COMMUNICATIONS

STUDIES ON GLAUCOMA RELATIVES*

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THE purpose of the present study is to find out if thorough screening of a small selected section of the population would be clinically valuable in the early diagnosis of glaucoma simplex. Mass screening of people over 40 years of age would certainly reduce the incidence of blindness due to glaucoma, but screening on such a scale would, for practical reasons, have to be limited to tonometry and optic disc inspection.

Relatives of patients with known glaucoma simplex were investigated. The study was carried out in two parts. In the first instance, siblings between the ages of 40 and 60 years were submitted to careful examination. This age range was chosen because glaucoma is rarely fully developed under 40 years of age. The results of these tests showed that, whilst many siblings had normal intra-ocular pressures and full fields, their coefficients of outflow were considerably reduced. The second part of the study was therefore extended to the investigation by tonography of the offspring of patients with simple glaucoma. The offspring were aged between 15 and 55 years at the time of examination.

Part I. Siblings

Fifty siblings of patients with known glaucoma simplex were invited to attend the glaucoma clinic at the High Holborn branch of Moorfields Eye Hospital for examination. Certain criteria were laid down for the diagnosis of glaucoma in the original patients before their siblings were selected. At the same time, fifty control persons were examined; they had no known family history of glaucoma and no intra-ocular disease, and were drawn from the Casualty, Orthoptic, and Refraction Departments of the hospital. The two groups were matched as nearly as possible for age and sex.

Subjects for examination were selected at random so that it was not known whether a sibling or a control was being examined. The family history was taken at the end of the examination.

The screening procedure for all who attended was as follows:

- (1) General medical and ophthalmic history.

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- (2) Family history of eye disease—with emphasis on age of parents at death.
- (3) General examination of the eye.
- (4) Applanation tonometry and weighted Schiötz tonometry.
- (5) Examination of the visual field on the Bjerrum screen. (Standard illumination and a 3 mm. white object at 2 m. Any doubtful fields were repeated with a 1 mm. object).
- (6) Tonography with the Schwarzer electronic tonometer.
- (7) Gonioscopy with the rimless Goldmann lens.

The coefficient of outflow was calculated on the Friedenwald Nomogram chart. The ratio P_0/C (outflow value—O.F.V.) where P_0 is the initial pressure and C the coefficient of outflow, was used to express the results. By the use of the O.F.V. the difference between normal and early glaucoma patients becomes evident in the earliest stages of the disease. The threshold of normality is 100, outflow values above this being abnormal.

Gonioscopy findings were grouped according to the simple classification suggested by Gorin and Posner (1957):

WIDE—All structures are visible.

MEDIUM—The trabeculae are visible but the ciliary body is obscured.

NARROW—Neither the ciliary body nor the posterior two-thirds of the trabeculae are visible.

As a result of the complete screening examination the subjects fall into one of three groups:

Definite; Suspect; No evidence.

Glaucoma Siblings.—The criteria for diagnosis of glaucoma simplex were two or more of the following in a patient with open angles:

- (1) Pressure of over 30 mm. Hg with a weighted Schiötz tonometer at some stage during the disease.
- (2) Pathologically-cupped disc.
- (3) Typical glaucomatous field defect.
- (4) Reduced coefficient of outflow.

Siblings fulfilling these criteria were regarded as having definite glaucoma simplex and were referred for treatment.

Suspects were siblings with an applanation tension of more than 20 mm. and/or an outflow value of more than 100. They were asked to return for a water-drinking test and tonography was repeated. Becker, Kolker, and Roth (1960) have shown that tonography after the ingestion of one litre of water is probably the best single test available for the detection of early simple glaucoma, as patients with this disease, unlike normals, display a lowered outflow after taking water. Tonography was started 20 minutes

after the water had been taken. This time was chosen on the basis of the studies of Drance (1958), who showed that maximum haemodilution occurs between 15 and 30 minutes after ingestion. The siblings were starved for 8 hours before this test. The results are shown in Table I.

TABLE I
RESULTS OF GLAUCOMA TESTS IN 50 SIBLINGS OF GLAUCOMA PATIENTS

Glaucoma	Number of Cases	Percentage of Total
Definite	4	8
Suspect	19	38
No evidence	27	54

Four siblings had definite glaucoma simplex:

(a) **Male aged 53 years**, already diagnosed and under treatment at another hospital. He was one-eyed (having lost the other eye through a war injury).

TENSION: 30 applanation.

33 with 7.5 weighted Schiötz.

P_0/C 800

The water-drinking test was not performed.

Open angle. Grossly constricted field. Deeply-cupped optic disc.

(b) **Female aged 50 years**, symptomless. Her brother was attending with glaucoma simplex. The mother also had glaucoma simplex.

TENSION: Right: 28 applanation. 36 with 7.5 weighted Schiötz } when first examined.
Left: 18 applanation. 28 with 7.5 weighted Schiötz }

P_0/C 600 right, 350 left.

Right field defect (arcuate scotoma in the superior temporal quadrant).

Right cupped disc.

The patient had a right anterior flap sclerotomy operation and is now using miotics in the left eye.

(c) **Female aged 57 years**. Her sister was attending with glaucoma simplex.

TENSION: Right: 28 applanation. 30 with 7.5 weighted Schiötz.

Left: 24 applanation. 28 with 7.5 weighted Schiötz.

P_0/C 500 right, 300 left.

Water-drinking test positive.

No field defect. Discs normal.

She is now on miotics which are controlling the situation.

(d) **Female aged 54 years**, sister of above.

TENSION: Right: 18 applanation. 22 with 7.5 weighted Schiötz.

Left: 18 applanation. 22 with 7.5 weighted Schiötz.

P_0/C 110 right, 110 left.

Negative water-drinking test.

Cupped disc. Field defect (arcuate scotoma in superior temporal quadrant).

She is controlled on miotics.

Nineteen water-drinking tests were carried out, three on siblings with definite glaucoma, and sixteen on siblings with suspected glaucoma. Three siblings failed to return for the test. The results are given in Table II, which also shows the average for the fifty controls.

RESULTS OF PROVOCATIVE TESTS IN 19 GLAUCOMA SIBLINGS AND AVERAGE OF CONTROL GROUP

Case No		1		2		3		4		5		6		7		8		9		10	
Eye		R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L
Rise in Tension (mm. Hg)		1	1	7	7	2	4	4	2	4	8	4	4	4	4	1	1	2	6	4	4
P ₀ /C	Before	158	158	140	140	110	110	170	170	140	180	80	106	600	280	138	200	110	110	121	121
	After	169	169	600	600	200	242	362	266	154	200	110	300	700	350	200	300	360	375	333	333

Case No.		11		12		13		14		15		16		17		18		19		20	
Eye		R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L
Rise in Tension (mm. Hg)		6	6	10	10	2	2	—	—	1	2	—	2	8	6	10	10	4	4	6	7
P ₀ /C	Before	130	140	130	130	80	80	80	133	172	135	150	260	500	300	166	166	180	200	157	200
	After	450	188	272	333	110	110	90	150	190	170	170	260	2600	450	300	400	180	244	200	220

CONTROL GROUP AVERAGE

Eye		R	L
Rise in Tension (mm. Hg)		—	5
P ₀ /C	Before	—	110
	After	—	162

The rise in tension was measured on the applanation tonometer. If a rise of 6 mm. measured on this instrument is taken as positive, eight tests proved positive and in sixteen cases the outflow was reduced even further under the water load.

Some of the siblings examined in the suspect group are almost certainly cases of early glaucoma with resting applanation levels of 18 to 19 mm. and highly-positive water-drinking tests. These patients are being followed carefully and are attending for tonography and central field examination every 6 months.

Results of Gonioscopy.—All the angles examined were either wide or medium except one which fell into the narrow category.

Controls.—The results for the control subjects are given in Table III.

TABLE III
RESULTS OF GLAUCOMA TESTS IN 50 CONTROL SUSPECTS

Glaucoma	Number of Cases	Percentage of Total
Definite	—	—
Suspect	1	2
No evidence	49	98

The one suspect had an outflow value of 110 and returned for a water-drinking test. The rise in tension after the water load was not significant but the outflow was reduced still further. She will be kept under observation.

In Fig. 1 the results of the two groups are given blocked together. The absence of any definite cases of glaucoma in the control series and the low incidence of suspects in that group compared with the glaucoma sibling group are of importance.

FIG. 1.—Results of glaucoma tests in fifty siblings of glaucoma patients and fifty controls.

Fig. 2 (overleaf) shows the outflow value plotted against age in all the subjects examined. It is interesting to note that only one control has an outflow value over 100 compared with 22 among the siblings of patients with glaucoma simplex.

The mean outflow was calculated for the two groups and is given with the relevant statistical data in Table IV (overleaf). The difference of the means in the glaucoma simplex group of siblings and the control group is statistically highly significant ($P < 0.001$).

FIG. 2.—Outflow value plotted against age in siblings of glaucoma patients and controls.

TABLE IV
MEAN OUTFLOW IN GLAUCOMA SIBLINGS AND CONTROLS

Group	Mean P_0/C	Standard Deviation	Standard Error of the Mean
50 Control	59.2	± 22.3	± 2.2
50 Glaucoma Siblings	121.0	± 110.3	± 11.1

Part II. Descendants

The results of this survey show that tonography is undoubtedly a very useful test for the early detection of glaucoma simplex. It was therefore decided to extend the survey to include another generation of relatives of patients with known glaucoma simplex. This time, the immediate descendants of such patients were invited to attend the glaucoma clinic and tonography only was performed. The same criteria for the diagnosis of glaucoma simplex in the parent and children were employed in this study.

The ages of the offspring investigated ranged from 15 to 60 years. 75 were examined along with a control group of fifty subjects having a negative family history of glaucoma and without intra-ocular disease. As far as possible, the controls were of the same age and sex range as the descendants. In the first instance, tonography was performed on the left eye only. If any of the subjects were found to have an outflow value of more than 100 they were asked to return for a water-drinking test. The possibility of a reduced coefficient of outflow was the main factor under investigation. The results are shown in Table V and Fig. 3.

TABLE V

RESULTS OF GLAUCOMA TESTS IN 75 DESCENDANTS OF GLAUCOMA PATIENTS

Glaucoma	No. of Cases	Percentage of Total
Definite	2	2.7
Suspect	23	41.3
No evidence	50	56

FIG. 3.—Results of glaucoma tests in 74 children of glaucoma patients and 50 controls.

Two cases of definite glaucoma were diagnosed:

(1) **Male aged 51 years.**

TENSION: Right: 55 applanation. 69 with 7.5 weighted Schiötz.

Left: 29 applanation. 30 with 7.5 weighted Schiötz.

P_0/C 230 left.

The initial tension in the right eye was too high for accurate tonography. No field defect. Open angles.

(2) **Male aged 45 years.**

TENSION: Right: 24 applanation. 30 with 7.5 weighted Schiötz.

Left: 28 applanation. 33 with 7.5 weighted Schiötz.

P_0/C 289 right, 233 left.

No field defect. Open angles.

The results of tonography after the water-drinking test in 25 glaucoma descendants are shown in Table VI.

TABLE VI
RESULTS OF WATER-DRINKING TESTS IN 25 GLAUCOMA DESCENDANTS
(Left eyes only)

Case No.		1	2	3	4	5	6	7	8	9	10	11	12	13
Rise in Tension (mm. Hg)		3	6	4	4	5	5	6	2	4	2	6	3	5
P_0/C	Before	145	105	146	85	123	150	125	105	133	121	185	150	130
	After	150	125	230	142	115	160	146	333	133	170	600	177	142

Case No.		14	15	16	17	18	19	20	21	22	23	24	25
Rise in Tension (mm. Hg)		2	2	4	4	16	2	5	3	3	3	2	6
P_0/C	Before	136	120	105	200	140	105	150	108	130	233	161	121
	After	266	300	130	260	2000	140	200	180	140	540	266	180

It is interesting to note that, in all but two cases, the outflow value was raised even further under the water load. These descendants have been subjected to the full glaucoma examination and will be kept under observation in the clinic.

Controls.—No case of definite glaucoma was discovered in this group, the outflow values of all examined being 100 or less.

Fig. 4 shows the outflow values of the glaucoma descendants and control subjects.

Fig. 4.—Outflow value plotted against age in children of glaucoma patients and 50 controls.

Fig. 5 (overleaf) shows the results of tonography in the descendants and also in the controls in 10-year groups. The following points should be noted:

- (1) The outflow value rises as age advances in the two groups.
- (2) The rise in the glaucoma group is steeper than that in the control group.
- (3) Even at the earliest age when it is possible to measure the outflow value, it is higher in the glaucoma group than in the control group.

The mean outflow for the two groups was calculated and is given with the relevant statistical data in Table VII (overleaf), which shows that the difference between the means of the two groups is highly significant ($P < 0.001$).

FIG. 5.—Outflow value in children of glaucoma patients and controls by age groups.

TABLE VII
MEAN OUTFLOW IN GLAUCOMA DESCENDANTS AND CONTROLS

Group	Mean P_0/C	Standard Deviation	Standard Error of the Mean
75 Descendants	101.3	± 41.9	± 4.8
50 Controls	68.2	± 19.3	± 2.7

Conclusions

As a result of these studies it can be concluded that there is a marked hereditary factor influencing the incidence of glaucoma simplex. The earliest lesion would appear to be an impairment of the drainage of aqueous humour from the anterior chamber, and the most useful test in the early diagnosis of this disease is tonography combined with the water-drinking test. This information may be employed clinically in the following way:

- By making a point of inquiring for a family history of glaucoma when interviewing a candidate for routine eye testing.
- By submitting the candidate with a positive family history to special testing in order to exclude glaucoma.
- By examining routinely all siblings of known cases of glaucoma simplex.

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