GENETIC CAUSES OF BLINDNESS IN BRAZILIAN SCHOOL CHILDREN

Carmen R. Serrano *, I. Neustein **, G. Taboada Lopes * and O. Frota-Pessoa ***

No survey undertaken for finding the frequency of genetic cases in a sample of blind persons has been published for Latin American populations. During our work in the Genetic Counseling Service of the University of São Paulo we studied clinically and genetically a sample of blind youngsters attending special classes. In this study emphasis was placed on disclosing the causes of the defect and counseling the families of the propositi. From this material the frequencies of cases classified according to etiology have been estimated.

MATERIAL AND METHODS

The 68 propositi forming our sample were ascertained among students who have learned or were learning braille reading under the supervision of the Service of Special Education (Serviço de Educação Especial) of the State of São Paulo, while attending regular classes in the public school system. Table 1 gives the age distribution in the sample. 91% of the subjects were less than 20 years old. Visual acuity was less than 2% in 91.2% of the propositi. The onset of the blindness was before the first year of age in 63.2% and before the 5th year of age in 80.7% of the cases. Since some of the propositi turned out to be relatives the 68 propositi belong to just 61 families.

Table 1 — Age distribution of the propositi.

Age (in years)	Number of cases	Percent
6 a 10	12	17.6
11 a 15	23	33.8
16 a 20	20	29.4
21 a 25	7	10.3
26 a 30	2	2.9
31 a 35	4	5.9
TOTAL	68	99.9

Clinical examinations were carried out in the Ophthalmology Department, Escola Paulista de Medicina ,and the genetic study and counseling were made in the Laboratory of Human Genetics, Universidade de São Paulo.

RESULTS

Tables 2 to 5 summarize the findings. The 68 cases of blindness in the sample are distributed in Table 2 according to an etiological classification. It is to be noted that pre-natal infectious diseases were included in section I and not in section V.

Since the 3 cases of retinoblastoma were bilateral and therefore, hereditary, section III in Table 2 must be combined with the "Inherited diseases" in section V to form a total of 35 cases in which a hereditary etiology has been stablished. This represents 51.5% of the sample. Considering that the blindness of any of the persons among the 2 propositi with "Unspecif-

Table 2 — Distribution of the cases in our samples according to an etiological classification (Hurlin, 1960).

Causes	Number of Cases		Percent	
I. INFECTIOUS DISEASES	20		29.4	
Unspecified infection		12		17.6
Syphilis		2		2.9
Gonococcal infection		2		2.9
Toxoplasmosis		1		1.5
Measles		1		1.5
German measles		1		1.5
Tuberculosis		1		1.5
II. POISONING TRAUMA AND ACCIDENTS	4		5.9	
Oxygen poisoning		3		4.4
Chemcial burns		1		1.1
III. NEOPLASIA (retinoblastoma)	3	3	4.4	4.4
IV. GENERALIZED DISEASES	3		4.4	
Lupus erithematosus		1		1.5
Brain tumor		1		1.5
Unspecified central nervous system disease		1		1.5
V. PRE-NATAL INFLUENCES	34		50.0	
Inherited diseases		33		48.5
Unspecified diseases		1		1.5
VI. UNDETERMINED ETIOLOGY	4	4	5.9	5.9
TOTAL	68	68	100.0	99.7

* Associated Researcher, Insttiuto de Genética Humana, Universidad Mayor de San Andrés, Casilla 2340, La Paz Bolivia. Ex-fellow of the Multinational Genetics Program, Organization of American States (OAS), in the University of São Paulo, Brazil.
** Departamento de Oftalmologia e Otorrinolaringologia, Escola Paulista de Medicina, São Paulo, Brazil, Seção de Oftalmo-pediatria.
*** Laboratório de Genética Humana. Departamento de Biologia, Universidade de São Paulo, Postal Adress: C.P. 11461, São Paulo, Brazil.

ied diseases" in section V and the 4 in section VI with "Undetermined etiology" could also be hereditary, it is safe to conclude that, in samples similar to this one, more than half of the cases of blindness are expected to have genetic etiology. There were 27 cases in which anenvironmental cause was established and 5 cases without known etiology.

Table 3 distributes the 68 cases according to the anatomical location of the defect. In Table 4 the genetic disorders are grouped by their type of inheritance. Table 5 gives the frequencies of the genetic and non-genetic conditions. The frequencies in Tables 3 and 4 refer not to the number of propositi, but to the total of the 61 families to which the 68 propositi belong.

Table 3 — Distribution of the cases in our sample according to anatomic location and type of affection following the classification of Hurlin (1960).

Location and affection	Number of Cases		Percent	
I. EYE BALLS	31		45.6	
Congenital glaucoma		15		22.6
Panophthalmitis		11		16.2
Anophthalmia		2		2.9
Coloboma		1		1.5
Microphthalmia		1		1.5
Unspecified		1		1.5
II. CORNEA (Unspecified)	1	1	1.5	1.5
III. LENS (cataract)	2	2	2.9	2.9
IV. UVEA	6		8.8	
Uveitis		3		4.4
Corioretinitis		3		4.4
V. RETINA	21		30.9	
Pigmentar retinosis		7		10.3
Leber's amaurosis		5		7.4
Retinoblastoma		3		4.4
Retrolental fibroplasia		3		4.4
Macular degeneration		2		2.9
Retina detachment		1		1.5
VI. OPTIC NERVE (optic atrophia)	5	5	7.4	7.4
VII. VITREOUS LIQUOR (Unspecified)	1	1	1.5	1.5
VIII. UNDETERMINED	1	1	1.5	1.5
TOTAL	68	68	100.1	100.2

Table 4 — Types and frequencies of genetic syndromes found among the 61 families forming our sample.

Affection	Number of families		Percent	
I. AUTOSOMIC DOMINANT	5		8.1	
Bilateral retinoblastoma		3		4.9
Congenital cataract		1		1.6
Severe myopia with bilateral retina detachment		1		1.6
II. AUTOSOMIC RECESSIVE	23		37.5	
Congenital glaucoma		14		22.9
Pigmentar retinosis		3		4.9
Leber's amaurosis		3		4.9
Stargardt disease (macular degeneration)		1		1.6
Anophthalmia		1		1.6
Laurence-Moon-Biedl syndrome		1		1.6
III. UNDETERMINED INHERITANCE (retina pigmentation)	1	1	1.6	1.6
TOTAL	29	29	47.2	47.2

DISCUSSION

The frequencies of cases of blindness due to pre-natal factors (including genetic ones) have been determined in samples from different countries on the basis of records from ophthalmological services. They vary (Table 6) from about 30% in Finland to 70% in New Zealand but such a spread must be due only partially to racial and geographical variables. The adequacy of prevention programs against accidental and infectious blindness and the degree in which modern therapy was in use in the populations from which the samples have been obtained are also influential on the balance between genetic and environmental cases. The age composition of the samples studied is yet another cause of discrepancy, the younger the propositi the higher the relative frequency of pre-natal causes. This tendency is illustrated by a comparison between the two determinations by Hatfield (Table 6, section I).

Ascertainment of cases through index reports is biased toward traumatic and infectious conditions because their causes are more readily recognized. Prospective data collected with the purpose of descriminating between genetic and environmental causes (Table 6 section II) are lesse hampered by such bias. This is probably why the range of the frequencies of genetic cases is higher in such surveys than those in Table 6, section I.

The works of Fraser and Friedmann (1967), Fraser (1968) and Merin **et al**. (1972) are more similar to ours than the others in matters of methodology. Therefore reference will be made mainly to them from now on.

Table 5 — Frequencies of families presenting genetic and non-genetic cases of blindness.

Causes	Number of families		Percent	
I. HEREDITARY	29	29	47.5	47.5
II. NON-HEREDITARY OR UNKNOWN	32		52.4	
Pre-natal		7		11.5
Peri-natal		6		9.8
Post-natal		18		29.5
Unspecified		1		1.6
TOTAL	61	61	99.9	99.9

Table 6 — Percent of blindness cases due to pre-natal influences obtained: I. from index reports; II. from direct ophthalmologic examinations.

Authors	Country	Sample	Ages	Percent
I. DATA FROM INDEX CARDS:				
Holst (1952)	Norway	3,181	15 to 65	45.9*
Kerby (1958)	U.S.A.	4.426	5 to 19	56.1
Hatfield (1963)	U.S.A.	7.757	5 to 19	47.8
Vannas and Raivio (1964)	Finland	2.283	Birth to 65	31.4
MacDonald (1965)	Canada	24,605	Birth to 65	32.0*
Parmelee et al. (1966)	U.S.A.	726	Birth to 18	40.7
Grosvenor (1966)	New Zeland	258	Birth to 15	65.5
Lindsted (1969)	Sweden	3,557	16 to 60	34.1
Hatfield (1972)	U.S.A.	3.115	Birth to 7	60.8
II. DATA FROM DIRECT EXAMINATIONS:				
Fraser and Friedman (1967)	England	776	Birth to 22	50.0
Fraser (1968)	Australia	50	5 to 18	44.0
Kaplan (1968)	Moscow	216	?	64.9**
Olurin (1970)	Nigeria	140	Birth to 14	42.0**
Sevel and Sochet (1972)	South Africa	253	?	75.8
Merin et al. (1972)	Cyprus	112	Birth to 40	79.0

* Hereditary etiology only.
** Pre-natal etiology, hereditary or non-hereditary.

Etiology

Our frequency of 47.5% for inheritable conditions compares well with those of 50%, found by Fraser and Friedmann (1967), and 44%, found by Fraser (1968). Merin **et al.** (1972) found a higher frequency of inherited conditions (79%) among which 50% were autosomic recessive in type. This is well explained by the high frequency of consanguineous marriages prevailing in the Cyprus Island, where the study was carried out. Hatfield (1972) in a great sample (3,115 children less than 7 years old) detected a genetic etiology in 47,4% of the cases. This agrees well with our data in spite of her methodology being different from ours.

The small frequency of pre-natal infectious conditions in our sample (11 5%) is actually an underestimate since congenital blindness due to toxoplasmosis, rubella and lues are in general complicated by other defects which excluded patients from the classe for the blind from which our sample was drawn. In the Australian sample of Fraser (1968) these types of blindness reach 20% specially because rubella cases associated to deafness were included. The low frequency (6%) found in England (Fraser and Friedmann, 1967) is attributable to the high level of sanitation of its population which allows good control of such diseases. On the other hand the low frequency (4%) found in Cyprus is considered by Merin **et al** (1972) as being the result of low hygienic level which makes more difficult the survival of congenital rubella cases.

Fraser and Friedmann (1967) registered 33% of peri-natal blindness. They were especially due to retrolental fibroplasia secondary to the exposure of premature babies to high concentrations of oxygen. In Australia, Fraser (1968) found the incidence of peri-natal blindness increased as a result of the same cause added to cases in which optic nerve atrophy was associated to other neurological problems (peri-natal damage syndrome). The lower frequency (9.8%) of peri-natal blindness in our sample is possibly due to:

a) better control of oxygentherapy nowadays;
b) the type of ascertainment adopted which excluded patients with neurological problems associated to blindness.

Post-natal causes presented relatively high incidence in our sample (29.5%) especially because of infectious disease (22.9%), a sign of poor hygienic level in the stracta of the population where the cases occurred.

Types of inheritance

Comparing our data with those from the literature (Table 6) we note:

1. No X-linked blindness happened to be included in our sample, although after the conclusion of this project a family with several members affected by Norrie Syn-

drome has been brought to our attention because two of them belonged to the public school system (Neustein, Moreira-Filho and Frota-Pessoa, in press).

2. The frequency of autosomic dominant conditions in our sample (8.1%) is small compared to those found in England (20.4%, Fraser and Friedmann. 1967) probably also because of the exclusion from it of complex syndromes.

3. The incidence of autosomic recessive conditions was relatively high (37.5%) in our sample mainly because of the very high frequency of congenital glaucoma in it (22.9%). Since in the absence of early surgery this condition leads to blindness, the lower frequencies found by Fraser and Friedmann (1967) and Hartfield (1972) might be explained by better medical care available to the populations from which their samples were drawn. However actual differences in gene frequencies are suggested by the extremely low incidence of the condition (1.7%) as a cause of blindness in Cyprus (Merin **et al.**, 1972), in spite of the high incidence there of autosomic recessive conditions in general. A second contribution to the high frequency of autosomic recessive conditions in our sample is made by the tapeto-retinian degenerations (11.4%), especially pigmentar retinopathies and Leber's amaurosis. Fraser (1968) found a predominance of coroido-retinian degenerations among the autosomic recessive conditions, which formed 24% of his sample. In Cyprus, Merin **et al.** (1972) also found high frequency (39.3%) of autosomic recessive blindness associated to albinism, microphthalmia and tapeto-retinian degeneration. There, as here, the incidence of consanguineous marriages is greater than in technologically more advaced populations and this could explain an excess of autosomic recessive conditions. Among our 23 propositi presenting autosomic recessive affections, 7 were born from consanguineous couples.

Genetic Counseling

No objective evaluation could be made of the effectiveness of the counseling which was offered to the families included in our sample. Ina number of cases the members of the families were not aware of the genetic nature of the blindness aflicting one or more of its members. We feel that the explanations they received have sensitized them to the recurrence risks to the point of inducing them to adopt effective methods of contraception.

In some families with more than one affected member there was already an awareness of risks but counseling was needed for quantitizing it and distinguishing couples subject to high risks from those free from them.

An important aspect of counseling was to put at rest the minds of members of the families under the imppression that they carried high risks when this was not the case.

ACKNOWLEDGMENTS

We thank the cooperation of the personel of the Serviço de Educação de Excepcionais da Secretaria de Educação do Estado de São Paulo in ascertaining the patients and sending them to us for examination.

This work had the support of the Multinational Genetics Program of the Organization of the American States (OAS), the Conselho Nacional de Pesquisas (CNPq) and the Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP).

SUMMARY

In the city of São Paulo, Brazil, a sample of 68 blind persons (belonging to 61 families) enrolled in public schools and learning braille were found to have the following characteristics:

1. Hereditary conditions were established as the cause of blindness in the majority (51.5%) of the cases and in 47.2% of the families.
2. Recessive autosomal conditions were responsible for the blindness in 37.5% of the families, with congenital glaucoma accounting for more than half of them.
3. Dominant autosomal disorders caused the blindness in 8.1% of the families, retinoblastoma having the greatest prevalence.
4. For one inherited case the data were not sufficient for deciding about the type of transmission.
5. No case of blindness was establised as being produced by X-linked or multifactorial disease.
6. In 27 individuals (39.7%) the blindness was related to environmental causes and in 5 cases (7.4%) etiology could not be established.

SUMÁRIO

Em uma amostra de 68 pessoas cegas, pertencentes a 61 famílias, averiguadas entre estudantes do sistema escolar público da cidade de São Paulo, Brasil, que estudavam braile, encontraram-se as seguintes características:

1. Determinou-se que a causa da cegueira era alguma doença hereditária na maioria dos casos (51,5%) e em 47,2% das famílias.
2. Em 37,5% das famílias a cegueira foi produzida por doenças autossômicas recessivas, sendo que o glaucoma congênito incidiu em mais da metade delas.
3. Em 8,1% das famílias, a cegueira foi devida a doenças autossômicas dominantes, entre as quais a mais comum foi o retinoblastoma.
4. Em um caso hereditário, os dados não foram suficientes para determinar o tipo de transmissão.
5. Nenhum caso de cegueira foi atribuído a herança ligada ao X ou a causa multifatorial.
6. Em 27 indivíduos (39.7%), a cegueira estava relacionada com fatores ambientais e em 5 casos (7.4%) não foi possível determinar a etiologia.

REFERENCES

FRASER. G. R. — The causes of severe sivual handicap among school children in South Australia. Med. J. Austr. 1: 615-20. 1968.

FRASER. G. R. & FRIEDMANN, A. I. — The causes of blindness in childhood. Baltimore, The Johns Hopkins Press. 1967. 245 p.

GROSVENOR, T. — Causes of blindness in New Zealand's maori and european children. Amer. J. Ophtal., 43: 17-26. 1966.

HATFIELD, E. M. — Causes of blindness in school children. Sight Sav. Rev., 33: 218-33. 1963.

HATFIELD. E. M. — Blindness in infants and young children. Sight Sav. Rev., 42: 69-89. 1972.

HOLST. J. C. — The occurrence of blindness in Norway. Amer. J. Ophthal., 35: 1153-66. 1952.

KAPLAN. A. I. — Genetic factors as a reason for blindness in children. Uch. zap. Mosk. Nauch-

issled. Inst. Glazn. Bolez. 14: 19-24, 1968. Apud Biological Abstracts, 51: 1155, 1970.
KERBY, C. E. — Causes of blindness in children of school age. Sight Sav. Rev., 28: 10-21, 1958.
LINDSTEDT, E. — Causes of blindness in Sweden. Acta Ophtal. (Kbh) (suppl.). 104: 1-80, 1969.
MACDONALD, A. E. — Causes of blindness in Canada. Canad. Med. Ass. J., 92: 264-79, 1965.
MERIN, S.; PAITHIS, A. G.; HOROWITZ, D. & MICHAELSON, I. C. — Childhood blindness in Cyprus. Amer. J. Ophtal., 74: 538-42, 1972.
OLURIN, O. — Etiology of blindness in Nigerian Children Am. J. Ophthalmol., 70: 538-40 Oct. 70.
PARMELEE, A. H.; WASCO, M. & ZIMMELMAN, H. — Blindness in children in the Los Angeles area. Sight Sav. Rev., 36: 23-6, 1966.
SEVEL, D.; SOCHET, S. — An ophtha.mic survey at the Worcester School for the blind. S.A. Med. J. 46: 295-6, 1972.
VANNAS, S. & RAIVIO, T. — Occurrence and causes of blindness in Finland. Acta Ophthal., 42: 307-17, 1964.