

## Ocular hypertension—a long-term follow-up of treated and untreated patients

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**SUMMARY** Sixty-one patients with ocular hypertension (117 eyes) were followed up for 1 to 11 years (average 40.7 months). Ten patients (12 eyes) developed visual field defects and optic disc lesions of glaucomatous type (10.2%). Their average age was lower than the average of the sample, and the defect appeared between 1 and 5 years (average 41.3 months).

The risk of developing glaucoma was related to the level of the intraocular pressure. Of the 75 eyes with pressures between 21 and 25 mmHg only 2 developed glaucoma, of the 25 cases with pressures of 26 to 30 only 3, but 7 of the 17 eyes with pressures of 31 mmHg or more did so. Prophylactic cryosurgery was carried out where indicated by the presence of lattice retinal degeneration or holes before starting miotic therapy.

Fifty eyes were given antiglaucoma therapy and compared with 67 eyes not treated. Treatment did not prevent the development of glaucoma and did not seem to influence the course of the ocular hypertension. The response to treatment was also valueless in predicting future glaucoma. Two untreated patients with high pressures developed central vein occlusion. As no harmful effect of treatment could be detected in the 50 treated eyes, elderly patients (more than 70 years) with intraocular pressure higher than 26 mmHg in the presence of systemic vascular disease should have their intraocular pressure lowered if possible before the development of field defects. In those with intraocular pressure below 26 mmHg there is no advantage in prescribing treatment. In the range 26 to 30 mmHg it is our practice to treat elderly patients over the age of 70 years, while younger patients are treated only if their intraocular pressure exceeds 30 mmHg.

Screening programmes to detect raised intraocular pressure (IOP) are widely used because of increasing awareness of both ophthalmologists and the general population of the symptomless presentation and progression of chronic open-angle glaucoma. After careful examination of those with raised intraocular pressure an ever growing group of patients is emerging who, in spite of a raised intraocular pressure, show neither pathological cupping of the optic disc nor a glaucomatous visual field defect. These patients are labelled 'ocular hypertensives'.

The incidence of ocular hypertension (OHT) in the general population is variously reported as 1% in the Oxford survey (Luntz *et al.*, 1963), 1.3% in the Birmingham study (Walker, 1974), and 5% in the Bedford survey (Perkins, 1973b). This is about five times higher than the incidence of glaucoma in the

latter two studies (0.31% in the Birmingham study and 0.93% in the Bedford survey (Bankes *et al.*, 1968)). The incidence in a glaucoma clinic population is much higher—according to one report 11% (Luntz, 1972).

Some authors believe that ocular hypertension represents a preglaucomatous stage (Richardson, 1972; and Goldmann, 1959). Others report on varying degrees of risk of patients with ocular hypertension for developing glaucoma. Graham (1968) and Armaly (1969) found it as low as 0.5%, Linner and Stromberg (1967) 2%, Perkins (1973a) 3.23%, and Walker (1974) as high as 20%. Kass *et al.* (1976) following up OHT eyes in patients with glaucoma in the second eye found 29% to develop visual field defects.

These reports leave little doubt that patients with ocular hypertension run a higher risk of developing chronic glaucoma than the rest of the population in a similar age group. Nevertheless, only the

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minority of patients with ocular hypertension will develop glaucoma, but the exact parameters that would indicate that a patient with ocular hypertension will develop glaucoma are not known. In this context, for example, there are conflicting views about the effect of treating intraocular pressure—does this reduce the risk of progression to glaucoma or not?

The results are reported of a prospective study to determine: (1) The incidence for the development of glaucoma in a population with ocular hypertension carefully monitored for intraocular pressure, visual field changes, and the appearance of the optic disc. (2) The time interval between first diagnosing ocular hypertension and the development of glaucoma. (3) If treatment of the intraocular pressure would protect the eye from developing glaucoma when compared to those not having been treated. (4) Any side effects or complications of long-term treatment.

### Definition of criteria

Patients attending our glaucoma clinics were diagnosed as OHT if: (1) The untreated intraocular pressure is found to be 21 mmHg or more on repeated measurements with the Goldmann applanation tonometer (Graham, 1972). The mean value of 3 pressures measured within the first few weeks of the patient's presenting to hospital is referred to in this paper as 'the mean initial intraocular pressure'. (2) The visual fields are normal when tested both with the Goldmann perimeter and the Bjerrum tangent screen. (3) The optic cup is separated from the edge of the disc by pink-coloured normal tissue (Drance, 1975). (4) There is no excavation of the disc margin by the optic cup. (5) The filtration angle is open.

### Material and methods

A total of 61 patients (117 eyes) with ocular hypertension have been followed for 1 to 11 years. All the patients attend the glaucoma clinics at the Johannesburg General Hospital and at the St. John Eye Hospital, Baragwanath. Fifty-six patients had bilateral ocular hypertension, 3 others unilateral ocular hypertension, the other eye being normal, and 2 patients had ocular hypertension in an only eye, the fellow eye being blind from disease other than glaucoma.

After the diagnosis of ocular hypertension is made—on the criteria mentioned above—the patients are reassessed at intervals of 2 to 6 months; intraocular pressure is measured at every visit and the optic disc examined by unioocular and binocular fundoscopy. The visual fields are tested on every occasion with the Goldmann perimeter and once or

twice a year with the Bjerrum tangent screen. For perimetry the 4eI and 3bIV targets on the Haag-Streit make of Goldmann perimeter were used in a dark room and standard background illumination. On the Bjerrum tangent screen the test was done at 1 m, with a 1 mm size white target. The Friedman analyser was used as a supplementary test to confirm paracentral scotomata when these appeared on one of the dynamic perimetries in a patient with previously normal fields.

The following field defects were considered significant: (1) Enlargement of the blind spot, particularly if this occurred in an upward or downward direction towards the Bjerrum area. (2) Paracentral scotomata in the Bjerrum area. (3) Typical arcuate scotoma. (4) Peripheral nasal scotomata in the 'nasal step' area. (5) Peripheral field loss, i.e., nasal step or altitudinal scotoma.

In all our cases the field defect could be correlated to a corresponding area of pathological cupping at the disc.

For some time tonographic studies and provocative tests were regularly performed, but they were abandoned when it was recognised that these have limited—if any—prognostic value, both from our own experience and that of others (Linner and Stromberg, 1964; Armaly, 1969; Graham, 1972; Kronfeld, 1975).

In 34 patients (67 eyes) we did not treat the raised intraocular pressure; the remaining 27 patients (50 eyes) were treated. The latter are patients with an initial intraocular pressure of at least 35 mmHg, ocular hypertension which is present in an only eye, and, thirdly, a randomly selected group of patients with intraocular pressure below 30 mmHg who were placed on treatment as part of this prospective study to evaluate the influence of treatment on the natural history of the condition.

The treatment is pilocarpine (2, 3, or 4%) 3 to 4 times daily, with adrenaline 2% twice daily added when necessary. A few patients are also on acetazolamide.

Before beginning treatment, however, all patients had their pupils dilated, and a careful search was made for equatorial lattice degeneration or holes in the retina. Peripheral retinal holes were found in 1 patient and these were closed by cryosurgery prior to the miotic treatment.

### Results

There are 36 females and 25 males, and the average follow-up is 42.8 months. Of the 117 eyes 48 (41%) have been followed up for more than 42 months, 69 (59%) for more than 3 years, and 29 (25%) for more than 5 years (Fig. 1).

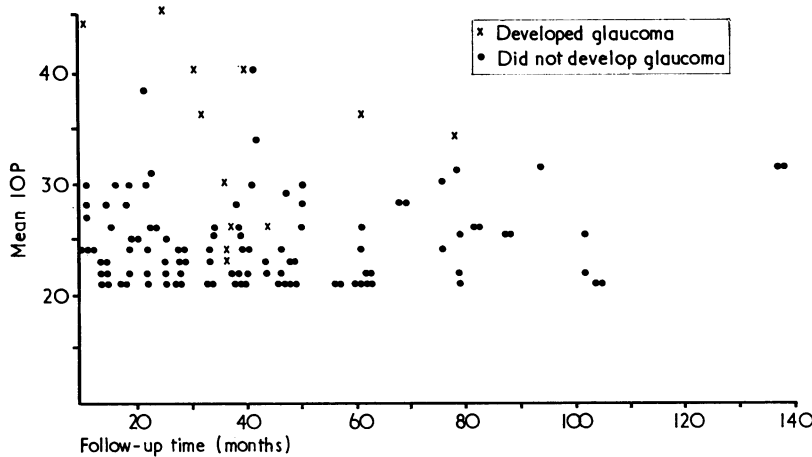


Fig. 1 Mean intraocular pressure in patients who did and did not develop glaucoma

In 75 eyes the means of their untreated intraocular pressure were between 21 and 25 mmHg, between 26 and 30 mmHg in 25 while 17 eyes had mean pressures higher than 31 mmHg measured on repeated occasions.

The age at which ocular hypertension was first diagnosed ranged from 36 to 83 years, 1 patient being 30 years of age. The mean was 61.2 years. The mean initial intraocular pressure and standard deviation were plotted for each age decade (Fig. 2). There appears to be no significant correlation in the mean intraocular pressure with advancing age.

Twelve eyes of 10 patients (10.2%) developed glaucoma, i.e., pathological cupping of their discs and glaucomatous field defect. Visual field defects appeared after 12 to 60 months of follow-up in 11

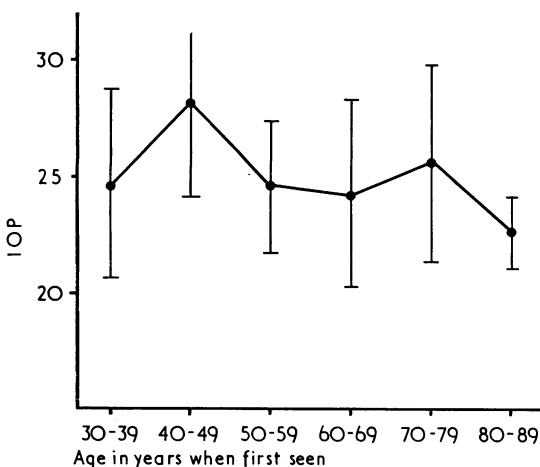


Fig. 2 Intraocular pressure when ocular hypertension was first diagnosed

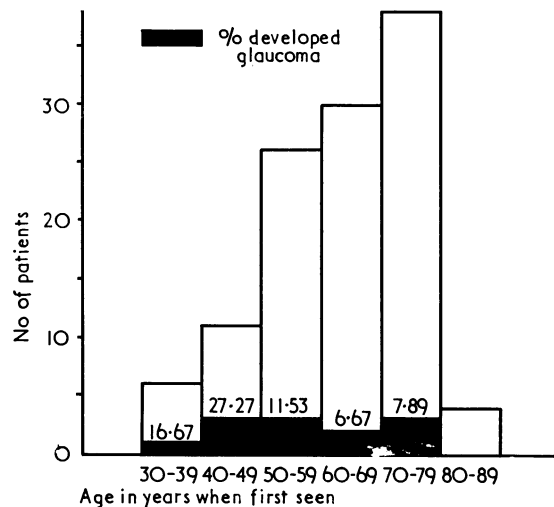


Fig. 3 Development of glaucoma in relation to age

of the 12 eyes and in 1 after 79 months, the mean being 41.3 months. Fig. 1 illustrates the relationship between the mean of the initial 3 intraocular pressure readings in each eye (follow-up in months), indicating also those eyes which developed glaucoma.

The highest pressure levels were measured in the age group 40 to 49, and it is in this decade that the highest incidence of glaucoma occurred (27.3%) (Fig. 3). In Fig. 4 we present the distribution of intraocular pressure for each eye in the various age groups, indicating those eyes that developed glaucoma (12 eyes). Of these 12 eyes 50% presented with ocular hypertension in the age decades 40 to 59 and subsequently developed glaucoma.

A number of factors which influence progression

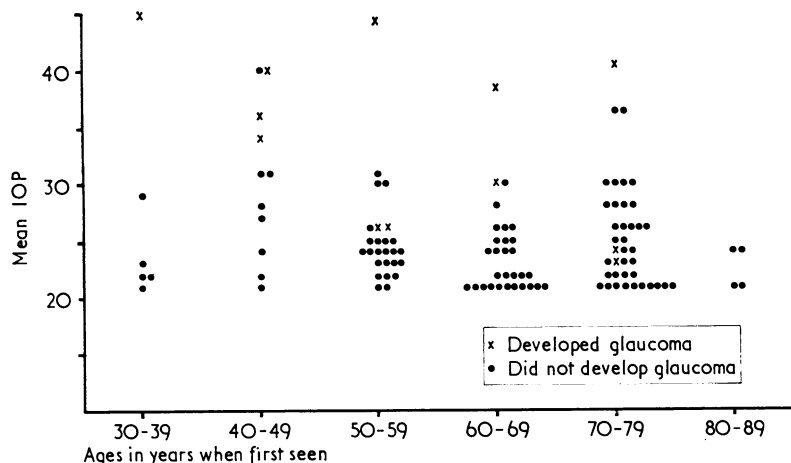


Fig. 4 Distribution of mean intraocular pressures and presence or absence of glaucoma in relation to age

of ocular hypertension to glaucoma were specifically looked at:

**Concomitant systemic disease.** Eleven patients are under medical care for systemic hypertension, 3 have well-controlled diabetes, 2 have chronic constrictive lung disease, and 1 is suffering from thyrotoxicosis. Only 1 of the hypertensive patients and 1 of the diabetics developed glaucoma.

**A family history** was noted in only 2 patients, but neither of these have so far developed glaucoma.

**Age of onset.** The 10 patients in our study who developed glaucoma were aged 36 to 75 with a mean age of 55.2 as compared with a mean of 62.1 in the total sample.

**Cup/disc ratio.** Of the 12 eyes that developed glaucoma only 9 had accurate cup/disc measurements documented. Four of these had a cup/disc ratio of less than 0.5, and 5 had cup/disc ratio of 0.5 (1), 0.7 (2), and 0.8 (2).

**The level of the mean initial intraocular pressures** (all patients initially untreated). Of the 12 eyes with ocular hypertension that developed glaucoma 7 had intraocular pressure of 31 mmHg or more, 3 between 26 and 30, and 2 of 21 to 25. In other words, of the 17 eyes with initial intraocular pressure of 31 mmHg or more 7 developed glaucoma (41.2%), 3 out of the 25 eyes with pressures between 26 and 30 mmHg (12%), and only 2 of the 75 eyes with pressures lower than 25 mmHg (2.7%) (Table 1).

**EFFECT OF TREATMENT**

**Response of treatment.** Fifty eyes with ocular hypertension (27 patients) are on antiglaucoma treatment, while the rest (34 patients, 67 eyes) receive no treatment. The response to treatment is considered 'good' when a drop of 11 mmHg or more was obtained, 'fair' when the decrease in the intra-

ocular pressure was 6 to 10 mmHg, and 'poor' when the treatment reduced intraocular pressure by 5 mmHg or less.

**Influence of treatment on development of glaucoma.** Nine eyes (7 patients) developed glaucoma while on treatment. The response to treatment in the various pressure groups is shown in Table 2, and the outcome of treatment in all patients in Table 3. In Fig. 5 the relationship between mean intraocular pressure, length of follow-up, and the eyes which

Table 1 The relationship between the level of mean initial intraocular pressure (IOP) and the development of glaucoma from ocular hypertension

IOP	Total eyes	Developed glaucoma	%
21-25	75	2	2.7
26-30	25	3	12
31 or more	17	7	41.2
Total	117	12	10.3

Table 2 Response to treatment

Initial mean IOP	Eyes that did not develop glaucoma				Eyes that did develop glaucoma				Total
	Response to treatment				Response to treatment				
	Good	Fair	Poor	Total	Good	Fair	Poor	Total	
21-25	6	4	15	25	2	—	—	2	27
26-30	5	—	3	8	—	1	—	1	9
31	6	2	—	8	6	—	—	6	14
Total	17	6	18	41	8	1	—	9	50

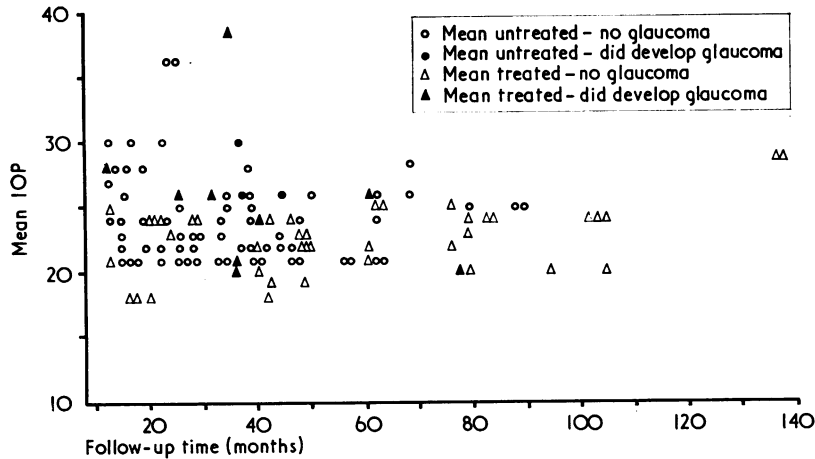


Fig. 5 Relation between mean intraocular pressure, length of follow-up, and development of glaucoma

developed glaucoma are plotted for both the untreated and treated eyes. In Fig. 5 mean intraocular pressure is the average of all intraocular pressures measured for each eye during the period of

Table 3 Influence of treatment on the outcome of ocular hypertension

IOP (Mean initial) (all patients initially untreated)	Patients left untreated (eyes)	Developed glaucoma (eyes)	Patients subsequently treated (eyes)	Developed glaucoma (eyes)
21-25	48	—	27	2
26-30	16	2	9	1
31 or more	3	1	14	6
Total	67	3	50	9

Table 4 Earliest manifestations of glaucoma (12 eyes)

Eye	Disc	Bjerrum	Goldmann
1	Upper temporal cupping	Inferiorly enlarged blind spot	Full
2	Inferotemporal cupping		Peripheral upper nasal scotoma
3	Inferotemporal cupping	Upper nasal scotoma	Full
4	Fundoscopically equivocal		Paracentral upper nasal scotoma
5	Fundoscopically equivocal		Paracentral upper nasal scotoma
6	Fundoscopically equivocal		Peripheral upper nasal scotoma
7	Fundoscopically equivocal		Peripheral lower nasal scotoma
8	Fundoscopically equivocal		Peripheral upper nasal scotoma
9	Inferotemporal cupping		Paracentral upper nasal scotoma
10	Inferotemporal cupping		Paracentral upper nasal scotoma
11	Temporal cupping		Paracentral nasal scotoma
12	Temporal cupping	Horizontally enlarged blind spot	—

follow-up in both the treated and untreated groups.

*Treatment in relation to observed complications.* Eight eyes (16%) showed a decrease of 2 lines or more in their visual acuity while on treatment owing to development of lens opacities, and 7 of these patients were over 70 years of age. In the untreated group 8 eyes (11.5%) showed increased lens opacities of similar degree, 5 of these in patients over 70. The difference is not significant.

During the follow-up period 3 patients developed occlusion of the central retinal vein. Two of these patients were not on antiglaucoma treatment, 1 is a hypertensive, both are over 70 years old, and their intraocular pressure was in the 26 to 30 mmHg range. The third patient is diabetic; the initial intraocular pressure was over 30 mmHg, and the patient responded well to pilocarpine.

Table 4 shows the earliest noted pathological

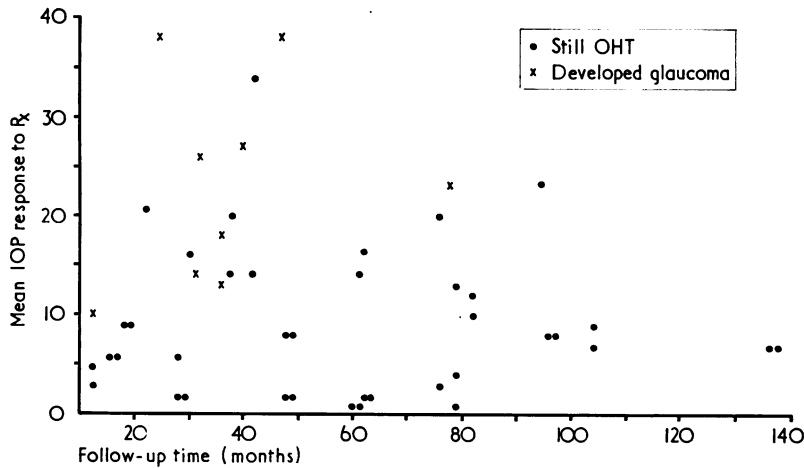


Fig. 6 Response of intraocular pressure to treatment

changes in the 12 eyes which developed glaucoma from ocular hypertension.

### Discussion

*Incidence of ocular hypertension progressing to glaucoma.* The 10.2% of glaucoma developing from ocular hypertension found in our series is higher than figures quoted by other authors (Graham, 1968; Armaly, 1969; Linner and Stromberg, 1967; and Perkins, 1973a), but lower than the 20% found by Walker (1974).

The patients who developed glaucoma were slightly younger than the average age of the sample (mean age 55.2 years as compared with 62.1 years). This suggests that glaucoma occurring in a patient with ocular hypertension will become manifest early in the course of the ocular hypertension. In this series we noted that if glaucoma developed it did so usually within 5 years of the first presentation with ocular hypertension.

*Earliest signs of glaucoma.* In 7 cases the earliest sign of glaucoma was pathological cupping of the optic disc. This was confirmed by a matching defect on the Goldmann field (4 cases) or the Bjerrum screen (3 cases). The other 5 patients presented with nasal scotoma either peripheral (3) or paracentral (2) documented on the Goldmann perimeter (Table 4).

### OTHER CLINICAL PARAMETERS

*Initial intraocular pressure.* The initial untreated intraocular pressure was the most consistent parameter for predicting the risk of glaucoma developing from ocular hypertension. As seen in Table 1, while the risk of glaucoma in patients with intraocular pressure of 25 mmHg or less was 2.7%, in the over 31 mmHg pressure group the risk was as high as 41.2%.

*Treated eyes.* The influence of treatment on the course of ocular hypertension is seen in Table 3 and Fig. 5. It is obvious that treatment did not prevent visual field loss, as more eyes on treatment developed glaucoma than those off treatment. Of 67 eyes not treated only 3 (4.5%) developed glaucoma, while of 50 treated eyes 9 (18%) developed glaucoma. The reason for this is that there are more patients with high intraocular pressure, who run the greatest risk of developing glaucoma in the group on treatment.

Furthermore from Table 3 it is clear that the same pattern of risk is seen in the eyes on or off treatment, i.e., those eyes in the highest range of intraocular pressure are at greater risk than those in the lower ranges (6 out of 14 treated eyes with intraocular pressure greater than 30 mmHg became glaucomatous).

While treatment did not prevent progression of ocular hypertension to glaucoma it did not, in this group of patients, do significant harm. The amount of cataract found in the treated group was similar to that in the untreated, and probably both were acceptable within the age-dependent incidence of cataract (Cinotti and Patti, 1968).

*Response to treatment.* The response of the intraocular pressure to treatment is recorded in Fig. 6 as the mean drop in intraocular pressure after treatment. Most of the eyes that developed glaucoma had responded well to treatment (a drop of 11 mmHg or more) but also had high initial intraocular pressure. On the other hand many of the eyes (about one-third) that did not develop glaucoma also responded well to treatment. Therefore, in reading the results documented in Fig. 6 the effect of the initially high intraocular pressure is probably more important in determining progression to

glaucoma than is the response to treatment, but both factors appear to play a part.

The patients had their intraocular pressure monitored at 3-monthly intervals and were measured at different times during the day. The mean drop in intraocular pressure resulting from therapy in the treated group as a whole was 10.5 mmHg, the pressure dropping from a mean initial pressure of 31.6 mmHg to a mean pressure on treatment of 21.1 mmHg. In spite of this considerable drop in intraocular pressures these patients were not adequately protected from developing glaucoma, as 18% of them developed the disease. It also did not seem to postpone the onset of glaucoma, as glaucoma developed on average within 3½ years.

The patients on treatment were not rigorously monitored in the sense of having regular diurnal variations of intraocular pressure measured at weekly or 2-weekly intervals to ensure that intraocular pressure was maintained under 20 mmHg at all times. It is possible but by no means certain that had such a rigorous regimen of control been followed these patients would have been adequately protected.

Our conclusion therefore is that, if the decision is made to treat a patient with ocular hypertension, then the ophthalmologist is committed to instituting treatment with a rigorous system of intraocular pressure control, by means of regular weekly or even daily (if the patient can do it himself) diurnal measurement of pressure to ensure that the intraocular pressure is constantly less than 20 mmHg. If this is not done then the patient is not protected against glaucoma.

If the intraocular pressure is not constantly maintained below 20 mmHg, either the medication must be increased, with the added risk of intensive medication, or the surgeon might as well abandon therapy. If intensive medication does not maintain intraocular pressure below 20 mmHg at all times of the diurnal curve, then the question of surgery arises. In our view ocular hypertensive patients run less risk if therapy is abandoned (only 10% of our patients developed glaucoma over 6 years, i.e., a 1.7% annual risk) compared to the risk of surgery.

Three patients suffered a central vein occlusion during the follow-up period and deserve some attention. All had an intraocular pressure higher than 26 mmHg. Only 1 was on treatment at the time the occlusion occurred, and this patient was diabetic and had intraocular pressure readings of 36 mmHg

prior to therapy. The other 2 received no treatment for their ocular hypertension, although 1 was hypertensive and on medical care.

As long-term pilocarpine treatment does not seem to be unduly harmful provided that degenerative retinal disease or retinal holes are treated prophylactically, it would seem reasonable that elderly patients (more than 70 years) with ocular hypertension and intraocular pressure measuring 26 mmHg or more should be treated in an attempt to improve perfusion at the optic head and to decrease the risk of vein occlusion. This is especially true if the patient has systemic vascular disease or is receiving antihypertensive drugs. On the other hand if the intraocular pressure does not respond to treatment with a fall of 5 mmHg or more, the treatment should be stopped.

Otherwise treatment seems to be unnecessary in ocular hypertension in which intraocular pressure without treatment is 30 mmHg or less, and can be postponed until frank glaucoma develops—if at all.

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