

## Family studies in glaucoma\*

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**SUMMARY** Two groups of patients with a family history of chronic open-angle glaucoma were compared with a normal population of 5919 individuals studied during the Bedford Glaucoma Survey. The mean screening intraocular pressure was significantly raised in both groups with a family history of chronic open-angle glaucoma. The prevalence rate of a raised intraocular pressure was 3.81 times that found in the normal population. This relationship was maintained when age-dependent prevalence rates were evaluated. No correlation between raised intraocular pressure and type of familial involvement could be determined. A 10- to 12-year follow-up of one group with a family history for open-angle glaucoma (101 patients) showed that 3% developed confirmed glaucoma, while an additional 5.9% were diagnosed as suspected chronic open-angle glaucoma. A letter survey of this group showed that 9 out of 63 respondents knew of additional family members who developed glaucoma over this 10-12-year period.

A well recognised risk factor in the development of chronic open-angle glaucoma is the presence of a family member with established disease. Perkins has demonstrated that, when family members of known cases of chronic open-angle glaucoma were evaluated, 11 new cases were found in 190 children and siblings of patients with the disorder.<sup>1</sup> In longitudinal studies in which first-degree relatives of patients with chronic open-angle glaucoma were followed up for 9-10 years a significant number had either developed chronic open-angle glaucoma or were highly suspect of having the disorder.<sup>2,3</sup>

It is the purpose of this paper to estimate by means of epidemiological methods the magnitude of the risk of developing a raised intraocular pressure as well as that of developing the disorder if one has a family member with the disease.

### Materials and methods

Two populations of patients with a family history of glaucoma were evaluated (designated study populations). One group came from the Bedford Survey<sup>4</sup> (Bedford study population) and consisted of 101

persons from 90 families collected during the two years the Bedford Survey was undertaken (1965-7), who provided the information that a family member had a history compatible with chronic open-angle glaucoma. The second group consisted of patients studied at the Institute of Ophthalmology in 1970-3 and previously reported on by Perkins<sup>1</sup> (Institute study population) and consisted of 167 patients from 90 families who were relatives of patients under the care of one of the authors (ESP) for confirmed chronic open-angle glaucoma. In both study populations the patients' records were evaluated retrospectively.

The general population to which each of the above populations were compared were the individuals reported upon in the Bedford Survey and included 5919 out of the 5941 persons screened (designated normal population).<sup>4</sup> The 22 individuals excluded were those with ocular disease in which the IOP was altered by the ocular pathology. The data from the normal population obtained from the Bedford Survey of 1965-7 were also analysed retrospectively. Table 1 displays the age and sex distribution of the normal population. All subjects included in this study were over the age of 30 years.

The screening IOP refers to that pressure obtained on the initial evaluation.

A 10-12-year follow-up study of the Bedford study population was undertaken to investigate how many individuals developed glaucoma over this time period.

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**Table 1** Normal population: Bedford glaucoma survey: 5919 persons

Age (years)	Female %	Male %
20-	0.05	0.05
30-	0.35	0.06
40-	18.14	14.50
50-	19.55	13.55
60-	14.87	7.66
70-	6.03	3.46
80+	0.76	0.37
Total	59.75	40.25

**Table 3** Standardisation (indirect) for age and sex: standard mortality ratio (SMR) (observed/expected)

	Bedford Study Population		Institute Study Population	
	SMR	SE	SMR	SE
Female	3.86	0.89	3.33	0.65
Male	3.23	1.02	5.36	1.26

Combining both study populations gives SMR=3.81; SE=0.45.

All individuals whose IOP was greater than 21 mmHg and who had no cupping or visual field loss were followed yearly from 1965 to 1977, and the data were obtained from the records of these visits. In addition a mail survey was undertaken in 1977 to determine if any additional members of the family had developed chronic open-angle glaucoma.

If one combines both study populations, the SMR=3.81±0.45. This indicates that, if one has a positive family history for chronic open-angle glaucoma, there is a 3.81 times greater risk of having a screening IOP greater than 21 mmHg than in the general population. No statistically significant differences exist either between populations or within populations with respect to sex.

**Results**

Fig. 1 displays the prevalence of an increased screening IOP with respect to age in the Bedford study population as compared with the normal population. Analysis of covariance shows that there

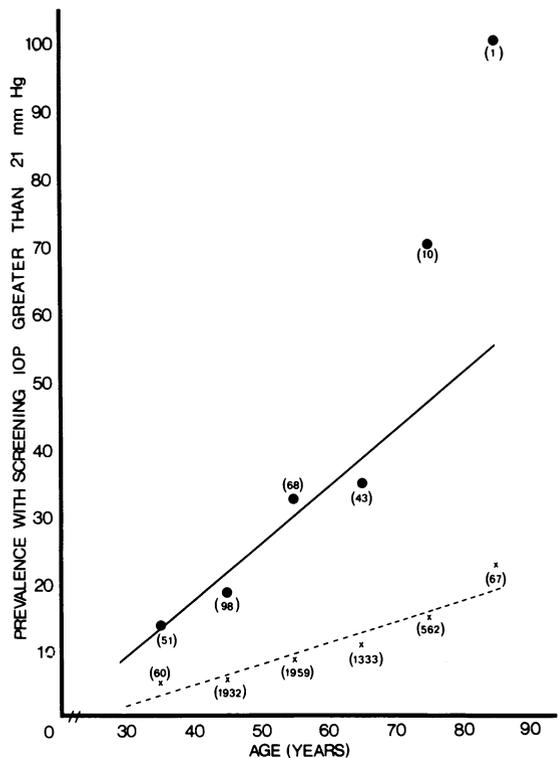
**Mean screening intraocular pressure.** The mean screening IOP of the two study populations was significantly higher ( $p<0.05$ ) than that in the normal population. Table 2 shows a comparison of the mean RE and LE IOP±SE in the three groups. Note that the mean values for both the study populations were comparable.

**Prevalence of IOP greater than 21 mmHg.** The prevalence of an increased IOP was three times greater in both study populations than in the normal population. In the normal population 508/5919 or 8.58% (SE=0.36) of individuals screened had a screening IOP greater than 21 mmHg. In contrast, 27/101 or 28.71% (SE=4.50) of individuals from the Bedford study population and 44/167 or 26.35% (SE=3.41) of individuals from the Institute study population had a raised intraocular pressure on initial testing.

Indirect standardisation for age and sex with respect to prevalence of increased IOP provides the standard mortality ratio (observed/expected) for both study populations with respect to sex (Table 3).

**Table 2** Screening intraocular pressure

	Normal population	Bedford study population	Institute study population
OD Mean	16.45	18.03	18.08
SE	0.043	0.35	0.46
	5914	101	167
OS Mean	16.11	17.82	17.50
SE	0.042	0.35	0.39
	5909	101	167



**Fig. 1** Prevalence of an increased screening intraocular pressure of greater than 21 mmHg with respect to age in a normal population and in a population of individuals who have a positive family history for chronic open-angle glaucoma. Parentheses indicate number of subjects in each age group.

is a statistically significant difference between the slopes of the two curves ( $p < 0.01$ ), indicating that the risk of having an increased IOP when there is a family history of chronic open-angle glaucoma exists throughout adult life.

*Relationship of screening IOP greater than 21 mmHg to type of familial involvement in the Bedford study population.* No correlation between elevated intraocular pressure and type of familial involvement could be determined. Fifteen of 69 or 21.7% of individuals who had at least one parent as the closest affected relative had an increased IOP. Five out of 17 or 29.4% of individuals who had at least one sibling as the closest affected relative had an increased IOP, and 5/15 or 33% who had as the closest affected relative a second-degree relative had an increased IOP.

*Longitudinal follow-up study of Bedford study population.* The 101 patients in the Bedford study population were followed up over a 10–12-year period. During this time 16 (15.8%) continued to carry a diagnosis of ocular hypertension, that is, an IOP consistently greater than 21 mmHg but no evidence of glaucomatous cupping of the optic nerve or visual field loss indicative of glaucoma. Six (5.9%) were started on antiglaucomatous therapy because of 'suspicious chronic open-angle glaucoma—that is, visual field and/or disc changes in the author's (ESP) opinion suggested early disease. An additional three (3%) developed visual field loss and/or optic nerve head cupping diagnostic of glaucomatous damage.

*Mail survey of Bedford study population.* The 101 patients from the Bedford study population were asked by mail if they knew of any additional members of their families who had developed chronic open-angle glaucoma. Of the 63 who responded 9 (14.3%) knew of other family members who had developed the disorder and were on treatment for it.

## Discussion

This study confirms the fact that having a family history of chronic open-angle glaucoma puts a person at higher risk not only of developing the disease but also of having an abnormal increase of intraocular pressure. The fact that there is agreement between mean IOP and prevalence of raised IOP in two independent groups of patients with a positive family history provides confidence that the results are accurate in spite of the fact that neither of the groups was randomly chosen.

One of the major problems in a study relative to family history of chronic open-angle glaucoma is to determine whether patients in fact have a family history when they say they do. In the Institute group the positive family history was entirely accurate, as

the individuals studied had family members under the care of one of the authors (ESP). In the Bedford Survey care was taken to ensure the accuracy of the family history, but in all cases one could not be sure it was entirely correct. Since the data from the two groups agree so well, we believe that the Bedford patients were moderately accurate with respect to their family history of chronic open-angle glaucoma.

The current study points out quite conclusively that, with aging, those individuals with a positive family history have an increasing chance of having an intraocular pressure greater than 21 mmHg. It also appears reasonable to assume that, with aging, the chance of developing suspected or frank glaucoma also increases, as it does in the general population. However, it is not inevitable that all patients with a positive family history who develop an increase in intraocular pressure actually develop glaucoma. A significant number studied had borderline IOPs for as long as four to five years without developing field loss and cupping. In fact the IOP of many of those studied returned to normal after several years of running in the low 20s. This observation has been reported previously in unselected patients with raised IOP.<sup>5</sup>

The individual with a family history of glaucoma who has a raised IOP must be followed up closely for the detection of changes related to the raised IOP. Older persons with a positive family history are probably at greater risk of developing glaucoma and should be watched more carefully. This hypothesis cannot be answered by this study, as the numbers of patients are too small and the follow-up period too short. Those factors which seem to have no role in the development of a raised pressure are sex and type of relative with raised pressure.

One can conclude from this investigation that the relative risk of having an increased IOP if a family member has chronic open-angle glaucoma is three to four times that in the general population. Furthermore, the percentage of patients who have a family history of chronic open-angle glaucoma who on long-term follow-up are found to develop either frank glaucoma or suspicious glaucoma is approximately 9%. This is almost 10 times the prevalence of glaucoma in the general population<sup>6</sup> and three times the incidence of glaucoma found by Perkins when he followed up for five to seven years the ocular hypertensives detected in the original Bedford Survey.<sup>7</sup> It is reasonable therefore to emphasise the importance of careful periodic ophthalmological examination of relatives of individuals who have chronic open-angle glaucoma.

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