COMPARATIVE PROVOCATIVE TESTS IN GLAUCOMA*†

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It is the purpose of this paper to compare the results of the lability test of Bloomfield and Lambert (1945) with those of its two components, the venous-congestion test of Schoenberg (1929) (referred to as the "cuff test") and the cold-pressure test of Kahler and Sallmann (1929) (referred to as the "ice test"), on a number of normal and glaucomatous eyes, in conditions which correspond as closely as possible. Further, the reaction is investigated of the same group of glaucomatous eyes to the water-drinking test of Marx (1925-28) and Schmidt (1928-31), the mechanism of which has been described in detail in a separate communication (Leydhecker, 1950). The results will be correlated to the spontaneous phasic variations of the ocular tension. These have been shown by Thomassen (1946) and Thomassen and Leydhecker (1950) to influence a number of provocative tests, all of which have in common the fact that they react on the vascular system of the eye.

Methods

Treatment with miotics was discontinued at least 12 hours before each test. The ocular tension was measured in all cases by the author with the same Schiötz X-tonometer, the patient lying supine with the head slightly elevated. One drop of pantocaine 1 per cent. was used for local anaesthesia. In most cases one reading only was taken each time, the patient's head being in a horizontal position, the eye looking vertically upwards towards the patient's suspended finger, and the tonometer being applied vertically on the middle of the cornea.

For the "cuff test" a sphygmomanometer-cuff was put round the patient's neck so that the cushion lay equally on both jugular veins. It was inflated to a pressure of 40-45 mm. Hg for one minute, the time being measured by a stop-watch. A higher pressure was regarded as too uncomfortable, especially in elderly patients. For the "ice test" one hand was immersed up to the wrist in a bowl of iced water for one minute. In the "lability test" both procedures were combined.

For an adequate comparison between the three tests it is desirable to compare groups of each type of test performed when the eye was in the same phase of its diurnal variation of pressure. This purpose was achieved by an assessment of the spontaneous phasic variations of the ocular tension as each test was performed or by applying all three tests at an interval of a few minutes. The latter procedure was adopted on 109 occasions in the series of glaucomatous eyes studied. In all cases tonometry was performed 30 minutes before the test and again at the end of the test, while the hand was still in the water or the cuff

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still inflated, or both. The tension returned to its previous level in approximately 3 to 5 minutes. Since in some cases it fell slightly below, or rose slightly above the values obtained before the test, tonometry was repeated before each new test. Thirty minutes after the last test the tension was taken again.

The order in which the 109 comparative tests were performed was: 1st the lability test, 2nd the cuff test, 3rd the ice test; immediately thereafter the patient massaged with a towel the hand chilled during the lability test.

Controls showed that a reversed order did not alter the results, if the intervals between the tests were sufficiently long (3-5 minutes) to allow the tension to return to approximately its previous level. Owing to the lightness of the instrument there was no fall in the ocular tension due to a massage effect of the repeated tonometry. Cuff tests repeated at intervals of a few minutes gave the same results, showing not only that the tension returns to the original level, but also that the conditions in the eye are not significantly altered by repeated venous congestion.

The water-drinking test was done on a separate day. The patients drank 500 or 1,000 ml. water before breakfast, and the tension was measured 30 minutes before, immediately before and 15, 25, 35, and 45 minutes after the ingestion of water. Miotics were discontinued 24 hours previously.

Results

Normal Eyes.—The lability test was done on 79 eyes and resulted in rises of 6 mm. Hg or less in eight cases, and of 7 or 8 mm. Hg in three cases. Since rises of 9 mm. Hg have been described in normal eyes (Bloomfield and Lambert, 1945; Sugar, 1948) only rises in tension greater than this are taken as abnormal in this paper.

The cuff test was done on 76 eyes and resulted in rises of 6 mm. Hg or less in 71 eyes, and rises of 7 mm. Hg in two eyes. This is the limit of variation described by Bloomfield and Lambert, and accordingly rises of 8 mm. Hg or more are taken as abnormal.

The ice test was performed on 72 eyes and resulted in rises of 2-4 mm. Hg in only twelve cases. This again is the same limit as that described by Bloomfield and Lambert, and accordingly a rise of more than 4 mm. Hg is regarded as pathological. In nine eyes the tension fell 2 mm. Hg during the test.

The reaction of the blood pressure to the immersion of the hand in ice water was measured in some patients, and rises in the systolic pressure of 0-20 mm. Hg were observed. There was, however, no conclusive correlation between the reaction of the ocular tension and the changes of the blood pressure. The ocular tension fell in some patients by 3 mm. Hg and rose in the same eyes by 6 mm. Hg on another day.

In 76 eyes lability and cuff tests were performed on the same eye after an interval of a few minutes. In fourteen eyes the lability test resulted in a rise 3 mm. Hg or more higher than that obtained with the cuff test; in five eyes the reverse occurred, and in 57 no marked difference was measured. It is interesting that the rise brought about by the lability test was not the sum of the results of the cuff test and the ice test.

Glaucomatous Eyes.—Only eyes suffering from primary glaucoma which had not been operated on are discussed in this paper. The series comprised 52 eyes, 21 of the chronic simple type, 31 of the congestive type. On these, 117 lability tests, 201 cuff tests, and 91 ice tests were performed, and in all of them an assessment of the spontaneous variation of the tension was attempted. The results are given in Table I. The lability test and the ice test showed approximately the same percentage of positive results (9 to 12·7 per cent.)* in the simple glaucoma group as in the congestive glaucoma group. The cuff test produced the largest number of positive results in the congestive glaucoma group (18 per cent.).

TABLE I

Results of the Lability, Cuff, and Ice Tests.

Type of Test	Type of Glaucoma	Patients	Eyes	Tests		
				Total	Positive	Negative
Lability ...	Simple	12	18	46	5	41
	Congestive	17	31	71	9	62
Cuff ...	Simple	12	21	68	6	62
	Congestive	17	31	133	24	109
Ice... ..	Simple	12	19	31	3	28
	Congestive	17	31	60	6	54

In Table II the incidence of positive or negative tests is related to the spontaneous variations of the ocular tension, the phases of which are referred to as "rising", "falling", "level", and "unknown".

A "rising" phase was assumed to exist if tonometry showed a higher tension immediately before the test than it had been 30 minutes previously, and if 30 minutes after the test a higher tension was again recorded. If the tension was rising so slowly that the difference between the first and the last reading (*i.e.*, the rise in one hour) was 7 mm. Hg or less, the test was not recorded as being performed during a rise, since in such cases the result of the test was found not to be influenced thereby.

* It will be noticed that reference is made to the number of positive or negative tests, not to percentage of eyes which have a positive reaction.

TABLE II

Results of the Lability, Cuff, and Ice Tests in relation to the Spontaneous Variations of the Ocular Tension.

Tests		Type of Glaucoma	Number of Tests done in each Phase of Spontaneous Variation of Ocular Tension*			
Type	No.		Rising	Falling	Level	Unknown
Lability ...	45	Simple	1 (1+)	3 (3—)	29 ⁽²⁺⁾ (27—)	12 ⁽²⁺⁾ (10—)
	71	Congestive	5 ⁽⁴⁺⁾ (1—)	5 (5—)	36 ⁽¹⁺⁾ (35—)	25 ⁽⁴⁺⁾ (21—)
Cuff ...	68	Simple	0	1 (1—)	45 ⁽⁴⁺⁾ (41—)	22 ⁽²⁺⁾ (20—)
	133	Congestive	4 (4+)	8 (8—)	67 ⁽⁸⁺⁾ (59—)	54 ⁽¹²⁺⁾ (42—)
Ice ...	31	Simple	1 (1+)	0	21 ⁽²⁺⁾ (19—)	9 ⁽¹⁺⁾ (8—)
	60	Congestive	4 (4—)	0	36 ⁽⁴⁺⁾ (32—)	20 ⁽²⁺⁾ (18—)

* Number of positive or negative tests in brackets (+) or (—)

Similarly a "falling" phase was recorded when the reading immediately before the test was lower than it had been 30 minutes previously, and when the reading 30 minutes after the test was again lower, the total fall of the tension in one hour being 8 mm. Hg or more.

The tension was regarded as "level" if the variations recorded within one hour were less than 3 mm. Hg.

Finally, the type of variation of the tension was recorded as "unknown" if:

- the change within one hour was more than 3 but less than 8 mm. Hg,
- the tension at the first and second readings was the same, but at the third higher or lower than before,
- the difference between the first and second readings indicated a rise or fall of tension, which then remained level when measured 30 minutes after the test,
- tonometry immediately before the test showed a higher or a lower tension than had been found half an hour before or after the test.

To summarize: a spontaneous rise or fall in tension was recorded only when it increased or decreased continuously through a range of 8 mm. Hg or more during the hour in which the test was done. The incidence of this type of spontaneous variation in tension is small (see Table II); most of the changes in tension occurred more quickly and irregularly, so that an assessment of how the tension changed at the actual time of the test was difficult or impossible. Spontaneous falls or rises in tension complying with the definition given here were observed in approximately 8 per cent. of all tests. All the lability tests (with one exception, which will be discussed later) and all the cuff tests carried out during a spontaneous rise of tension gave a positive result, and those carried out during a spontaneous fall gave a negative result. The incidence of positive tests amongst those done in a level phase was only 2.8 to 11.9 per cent. The ice test, in contrast to the two other tests, was always negative during a spontaneous rise.

TABLE III

*Relative Increases of the Ocular Tension produced by the Lability and Cuff Tests performed consecutively or simultaneously on the Same Eye.**

Order of Tests	Type of Glaucoma		Normal Eyes
	Simple	Congestive	
Lability > Cuff ...	13	22	14
Lability = Cuff ...	27	35	57
Lability < Cuff ...	2	10	5

* Only differences of 3 mm. Hg or more are evaluated.

A comparison of the relative increases of tension obtained with the lability and cuff tests by successive tests after a short interval is given in Table III. For both types of glaucoma the difference was smaller than 3 mm. Hg in more than half the cases. In the remainder, the lability test more frequently produced rises at least 3 mm. Hg higher than those brought about by the cuff test.

In the practical application of both tests, however, these differences are irrelevant, since the occurrence of a positive or negative result is the only thing that matters. In Table IV, therefore, the same tests are compared from this point of view. The comparison shows that in 90.5 per cent. of simple glaucomas,

and in 83.6 per cent. of congestive glaucomas, the same clinical results were obtained with either test, both being positive or both negative when done on the same glaucomatous eye after one another.

TABLE IV
Evaluation of the same Tests as in Table III according to the Clinical Result (positive or negative).

Clinical Results	Type of Glaucoma	
	Simple	Congestive
Lability test + Cuff test —	3	4
Both tests + or —	38	56
Lability test — Cuff test +	1	7

TABLE V
Comparison between the Clinical Results of the Lability Test and the Water-Drinking Test in the same Group of Eyes.

Clinical Results	Type of Glaucoma	
	Simple	Congestive
Lability test + Drinking test —	0	1
Both tests + or —	5	9
Lability test — Drinking test +	10	10

When the results of the water-drinking test are compared with those obtained with the lability test in the same eyes (Table V) it becomes obvious that the former is more reliable. It was positive in twenty eyes, in which repeated lability tests had negative results, and the reverse occurred in one eye only. In fourteen eyes both tests were either positive or negative.

Finally, when all the 116 water-drinking tests of this study are reviewed (Table VI), the high incidence of positive tests (58 per cent. in simple glaucoma, 67 per cent. in congestive glaucoma) contrasts favourably with the poor results of the other tests reported in Table I.

TABLE VI
Incidence of Positive Results with the Water-Drinking Test.

Type of Glaucoma	Number of Tests		
	Total	Positive	Negative
Simple	50	29	21
Congestive	66	44	22

The results of the water-drinking tests were not influenced by a spontaneous rise or fall in the ocular tension preceding the ingestion of water.

The depth of the chamber angle did not influence the result of any of the tests.

Discussion

The first significant result is that both lability and cuff tests were positive in 8.8 to 18 per cent. of all applications to glaucomatous eyes not under the influence of miotics. These figures do not compare directly with those reported by other observers, since it has been the custom to perform one test of each type on each eye and to evaluate the percentage of eyes reacting positively. In contrast to this method it is the aim of the present paper to study the conditions in which positive or negative results are obtained in repeated applications of the same test to the same eyes. When so many tests of each type are done on a single eye, a considerable percentage of them gives a positive result at some time, so that a report of this kind may appear misleading; but when Tables I and VI are compared, it will be seen that valuable results have been obtained by this method of evaluation. The poor results of the lability, cuff, and ice tests may partially be explained by the lower pressure used for the compression of the jugular veins (45 mm. Hg) as compared with the technique of Bloomfield and Kellermann (1947), Sykowski (1948), and Stine (1948). On the other hand, they are confirmed by Sugar (1948) who obtained positive lability tests in less than half his glaucomatous patients,

though he employed a pressure of 55 mm. Hg. It is felt that Kronfeld (1949) is right when he states that the clinical application of the lability test is discouraging. The ice test was as unreliable as the two other tests.

The water-drinking test, on the other hand, showed an incidence of 58 per cent. positive tests in simple glaucoma (as compared with 10.9 per cent. with the lability test, 8.8 per cent. with the cuff test, and 9 per cent. with the ice test), and 67 per cent. in congestive glaucoma (lability test, 12.7 per cent.; cuff test, 18 per cent.; ice test, 10 per cent.). The better results of the water-drinking test are also obvious when the numbers of positively reacting eyes on which numerous water-drinking and lability tests were performed are compared. In twenty of these the former test was positive and the latter negative, whereas the reverse was observed in one eye only.

A discussion of the mechanism of these tests is unnecessary here since this has been dealt with in previous communications (the lability test by Thomassen and Leydhecker, 1950; the water-drinking test by Leydhecker, 1950); it may suffice to repeat that the water-drinking test acts by changing the osmotic equilibrium between the blood serum and the intra-ocular fluids in contrast to the other three tests which influence the vascular system of the eye. This fundamental difference in mechanism explains why the water-drinking test is uninfluenced by changes in the intra-ocular vascular state as are the lability and cuff tests.

In a previous communication (Thomassen and Leydhecker, 1950) it was pointed out that the lability test is usually positive in a rising and negative in a falling phase of the ocular tension, and that it can be either positive or negative when the tension is level. An analysis of the tests described in the present paper shows that this also applies to the cuff test, while the ice test seems to follow the reverse rule, if any. Only one negative lability test was observed in a rising phase of the tension; and when the same patient was seen again the test was positive during a spontaneous rise. In the first instance the tension was high before the test, so that an error of reading of half a point on the scale of the tonometer may have caused the exceptional result.

The ice test was always negative when performed during a spontaneous rise of tension. It seems likely, therefore, that the regular influence of spontaneous variations in the ocular tension on the result of the lability test is due exclusively to the influence of venous congestion. The combination of the production of view, a disturbing factor which may have caused the negative lability test during a spontaneous rise of tension described above.

It would seem that the combination of the cuff test with the ice test in the lability test offers no clinical advantages as compared with the cuff test by itself (Table IV). Indeed, it would seem a fair conclusion that for clinical purposes all these three tests are of only limited value, and that the cuff test by itself is certainly as good as the lability test and may, in fact, be better since the immersion of the hand into ice water introduces other factors the nature of which is little understood. In any event the practical clinical value of the phasic relations of the tests is small. A positive test means that the ocular tension is abnormally unstable regardless of the phase, while a negative test in a falling or level phase is without significance in the elucidation of the diagnosis of glaucoma. Phasic variations in the ocular tension smaller than 7 mm. Hg in an hour do not affect the outcome of the test, and greater variations themselves demonstrate the instability of the tension without any further test.

Some observations incidental to the main theme of this paper may be of interest.

In some cases of congestive glaucoma gross and rapid variations of the ocular tension have been observed to occur; in some patients the rise of tension almost invariably began after 9 a.m., rose to 60-80 mm. Hg, and showed a spontaneous fall subsiding about 1 p.m. These great variations are not always recognized, for when a diurnal variation curve is plotted with the usual two or three readings (morning, noon, and evening), variations much smaller than those which actually occur may be recorded. These spontaneous rises of tension were frequently not associated with any subjective sensations. It would therefore seem wise that the tension should be measured hourly in hospitalized patients throughout the morning when the presence of glaucoma or an unstable post-operative tension is suspected. In the author's opinion continuous treatment with miotics is unsafe if these gross variations in tension are found 12 hours after the cessation of miotics, as happened in some of the patients in this series. Moreover, patients should also be advised to discontinue miotic treatment for at least this interval before they attend hospital for a routine check-up.

It has also been observed that miotics did not often become effective until 40 minutes after their instillation, during which interval a spontaneous rise of tension continued. Operations should therefore be timed to avoid the hours in which spontaneous rises have previously been observed, since the usual pre-operative preparation with miotics may not control the tension soon enough.

Lastly, spontaneous variations in tension should be taken into account in all procedures expected to change the ocular tension; they may themselves be mistaken for an experimental effect, or may neutralize, or even reverse, the outcome of any such experiment in glaucomatous eyes.

Summary

(1) In 52 eyes suffering from chronic simple or congestive glaucoma which had not been subjected to operation, 117 lability tests, 201 venous-congestion tests, and 91 cold-pressure tests were performed. A positive result was obtained in fourteen lability tests, thirty venous-congestion tests, and nine cold-pressure tests.

(2) The spontaneous phasic changes of the ocular tension at the time of each test were observed: a rising phase was observed

fifteen times, and a falling phase seventeen times, whereas the tension was level in 234 instances, and on 142 occasions the phase could not be assessed.

(3) During spontaneous rising phases of the ocular tension of at least 8 mm. Hg per hour, all venous-congestion tests were positive. During spontaneous falling phases they were all negative. With one exception, the lability test followed the same rules. The cold-pressure test was always negative in a rising phase. It is suggested therefore that the influence of the spontaneous variations of tension on the lability test is due to one of its components only, viz., the venous congestion.

(4) The lability test offers no clinical advantages over the venous-congestion test and its results are complicated by its two different components. As long as the mechanism of both tests is yet insufficiently understood it seems advisable to study the venous-congestion test separately.

(5) In the same eyes, 116 water-drinking tests were performed. Positive results were obtained in 58 per cent. in simple glaucoma, and in 67 per cent. in congestive glaucoma. This test is therefore more reliable than the lability test.

(6) The significance of spontaneous phasic variations of the ocular tension in the diagnosis and treatment of glaucoma is discussed. It is suggested that the spontaneous phasic variations of the ocular tension should be taken into account in all experiments on glaucomatous eyes in which the ocular tension is expected to be altered.

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