CLINICAL METHOD OF OBSERVING CHANGES IN THE RATE OF FLOW OF AQUEOUS HUMOUR IN THE HUMAN EYE*†

II. IN GLAUCOMA

BY

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IN a previous paper (Langley and MacDonald, 1952), the fluorescein instillation test was described and the results obtained in normal human eyes discussed. It was seen that the instillation of 10 per cent. fluorescein solution into the conjunctival sac resulted in the appearance of the dye in the aqueous humour, and that the concentration in the aqueous of normal eyes fell off slowly and evenly over a period of as long as 24 hours. The concentration was reduced by approximately 1 part per 100 million parts per hour. The level at any moment was held to represent a steady state between the concentration of fluorescein in the cornea and that in the aqueous, modified by the normal steady flow of aqueous; and this flow was responsible for the eventual disappearance of the dye from the anterior chamber. It was also emphasized that any sudden fall in fluorescein concentration indicated an increase in the rate of flow of aqueous, and that drainage of aqueous from the anterior chamber without its replacement by clear fluid would produce no change in the concentration.

In the present paper, the results in glaucomatous eyes are described, and the significance of these results in relation to certain of the known features of the disease is discussed.

METHOD.—The test was carried out as described in the previous paper. Miotic treatment, if used, was withheld for 24 hours before the test. The patient instilled the fluorescein drops himself either on rising on the morning of the test or before retiring the previous evening. In this way the concentration of fluorescein in the aqueous would have reached and passed its maximum before the observations commenced at 9.30 a.m. After a period of observation, a miotic (usually pilocarpine 1 per cent. or 2 per cent. and in some cases eserine $\frac{1}{4}$ per cent.) was instilled and further observations recorded. The fluorescein concentration was estimated by the method of Amsler and Huber (1946) and transposed into terms of actual concentration of the dye from the conversion curve shown in the previous paper. The ocular tension was taken at intervals with a Schiötz X-tonometer, pantocaine 1 per cent. anaesthesia being used for this purpose. Following the instillation of miotics the pupil in some eyes became so small that readings with the usual breadth of the beam of light became difficult, and it was found that when this occurred, the readings could be accurately checked by using the smallest aperture of the Haag-Streit slit lamp. Readings taken with the smallest beam were checked against those taken with the usual aperture in the calibrated apparatus, and were found to be consistently 0.1 amp. lower except in the highest ranges of fluorescein concentration.

* Received for publication May 7, 1952.

†Dedicated to Professor Lindner on the occasion of his 70th birthday.

RESULTS

IN CHRONIC CONGESTIVE GLAUCOMA.—Fifteen patients (29 eyes) were observed for 2 hours, after which pilocarpine 1 or 2 per cent. was instilled and further readings taken. Three eyes had been operated on and the results in these are reported separately below.

In nineteen eyes the tension was low and steady (between 20 and 25 mm. Hg Schiötz) and was associated with either a steady or slightly falling concentration of fluorescein in the aqueous during the initial period of observation.

In two eyes the tension was steady at a high level (68 mm. Hg Schiötz) and was also associated with a steady concentration of fluorescein.

In three eyes the tension was falling spontaneously, and in these the fluorescein concentration fell off at a rate greater than normal.

The two remaining eyes (both in the same subject) showed a falling fluorescein concentration occurring in a rising phase of tension.

The instillation of pilocarpine produced great changes in the concentration of fluorescein. In 24 eyes the concentration fell significantly, and in many cases dramatically, this change being accompanied by a fall of tension which in the majority amounted to only 3 or 4 mm. Hg. One patient arrived for the test with a tension of 68 mm. Hg in both eyes and a fluorescein reading of 2.5 ampères, which represents a level higher than is accounted for in our conversion curve.* In spite of repeated instillations of pilocarpine 2 per cent. and eserine 1 per cent. over 5 hours, the concentration remained steady at about this level and the tension remained high. Subsequently the tension fell to normal after admission to hospital, but we were unable to take readings during this fall. In this case, therefore, the high tension was associated with a relatively stagnant aqueous, as might be expected.

Many of the cases described above demonstrated such a great increase in the rate of flow of aqueous that the dye was completely washed out of the anterior chamber within an hour or so, and in some instances within less than 30 minutes (Fig. 1, see p. 501).

The increased flow of aqueous often manifested itself in an interesting way. Normally, the dye is seen in the anterior chamber in the form of a green flare extending from the back of the cornea to the lens capsule. In many cases this green flare became truncated so that it no longer extended as far back as the lens, and an optically empty zone appeared between the flare and the lens. In some instances the clear zone extended further forward than the mid-point between lens and cornea. A drawing of this phenomenon is reproduced in Fig. 2 (opposite). This effect is believed to be due to an excessive volume of aqueous entering the anterior chamber through the pupil and washing away the dye in its vicinity. The clear zone may remain so for an hour or more until the rate of flow of aqueous settles down, after which the dye again becomes homogeneously distributed.

* See Langley and MacDonald (1952), Fig. 1.

FIG. 2.—Case of glaucoma simplex.
(a) before pilocarpine.
(b) 30 minutes after instillation of pilocarpine.

FIG. 1.—Case of chronic congestive glaucoma. Right eye trephined. Pilocarpine 2 per cent. instilled where indicated by arrow.

FIG. 3.—Case of advanced glaucoma simplex (right eye). A large fall in tension from a high level was not accompanied by any change in fluorescein concentration. The latter fell rapidly during a further drop in tension, and continued to fall off slowly during a subsequent rise.

IN GLAUCOMA SIMPLEX.—In 28 patients (56 eyes) examined, six eyes had been operated on. In the fifty non-operated eyes, it was found that, when the tension was steady or rising, the fluorescein concentration fell at approximately the normal rate. When a significant fall of tension occurred spontaneously, it was accompanied by an increased rate of fall in the fluorescein concentration. An exception to this occurs when the tension is particularly high; here there may be a large spontaneous fall in tension to a level which is still well above normal, while the fluorescein concentration remains unaltered. Fig. 3 shows a spontaneous fall of tension from 90 mm. Hg to 68 mm. Hg, with the fluorescein level remaining steady. A further fall to 59 mm. Hg was accompanied by a fall in fluorescein concentration from 20 to 12 parts per 100 million. The tension subsequently rose again to 68 mm. Hg, and during this rise the rate of flow of aqueous slowed again as was indicated by the fact that fluorescein fell by only 2 parts per 100 million in 4 hours. This would appear to indicate that, in cases with a high tension, the circulation of aqueous through the anterior chamber is considerably retarded, but when the tension falls sufficiently the outflow of aqueous is allowed to proceed, and does so at a rate greater than normal.

The instillation of miotics again had a profound effect in the majority of cases. Thus in 47 out of the fifty non-operated eyes, the fluorescein concentration was reduced by 50 per cent. or more in less than an hour.

FIG. 4.—Case of bilateral glaucoma simplex. Pilocarpine 2 per cent. instilled where indicated by arrow caused a fall in tension and an increased flow of aqueous which washed the fluorescein out of the anterior chamber. Later the flow of aqueous slowed down, allowing more fluorescein to enter the aqueous from the cornea.

The dye was completely washed out of the anterior chamber in many eyes, and truncation of the green flare was observed in many others. Fig. 4 shows a case in which the instillation of pilocarpine 2 per cent. resulted in a fall of fluorescein concentration from a high level to zero in both eyes within 30 min., the tension falling at the same time. The subsequent slowing of the flow of aqueous allowed the fluorescein level to rise again.

Fig. 5 shows a case in which was seen the phenomenon of truncation of the flare. Following the instillation of pilocarpine 2 per cent., the reading in that part of the flare nearest the cornea was 6.5 parts per 100 million whereas that near the lens was zero. After a further 40 min., the dye again became evenly mixed, the reading throughout the whole depth of the anterior chamber being 7.5 parts per 100 million.

FIG. 5(a).

FIG. 5(b).

FIG. 5.—Eye in which truncation of the flare was observed. After the instillation of pilocarpine, the concentration of fluorescein near the lens (b) fell to zero, whereas that near the cornea (a) was less altered (see Fig. 5b). Subsequently the dye again became homogeneously mixed.

IN OPERATED EYES.—Three eyes had been operated on successfully for congestive glaucoma, one having been trephined and two having had a broad

iridectomy. The tension was low and steady and was accompanied by a steady fluorescein level. The instillation of pilocarpine produced no fall in the fluorescein concentration but caused the tension to fall slightly. These eyes therefore behaved in a manner similar to that of the normal eye. The results in a successfully operated eye (Fig. 1, right eye) may be compared with those in the fellow eye.

Six eyes had been operated on for glaucoma simplex, three of which could be regarded as clinically successful, the tension remaining below 25 mm. Hg over the 24 hours. Two of these eyes had been trephined and one had had a flap sclerotomy. The tension in the trephined eyes remained steady and the fluorescein concentration either fell off at the normal rate or remained unaltered even after pilocarpine or eserine was instilled. The other successful case showed a spontaneous drop in tension from 16 to 13 mm. Hg, this small change being accompanied by a large fall in the fluorescein level from 20 to 10 parts per 100 million in 2 hours. This case (Fig. 6) shows that although the operation had damped down the height and amplitude of the variations in tension, there still remained a tendency to spontaneous acceleration in the rate of flow of aqueous.

The three eyes in which the operation was clinically unsuccessful were interesting. One case had had a complete iridectomy, yet the tension still rose to 40 mm. Hg at times during the day. Miotics produced a marked fall in fluorescein concentration and a fall in tension. The second case (a flap sclerotomy) showed a rapid spontaneous fall in fluorescein concentration with a tension steady at 35 mm. Hg. A miotic was not used on this case. The third eye was one which had been trephined on two occasions because the first operation had not altered the height or variations in tension over the 24 hours. As the first trephine hole was blocked with iris tissue, the operation had been repeated at another site, and although the second trephine hole was gonioscopically patent and the overlying conjunctiva oedematous, the behaviour of the tension was again little altered. In this eye the fluorescein concentration fell during a rise in tension from 40 to 45 mm. Hg. A subsequent spontaneous fall to 30 mm. Hg was not accompanied by any further change in the fluorescein level. The results in this eye could be explained by a rapid flow of aqueous producing both a rise in tension and a fall in fluorescein concentration, the subsequent slowing down of the flow allowing the tension to fall and the fluorescein level to remain stationary.

FIG. 6.—Spontaneous changes in an eye with glaucoma simplex which had been successfully operated upon. Fluorescein had been instilled 12 hrs previously. A large drop in the concentration of fluorescein accompanied a small change in tension.

It may be that in some cases of glaucoma the variations in tension are due to periods of increased formation of aqueous.

DISCUSSION

Observations on aqueous veins have established that the outflow of aqueous in glaucomatous eyes is not constant but varies according to whether the tension is in a rising or falling phase (Thomassen, 1947; Thomassen, Perkins, and Dobree, 1950). These findings can be correlated with the results observed in the fluorescein instillation test. When the tension is in a rising phase, aqueous veins are often observed to fill with blood. In many of our cases in the same phase of tension, the flow of aqueous through the anterior chamber was retarded or proceeded at the normal rate. A falling phase of tension was usually accompanied by a more rapid flow of aqueous; in the same phase of tension, aqueous veins would be expected to be clear.

In some cases, however, it appeared that a rapid flow of aqueous may have been responsible for a rise in tension. In others, when the tension was very high, a fall was not accompanied by any demonstrable flow of aqueous. In such an event, a considerable fall in tension could be accomplished simply by the release of a very small volume of aqueous from the eye, the contents of the anterior chamber remaining relatively stagnant.

In glaucoma, miotics produce a great increase in the rate of flow of aqueous through the anterior chamber, and they are known to cause the aqueous veins to become clear (Ascher, 1942; Gartner, 1944). Thomassen and others (1950) confirmed the latter observation only if the miotic caused a fall of ocular tension.

It may be suggested that the miotic produces the sharp fall in fluorescein concentration by causing constriction of the pupil, thus presenting a larger surface area of iris tissue through which the dye could be absorbed. This possibility is discounted by our observations on glaucomatous eyes in which there was marked atrophy of the iris, or iridoschisis, or in which a large iridectomy had been performed. In addition, we were able to perform the test on a case of glaucoma with congenital aniridia in which the stump of the iris was diminutive and did not obstruct the broad chamber angle in any part. In all these cases, miotics produced the same effects as those seen in glaucomatous eyes with normal irides. Moreover, in those cases where truncation of the flare was visible, the dye could actually be seen to be displaced by the clear aqueous entering the anterior chamber through the pupil.

Miller (1952) reports that withdrawal of miotic treatment in cases of congestive glaucoma often reveals a lessened ability to compensate for a tendency to a rise in tension, whereas before the treatment was begun, the eyes had recovered spontaneously from innumerable minor congestive attacks over many years. To establish whether the effects of miotics were

related to previous miotic treatment, the results in twelve of our cases which had never been treated were compared with the remainder. In addition, four cases were investigated before and after a period of treatment. No significant differences were noted.

At this stage in this investigation, it cannot be decided whether the test will prove useful from the clinical point of view. Where a rapid flow of aqueous occurs spontaneously or is produced by the instillation of a miotic, the eye can be said to differ from the normal; and glaucoma is one condition in which such effects are found.

The test, however, does provide a means of studying some aspects of the hydrodynamics of the living glaucomatous eye, and further investigations may produce additional information.

SUMMARY

The results of the fluorescein instillation test in glaucomatous eyes are reported.

These eyes differ from the normal in that the rate of flow of aqueous does not remain steady, but undergoes fluctuations throughout the day which are reflected in the variations of ocular tension. Miotic drugs commonly produce a great increase in the rate of flow of aqueous with a simultaneous fall in tension.

An eye which has been operated on successfully for glaucoma usually shows responses similar to the normal eye, whereas in clinically unsuccessful operations the rate of flow of aqueous continues to vary spontaneously or can be made to do so by the instillation of a miotic.

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