Journal of Medical Genetics 1987, **24**, 584–588

Prevalence and mode of inheritance of major genetic eye diseases in China

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SUMMARY The prevalence and mode of inheritance of major genetic eye diseases have been investigated in China since the establishment of the Section of Ophthalmic Genetics of the Chinese Society of Genetics. Mass screening of genetic eye diseases has been undertaken in many districts in China, covering more than 700 000 people, and more than 5000 pedigrees of genetic eye diseases have been collected and analysed all over China. Based on these data, the prevalence and mode of inheritance of dyschromatopsia, degenerative myopia, retinitis pigmentosa, congenital ptosis, congenital microphthalmos, congenital cataract, congenital glaucoma, Leber's optic atrophy, corneal dystrophy, congenital nystagmus, coloboma of the eye, congenital aniridia, retinoblastoma, macular dystrophy, simple myopia, primary glaucoma, and strabismus have been investigated, and the results are presented.

The Section of Ophthalmic Genetics of the Chinese Society of Genetics was established in 1979. Before 1979, few ophthalmologists paid attention to the field of ophthalmic genetics, but since then an increasing number of ophthalmic genetic clinics and laboratories have been established in China. In June 1980, the First Chinese Congress of Ophthalmic Genetics was held. During this meeting, the prospects were also discussed for the Chinese Ophthalmic Genetics Programme Planning, the main content being to investigate the prevalence and mode of inheritance of major genetic eye diseases in China. The criteria for diagnosis and method of mass screening of genetic eye diseases were established and unified.

The Second, Third, and Fourth Chinese Congresses of Ophthalmic Genetics were held in 1982, 1984, and 1986, respectively. Nine hundred and fifty-six ophthalmologists and geneticists attended these meetings, and 886 papers were read. Most of the Chinese ophthalmic centres joined our activities, including more than 500 members. Mass screening of genetic eye diseases has now been undertaken in many districts in China, covering 700 000 people, and the results are presented in table 1. More than 5000 pedigrees of genetic eye diseases have been collected and analysed from all over China. Based on these data, the prevalence and mode of inheritance of major genetic eye diseases have been documented.

Received for publication 23 December 1986.
Accepted for publication 7 January 1987.

TABLE 1 *Prevalence of major genetic eye diseases in China.*

Disease	*No of people examined*	*Prevalence (%)*
Dyschromatopsia (male)	278 001	4·89 (1:20)
Degenerative myopia	26 084	0·95 (1:105)
Congenital ptosis	247 389	0·18 (1:552)
Congenital cataract	207 319	0·037 (1:2728)
Retinitis pigmentosa	196 777	0·03 (1:3784)
Congenital nystagmus	272 931	0·025 (1:4014)
Congenital microphthalmos	310 162	0·009 (1:11 077)
Congenital coloboma	199 525	0·007 (1:15 348)
Congenital glaucoma	199 525	0·004 (1:24 941)
Congenital aniridia	267 863	0·00075 (1:133 931)

Congenital dyschromatopsia

The prevalence of congenital dyschromatopsia (deutan and protan types) in 29 races in China have been thoroughly investigated. In the Han race, which is the major racial group in China, the prevalence of dyschromatopsia in males was 4·89% (among 128 357 men) and 0·7% in females (among 56 580 women). In some minor races, the prevalence was lower or higher, for example, the prevalence was only 1·75% in the Miao race (128 out of 5458 men), but as high as 7·61% in the Hasaka race (a minor race of Caucasian origin). The mode of inheritance of dyschromatopsia (deutan and protan types) is X linked recessive in China as in other countries.

Degenerative myopia

The prevalence of degenerative myopia in East, Mid-south and North-east China was 0·95% (based on mass screening of 26 084 people). Hu[1] collected 61 pedigrees of degenerative myopia and found that it was inherited as an autosomal recessive trait; numerous other reports have been published since then (Geng, 87 pedigrees; Li, 96 pedigrees; Xia, 177 pedigrees; Nie, 16 pedigrees; Zhang, 70 pedigrees). All of these authors agreed that degenerative myopia was inherited as an autosomal recessive trait. When both parents were affected, 42 out of 45 offspring were affected (93·3%). When both parents of the probands appeared normal, 22·3% of the offspring were affected (Lenz's correction). When one of the parents of the probands was affected, 257 out of 564 offspring were affected (45·6%). These figures suggest autosomal recessive inheritance.

Retinitis pigmentosa

The prevalence of retinitis pigmentosa was 0·03% (1:3784) in East, Mid-south, North-west, South-west, and North China (based on mass screening of 196 777 people). Several large series of pedigrees of retinitis pigmentosa have been reported (320 pedigrees); the percentages of autosomal recessive (including sporadic cases), autosomal dominant, and X linked recessive were 91·8%, 5·2%, and 3·0% respectively. Compared with data from Western countries, the percentages of X linked recessive and autosomal dominant inherited retinitis pigmentosa in China is rather low, and the percentage of autosomal recessive retinitis pigmentosa is relatively high.[2]

Congenital ptosis

The prevalence of congenital ptosis in China was 0·18% (1:552), based on mass screening of 247 389 people. Two large series of pedigrees have been reported (76 pedigrees). The percentages of sporadic, autosomal dominant, and autosomal recessive cases were 67·1%, 18·4%, and 14·5% respectively. Ptosis with epicanthus inversus and blepharophimosis (Komoto's syndrome) is common in China, accounting for 8·3% of cases of congenital ptosis. It was inherited as an autosomal dominant trait with full penetrance.

Congenital microphthalmos

The prevalence of congenital microphthalmos was 0·009% (1:11 077) in 12 provinces in China, based on mass screening of 310 162 people. In certain areas the prevalence was somewhat higher. For example, the prevalence was 0·057% (1:1758) in East Henan. Most of the cases reported in China were sporadic (75 to 90%); only 10 to 25% of cases had familial occurrence, all modes of inheritance being observed. Microphthalmos associated with aniridia or congenital cataract were inherited as autosomal dominant traits and most of the cases associated with corneal opacities or coloboma were sporadic or inherited as autosomal recessive traits.

Congenital cataract

The prevalence of congenital cataract was 0·037% (1:2728) in some districts in China, based on mass screening of 207 319 people. Several large series of congenital cataract have been published.[3] In 677 cases of congenital cataract reported in China, the percentages of sporadic, autosomal dominant, and autosomal recessive inheritance were 70·2%, 21·0%, and 8·8%, respectively. Some X linked recessive cases have been reported also.

Congenital glaucoma

The prevalence of congenital glaucoma was 0·004% (1:24 941) in China based on mass screening of 199 525 people. A number of authors have reported large series of pedigrees of congenital glaucoma. In 234 cases reported in China, the frequency of parental consanguinity was 2·3% (compared with an average of 1% in the general population). The corrected prevalence in sibships was 12·5 to 20·9%, suggesting autosomal recessive inheritance. Since the prevalence was higher in males (male:female ratio 3·3:1), and three cases of parent to child transmission have been reported, the possibility of multifactorial inheritance must also be considered.

Leber's optic atrophy

Many pedigrees of Leber's optic atrophy have been reported in China.[4] The most striking feature is the relatively high incidence among females. In Chinese publications, we were able to find 354 cases, the ratio of affected females to males being 44·9%:55·1%. This ratio is much higher than that reported in Western countries (15%:85%), but is similar to the Japanese figure (41%:59%).[5] The average age of onset was 18·8 years, which is earlier than that reported in Western countries and is close to the Japanese figure.[5]

Corneal dystrophy

The three most common types of corneal dystrophy

reported in China were: nodular type (164 cases, inherited as autosomal dominant with high penetrance), reticular type (34 cases, inherited as autosomal dominant with high penetrance), and macular type (five pedigrees, inherited as autosomal recessive).

Congenital primary nystagmus

The prevalence of congenital nystagmus in China was 0·025% (1:4014, including both primary and secondary congenital nystagmus), based on mass screening of 272 931 people. The Section of Ophthalmic Genetics of the Chinese Society of Genetics collected and analysed 208 pedigrees from 17 provinces. The mode of inheritance was sporadic in 64·4%, autosomal dominant in 18·3%, autosomal recessive in 8·7%, X linked recessive in 7·2%, and unknown in 1·4%. No definite X linked dominant inheritance has been identified.

Congenital coloboma of the inner eye

The prevalence of coloboma in Mid-south, South-west, East, North-west, and North China was 0·007% (1:15 348), based on mass screening of 199 525 people. The Section of Ophthalmic Genetics of the Chinese Society of Genetics collected and analysed 142 pedigrees from 21 provinces. Among 104 pedigrees of simple coloboma of the uvea, the percentages of sporadic, autosomal dominant, and autosomal recessive inheritance were 93·3%, 3·9%, and 2·9% respectively. Among 12 pedigrees of coloboma of the macula, the percentages of sporadic, autosomal dominant, and autosomal recessive were 58·3%, 33·3%, and 8·3%. Among 22 pedigrees of coloboma of the optic nerve, the percentages of sporadic and autosomal dominant cases were 86·4% and 13·6%. Among four pedigrees of coloboma of the lens, two pedigrees showed sporadic and the other two autosomal dominant inheritance.

Congenital aniridia

The prevalence of aniridia in China was 0·00075% (1:133 931), based on mass screening of 267 863 people. The mode of inheritance in 26 pedigrees reported in China was autosomal dominant with full penetrance.

Retinoblastoma

The incidence of retinoblastoma in living newborns in Shanghai was 1:11 800.[6] Most of the cases reported (1166 cases) were sporadic, only 2·8% cases having a positive family history.[7] The possible explanation was that in the past the survival rate of retinoblastoma was low, so that most cases were either inherited through a carrier or occurred as a new mutation. Bilateral cases accounted for 14·3%. Two cases of deletion of the long arm of chromosome 13 (13q14–) have been reported.

Macular dystrophy

In Stagardt's disease, the frequency of parental consanguinity was 13·3% and the corrected prevalence among sibs was 23·8%, indicating autosomal recessive inheritance. In progressive cone-rod dystrophy, the frequency of parental consanguinity was 38·9% and the corrected prevalence among sibs was 28·2%, indicating autosomal recessive inheritance and heterogeneity.

Simple myopia

Simple myopia is common in China; in a mass screening of 130 000 students in Liaoning Province in 1983, the prevalence of reduced vision was 35·4% (myopia accounted for 85 to 95% of cases). In the large cities, the prevalence was high, being 59·4% in high school students in Shanghai city. There is disagreement concerning the aetiology of myopia. Some authors believe that myopia is related to genetic factors and others emphasise environmental factors. Hu investigated this problem through a twin study. In 90 pairs of twins with myopia, the concordance rate of myopia was 81·6% in monozygotic twins and 57·6% in dizygotic twins ($p<0·05$). The correlation coefficient was 0·71 in monozygotic twins and 0·26 in dizygotic twins ($p<0·01$). The heritability index of myopia was 61%.[8] Chu and Wang[9] studied these problems in another group of twins, with similar results: the heritability index of myopia, radius of the cornea, axial length of the eyeball, and depth of the anterior chamber were 65%, 49%, 56%, and 72%, respectively. These results indicated that both genetic and environmental factors play a role in the occurrence of myopia. Based on these data, Hu proposed a hypothesis of multifactorial inheritance of myopia. Li studied the role of inheritance of myopia in Shandong Province; the familial occurrence rates in first and second degree relatives of myopic patients were 15·1% and 6·3% and the prevalence of myopia in the same area was 3·3%. The heritability of myopia as calculated from these data was 61·6%. This pattern conformed with multifactorial inheritance.

Primary glaucoma

The prevalence of glaucoma in people over 30 years

TABLE 2 *Recurrence risks of exotropia.*

No of affected parents			0			1			2		
No of affected children			0	1	2	0	1	2	0	1	2
Grandparents		*No of normal children*									
No of normal	*No of affected*										
4	0		0·5	5·1	12·2	6·3	15·6	24·5	38·4	43·8	48·6
3	1	0	1·8	8·4	16·3	8·1	18·8	27·5	43·8	48·9	53·3
2	2		5·5	14·2	22·1	19·9	29·6	37·2	49·3	54·0	58·0
4	0		0·5	4·7	11·2	5·7	14·0	22·0	35·0	40·1	44·7
3	1	1	1·6	7·7	14·9	7·2	16·2	24·6	40·0	44·7	49·0
2	2		5·0	12·9	20·2	17·5	26·4	33·6	44·7	49·3	53·3
4	0		0·4	4·4	10·4	5·2	12·7	20·1	32·2	37·0	41·1
3	1	2	1·5	7·1	13·7	6·5	14·6	22·3	36·5	41·2	45·4
2	2		4·6	11·8	18·6	15·7	27·8	30·6	40·9	45·4	49·3

old was 1% in China. Closed angle glaucoma is more common than open angle glaucoma in China. Wang investigated the mode of inheritance of primary closed angle glaucoma in 100 cases. The familial occurrence rates in first and second degree relatives was 7·1% and 2·33%, respectively. The prevalence of closed angle glaucoma in the same district was 0·96%.[10] The heritability of closed angle glaucoma as calculated from these data was 65%.

Strabismus

Hu investigated the mode of inheritance of exotropia in 425 persons. The familial occurrence rate in first, second, and third degree relatives was 9·0%, 2·2%, and 1·1% respectively. The prevalence of exotropia was 0·58%. The heritability of exotropia as calculated from these data was 81·3%.

Other genetic eye diseases

CRYSTALLINE RETINOPATHY

This is a very rare disease in Western countries, according to Grizzard *et al.*[11] There have been only 14 reported cases in the West, but it is quite common in China. During 1978 to 1980, we observed 25 families (35 patients) in our clinic. All of the parents and offspring of the probands appeared normal, but some of their sibs were affected, the corrected prevalence among the sibs being 19·2%. The frequency of parental consanguinity was 20·0%, indicating autosomal recessive inheritance.

OGUCHI'S DISEASE

According to François,[5] about 80 cases have been reported in Japan, but only 26 cases have been reported in Caucasians. There have been 16 cases reported in China. Families with several cases in sibs and consanguinity of parents have been reported, indicating autosomal recessive inheritance.

Genetic counselling

We established a clinic for genetic eye disease and genetic counselling in 1978. More than 1500 patients have visited the clinic or have written for genetic counselling. We have designed genetic counselling tables for some monogenic inherited eye diseases, including degenerative myopia, corneal dystrophy, and aniridia, based on the genetic percentages, mode of inheritance, degree of penetrance, and the gene frequency among the Chinese.

We have developed a computer programme to estimate recurrence risks for multifactorial inherited genetic diseases based on Smith's formula.[12] Using this programme, we have prepared tables for estimating recurrence risks for a variety of family situations in several multifactorial inherited eye diseases, such as exotropia and primary closed angle glaucoma (table 2).

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