness (bil)	—	—	1 ☐ 1 ☐
120 DC	M	Sensorineural deafness (bil)	—	—	1 ☐ 1 ☐
121 JM	M	Sensorineural deafness (bil)	—	Mother's 2 sisters' sons	1 ☐ 1 ☐
122 SW	F	Sensorineural deafness (bil)	—	—	1 ☐ 1 ☐
123 GE	M	Sensorineural deafness (bil)	—	—	3 ☐ 3 ☐
124 *KL	F	Sensorineural deafness (bil), sickle-cell trait	—	—	2 ☐ 2 ☐
125 AC	M	Sensorineural deafness (bil)	—	—	2 ☐ 2 ☐
23 *LH	F	Sensorineural deafness (bil)	—	M; otosclerosis	—
126 JT	F	Sensorineural deafness (bil)	—	—	2 ☐ 2 ☐
127 AC	M	Sensorineural deafness (bil)	—	—	2 ☐ 2 ☐
128 DI	F	Sensorineural deafness (bil)	—	Unknown (adopted)	Unknown
28 *DD	F	Sensorineural deafness (bil)	—	F; otosclerosis	—
129 SG	F	Sensorineural deafness (bil)	—	—	1 ☐ 1 ☐
130 SN	F	Sensorineural deafness (bil)	—	—	2 ☐ 2 ☐
26 *NB	M	Sensorineural deafness (bil), Meniere's disease	—	M; Meniere's disease	1 ☐ 1 ☐
131 KL	M	Macular degeneration (bil)	—	—	3 ☐ 3 ☐
132 PD	M	Myopia, nystagmus	—	—	1 ☐ 1 ☐
133 BW	F	Myopia	—	—	3 ☐ 3 ☐
134 RG	M	Myopia, nystagmus	—	—	2 ☐ 2 ☐
135 SP	M	Nystagmus	—	—	2 ☐ 2 ☐
136 MB	M	Nystagmus	—	—	1 ☐ 1 ☐
137 JB	F	Idiopathic scoliosis	—	—	2 ☐ 2 ☐
138 TC	M	Idiopathic scoliosis	—	—	—
139 *BD	F	Cystic fibrosis, retrolental fibroplasia	—	—	1 ☐ 1 ☐
53 *TC	M	Myopia, blepharophimosis	—	F; father's sister's son, daughter, blepharophimosis	1 ☐ 1 ☐
LOW RISK (LESS THAN 1 IN 40)					
140 AB	M	Muscular dystrophy (Becker type)	—	M; carrier	1 ☐ 1 ☐
141 IP	M	Pelvic limb-girdle muscular dystrophy	—	—	2 ☐ 2 ☐
142 ML	M	Limb-girdle muscular dystrophy (atypical)	—	Unknown	Unknown
143 SN	F	Myelodysplasia	LMN lesion	—	1 ☐ 1 ☐
144 SA	F	'Neuropathy'	—	—	1 ☐ 1 ☐
145 RW	M	Benign congenital hypotonia	—	—	1 ☐ 1 ☐
146 YN	F	Spastic diplegia	—	—	3 ☐ 3 ☐
147 MS	M	Hemiplegia	—	—	—
148 AM	M	Hemiplegia and epilepsy	—	—	1 ☐ 1 ☐
149 KMcl	M	Arthrogryposis	—	—	—
150 JMca	F	Arthrogryposis	—	—	2 ☐ 2 ☐
151 MM	M	Arthrogryposis	—	—	2 ☐ 2 ☐
152 LI	M	Arthrogryposis	—	—	2 ☐ 2 ☐
153 IB	M	Arthrogryposis	—	—	3 ☐ 3 ☐
154 PU	M	Arthrogryposis	—	—	1 ☐ 1 ☐
155 MR	M	Aplastic femoral heads, triphalangeal thumbs	—	—	3 ☐ 3 ☐
156 SH	M	Disdiadochonesis (L)	Cerebral angioma	—	1 ☐ 1 ☐
157 RW	F	Temporal hemianopia	Cranioopharyngioma	—	3 ☐ 3 ☐
158 NA	M	Temporal hemianopia	Astrocytoma	—	4 ☐ 4 ☐
159 SF	F	Epilepsy	Intracranial haemangioma	Unknown	Unknown
160 LS	M	Hemiplegia	Porencephalic cyst	—	1 ☐ 1 ☐
161 WP	M	Speech disorder	—	—	2 ☐ 2 ☐
162 SS	F	Amelia, right forearm	—	—	2 ☐ 2 ☐
163 EG	F	Ectromelia, transverse, left forearm	—	—	—
164 JR	F	Ectromelia, transverse, left forearm	—	—	1 ☐ 1 ☐
165 JC	F	Ectromelia, transverse, left forearm	—	—	1 ☐ 1 ☐

APPENDIX—continued

Name	Sex	Handicap	Cause	Family history	Sibs
166 RW	M	Spondylolisthesis	—	—	1 □ 1 ○
167 MR	F	Hydronephrosis	Bladder neck obstruction	—	4 ○
168 *AA	M	Sickle cell anaemia, sensorineural deafness (bil)	Meningitis	—	1 □ 1 ○
124 *KL	F	Sickle cell trait, sensorineural deafness (bil)	—	—	2 □ 3 ○
169 IZ	M	β-thalassaemia	—	—	1 □ 1
170 SW	F	Gaucher disease	—	—	1 □ 2 ○
171 CL	F	Malformed pinnae, conductive deafness, PDA, VSD	—	—	1 □ 2 ○
172 SL	M	Fibrocystic disease	—	—	1 □ twin of CL
173 IN	M	Partial albinism, ocular albinism	—	—	3 □ 2 ○
174 BW	F	Albinism	—	—	1 □ 1 ○
175 PW	F	Albinism	—	—	1 □ 1 ○
176 AM	M	Albinism	—	—	1 □ 1 ●
177 PM	F	Albinism	—	—	4 □ 1 ●
178 MS	F	Albinism	—	—	3 □ 1 ○
179 MS	M	Albinism	—	—	1 □ 4 ○
180 JE	M	Albinism	—	—	1 □ 1 ○
181 DH	M	Albinism	—	—	5 □ 4 ○
182 LM	F	Rod monochromatism	—	—	3 □
183 TR	M	Rod monochromatism	—	—	1 □
184 PR	M	Macular aplasia, rod monochromatism	—	—	1 ○
185 PA	M	Macular dystrophy	—	—	2 □
186 DO	F	Macular defect	—	—	2 □
187 DG	M	Macular aplasia	Mat; g/parents were cousins Mother's 4 brothers, mother's 2 sisters' sons	—	1 □ twin of DG
188 TF	M	Optic atrophy	—	—	1 □
189 SB	M	Optic atrophy	—	—	2 □
190 VP	F	Chorioretinal atrophy	—	—	1 □ 3 ○
191 PW	M	Retinal aplasia	M and F first cousins	1 □	1 □ 1 ○
192 CF	F	Retinal aplasia	—	—	1 □ 1 ○
193 MB	M	Retinitis pigmentosa	—	—	2 □ 2 ○
194 PL	M	Cataracts	—	—	2 □ 1 ●
195 CL	F	Cataracts	—	—	1 □ 1 □
196 DS	M	Cataracts	—	—	2 □
197 AE	M	Cataracts, malformed maculae	—	—	1 □ 1 ○
198 DW	M	Corneal dystrophy, 'unclassical'	—	—	2 □ 1 ○
199 SH	F	Myopia, nystagmus	—	—	1 □
200 IO	M	Myopia, night blindness	—	—	4 □ 1 ●
201 MD	M	Myopia	—	—	1 □
202 SH	M	Hypermetropia	—	—	1 □ 3 ○
203 *MP	F	Hypermetropia, epilepsy	Birth trauma	—	3 □ 1 ○
204 RS	M	Wolfram-Tyler syndrome	—	—	1 □ 1 ○
205 AS	M	Riley-Day syndrome	—	—	1 □ 1 ○
206 SN	F	Iridocyclitis	Still's disease	—	1 □ 1 ○
207 DC	M	Iridocyclitis, secondary cataracts	Still's disease	—	2 □ 1 ○
NO INCREASED RISK					
208 TW	M	Epilepsy	Birth trauma	—	—
209 DF	F	Epilepsy, nystagmus	Neonatal septicaemia	—	—
210 MR	M	Epilepsy, optic atrophy	Prematurity	—	3 ○
211 EA	F	Epilepsy, partial sensorineural deafness	Kernicterus	—	1 □ 1 ○
203 *MP	F	Epilepsy, hypermetropia	Birth trauma	—	1 □ 1 ○
212 DC	F	Spastic diplegia	Prematurity	—	2 □ 1 ○
213 NW	M	Spastic diplegia	Prematurity	—	1 □ 1 ○
214 AB	F	Spastic diplegia	Prematurity	—	2 □ 1 ○
215 DP	F	Athetoid diplegia	Birth trauma	—	1 □ 1 ○
216 AR	M	Athetoid diplegia	Birth anoxia	—	1 □ 1 ○
217 BS	M	Athetoid diplegia	Birth trauma	—	2 □ 2 ○
218 JP	F	Hemiplegia, epilepsy	Birth trauma	—	1 □ 1 ○
219 NA	M	Hemiplegia	Birth anoxia	—	1 □ 1 ○
220 SJ	F	Hydrocephalus	Meningitis	—	1 □ 1 ○
221 JM	F	Hydrocephalus	Meningitis	—	1 □ 1 ○
222 GK	M	Bronchiectasis	Recurrent infections	—	1 □ 1 ○
223 TW	F	Cataracts	Rubella	—	1 □ 1 ○
224 WMcC	M	Cataracts	Prematurity	—	2 □ 1 ○
225 AP-C	F	Cataracts	Rubella	—	2 □ 1 ○
226 RP	M	Cataracts	Rubella	—	1 □ 1 ○
227 NL	M	Cataracts	RTA	—	2 □ 3 ○
228 RW	M	Cataracts	Rhesus incompatibility	—	1 □

APPENDIX—continued

	Name	Sex	Handicap	Cause	Family history	Sibs
229	CC	M	Cataracts	Prematurity	—	1 □ 2
230	AR	M	Cataracts	Rubella	—	1 □ 2
231	SW	F	Sensorineural deafness	Prematurity	—	1 ○
232	TC	F	Sensorineural deafness, cataracts, thrombocytopenia	Rubella	—	1 ○
233	DI	M	Cataracts, microphthalmos, sensorineural deafness	Rubella	—	2 □ 1
234	CL	M	Optic atrophy, hydrocephalus	Birth trauma	—	1 □ 2
235	JH	F	Optic atrophy	Measles encephalitis	—	1 □ 2
139	*BD	F	Retrolental fibroplasia, fibrocystic disease	Prematurity, oxygen therapy	—	1 □ m½
236	PB	M	Microphthalmos (bil), aphakia (bil), nystagmus, sensorineural deafness (bil)	Rubella	—	2 □ 1
237	DG	M	Sensorineural deafness (bil)	Rubella	—	1 ○ 3
238	DB	M	Sensorineural deafness (bil)	Meningitis	—	2 ○
239	JE	F	Sensorineural deafness (bil)	Meningitis	—	1 ○
240	DG	M	Sensorineural deafness (bil)	Meningitis	—	2 ○
241	CH	M	Sensorineural deafness (bil)	Rhesus incompatibility	—	5 ○
242	DA	M	Sensorineural deafness (bil)	Rubella	—	1 ○
243	NB	M	Sensorineural deafness (bil)	Rubella	—	2 ○
244	DC	F	Sensorineural deafness (bil)	Rubella	—	2 ○
245	ME	M	Sensorineural deafness (bil)	Rubella	—	3 ○
246	AM	M	Sensorineural deafness (bil)	Rubella	—	2 ○
247	AS	M	Sensorineural deafness (bil)	Rubella	—	1 ○
248	RW	M	Sensorineural deafness (bil)	Rubella	—	1 ○
249	AW	F	Sensorineural deafness (bil)	Rubella	—	1 ○
250	JJ	M	Sensorineural deafness (bil)	Rubella	—	1 ○
251	SS	M	Sensorineural deafness (bil)	Rubella	—	1 ○
252	WC	F	Sensorineural deafness (bil)	Rubella	—	1 ○
253	PY	M	Sensorineural deafness (bil)	Rubella	—	1 ○
254	JW	M	Sensorineural deafness (bil)	Rubella	—	2 ○
255	SK	M	Sensorineural deafness (bil)	Rhesus incompatibility	—	1 ○
256	AH	F	Sensorineural deafness (bil)	Streptomycin	—	1 ○
257	AV	M	Sensorineural deafness (bil)	Birth trauma	—	1 ○
258	IS	M	Sensorineural deafness (bil)	Measles	—	3 ○
259	AMcL	F	Sensorineural deafness (bil)	Streptomycin	—	1 ○
260	CS	F	Sensorineural deafness (bil)	Meningitis	—	1 ○
261	KM	M	Sensorineural deafness (bil)	Prematurity	—	4 ○
262	RS	M	Sensorineural deafness (bil)	Rubella	—	2 ○
263	AG	M	Sensorineural deafness (bil)	Streptomycin	—	1 ○
264	HH	F	Sensorineural deafness (bil), epilepsy	Prematurity	—	1 ○
265	NT	M	Sensorineural deafness	Meningitis	—	1 ○
266	JP	M	Sensorineural deafness	Measles, recurrent ear infections	—	1 ○
267	GR	M	Sensorineural deafness (bil) left hemiplegia	Prematurity	—	3 □ 2
268	GB	M	Sensorineural deafness (bil)	Meningitis	—	3 □ 1
269	TW	M	Sensorineural deafness (bil), panuveitis, left cataract	Meningitis	—	1 □ 5
270	BV	M	Sensorineural deafness (bil), microphthalmos, cataracts	Rubella	—	2 □ 2
271	MF	M	Sensorineural deafness (bil)	Meningitis	—	1 □ 1
272	MW	F	Sensorineural deafness (bil)	Measles	—	1 □ 1
273	CM	F	Sensorineural deafness (bil)	Rubella	—	1 □
274	CH	M	Sensorineural deafness (bil)	Rhesus incompatibility	—	5 ○
275	ER	M	Sensorineural deafness (bil)	Kernicterus	—	1 □ 1
276	SH	F	Sensorineural deafness (bil)	Mumps	—	1 □
277	GN	M	Sensorineural deafness (bil)	Rubella	—	1 □ 1
278	SR	M	Sensorineural deafness (bil)	Rhesus incompatibility	—	1 ○
279	CD	M	Sensorineural deafness (bil)	Rubella	—	1 ○
280	NH	M	Sensorineural deafness (bil)	Rhesus incompatibility	—	2 ○
168	*AA	M	Sensorineural deafness (bil), sickle-cell anaemia	Meningitis	—	1 □ 1
281	DG	M	Sensorineural deafness (bil)	Rubella	—	1 □ 2
282	EB	F	Sensorineural deafness (bil)	Rubella	—	1 □ 1
283	AC	F	Sensorineural deafness (bil)	Rubella	—	1 □ 1
284	SP	M	Sensorineural deafness (bil)	Rubella	—	2 □ 1
285	IC	M	Sensorineural deafness (bil)	Rubella	—	2 □ 1
286	TB	M	Sensorineural deafness (bil)	Rubella	—	1 ○
287	KB	M	Sensorineural deafness (bil)	Rubella	—	1 ○

* 1 proband with 2 diagnoses. F = father; M = mother; g/f = grandfather; g/m = grandmother; pat = paternal; mat = maternal