Family studies in glaucoma

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There is now strong evidence for a genetic basis to glaucoma. Numerous family histories have been recorded, and Dodinval, Prijot, and Weekers (1970) consider that at least 20 per cent. of cases of open-angle glaucoma are of a familial and hereditary character. Additional evidence derives from studies of the families of patients with glaucoma. Kellerman and Posner (1955) examined 192 relatives and detected eight cases of chronic simple glaucoma; Becker, Kolker, and Roth (1960) examined 110 parents, siblings, and children of patients with chronic simple glaucoma and diagnosed the condition in six. Miller and Paterson (1962) found an incidence of 8 per cent in the first-degree relatives over the age of 40 years of 125 sibs and children of patients with chronic simple glaucoma. Two additional cases were diagnosed on further follow-up (Paterson, 1970).

Although it is recognized that the relatives of patients with closed-angle glaucoma are likely to have similar anatomical characteristics, the frequency of the overt disease in relatives is not well documented. Kellerman and Posner (1955) examined 24 relatives (48 eyes) of patients with closed-angle glaucoma and found two suspicious cases.

We have examined the relatives of cases of chronic simple, closed-angle, and some other types of glaucoma at the Institute of Ophthalmology, London. A preliminary report on 201 subjects was given by Leighton (1968) and this paper extends the findings to cover a total of 376 subjects who have attended the clinic.

Methods

Patients diagnosed at the Institute Glaucoma Clinic as having glaucoma were requested to ask their relatives to attend for screening. No age limit was set, and not only children and siblings but other relatives were seen. As many as fourteen members of one family attended and there were seven families in whom more than five members were examined. A small number of people also attended whose relatives were said to have glaucoma but had not been seen at the Institute.

At the first visit a slit-lamp examination, tonometry using the Goldmann applanation tonometer, and fundus examination were carried out. If the tension was 20 mm.Hg or more in one or both eyes, the optic discs were considered suspicious, or the angles appeared narrow, an appointment was made for fuller investigation. This consisted of visual field examination, using the Globuck screen and the Goldmann perimeter in all cases, gonioscopy, and provocative tests and tonography where indicated.

The criteria for making a diagnosis of chronic simple glaucoma were a tension of over 21 mm.Hg on more than one occasion, combined with a glaucomatous field defect and no evidence of angle closure.

Patients with glaucomatous field defects and cupping of the disc but with tensions below 21 mm.Hg were diagnosed as having low tension glaucoma. Closed-angle glaucoma was diagnosed in patients with a raised tension in the presence of a gonioscopically closed angle.

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Results

376 subjects were examined altogether, but seventeen were excluded from analysis because there was doubt whether the relative had glaucoma; none of these seventeen had any evidence of glaucoma. The remaining 359 have been divided for the purposes of analysis into the groups shown in Table I. The more distant relatives were nieces, nephews, cousins, and grandchildren.

Table I *Classification of 359 relatives of patients with glaucoma*

<i>Type of glaucoma</i>	<i>Children and siblings</i>	<i>More distant relatives</i>
(a) Chronic simple	190	22
(b) Closed-angle	67	14
(c) Other types	29	14
(d) Not known	19	4
Total	305	54

(I) CHILDREN AND SIBLINGS

(a) *Of patients with chronic simple glaucoma*

This group comprised 190 subjects, 103 female and 87 male. The mean age was 41.54 years (S.D. ± 14.79). The age distribution is shown in Table II. Chronic simple glaucoma

Table II *Age distribution of children and siblings of patients with glaucoma*

<i>Type of glaucoma</i>	<i>Age group (yrs)</i>							<i>Total</i>
	10-19	20-29	30-39	40-49	50-59	60-69	70-79	
Chronic simple	13	34	38	52	26	21	6	190
Closed-angle	4	14	10	22	8	9	0	67
Other types	2	8	3	5	6	4	1	29

was diagnosed in ten subjects (5.26 per cent.) and a brief summary of the clinical findings is given in Table III. In four further cases (Table IV), raised tension (over 30 mm.Hg in two cases) combined with abnormal discs and low outflow values or a positive water-drinking test made the diagnosis so likely that treatment was instituted although no field defects could be elicited. No. 178 was particularly surprising: he was only 14 years of age and his tensions on screening were R. 17; L. 31 mm.Hg. Phasing showed wide swings of tension in the left eye; the angle was wide and appeared normal and the coefficient of outflow was R. 0.14; L. 0.12.

The incidence of glaucoma (5.26 per cent.) is high considering the age structure of the population screened; had the screening been confined to the 105 subjects over the age of 40 years, the incidence would have been 7.62 per cent.).

Table III Summary of clinical findings in ten children and siblings diagnosed as cases of chronic simple glaucoma

Case no.	Age (yrs)	Sex	Relative with glaucoma	Clinical findings
26	45	M	Father	Raised tension, cupping of disc, field defect
144	73	F	Brother	Raised tension, ? physiological cupping, field defect
182	73	M	Sister	Raised tension, suspicious disc, field defect
196	39	M	Father	Raised tension, cupping of disc, field defect
210	42	M	Father	Raised tension, suspicious disc, field defect
230	59	M	Mother	Raised tension, suspicious disc, field defect
257	23	M	Father	Raised tension, suspicious disc, field defect
286	63	M	Brother	Raised tension, cupping of disc, field defect
294	54	M	Mother and father	Raised tension, cupping of disc, field defect
350	60	F	Mother	Raised tension, cupping of disc, field defect

Table IV Details of four children and siblings receiving treatment for chronic simple glaucoma but without field defects

Case no.	Age (yrs)	Sex	Relatives with glaucoma	Clinical findings
12	51	F	Mother	Raised tension, suspicious disc, positive water-drinking test
60	61	M	Brother	Raised tension, suspicious disc, low facility of outflow
178	14	M	Father	Raised tension (over 30 mm.Hg in one eye), low facility of outflow
188	30	M	Mother, uncle, aunt	Raised tension, cupping of disc

There is a preponderance of males in those diagnosed as cases of chronic simple glaucoma, and it is interesting to note that seven were children or sibs of a man with glaucoma, although there were only 62 male probands in the group.

In addition to the cases of chronic simple glaucoma, one was diagnosed as having low tension glaucoma. Further follow-up because of ocular hypertension or suspicious discs was advised in 53; seventeen of these were later discharged, but 31 failed to attend, and five are still being followed up.

It should be noted that in three of the cases of chronic simple glaucoma the original diagnosis of the proband was chronic closed-angle glaucoma. Subsequent re-evaluation suggested that chronic simple glaucoma with narrow angles could not be excluded.

(b) Of patients with closed-angle glaucoma

There were 67 subjects in this group, 43 female and 24 male. The mean age was 41.08 years (S.D. ± 13.83); the age distribution is shown in Table II. Closed-angle glaucoma was

diagnosed in four subjects (5.97 per cent.) and brief details are given in Table V. It will be seen that all the cases of closed-angle glaucoma were female—an incidence of 9.3 per cent. of the 43 women screened, and an incidence of 16 per cent. of the 25 female probands. All were over the age of 40 years and constituted 10 per cent. of subjects in these age groups. Further follow-up was advised in eleven, seven of whom were later discharged, three failed to attend and one is still being followed up.

Table V *Summary of clinical findings in four children and siblings diagnosed as cases of closed-angle glaucoma*

Case no.	Age (yrs)	Sex	Relative with glaucoma	Clinical findings
7	43	F	Sister	Raised tension with angle closure
8	68	F	Mother, sister, and two brothers	Narrow angles, positive dark-room test
9	66	F	Mother	Raised tension, field defect, narrow angles
137	60	F	Sister	Acute attack while under investigation

(c) Of patients with other types of glaucoma

There were 29 subjects in this group and the types of glaucoma in their relatives are shown in Table VI. The mean age was 41.38 years; the age distribution is shown in Table II. Two cases of glaucoma were diagnosed in this group. One was a man aged 48 whose mother had low-tension glaucoma; he was found to have cupping of the disc with an arcuate scotoma in the left eye and was diagnosed as having low-tension glaucoma. It was later found that a brother was also under treatment for glaucoma. The second was a woman aged 62 who was found to have typical chronic simple glaucoma; her sister was under observation for ocular hypertension without field defects. Further follow-up was advised in thirteen, five of whom were later discharged; six failed to attend and two are still being followed up.

Table VI *Classification of 29 probands with other types of glaucoma*

Type of glaucoma	No. of cases
Low tension	10
Secondary	10
Suspected	6
Pigmentary	1
Juvenile	1
Retinitis pigmentosa and glaucoma	1
Total	29

(d) Of patients in whom the type of glaucoma was not known

There were nineteen subjects in this group and the mean age was 44.57 years. No cases of glaucoma were detected in this group, but two subjects were advised to attend for follow-up as the discs were suspicious.

Summary of results of screening children and siblings

The results of screening the children and siblings are shown in Table VII. If screening had been limited to the 171 subjects over the age of 40 years, two cases of glaucoma would have been missed, but the proportion of positives would have been higher (Table VIII).

Table VII *Results of screening 305 children and siblings of patients with glaucoma*

<i>Type of glaucoma in relative</i>	<i>No. screened</i>	<i>No. of cases of glaucoma diagnosed</i>			
		<i>Chronic simple</i>	<i>Closed-angle</i>	<i>Low tension</i>	<i>Per cent. positive</i>
Chronic simple	190	10	—	1	5.26
Closed-angle	67	—	4	—	5.97
Other	29	1	—	1	6.90
Not known	19	—	—	—	—
Total	305	11	4	2	5.57

Table VIII *Results of screening 171 children and siblings over the age of 40 years*

<i>Type of glaucoma in relative</i>	<i>No. screened over age 40</i>	<i>No. of cases of glaucoma diagnosed</i>			
		<i>Chronic simple</i>	<i>Closed-angle</i>	<i>Low tension</i>	<i>Per cent. positive</i>
Chronic simple	105	8	—	1	7.62
Closed-angle	39	—	4	—	10.26
Other	16	1	—	1	12.5
Not known	11	—	—	—	—
Total	171	9	4	2	8.77

(2) DISTANT RELATIVES

There were 54 subjects in this group and no cases of glaucoma were detected. Nine were advised to attend for further follow-up because of ocular hypertension or suspicious discs; four are still under observation, three have been discharged, and two have been lost to follow-up.

Discussion

These results confirm previous reports of a high familial incidence of chronic simple and closed-angle glaucoma. Although screening was not confined to subjects over 40 years of age, open-angle glaucoma was diagnosed in 5.26 per cent. of children and siblings of known cases and closed-angle glaucoma in 5.97 per cent. of children and siblings of patients with

this condition. No cases of glaucoma were found in more distant relatives. Four other cases were considered to require treatment although no field defect could be elicited.

Population surveys, such as those at Ferndale (Hollows and Graham, 1966) and Bedford (Bankes, Perkins, Tsolakis, and Wright, 1966; Perkins, 1973), suggest that the prevalence of glaucoma in the general population is less than 1 per cent, so that the prevalence in first-degree relatives is significantly higher. The expense and organization required to screen relatives of known cases is very much less than that required for mass population screening, and although sporadic cases will not be detected in this way it is possible that many apparently sporadic cases do in fact have an affected relative, and would be detected through a family clinic. Relatives living at a distance could be informed by letter and advised to attend a local clinic.

As with any screening programme, borderline cases always present some problems, and 91 subjects (25.35 per cent. of the total screened) were advised to attend for further follow-up: ten are still attending, 36 have been discharged, and 45 have been lost to follow-up. However, if a family clinic is run in conjunction with a normal glaucoma clinic, the follow-up of borderline cases can be carried out as part of its routine work.

One of the most gratifying aspects of the present screening programme has been the fact that the glaucoma has been diagnosed in a presymptomatic stage and in most cases before any serious visual loss has occurred. The mean age of the cases of open-angle glaucoma was 53 years—at least 10 years less than the peak age for cases diagnosed in a routine glaucoma clinic. Although two cases of definite glaucoma and two of suspected glaucoma were found in subjects under the age of 40 years, it is probably reasonable to confine screening to first-degree relatives over this age. It must be realized however, that a single negative screening examination does not exclude the later development of the disease, and re-screening at 5-year intervals should be recommended.

Less attention has been paid to the presymptomatic diagnosis of closed-angle glaucoma, but the results of this family study have shown an incidence of 5.97 per cent. in the 6 children and siblings studied. All the cases were over the age of 40 years (10.26 per cent. of the subjects in this age group). As the prophylactic treatment of this condition by peripheral iridectomy or laser iridotomy (Perkins and Brown, 1973) is so satisfactory, and the visual sequelae of an acute attack so serious, early diagnosis is particularly important. Although gonioscopy is required to confirm the diagnosis, slit-lamp examination of the periphery of the anterior chamber is a rapid and simple screening test and will indicate the subjects who require further investigation.

Low tension glaucoma is much less common than either chronic simple or closed-angle glaucoma, but also appears to have a familial incidence, and one out of ten children and siblings of such patients was found to have the condition.

Summary

359 relatives of glaucoma patients were screened for glaucoma. Screening was not limited to subjects over the age of 40 years. Eleven cases of open-angle glaucoma (ten of chronic simple glaucoma and one of low tension glaucoma) were found in 190 children and siblings of patients with chronic simple glaucoma. Four cases of closed-angle glaucoma were diagnosed out of 67 children and siblings. One further case of chronic simple glaucoma was diagnosed in the sister of a patient under observation for ocular hypertension, and one case of low tension glaucoma was diagnosed out of ten children and siblings of patients with this condition. Four further cases were suspected of having chronic simple glaucoma.

and treatment was initiated although no field defect could be detected. No cases of glaucoma were diagnosed in 54 more distant relatives of patients with glaucoma.

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