

PRIMARY ANGLE-CLOSURE GLAUCOMA*†

A REVIEW OF PROVOCATIVE TESTS

BY

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A PROVOCATIVE test is one that "calls forth" a particular response under a defined set of conditions. For many years, a rise in intra-ocular pressure has been known to follow various circumstances. In attempts to detect glaucoma before serious eye disease occurred or to assess its control, various provocative tests have been elaborated (Leydhecker and Miller, 1949).

Because acute angle-closure glaucoma frequently damages eyes and vision yet may show no obvious evidence of its presence between attacks, and because in favourable circumstances it can be cured by relatively simple surgery, appropriate provocative tests appear highly desirable to facilitate its detection before an all too obvious acute attack develops.

Development of Angle-Closure Tests

Over a century ago von Graefe realized that belladonna made acute glaucoma worse and in later years many authors presented case reports of acute glaucoma caused by mydriatics. When eserine and pilocarpine were introduced for the treatment of glaucoma in 1876, fierce controversy ensued about their value for acute glaucoma, but their benefits were too great to be denied for long. Cases of acute glaucoma caused by atropine and cured by eserine were reported (Snell, 1882), and the importance of mydriatics as a cause of acute glaucoma became firmly established.

Different authors thought that the glaucoma-inducing effects of mydriatics were produced by different mechanisms, but between 1920 and 1932 Siedel and Serr showed convincingly that the rise in intra-ocular pressure was dependent upon pupil dilatation. Their papers were summarized by Leydhecker and Miller (1949):

Siedel found: (a) that the mydriatic test is dependent upon the width of the pupil, not on the method of its enlargement, and that the increased tension can be reduced by any factor which causes contraction of the pupil; (b) that the test is positive only in eyes with shallow anterior chambers; (c) that in eyes that react with a rise in tension there is a critical threshold of pupillary dilatation beyond which the rise occurs; (d) that the positive test is the result of obstruction to the outflow. Pressure with a weight of 15 g. on an eye with a shallow anterior chamber and a constricted pupil produced a fivefold greater drop in tension than when the same pupil was dilated.

Siedel and Serr also investigated the rise in intra-ocular pressure after a stay in darkness and concluded that mydriasis was responsible for it.

Induced pupil dilatation became the favoured provocative test for angle-closure glaucoma. A significant yet controllable rise in tension was sought and later, when tonography became an accepted procedure, a significant reduction in outflow was

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determined (Foulds, 1956; Becker and Thompson, 1958).

However, it soon became obvious that, although the rise in tension was usually readily controlled by miosis, a severe acute glaucoma was sometimes precipitated with all its urgency and destructive consequences. The stronger the mydriatic the more frequently a positive result was achieved, but the more likely was the occurrence of a severe acute glaucoma. On the other hand provocative tests were frequently negative and the patient later developed an acute angle-closure glaucoma. Compromises were therefore necessary so that relatively weak mydriatics (such as eucatropine) were used or the dark-room test was favoured.

Furthermore, tensions sometimes rose while angles remained open so that gonioscopic control became an added requirement. Gonioscopy is relatively reliable with pupils fixed by mydriatics but less accurate after dark-room tests, when angles may open quickly with the examining light or angle depths be hidden by iris convexity.

More serious uncertainties arose when it was shown that, even after the angle-closure glaucoma had been cured by a peripheral iridectomy, a considerable number of patients still gave positive provocative angle-closure tests after the instillation of tropine mydriatics (Lowe 1964), or after dark-room tests (Higgitt, 1954; Lowe, 1964). Therefore the uncertainty of angle-closure provocative tests from the many false negatives pre-operatively was increased by many false positives post-operatively.

Principles of Pupil Dilatation Tests

The above pupil dilatation provocative tests depend upon two mechanisms:

- (a) Increase in relative pupil block followed by angle-closure due to pupil block;
- (b) Angle-closure by the iris folding into the angle and smothering the trabeculae.

In eyes with shallow anterior chambers, the iris rests more firmly against the anterior surface of the forward lens than it does in normal eyes with flat irides. This leads to a relative pupil block which is enhanced as the pupil dilates and the iris becomes thicker. Thus pupil dilatation from any cause tends to increase pupil block by this mechanism. However, if the pupil dilatation is produced by iris sphincter muscle paresis (as by the application of tropine drugs or the dark-room test), the medially-acting component of sphincter muscle activity which tends to draw the pupil margin towards the lens is greatly weakened. This induced paresis of the sphincter muscle tends to weaken the pupil block (Lowe, 1966a).

Thus tropine drugs and the dark-room test increase pupil block by pupil dilatation but reduce it by sphincter muscle paresis, and this is a probable explanation of a large number of false negative results with these tests.

But iris sphincter muscle paresis causes another effect, namely, the closure of narrow angles by peripheral iris folding against the trabeculae because the dilator muscle acts without the antagonism of the sphincter (Lowe, 1966a). This form of angle-closure depends on the narrowness of the angle and the strength of the tropine drug as well as on the duration of application of the test. For this reason a considerable number of narrow-angle eyes still give positive provocative tests after pupil block has been by-passed and clinical angle-closure glaucoma has been cured by a peripheral iridectomy (Lowe, 1966b). Tropine drugs have a further effect that is not related to angle-closure. After their application some eyes show a rise in tension and a fall in outflow yet the widths of the angles remain unchanged. These alterations in tension

and outflow are usually not sufficient to confuse interpretation of the test result, but may sometimes do so. This is a further reason why gonioscopy must form part of the provocative test.

Thus tropine drugs and dark-room tests must be considered theoretically unsatisfactory as provocative tests for angle-closure glaucoma because:

(a) They only increase pupil block by thickening the iris or positioning the pupil so that it may grip the lens more firmly;

(b) They diminish pupil block by sphincter pupillae paresis;

(c) They can cause angle-closure by iris folding into the narrowed angle, and this is not a significant feature of the usual angle-closure glaucoma because it frequently persists after the clinical glaucoma has been cured by iridectomy;

(d) They may cause apparently significant rises in pressure and reduction of outflow without angle-closure.

Pupil Block

The main mechanical factor that initiates attacks is relative pupil block. In eyes with shallow anterior chambers, pupil block may be increased by:

(a) Thickening the iris by partial pupil dilatation;

(b) Stimulation of the dilator pupillae while the sphincter maintains its tone;

(c) Strong stimulation of the sphincter pupillae.

The maximum effect is achieved when all these factors act together.

Adrenalin-type drugs produce pupil dilatation by stimulation of the dilator pupillae and they very rarely cause angle-closure in the presence of a peripheral iridectomy (Lowe, 1965). The sphincter pupillae appears to maintain its tone during their action. They tend to draw the iris against an anteriorly-placed lens and this effect will be further increased if the sphincter pupillae is stimulated by a miotic (Lowe, 1966c). They can increase relative pupil block even in the presence of small pupils. They cause little change in outflow or increase it. They appear to mimic the pupil-block-angle-closure mechanism more appropriately than the tropine drugs or the dark-room test.

But adrenalin-type drugs have a serious risk. Reversal of the pupil dilatation requires the application of a miotic, and miotics acting with adrenalin-type drugs increase the pupil block which may intensify the angle-closure (Lowe, 1966c). Strong adrenalin solutions or their counterparts (such as 10 per cent. phenylephrine) can overcome even strong miotics and, in the presence of a raised intra-ocular pressure, the iris cannot be drawn away from the smothered trabeculae. The patient may need urgent admission to hospital for adequate tension control and surgical release of the pupil block (Lowe, 1965). All the severe destruction of angle-closure glaucoma is likely, especially if the induced acute glaucoma occurs after the patient has left the clinic.

Indications for Provocative Tests

Angle-closure glaucoma is fraught with severe consequences yet its cure is possible by means of a relatively simple operation provided the eye is not damaged. The benefits of surgery are so pronounced that, if mild angle-closure glaucoma could be provoked and controlled, peripheral iridectomy would be justified to prevent much visual loss and save much distress to the patients involved.

There appear to be three indications for angle-closure provocative tests:

- (1) The second eye after definite angle-closure glaucoma in one eye;
- (2) Eyes suspected of having intermittent attacks or a relieved acute attack;
- (3) Symptom-free eyes with shallow anterior chambers and narrow angles discovered by routine examinations.

The second eyes of patients who have had definite angle-closure glaucoma in the other eye have such a high risk of future angle-closure glaucoma and damage to vision that they should be made safe by surgery before the patient is discharged from hospital or even before surgery upon the first eye involved. Not all these patients would develop an acute angle-closure glaucoma in the second eye, but the chance has been estimated at approximately 75 per cent. Provocative tests give much lower percentages and at the present time negative tests appear dangerous in that they may lead to postponement of surgery. If a provocative test could be shown to be likely to distinguish those with high and low risks of angle-closure in the second eye, and the test results were confirmed by following a series of patients at least 15 years, then prophylactic surgery might be avoided on some second eyes. Until such a provocative test has been proved, second eyes accompanying angle-closure glaucoma should receive the curative benefits of surgery although there may be some surgical risks.

Second eyes accompanying angle-closure glaucoma have featured largely in the statistics of angle-closure provocative tests, but because these eyes have a known high risk of angle-closure glaucoma, the results obtained with provocative tests upon them should not be transposed to other eyes that may appear anatomically similar but have suffered no angle-closure attacks.

Attacks of intermittent angle-closure glaucoma are frequently difficult to diagnose. As with many diseases the basis of diagnosis is a careful and detailed history. Unfortunately, patients are often vague about the cardinal symptoms of eye-ache, blurred vision, haloes, and nausea, and frequently the symptom complex is incomplete. Certain diagnosis depends upon examining the patient during an attack and checking for corneal oedema, pupil dilatation, raised tension, or angle-closure. This necessitates the patient being in a situation where an ophthalmologist or eye hospital can be attended, usually at night. Often there is a particular circumstance that precipitates the attacks and its intensive application should be encouraged to try to induce an attack for examination. If successful this is the best test as it is produced under the natural conditions causing the intermittent angle-closure glaucoma.

Some people have true acute attacks of angle-closure glaucoma that resolve spontaneously. They may be diagnosed in retrospect by careful history-taking or perhaps by the presence of a segment of slight iris atrophy at the pupil margin. These attacks are usually of insufficient severity to form *glaukomflecken*, but the characteristic faint flecks should be sought.

When cases of suspected angle-closure glaucoma are seen, the clinician should assess the probabilities, and if the diagnosis of a past attack is reasonably certain, surgery should be advised. Most decisions do not need the support of uncertain provocative tests, but sometimes the patient and not the ophthalmologist needs a positive provocative test to be convinced of the necessity for surgery.

Symptom-free eyes with shallow anterior chambers and narrow angles are found not rarely during routine examinations and these eyes usually have full vision. Some

will develop angle-closure glaucoma and some will suffer loss of vision despite warnings that may be given to the patient. Unfortunately also, warnings will unduly scare some patients who will never develop angle-closure, but if warnings are not given, any attack that develops is likely to be neglected until damage to eye and vision occurs. It is in this group that provocative tests are particularly required. Furthermore, it is especially in this group that severe acute glaucoma should not be induced by the provocative test. Törnquist (1958), using the dark-room test, found that very few such eyes gave rises of tension over 8 mm. (5 per cent. of anterior chambers less than 2.0 mm. deep and 1.5 per cent. of anterior chambers deeper than 2 mm.). Mills and Becker (1963), using the 5 per cent. eucatropine pupil dilatation test on 68 people referred only because of narrow angles discovered on routine gonioscopy, found that only 7 per cent. gave a positive result by this provocative test. The few positive results with the dark-room test indicate the total effort is not worth while. The 7 per cent. positive selection with the eucatropine test would justify the total effort only if the test were shown to sort the selected population accurately into those at risk and those probably free from danger. These requirements have not been met—it would take 15 years to do so.

Kirsch (1965) has described a triple provocative test consisting of partial mydriasis with 1 or 3 per cent. eucatropine and 0.5 per cent. cyclopentolate combined with miosis from 4 per cent. pilocarpine at the same time as a water-drinking test. This test provides reasonably close parallels to the known factors producing angle-closure glaucoma attacks. Kirsch states that the test was frequently positive when a mydriatic or dark-room test had been previously negative but, of 139 asymptomatic eyes found with narrow angles on routine examination, only 10 per cent. gave a positive triple provocative test and two developed frank acute angle-closure glaucoma.

Probably the percentage of positive tests could be increased by using adrenalin or phenylephrine instead of the tropine drugs, but more acute angle-closure glaucoma would be likely to occur. Severe eye damage has been seen to follow 10 per cent. phenylephrine provocative tests (Lowe, 1965).

The relative frequency with which eyes with shallow anterior chambers and narrow angles are found in the general population compared with the infrequency of angle-closure glaucoma, indicates that the percentage of narrow-angle eyes that will develop angle-closure glaucoma is only about 7 to 10 per cent. If the percentage from provocative tests were high, an excessive number would be provoked artificially.

Discussion and Conclusions

Provocative tests for angle-closure glaucoma remain unsatisfactory. For the fellow eye with similar anatomical configuration to an eye that has developed angle-closure glaucoma, provocative tests need to yield approximately a 75 per cent. positive response, and eyes with negative tests need to be followed for at least 15 years for the negative results to be sufficiently proved. A somewhat similar response should be expected from eyes that have been carefully selected as suspect for a previous angle-closure attack. At present in both the above groups careful clinical history and examination can give a better guide for surgery than provocative tests.

Clinically accurate provocative tests for asymptomatic eyes with shallow anterior chambers and narrow angles are highly desirable so that the curative benefits of

peripheral iridectomy may justify the risks of surgery. As the measurement of anterior chamber depths with slit-lamp measuring devices becomes routine practice, the results should be correlated. The main mechanical feature of the provocative tests will need to be relative pupil block rather than pupil dilatation. The tests must entail very little risk of precipitating frank angle-closure glaucoma, otherwise they will find no place in clinical practice away from hospitals. It is in general ophthalmic practice that they are most needed. At present not only is the percentage of false negatives known to be too high but positive tests are usually taken as indications for medical or surgical action without any assessment of the validity of the positive results, especially in asymptomatic eyes.

The problem therefore appears to be one of considerable magnitude and requiring much time, somewhat comparable with but even more difficult than the assessment of the validity of borderline ocular tensions for chronic simple glaucoma found by routine examinations or surveys. Nevertheless, it is important that attempts should be made to devise better provocative tests for angle-closure glaucoma and that their accuracy should be checked over a long time. At present, for ordinary clinical practice, it appears that provocative tests for angle-closure glaucoma are too inaccurate, too time-consuming, or too dangerous, and they can frequently be rendered unnecessary by careful and skilled clinical examination.

Summary

Provocative tests for angle-closure glaucoma are highly desirable but pupil dilatation with tropine drugs and dark-room tests are theoretically unsuitable. At present, careful clinical history-taking and examination are more accurate than provocative tests for deciding in favour of surgery upon second eyes or eyes suspected of having had a previous angle-closure attack.

Present provocative tests are too inaccurate, too time-consuming, or too dangerous for symptom-free eyes found to have shallow anterior chambers and narrow angles on routine examinations. Attempts to find better provocative tests should continue.

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