MIXED GLAUCOMA*

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DURING the past 20 years it has become widely accepted that primary glaucoma consists of two distinct conditions: chronic simple glaucoma and closed-angle glaucoma. The main features of these are well known and in their classical forms their early stages are quite different. Chronic simple glaucoma may present with a history of visual field loss, perhaps affecting visual acuity, or the condition may be so slow and insidious that it may be discovered only by a routine tonometry or fundus examination. The history in closed-angle glaucoma is much more dramatic, the patient usually presenting with episodic mistiness of vision in association with which there may be haloes and discomfort. Occasionally a full-blown attack of acute glaucoma may be the first episode.

The cardinal signs of chronic simple glaucoma are a raised ocular tension, in spite of gonioscopically open angles, and progressive field loss in association with pathological cupping of the disc.

In closed-angle glaucoma, the episodic nature of the condition may cause the patient to seek advice when the ocular tension is not raised and the collateral signs only may give the clue to the diagnosis. These are well known and hinge on the gonioscopic appearance of a narrow angle and other signs indicative of crowding in the anterior segment, *viz.* shallow anterior chamber and small corneal diameter in a hypermetropic eye.

The course of the two conditions is also very different. In simple glaucoma control of the ocular tension (by whatever means) is felt by many to be no guarantee that the disease will cease to progress, although this may not be true of the earlier stages. On the other hand effective control of the ocular tension in closed-angle glaucoma is an effective guarantee that further visual damage will be prevented.

From this simplified presentation it would seem surprising that the two types should ever be confused. Yet there is a considerable number of cases in which the history, signs, and course do not fit into either group, and it is the purpose of this paper to consider the overlap of the two conditions. Their co-existence is very uncommon and there are theoretical reasons for their mutual exclusiveness.

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A series of 47 patients out of 1,861 successive cases seen at the Glaucoma Clinic at the Institute of Ophthalmology, London, had each been diagnosed as a case of "mixed glaucoma". The various surgeons who have seen these cases have different views on what "mixed glaucoma" is, as will be seen from the analysis that follows, which was made in an effort to determine from the records whether there was conclusive evidence that any eye could be said to be affected by simple glaucoma and closed-angle glaucoma at the same time. The cases fall into five groups (Table I):

TABLE I
CLASSIFICATION OF 47 CASES

Group	No. of Cases	Probable Diagnosis
1	22 (Nos 1-22)	Chronic simple glaucoma
2	10 (Nos 23-32)	Closed-angle glaucoma
3	7 (Nos 33-39)	Could be either type of primary glaucoma
4	5 (Nos 40-44)	Too doubtful for classification
5	3 (Nos 45-47)	Mixed glaucoma

In the 22 cases allocated to Group 1, there were certain findings suggestive of mixed glaucoma. These are set out in Table II.

TABLE II
PROBABLE CHRONIC SIMPLE GLAUCOMA (Cases 1-22)

Group 1	Findings Suggesting Mixed Glaucoma
Cases 1-16	Narrow but open angles
Cases 17-19	Haloes, high tension associated with narrow but open angles
Case 20	Very doubtful history of haloes, narrow angle, cupped discs
Case 21	Medium narrow angle, doubtfully positive dark-room test, cupped discs
Case 22	Narrow angle, positive dark-room test, cupped disc

Cases 17-19.—It is recognized that in chronic simple glaucoma haloes may be experienced. Independently of the present series of cases, the writer found that, of 557 successive patients with chronic simple glaucoma seen at the Glaucoma Clinic of the Institute of Ophthalmology, 54 had experienced haloes, and in 23 of them haloes were the presenting symptom. (Some of these were classifiable as "pigmentary glaucoma", if this is a separate entity.)

Case 20.—This patient had one blind eye due to thrombotic glaucoma. The eye in which mixed glaucoma was diagnosed had several pre-operative gonioscopies while on miotics and the angle was reported first as narrow but open and later as very narrow

with "considerable peripheral anterior synechiae probably". After an iridencleisis the angle was found to be wholly open with no peripheral anterior synechia. (In Case 17 the angle after miotics appeared narrower than before.)

Cases 21 and 22.—A positive dark-room test in each of these cases suggested a mixed glaucoma. Unfortunately there is no record of gonioscopy at the time when the tension was provoked by the test. However, it is known that a positive dark-room test does occasionally occur in simple glaucoma though the mechanism is obscure. (See Case 32.)

The findings suggestive of mixed glaucoma in the ten cases in Group 2 are set out in Table III.

TABLE III
PROBABLE CLOSED-ANGLE GLAUCOMA (Cases 23–32)

Group 2	Findings Suggesting Mixed Glaucoma
Cases 23–26	Advanced cupping, mainly closed angles
Case 27	Isolated raised ocular tension reading and slightly reduced outflow in fellow eye of case of acute glaucoma
Case 28	Typical congestive history, disc cupping, and very narrow angles; degree of obstruction could not be gauged
Case 30	Previous typical closed-angle glaucoma but superimposed aphakic element
Case 31	Bilateral cupping, angles very narrow, extensive iridocorneal contact relieved by peripheral iridectomy
Case 32	Possibly "angle shortening"

Case 32.—A positive dark-room test suggested the closed-angle element but raised ocular tension was present with the angles "open" and there was no history to support angle closure. The angle was described as peculiar in being mainly broad but with a very prominent arterial roll and the iris encroaching on the trabecula "from behind". This may have been simple glaucoma with a positive dark-room test, but, in retrospect, it would seem from the angle appearance that this might have been the "angle-shortening" type of closed-angle glaucoma described by Gorin (1960).

The findings suggestive of mixed glaucoma in the seven cases in Group 3 are set out in Table IV.

TABLE IV
COULD BE EITHER TYPE OF PRIMARY GLAUCOMA (Cases 33–39)

Group 3	Findings Suggesting Mixed Glaucoma
Cases 33–37	No congestive history, disc cupping, narrow angles (? closed); two had positive dark-room tests
Case 38	Congestive history, disc cupping, narrow angle with normal ocular tension at time of examination
Case 39	Congestive history in one eye, controlled by iridencleisis; other eye symptomless with medium open angle and reduced outflow

Cases 33–37.—These cases illustrate the difficulties of estimating the degree of organic obstruction or closure of an extremely narrow angle.

Case 39.—This may have been simple glaucoma in one eye and closed-angle glaucoma, pre-operatively, in the other.

The findings suggestive of mixed glaucoma in the eight cases in Groups 4 and 5 are set out in Tables V and VI.

TABLE V
TOO DOUBTFUL FOR CLASSIFICATION (Cases 40–44)

Group 4	Reasons for Difficulty in Classification
Cases 40, 41	Probably late juvenile glaucoma
Case 42	Severe arteriosclerotic retinopathy confusing the field picture
Cases 43, 44	Element of secondary glaucoma due to uveitis complicating clinical picture

TABLE VI
PROBABLE MIXED GLAUCOMA (Cases 45–47)

Group 5	Findings Suggesting Mixed Glaucoma
Case 45	Haloes years before but not recently, disc cupped, ocular tension just controlled with miotics; angle broad where open, 30 per cent. peripheral anterior synechiae elsewhere (only eye)
Case 46	Acute attack in one eye. Ocular tension not controlled by iridectomy alone. 50 per cent. open angle, disc cupped with new vessels. Evidence of simple glaucoma in fellow eye
Case 47	Acute attack in one eye. Ocular tension reported as normalized by miotics; peripheral iridectomy later. Tension now controlled only by miotics in both eyes. Angles open all round (narrow in unoperated eye, medium in operated eye). Discs normal

Case 45.—A closed-angle glaucoma had obviously existed at some time in this patient's eye, but the broad remainder of the angle suggests that simple glaucoma was predominant at the time of examination.

Case 46.—The eye affected by acute glaucoma had had symptoms for 3 months and it is therefore possible that the 50 per cent. open angle had trabecular damage.

Discussion

The above analysis points to the actual co-existence of chronic simple and closed-angle glaucoma as being very uncommon. It is impossible to give any accurate figures of the extent of the overlap of the two conditions for two reasons. First, some of the cases in Group 3 (in which either type of glaucoma could explain the picture) may, in fact have been cases of true mixed glaucoma. Secondly, the population at risk is quite unknown.

It may be asked what criteria should be used to make sure that the two types of primary glaucoma were co-existent in the same eye at the same time. Presumably a patient with established chronic simple glaucoma in which it had been definitely observed that the ocular tension was raised in spite of open angles, might then start to develop congestive attacks in which the angle was seen to be closed. None of the above patients was observed frequently enough to say that this was true, but the last two probably did develop a closed-angle during simple glaucoma; significantly, the tendency to angle closure in these two cases was severe enough to produce an acute attack. The clinical impression that the development of congestive attacks in the course of established unoperated simple glaucoma is very rare indeed seems to be confirmed by the cases analysed above.

The reverse state of affairs, in which simple glaucoma supervenes on established closed-angle glaucoma, appears to occur more frequently, but here it is difficult to be sure that the simple glaucoma element is, in fact, primary, and that it is not secondary to damage, by repeated angle closure, to the trabeculae or to Schlemm's canal and its efflux channels. It must be admitted that there can be no direct proof *in vivo* that this damage does in fact occur, and that wherever the question arises the possibility of a pre-existing simple glaucomatous element cannot be ruled out. Certainly gonioscopic visualization of the trabeculae will give no clue to the nature of the trabecular or post-trabecular obstruction.

The place of gonioscopy in the diagnosis of the primary glaucoma needs no extended discussion here, but when the history is equivocal the gonioscopic findings may not help to classify the glaucoma. There is, of course, no *a priori* reason why simple glaucoma should not be accompanied by any width of open angle, but it may be remarked that, although miotics will usually widen the angle, they may sometimes increase *iris bombé* and give an impression of a narrow angle which had not necessarily been present before treatment was instituted. Gonioscopy before miosis would thus appear to be advisable in all cases. It may be that some of the patients in Group 1 of the present series have angles narrowed by miotics, thus suggesting a closed-angle element.

The difficulty of determining whether the iris in contact with the cornea or with Schwalbe's line in unoperated eyes (Phillips, 1956) is organically adherent, is a feature common to many of these cases. The effect of miotics in a case of simple glaucoma with a very narrow angle and physiological *iris bombé* could be to increase the relative pupillary block and suction on the iris root (as a result of the decreased resistance to aqueous outflow through the trabecular drainage channel system) so much that the angle becomes even narrower. Could this irido-corneal contact aggravated by miosis be itself in certain cases a factor resisting the flow of aqueous? A simple glaucoma might thereby be converted to a type of chronic closed-angle glaucoma such as that described by Foulds and Phillips (1957). In

such cases in which the iris may stretch through the use of miotics over a long period one type of outflow resistance may be replaced by another. Certainly it might be expected that miotics in this type of case would be more effective after iridectomy provided that access to the angle had been made more free by this procedure. In some eyes in which fistulizing operations have failed to drain, the tension may be controlled by miotics because the associated iris surgery makes medical treatment more effective.

If simple glaucoma can be accompanied by any width of angle the same cannot be said of the vast majority of cases of closed-angle glaucoma. The angle, if not obscured by *iris bombé* is narrow at least at its neck, and the usual difficulty is to decide whether the angle is open at all and whether, if obstructed, this blockage is due to mere contact or to peripheral anterior synechiae. In an eye with an angle such as this, accompanied by a pressure not controlled by miotics and, possibly, by cupping with field loss, it is not unnatural for surgeons to embark on a drainage operation rather than to risk peripheral iridectomy alone. This latter procedure sometimes produces a more easily visible and largely open angle with normal tension (Foulds and Phillips, 1957, as in the present Case 31), but here again, should a peripheral iridectomy fail to control the tension and yet produce sufficient opening of the angle for the trabeculae to be visible, one cannot say whether the case was initially one of simple glaucoma or was always one of closed-angle glaucoma with consequent trabecular damage. Presumably a raised tension with complete absence of peripheral anterior synechiae after a basal iridectomy would favour simple glaucoma. It is difficult to imagine trabecular damage without the formation of at least some organic adhesions; this may, however, be an unwarranted assumption.

In some degree the age incidence of the two primary forms of glaucoma may make co-existence unlikely, but the age groups overlap enough to make this far from impossible. There may be mechanical reasons against their co-existence, however. Even on the relative pupillary block theory of closed-angle glaucoma of the usual type, it seems to be generally agreed that expulsion of the aqueous from the anterior chamber is the "final act" (Shaffer, 1956). The nature of the precipitating factor is uncertain, but much more attention is paid to angle blockage due to a bowed forward iris than to a crowding of iris tissues. It is well known that mydriasis alone is often insufficient to cause angle blockage in these eyes, and the occurrence of angle blockage with a small pupil or even as a direct consequence of the use of a miotic is also occasionally encountered. In the presence of pupillary block, it is difficult to imagine that angle closure would occur without aqueous passing out through the drainage channels.

The suction theory of Posner (1953) again demands that the aqueous in the sequestered peripheral sinus of the anterior chamber be pushed out by the *vis a tergo* of pressure behind the iris in relation to "suction" *via* the drainage channels.

In either case a marked obstruction of the outflow channels in simple glaucoma would appear to reduce the likelihood of angle closure. One may conceive that a comparatively mildly raised outflow resistance would allow angle closure if the predisposing anatomical and physiological factors are marked; here it may be recalled that the two cases considered as possible mixed glaucoma both had acute attacks. If outflow variations (such as may be responsible for the phasic variations of ocular tension in simple glaucoma) occur, it would be expected that the tendency to angle closure would be most likely when the outflow is at its maximum. It would seem, however, that a patient with a tension high enough to produce haloes in simple glaucoma must have a markedly obstructed outflow and is therefore unlikely to develop angle closure.

The role of an abnormally free aqueous outflow *via* the trabeculae in closed-angle glaucoma has never been fully investigated, but there is no doubt from the practical point of view that cyclodialysis without iris surgery in closed-angle glaucoma (increasing the loss of aqueous from the anterior chamber without relieving the relative pupillary block) is a dangerous procedure (Chandler, 1952).

Is it important from the practical point of view to try to put difficult cases into one or other category of primary glaucoma? The writer believes that the answer to this question is uncertain at present. There are some cases of closed-angle glaucoma which are difficult to recognize but will respond to peripheral iridectomy alone, thus obviating the dangers attendant on drainage operations in this type of case. Against this is the difficulty of being certain of the response to iridectomy alone and the natural desire to avoid submitting an eye to more than one operative procedure if possible, particularly in view of the difficulty of interpreting gonioscopic findings as discussed previously.

There are many surgeons who vary their drainage operations according to the type of glaucoma or according to the type of angle or the depth of the anterior chamber. Assessing the case after the use of miotics may be misleading here; both the width of the angle and even the depth of the anterior chamber (Bleeker, 1960) may decrease as a consequence of their use. In any case, as surgeons who use one drainage procedure for all types of glaucoma usually incorporate iris surgery in their techniques, the "curable" part of the closed-angle element is incidentally taken care of.

From the point of view of the prognosis, it is again uncertain whether simple glaucoma, if diagnosed before cupping has occurred, is definitely of worse prognosis than early closed-angle glaucoma, or, conversely, that cupping or field loss in closed-angle glaucoma are any less likely to advance in spite of control of the tension than in simple glaucoma. Further, as regards unilateral cases, no distinction can be made, as a high proportion of both types of glaucoma is eventually bilateral.

Whatever doubt there may be about the practical advantage of trying to separate the two primary glaucomas in difficult cases, the diversities of closed-angle glaucoma are obvious and a narrowing of the group of cases referred to as simple glaucoma can only help the search for the ultimate factors responsible for both types of the disease and the clarification of our knowledge of prognosis and treatment.

Summary

(1) A series of 47 cases diagnosed as mixed glaucoma is presented and analysed from the standpoint of the present classification of primary glaucoma. Five groups were reviewed:

- (a) 22 were considered to be chronic simple glaucoma.
- (b) 10 were considered to be closed-angle glaucoma.
- (c) 7 could on present criteria be considered as either (a) or (b), although the co-existence of the two conditions could not be excluded.
- (d) 5 cases were insufficiently investigated or too complex and doubtful for classification.
- (e) 3 were probably cases of true "mixed glaucoma", in the sense of co-existent closed-angle and simple glaucoma.

(2) Mixed glaucoma in this sense is probably very rare and can often be excluded from the diagnosis.

(3) Certain difficulties of classification are mentioned, especially those presented by angles which appear very narrow with the gonioscope.

(4) Some theoretical reasons for the rarity of the association of the two types of glaucoma are presented.

(5) The practical use of classifying difficult cases is questioned, but it may ultimately help to clarify such matters as the reputedly poor long-term prognosis of simple glaucoma.

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