

CLINICAL STUDY OF EARLY CHRONIC SIMPLE GLAUCOMA:
DAILY CURVE OF PRESSURE, VISUAL FIELDS AND EYE FUNDUS:
FOLLOW-UP OF 5-15 YEARS

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INTRODUCTION

It is well known that the persistently high IO pressure determines irreversible visual field loss and glaucomatous cup.

Relatively recent papers (LEYDHECKER, 1958) have shown that the time interval necessary for the appearance of visual field defects is around 10 years. This interval represents the resistance of the optic nerve to the hypertension and wide individual variations may occur (LINNÉR & STROMBERG, 1967) specially when there is a good gradient Ophthalmic Artery Pressure/Po as LOBSTEIN (1963, 1968) and others have shown some years ago.

In this paper we have studied a group of 143 patients followed systematically for more than 5 years in which there has not been any significative change in the visual fields that could be related to the ocular hypertension.

The Daily Curve of Pressure, systematized as a semiotic method by SAMPAOLESI & RECA (1961) and introduced for the control of clinical or surgical treatment by CALIXTO, SAMPAOLESI, CARVALHO, and RECA (1966) is the only available direct method for the tensional control, before or during treatment. Before its systematization, this control was only indirectly evaluated by single tonometries, visual fields and optic disc examinations.

The follow-up of patients through the DCPO gives the ophthalmologist good conditions for the judgement of treatment: daily schedule for the administration of the eye drops, combination of hypotensive drugs, and choice of the best drug or drugs for each patient "per se".

We believe that its systematic use determined a radical change in the evaluation of the treatment: before its introduction we selected more cases for surgical treatment due to the lack of a good criterium for the therapeutic evaluation. New drugs, acting by different mechanisms in the tensional regulation, associated with the classical medication (pilocarpine) have also contributed, without doubt, to the substancial change in the treatment.

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MATERIAL AND METHODS

In December 1969, ten years after the establishment of the Glaucoma Clinic of the Medical School of the Federal University of Minas Gerais (at São Geraldo Hospital), we had 1837 patients registered. From these, we were able to select 143 patients in whom the diagnosis was made in the hypertensive phase of the disease i.e., before the occurrence of visual field loss and with normal or moderately glaucomatous cups. It was included in the sample one patient with visual field loss due to glaucoma, but present since the first examination. With proper treatment it did not progress during a 9 year follow-up. All the other patients had normal visual fields.

These patients were followed from 5 to 15 years and showed regular control of treatment (eye fundus, visual fields, and DCPo). They correspond to only 7.8% of all the patients registered in the period of ten years. This percentage represents a very low proportion of recognition of the disease in the ideal phase of diagnosis, i.e., the phase that preceds the visual field and optic disc changes.

Our routine examination was as follows:

1. Biomicroscopy (Haag-Streit slit lamp, mod. 900), ophthalmoscopy (Bausch & Lomb binocular ophthalmoscope) and gonioscopy (Goldmann's contact lens and Haag-Streit slit lamp, mod. 900). During the first years we used the old Haag-Streit slit lamp, mod. 360.
2. Visual fields — obtained in the Goldmann's perimeter, studying 4 isopters and exploring the Bjerrum area for the presence of scotomas unconnected to the blind spot. Since 1974 we began to perform the selective perimetry, as proposed by ARMALY (1969).
3. Ophthalmodynamometry — according to WEIGELIN and LOBSTEIN (1963).
4. Daily Curve of pressure (SAMPAOLESI and RECA, 1961).
5. Grant Tonography (1950) and Leydhecker tonographic test (1958) made one or more times in all patients.

Since 1962 we have introduced the applanation tonometry in the routine of the ophthalmologic examination made by the residents of the Eye Department. The initial suspicion of glaucoma usually arises from the systematic applanation tonometry, less often from the optic disc morphology, and even less often from the familiar history of the patient, generally obtained "a posteriori".

The periodic controls, performed once or twice every year, included systematically the study of the visual fields, ophthalmoscopy, ophthalmodynamometry and the DCPo. In 33 patients (66 eyes) we also performed tonography (once or more) for the control of treatment; we will discuss its value as a method of control.

From the 143 patients of our study, 94 were women (66%) and 49 men (34%).

We divided our patients in 6 groups, according to the parameters of the Daily Curve of Pressure (Mean Pressure —Pm, and Standard deviation of the seven daily measurements — V), as we will discuss below. The

types of camerular sinus and the Cup/Disc ratio are represented in Table 1; the drugs used for the treatment in each group, in Table 2. The other features of the six groups were:

Group I — Composed of 10 patients (8 women and 2 men, aged from 27 to 55 years). The diagnosis of glaucoma in this group arised from the yearly tonometric curve, i.e., the repeated tonometry showed pathologic values (generally ranging from 16 to 24 mm Hg) but the values of the DCPo were only suspect and did not contribute significantly for the diagnosis.

Group II — Formed by 38 patients (24 women and 14 men, aged from 20 to 70 years). In this heterogeneous group, the DCPo showed quite different results for the two eyes of each patient: the pathologic parameters for one eye were not the same for the other eye. Despite this fact, the DCPo contributed for the diagnosis of glaucoma in the patients of this group.

Group III — Constituted by 38 patients (24 women and 14 men, aged from 16 to 58 years). The feature of this group was the normal mean Pressure (Pm) and the significantly pathologic V in both eyes. It is interesting that the clinical history revealed the occurrence of rainbows (haloes) in 6 cases from this group and in only two patients from group five, of all the 143 patients studied.

Group IV — Constituted by 5 patients (3 women and 2 men, aged from 18 to 66 years). The feature of this group was the pathologic mean pressure, with normal V in both eyes of all patients.

Group V — Constituted by 13 patients (10 women and 3 men, aged from 34 to 64 years). The main feature of this group was that the two parameters of the DCPo (Pm and V) were pathologic in both eyes.

Group VI — Constituted by 50 patients (29 women and 21 men, aged from 14 to 71 years). In this group the diagnosis was made before we began to perform the DCPo as a systematic semiotic method or when we found single applanation tonometries around 30 mm Hg or more, making the DCPo unnecessary for the diagnosis. Therefore, in this group we have DCPo only for the control of treatment.

RESULTS AND COMENTS

I — Daily Curve of Pressure

Previously we tested the difference between the left and right eyes with the paired-t test in all the 143 patients considered together, in relation to the DCPo parameters (Pm and V) and tonographic coefficients (Co-4, F, and C3-7). No statistically significant difference was found. Therefore, for the continuation of the statistical analysis we considered left and right eyes together in every group.

Before studying the results in each group, we made histograms with the Pm and V values of those patients in which we had these values before and during treatment. This included the patients of the first five groups, considered together (186 eyes or 93 patients). These histograms (fig. 1 and 2) indicate that the treatment lowered the Pm and V values, moving them in the direction of the normal values. As the "during treatment" values we considered the last DCPo of control.

For the analysis of the data from each of the six groups we have first calculated, for every one, the mean and standard deviation of Pm and V, before and during treatment. Then, by the paired-t test we compared, in each group, the values before and during treatment (Table 3).

Highly significant differences were found for both Pm and V values in all groups, except group IV. In this group we did not find any significant difference in relation to the V values, probably because this group was previously selected by the high Pm and normal V value of its patients.

In group I (10 patients) the PCPo was "borderline" and the diagnosis of glaucoma came effectively from single tonometries (annual curve) with pathologic values. In this group, which represents 7% of our material of study, the DCPo was unable to make the diagnosis of the disease. It is important to emphasize that in this group both methods (DCPo and single tonometries) were complementary.

In group VI it was impossible to apply the paired-t test (see Material and Methods).

We were also interested in comparing the parameters of the PCPo of our glaucomatous patients under treatment with the normal values (obtained in 86 eyes; CALIXTO, 1967). So, we tested, with the t test, the difference between the Pm and V means of each one of the six groups under treatment and those of a normal sample (Table 4). In all groups highly significant differences were found in relation to Pm. In relation to the V values, the statistical analysis did not show any statistical difference in all the groups, except group I. In this group the V value before treatment was normal and the treatment lowering the V values, made it smaller than that of the normal sample.

The above findings can be visualised in Fig. 3, where we have plotted the means of Pm and V before and during treatment, in comparison with the normal sample (86 eyes). This graph shows very well the following facts: a) The treatment lowered the Pm values, but they were still slightly greater than the mean of the normal sample (the difference was statistically significant); b) The treatment normalized the V values (no significant difference in relation to a normal sample).

II — Tonography

Table 3 shows the mean and standard deviation of the tonographic coefficients, obtained in all the six groups before treatment. Except for group IV, the values do not differ significantly from each other. Group IV

is the smallest one, with only 5 patients; maybe the difference depends on this fact.

On a previous study, we determined the tonographic coefficients of 240 normal eyes, obtaining their mean and standard deviation. From these data we have calculated the normal range of variation, the suspect and the pathologic values. Table 5 shows the distribution of the values of C_{0-4} and C_{3-7} of the glaucomatous patients, that were found in the normal, suspect and pathological range of each of these coefficients.

Table 5 shows: — a) From the 273 eyes studied tonographically, 71% of the values of C_{0-4} were on the normal range of variation and only 2% showed pathologic values; b) On the same eyes, the values of C_{3-7} showed 16% in the normal range of variation and 57% on the pathological. These findings indicate clearly that the C_{3-7} coefficient was more discriminative between normal and early glaucomatous eyes than the C_{0-4} .

Fig. 4 confirms in another way the same findings of Table 5: a) The mean values of C_{0-4} are in the normal range of variation, with the exception of group IV, whose mean was in the suspect range; b) The mean values of C_{3-7} were in the suspect or pathological range.

The above conclusions in relation to these coefficients agree with those obtained by LEYDHECKER (1958), but disagree with those recently obtained by PORTNEY and SOUSA (1974).

In relation to the minute-volume of aqueous humor determined tonographically (F) there has not been any significant difference between the normal and the glaucomatous means. We do not ignore the sources of error, neither the critics to the tonographic method for the evaluation of this coefficient, but they were systematically found in the two samples (normal and glaucomatous).

In 33 patients (66 eyes) in which tonography was performed before and during treatment, we were able to apply the paired-t test for the comparison of these values (Table 6; Fig. 5 and 6). It is important to stress that these 33 patients, in whom tonography was carried out during treatment, were selected at random, without any specific clinical reason to repeat the examination. We did so only to study its possible merit as a method for the control of treatment. Our findings were: a) The test pointed out a significant difference between the means of C_{0-4} (before and during treatment), although they were very close each other (Fig. 5); b) It was found no significant difference between the means of the minute volume measurements, before and during treatment; c) Similarly, there has not been a significant difference between the C_{3-7} means during and before the hypotensive treatment.

Yet on the same group of patients we have compared the means of tonographic coefficients during treatment with that of normal eyes, using the t test. Highly significant differences for C_{0-4} and C_{3-7} , but not for the minute volume were found (Table 6). These findings, when compared with those obtained from the study of Table 5 led us to the following conclusions: a) Although the mean of C_{0-4} from our glaucomatous patients was

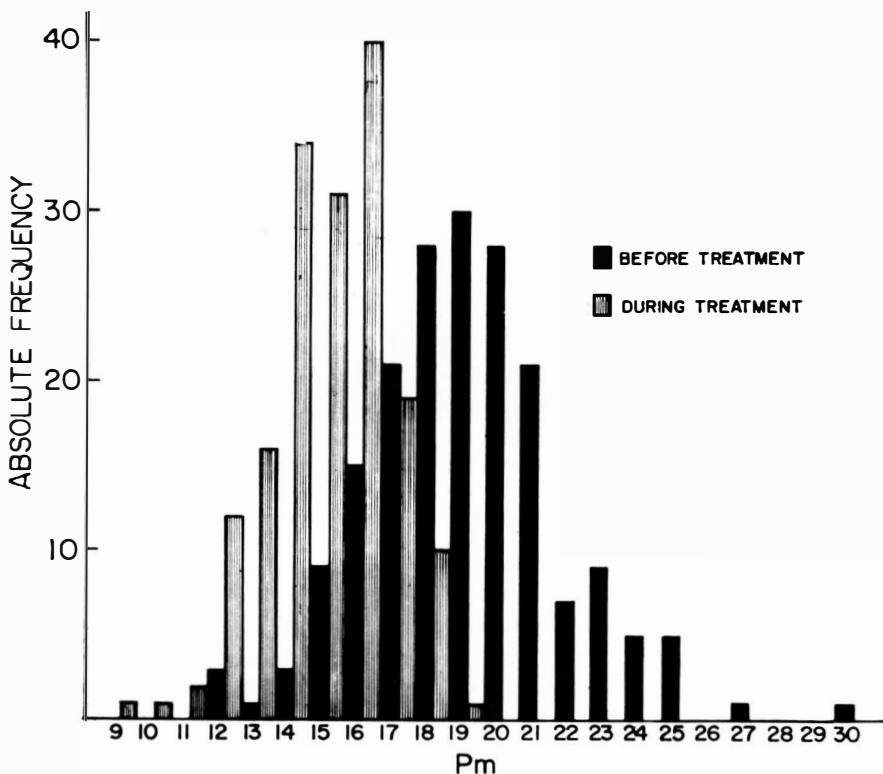


Fig. 1 — Daily Curve of Pressure. Frequency of Pm values in 93 patients (186 eyes) with early chronic simple glaucoma, before and during treatment.

significantly different ($p < 0.001$) but the overlap of the glaucomatous range of C_{0-4} values from the glaucomatous sample fell in the normal range of variation, what limits the use of this coefficient as a semiotic element for the individual patient; b) In relation to the C_{3-7} , the mean was also significantly different ($p < 0.001$) but the overlap of the galucomatous values with those from a normal sample was much smaller. This makes the C_{3-7} more meaningful as a semiotic test for the individual patient than the C_{0-4} .

III — Visual Fields

The careful study of the visual fields, with proper and well applied technique, besides the DCPo, is a fundamental element for the diagnosis and control of the glaucomatous patient.

In this study we have selected 143 patients in whom, at the first examination, the visual fields were normal in both eyes, with just one excep-

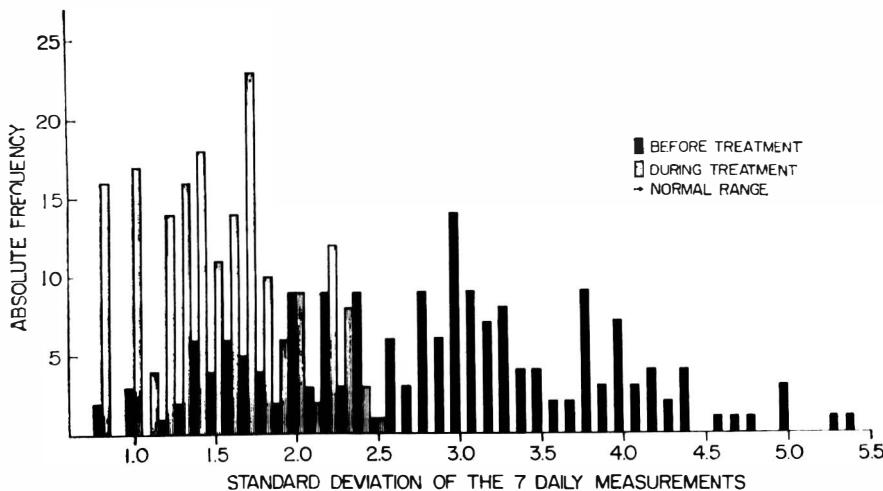


Fig. 2 — Daily Curve of Pressure. Frequency of V values in 93 patients (186 eyes) with early chronic simple glaucoma, before and during treatment.

tion. These patients were followed for 5-15 years for the study of visual field defects due to glaucoma.

We included in the present study one patient (group I) with visual field defect of glaucomatous type since the first examination. However, with good control of the intraocular pressure, the defect did not progress (time of control: 9 years).

In patients older than 60 years, we had always in mind the possibility of occurrence of senile lenticular changes mainly lenticular sclerosis, that could be responsible for the retraction of the internal isopters (specially 2/1) in the Goldmann perimeter. These changes would be independent from the IO pressure level and were not considered significant.

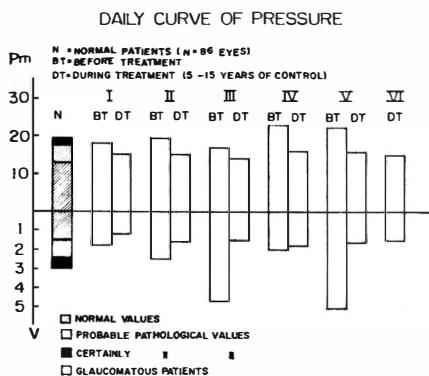


Fig. 3 — Comparison of the mean values of Pm and V in six groups of glaucomatous patients before and during treatment, in relation to a sample of normal patients.

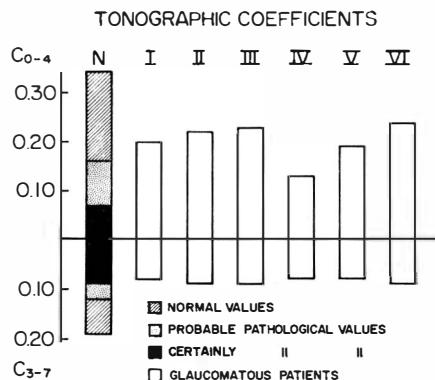


Fig. 4 — Comparison of the mean values of the tonographic coefficients (C_{0-4} and C_{3-7}) in six groups of glaucomatous patients before treatment, in relation to values of a normal sample.

Along the years, 15 patients (10,4%) developed cataract (24 eyes) with worsening of the visual acuity and visual fields (retraction and deformation of the isopters) not related to the glaucoma. The IO pressure was always maintained in satisfactory level and the eye fundus, when seen, did not show an increase of the optic disc cup. In some of these eyes we noted that the IO pressure lowered with the development of the cataract.

The presence of paracentral scotomas, unconnected with the blind spot, was always searched for in the Bjerrum area.

In only 3 eyes of 2 patients we were able to detect a worsening of the visual fields attributed to glaucoma. In one patient (both eyes) the worsening was due to irregular treatment and appeared in 1972, without any further progression. In the other patient, the visual field loss appeared in the left eye despite regular treatment during 8 years, but in this case the DCPo

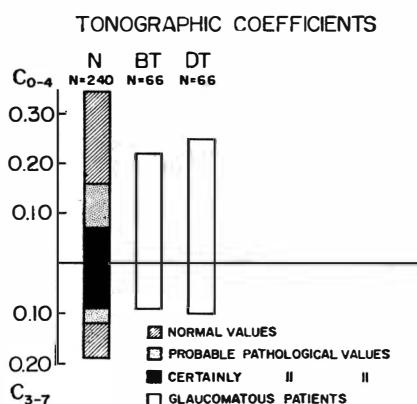
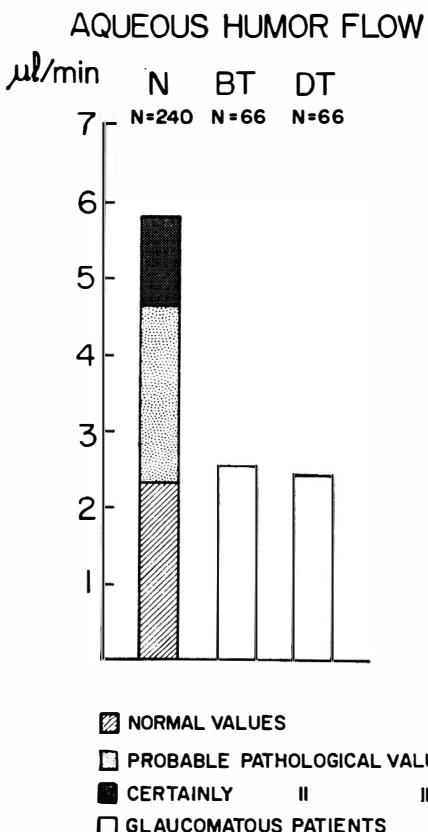


Fig. 5 — Mean C_{0-4} and C_{3-7} from 33 early glaucomatous patients, before and during treatment, compared with values from a normal sample.



6. GRANT, M. G. — Tonographic Methods for measuring the facility and rate of and during treatment, compared with values from a normal sample.

was always slightly abnormal (Fig. 7). This patient has been followed since 1967. The first visual fields were obtained on July, 20th 1967 and the last on March, 20th 1975. On the right eye the visual field has been approximately the same from 1967 to 1975 (Fig. 8), but on the left eye, despite mild concentric retraction in the first examination, we noted a visual field loss in the last examination: peripheral depression, mainly in nasal inferior quadrant and a Ronne's nasal step (Fig. 9). The daily curve of pressure before and during treatment, made annually, showed the difference between both eyes (Fig. 7). The cups were unequal: in the right eye the cup/disc ratio was 0.5 and in the left it was 0.8, the margin of the cup coinciding with the optic disc margin. It is important to refer that: a) This patient had normal systemic arterial pressure; b) There was no difference in ophthalmodynamometric pressures between right and left eyes.

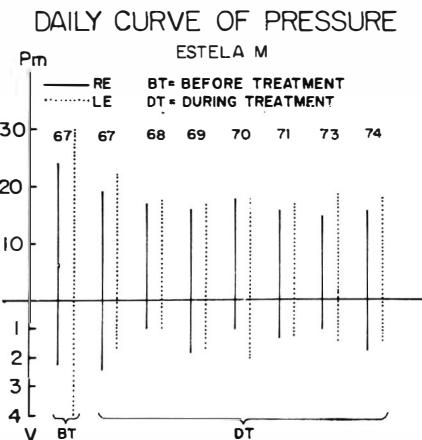


Fig. 7 — DCPo from 1967 to 1975 of the patient who lost visual field in the left eye.

IV — Eye Fundus

Since 1962 we have adopted a criterium for optic disc cup classification: it is based on the comparison between the horizontal diameter of the cup and the horizontal radius of the optic disc; our classification does not differ significantly from the cup/disc ratio suggested by ARMALY (1969).

Our classification is (Fig. 10):

1. Cup 0 = optic disc without cup, or flat.
2. Cup + = The diameter of the cup is smaller than the radius of the optic disc.
3. Cup ++ = The diameter of the cup is equal to the radius of the optic disc.
4. Cup +++ = The diameter of the cup is greater than the radius of the optic disc.
5. Cup ++++ = The diameter of the cup is equal to the diameter of the optic disc (total cup or complet cup).

It is possible to insert grades between the 5 fundamental types, allowing possibilities (in Armaly's classification there are 10 types). The C/D ratio of Armaly is more analytical and therefore somewhat more difficult to evaluate in longitudinal study or when 2 ophthalmologists examined independently the same eye; we can better use Armaly's classification when using retinographies or stereoretinographies.

In the 143 patients studied (286 eyes), the cup/disc ratio was: a) Normal optic discs (0 and +) or C/D < 0.5 in 180 eyes; b) Cup ++ or C/D = 0.5 in 48 eyes; c) Cup +++ or C/D > 0.5 in 58 eyes. (Table 1).

We have sometimes made contradictory evaluations of the C/D ratio in successive controls. For example, in the first examination we analysed the

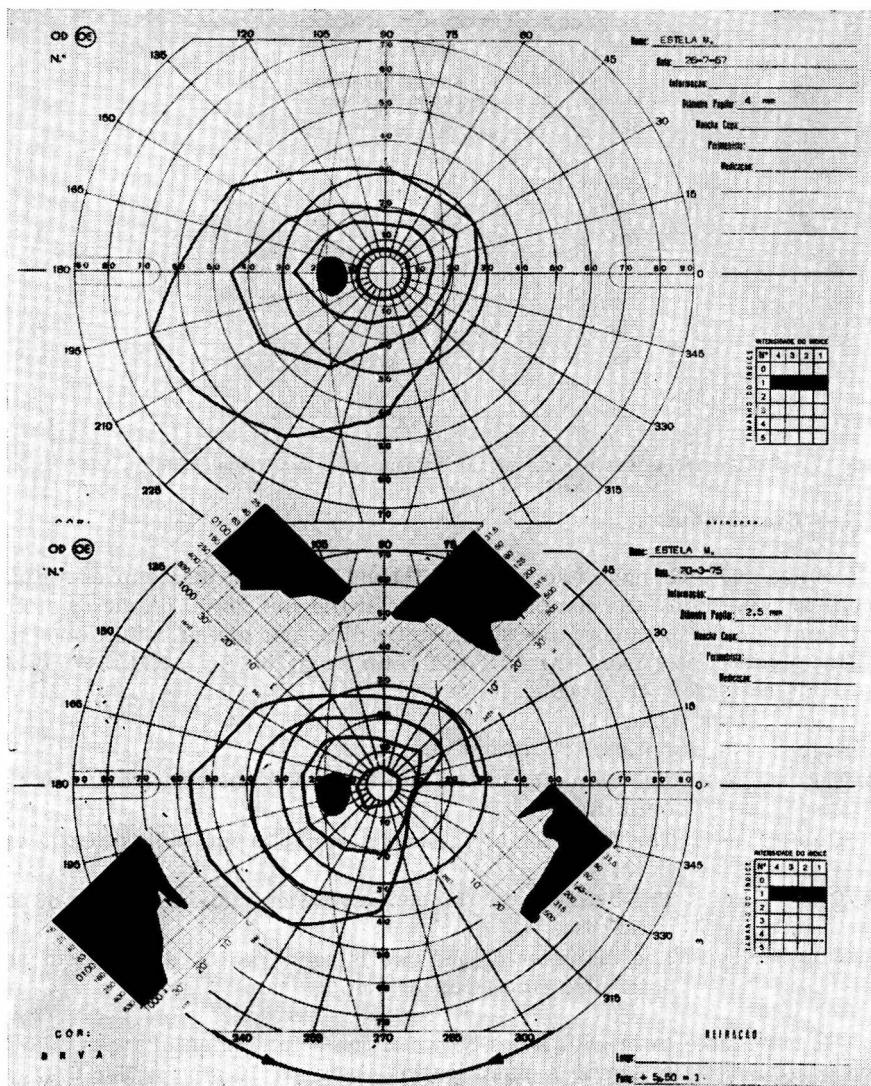
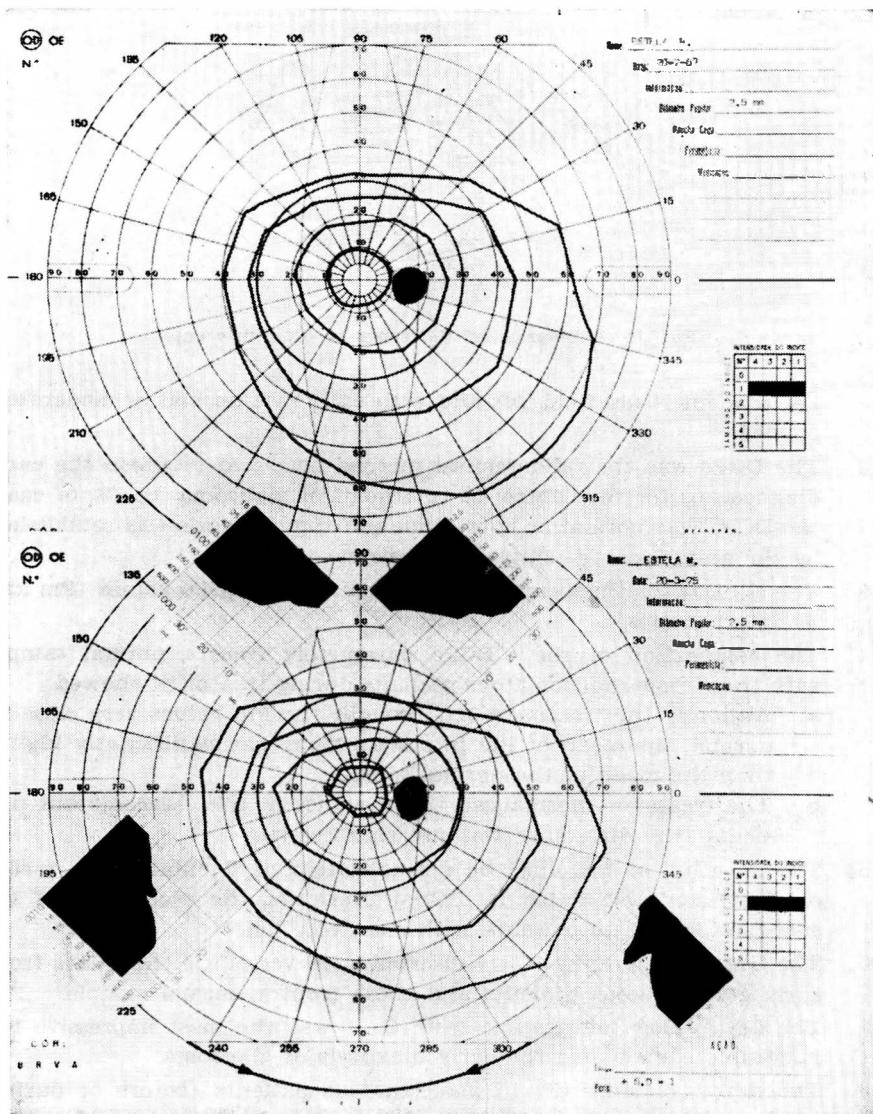


Fig. 8 — Visual fields (kinetic and static) of the right eye (1967 and 1975, respectively) from the same patient of fig 7.

cup as ++ and in a posterior one as +. We have seldom found this variation and it does not lessen the merits of both classifications.

In relation to the "parallelism" between visual field defects and glaucomatous cup, our data do not support, in general, this parallelism (58 eyes with cups greater than 0.5 had no evident visual field defects).



CONCLUSIONS

1. Only 7.8% of the patients, registered in the Glaucoma Clinic during 10 years, were diagnosed as glaucomatous in the hypertensive phase,

TYPES OF OPTIC DISC CUP (in normal and glaucomatous patient)

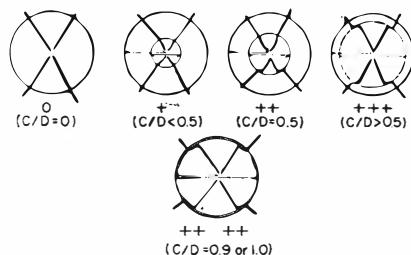


Fig. 10 — Diagram of the types of optic disc cup.

i.e., without visual field loss and with optic disc normal or moderately cupped.

2. The DCPO was the fundamental method either to establish the early diagnosis or for the control of treatment of glaucoma. In 7% of cases the DCPO was normal or borderline and the diagnosis was established by the annual curve (single tonometries).
3. The clinical treatment lowered significantly the DCPO values (Pm and V) in all groups.
4. The comparison of the DCPO parameters from a normal sample with those from glaucomatous patients during treatment showed:
 - a. Although the treatment has brought the Pm values very close to normal, the mean of Pm in our 6 groups was significantly higher than the mean of the normal sample.
 - b. The treatment normalized the V values in the glaucomatous patients (the difference was not significant).
5. The lowering of Pm and the normalization of V obtained by medical treatment (evaluated by DCPO) prevented the occurrence of visual field loss in all patients, with one exception.
6. The Grant tonography (C_{0-1}) discriminated very little the values from early glaucomatous patients and those from a normal sample.
7. The Leydhecker tonographic test (C_{3-7}) was the most impressive tonographic element for the early diagnosis of glaucoma.
8. The minute-volume (F) in glaucomatous patients (before or during treatment) was not significantly different from the values of a normal sample.
9. The Grant tonography and the Leydhecker tonographic test were not useful for the control of treatment.
10. There was no "parallelism" between the C/D ratio and the visual fields in our patients; it is possible that in more advanced phase of the disease it may occur a better correspondence ($C/D > 0.8$ with visual field loss).

SUMMARY

In this paper the Author presents a study of 143 early glaucomatous patients followed from 5 to 15 years with annual daily curve of pressure (DCPo), visual fields and ophthalmoscopy. These 143 patients correspond to 7.8% of the 1837 patients registered in the Glaucoma Clinic in a period of ten years. This is the percentage of patients that were diagnosed as glaucomatous in the hypertensive phase, i.e., without visual field loss and with normal or moderately cupped optic discs.

It is emphasized the importance of DCPo not only for the diagnosis, as well as for the control of treatment. Tonography has limited value for the diagnosis and almost no value for the control of treatment; the tonographic test of Leydhecker (C3-7) is the most important tonographic element for the diagnosis of glaucoma, but it is also useless for the control of treatment.

The treatment modified the parameters of the daily curve of pressure (P_m = arithmetic mean of the seven daily measurements, and V = standard deviation of the 7 daily measurements) as follows:

- a) The P_m values were lowered, and were brought very close to normal. Nevertheless, the mean of the treated glaucomatous patients was yet significantly higher than the mean of a normal sample.
- b) The V values were normalized (the difference in relation to a normal sample was not statistically significant).

REFERENCES

1. ARMALY, M. F. — Ocular Pressure and Visual Fields A ten-year follow-up study. *Arch. Ophth.*, 81: 25-40, 1969.
2. ARMALY, M. F. — Genetic determination of the Cup/Disc ratio of the optic nerve. *Arch. Ophth.*, 78: 35-43, 1967.
3. ARMALY, M. F. — Cup/Disc ratio in early open-angle glaucoma. *Doc. Ophth.*, 26: 526-533, 1969.
4. CALIXTO, N.; SAMPAOLESI, R.; CARVALHO, C. A. and RECA, R. — Valuation of medical therapy of primary glaucoma. 1st South Am. Glaucoma Symp., Bariloche 1966, pp 171-9 (Mod. Probl. Ophth., vol. 6, Karger, Basel/New York, 1968).
5. CALIXTO, N. — Pressão intraocular. Curva Diária de Po. Rígidez parietal. Coeficientes tonográficos (Médias de normalidade em Diferentes grupos etários). Tese de Livre Docência, 1967.
6. GRANT, M. G. — Tonographic Methods for measuring the facility and rate of aqueous flow in human eyes. *Arch. Ophth.*, 44: 204-214, 1950.
7. LEYDHECKER, W. — Ein neues Verfahren der Klinischen Tonographie. *Klin. Mbl. Eugenheilk.*, 132: 77-95, 1958.
8. LEYDHECKER, W. et al. — Der intraokulare Druck gesunder menschlicher Augen. *Klin. Mbl. Augenheilk.*, 133: 662-670, 1958.
9. LINNÉR, E. and STRÖMBERG, U. — Ocular hypertension. A five year study of the total population in a Swedish town skövde. In: Glaucoma Symp. Tutzing Castle 1966, pp 187-214 (Karger, Basel/New York, 1967).
10. LOBSTEIN, A. — Factors affecting the susceptibility of the glaucomatous eye to raised intraocular pressure. 1st South Am. Glaucoma Symp., Bariloche 1966, pp. 73-93 (Mod. Probl. Ophth., vol. 6, Karger Basel/New York, 1968).
11. PORTNEY, G. L. and SOUSA, F. J. — Negative findings on the seven-minute coefficient outflow. *Am. J. Ophth.*, 78: 848-851, 1974.
12. SAMPAOLESI, R. and RECA, R. — La courbe tensionnelle journalière dans le diagnostic précoce du glaucome. *Bull. et Mém. de la Soc. Franç. d'Ophthal.*, 77, 252-261, 1964.
13. WEIGELIN, E. and LOBSTEIN, A. — Ophthalmodynamometry S. Karger, Basel/New York, 1963.