The fellow eye

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SUMMARY The result of a 10-year longitudinal study of the fellow eye at risk of developing closed-angle glaucoma (because the presenting eye had the disease) is described. 202 eyes were observed between 1 August 1970 and 31 July 1980. Each eye was provoked shortly after presentation using a pilocarpine phenylephrine provocative test. If the test produced a closed-angle glaucoma an iridectomy was done; if closed-angle glaucoma did not occur the eye was observed and it was reprovoked at yearly intervals. There were 3 possible outcomes for any one eye. Either the eye developed closed-angle glaucoma; or it was lost to follow-up; or at the end of the study the patient was alive, under observation, without having developed glaucoma. 90% of acute attacks occurred within 6 months of presentation. If an eye survived the first year without getting glaucoma the probability of its development in any one year period up to the fifth anniversary was 0.05; thereafter it was zero. The cumulative probability of an eye surviving to the fifth anniversary without glaucoma was 0.34, remaining constant thereafter; that is 34% of iridectomies are unnecessary. A high prevalence of ocular hypertension was seen in eyes that did not have an iridectomy (26%). It was concluded that a routine iridectomy is not necessary and that the fellow eye that will get glaucoma can usually be detected. The untreated fellow eye presents a naturally occurring model of one of the mechanisms involved in the production of ocular hypertension.

The presence of spontaneous closed-angle glaucoma in one eye is an indication for doing a peripheral iridectomy in its fellow. The evidence on which this decision is based comes from retrospective studies involving fellow eyes. These show^{1,2} that if the fellow eye is treated conservatively 45 to 70% eventually develop an acute glaucoma. It is a necessary consequence that 30 to 55% of iridectomies are unnecessary, but that fact causes no disquiet because there are few operative complications, and another acute attack rarely occurs.²⁻¹²

If the fellow eye that will develop closed-angle glaucoma could be identified before the event, unnecessary iridectomies would be eliminated. This paper describes the result of a 10-year longitudinal study the purpose of which was to devise a scheme for selecting the eye that needs an iridectomy and to observe the behaviour of the untreated fellow eye.

Material and methods

The study began on 1 August 1970 and finished on 31 July 1980. During that 10-year interval all patients seen at the glaucoma clinic with unilateral spontaneous closed-angle glaucoma (acute, inter-

mittent, or chronic) were managed in the way now described.

At entry into the study any treatment being given to the fellow eye was stopped. During the first 2 weeks after presentation a pilocarpine-phenylephrine provocative test was done. The details of the method have varied over the years, but in essence the test has 3 stages.

Stage 1. Intraocular pressure is measured, the presence and distribution of iridocorneal contact noted, and a tonography trace recorded. One drop each of pilocarpine 2% and phenylephrine 10% are instilled and gonioscopy is done. The patient is left for 1 hour. *Stage 2.* If now intraocular pressure has increased by 8 mmHg or more, together with total angle closure, the test is terminated by intravenous acetazolamide 500 mg and 1 drop of gutt. thymoxamine 0.5%. If the pressure increase is less than 8 mmHg, stage 1 is repeated without doing gonioscopy. *Stage 3.* As for stage 1 (but no gonioscopy, it is unnecessary because iridocorneal contact extends well on to the corneal side of the limbus and can be seen with a slit-lamp). If the test is positive the eye is treated as described in stage 2. If negative, gutt. thymoxamine 0.5% is instilled and the test terminated.

A fellow eye showing a positive provocative test

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had a peripheral iridectomy done. If the test was negative no treatment was given, the patient was seen at 6-monthly intervals, and the eye reprovoked at yearly intervals. (In the early stages of the study this regimen was, on occasion, violated and a test done at less than yearly intervals. It soon became apparent that this was unnecessary.) If the provocative test subsequently became positive, an iridectomy was done. Similarly, if an eye developed a spontaneous acute attack, an iridectomy was done.

As a help in interpreting the results the intraocular pressure, facility of outflow, and the frequency and extent of angle closure produced by a provocative test are described for 4 groups of eyes.

(1) Eighty-eight eyes from 88 patients were selected as a control group on these criteria: (a) a minimum age of 67 years; (b) their first attendance at the eye hospital by direct clinic referral; (c) no patient referred because of a raised intraocular pressure was included in the control group. The intention was to get as near as possible to a random sample of patients with ageing eyes, but to exclude the bias that would be introduced if they were known before referral to have a raised pressure.

(2) One hundred and four fellow eyes in this study developed closed-angle glaucoma at the time of the first provocative test and subsequently had a peripheral iridectomy. Fifty-seven of those patients still attending the glaucoma clinic make up the second group. Six of the eyes need treatment to maintain a normal pressure.

(3) Fifty-eight of the fellow eyes were free of glaucoma at study termination. The details of their last provocative test are recorded.

(4) Twenty-six fellow eyes were found which were at risk because the other eye had had closed-angle glaucoma. They had been treated with prophylactic pilocarpine drops for at least 10 years (mean 13.4 years, standard error 1.1 years). The details of their most recent provocative test are recorded.

Results

The number of fellow eyes observed was 202 (in the presenting eye 150 had acute, 39 intermittent, and 13 chronic closed-angle glaucoma). Their fates during the 10-year period were as follows.

(1) One hundred and fifteen eyes developed closed-angle glaucoma as a result of a provocative test. One hundred and four occurred at the time of the first test, within 2 months of presentation. In 11 eyes the first test or tests were negative but became positive at a later date (1 within 2 months, 1 within 2–6 months, 3 within 6 months–1 year, 4 within 1–2 years, 1 within 2–3 years, and 1 within 6–7 years).

(2) Nine eyes developed spontaneous acute

closed-angle glaucoma in spite of negative provocative tests. (3 occurred within 2 months of presentation, 3 within 2–6 months, and 1 each within 2–3, 3–4, and 4–5 years). Seven patients presented within 12 hours of onset, the other 2 within 48 hours. In 1 patient vision was reduced from 6/9 to 6/18; the other patients retained the vision they had.

(3) Five patients were lost to follow-up: 3 within 1 month of presentation, 1 within 2–3 years, and 1 within 4–5 years.

(4) Fifteen eyes were classed as lost to follow-up because 3 needed a cataract extraction before closed-angle glaucoma occurred and 12 died without getting glaucoma.

(5) Fifty-eight eyes have never developed glaucoma and were still being observed at study termination on 31 July 1980. Their intraocular pressure has increased significantly during the interval between presentation and termination (mean = 2.4 mmHg; $t = 4.78$, $p < 0.001$).

These data are amenable to a life table analysis.^{13 14} The survivorship table (Table 1) is made up in the following way: column 1 records the time that has elapsed since entry to the study; column 2 records the number of fellow eyes under observation at the beginning of the relevant interval in column 1; column 3 records the number of eyes that developed an acute closed-angle glaucoma during the interval (there are 2 possibilities, either the glaucoma was induced or it was spontaneous); column 4 records the number of eyes withdrawn from the study during the relevant interval without getting glaucoma (there are 4 possibilities, death, lost to follow-up, cataract extraction, or an acute attack had not occurred at study termination).

The next four columns are derived from these raw data: column 5 records the probability of an eye developing an acute glaucoma during the interval recorded in column 1; column 6 records the prob-

Table 1 *Survivorship for the fellow eye*

1	2	3	4	5	6	7	8
0–2 months	202	108	4	0.54	0.46	0.46	0.035
2–6 months	90	4	8	0.047	0.95	0.44	0.035
6–12 months	78	3	4	0.039	0.96	0.42	0.035
1–2 years	71	4	23	0.058	0.94	0.39	0.033
2–3 years	44	2	14	0.054	0.95	0.37	0.034
3–4 years	28	1	5	0.039	0.96	0.36	0.036
4–5 years	22	1	11	0.061	0.94	0.34	0.04
5–6 years	10	0	3				
6–7 years	7	1	2				
7–8 years	4	0	1				
8–9 years	3	0	3				
9–10 years	0	0	0				

ability of not getting an acute attack during that interval; column 7 represents the cumulative probability that an eye will survive to any stated interval without getting an acute attack; finally, column 8 is the standard error of the figure in column 7.

For example, 28 eyes survived to the third anniversary without getting glaucoma. During the 3-4-year interval 1 eye developed closed-angle glaucoma and 5 were removed because study termination had been reached. The probability of an eye getting glaucoma during the 3-4-year period was 0.04 (or of not getting glaucoma 0.96). Finally, the probability of a fellow eye surviving to the fourth anniversary without glaucoma was 0.36. Table 1 also shows that if an eye survives to the fifth anniversary the probability of getting glaucoma thereafter is effectively zero.

Tables 2 and 3 record data from four groups of patients: (1) A control group of 88 right eyes from 88 patients. (2) A group of 57 fellow eyes from this series which had had a positive provocative test and an iridectomy; the figures recorded here were obtained at a variable interval after the iridectomy (mean 3 years, standard error 0.4 years). (3) Fifty-eight of the fellow eyes which had not developed glaucoma by the time study termination was reached. (4) Twenty-six fellow eyes, not connected with the present study, which had been treated with prophylactic pilocarpine for a mean period of 13.4 years (standard error 1.1 years).

In both tables P_0 and C refer to the values obtained

Table 2 P_0 and C values in 4 groups of eyes

	No.	$P_0 \geq 21$	$C < 0.18$	$P_0/C \geq 100$	Age
Control eyes	88	10 (11%)	9 (10%)	12 (14%)	74.0 (0.9)
Fellow eyes: 57 iridectomy	57	16 (27%)	14 (25%)	14 (25%)	67.1 (1.6)
Fellow eyes: 58 no treatment	58	15 (26%)	14 (25%)	18 (32%)	65.1 (1.7)
Fellow eyes: 26 miotics	26	10 (38%)	11 (42%)	13 (50%)	70.3 (1.5)

P_0 =intraocular pressure. C=facility of outflow. Age refers to the mean age of the sample with the standard error of the mean in brackets.

Table 3 Prevalence and extent of irido-corneal contact

	No.	ICC	Extent
Control eyes	88	10%	34%
Fellow eyes: iridectomy	57	Nil	Nil
Fellow eye: no treatment	58	84%	44%
Fellow eye: miotics	26	88%	51%

ICC=irido-corneal contact. Extent refers to the proportion of the corneal circumference involved.

at the start of the provocative test. ICC refers to the number of eyes showing iridocorneal contact at the end of the test together with the extent of the corneal circumference involved.

Discussion

Table 1 shows that, if a fellow eye survives the first year of follow-up without developing a positive response to a provocative test or a spontaneous acute attack, the probability of getting closed-angle glaucoma in any one year period thereafter is about 0.05 (Table 1, column 5). After 5 years the probability is effectively zero. In contrast Lowe² stresses the 5-10 year-period because 40% of his recorded acute attacks occurred then. Several consequences necessarily follow from this diverging experience.

Firstly, the pilocarpine-phenylephrine provocative test can predict which fellow eye will probably get closed-angle glaucoma, leaving a group for follow-up in which the probability is low. It also means that the factor or factors that predispose to, and cause, closed-angle glaucoma are already present in the fellow eye at the same time as the presenting eye develops symptoms. Secondly, the ability of the test to abstract from the sample those eyes that have, or will get, disease (its sensitivity) is $115/124=93\%$. The calculation begs the question, so that a more immediately valuable measure is the predictive value of a negative test (that is, the probability that an eye with a negative test does not have and/or will not get closed-angle glaucoma). This depends upon the time that has elapsed between presentation and doing the test, but is never less than 0.94. By the time of the fifth anniversary the predictive value is almost certain, that is, if any eye has survived that long and if the test is negative, a fellow eye managed in the manner described in this paper will not get spontaneous closed-angle glaucoma.

Thirdly, because there are few false negatives it is a reasonable inference that the event (or combination of events) involved in the pathogenesis of the disease process is similar to those that occur during a positive provocative test. There is experimental evidence to suggest that this is largely a consequence of parasympathetic activity.¹⁵

The prevalence of ocular hypertension and reduced outflow values in the 58 eyes that have not developed closed-angle glaucoma is 26% (Table 2). This is not because of peripheral anterior synechiae (present in one eye and involving less than 5% of the angle circumference). Neither is it a consequence of the increasing prevalence of ocular hypertension that occurs with age (both the control group and the 58 fellow eyes are from ageing populations, yet the prevalence of ocular hypertension in the fellow eyes

is significantly greater than in the control group— $Z=2.16$, $p<0.05$).

Table 2 also shows that if a fellow eye develops a positive provocative test and has a peripheral iridectomy, ocular hypertension is also more frequent than in the control group. Again, in the miotic treated fellow eyes the prevalence of ocular hypertension is highest of all—36%. Finally, the intraocular pressure of the 58 untreated fellow eyes is now significantly higher than it was at presentation ($t=4.78$, $p<0.001$). The increased prevalence is therefore unrelated to age, increases with follow-up, and is not prevented by doing an iridectomy. What is the mechanism?

Table 3 shows that about 80% of the miotic treated and no-treatment fellow eyes developed substantial iridocorneal contact at the end of a provocative test. In the control group the figure was 10%, but no eye that had an iridectomy developed any contact.

It is also relevant that 39 eyes of the 202 in this series presented with intermittent closed-angle glaucoma, subsequently confirmed by a positive provocative test. At the first attendance, 17 or 44%, had ocular hypertension. There is good reason to suppose, from the history and the positive test, that these eyes had had episodes of raised pressure and angle closure in the past, and it is reasonable to ascribe the ocular hypertension to these episodes. By analogy too it seems reasonable to suppose that the ocular hypertension and reduced outflow values found in the 58 fellow eyes and in the 57 fellow eyes that had had an iridectomy result from a similar mechanism.

The implication is that at the time of presentation or in the succeeding few years a significant proportion of fellow eyes already have signs of an active disease process in the absence of any story to suggest an acute attack. Acute closed-angle glaucoma is therefore merely an incident (but an obvious one) in the evolution of a disease process that can have other more subtle consequences too.¹⁵

How then should the fellow eye be treated? Miotics are not the answer, because they do not prevent disease. Routine iridectomies are also unsatisfactory, 34% are unnecessary, and there is a small, but finite, morbidity. Its very success too has inhibited thought and research into closed-angle mechanisms.

Equally clear is the inescapable fact that the scheme followed in this paper is also unsatisfactory. Nine patients developed spontaneous glaucoma in spite of negative tests and 5 were lost to follow-up. There is in fact no reason to suppose that the patients are any better off than if they had all had a routine iridectomy.

Perhaps there is no best way to treat the fellow eye. Whether selective or routine iridectomies are done, both methods are 'right' and both are 'wrong' in their several different ways. If the visual health of a patient is used as the ultimate criterion for making a decision, there is no necessary reason why one method should be chosen in preference to the other.

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