CLOSED - ANGLE GLAUCOMA

A study of the Mechanism

of Angle Closure.

by

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C O N T E N T S

INTRODUCTION

Since the first systematic description of the disease was published by Sir William McKenzie in 1830 much has been written on the subject of glaucoma. Even now, more than one hundred years later, in spite of an enormous volume of experimental work a complete understanding of the condition has yet to be reached.

One of the main stumbling blocks to the attainment of this understanding has been a lack of recognition that primary glaucoma is not one disease but several, and much of the confusion of terminology and of concept has been due to an attempt to fit the various clinical appearances of the several types of primary glaucoma into imagined stages in the development of a single disease entity. It is now generally agreed that cases of primary glaucoma can be subdivided into two main types, each so different from the other that they may be considered to be entirely different diseases.

The first of these conditions, now known as closed angle glaucoma* (Duke Elder, 1955) is characterised by a shallow anterior chamber, a narrow entrance to

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* See note on terminology, p. 140

to the angle of the anterior chamber and a tendency to develope sudden rises in ocular tension apparently precipitated by mechanical obstruction of the angle. This obstruction is itself brought about by several factors whose mode of action has not yet been fully elucidated and of which more will be said later.

In the second condition, chronic simple glaucoma, the raised ocular tension is thought to be due to a more or less permanent interference with the egress of aqueous humour from the eye. The exact location of the obstruction in this disease, however, has not yet been determined. Clinically, the condition is characterised by its insidious onset, cupping of the optic disc with increasing visual field loss and the fact that the depth of the anterior chamber and the width of the angle of the anterior chamber is not different from that found in normal eyes.

Difficulty in diagnosis arises in those cases of closed angle glaucoma which do not develope an acute attack of the disease, and may, as a result mimic chronic simple glaucoma, and in those few eyes which are affected by both conditions simultaneously.

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It is mainly with some of the problems of closed angle glaucoma that this thesis will deal.

SUMMARY

Presented in this thesis is a new conception of the mechanism underlying the development of closed angle glaucoma. It is based upon a study of the ocular tension and facility of aqueous outflow in normal eyes and those affected by the disease, in response to provocative tests, together with observations upon cases of chronic closed angle glaucoma and upon the apparently healthy eyes of cases wherein the disease is unilateral.

The development of currently accepted views on the aetiology of closed angle glaucoma is traced in a review of the literature on the subject and it is shown that the disease is believed to be due to mechanical obstruction of the angle of the anterior chamber by the root of the iris in an eye wherein the lens is disproportionately large. It has been generally held until now that in an eye affected by this disease the ocular tension and facility of aqueous outflow between attacks of hypertension are completely normal and that the angle of the anterior chamber at these times is open and functioning freely. That this view is erroneous

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in many cases, however, is the deduction to be drawn from the work presented in this thesis, for all the evidence supports the view that even in the early stages of the disease a variable portion of the angle of the anterior chamber is habitually closed and that the ocular tension and facility of aqueous outflow in such an eye, although still within the accepted limits of normality, is in fact already abnormal for the eye in question.

The darkroom test is studied in detail and an analysis of the results of the test on normal eyes and those affected by closed angle glaucoma is presented. It is shown, contrary to the generally accepted view, that the rise in ocular tension occasioned by the test is influenced by the initial tension in the eye tested and probably by the degree of angle closure existing prior to the test. It is calculated that a rise in ocular tension of over 8.5 mm. Hg with the darkroom test is evidence in favour of a diagnosis of closed angle glaucoma.

The development of the tonographic method of measuring the facility of aqueous outflow is outlined

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and a new provocative test, the "darkroom outflow test" is described. In this test, measurements of the facility of aqueous outflow are made before and after one hour in the dark; the occurrence of angle closure being indicated by a measurable fall in the level of aqueous outflow. From a study of the results of this test on normal eyes and those affected by closed angle glaucoma it is concluded that a fall in the outflow level of at least 30% with this test is of significance. Contrary to the generally accepted view, it is shown that in cases of closed angle glaucoma, even where the resting ocular tension is within normal limits, the facility of outflow is lower than that found in comparable normal eyes, indicating the existance of some degree of angle closure in the affected eyes. It is also demonstrated that the rise in ocular tension occuring with the darkroom test is directly related to the level of aqueous outflow existing prior to the test and thus to the degree of angle closure present at that time.

From a study of the effect of the darkroom test and the darkroom outflow test on normal eyes it is concluded, contrary to the generally accepted view,

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that variations in the rate of aqueous inflow play a more important part in the causation of changes in ocular tension than do alterations in the rate of aqueous outflow.

It is shown that the operation of peripheral iridectomy on eyes with closed angle glaucoma completely prevents the development of closure of the angle on provocation with the darkroom outflow test.

It is postulated that advanced chronic closed angle glaucoma with cupping of the disc and visual field loss may develop insiduously by a gradual extension of the area of occlusion of the angle which commences early in the disease and that this advanced stage of the disease need not necessarily indicate the presence of goniosynechiae as is at present thought. A study of the ocular tension, facility of aqueous outflow and appearance of the angle after the operation of peripheral iridectomy in such cases supports this view.

It is found that a large number of apparently healthy "second" eyes in cases of unilateral closed angle glaucoma are in fact affected by the disease and that the absence of symptoms is no guide to whether or

not an eye under consideration is so affected.

Finally the results of all these separate investigations are correlated and views, differing from those generally accepted, on the natural history of closed angle glaucoma in both its acute and chronic forms are presented.

CHAPTER I

REVIEW OF THE LITERATURE

SUMMARY

The literature apertaining to closed angle glaucoma is reviewed and the development of current views on the mechanism of the disease outlined.

In his original description of glaucoma, McKenzie (1830) noted that in this condition there was usually an abnormal hardness of the eye, a finding which he ascribed to the formation of a superabundance of aqueous fluid. He also noted that some cases ran an acute and others a chronic course. von Graefe (1857) describing the operation of iridectomy also noted the acute and chronic forms of the disease and stated that the anterior chamber was frequently shallow in eyes affected by glaucoma. Priestly Smith (1887) pointed out that shallowness of the anterior chamber was not found in all eyes affected by glaucoma but was characteristic of the

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acute congestive form of the disease.

In 1922 Raeder attempted to classify glaucoma into a group of cases in which the anterior chamber was shallow and one in which it was of normal depth. The significance of shallowness of the anterior chamber became more apparent as the result of work by Rosegren (1930-31). This author measured the depth of the anterior chamber in a large number of normal and glaucomatous eyes. In the normal eyes, he found that the depth of the anterior chamber diminished with age and that when, taking this factor into account, a comparison was made between the glaucomatous and normal eyes, the depth of the anterior chamber was found to be significantly less in the former. On further analysis he found that this difference was due to the presence in this group of glaucomatous eyes of a small number of eyes in which the anterior chamber was extremely shallow. These cases almost without exception were affected by so-called congestive glaucoma. When the depth of the anterior chamber in the remaining non-congestive eyes was compared with that in the normal series, no significant

difference was found. From these observations it became apparent that cases of primary glaucoma in which the anterior chamber was shallow were of a different type to those in which the anterior chamber was of normal depth.

The relationship between shallowness of the anterior chamber and the raised ocular tension in glaucoma has been the subject of much controversy, some authors believing the decreased depth of the anterior chamber to be the result of raised ocular tension, others holding that it was an anatomical pecularity of the affected eyes and itself a factor predisposing to raised ocular tension. One of the earliest supporters of the view that shallowness of the anterior chamber was the result rather than the cause of raised ocular tension was von Graefe (1857) who believed that a high intra-ocular pressure by making the eye more spherical would flatten the corneal curve thus reducing the depth of the anterior chamber. These postulated changes in corneal curvature could, however, not be supported by actual measurement (Scheslske, 1864;

Coccius ....

Coccius, 1872; Eissen, 1888).

A more popular hypothesis and one which again received support from von Graefe (1857) was that the raised ocular tension in glaucoma was due to an increase in the volume of the vitreous, which in turn resulted in an anterior displacement of the lens. Rheindorf (1887) believed that swelling of the vitreous was due to retention of fluid in the vitreous chamber as the result of decreased permeability of the zonule. Priestly Smith (1897) also thought that there was an anterior displacement of the lens during an acute attack of glaucoma but he believed that the anterior chamber in these cases was already abnormally shallow before the development of the acute attack.

Although it is true that a change in the volume of the vitreous can be brought about by altering its pH there is no evidence that this can occur in vivo and in fact there is good evidence to show that it does not. Baurman (1924) and Lobeck (1929) found that the pH change necessary to alter the volume of the vitreous was well outside that which would obtain in vivo. Schmerl (1928)

was unable to demonstrate any significant alteration in the pH of the blood in cases of glaucoma. Duke Elder, Davson and Benham (1936) showed that the swelling pressure of the vitreous from an eye known to have had glaucoma was less than 2 mm. of saline even when dehydrated by over 99%. More recently von Sallman (1941) has shown that although the volume of the vitreous is increased in the very high and very low pH range it is actually less at a pH just above and just below 7 than it is at neutrality, i.e., within the pH range expected in the living eye.

It may be taken therefore that the depth of the anterior chamber does not reflect changes in the volume of the vitreous although as late as 1955, the opinion that there was oedema and swelling of the vitreous in acute glaucoma was expressed by Sheie (see Newell, 1955).

Gronhölm (1910) suggested that shallowness of the anterior chamber resulted from swelling of the ciliary body in glaucoma. Oedema and swelling of the ciliary processes in acute glaucoma were

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demonstrated histologically by Friedenwald (1930) but as Törnquist (1953) has observed, in cyclitis where swelling of the ciliary body is probably at its maximum the anterior chamber is usually deep.

The opposite view, that the shallow anterior chamber found in some cases of glaucoma was an anatomical pecularity of the affected eye and that this defect predisposed to the development of the disease was strongly supported by Priestly Smith (1883-1910) who was of the opinion that in these eyes there was a disproportion between the size of the lens and that of the eye. This theory had earlier been suggested by Bowman (1862) but was greatly strengthened by the experimental work of Priestly Smith who, in 1883, demonstrated the continuous growth of the lens throughout life and correlated this with the increased incidence of glaucoma with advancing years (1886). He also noted that the corneal diameter of glaucomatous eyes tended to be smaller than that seen in normal eyes (1891) and that this tendency affected both eyes even when the glaucomatous process was unilateral.

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He pointed out (1891) that although hypermetropia was common in eyes affected by glaucoma, it was the relative size of the lens to the eye rather than the existence of this refractive error which resulted in shallowness of the anterior chamber. Czermak, (1897) also observed that in unilateral acute glaucoma the anterior chamber was shallow in the unaffected as well as the affected eye. He too believed this to be due to a disproportionately large lens but thought that in these cases there was superadded a failure to form sufficient aqueous fluid. It says much for the observations of Priestly Smith that although the mechanism underlying closed angle glaucoma is more fully understood now than it was sixty years ago, current thought still regards disproportion between the size of the lens and that of the eye to be the major predisposing factor in the development of this type of glaucoma.

The accurate measurements of Rosengren (1930-31) virtually proved that shallowness of the anterior chamber was a primary condition and one which was probably an aetiological factor in the

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development of what was then known as congestive glaucoma. He measured the depth of the anterior chamber in four cases before and during an acute "congestive" attack and found no significant alteration in the axial depth of the anterior chamber with the attack. He correlated the respective depths of the anterior chambers of each eye in cases of unilateral glaucoma and showed that in general the two eyes were anatomically similar as regards the depth of the anterior chamber. Sugar (1951) was of the opinion that in unilateral acute primary glaucoma a deep anterior chamber in the unaffected eye was of rare occurrence if indeed it occurred at all.

In a recent study, Törnquist (1953) has shown that a shallow anterior chamber is commoner in the eyes of relatives of patients suffering from acute glaucoma than in the eyes of other normal persons of corresponding age. He has also demonstrated by a study of the eyes of uniovular and binovular twins that the structures which determine the depth of the anterior chamber are influenced more by genetic than environmental factors, again suggesting that shallowness of the anterior chamber is a pre-existing and predisposing factor in acute

glaucoma ....

glaucoma. The same author (1957) has shown that the corneal radius is significantly smaller in eyes with closed angle glaucoma than in comparable normal eyes.

It is thus clear that shallowness of the anterior chamber is an anatomical peculiarity of some eyes and most probably determined by genetic factors. In addition, the depth of the anterior chamber becomes progressively less as the lens increases in size with passing years, and this eventually predisposes to the development of acute glaucoma in affected eyes.

An explanation of the way in which shallowness of the anterior chamber might lead to glaucoma had to await the development of gonioscopy. Attention was first drawn to the angle of the anterior chamber when Leber (1873) demonstrated by the injection of dyes that the aqueous humour passed by way of the angle of the anterior chamber to be absorbed in the canal of Schlemm. The independent discovery of peripheral anterior synechiae in eyes with long standing glaucoma by Knies (1876) and Weber (1877) appeared to offer an explanation of the raised ocular tension in glaucoma until it was proved that these synechiae were only present in some

cases of glaucoma and in fact appeared to be the result rather than the cause of the disease (Elschnig, 1896; Priestly Smith, 1910; Reese, 1933).

Although the anatomy of the angle of the anterior chamber had been described in detail by Rochon-Duvingeaud (1892) it was not until 1914 that examination of the angle in the living eye was achieved by Salzman who not only described the appearance of the normal angle but was able to give a description of such abnormalities as peripheral anterior synechiae. An earlier attempt to see the angle by ophthalmoscopy and indentation of globe was made by Trantas (1907) but this author was more particularly interested in the appearance of the pars plana ciliaris than that of the angle of the anterior chamber. Further development of the method devised by Salzman was carried out by Koeppe (1920) and Troncoso (1925). The last author suggested the now generally used term, "gonioscopy" to describe the procedure. Troncoso (1925) noted that the width of angle of the anterior chamber varied greatly from eye to eye and that it appeared to be greater in youth than in old age. He could find no correlation between the occurrence

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of goniosynechiae and any particular type of glaucoma.

One of the greatest advances in the understanding of glaucoma came with the recognition by Barkan (1936-38) that primary glaucoma could be divided into two main groups on the basis of the width of the angle of the anterior chamber. He designated these groups wide angle and narrow angle glaucoma and showed that in the latter group, the ocular tension remained within normal limits so long as the entrance to the angle of the anterior chamber was unobstructed by the root of the iris. When, however, the root of the iris closed the entrance to the angle there occurred a precipitate rise in ocular tension which was restored to normal levels on the re-opening of the angle by the use of miotics or following an iridectomy. Failure of the ocular tension to return to normal occurred if goniosynechiae had formed during the period that the angle had been closed. In the group of cases designated wide angle glaucoma no such tendency for mechanical obstruction of the angle to occur was demonstrable.

The suggestion that the raised ocular tension in what had previously been known as congestive glaucoma

was due to mechanical obstruction of the filtration angle was strongly supported by various workers. Bangaerter and Goldmann (1941) showed that in a group of eyes affected by frank or prodromal acute glaucoma, the ocular tension was high when the angle was closed but fell to normal again when the angle reopened. Sugar (1941) stated that "all evidence indicates that in cases of acute congestive glaucoma the angle is normal before the onset of the attack but is closed during the attack". Kronfeld (1949) in a review of current thought at that time, noted that narrow angle glaucoma was distinguished by "rises of ocular tension due to transient reversible obstructions of the entrance to the chamber angle". He thought that these obstructions were dependant upon "a pre-existing chronic narrowness of the passage into the angle" and "the action of acute secondary angle crowding factors".

Attention was then turned from the possible reasons for the existence of a shallow anterior chamber to a consideration of the factors responsible for narrowness of the angle of the anterior chamber. Although it was recognised that the depth of the anterior chamber and the width of the angle were probably directly related,

Gradle ....

Gradle and Sugar (1940) were able to show by direct measurement that this was not always the case. While they found a gross correlation between the axial depth of the anterior chamber and the width of the angle of the chamber (estimated by "goniometry") they pointed out that in some eyes a deep anterior chamber was associated with a narrow entrance to the angle.

Most authors (Barkan, 1936; Sugar, 1941) stressed the importance of a disproportionately large lens in causing narrowness of the angle, believing this narrowness to be due entirely to an anterior displacement of the plane of the iris. An eye with a large lens and a relatively small cornea is likely to be hypermetropic and the high incidence of hypermetropia in eyes subject to acute glaucoma was pointed out by several workers (Rosengren, 1930-31; Hird, 1933; Sugar, 1941: 42: 47).

Although it was realised that in an eye in which the lens was disproportionately large the entrance to the angle of the anterior chamber would be narrowed by the consequent anterior displacement of the iris, an alternative explanation for the occurrence of a narrow angle in these cases had already been postulated by

Curran (1920). In the normal eye there is a constant flow of aqueous humour from the posterior chamber, through the pupil to the anterior chamber. For this flow to occur there must be a pressure gradient from the posterior to the anterior chamber. The fact that the aqueous pressure behind the iris is greater than that in front of it was demonstrated by Ulbrich (1908) and Heine (1913) each of whom described a case in which part of the iris stroma was weaker than the rest, noting that the weakened area bulged towards the anterior chamber especially when the pupil in the affected eye was constricted by the instillation of physostygine.

A similar case of congenital aplasia of an area of the iris was described by Urbanek (1922). Miller (1956) published details of a case of closed-angle glaucoma in which an attempted peripheral iridectomy resulted in the removal of only part of the iris stroma leaving the pigment epithelium intact. In this case also, bulging of the weakened area towards the anterior chamber was very noticeable, and demonstrated the fact that in an eye affected by closed-angle glaucoma the pressure in the posterior chamber is markedly higher than that in

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anterior. Priestly Smith (1910) noted that there was a definite resistance to the passage of aqueous fluid from the posterior chamber to the anterior and postulated that this was due to the close apposition of the pupillary margin of the iris to the anterior lens capsule. Curran (1920) advanced the theory that in glaucoma where the anterior chamber was shallow and the lens large the consequent area of contact between the iris and the anterior lens capsule would be much greater than in the normal eye. The tonic action of the sphincter pupillae in such an eye would obstruct the flow of aqueous from the posterior to the anterior chamber so that the pressure in the posterior chamber might be high enough to balloon the periphery of the iris forwards to obstruct the entrance to the angle, thus preventing the normal egress of aqueous and precipitating a rise in ocular tension. He suggested that the efficacy of an iridectomy in cases of acute glaucoma depended upon the equalisation of the pressures in the anterior and posterior chambers.

Bænziger (1922) was able to prevent sub-acute glaucomatous attacks in one patient by performing a peripheral iridectomy. He too thought that acute glaucoma was

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due to an increase in the pressure within the posterior chamber and that this forced the iris root into contact with the cornea.

Chandler (1952) supported the mechanism of "relative pupillary block" postulated by Curran. He noted that the gonioscopic appearance of eyes affected by closed-angle glaucoma was consistent with the existence of a degree of iris bombé. He was able to show that in these eyes a peripheral iridectomy, by collapsing this iris bombé, was followed by the reopening of the whole of the previously closed angle. He confirmed the earlier work of Curran that it was impossible to provoke a further attack of acute glaucoma in an eye upon which a peripheral iridectomy had been performed.

That true iris bombé results in closure of the angle of the anterior chamber and a secondary rise in ocular tension had been known from clinical experience for a long time. Scheie and Fraÿer (1950) found that when air was injected into the anterior chamber of a rabbit's eye, the resulting obstruction to the flow of aqueous fluid through the pupil was followed consistently by the development of an iris bombé and an acute rise

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in ocular tension. Barkan (1947) had previously noted that in the operation of cyclodialysis with injection of air into the anterior chamber, the bubble of air so introduced could obstruct the normal flow of aqueous through the pupil and lead to the formation of an iris bombé and closure of the angle of anterior chamber. The iris bombé would collapse and the ocular tension return to normal if the bubble were displaced from the pupil area by a suitable alteration in the position of the patient's head.

Haas and Scheie (1952) used the operation of peripheral iridectomy to treat their early cases of closed angle glaucoma. They found that when the ocular tension in these cases was raised the angle of the anterior chamber was invariably closed but after the iridectomy had been performed the previously closed angle reopened, not only in the operated sector but in the whole circumference of the anterior chamber.

Barkan (1954) made a detailed study of the periphery of the iris in glaucomatous and normal eyes. He noted an anterior convexity of the iris in all hypermetropic and emmetropic eyes but not in myopic eyes. (This

convexity he found to become more marked with the pupil in miosis.) He noted also that this "physiological iris bombé" was much more marked in the eyes of older patients and was apparently absent from the eyes of children and those in whom the anterior chamber was of greater than average axial depth. He correlated the flat appearance of the iris in children with their greater average depth of anterior chamber and assumed that in these eyes there was a minimal area of contact between the iris and anterior lens capsule.

Barkan believed that an anterior displacement of the lens was the main factor in the production of increased pupillary resistance to aqueous flow. He regarded a disproportion in the size of the lens as an alternative aetiological factor and was of the opinion that both the position and the size of the lens could contribute to the closure of the angle by the root of the iris.

His belief that the pupillary block in eyes affected by closed-angle glaucoma was due to an anterior displacement of the lens was based on his measurements of the axial depth of the anterior chamber in such eyes. He found that over the course of years the axial depth

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of the anterior chamber in these eyes became noticeably less. This could, however, have been due merely to the known increase in the thickness of the lens which occurs with advancing years. He also thought that in closed-angle glaucoma after a peripheral iridectomy there was a deepening of the anterior chamber due to a backward movement of the lens. While it is true that the periphery of the anterior chamber deepens with the abolition of the iris bombe in these eyes, most workers have been unable to show any axial deepening of the anterior chamber after this operation. As has already been noted, Rosengren (1930) was unable to show any alteration in the depth of the anterior chamber before and after an acute attack of glaucoma and Tørnquist (1956) in a recent paper found no significant change in the depth of the anterior chamber following iridectomy in closed-angle glaucoma.

That an anteriorly placed lens can cause pupillary block and iris bombé, however, was clearly demonstrated by Barkan (1953) who described a case of secondary glaucoma in which the lens was drawn forward by a fibrous band arising from the cornea and inserted into the anterior

lens capsule. In this eye although there was marked iris bombé and closure of the angle by the iris root the appearance of the angle returned to normal and the iris bombé disappaared when the fibrous band was divided, allowing the lens to move back into what was presumably its normal position.

Whether in closed-angle glaucoma an anterior displacement of the lens does account in part for shallowness of the anterior chamber or whether the iris bombé is entirely the result of the lens being too large is still undecided, although most workers favour the latter rather than the former view. The fact that following an iridectomy for acute glaucoma, there is usually little change in the degree of hypermetropia would suggest that there is no backward movement of the lens as a result of the operation.

Thus was evolved the concept that in closed-angle glaucoma the entrance to the angle of the anterior chamber was basically narrow doe to the anatomical configuration of the affected eye. This narrowing of the entrance to the angle was thought usually to be due to increased resistance to the flow of aqueous through the pupil and the occurrence of physiological

iris bombé. In some cases of closed-angle glaucoma (20% of the total according to Barkan, 1954) however the angle of the anterior chamber was seen to be narrow although there was no evidence of iris bombé.

The existence in any eye of a narrow angle however does not necessarily mean that the eye is affected by closed-angle glaucoma. It is only when the entrance to the angle has become so narrow that it can be obstructed by secondary angle crowding factors that one can speak of such an eye as being affected by closed-angle glaucoma.

Of the factors which determine whether a previously narrow but open angle will be converted into a closed one, changes in the size of the pupil are undoubtedly important. It has long been known that dilatation of the pupil by a mydriatic may be followed by an attack of acute glaucoma in a suitably predisposed eye. Derby (1867) published details of two cases in which an acute rise in ocular tension was precipitated by the local use of atropine drops. In the affected eyes of each of these cases the anterior chamber was noticeably shallow. This author also quoted a similar case recorded earlier by Wharton Jones (1865). Gronholm (1910) noted that

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in some cases of glaucoma the ocular tension rose when the patient was kept in a darkened room and fell again when the eyes were exposed to bright light. He correlated these changes in ocular tension with alterations in pupillary diameter. He also found that a mydriatic instilled into an affected eye was followed by a rise in ocular tension and a miotic by a fall in tension. Priestly Smith (1910) believed that pupillary dilatation could cause mechanical obstruction of the angle of the anterior chamber but thought that this effect was not of great significance in the pathogenesis of glaucoma.

Seidel (1922) correlated changes in the pupillary diameter produced by miotics and mydriatics with coincidental changes in ocular tension. He believed that the effect of dilating the pupil was to crowd the iris into the angle of the anterior chamber and so obstruct that outflow of aqueous. Serr (1929) by varying the external illumination of the eye produced changes in pupil size and ocular tension. He was of the opinion that for any particular glaucomatous eye there was a critical pupil size which would precipitate a rise in ocular tension. He noted that, in one case of glaucoma, although a period in the

dark had resulted in a rise in ocular tension, full dilation of the pupil by cocaine and adrenalin was followed by a fall in ocular tension. This finding is in keeping with the theory of relative pupillary block for, with the pupil fully dilated, there is no longer any contact between the iris and anterior lens capsule and thus no tendency for abnormally increased pressure to develop in the posterior chamber. Sugar (1941) by means of gonioscopy was able to demonstrate closure of the angle by the root of the iris in eyes affected by closed-angle glaucoma in which the pupil had been dilated by mydriatic drugs.

The hypothesis that angle closure is more likely to occur at one particular pupil size than any other had recently received support from Chandler (1952) who believed that attacks of acute glaucoma were most likely to occur when the pupil was semi-dilated (3-6mm. diameter). He felt that when the pupil was in this state, there still existed a degree of "pupillary block" sufficient to ensure that the pressure in the posterior chamber was higher than that in the anterior, but that in addition, the periphery of the iris was in a relaxed condition and so able to balloon forward more readily and so obstruct

the entrance to the angle. In support of this theory he quoted the occurrence of a spontaneous fall in the ocular tension of some eyes affected by acute glaucoma in which the pupil was widely dilated. Miller (1956) also noted the apparently anomalous result of a fall in ocular tension with full dilation of the pupil in a case of closed-angle glaucoma in whose eyes atropine had been mistakenly instilled.

Although it is generally recognised that obstruction of the angle may occur when the pupil dilates, it has also been suggested that such an obstruction can occur if the pupil is very strongly constricted. Shaffer (see Newell, 1955) noted that if extreme pupillary constriction were effected in an eye by the use of a very strong miotic, the ocular tension would rise. He noted that disopropylflurophosphate (DFP) caused a marked rise in ocular tension when instilled into the eye of a rabbit. This substance is markedly irritant however and the change in ocular tension which it causes may well be related to the resulting vasodilatation.

Chandler (1952) however noted that in closed-angle glaucoma instillation of DFP into an affected eye was

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followed by obstruction of the angle. He believed that the extreme pupillary constriction which followed the use of this drug created an almost complete pupillary block in these cases with the formation of a marked iris bombé in spite of the fact that the body of the iris was tense and one would have presumed incapable of ballooning into the anterior chamber. It is of course possible that vasodilatation within the ciliary body might have been responsible for the angle closure seen in these eyes. It is unlikely however that the degree of miosis which might occur under physiological conditions could ever produce enough iris bombé to result in angle closure. That a sufficient degree of pupillary dilation to cause closure of the angle might occur under physiological conditions however is well recognised (Shaffer, 1955).

Another factor which might result in the closure of an already narrow angle was thought to be accommodation. Sugar in his monograph "The Glaucomas" (1957) noted that a narrowing of the angle could be seen gonioscopically when the eye being examined was made to accommodate. He also noted that this change in the width of the angle was more marked in young individuals than in

those of the older age groups in which the incidence of closed-angle glaucoma was higher. Higgitt and Smith (1955) described two cases in which the ocular tension rose after twenty to thirty minutes of reading. Both of these cases were young adults (25 years and 44 years old) and although both showed angles which were anatomically narrow in neither was the iris noticeably bombé. Duke Elder (1955) was of the opinion that in these cases the obstruction of the angle was due to a forward movement of the ciliary body and believed that vasodilatation in this region might similarly result in the closure of a narrow angle.

The occurrence of an acute attack of primary glaucoma following emotional stress has long been recognised. Priestly Smith (1886) thought that the increased liability of the female to develop acute glaucoma was due to vascular instability. Goldenburg (1928) believed that acute glaucoma was precipitated by swelling of the ciliary body in response to some circulating toxin. Friedenwald (1930) showed histologically that in eyes which had suffered an acute attack of glaucoma evidence of a vascular lesion in the ciliary body could be detected.

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The eyes which he examined however were excised some considerable time after the attack of glaucoma and are unlikely to have given a true picture of the pathological changes present at the onset of the attack. Fiegenbaum (1931) noted that a change in the intensity of the illumination of one eye could affect the ocular tension in the other and postulated a nervous reflex to explain this. Magitot (1948) expressed the belief that the ocular tension was controlled centrally by means of a hypothalamic reflex and that pupillary dilatation and changes in ocular tension were both manifestations of this same neuro-vascular control. Duke Elder (1955) at the C.I.O.M.S. symposium on glaucoma, while agreeing that mechnical blockage of the angle by the "Curran-Chandler" mechanism could occur, felt that this mechanical obstruction was itself the result of some underlying vascular change within the eye.

Various theories to explain how emotional disturbance could precipitate an acute attack of glaucoma have been postulated. Thus Sugar (1941) favoured the pupillary dilatation which accompanies emotional stress as the chief factor responsible. Chandler (1952) felt

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that closure of the angle could result from vascular congestion in the uveal tract. Grant (1952) noted a sudden increase in ocular tension coincident with blushing on the part of the patient and assumed it to be due to vasodilatation in the choroid. Barany (1955) suggested that tenseness in the extra-ocular muscles might play a part in raising the ocular tension. The fact that a visit to a cinema precipitated an acute attack of glaucoma in a patient whose ocular tension did not rise following a darkroom test was cited as evidence of the importance of psychic factors in the development of the disease by Miller (1953). It has however been found impossible to determine whether there is a particular type of psyhological make-up which predisposes to the development of glaucoma (Ripley, 1948-50).

It thus appeared that although the rise in ocular tension occurring in closed-angle glaucoma was the result of mechanical obstruction of the angle of the anterior chamber in a suitably predisposed eye there was no definite agreement on the factors responsible for this.

That closure of the angle did indeed precede

the rise in ocular tension in this disease was shown by Bangaerter and Goldman (1941), Froncois (1948) and Vannini (1952). These same authors showed that as the pupil contracted under the influence of miotics, the angle opened again and the tension returned to normal provided that no permanent adhesion had formed between the root of the iris and the previously occluded trabeculum.

When Barkan (1936) separated primary glaucoma into narrow and wide angle glaucoma he noted that some of his cases of narrow angle glaucoma presented initially with complete angle closure and an acute rise in ocular tension while others, as the result of numerous moderate attacks of transient obstruction of the angle leading to the formation of peripheral anterior synechiae, presented as cases of chronic progressive deterioration of vision which could only with difficulty be distinguished from that found in chronic simple glaucoma. He noted that as a rule the angle of the anterior chamber was narrower above than below and that it was in this upper sector that closure of the angle usually started and in which peripheral anterior synechiae first formed. He

also ....

also thought that this narrowness of the angle of the anterior chamber superiorly was the explanation of the vertically oval pupil seen in eyes affected by acute glaucoma. The changes in the symmetry of the iris pattern noted by Riddell (1946) as an early sign in primary glaucoma may also reflect the asymmetry of the angle described by Barkan.

Shaffer (1955), as the result repeated gonioscopic examination of eyes affected by closed-angle glaucoma over a period of years, was of the opinion that the angle of the anterior chamber was initially closed in its upper sector but that the area so obstructed gradually increased until finally only a very small proportion of the circumference of the angle below was left unobstructed. Phillips (1956) showed that the incidence of goniosynechiae in cases of closed-angle glaucoma was significantly greater in the upper half of the angle than in the lower. He also believed as the result of direct gonioscopic observation that in the early stages of the disease the angle of the anterior chamber was obstructed initially in the upper sector by contact between the root of the iris and the posterior surface of the cornea and that

this area of "irido-corneal contact" slowly implicated more and more of the angle from above downwards until eventually the maintenance of normal tension in the eye was dependant upon the outflow of aqueous through the one remaining open sector of the angle below. He felt that it was the sudden obstruction of this remaining open sector of the angle that finally resulted in the development of an attack of acute glaucoma.

Kronfeld (1944) was of the opinion that the outflow of aqueous from the eye could still be normal when only one quarter of the circumference of the angle was unobstructed, while Troncoso (1947) and Sugar (1945) thought that an even smaller area of open angle was compatible with normal drainage.

It would appear to be a simple matter to determine by gonioscopy whether or not the angle of the anterior chamber in early closed-angle glaucoma is partly obstructed and to relate the resting ocular tension and facility of aqueous outflow to the degree of obstruction present. Unfortunately where the angle is very narrow it is usually impossible on gonioscopy to tell whether the angle is open or closed as the anterior

convexity ....

convexity of the iris obstructs the view of the deeper part of the angle. Even where the angle can be seen clearly it is not possible by observation alone to determine whether closure of any sector is actual or only apparent. Support for the hypothesis that in early closed-angle glaucoma a habitual although variable degree of contact between the iris and cornea exists in some part of the angle must therefore be sought by some other means.

As the writer, contrary to the generally accepted view, was of the opinion that closure of even a portion of the angle in any particular eye was unlikely to be consistent with either a normal ocular tension or a normal outflow of aqueous for that eye, it seemed reasonable that information on the state of the angle might be forthcoming from a detailed study of the ocular tension and aqueous outflow in eyes affected by the disease. It also seemed probable that the response of an eye to the usually employed provocative tests might be greatly influenced by the degree of angle closure existing prior to the test, and so it was decided to study the variations in the tension and outflow of aqueous

in eyes affected by closed-angle glaucoma both in the resting condition and following provocation.

The results of these investigations are now presented and include a statistical evaluation of the darkroom test and details of a new provocative test; the "darkroom outflow" test. Several factors of significance in the surgical treatment of closed-angle glaucoma have emerged from this study and these will also be discussed.

CHAPTER II

THE DARKROOM TEST

SUMMARY

In this chapter the results of the darkroom test on a series of normal eyes and on a similar series of eyes presumed to have closed-angle glaucoma are presented.

A small but real rise in ocular tension occurred in those normal eyes submitted to the darkroom test.

The conclusion is reached that an eye must develop a rise in ocular tension of at least 8.5 mms. Hg for the result of the darkroom test to be considered positive.

It is shown that a positive result with the darkroom test is more likely to occur if the resting ocular tension in the eye tested is higher than 25 mm. Hg and that the magnitude of the rise in tension occurring with the test also depends upon the resting ocular tension at the start of the test.

The existence in an eye of a shallow anterior

chamber and a narrow entrance to the angle of the anterior chamber does not constitute a diagnosis of closed-angle glaucoma. Kronfeld (1949) noted that 20% of his cases in which the angle of the anterior chamber was found to be extremely narrow did not develop any sign of closed-angle glaucoma over a five year period of observation. In order to make a diagnosis of closed-angle glaucoma, evidence of actual obstruction of the angle of the anterior chamber must be sought. The usual indication that obstruction of the angle has occurred is the finding of a pathologically raised ocular tension. As the ocular tension in closed-angle glaucoma between attacks is usually within normal limits the use of a suitable provocative test is often necessary to establish the diagnosis. The simplest and most often used of these tests is the darkroom test. In this test the patient is confined to a darkened room for a period of one hour and the resulting change in ocular tension noted.

As has already been noted (p. 29) Gronholm in 1910 was the first to observe that a period of time in a darkened room could be followed by a rise in ocular

tension ....

tension in patients suffering from primary glaucoma. Seidel (1922) believed that this rise in ocular tension was due to angle block secondary to pupillary dilatation and Serr (1925) was of the opinion that the rise in tension only occurred if the pupil of the affected eye was dilated to a critical size. From these observations there was developed the provocative test now known as the darkroom test. Further work on the effect of darkness on the ocular tension was published by Sallman, 1930; Gradle, 1931; Ohm, 1936; Wetzlich, 1934; Bloomfield and Kellerman, 1947; Kronfeld, 1948; Magitot, 1948; Zaretskaya, 1948; Weinstein, 1953; Ross, 1953, and Higgitt, 1954.

Conflicting opinions on the value of the darkroom test were expressed by these authors some finding that a substantial rise in ocular tension was of frequent occurrence in cases of glaucoma, others that such a rise was rare and of little diagnostic assistance. The application of the darkroom test to cases of chronic simple glaucoma which as a rule do not develop a rise in ocular tension with the test probably explains the disappointing results found by some workers (Gradle, 1931; Ohm, 1936; Bloomfield and Kellerman, 1947; Magitot,

1948). Later workers (Kronfeld, 1948; Higgitt, 1954) who applied the test only to cases of suspected closed-angle glaucoma were more enthusiastic in their estimate of its diagnostic value in these cases.

Even when the test is applied to cases presumed to have closed angle glaucoma, however, a significant rise in ocular tension is not found in every case. Higgitt (1954) found that 78% of his cases of "congestive" glaucoma gave a positive rise of ocular tension with the test, whereas Leydhecker (see Duke Elder, 1955) found that only 11% of his "congestive" and "narrow angle" glaucoma cases did so. Consequently the latter author concluded that the test was of little value in the diagnosis of closed-angle glaucoma. Kronfeld (1949) noted the development of an acute attack of glaucoma in a patient who had previously failed to produce a rise of ocular tension with the darkroom test and Miller (1953) pointed out that a visit to the cinema had been known to result in an acute attack of glaucoma in a patient in whom the darkroom test had been negative.

Leydhecker (see Duke Elder, 1955) in assessing the results of the darkroom test considered the rise

of ....

of 9 mms. Hg suggested by Higgitt (1953) as the measure of a positive test to be too low, pointing out that this figure was derived from the latter authors' data without any real statistical analysis. No such analysis had in fact been published at that time.

In the present investigation the darkroom test was chosen for further study not only because it might help to elucidate the mechanism of angle closure but because it was simple to perform, not particularly distressing to the patient and relatively safe. Some authors (Sugar, 1948) have expressed the opinion that a rise in ocular tension in an eye affected by closed-angle glaucoma can be demonstrated more readily by the instillation of a mydriatic than by any other provocative test. The mydriatic test was considered unsafe by Kronfeld (1949) and it has not been made the subject of any part of this investigation.

The results which are presented now are all of tests performed at the Institute of Ophthalmology carried out by the author under standard conditions. The method used was similar to that described by Higgitt (1954).

The eyes of the patient to be tested were anaesthetised by the instillation of several drops of

one per cent amethocaine hydrochloride in each and a measurement of the ocular tension was made with a standard Schiøtz X-tonometer, the patient being recumbent while the measurement was made. The patient was then kept in total darkness for one hour, being cautioned not to fall asleep during this period. At the end of an hour another measurement of the ocular tension was made with the same instrument as before. Both the initial and final measurements were made under normal room lighting.

The effect of the darkroom test on a series of 57 normal cases was first investigated. All the cases included in the normal series were investigated to exclude their having closed-angle glaucoma. Gonioscopy was performed on each and only those eyes in which the angle of the anterior chamber was not unduly narrow included in the series to be tested. The angle of the anterior chamber in these cases had to be open in all sectors and the trabeculae visible in the whole circumference of the angle. Clinically these cases were classed as having wide or medium angles. A careful case history was taken to exclude any patient with a history of haloes or attacks of blurred vision. In each case the central and peripheral visual fields

were ....

were plotted and no case with a field defect included in the normal series. Apart from the question of closed-angle glaucoma, none of the normal eyes had evidence of past or present uveitis or any other pathological condition which could be recognised by the usual methods of clinical examination.

The group of cases so selected consisted of 32 males and 25 females with a mean age of 56.8 years ($\pm$ 11.8). That the variance of the results might not be minimised by the similarity of fellow eyes, the result of the test on only one eye chosen at random from each patient tested was used in the subsequent analysis. (The random selection of right or left eyes was effected by the toss of a coin for each patient tested.)

Of the 57 eyes submitted to the darkroom test 36% showed a rise in ocular tension; in 9% the ocular tension fell while in the remaining 55% there was no appreciable change. Taken as a whole, the group showed a small mean rise in ocular tension with the test (+0.97 mm. Hg with a standard error of $\pm$ 0.33). The distribution of the results was Gaussian with a standard deviation of $\pm$ 2.54 mm. Hg (Fig. I).

Although ....

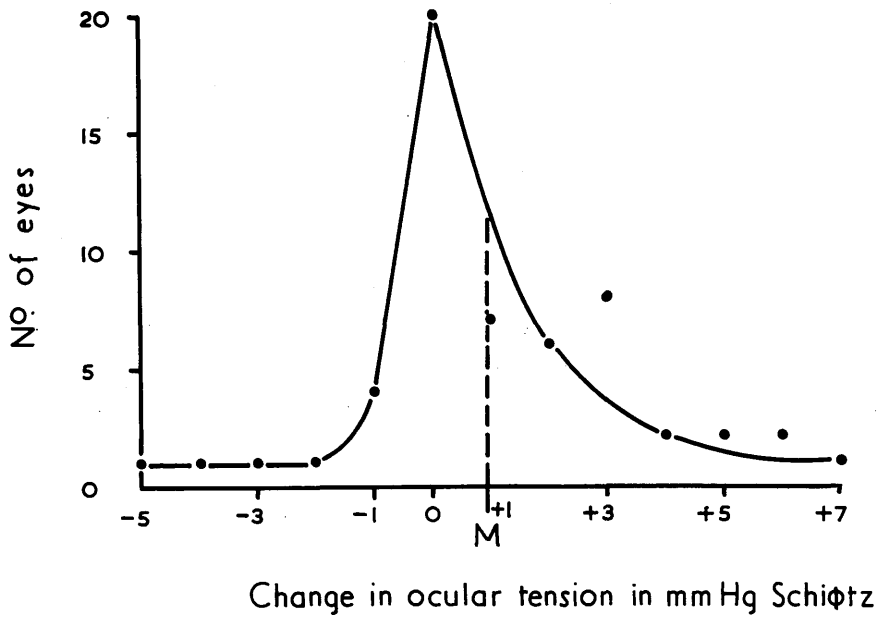

Fig. 1.

Graph to illustrate the results of the darkroom test on 57 normal eyes. A small mean rise in ocular tension (M) occurred with the test in these eyes.

Although the mean rise in ocular tension in these normal eyes was small, it was significantly different from the expected value of zero and so may be considered real. (Students $t = 2.89$: $n = 56$: $P = < 0.01$.)

From the behaviour of this series of normal eyes it is possible to deduce what may be considered a pathological rise in ocular tension with the darkroom test. A rise in ocular tension of more than three times the standard deviation of the mean change in ocular tension found in normal eyes with test is likely to have occurred by chance less than once in one hundred times and such a rise may reasonably be regarded as evidence in favour of a diagnosis of closed-angle glaucoma. In the present series of normal eyes it has been noted that following the darkroom test there was a mean rise of ocular tension of + 0.97 mms. Hg with a standard deviation of $\pm$ 2.54 mms. Hg. To be significant at the 99% level of probability therefore, an eye under test would have to produce a rise in ocular tension of at least 8.6 mms. Hg ($M + 3\sigma$).

As the series of normal eyes submitted to the darkroom test might not be truly representative of normal eyes in general, it was decided to calculate 95% confidence

limits ....

limits for the mean change in ocular tension with the darkroom test. These showed that the true mean change in tension with the test could lie anywhere between + 0.18 mms. Hg and + 1.78 mms. Hg.

To be considered pathological, therefore, the rise in ocular tension resulting from the test should be greater than a figure lying between + 7.8 mms. Hg and + 9.4 mms. Hg. This is in close agreement with the figure of + 9 mms. Hg rise suggested on clinical grounds as the measure of a positive test, by Higgitt (1954).

The fact that the darkroom test should be followed by a rise in ocular tension in normal eyes in which the factor of angle closure can almost certainly be ruled out is difficult to explain. Duke Elder (1940) noted that it had been repeatedly shown that a small rise in ocular tension occurred when normal eyes were subjected to a period of darkness. This effect was said to be abolished by a retrobulbar injection of alcohol or an optico-ciliary neurectomy, an observation which could support the view that the change in tension was reflex in origin. Duke Elder (1932) states that light directly constricts, while darkness dilates the vessels of the

choroid ....

choroid and that this dilatation in the dark causes the rise in ocular tension which occurs when light is excluded from a normal eye. In the presence of an adequate drainage mechanism however any increase in the volume of the choroid would be likely to result in an increase in the rate of outflow of aqueous so that the rise in ocular tension would be transient, and one would imagine, unlikely to be present after one hour in the dark.

In none of the normal eyes studied in this investigation was the angle abnormally narrow nor did gonioscopy reveal angle closure in any of these cases after the darkroom test. As will be seen later (p. 78) no significant alteration in the rate of aqueous outflow during the darkroom test was discovered when this aspect of the problem was studied. It would seem unlikely therefore that the rise in tension occasioned by the darkroom test in these normal eyes was due to obstruction of aqueous outflow. Similarly if the outflow of aqueous in these cases was normal (as indeed it was found to be) any reflex vasodilatation occurring within the eye would have precipitated only a transient rise in ocular tension unlike the prlonged rise noted. The explanation of the rise in tension must

therefore lie in an increase in the rate of aqueous formation so that with no change in the rate of outflow, the pressure equilibrium within the eye would assume a higher base level. Such an increase in the rate of aqueous formation might itself be the result of reflex vasodilation within the ciliary body or might reflect some wider response on the part of the hypothalamus or autonomic nervous system induced by the change in illumination. Small changes in ocular tension comparable with those occurring with the darkroom test are seen in the diurnal intra-ocular pressure variations which are reasonably believed to result from rhythmic alterations in the activity of the autonomic nervous system.

The effect of the darkroom test on the ocular tension of eyes presumed to have closed-angle glaucoma was next investigated. For this purpose a group of 108 cases each of whom was believed to be suffering from closed-angle glaucoma was submitted to the darkroom test. In each case a presumptive diagnosis of closed-angle glaucoma had been made on the appearance of the angle of the anterior chamber and on the history of symptoms. All of the cases in this group had noticeably narrow

angles as seen gonioscopically. In some cases a presumptive diagnosis of closed-angle glaucoma was made because of a frank acute closed-angle attack in either the eye to be examined or its fellow. Where there had been no such acute attack a definite history of haloes and blurred vision lasting at least one hour and relieved by either sleep or miotics was obtained.

As with the series of normal eyes only one eye from each patient tested was included in the analysis. Where both eyes were tested a random choice was made between them. Where one eye had been operated on for acute glaucoma the result of the test on the fellow eye was taken. The resulting group consisted of 108 cases, 55 of whom were male and 53 female. The mean age of these cases was 57.6 years ($\pm$ 11.0). The sex distribution was similar to that in the series of normal cases and analysis by a χ^2 test did not reveal any significant difference between the two series in this respect (Table I). ($\chi^2 = 0.406$: $n = 1$: $P = > 0.50$).

A comparison of the age compositions of the two series revealed no significant difference in this respect either (Table II). In the control series the mean age

T A B L E I

Series	Number of Cases	
	Male	Female
Control	32 (56%)	25 (44%)
Closed-angle glaucoma	55 (51%)	53 (49%)

Comparison of the age distribution in 57 normal cases and 108 cases of closed-angle glaucoma submitted to the darkroom test. The two series are similar in age distribution. (χ^2 = 0,406 : n = 1 ; P = > 0.50.)

T A B L E I I

Series	Mean age (years)		Comparison of Mean Ages of Males and Females	Total Mean Age (Years)	Comparison of Total Mean Age in Control and Test Series
	Male	Female			
Control	55.7 (± 13.0)	57.8 (± 10.2)	t = 1.11 : n = 55 : P = > 0.10	56.8 (± 11.8)	t = 0.433 : n = 163 : P = > 0.10
Test	57.4 (± 10.4)	57.8 (± 11.8)	t = 0.18 : n = 106 : P = > 0.10	57.7 (± 11.0)	F = 1.07 : n_1 = 56 : n_2 = 107 : P^2 = > 0.20

Comparison of age distribution in 57 normal eyes and 108 cases with closed-angle glaucoma submitted to the darkroom test. The age distribution is similar in each series.

of the males (55.7 years $\pm$ 13.0) did not differ significantly from that of the females (57.8 years $\pm$ 10.2) ($t = 1.11$: $n = 55$: $P => 0.10$). In the series of cases affected by closed-angle glaucoma the mean age of the males (57.4 years $\pm$ 10.4) similarly did not differ from that of the females (57.8 years $\pm$ 11.8) ($t = 0.18$: $n = 106$: $P => 0.10$). In addition, the mean age of all cases in the normal series (56.8 years $\pm$ 11.8) did not differ significantly from that in the glaucomatous series (57.7 years $\pm$ 11.0) ($t = 0.433$: $n = 163$: $P => 0.10$). ($F = 1.07$: $n_1 = 56$: $n_2 = 107$: $P => 0.20$).

In the group of cases presumed to have closed-angle glaucoma the darkroom test produced a well marked rise in ocular tension. The mean change in tension was + 11.12 mms. Hg with a standard deviation of $\pm$ 12.08 mms. Hg.

As was expected, this mean rise in ocular tension was significantly greater than that found in the series of normal eyes ($t = 6.26$: $n = 163$: $P =< 0.001$).

The fairly large standard deviation for the results of the darkroom test in the cases of closed-angle glaucoma indicated a wide range and suggested that there

might ....

might not be a clear demarcation between the results of the test on normal and glaucomatous eyes. This was indeed found to be the case for, of the 108 eyes presumed to have closed-angle glaucoma, only 56 (51.9%) developed a rise in ocular tension of more than 8 mms. Hg with the test and of these 17 had ocular tensions at the beginning of the test of more than 31 mms. Hg. The results of the test on the normal and glaucomatous eyes are shown graphically in Fig. 2 where it is apparent that there is considerable overlap of the two series. From this alone it would appear that while a positive darkroom test is of value in establishing the diagnosis of closed-angle glaucoma the reverse is certainly not true.

If it is the case that in an eye affected by early closed-angle glaucoma, part of the angle of the anterior chamber may be more or less permanently obstructed although the ocular tension might still be within normal limits, one would expect that in any group of such eyes those in which the angle was already largely obstructed would be more likely than the others to develop a rise in ocular tension on suitable provocation.

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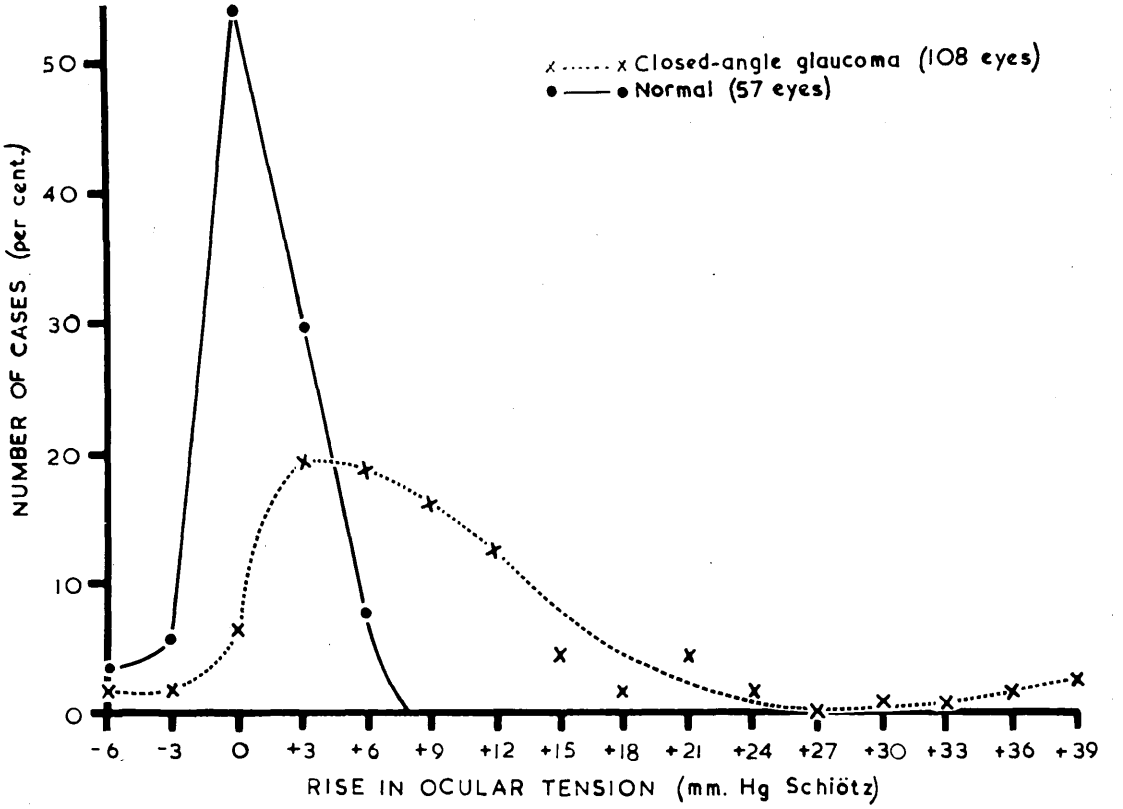

Fig. 2.

Graph to illustrate the distribution of 57 normal eyes and 108 eyes with closed-angle glaucoma in relation to the change in ocular tension with the darkroom test. There is considerable overlap between the normal and glaucomatous results.

Although the ocular tension in such eyes might be within normal limits (i.e., below 31 mms. Hg) it seemed reasonable that it would be higher in those eyes in which the angle of the anterior chamber was partly obstructed than in those not so obstructed. Thus one might expect a higher incidence of positive darkroom tests among those cases in which the ocular tension at the start of the test was in the upper reaches of the normal range than where this ocular tension was lower.

Leydhecker (see Duke Elder, 1955) has stated that for provocative tests in general, the initial resting ocular tension does not influence the result of the test (at least for ocular tensions of less than 30 mms. Hg). From clinical experience and for the reasons mentioned above it was believed that the result of the darkroom test was greatly influenced by the initial ocular tension. To establish whether indeed this was the case, the results of the darkroom test were classified in groups according to the resting tension in each eye at the start of the test. The incidence of positive results with the darkroom test was found to rise steadily with increasing initial ocular tension levels (Fig. 3).

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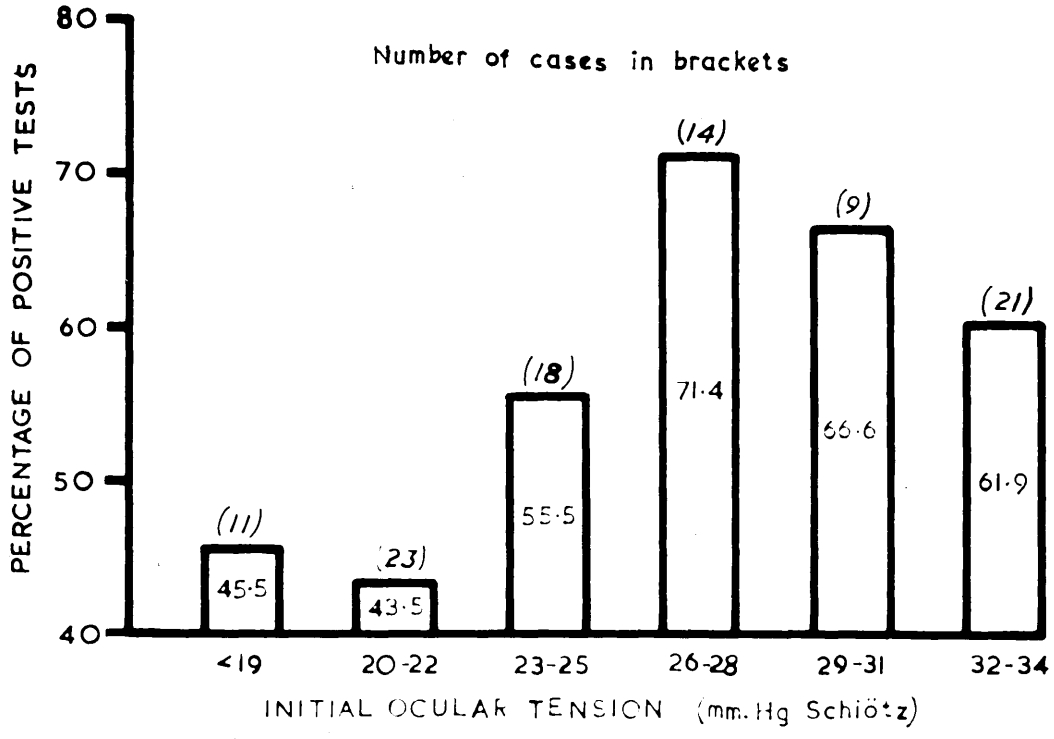

Fig. 3.

Comparison of the incidence of positive results with the darkroom test on eyes with closed-angle glaucoma at differing initial levels of ocular tension. The greatest number of positive tests occurs in the group with an initial ocular tension of 26-28 mm. Hg.

As there appeared to be a greater likelihood of a positive result where the initial tension in the eye tested was above 25 mms. Hg than where it was lower than this figure, a comparison was made between the percentage of positive results occurring at an initial level of ocular tension of less than 25 mms. Hg and that found where the initial tension was 26-30 mms. Hg. The results of the darkroom test in those eyes wherein the resting tension was above 30 mms. Hg were not included in this comparison as the tension in these eyes was already abnormal before the start of the test. The result of the comparison is shown in Table III. A

TABLE III

Initial tension (mm. Hg)	Result of Darkroom Test	
	Positive	Negative
Less than 25 (41 eyes)	17 (41.5%)	24
26-30 (32 eyes)	23 (71.9%)	9

Comparison of the results of the darkroom test on eyes with closed angle glaucoma and differing initial level of ocular tension. The greatest incidence of positive results occurs in the

group ....

group of eyes with the higher initial ocular tension ($\chi^2 = 5.54 : n = 1 : P = < 0.02$)

χ^2 test disclosed a significantly greater incidence of positive results with the darkroom test where the initial tension in the eye tested was in the higher of the two ranges described. ($\chi^2 = 5.54 : n = 1 : P = < 0.02$)

The increased incidence of positive results at higher levels of initial ocular tension suggested that the actual magnitude of the rise in tension with the darkroom test might be similarly influenced by the resting ocular tension. The change in ocular tension occurring with the test on cases of closed-angle glaucoma was accordingly plotted against the initial ocular tension. The results are illustrated graphically in Fig. 4. At an initial ocular tension of up to 25 mms. Hg and over 30 mms. Hg the test appeared to be followed by a mean rise of tension of about 10 mms. Hg. The mean rise in ocular tension from an initial level of 26-30 mms. Hg however was found to be unexpectedly large (+26.1 mms. Hg). To determine whether this large mean rise in tension was significantly different from

that ....

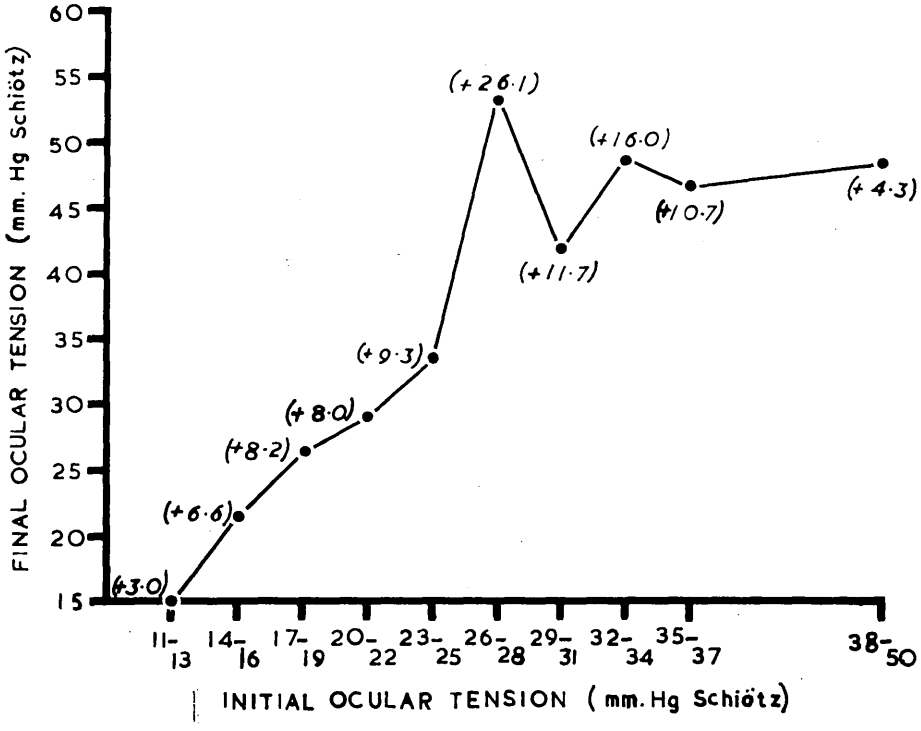

Fig. 4.

Graph to show relationship between the initial and final ocular tension of 108 eyes with closed angle glaucoma submitted to the darkroom test. The rise in tension from an initial level of 26-28 mm. Hg is greater than that from any other initial ocular tension.
The figures in brackets represent mean changes in ocular tension.

that occurring at other levels of initial tension a comparison was made between the mean rise in tension for those cases in which the resting tension was from 26-30 mms. Hg inclusive and that of all the other cases submitted to the test. The former mean rise was found to be + 23.7 mms. Hg ($\pm$ 29.8) and the latter + 8.6 mms. Hg ($\pm$ 8.18). On testing, there is a significant difference between these results ($t = 4.14 : n = 106 : P = < 0.001$).

As this might merely mirror the fact that the group of eyes with the lower resting tension contained a smaller proportion of positive results than the other, the comparison was repeated for those cases giving a rise in ocular tension of at least 8 mms. Hg with the test. It was again found that the mean rise in ocular tension for those cases in which the resting tension was 26-30 mms. Hg was significantly greater than the rise occurring from other initial levels of ocular tension (+ 34.8 mms. Hg $\pm$ 15.8 mms. Hg compared with + 14.8 mms. Hg $\pm$ 8.9 mms. Hg : $t = 5.4 : n = 52 : P = < 0.001$).

With the exception of the unexpectedly large rise in ocular tension where the initial tension was in the region of 25 mms. Hg there appeared to be a direct relationship between the initial ocular tension

and ....

and the rise in tension following the darkroom test. To establish whether a simple relationship did in fact exist between these two variables, the change in ocular tension with the test was plotted against the initial tension for each eye in the suspected closed-angle glaucoma series and the correlation coefficient determined (Fig. 5). Only those cases wherein the initial ocular tension was within normal limits were accepted for this analysis and of these there were 73. Although the correlation is not high ($r = -0.368$) it is significant ($n = 71$: $P = < 0.01$).

From the regression line of y upon x one can calculate what rise in ocular tension is to be expected from any particular initial level of ocular tension. The equation of this regression line was found to be $y = 1.05\ x - 11.4$ mms. Hg, so that, if the ocular tension at the start of the darkroom test were 20 mms. Hg, one would expect a rise in tension of + 9.6 mms. Hg with the test, whereas with an initial ocular tension of 30 mms. Hg the expected rise would be + 20.1 mms. Hg. The residual variance however is rather high ($\pm$ 12.10 mms. Hg) so that any estimate of the expected rise

in ....

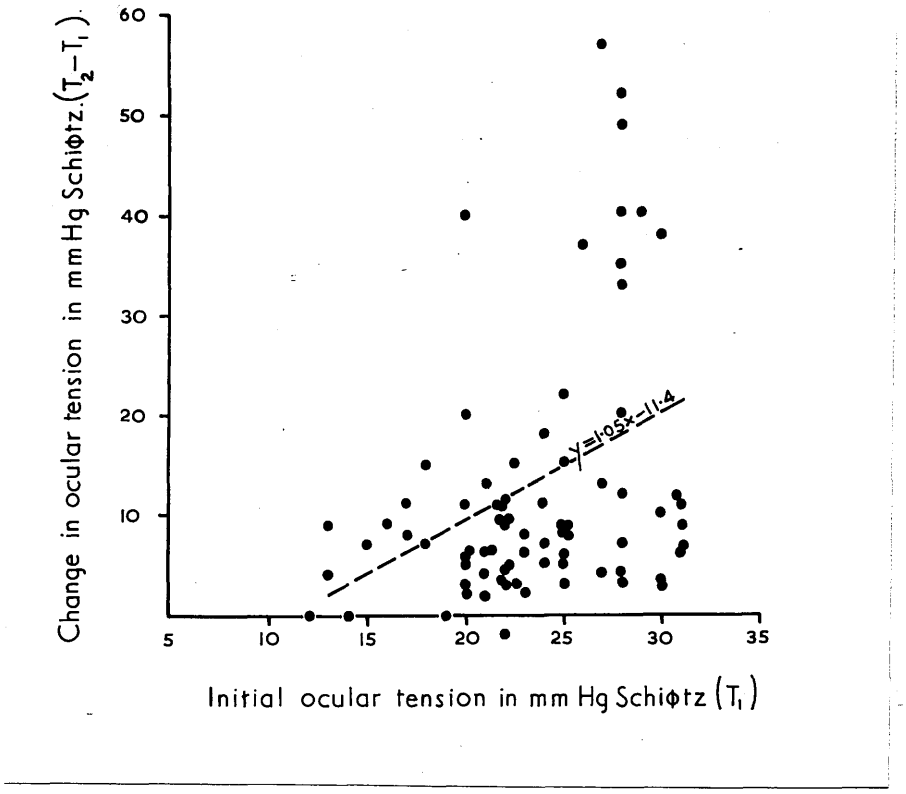

Fig. 5.

Diagram to illustrate the relationship between the initial ocular tension (T_1) and the change in ocular tension ($T_2 - T_1$) occurring with the darkroom test on 73 eyes with closed-angle glaucoma.

High resting levels of ocular tension are associated with greater rises in ocular tension with the test than is the case where the initial ocular tension is low.

in tension with the test from known values of the resting ocular tension would of necessity be imprecise.

It was thus apparent that not only was the likelihood of a positive result with the darkroom test influenced by the initial tension in the eye to be tested but, in addition, the actual magnitude of the change in ocular tension with the test was similarly related to the resting level of ocular tension. The significance of these findings will be discussed later.

CHAPTER III

THE DARKROOM OUTFLOW TEST

SUMMARY

The development of the tonographic method of assessing the facility of aqueous outflow is described.

It is suggested that tonography provides a quantitative method of estimating the degree of obstruction of the angle in cases of closed-angle glaucoma.

The details of a new provocative test, the "Darkroom Outflow Test" are described. In this test the facility of aqueous outflow is assessed before and after an hour in the dark.

In normal eyes no significant alteration in the rate of aqueous outflow occurs with the test whereas in eyes affected by closed-angle glaucoma there is usually a marked fall in the level of aqueous outflow. A 30% fall in the outflow level with the test is considered to be indicative of the occurrence of degree of angle closure sufficient to warrant the diagnosis of closed-angle glaucoma.

The ocular tension in 85 normal eyes is

investigated ...

investigated with the tonometer used throughout the present investigation and it is concluded that an ocular tension of 31 mm. Hg may be considered as the upper limit of the normal range for this instrument.

From a study of the ocular tension and facility of aqueous outflow it is concluded that in cases of closed-angle glaucoma a resting ocular tension of 24 mm. Hg indicates the closure of enough of the angle to reduce the facility of outflow to a pathologically low level.

It is shown that in closed-angle glaucoma, the results of the darkroom test are influenced greatly by the level of aqueous outflow prevailing at the start of the test, a greater incidence of positive results and a greater mean rise in ocular tension occurring in eyes in which the level of outflow is low initially than where the outflow factor is normal or high.

It is concluded that some degree of obstruction of the angle may be present in eyes affected by closed-angle glaucoma even where the ocular tension is apparently normal.

Although large changes in the tension of an

eye affected by closed-angle glaucoma undoubtedly reflect alterations in the degree of obstruction of the angle, a direct measurement of the area involved at any particular time would obviously provide more precise information on this point. Unfortunately gonioscopy is of little help in assessing the degree of angle closure present at any time as the light from the slit-lamp immediately causes the pupil to contract and the width of the angle to alter (Smith, 1954). It is possible, however, to assess the degree of obstruction of the angle by means of tonography.

Schiøtz (1905) when describing the use of his tonometer noted that tonometry repeated at short intervals lowered the tension in normal eyes. In 1915 Priestly Smith observed that prolonged application of a tonometer to a normal eye resulted in a definite lowering of the ocular tension. He postulated that this was due to an increase in the rate of escape of aqueous fluid from the eye. He suggested that absence of this softening of the eye was indicative of obstruction at the filtration angle. Polack von Gelden (1911) made repeated tonometric measurements on the same eye with

a 5.5 or 7.5 g. weight. These readings were made at four- to five-second intervals until a constant value was obtained. He found that in normal eyes repeated tonometry resulted in a definite reduction in the ocular tension. Wegner (1925) developed the method of protracted tonometry. He kept a tonometer on the eye for five or six minutes and found that in normal eyes the ocular tension would fall by at least a third of the initial measurement and sometimes by as much as one half during this procedure. He found that the phenomenon was unaffected by the age of the patient or by the instillation into the eye of either a miotic or a mydriatic. Although Polack von Gelden found that the expected fall in ocular tension with repeated tonometry did not occur in cases affected by glaucoma, Wegner was unable to verify this.

Baillairt who had developed the dynamometer that bears his name, noted (1931) that the application of his instrument to a normal eye resulted in a marked fall in the ocular tension. He was of the opinion that this was due to an alteration in the volume of blood in the choroid. Shope (1932) found that a fall in tension

after ....

after the application of a tonometer to an eye was the rule both with normal and with glaucomatous eyes seeming to have little, or no relation to obstructive changes at the filtration angle. It is possible that the cases of glaucoma which he studied were of the closed-angle type in which between attacks the angle of the anterior chamber may be open and apparently normal.

Bock, Kronfeld and Stough (1934) made a detailed study of the effect on normal and glaucomatous eyes of tonometry with a 15 gram weight maintained for a period of two minutes. They concluded that a fall of from 5-15 mms. Hg was the rule in all normal eyes tested. They found that in normal eyes the higher the initial tension, the greater was the fall in the tension with the test. When a comparison was made between the result of the test in patients of over fifty years in age and those obtained from younger subjects no appreciable difference was found. In eyes affected by glaucoma too the results of the test were influenced by the initial tension level. Where the initial tension was below 26 mms. Hg a normal result was obtained whereas in eyes in which the initial tension was between 27

and ....

and 36 mms. Hg the fall in ocular tension during the application of the tonometer was much less than that found in normal eyes.

In spite of all this work however prolonged tonometry was not used as a clinical procedure in the investigation of glaucoma until the development of tonography by Grant (1950). The development of the Mueller electronic tonometer, the sensitivity of which made possible a more accurate estimate of the fall in ocular tension on prolonged tonometry, stimulated further work on this aspect of the subject.

Moses and Bruno (1950) used this instrument to determine the relationship between the rate of volume loss from the eye and the total intra-ocular pressure during tonometry for two minutes. They neglected however to take into account the distensibility of the eye, relating the change in volume only to the corneal indentation produced by the tonometer plunger. Grant (1950) also used the Mueller tonometer in the development of the technique which he named tonography.

As Grant pointed out, application of a tonometer to the eye increases the intra-ocular pressure, indents

the cornea and distends the globe. This increase in intra-ocular pressure leads to an increase in the rate of outflow of aqueous from the eye with a consequent decrease in the volume of the globe. In the absence of any profound change in the rate of aqueous formation, the rate of volume loss is equal to the rate of aqueous outflow from the eye.

The volume of fluid displaced by the indentation of the cornea has been determined by Friedenwald (1937) for different plunger weights and different intra-ocular pressures. This same author taking into account the elasticity of the coats of the eye has calculated the total volume change resulting from the application to an eye of a tonometer with differing plunger weights at different levels of intra-ocular pressure. He has shown that the change in volume resulting from the application of a tonometer to the eye bears a logarithmic relationship to the resulting change in pressure.

Grant used Friedenwald's data to calculate the increased rate of aqueous outflow from the eye during tonometry. He found that the rate of volume loss (ΔV) is proportional to the pressure increment

due ....

due to the weight of the tonometer ($\triangle P$) and to the duration of the procedure (t), i.e.,

$$\Delta V \propto \Delta P \times t$$

$$\therefore \Delta V = C. \Delta P.t$$

In this expression the pressure increment is the difference between the intra-ocular pressure prior to the application of the tonometer and the changing intra-ocular pressure during the application of the instrument. Grant found that this latter figure could be represented approximately by the arithmetic average of the intra-ocular pressures at successive half-minute intervals. Both the resting intra-ocular pressure and that obtaining during tonometry were calculated from the recorded ocular tensions by the use of Friedenwald's data. The equation thus derived became:

$$\Delta V = c\ (Av\ Pt - Po).t$$

from which

$$c = \frac{\Delta V}{(Av\ Pt - Po)} .t$$

where ....

where c = co-efficient of aqueous outflow (i.e., the increased rate of aqueous outflow in cu.mm. per mm. Hg intra-ocular pressure increment per minute),

Pt = intra-ocular pressure during tonometry,

Po = intra-ocular pressure before tonometry,

t = time of application of the tonometer in minutes,

ΔV = change in ocular volume in mm^3.

For normal eyes Grant (1950) found that the average co-efficient of outflow was 0.243 with a range of 0.15 to 0.34. In chronic simple glaucoma the co-efficient was much lower, usually below 0.10. Grant was of the opinion that the figure he derived did in fact largely represent the increased rate of aqueous outflow rather than either a change in the rate of aqueous formation or an alteration in the choroidal blood volume, for he discovered that in rabbits the facility of outflow was similar after death to that recorded during life. In addition, in enucleated human eyes when allowance was made for the lack of aqueous inflow the facility of outflow determined by tonography agreed well with that found in normal human eyes in vivo. The injection

of a viscous solution such as methyl cellulose into the anterior chamber greatly lowered the facility of outflow.

In cases of closed-angle glaucoma, Grant (1951) noted that during an acute attack of hypertension when the angle was closed the facility of aqueous outflow was very low (0.01 - 0.06) but between attacks of raised tension, the outflow of aqueous was comparable to that found in normal eyes. Where peripheral anterior synechiae had been formed, however, there was a decrease in the facility of outflow commensurate with the area of angle occluded and this obstruction to aqueous outflow persisted even after enucleation. In sub-acute closed-angle glaucoma where the ocular tension was raised and the angle appeared to be partially obstructed when viewed with a gonioscope, the facility of aqueous outflow was found to be correspondingly decreased.

Grant (1955) pointed out that the rise in ocular tension in acute glaucoma is entirely explicable by the occurrence of angle closure, for without any change in the rate of aqueous formation, assuming it to be 1 cu.mm./min., a decrease in the facility of outflow from a normal value

of 0.20 to one of 0.02 such as is found in acute glaucoma would result in a rise in ocular tension from an initial level of 16 mms. Hg to one of 58 mms. Hg.

From the foregoing it would seem reasonable that tonographic measurement of the facility of aqueous outflow in cases of closed-angle glaucoma would enable one to estimate the degree of angle closure existing at any time. Measurement of the change in the facility of aqueous outflow occurring in such an eye with the darkroom test might therefore be more likely to reveal the existence of the disease than the usually employed measurement of the change in ocular tension.

It was decided therefore to measure the facility of aqueous outflow before and after the darkroom test in cases suspected of having closed-angle glaucoma and to compare the results so obtained with those found in normal eyes. In the majority of cases of closed-angle glaucoma such measurements revealed a diminution in the co-efficient of aqueous outflow of sufficient magnitude to enable these cases to be distinguished from normal. This procedure, which is described in detail below, will be referred to as the "darkroom outflow" test.

METHOD

The eye to be tested was anaesthetised by the instillation of two to three drops of 1% amethocaine hydrochloride. A drop of sterile liquid paraffin was instilled to protect the cornea. The ocular tension was measured with a standard Schiøtz X-tonometer. The facility of aqueous outflow was then determined by applying the Mueller electronic tonometer to the eye and noting the resulting change in ocular tension during a period of four minutes. From this the coefficient of aqueous outflow was determined by the use of the conversion tables published by Grant (1951). The patient was next asked to sit quietly for half an hour under normal room lighting. At the end of this period the ocular tension was again measured with the same tonometer as before. The patient was then seated in a darkened room for one hour, being cautioned not to fall asleep. At the end of this hour the ocular tension was again measured with the same tonometer and a further determination of the facility of aqueous outflow made. The initial measurements of ocular tension and facility of outflow were made under similar conditions of artificial lighting while

the ....

the final measurements were made in standard conditions of dim illumination. (Enough light was provided to allow of accurate positioning and reading of the tonometer scale.) All measurements were made with the patient recumbent. In assessing the facility of outflow, the ocular tension during the first half minute after application of the tonometer was ignored and the facility calculated for the succeeding four minutes, for it was found that the readings of ocular tension with the electronic instrument were erratic just after its application to the eye. In all cases it was found that the ocular tension returned to within a few mms. Hg of the first measurement after half an hour, in spite of the intervening tonography.

In all, the test was applied to a series of 97 cases presumed to have closed-angle glaucoma and a further series of 42 normal eyes. The criteria upon which a presumptive diagnosis of closed-angle glaucoma or of normality was based, were the same as those already detailed for the darkroom test (p. 47).

As in the case of the darkroom test only one eye chosen at random from each patient was included in the series to be analysed. None of the normal eyes

had ....

had a narrow angle so that closure of the angle as a result of the test was considered unlikely. This view was confirmed by gonioscopic examination of a number of the normal eyes before and after the test, which, in the cases examined, revealed no apparent alteration in the width of the angle. Because of this, no appreciable alteration in the facility of aqueous outflow of normal eyes was expected with the test and none was found.

It was originally expected that the arithmetic difference between the initially determined value of the outflow factor and that obtained after the period in the dark would give a reasonable estimate of the area of angle closure which had developed in the eye tested. This, however, failed to take into account the existing level of outflow prior to the test which in cases of closed-angle glaucoma was found to vary from as little as 0.06 in some eyes to 0.30 in others. A reduction in the facility of outflow of say 0.03 from an initial level of 0.06 is obviously very different from a similar fall in outflow where the initial outflow was 0.30, for in the first case the change in outflow is one of 50% of the resting outflow level while in the second

case the change is of 10% only. In order that the influence of the initial outflow level might not be ignored it was decided to express the change in outflow as a fraction of the initial outflow level so that instead of taking the arithmetic difference between the two readings, the logarithmic difference was used. In analysing the results of the darkroom outflow test the difference between the logarithms of the initial and final outflow determinations results in a positive figure if there has been a diminution in the outflow factor with the test and in a negative figure if the test has been followed by an increase in the rate of outflow.

In the series of normal eyes submitted to the test the resulting change in outflow was small. The distribution of the results was Gaussian with a mean change in outflow of log 0.006 ($\pm$ 0.055). (Fig. 6.) When this small mean change in outflow was compared with the expected value of zero by means of Students "t"-test it could be seen that it did not in fact differ significantly from zero. ($t = 0.14 : n = 41 : P = > 0.1$). It is interesting to note that although

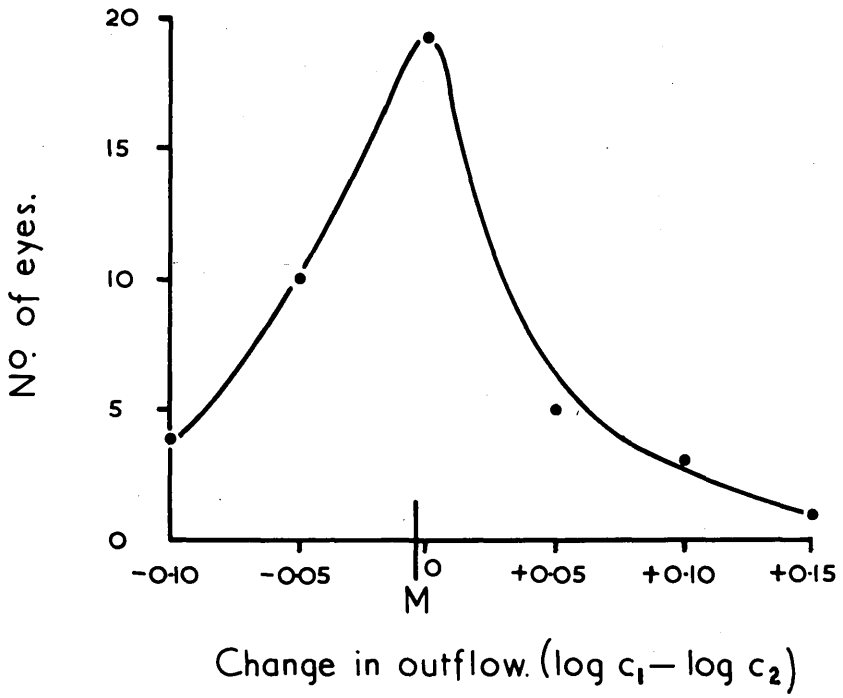

Fig. 6.

Graph to illustrate the change in the facility of outflow occurring in 42 normal eyes with the darkroom outflow test. The mean log. change in outflow is not significantly different from zero.

a small mean rise in ocular tension was found in the normal eyes submitted to the darkroom test (p. 51) no corresponding diminution in the facility of aqueous outflow was discovered in such eyes in the present investigation.

As was the case with the darkroom test, from the behaviour of the normal eyes it was possible to estimate what change in the facility of aqueous outflow with the darkroom outflow test might be considered as lying outside the likely range of normality. A decrease in the outflow factor of more than three times the standard deviation of that change found in normal eyes with the test carries at least a 99% probability of being due to factors other than chance. As noted above, the standard deviation found in the present normal series was $\pm$ log 0.055, making a positive result a change in the value of the outflow factor at least + log 0.160 ($M + 3\sigma$). This figure is equivalent to a fall in outflow of 30% of the initial outflow level.

It had next to be seen how eyes affected by closed-angle glaucoma would react to the test. The series of apparently glaucomatous eyes upon which

this part of the investigation was carried out, consisted of eyes in which a presumptive diagnosis of closed-angle glaucoma had been made, using the criteria already described (p. 47). To avoid repetition these eyes will be referred to as belonging to the glaucomatous series although it may be that not all of the eyes so designated were, in fact, affected by the disease. As a result, any differences noted between the normal and glaucomatous series are likely to be less than those which in fact do exist, thus increasing the validity of the deductions drawn therefrom.

In order that these glaucomatous eyes might be compared with the normal eyes tested, it was necessary to ensure that the age and sex distributions in the two series were similar. Of the 97 cases in the glaucomatous series, 40 were male and 57 female. In the series of normal cases the sex distribution was 14 male and 28 female cases. No significant difference was found in the sex distribution of the two series by means of a χ^2 test. (Table IV). ($\chi^2 = 0.77 : n = 1 : P = > 0.10.$) Similarly no significant differences were found in the age distributions within and between the two series

of ....

of cases (Table V).

T A B L E IV

Series	Number of cases		
	Male	Female	$\chi^2 = 0.77$
Normal	14 (33.3%)	28 (66.7%)	n = 1
Closed-Angle Glaucoma	40 (41.2%)	57 (58.8%)	P => 0.10

Comparison of the sex distribution in a series of 42 normal cases and 97 cases affected by closed-angle glaucoma submitted to the darkroom outflow test. The sex distribution is similar in the two series. ($\chi^2 = 0.77$: n = 1 : P => 0.10)

T A B L E V

	Mean Age (Years)		Comparison of Mean Ages of Males and Females	Total Mean Age (Years)	Comparison of Total Mean Age in each Series.
	Male	Female			
Normal	56.2 (±16.7)	60.9 (±11.7)	t = 1.05 n = 40 P => 0.10	59.3 (±13.5)	t = 1.56 n = 137 P => 0.10
Closed Angle Glaucoma	55.9 (± 9.2)	56.2 (±15.7)	t = 0.08 n = 95 P => 0.10	56.1 (±10.0)	F = 1.35 n_1 = 41 n_2 = 96 P => 0.10

Comparison of the age distribution of 42 normal cases and 97 cases affected by closed angle glaucoma submitted to the darkroom outflow test. The age distribution is similar in the two series.

In the normal series, the mean age of the males

(56.2 .....

(56.2 years $\pm$ 16.7) was not significantly different from that of the females in the same series (60.9 years $\pm$ 11.7) ($t = 1.05$: $n = 40$: $P = > 0.10$). In the glaucomatous series the mean age of the males was 55.9 years $\pm$ 9.2 while that of the females was 56.2 years $\pm$ 15.7. Again there was no significant difference between these figures ($t = 0.08$: $n = 95$: $P = > 0.10$). Comparing the total mean age of all the normal cases (59.3 years $\pm$ 13.5) with that of the glaucomatous series (56.1 years $\pm$ 10.0) it could be seen that both series were entirely comparable in respect of age distribution. ($t = 1.56$: $n = 137$: $P = > 0.10$: $F = 1.35$: $n_1 = 41$: $n_2 = 96$: $P = > 0.10$.)

When the results of the darkroom outflow test on the glaucomatous series of eyes were examined it was found that in general there was a gross diminution in the facility of outflow in these eyes with the test. The mean change in outflow being + log 0.271 ($\pm$ log 0.253). This figure is very different from that found for the normal series (+ log 0.006 $\pm$ log 0.055) and on testing, the difference is seen to be significant ($t = 6.69$: $n = 137$: $P = < 0.001$). This mean decrease in the

facility of aqueous outflow occurring with the darkroom outflow test in cases presumed to have closed-angle glaucoma is equivalent to a fall in the facility of aqueous outflow of nearly 50% (47.5%) of the initially determined outflow factor.

If it is true that in early cases of closed-angle glaucoma, the angle of the anterior chamber is progressively closed by contact between the root of the iris and the back of the cornea one might expect that a group of eyes so affected would present a lower mean facility of aqueous outflow than a similar group of normal eyes, even when the ocular tensions in the former group were within the accepted limits of normality. Unfortunately there is no general agreement upon what constitutes the upper limit of the normal ocular tension. It was decided therefore to calculate, from a series of normal cases investigated personally by the writer, the limits of what might reasonably be regarded as the normal range of ocular tension (for the same standard Schiøtz X-tonometer as was used in the darkroom and darkroom outflow tests).

A series of 85 normal eyes was investigated

and ....

and the resting ocular tension of each measured with the Schiøtz X-tonometer. The tonometer reading was translated into mms. Hg in accordance with the 1929 conversion chart for this instrument. The mean ocular tension of this series was found to be 19.6 mms. Hg ± 3.6 mms. Hg. Thus the expected range of normal ocular tensions with this instrument would lie between 12.4 and 26.8 mms. Hg at the 95% level of probability or 8.8 and 30.4 mms. Hg at the 99% level of probability. The upper limit of normal ocular tension so calculated is higher than the true value as the variance of the results from which it is derived is affected by observational errors and instrumental errors inherent in the design of the tonometer together with errors due to such factors as the variability of corneal curvature and scleral rigidity. The increased variance resulting from these errors extends the estimated range of the normal ocular tension so that the limits quoted above can by no means be regarded as absolute measurements of ocular tension. The figures so derived however are useful and valid for the comparative purposes to which they are applied in this investigation.

It ....

It is interesting to note that an ocular tension of over 26 mms. Hg would be encountered in normal eyes less than five times in a hundred cases, for it was found, with both the darkroom test and the darkroom outflow test that eyes, in which the ocular tension was above 26 mms. Hg initially reacted very differently to those in which the tension was below this figure. For the purposes of the present investigation, an ocular tension of up to 31 mms. Hg was taken as being within the normal range and any tension of more than this figure as being pathologically raised.

To establish whether, in a group of eyes presumed to be suffering from closed-angle glaucoma there was evidence of obstruction of the angle even when the ocular tension was apparently normal, a comparison was made between the resting outflow, measured by tonography, in a series of normal eyes and in a comparable series of glaucomatous eyes. In spite of the fact that the ocular tension of the eyes in the glaucomatous series was below 31 mm. Hg, the mean level of outflow in these eyes (0.168 ± 0.058) was significantly lower than that found in the normal series (0.19 ± 0.046). ($t = 2.06$:

n = 137 : P = < 0.05.) The importance of this fact in the treatment of closed-angle glaucoma will be discussed later (p.125).

The distribution of the outflow levels in the series of normal eyes was in accordance with the usual biological curve. Calculating the range of values for the co-efficient of aqueous outflow to be expected in normal eyes from the mean and standard deviation of the present series, it can be concluded that the normal outflow level should lie between 0.10 and 0.28 (at the 95% level of probability) and that values below 0.10 should be considered pathological.

The mean resting outflow (0.189) determined for the eyes in the normal series in this investigation differs from that published by Grant (c = 0.243) but as Grant has pointed out (see Duke Elder, 1955) a difference in the curvature of the edge of one tonometer plunger as compared with another can account for differences of this order in the calculated values of the facility of outflow. As all the determinations of aqueous outflow in this investigation were carried out by the writer using the same electronic tonometer,

the figures so obtained, while probably not representing absolute values of aqueous outflow are nevertheless valid for comparative purposes.

The ocular tension in any eye is the result of a balance between the inflow and outflow of aqueous together with the effect of the rigidity of the coats of the eye and the blood pressure in the intra-ocular vessels. In any series of normal eyes there are likely to be differences in the rates of aqueous inflow and a similar spread in the calculated facilities of aqueous outflow, the actual level of ocular tension in any particular eye being the result of whatever combination of these factors prevails at the time of measurement. One might imagine therefore that two eyes with the same ocular tension might nevertheless have very different rates of inflow and outflow. This was indeed found to be true of those normal eyes investigated, the eyes with the same ocular tension often having different facilities of aqueous outflow as measured tonographically. As would be expected from this no correlation could be demonstrated between the measurements of ocular tension and aqueous outflow in these normal eyes ($r = -0.178$:

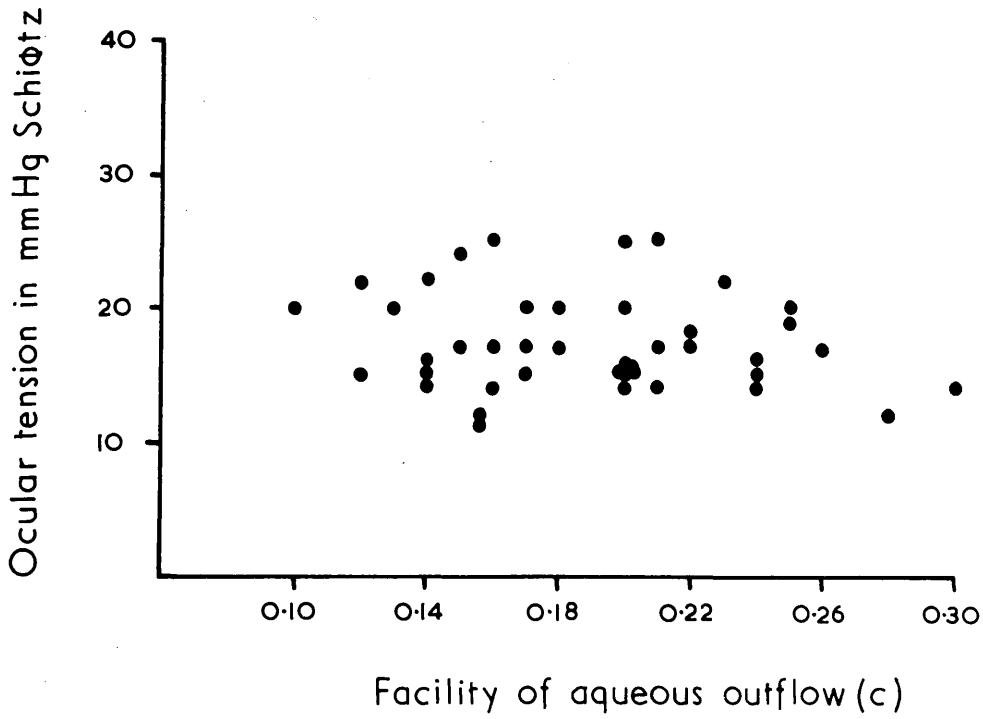

Fig. 7.

Diagram relating the ocular tension and facility of aqueous outflow in 42 normal eyes. Eyes with the same tension may have very different levels of aqueous outflow.

$n = 40 : P = > 0.10$)(Fig. 7).

The fairly small range of ocular tensions found in this series of normal eyes in spite of the wide variation in outflow levels is evidance in favour of the existence of some controlling factor adjusting the inflow level to suit the outflow, for as has already been noted the facility of aqueous outflow as measured tonographically appears to be relatively stable, and the fact that the value determined for the enucleated eye is similar to that derived from the living eye (Grant, 1950) would suggest that the maintenance of the normal ocular tension might depend more upon suitable alterations in the rate of aqueous inflow than upon compensating changes in the rate of outflow.

When, however, a comparison is made between the facility of aqueous outflow and the ocular tension in the case of eyes with closed-angle glaucoma it can been seen that there is a definite tendency for lower outflow levels to be associated with higher levels of ocular tension (Figs. 8 & 9). This is borne out by a correlation factor of - 0.455 which is significant at the 99.9% level ($r = - 0.455 : n = 95 : P = < 0.001$).

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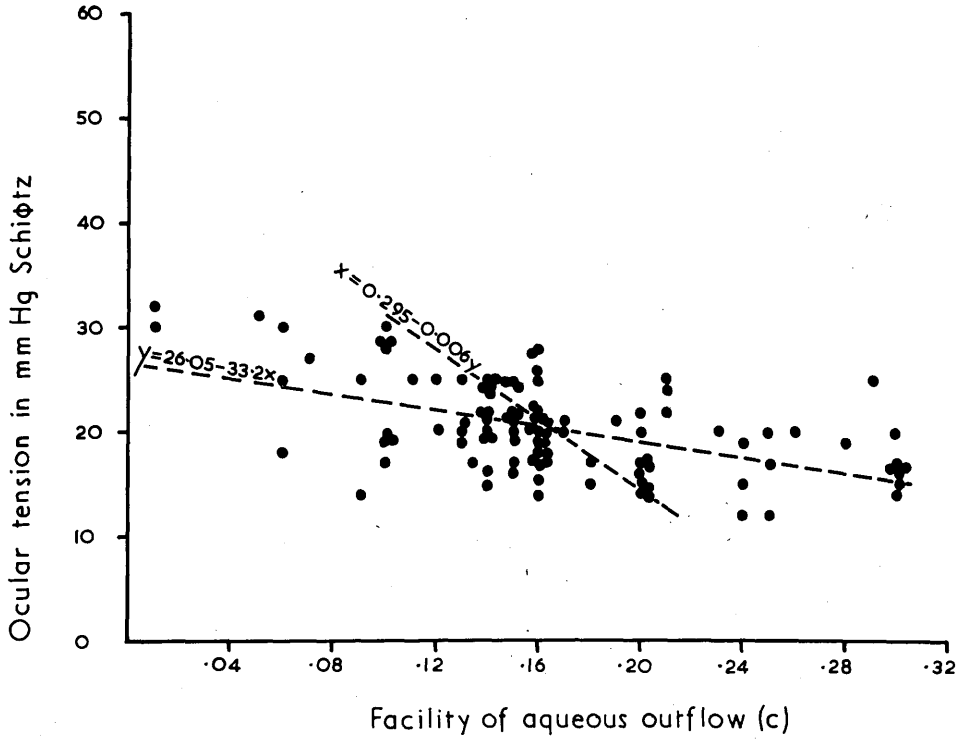

Fig. 8.

Diagram to illustrate the relationship between ocular tension and facility of aqueous outflow in eyes with closed angle glaucoma. In contrast to normal eyes, in closed angle glaucoma, where the resting ocular tension is within normal limits, the higher levels of ocular tension are associated with low values of aqueous outflow. The regression lines are superimposed.

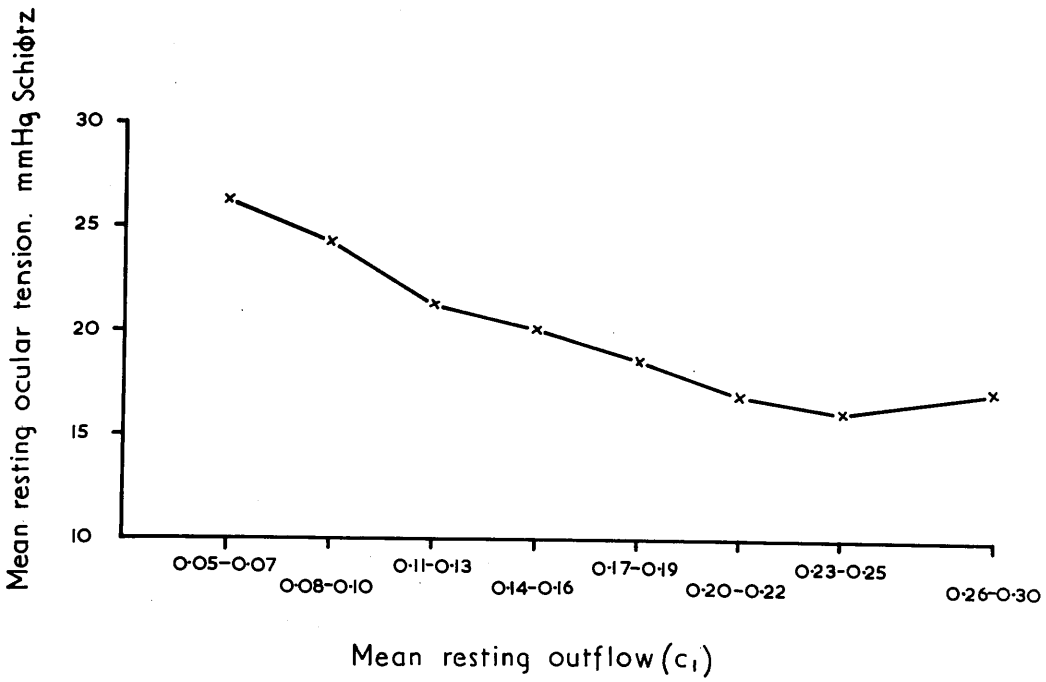

Fig. 9.

Graph to illustrate the mean ocular tension at differing levels of aqueous outflow in eyes with closed angle glaucoma. The lower the facility of outflow the higher is the ocular tension.

This latter graph differs from that for the eyes in the normal series in another respect also. In the case of the normal eyes none of the outflow levels is less than 0.10 whereas in the group of glaucomatous eyes such readings are not uncommon. The presence of these lower values of aqueous outflow in the eyes affected by closed-angle glaucoma is indicative of angle closure, although in none of the affected eyes was the tension greater than 31 mms. Hg. In addition if it is accepted that the rate of aqueous inflow in eyes with closed-angle glaucoma is similar to that found in normal eyes (and there is no evidence to the contrary) the correlation which exists between the ocular tension and the facility of outflow in closed-angle glaucoma must also be related to the existence of varying degrees of occlusion of the angle in these eyes. As can be seen from the graph (Fig. 8) this correlation continues down to ocular tensions of less than 20 mms. Hg suggesting that a degree of angle obstruction exists in some glaucomatous eyes even when the ocular tension is as low as this figure.

As has been noted, the apparatus used in this investigation has been found to give a co-efficient

of aqueous outflow of 0.10 as the lower limit of normality.

From the equation of the regression line of ocular tension on aqueous outflow in cases of closed-angle glaucoma, it can be seen that where the outflow factor is in the region of 0.10, indicative of some obstruction to the outflow of aqueous the resting ocular tension is likely to be in the region of 23 mms. Hg ($y = 26.05 - 33.24$). From this one may reasonably deduce that in closed-angle glaucoma where the ocular tension is greater than 24 mms. Hg, there may already exist a degree of angle closure, which if untreated may eventually lead to the permanent occlusion of the affected area by the development of goniosynechiae.

From the foregoing, one would expect that the result of a provocative test such as the darkroom test might be influenced by this obstruction to aqueous outflow which has been shown to occur in affected eyes when the ocular tension is in the upper reaches of the normal range.

To test this supposition, the incidence of positive darkroom tests in the series of glaucomatous eyes was related to the coefficient of aqueous outflow

determined for these eyes at the start of the test. The percentage incidence of positive results with the darkroom test was calculated for groups of eyes with decreasing levels of aqueous outflow and it was found that whereas the number of positive results was small where the outflow level was initially high, the incidence of positive results rose progressively with decreasing values of outflow coefficient (Fig. 10).

To test the significance of this finding a comparison was made between the incidence of positive results with the darkroom test in those cases where the initial outflow was greater than 0.13 and that where the outflow was lower than 0.12. In the former category where the initial level of aqueous outflow was within normal limits only 14 out of 79 cases (17.7%) gave a positive result with the darkroom test, whereas in the latter group in which the level of outflow initially was lower than normal, 15 cases out of 18 (83.3%) gave a positive result with the test. A χ^2 test reveals a significant difference between these two categories (Table VI)($\chi^2 = 27.06$: $n = 1$: $P = < 0.001$).

When the mean initial level of aqueous outflow

for ....

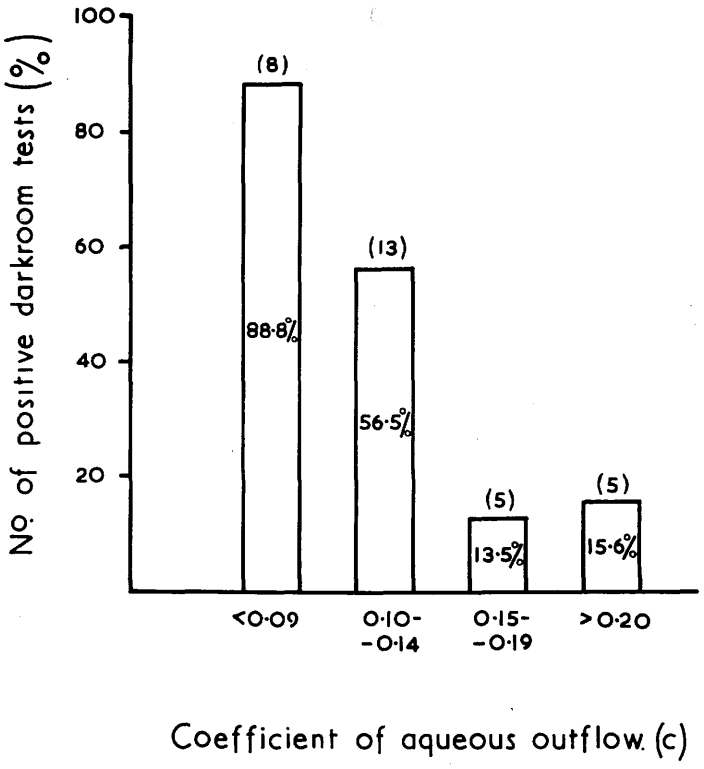

Fig. 10.

Diagram relating the resting facility of outflow and the incidence of positive results with the darkroom test in eyes with closed angle glaucoma. The greatest incidence of positive results with the test occurs where the initial level of outflow is low.

TABLE VI

Facility of Aqueous Outflow	Result of Darkroom Test	
	Positive	Negative
Greater than 0.13 (18 eyes)	15 (83.3%)	3
Less than 0.12 (79 eyes)	14 (17.7%)	65

A comparison of the incidence of positive results with the darkroom test on two series of eyes with closed-angle glaucoma with differing levels of aqueous outflow initially. The darkroom test is more often positive where the initial level of outflow is low than where it is normal or high ($\chi^2 = 25.85$: $n = 1$: $P = < 0.001$).

for all cases of closed-angle glaucoma giving a positive result with the darkroom test ($c = 0.133 \pm 0.064$) was compared with that calculated for these cases giving a negative result with the test (0.181 ± 0.050) it was found that, in spite of the fact that the ocular tension of the eyes in both groups at the start of the test was within normal limits, the group of cases giving a positive result with the darkroom test had a significantly lower level of aqueous outflow initially than had the

group ....

group in which the result of the test was negative. ($t = 3.6 : n = 95 : P = < 0.001.$)

It thus appeared reasonably certain that not only was there evidence of obstruction of the angle in some eyes with closed-angle glaucoma where the ocular tension was within normal limits, but that the result of the darkroom test depended largely upon whether or not this obstruction was present.

It has already been noted (p.62) that the magnitude of the rise in ocular tension occurring with the darkroom test in cases of closed-angle glaucoma was greater where the initially determined tension was in the upper reaches of normality. It was decided to investigate whether or not the actual magnitude of the rise in tension in these cases was also directly related to the facility of aqueous outflow at the start of the darkroom test.

When the rise in ocular tension occurring with the darkroom test in cases of closed-angle glaucoma was plotted against the initial level of outflow in these eyes it was found that the lower the facility of outflow at the start of the test the higher was

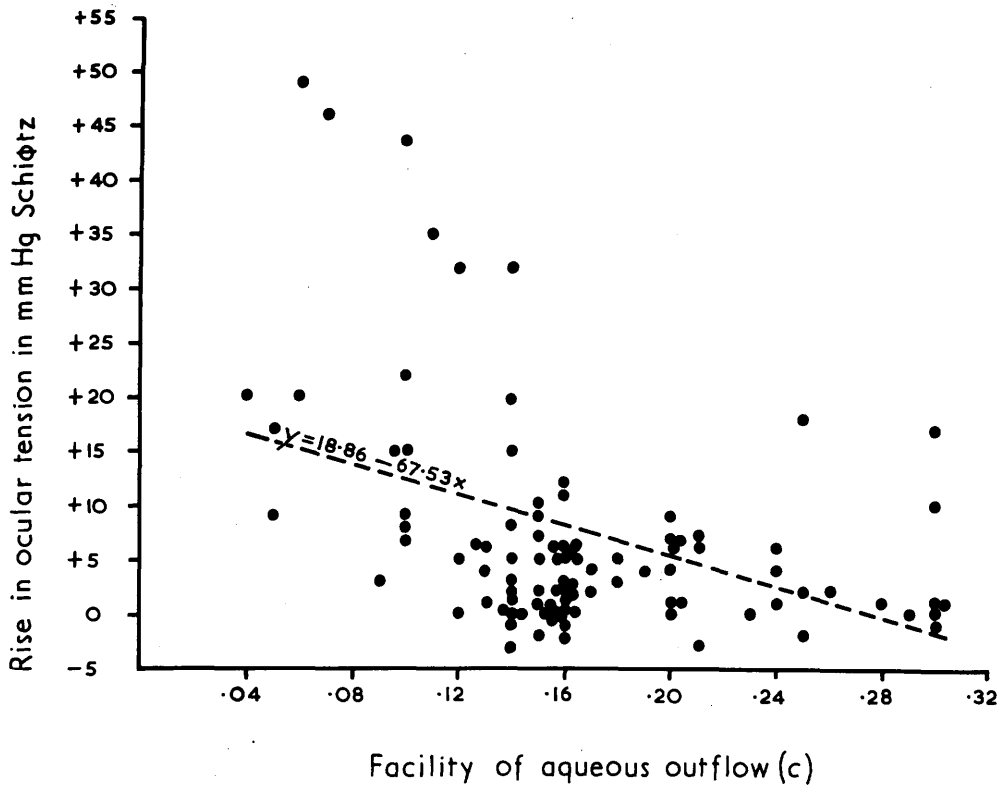

Fig. 11.

Diagram to illustrate the relationship between the resting facility of aqueous outflow (c) and the rise in ocular tension with the darkroom test on eyes with closed angle glaucoma. Low initial levels of outflow are associated with greater rises in ocular tension with the test than is the case with higher levels of outflow. The regression line of ocular tension on aqueous outflow is indicated.

the resulting rise in ocular tension (Fig. 11). Calculating the correlation coefficient for these two variables, a significant degree of correlation is found to exist ($r = -0.332 : n = 95 : P = < 0.01$).

When consideration was given to the influence of the resting level of aqueous outflow on the magnitude of the change in the outflow factor occurring in the darkroom outflow test in cases of closed-angle glaucoma some unexpected results became apparent. It might be thought that in these eyes an hour in the dark would be likely to result in a fall in the facility of outflow of say 30% irrespective of the level of outflow at the start of the test, provided that enough of the angle was open to allow of a reduction in outflow of this magnitude. When however the resting outflow level is plotted against the change in outflow occurring with the test in these eyes it is seen that lower initial levels of outflow are associated with much greater reductions in the outflow factor than are the higher levels (Fig. 12). This correlation is significant ($r = -0.363 : n = 95 : P = < 0.001$). This suggests that where the angle is largely obstructed prior to

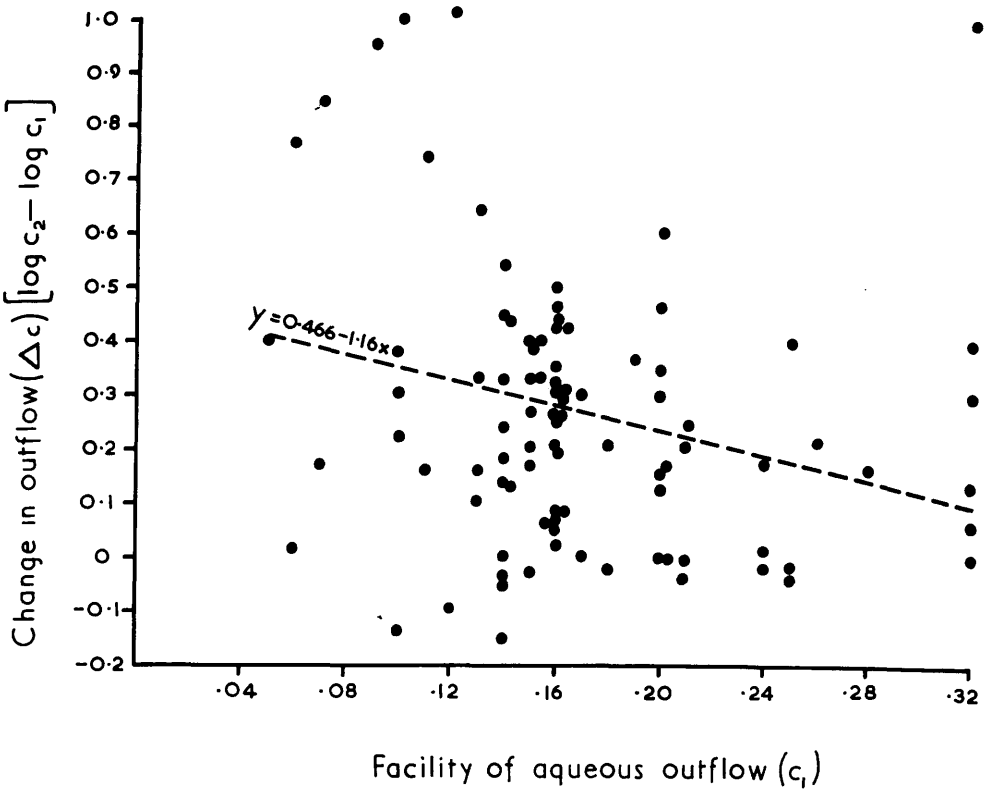

Fig. 12.

Diagram to illustrate the relationship between the initial facility of outflow (c_1) and the change in outflow (Δ c) occurring as a result of the darkroom outflow test on eyes with closed-angle glaucoma. Low levels of outflow initially, are associated with greater changes in outflow with the test than is the case where the initial level of outflow is high.

the test, the remaining unobstructed area is much more sensitive to changes in illumination than is the case when all the angle is open.

CHAPTER IV

A COMPARISON OF PROVOCATIVE TESTS

SUMMARY

A comparison is made between the results of the darkroom test and the darkroom outflow test on a series of eyes with closed-angle glaucoma. The darkroom outflow test is found to be positive in a significantly greater number of cases than the darkroom test. An attempt is made to assess how quickly angle closure occurs in the dark by measuring the change in the facility of outflow during the darkroom test at intervals of 15 minutes.

The efficacy of a peripheral iridectomy in the prevention of angle closure is assessed by means of the darkroom outflow test. In none of the eyes which had been subjected to this operation could closure of the angle be induced.

As has already been mentioned, it was expected that the darkroom outflow test might prove a more discriminating provocative test in the investigation

of ....

of closed-angle glaucoma than the standard darkroom test. A comparison of the results of the two tests performed on the same group of glaucomatous eyes justified this expectation.

In order to decide whether the darkroom outflow test was more useful than the standard darkroom two questions had to be answered:

(1) Did the darkroom outflow test separate the normal eyes from the abnormal more clearly than the darkroom test;

(2) was the darkroom outflow test more often positive in the same group of closed-angle glaucoma cases than the darkroom test.

When the initially determined coefficients of aqueous outflow in eyes subjected to the darkroom outflow test were plotted against the final values, it was found that in the case of normal eyes the results were symmetrically disposed about a line which represented no change in outflow level with the test (Fig. 13). In none of these eyes was there a fall in the level of outflow of as much as 30%.

It will be remembered that when the darkroom

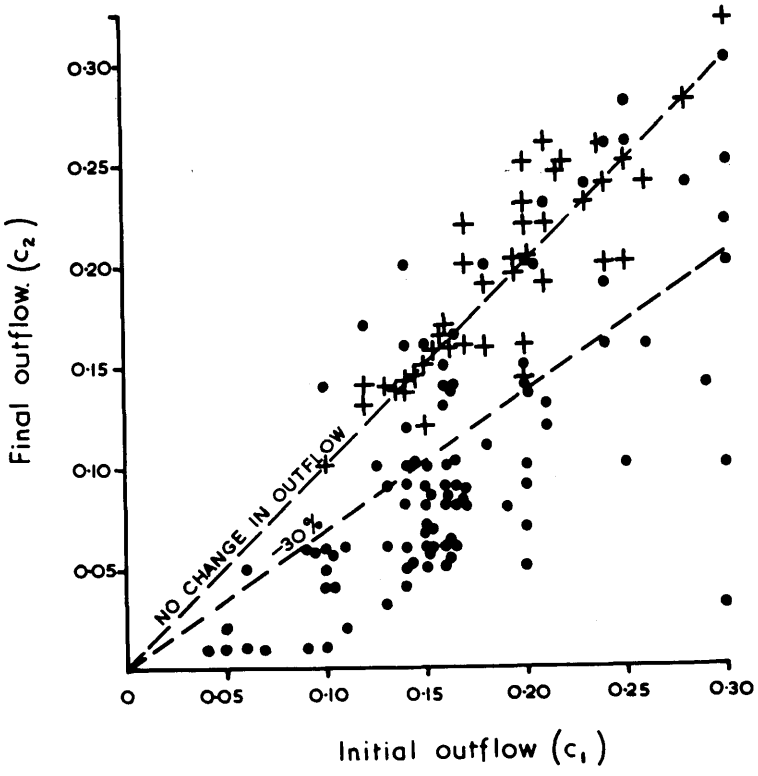

Fig. 13.

Scattergram relating the initial level of outflow (c_1) and the final level (c_2) in 42 normal eyes (+) and 97 eyes with closed angle glaucoma (•) submitted to the darkroom outflow test. In all the normal eyes the change in outflow with the test was less than 30%. A fall in outflow of over 30% occurred in the majority of eyes with closed angle glaucoma.

test was studied, considerable overlap was found between the results with the test in normal and glaucomatous eyes. When the results of the darkroom outflow test were similarly compared it was apparent that there was a much clearer separation of the two groups of cases with this test (Fig. 14), (cf. Fig. 2).

When the incidence of positive results with the darkroom test was compared with that of the darkroom outflow test, it was found that in the same series of eyes with closed-angle glaucoma a significant change in outflow level was more often found than a significant rise in ocular tension. Of the 97 cases studied the darkroom test was positive in 30% while the darkroom outflow test was positive in 67%. This difference is significant ($\chi^2 = 24.6 : n = 1 : P =< 0.001$)(Table VII).

At first sight this might appear strange as both the rise in ocular tension and the change in the facility of outflow result from the same mechanical blockage of the angle. The difference however is explicable when the time factor is considered for it must take some appreciable time for obstruction of

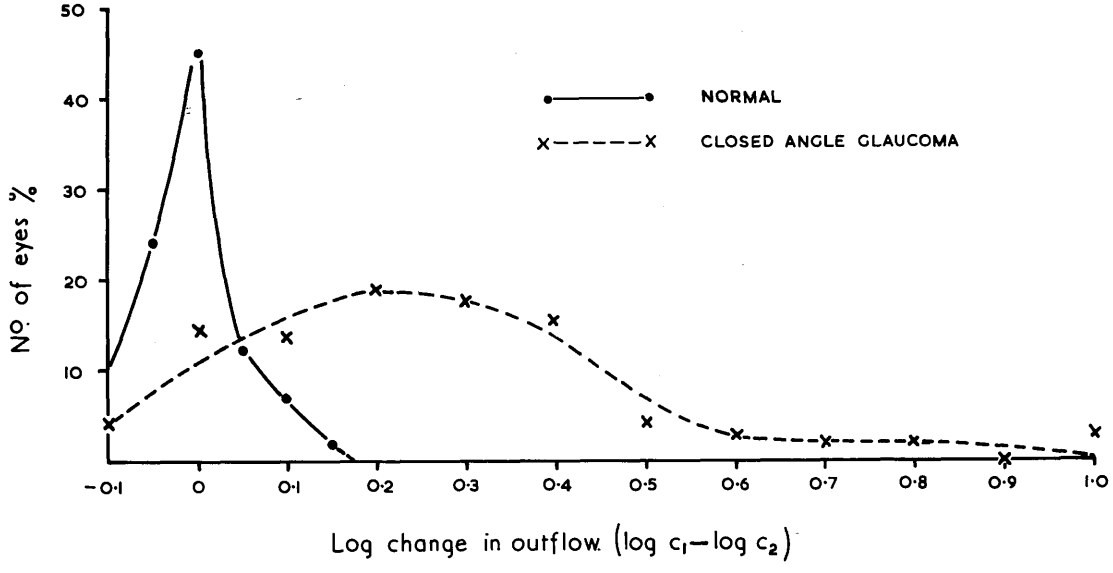

Fig. 14.

Diagram to illustrate the distribution of 42 normal eyes and 97 eyes with closed angle glaucoma in relation to the change in outflow occurring with the darkroom outflow test. There is a fairly clear demarcation between the two series of eyes.

TABLE VII

Test Employed	Result of Test	
	Positive	Negative
Darkroom test	29 (30%)	68
Darkroom outflow test	65 (67%)	32

Comparison of the results of the darkroom test and darkroom outflow test on the same series of 97 eyes with closed-angle glaucoma. The darkroom outflow test is more often positive than the darkroom test. ($\chi^2 = 24.6 : n = 1 : P = < 0.001$)

the angle which is immediately recognisable by tonography to cause a significant rise in ocular tension. Presumably all cases giving a positive result with the darkroom outflow test would also give a positive result with the darkroom test if given sufficient time. This view is supported by the fact that in some cases a significant rise in tension occurred after two hours in the dark when such a rise was absent after only one hour in the dark.

In order to determine how quickly obstruction of the angle occurring with the darkroom test could be appreciated by tonography a small series of cases

of ....

of closed-angle glaucoma was submitted to darkroom outflow tests of 15 minutes, 30 minutes, 45 minutes and 60 minutes duration. As this investigation required eight tonographic determinations of the facility of outflow on four different days for each patient the number of cases investigated was small and no significant statistical results were obtained.

The change in outflow factor for each test was expressed as a fraction of the initially determined level of outflow. When the mean change in outflow occurring at intervals of fifteen minutes was plotted against time (Fig. 15) it could be seen that in the cases investigated a measurable degree of angle obstruction occurred after 30 minutes in the dark whereas a significant rise in ocular tension did not occur until after one hour in the dark.

In order to make the results of the darkroom outflow test more easily interpreted a graph relating the initial and final determinations of aqueous outflow was prepared (Fig. 16). Results lying below the heavy line are indicative of angle closure with the test while those above it may be considered negative. The area

bounded ....

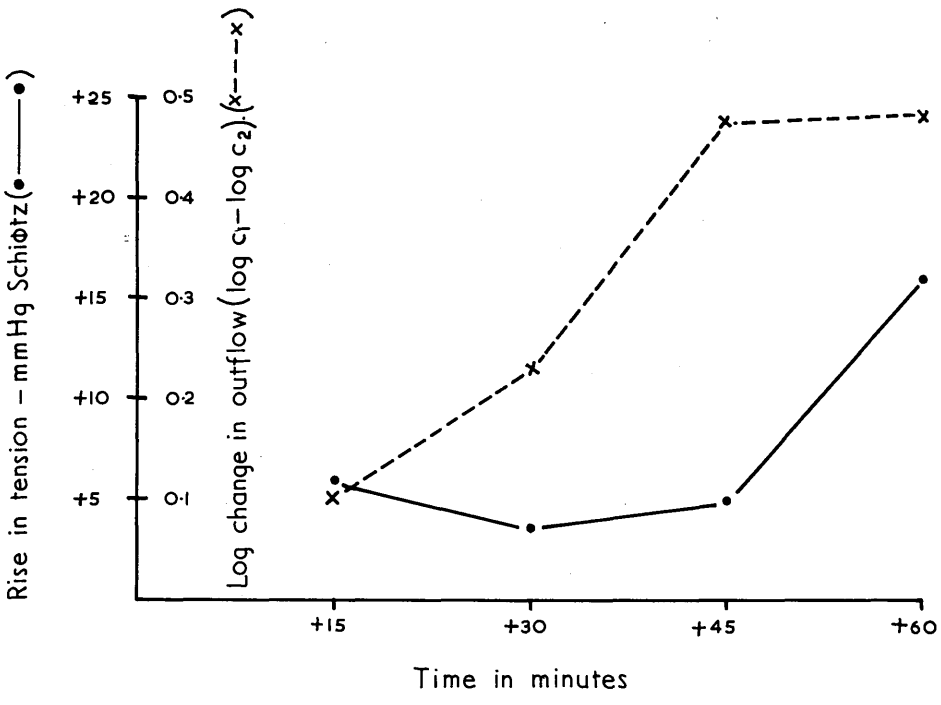

Fig. 15.

Diagram to illustrate the relative mean rates of change in ocular tension and aqueous outflow occurring in eyes with closed angle glaucoma subjected to the darkroom outflow test. The level of outflow falls before the ocular tension rises.

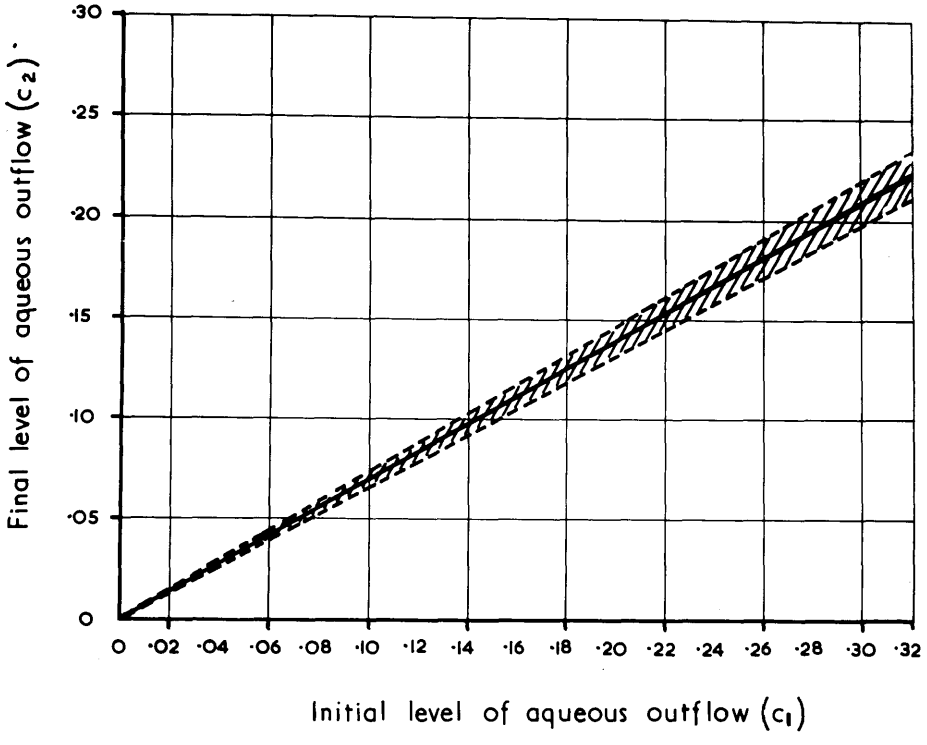

Fig. 16.

Diagram to facilitate the interpretation of the results of the darkroom outflow test. Results lying below the heavy line are indicative of the occurrence of angle closure with the test while those above the line may be regarded as negative. Results lying within the shaded area are borderline.

bounded by the broken lines represents 95% confidence limits between which the results of the test may be taken as borderline.

As the darkroom outflow test appeared to offer a method of assessing the ease with which the angle could become obstructed it was thought a suitable test for an investigation into the efficacy of peripheral iridectomy in closed-angle glaucoma. For this investigation 11 cases of closed-angle glaucoma upon which a peripheral iridectomy had been performed were submitted to the test. None of the cases tested had peripheral anterior synechiae. Pre-operatively each of these cases had a narrow angle in the affected eye and suffered attacks of raised ocular tension together with haloes and misty vision. Most of the cases had experienced an acute closed-angle attack in the affected eye while those which had not done so presented other evidence of angle closure such as a positive darkroom test.

The results of provocation with the darkroom outflow test on these operated eyes are shown in Table VIII where it can be seen that the pre-operative tendency in these eyes to develope closure of the angle has been

TABLE VIII

Sex	Age	Eye	Darkroom Test				Darkroom Outflow Test		
			T_1	T_2	$T_1 - T_2$	Result	c_1	c_2	Result
F	55	R	17	20	+ 3	Negative	0.20	0.18	Negative
F	70	L	25	25	0	"	0.14	0.14	"
F	62	L	20	19	- 1	"	0.20	0.20	"
M	42	R	20	20	0	"	0.14	0.18	"
F	48	R	16	15	- 1	"	0.19	0.20	"
F	54	L	20	19	- 1	"	0.17	0.13	"
F	71	R	21	17	- 4	"	0.14	0.11	"
M	62	R	25	24	- 1	"	0.18	0.21	"
M	54	L	20	24	+ 4	"	0.16	0.14	"
F	64	L	29	27	- 2	"	0.10	0.10	"
F	34	L	24	25	+ 1	"	0.16	0.15	"

Results of the darkroom test and darkroom outflow test on eleven eyes with closed-angle glaucoma upon which peripheral iridectomies had been performed. In each case the result of the provocative test was negative. (T_1 and T_2 = ocular tensions in mm. Hg: c_1 and c_2 = facilities of aqueous outflow.)

completely abolished by the peripheral iridectomy. In none of the eyes tested was the darkroom outflow test positive nor was there any significant rise in ocular tension on provocation. As there was no subconjunctival

drainage ....

drainage of aqueous in any of these eyes post-operatively the control of ocular tension and aqueous outflow exercised by the peripheral iridectomy is good evidence in favour of the existence of an iris bombé mechanism in these eyes prior to the operation.

CHAPTER V

CHRONIC CLOSED-ANGLE GLAUCOMA

SUMMARY

It is shown that in some cases of chronic closed-angle glaucoma where cupping of the optic disc and visual field loss has occurred, that although the obstruction of the angle in these eyes may appear to be permanent and due to goniosynechiae, it is in fact variable and due to contact rather than adhesion between the root of the iris and the posterior surface of the cornea.

This deduction is based on measurements of the facility of outflow and ocular tension together with observations of the appearance of the angle in these cases following the instillation of strong miotics or after peripheral iridectomy.

It is known that some long standing cases of closed-angle glaucoma develop pathological cupping of the optic disc accompanied by visual field loss. Clinically, the development of pathological changes

in ....

in the nerve head in such cases has usually been taken as an indication that the angle has become permanently obstructed by the development of peripheral anterior synechiae. However, the finding that a variable degree of obstruction of the angle was often present even in early cases of closed-angle glaucoma suggested that such changes in the optic disc and visual field might result from long standing but not necessarily permanent obstruction of the angle by contact rather than adhesion between the root of the iris and the cornea.

It was noted that in some cases of closed-angle glaucoma the resting outflow was often as low as that found in chronic simple glaucoma but that it could be raised to near normal levels by the instillation of a suitable strong miotic. An actual example will illustrate this.

Case I: a male aged 63 had developed an acute hypertensive episode in the right eye early in 1954. The attack responded to miotic therapy and thereafter the patient had been instilling pilocarpine 2% twice daily into this eye. In June, 1955 the vision in the right eye was 6/9 unaided and the visual field full.

Gonioscopy revealed a "very narrow angle, closed above but just open below". The ocular tension was found to be 28 mm. Hg some 7 hours after the instillation of pilocarpine 2%; the facility of aqueous outflow was 0.10. One hour in the dark caused the ocular tension to rise to 34 mms. Hg while the facility of aqueous outflow fell to 0.05. Immediately after the instillation of pilocarpine 2% the ocular tension was found to be 28 mms. Hg but the facility of outflow had risen to 0.14. A further hour in the dark resulted in a rise of ocular tension to 30 mms. Hg and a fall in the facility of outflow to 0.08. This indicated that part of the angle was more or less habitually obstructed by irido-corneal contact. Just after the instillation of pilocarpine however the level of aqueous outflow rose to within normal limits, indicating that the obstructive changes at the angle were by no means permanent.

In this case, for most of the time the facility of outflow was as low as that usually found in cases of chronic simple glaucoma, and it seemed reasonable to postulate that such a case might eventually develop cupping of the optic disc and visual field loss without however

necessarily ..

necessarily forming goniosynechiae. It would obviously be possible to prove that this advanced stage of chronic closed-angle glaucoma could result from reversible obstruction of the angle if the facility of aqueous outflow and the ocular tension could be normalised by a peripheral iridectomy and the angle of the anterior chamber subsequently shown to be open and free from goniosynechiae.

Several cases of chronic closed-angle glaucoma with varying degrees of cupping of the optic disc and visual field loss were studied and those in which the obstruction of the angle appeared to be variable and probably reversible submitted to the operation of peripheral iridectomy. In deciding which cases were suitable for operation more reliance was placed upon the changes in ocular tension and facility of outflow following the instillation of a strong miotic, than upon the gonioscopic appearance of the angle for where there was marked iris bombé it was usually impossible to tell whether the angle was closed by goniosynechiae or merely by contact between the iris and cornea. The absence of a history of an attack of acute congestive glaucoma was also regarded as a point in favour of the obstruction of the angle being

reversible rather than permanent.

Details of the cases studied are given below. In all the cases described the ocular tension had been high enough for a period of time sufficient to result in cupping of the optic disc and thedevelopment of scotomata in the visual fields. This long standing high tension coupled with a low outflow factor was indicative of continuous obstruction of the angle in these eyes, while the fact that the instillation of a strong miotic was able to normalise the tension and outflow reading for a short time indicated that the closure of the angle was unlikely to be due to goniosynechiae. The truth of this deduction was demonstrated in those cases submitted to peripheral iridectomy, for, following the operation the ocular tension and facility of aqueous outflow were found to be within normal limits while the previously closed angle of the anterior chamber was seen to be open and free from goniosynechiae.

Case II: a male, aged 49, complained of attacks of blurred vision in the right eye for one year. He was found to have corneal oedema in the affected eye and an ocular tension of 60 mms. Hg (Schiøtz) which

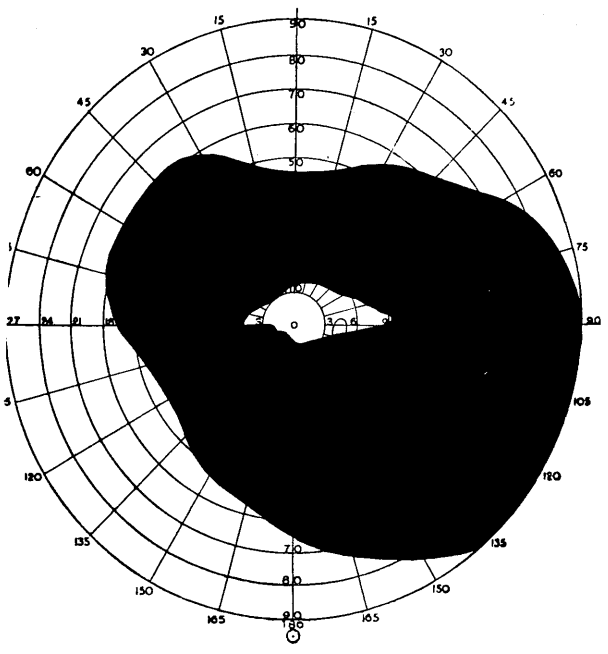

Fig. 17.

Visual field of Case II to show the extent of field loss.

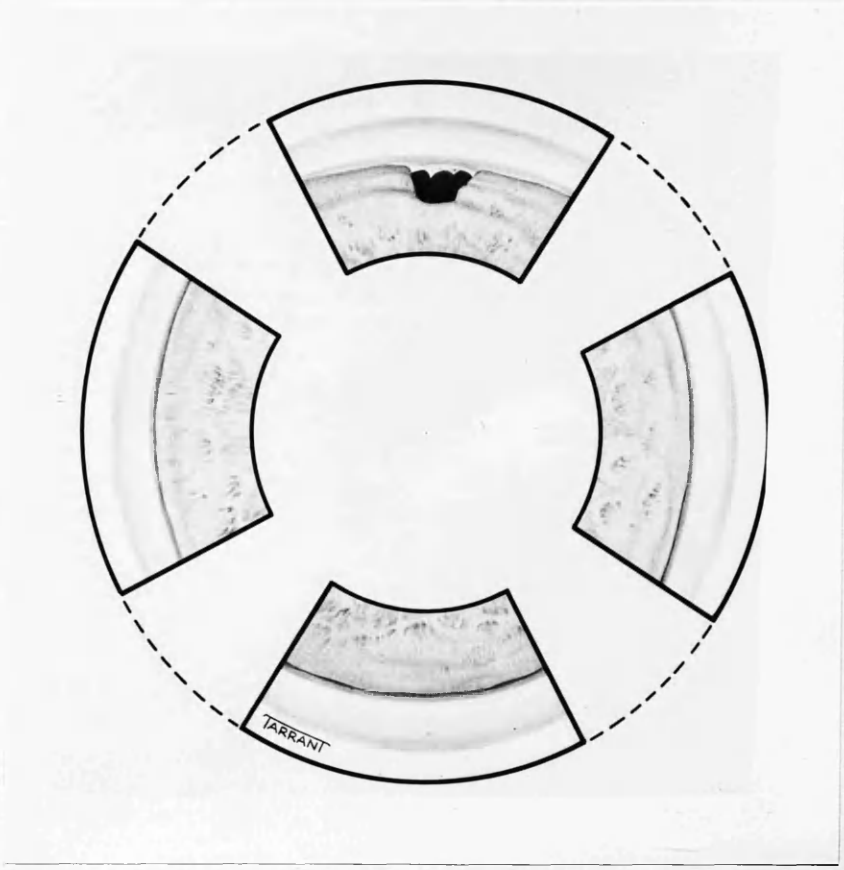

Fig. 18.

Drawing to illustrate the post-operative appearance of the angle of the anterior chamber in Case II. The angle is open and free from goniosynechiae.

was reduced by miotics to 48 mms. Hg. Gonioscopy revealed a very narrow angle apparently entirely closed. The optic disc was pathologically cupped and the visual field constricted to within 10° of the fixation point (Fig. 17).

A peripheral iridectomy was performed, after which the angle of the anterior chamber could be seen to be open and free from goniosynechiae (Fig. 18). The ocular tension thereafter did not rise above 20 mms. Hg and the facility of aqueous outflow was 0.25.

Case III: a male aged 72, complained of discomfort in the right eye and failing vision for nine months. The ocular tension was found to be 70 mms. Hg reduced by miotics to between 30 and 40 mms. Hg. The optic disc was deeply cupped and the visual field showed nasal loss within 5° of the fixation point, together with a typical Bjerrum scotoma (Fig. 19).

Gonioscopy shortly after the instillation of eserine 0.5 per cent. and pilocarpine 2 per cent. revealed a narrow angle, open in the lower segment but closed in the upper (Fig. 20). The facility of aqueous outflow at that time was 0.14 in the affected (compared

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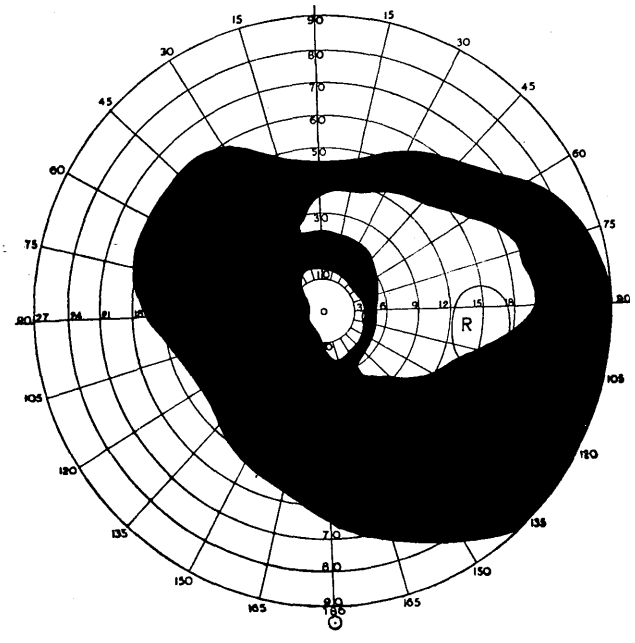

Fig. 19.

Visual field in Case III to show the extent of field loss.

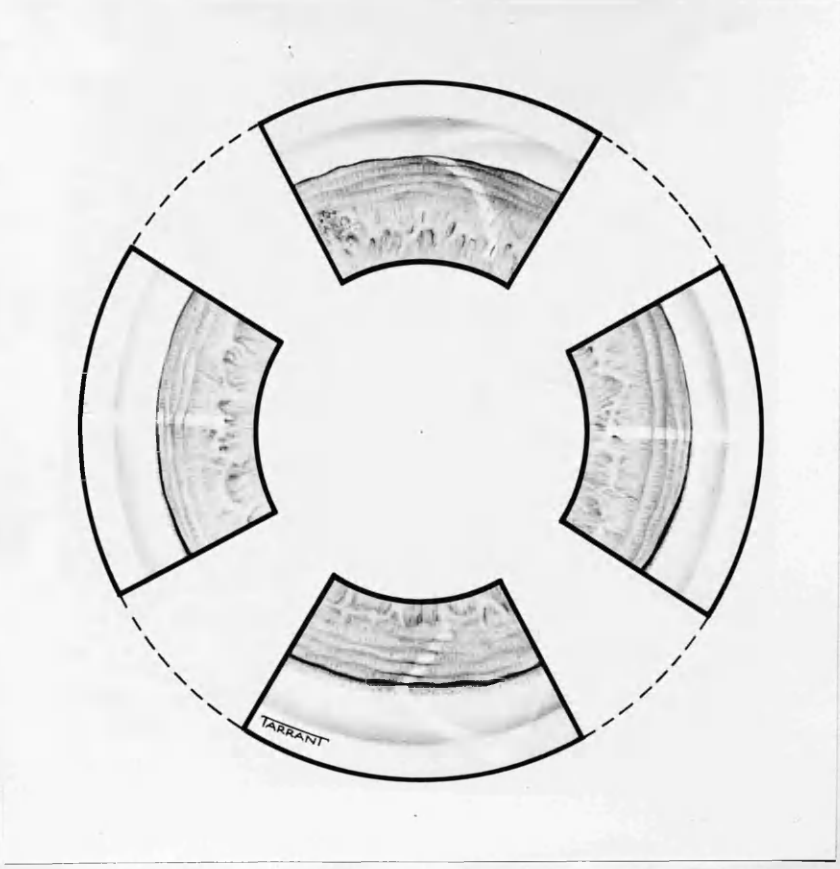

Fig. 20.

Drawing to illustrate the pre-operative appearance of the angle in Case III. The angle is closed above and just open below.

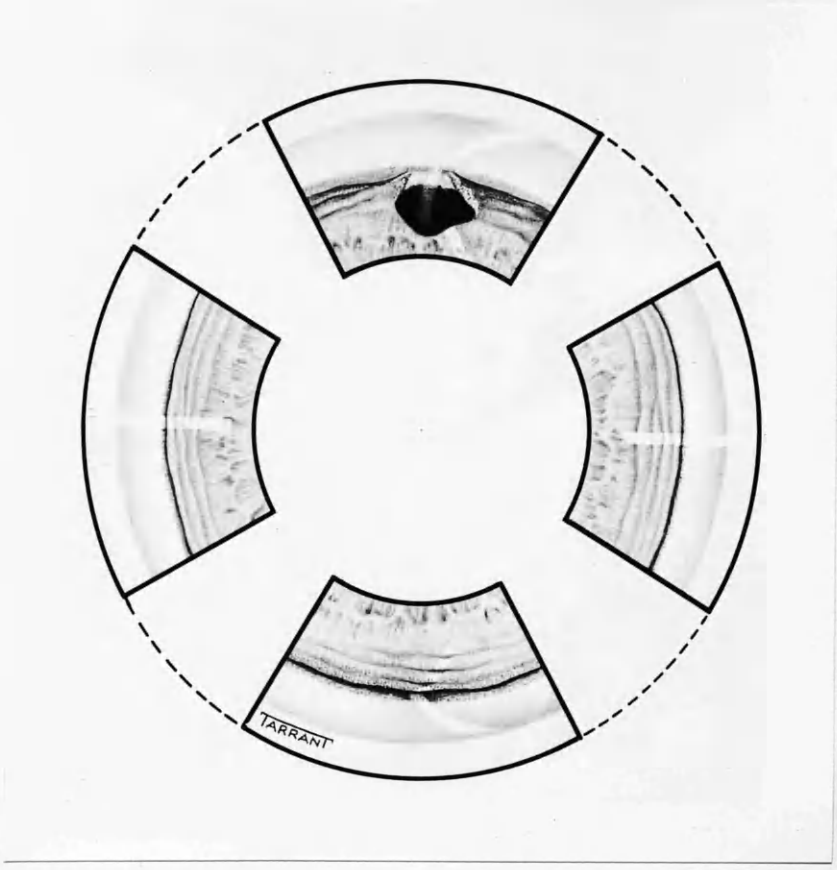

Fig. 21.

Drawing to illustrate the post-operative appearance of the angle in Case III. The angle is now open and free from goniosynechiae.

with 0.20 in the unaffected) eye.

A peripheral iridectomy was performed on the right eye, after which the previously closed sector of the angle could be seen to be open and free from goniosynechiae (Fig. 21). The ocular tension remained in the region of 20 mms. Hg while the facility of aqueous outflow was 0.28.

Case IV: Male aged 51. Presented with a history of haloes and mistiness of vision in the left eye for six months. The left optic disc was found to be cupped and there was a typical Bjerrum scotoma in the left field of vision (Fig. 22). The ocular tension four hours after the instillation of pilocarpine was 34 mms. Hg. Gonioscopy revealed that at least 70% of the angle of the anterior chamber was closed. Immediately after the instillation of pilocarpine 2% and eserine 1% the angle appeared to be open while the facility of aqueous outflow was 0.16. The ocular tension was then 25 mms. Hg. A peripheral iridectomy was performed on the left eye following which, without miotics the angle could be seen to be open and free from goniosynechiae. The ocular tension was 22 mms. Hg even after provocation

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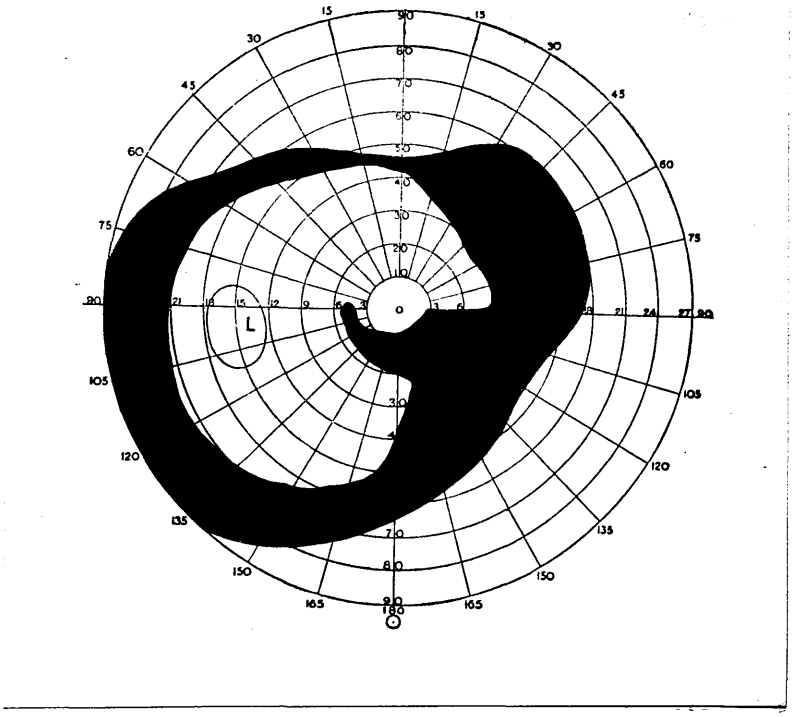

Fig. 22.

Visual field of Case IV to show the typical glaucomatous field loss.

with the darkroom test and the facility of aqueous outflow was 0.16 with no significant reduction in this figure with the darkroom outflow test.

Case V: male aged 62, complaining of haloes and misty vision in the right eye for three months, was found to have cupping of the optic disc and a visual field defect although the ocular tension in the affected eye could be normalised by the use of miotics (Fig. 23).

A peripheral iridectomy was performed following which the angle of the anterior chamber could be seen to be open and free from goniosynechiae. The ocular tension remained below 25 mms. Hg in spite of provocation with the darkroom test. The darkroom outflow test was negative, the facility of aqueous outflow in the affected eyes being 0.21.

Case VI: female aged 68, complaining of mistiness of vision and haloes for two months. The right visual field was found to be full whereas that on the left revealed extensive glaucomatous field loss (Fig. 24). The ocular tension in the left eye was 27 mms. Hg rising to 72 mms. Hg with the darkroom test. The facility of aqueous outflow was 0.07 falling to 0.01 with the

darkroom ....

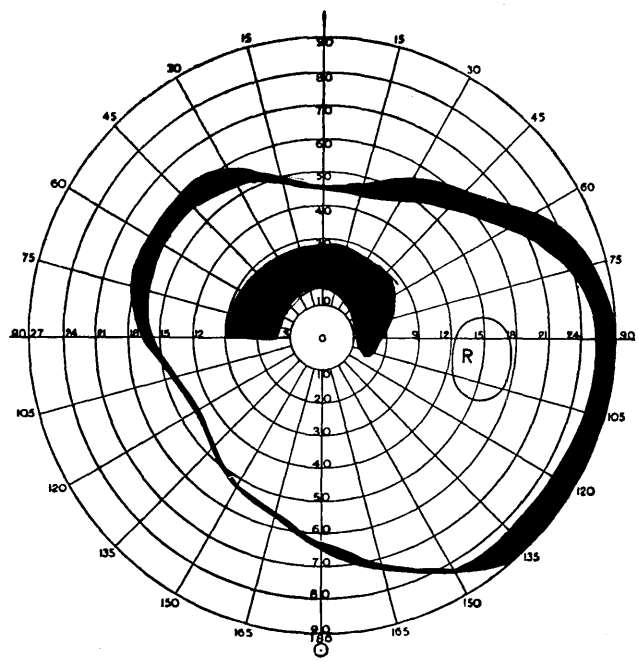

Fig. 23.

Visual field of Case V to show the typical glaucomatous field loss.

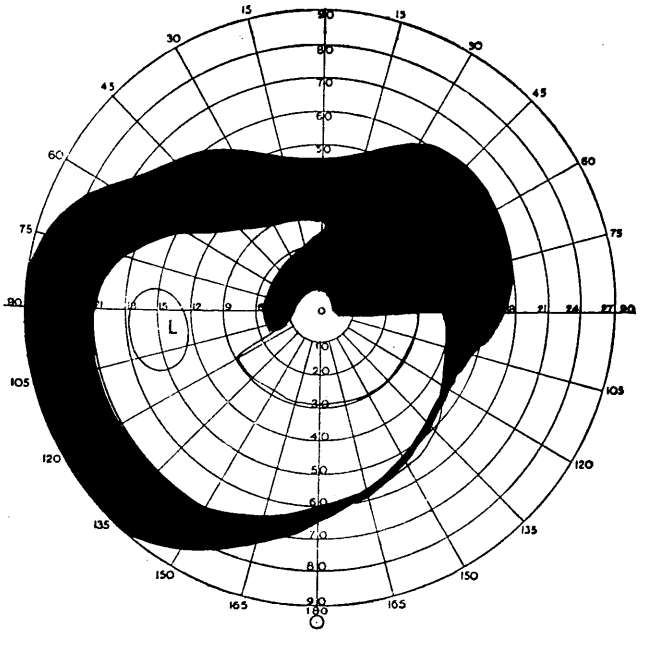

Fig. 24.

Visual field of Case VI to show the defect present.

darkroom outflow test. When using guttae pilocarpine 2% however the ocular tension in the affected eye did not rise above 25 mms. Hg with the darkroom test nor did the facility of aqueous outflow fall below 0.15. This patient has not been operated upon, but the normal outflow level, ocular tension and appearance of the angle after the instillation of pilocarpine drops indicate that the obstruction of the angle which had been present long enough to produce optic atrophy and a field defect, must have been due to irido-corneal contact and not to goniosynechiae.

Case VII: male, aged 68, complained of blurred vision and haloes affecting the left eye for 5 years. The left optic disc was found to be cupped and there was typical glaucomatous field loss (Fig. 25). The ocular tension in the affected eye was 45 mms. Hg while gonioscopy revealed that at least 50% of the angle was closed. Instillation of guttae pilocarpine 2% caused the angle to re-open and the tension to fall to 20 mms. Hg. The facility of aqueous outflow at this time was 0.33.

A peripheral iridectomy was performed on the left eye but as there was evidence of subconjunctival

drainage ....

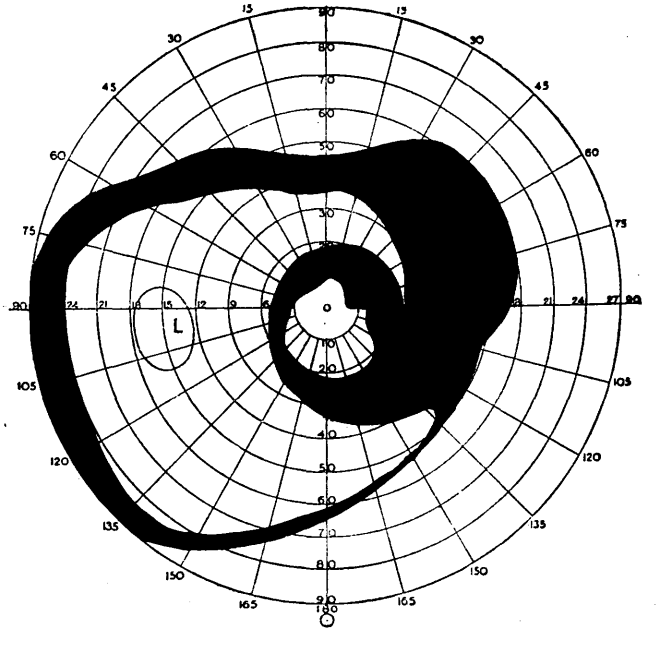

Fig. 25.

Visual field of Case VII to show the defect present.

drainage of aqueous subsequently no deductions on the functional state of the angle could be drawn from the fact that the ocular tension remained within normal limits post-operatively. As in Case V, however, the low ocular tension and high facility of outflow found pre-operatively after the instillation of pilocarpine together with the gonioscopic appearance of the angle ruled out the presence of goniosynechiae in this case.

The behaviour of these eyes clearly demonstrates that obstruction of the angle in cases of advanced chronic closed-angle glaucoma may be due to contact between the iris and cornea sufficient to reduce the outflow of aqueous to abnormally low levels and maintained for a period of time long enough to result in cupping of the optic disc and loss of part of the visual field without the formation of goniosynechiae.

It is well recognised that in chronic closed-angle glaucoma, goniosynechiae do eventually form and this present study underlines the importance of adequate treatment of such eyes in the early stages where the obstruction of the angle is still reversible.

CHAPTER VI

UNILATERAL CLOSED-ANGLE GLAUCOMA

SUMMARY

The bilateral incidence of closed-angle glaucoma is to be expected from the anatomical similarity of fellow eyes.

The second eye in a series of cases of unilateral closed-angle glaucoma is investigated by means of the darkroom test and the darkroom outflow test.

Positive evidence of closed-angle glaucoma was discovered in approximately two-thirds of the eyes investigated.

The darkroom outflow test was more often positive in these eyes than the standard darkroom test.

In the cases investigated, demonstrable angle closure was found in most of those having symptoms of the disease. The occurrence of angle closure was also demonstrated in a large number of eyes which were symptom free.

As the anatomical configuration of an eye principally determines whether or not it will develop closed-angle

glaucoma, it is to be expected that the similarity which exists between the two eyes in any one patient would result in the bilateral, rather than unilateral, incidence of the disease. It has long been known from clinical experience that where one eye is affected by glaucoma, sooner or later the other eye is likely to follow suit. Mackenzie (1854) noted that "when glaucoma has commenced in one eye it generally extends also to the other".

Bain (1956) has recently stressed the advisability of thorough investigation of the fellow eye where one eye has developed an acute attack of closed-angle glaucoma. He has shown that of 200 cases (which had suffered a unilateral attack of acute glaucoma) the second eye developed clinical evidence of the disease in more than half the cases studied (53%). He noted that the darkroom test was positive in ten cases (out of a total of 60) wherein the second eye was symptom free and suggested that a more efficient provocative test would have revealed the existence of the disease in a much greater number of these apparently normal eyes.

As the darkroom outflow test is more often

positive than the standard darkroom test in cases of closed-angle glaucoma it was decided to use this test to investigate the fellow eyes of a number of cases wherein one eye was known to have closed-angle glaucoma. The affected eye in each case had either had a frank attack of acute glaucoma or had been seen in a sub-acute attack with raised tension and a closed angle. Seventy-nine such cases were investigated and of these 32 were male and 47 female. Of these 79 eyes investigated, 22 (27.8%) showed a positive rise in ocular tension with the darkroom test while a significant fall in the facility of aqueous outflow occurred in 45 (57%). The number of cases showing a significant change in the facility of outflow is significantly greater than those giving a positive result with the darkroom test ($\chi^2 = 12.07$: $n = 1$: $P = < 0.001$) (Table IX).

In an attempt to determine whether the diagnosis of closed-angle glaucoma in these cases could have been made on the history of symptoms suggestive of the existence of the disease rather than by the use of provocative tests, the results of the darkroom test and the darkroom outflow test were related to the

TABLE IX

Test Employed	Result of Provocative Test	
	Positive	Negative
Darkroom test	22 (27.8%)	57
Darkroom outflow test	45 (57%)	34

Comparison of the results of the darkroom test and darkroom outflow test on 79 unaffected eyes in cases of apparently unilateral closed angle glaucoma. The darkroom outflow test is more often positive in these cases than the darkroom test. ($\chi^2 = 12.07$: $n = 1$: $P = < 0.001$).

presence of symptoms in each particular case. Where there was a definite history of haloes and blurred vision the eye was considered to have positive symptoms of closed-angle glaucoma. In the absence of such a history the eye was considered to be negative in this respect.

Of the 79 fellow eyes studied, a positive history of symptoms was found in only 17 (21.5%). Of these 17 only 8 eyes gave a positive result with the darkroom test. Of the remaining 62 eyes which were symptom-free 14 showed a significant rise in ocular tension with the darkroom test. The difference in the

incidence ....

incidence of positive results with the darkroom test in the group of eyes with positive symptoms (47.1%) is significantly higher than that in the other group (27.5%) (Table X) (χ^2 = 7.34 : n = 1 : P = $<$.01).

TABLE X

Presence or absence of Symptoms	Result of Darkroom Test	
	Positive	Negative
Positive symptoms of closed angle glaucoma	8 (47.1%)	9
No symptoms	14 (27.5%)	48

Results of the darkroom test in the apparently unaffected eyes of cases with unilateral closed-angle glaucoma. The results of the test are more often positive in those eyes with symptoms of the disease than in those which are symptom free. (χ^2 = 7.34 : n = 1 : P = $<$ 0.01.)

While it is true that the incidence of positive results with the darkroom test was higher in the group with positive symptoms than in the other negative group, the observation that less than half the cases with a definite history suggestive of closed-angle glaucoma gave a positive result with the test underlines the

fact that a negative darkroom test is of little clinical value in assessing whether or not an eye is affected by the disease.

When the results of the darkroom outflow test were similarly related to the symptomatology in this series of cases it was found that of the 17 cases with positive symptoms 14 (82.4%) showed a significant fall in the facility of aqueous outflow with the test while in one of the three remaining eyes tested the facility of outflow prior to the test was already abnormally low (c = 0.05). Of the 62 eyes which were symptom-free 30 (48.4%) gave a positive result with the darkroom outflow test. Although the darkroom outflow test was positive in nearly all eyes exhibiting symptoms of the disease, it was also positive in a large number of those eyes which were symptom-free, and in fact the incidence of positive results with this test is not significantly different in the two categories (χ^2 = 1.40 : n = 1 : P = $>$ 0.10).

Thus a positive history of symptoms in the fellow eye where one eye is already affected by closed-angle glaucoma is good evidence in favour of the second eye's

being ....

being affected by the disease. No reliance however can be placed on the absence of symptoms in ruling out the existence of the disease, for both the darkroom test and the darkroom outflow tests will frequently reveal the presence of the disease in the absence of positive symptoms.

The existence of demonstrable closed-angle glaucoma in the great majority of these "second" eyes stresses the importance of adequate investigation and treatment of the apparently healthy fellow eye where the disease appears to be unilateral.

CHAPTER VII

CONCLUSION

SUMMARY

The observations recorded in the previous chapters are correlated and views on the natural history of closed-angle glaucoma in both its acute and chronic forms are presented.

In the first chapter of this thesis the evolution of the corrently accepted views on the aetiology of closed-angle glaucoma was traced. It was noted that the disease was believed to be the direct result of the presence of a disproportionately large lens in an eye too small to accommodate it. This disproportion was thought to lead to the formation of an iris bombé with consequent narrowing of the angle of the anterior chamber.

An eye so affected, but in which the angle of the anterior chamber was open although narrow and wherein the ocular tension was comparable to that found in an unaffected normal eye, was considered to

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be pre-glaucomatous. Such an eye was thought to differ from its normal counterpart only in its possible predisposition to the development of hypertension as the result of the obstruction of the angle by the action of some secondary angle crowding factor.

In an eye in which such hypertensive episodes occurred it was considered that between attacks when the ocular tension was not raised, the angle of the anterior chamber was open and functioning normally. Closed-angle glaucoma in such an eye was understood to progress in one or other of two different ways. As the result of the action of some more vigorous stimulus to angle closure an acute attack of "congestive" glaucoma might result or, following repeated minor attacks of this nature, goniosynechiae would be formed and these by permanently reducing the level of aqueous outflow would lead to the development of chronic closed-angle glaucoma with its attendant cupping of the optic disc and visual field loss.

Owing to the presence of goniosynechiae in this latter instance the surgical treatment of such a case was always by a drainage operation rather than by simple

iridectomy.

The state of the angle between attacks of hypertension is of importance in the treatment of closed-angle glaucoma. Consideration of the observations presented in this thesis would suggest that a degree of angle closure exists in most eyes affected by the disease even when the ocular tension is not apparantly raised.

The suggestion that the angle of the anterior chamber was already partly closed in the upper sectors before there was any other objective or subjective evidence of the disease (Shaffer, 1955; Phillips, 1956) received support from several observations. The fact noted by Barkan (1938) that the angle was narrowest in its upper sector suggested that if angle closure were to occur, it would do so preferentially in this upper narrow region. This conclusion was supported by the usual finding of a vertically oval pupil in acute glaucoma. The evidence that goniosynechiae occurred more often above than below in closed-angle glaucoma (Phillips, 1956) also lent support to the view that angle closure was more likely to affect the upper narrow part of the angle than the lower and wider

portion ....

portion.

This latter observation however is not direct evidence that any degree of angle closure is present in closed-angle glaucoma between attacks of hypertension for goniosynechiae are known to follow hypertensive episodes and the inflammatory reaction which produces them is probably itself a response to the prolonged interference with the local blood circulation which undoubtedly occurs during an acute attack of glaucoma. Gonioscopic verification of the view that in an affected eye the angle is closed initially in the upper sectors is usually impossible for reasons which have already been discussed (p. 39).

Evidence that there is some degree of angle closure present in eyes affected by the disease even where the tension is apparently within normal limits is to be found however in the results of the darkroom test and darkroom outflow test on such eyes and from the study of cases of chronic closed-angle glaucoma.

The existence, in eyes with closed-angle glaucoma (where the ocular tension is still within normal limits), of an average level of aqueous outflow which is lower

than that found in comparable normal eyes suggests that in the early stages of the disease some part of the angle is already obstructed and that the ocular tension, although apparently normal, is already higher and the outflow of aqueous lower than it would have been had the angle been fully open. In addition, where the ocular tension in affected eyes is in the upper reaches of normality there is found to be an increased predisposition to the development of further angle closure on provocation with the darkroom test.

These observations indicate the habitual presence in such eyes of some degree of angle closure. The variability of both the ocular tension and the level of aqueous outflow in these eyes however it good evidence that the area of angle obstructed is not fixed and that the obstruction itself is due to contact between the root of the iris and the trabeculae rather than to goniosynechiae. This conclusion is also to be drawn from the study of cases of chronic closed-angle glaucoma where it was shown that a habitual degree of angle closure sufficient to reduce the outflow of aqueous to pathologically low levels might be present for long enough to result

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in cupping of the optic disc and yet still be reversible and not necessarily accompanied by the formation of goniosynechiae.

These findings have a direct bearing on the treatment of cases of closed-angle glaucoma. As the raised ocular tension in this disease is the direct result of mechanical obstruction of the angle which is itself still capable of functioning normally, the logical treatment of the condition would be by the prevention of angle closure. As has been seen, in most cases this closure of the angle follows upon the development of an iris bombé due to an increase in the pressure within the posterior chamber relative to that obtaining within the anterior chamber. As is well recognised, an iridectomy (either peripheral or complete) by equallising the pressures in the two chambers will aholish this state of iris bombé. The beneficial effect of a peripheral iridectomy in preventing the occurrence of angle closure is well seen in those cases of closed-angle glaucoma upon which this operation had been performed, which were studied by means of the darkroom outflow test (Chapter IV).

The treatment of this disease by the use of

miotic drugs has several disadvantages. Absence of symptoms and an ocular tension within the normal range have in the past been the criteria upon which the efficacy of miotic treatment has been judged. As has been seen in Chapter VI, however, the absence of symptoms is no guide to whether or not angle closure is present, many eyes which were entirely symptom-free revealing frank evidence of the disease on further investigation.

It has also been shown that an ocular tension within the normal range is not proof that the angle in these cases is fully open, for the apparently normal tension found in any particular eye with this disease may in fact be higher than the basic normal tension for that eye. An ocular tension of over 26 mms. Hg in an eye with closed-angle glaucoma is indicative of the existence of some degree of angle closure. An eye with such a resting tension is in an unstable state and likely to develop a severe rise in tension on suitable provocation. If this is so, it follows that in an eye, on treatment with miotics, wherein the resting ocular tension is between 25 and 30 mms. Hg, the angle is partly closed and thus the eye is still in danger of developing

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either an acute attack of glaucoma or of forming goniosynechiae. Such an eye would be better treated surgically, for the risks attendant upon a peripheral iridectomy at this stage are probably less than those to be expected if the eye is left to form goniosynechiae.

In this latter instance the potentially normal angle is permanently damaged and no alternative remains but to provide exterior drainage for the aqueous, a procedure which carries a far greater risk to the eye than the comparatively simple operation of peripheral iridectomy performed in the early stages of the disease.

The fact that such a large proportion of fellow eyes in cases of apparently unilateral acute glaucoma can be shown to be affected by the disease gives support to the view that a prophylactive peripheral iridectomy should be performed on the second eye of such cases provided that the two eyes are anatomically similar. In this connection the value of provocative tests is again stressed and it is to be noted that in the early stages of the disease the darkroom test is usually negative while the result of the darkroom outflow test may well be positive.

Although ....

Although a narrow angle is a necessary pre-requisite to the development of acute glaucoma its presence alone does not explain the occurrence of such an attack. Undoubtedly partial closure of the angle is the usual precursor of an acute attack of glaucoma, and the results of the darkroom outflow test would suggest that where the angle is already largely obstructed very little additional stimulus is required to produce complete closure. It is of interest to consider what possible triggering mechanisms exist.

As has been mentioned earlier, it has long been known that dilatation of the pupil in a suitably predisposed eye may be followed by an acute attack of glaucoma. This pupillary dilatation may be the result of changes in illumination as in the darkroom test or reflect some alteration in the activity of the autonomic nervous system.

Prolonged accommodative effort too, may be followed by angle closure and a rise in ocular tension. On accommodation the anterior lens capsule becomes more convex so that there is further impediment to the free passage of fluid from the posterior to the anterior chamber, with consequent exaggeration of the "physiological"

iris bombé present. In addition the ciliary body alters shape and position and may directly close the angle. The rise in ocular tension which is sometimes found on prolonged accommodation forms the basis of the reading test (Higgitt and Smith, 1955).

The role of vasodilatation within the eye is difficult to assess. It is known that passive venous congestion may raise the intra-ocular pressure (as in the lability test) while it has been shown that blushing may be accompanied by a large rise in ocular tension (Grant, 1955). As by far the largest part of the intra-ocular circulation lies behind the iris-lens diaphragm, a sudden vasodilation in this region would increase the pressure within the vitreous chamber in first instance. This might result in an anterior displacement of the lens and iris but, as has been already noted, repeated measurements by various workers have failed to displose such a forward movement of the lens with the development of an attack of ocular hypertension.

In the absence of any movement of the lens however, vasodilatation within the choroid and ciliary body could result in an increase of pressure within the

posterior ....

posterior chamber, for the zonule offers no impediment to the free passage of fluid from within the vitreous chamber. Such an increase in the pressure of the posterior chamber would be likely to cause a forward ballooning of the iris provided that some of the fluid within the anterior chamber could be forced out of the eye. As any open sector of the angle in such an eye might be expected to function normally an increase in the rate of outflow would follow the changes described. It is a reasonable deduction therefore that ballooning of the iris and angle closure could follow upon vasodilatation within the ciliary body and the choroid in a suitably predisposed eye. Apart from the question of vasodilatation, a sudden increase in the capillary blood pressure within the eye leading to the diffusion of fluid at a higher than normal pressure into the posterior segment of the eye might also result in a forward ballooning of the iris in the same way as would vasodilation in this region.

Finally the influence of the rate of aqueous formation must not be overlooked.

In normal eyes (and in chronic simple glaucoma) where mechanical obstruction of the angle does not occur

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the level of aqueous outflow appears to be fairly stable. Grant and Trotter (1955) have shown that in the enucleated eye the facility of outflow measured by tonography is comparable to that found in vivo. Normal eyes submitted to the darkroom outflow test in the present investigation showed no significant change in outflow with the test although a small rise in ocular tension occurred. De Roeth (1954) has shown that the diurnal variations in ocular tension which occur in normal eyes are unaccompanied by any measurable alteration in the facility of aqueous outflow.

In view of the apparent stability of the outflow factor as measured by tonography, it is reasonable to assume that the phasic variationsin ocular tension which are constantly occurring reflect alterations in the rate of aqueous inflow, for in the presence of a normally functioning angle any increase in the volume of blood within the eye would be likely to produce only a transient change in the level of ocular tension. In this connection aqueous formation must be held to include the diffusion of fluid from the intra-ocular arterial capillaries for a prolonged rise, for example,in the capillary blood

pressure would result in a rise in the level of intra-ocular pressure if the outflow of aqueous were to remain unaltered.

It was seen that when normal eyes are submitted to the darkroom test a small mean rise in ocular tension results without any corresponding decrease in the facility of outflow. As this effect is apparent after the lapse of one hour, it too is likely to be due to an increase in the rate of aqueous formation. As the relatively slow change in ocular tension which occurs with the diurnal cycle is thought to be part of a more widespread cyclic alteration in autonomic tone it would appear that changes in the rate of aqueous formation may be directly influenced by the autonomic nervous system.

Where the drainage mechanism of the eye is functioning normally a small increase in the rate of aqueous inflow will not raise the intra-ocular pressure to any great extent. Where the outflow is diminished however even a small increase in the rate of inflow will result in a considerable rise in ocular tension. It may be, therefore, that the rise in tension which occurs with the darkroom test in cases of closed-angle glaucoma while principally the result of obstructive

changes at the angle, is also partly explicable by an increase in the rate of aqueous inflow in such eyes in the dark. It is interesting to note that a positive darkroom test may occur in cases of juvenile glaucoma where no evidence of angle closure is forthcoming and where the rate of aqueous outflow, always low in these cases is not further reduced by the provocative test. Details of such a case will illustrate this.

Case VIII: a male, aged, 26, who complained of attacks of misty vision and haloes on and off for a year, the attacks only occurring during the hours of darkness when the patient, a seaman, was on watch. The angle of the anterior chamber in each eye was found to be wide and free from goniosynechiae although the trabecular appeared to be poorly developed, resembling the appearance found in cases of buphthalmos. The resting ocular tension in the left eye was 20 mms. Hg and the facility of outflow 0.06. An hour in the dark resulted in a rise of tension to 40 mms. Hg while the facility of aqueous outflow and the gonioscopic appearance of the angle remained unchanged. In the absence of any change in the rate of outflow such a rise in ocular

tension could only result from an increased rate of inflow possibly associated with raised intra-ocular capillary blood pressure.

The immediate effect of a sudden increase in the rate of aqueous formation would be to increase the pressure within the posterior chamber. This increase in pressure would be transmitted through the body of the iris to the anterior chamber where it would result in an increase in the rate of escape of fluid from there. This would lead to a forward ballooning of the body of the iris and in an eye with a narrow angle, to obstruction of the angle. Such an increase in the rate of aqueous formation, determined by a change in autonomic activity may well explain the occurrence of an acute attack of glaucoma following emotional stress.

While it is true that for a particular eye, the facility of aqueous outflow as measured by tonography would appear to be constant, what is being measured is an artificially raised level of outflow which is dependant upon the anatomy of the outflow channels of the eye and the additional weight of the tonometer. While this method is quite capable of revealing mechanical obstruction of the angle such as occurs in closed-angle glaucoma it

may well be too insensitive to measure the small changes in outflow which may occur in the undisturbed eye.

There is indeed evidence that the outflow of aqueous is a variable factor, for Langley and Macdonald (1952) have shown that the rate of disappearance of fluorescein from the anterior chamber of the normal eye is related to the phasic variations in ocular tension suggesting that the changes in tension are due to alterations in the rate of both the inflow and outflow of aqueous.

In theory a sudden increase in the rate of aqueous outflow could precipitate angle closure in an eye with a narrow angle by sucking the root of the iris against the trabeculum.

While the various angle crowding factors which may result in the final closure of the angle have been discussed as separate entities it is of course much more likely that several of these factors would act together to produce an acute attack of glaucoma.

It is now possible to summarise the evolution of a typical case of closed-angle glaucoma. In the affected eye the lens is relatively too large and leads to the formation of an iris bombe. As time goes on the

lens ....

lens continues to grow and the iris bombe increases in depth until eventually the root of the iris touches the trabeculae in the narrowest sector of the angle, usually above. This area of contact gradually increases in size so that more and more of the angle is obstructed. From the onset of this obstruction the outflow of aqueous is somewhat impeded and the resting ocular tension for the eye in question, although at this stage still apparently normal, is higher than it was. As more of the angle is obstructed, the resting ocular tension rises to the upper limits of the normal range and at this stage complete obstruction of the angle with the development of an acute attack of glaucoma may supervene as the result of the action of one or more of the angle crowding factors discussed above. Such an acute attack may resolve spontaneously, or following treatment, and may be accompanied by an inflammatory reaction leading to the development of goniosynechiae. These goniosynechiae present a premanent and irreversible obstruction to the outflow of aqueous so that the ocular tension remains pathologically raised and cupping of the optic disc and eventually absolute glaucoma supervenes.

This ....

This advanced stage of chronic closed-angle glaucoma may also arise without a preceding acute attack of hypertension. The angle of the anterior chamber may be so asymmetrical that although closed by contact between the iris and cornea in its narrower sectors so that the outflow of aqueous is grossly reduced, there remains an unobstructed wider sector sufficient to prevent the onset of an acute attack but insufficient to keep the resting ocular tension below the level at which damage to the optic nerve head occurs.

It is possible too that an eye which differs little from one developing an acute attack of glaucoma may, in the absence of such additional stimulus as is required to produce complete closure of the angle, develop the chronic stage of the disease. In this latter instance the slow closure of the angle from above downwards over the years would eventually affect so much of the angle that the resting ocular tension might remain constantly elevated with the consequent development of cupping of the optic disc and visual field loss.

Thus all the clinical varieties of closed-angle glaucoma can be related to the same basic anatomical mischance. As the severity of the condition in all cases

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is steadily progressive the rational treatment of the disease is the correction of the iris bombe by performing a peripheral iridectomy early in the course of the disease before the occurrence of irreparable damage.

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APPENDIX.

Terminology

At the 1955 symposium on glaucoma organised by the Council for International Organisations of Medical Science under the chairmanship of Sir Stewart Duke-Elder, it was decided that the terms "congestive glaucoma" and "narrow angle glaucoma" should be dropped from international usage, and that the term "closed angle glaucoma" be used to describe this variety of the disease. The new terminology has been used in this thesis, except where direct reference has been made to previous work wherein the descriptive term "congestive glaucoma" has been employed by the author cited.

Detailed results of the Darkroom Test
on a Random Sample of non-glaucomatous eyes.

Sex	Age.	Initial ocular tensions. (mm. Hg)	Final ocular tension. (mm. Hg)	Change in ocular tension. (mm. Hg)
F	48	17	17	0
M	66	28	28	0
M	71	23	26	+3
M	55	21	17	-4
F	47	20	20	0
M	54	16	17	+1
M	50	22	21	-1
M	49	17	19	+2
F	42	24	25	+1
M	57	20	20	0
F	78	21	24	+3
F	42	20	20	0
M	75	21	28	+7
F	44	24	30	+6
M	67	20	20	0
F	75	22	21	-1
F	59	15	16	+1
M	75	20	21	+1
M	50	20	24	+4
F	70	22	22	0
M	48	17	22	+3
M	46	15	17	+2
M	64	21	21	0
M	59	24	25	+1
F	59	25	31	+6
M	26	17	19	+2
M	27	19	20	+1
F	57	19	19	0
M	28	21	24	+3
M	58	20	23	+3
M	47	17	20	+3
M	61	16	20	+4
F	50	21	20	-1
M	53	20	21	+1
M	43	20	25	+5
F	51	25	25	0
M	70	20	22	+2
M	67	14	17	+3
M	57	20	20	0
F	68	15	17	+2
F	54	22	20	-2
F	53	25	18	-7
F	54	17	17	0
F	71	23	23	0
F	55	22	22	0

M	50	17	20	+3
M	47	17	22	+5
F	61	25	25	0
F	72	26	25	-1
F	56	15	15	0
F	61	23	23	0
F	64	23	23	0
M	65	20	15	-5
M	73	25	28	+3
M	59	25	25	0
M	65	18	20	+2

Detailed results of the Darkroom Test on a random sample of eyes presumed to have closed-angle glaucoma.

Sex	Age.	Initial ocular tension (mm. Hg)	Final ocular tension (mm. Hg)	Change in ocular tension (mm. Hg)
M	59	25	31	+6
M	67	35	60	+25
M	67	30	40	+10
M	63	25	30	+5
M	67	21	27	+6
M	25	20	40	+20
M	66	27	60	+33
M	53	18	33	+15
M	45	31	40	+9
M	69	25	28	+3
M	59	13	17	+4
M	60	28	35	+7
M	48	40	45	+5
M	48	25	33	+8
M	50	26	63	+37
M	34	28	40	+12
M	62	55	77	+22
M	71	22	33	+11
M	53	35	55	+20
M	68	22	25	+3
M	58	35	45	+10
M	59	35	40	+5
M	56	52	62	+10
M	76	77	75	-2
M	64	35	37	+2
M	41	42	55	+13
M	47	28	48	+20
M	48	22	33	+11
M	62	24	35	+11
M	58	31	37	+6
M	72	28	68	+40
M	63	70	70	0
M	33	28	80	+52
M	60	37	42	+5
M	57	20	23	+3
M	67	25	32	+8
M	75	16	25	+9
M	69	28	63	+35
M	47	35	37	+2
M	67	20	31	+11
M	63	23	29	+6
M	48	20	60	+40
M	48	35	51	+18
M	52	32	63	+31
M	56	32	45	+13

M	57	35	51	+16
M	57	33	82	+45
M	47	18	25	+7
M	58	19	19	0
M	57	22	25	+3
M	57	33	47	+14
M	67	15	22	+7
M	56	22	31	+9
M	62	22	26	+4
M	60	14	14	0
F	56	33	42	+9
F	47	20	23	+3
F	60	23	23	0
F	45	40	40	0
F	72	20	25	+5
F	61	30	33	+3
F	34	45	40	-5
F	55	21	34	+13
F	61	22	31	+9
F	59	25	40	+15
F	48	27	40	+13
F	74	17	25	+8
F	63	35	35	0
F	41	21	27	+6
F	52	21	25	+4
F	51	31	37	+6
F	59	13	22	+9
F	43	31	42	+11
F	64	23	31	+8
F	63	29	40	+11
F	66	28	31	+3
F	69	12	12	0
F	35	25	28	+3
F	56	20	25	+5
F	41	22	20	-2
F	52	24	31	+7
F	55	28	77	+49
F	50	63	67	+4
F	30	22	26	+4
F	43	24	29	+5
F	42	21	23	+2
F	61	30	68	+38
F	61	37	48	+11
F	48	45	48	+3
F	70	25	33	+8
F	55	31	42	+11
F	52	40	35	-5
F	60	72	78	+6
F	70	25	48	22
F	77	27	84	+57
F	51	35	37	+2
F	56	28	31	+3

F	64	24	42	+18
F	75	33	33	0
F	52	35	58	+23
F	68	33	40	+7
F	76	33	42	+9
F	77	25	40	+15
F	68	22	31	+9
F	67	17	28	+11
F	76	27	31	+4
F	69	20	26	+4
F	64	25	33	+8

Detailed results of the Darkroom Outflow Test on a series of non glaucomatous eyes.

Sex	Age	Initial Tension (mm. Hg)	Final Tension (mm. Hg)	Change in Tension (mm. Hg)	Initial Outflow (c_1)	Final Outflow (c_2)	Change in Outflow ($\log c_1 - \log c_2$)
M	52	14	15	+1	0.20	0.20	0.000
F	52	14	17	+2	0.21	0.22	- 0.020
F	52	14	17	+2	0.24	0.26	- 0.035
F	71	20	20	0	0.13	0.14	-0.032
M	56	20	20	0	0.18	0.16	+0.051
F	62	17	16	-1	0.21	0.19	+0.043
F	58	16	16	0	0.14	0.14	0.000
M	56	24	26	+2	0.15	0.15	0.000
F	50	17	17	+0	0.22	0.25	-0.056
F	57	18	17	-1	0.22	0.25	-0.056
M	66	12	14	+2	0.16	0.17	-0.026
F	76	15	15	0	0.20	0.14	0.155
F	92	11	11	0	0.16	0.16	0.000
M	58	17	15	-2	0.17	0.16	0.026
F	50	15	14	-1	0.20	0.16	0.097
M	54	15	15	0	0.12	0.13	-0.035
F	61	17	16	-1	0.18	0.19	-0.024
F	68	20	22	+2	0.20	0.23	-0.061
M	21	15	17	+2	0.20	0.25	-0.097
F	69	17	16	-1	0.26	0.24	0.035
F	74	25	24	-1	0.21	0.26	-0.093

F	58	16	16	0	0.24	0.24	0.000
F	42	20	19	-1	0.25	0.25	0.000
F	65	15	16	+1	0.24	0.20	0.079
M	66	20	24	+4	0.17	0.20	-0.071
F	54	14	15	+1	0.30	0.34	-0.054
F	53	14	14	0	0.16	0.16	0.000
F	64	25	24	-1	0.20	0.20	0.000
M	54	17	17	0	0.15	0.12	0.097
F	57	14	15	+1	0.14	0.14	0.000
F	72	22	20	-2	0.14	0.14	0.000
F	61	25	25	0	0.16	0.16	0.000
M	54	15	20	+5	0.17	0.22	-0.112
F	71	17	17	0	0.16	0.16	0.000
F	66	15	17	+2	0.20	0.20	0.000
M	60	15	16	+1	o.14	0.14	0.000
F	54	22	20	-2	0.12	0.14	-0.097
F	63	22	25	+3	0.23	0.23	0.000
M.	27	19	17	-2	0.25	0.20	0.097
F	32	12	12	0	0.28	0.28	0.000
M	82	20	19	-1	0.10	o.10	0.000
M	81	15	14	-1	0.20	0.22	0.041

Detailed results of the Darkroom Outflow Test on a series of eyes presumed to have closed angle glaucoma.

Sex	Age	Initial Tension (mm. Hg)	Final Tension (mm. Hg)	Change in Tension (mm. Hg)	Initial Outflow (c_1)	Final Outflow (c_2)	Change in Outflow (log c_1 -log c_2)
F	62	20	18	-2	0.25	0.28	-0.049
M	53	17	17	0	0.30	0.20	0.176
M	59	25	27	+2	0.15	0.09	0.222
F	69	17	21	+4	0.20	0.20	0.000
F	59	16	17	+1	0.30	0.25	0.079
M	50	20	20	0	0.12	0.17	-0.151
F	54	15	14	-1	0.30	0.30	0.000
M	52	21	25	+4	0.19	0.08	0.376
F	50	21	28	+7	0.15	0.07	0.331
F	73	20	25	+5	0.16	0.09	0.350
M	49	15.5	17.5	+2	0.15	0.16	-0.028
M	55	28	34	+9	0.10	0.06	0.222
F	33	17	24	+7	0.20	0.10	0.301
F	67	16	21	+5	0.14	0.10	0.146
F	60	20	22	+2	0.16	0.06	0.326
F	53	19	20	+1	0.24	0.25	-0.018
M	54	19	24	+5	0.10	0.14	-0.146
M	50	24	21	-3	0.14	0.14	0.000
M	59	22	22	0	0.14	0.20	-0.155
M	43	17	34	+17	0.30	0.03	1.000

M	62	16	15	-1	0.20	0.14	0.155
F	71	26	25	-1	0.16	0.13	0.090
F	34	19	34	+15	0.095	0.04	0.375
F	46	25	26	+1	0.14	0.09	0.192
F	71	21	21	0	0.16	0.09	0.250
M	80	15	16	+1	0.20	0.20	0.000
F	59	19	20	+1	0.28	0.24	0.167
F	50	19	17	-2	0.16	0.15	0.028
F	50	15	21	+6	0.24	0.19	0.101
F	61	20	22	+2	0.17	0.08	0.327
M	42	20	20	0	0.16	0.13	0.090
F	66	15	16	+1	0.16	0.14	0.058
F	67	22	22	0	0.16	0.10	0.204
F	58	20	21	+1	0.20	0.15	0.125
F	46	20	30	+10	0.15	0.10	0.176
M	53	14	19	+5	0.16	0.10	0.204
F	70	12	16	+4	0.24	0.16	0.176
M	58	22	31	+9	0.20	0.05	0.602
F	68	27	73	+46	0.07	0.01	0.845
F	50	19	20	+1	0.13	0.09	0.160
M	35	25	28	+3	0.09	0.06	0.176
F	54	25	31	+6	0.16	0.14	0.058
M	59	25	60	+35	0.11	0.02	0.740
F	37	28	39	+11	0.16	0.05	0.505
M	48	20	20	0	0.15	0.06	0.398
F	35	31	40	+9	0.05	0.02	0.398
F	52	24	31	+7	0.21	0.13	0.208
F	55	28	72	+44	0.10	0.01	1.000
M	66	14	14	+0	0.20	0.14	0.155
M	62	25	25	+0	0.15	0.07	0.331
M	62	14	82	+68	0.09	0.01	0.954
F	37	28	40	+12	0.16	0.05	0.477

F	61	20	28	+8	0.14	0.08	0.243
M	52	20	31	+11	0.13	0.03	0.637
M	45	20	52	+32	0.14	0.04	0.544
M	67	18	67	+49	0.06	0.01	0.778
M	64	25	57	+32	0.12	0.01	1.079
M	59	22	28	+6	0.16	0.06	0.426
M	67	17	28	+11	0.13	0.06	0.336
M	42	25	45	+20	0.06	0.05	0.079
F	58	15	20	+5	0.18	0.20	-0.046
F	60	21	24	+3	0.14	0.10	0.146
F	55	25	40	+15	0.14	0.05	0.447
M	58	25	25	0	0.29	0.14	0.316
M	36	15	22	+7.0	0.20	0.07	0.456
M	59	32	52	+20	0.04	0.01	0.602
M	54	30	47	+17	0.05	0.01	0.698
M	62	30	52	+22	0.10	0.06	0.222
F	76	17	25	+8	0.10	0.04	0.398
F	54	21	25	+4	0.17	0.17	0.000
F	64	20	20	0	0.23	0.24	-0.019
M	68	18	20	+2	0.16	0.09	0.250
M	68	25	25	+0	0.15	0.05	0.398
F	57	25	45	+20	0.14	0.05	0.447
F	54	22	28	+6	0.21	0.12	0.243
F	59	17	20	+3	0.16	0.06	0.426
F	53	22	28	+6	0.16	0.08	0.301
F	53	20	30	+10	0.30	0.10	0.477
F	56	17	17	0	0.16	0.09	0.250
F	74	17	22	+5	0.15	0.08	0.273
M	61	15	15	0	0.14	0.16	-0.058
F	54	17	19	+2	0.25	0.26	-0.017
F	70	22	20	-2	0.15	0.15	0

F	36	20	22	+2	0.26	0.16	0.211
F	58	17	24	+7	0.20	0.09	0.347
F	62	19	25	+6	0.16	0.08	0.301
F	54	20	20	0	0.15	0.06	0.398
F	59	17	20	+3	0.16	0.06	0.426
F	53	17	20	+3	0.16	0.14	0.058
F	53	22	28	+6	0.16	0.08	0.301
M	53	25	29	+4	0.13	0.10	0.114
M	63	28	35	+7	0.10	0.05	0.301
M	58	17	20	+3	0.18	0.11	0.214
F	45	25	22	-3	0.21	0.23	-0.040
M	56	12	30	+18	0.25	0.10	0.398
F	72	21	30	+9	0.15	0.15	0
F	42	22	23	+1	0.15	0.07	0.331
F	50	14	15	+1	0.30	0.22	0.135