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COMMUNICATIONS

THE WATER-DRINKING TEST* †

BY

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THIS paper is a contribution to the study of the mechanism of the water-drinking test, attempting to answer the question whether it is a test for the function of the capillary endothelium, as the first investigators of this test assumed, or whether the osmotic changes of the blood account for the rise of the ocular tension. The first conception implies that chronic simple glaucoma is a general disease caused by dysfunction of the capillary endothelium. The second theory suggests that the defect lies in the eye itself. Each opinion has been strongly advocated by a clinic, the first at Bonn, the second at Heidelberg. Since an understanding of the arguments in the controversy may help to assess the present investigation, a short review of the literature follows.

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Literature

Experiments at Bonn.—Marx (1925; 1926 a, b, c, d; 1928), working at the Medical Clinic at Bonn, investigated the drinking test (1 litre water within a few minutes in a state of fasting). The haemoglobin percentage of the blood was measured every 15 minutes and the volume and specific gravity of the urine every 30 minutes. In normal cases the haemoglobin curve showed a dilution of the blood with a peak between 20 and 40 minutes, and a smaller maximum between 50 and 80 minutes. The original level was regained in 4 to 5 hours. Identical curves were obtained after drinking 1,000 cc., 250 cc., or 50 cc. water or normal saline. The diuresis was less constant. The specific gravity showed one phase of dilution only. Abnormal reactions, found in diseases of kidney and heart or in glandular insufficiency, were attributed to a general disturbance of the capillary endothelium, which was regarded as the barrier to the exchange between blood and tissue.

Schmidt, also at Bonn, took the interpretation of this test for granted and reported on sixteen cases of chronic simple glaucoma in which only these systemic responses were studied (Schmidt, 1928a). The ocular tension was not measured. Eight of the sixteen haemoglobin curves were abnormal, but in his opinion fifteen patients reacted abnormally because of delayed diuresis and/or irregular dilution of the urine. His conclusion was that in chronic simple glaucoma a disturbance of the capillary endothelium is present.

In later publications (1928b, c; 1929; 1931) he also reported a rise of the ocular tension during the test in all cases of untreated simple glaucoma, which was the same after drinking 1,000 cc., 250 cc., 50 cc., or 20 cc. water (1931). This is his only valid argument against an osmotic basis for the drinking test, his others being erroneous, *e.g.*, when he pointed out that hydraemia produced by heat or by the injection of hypertonic solutions did not produce a rise of the intra-ocular pressure (1928c).

His views were shared by his teacher Römer (1928) and his co-worker de Decker (1929a, b) who applied the water test in seventeen cases of retinal detachment and obtained a significant rise of tension in seven of them. This disease, too, was therefore attributed by de Decker and by Römer to a disturbance of the intra-ocular capillaries.

Although in a control test with normal saline de Decker obtained smaller rises, which were within the error of tonometry (the report on a second case is misleading), he attributed the effect to the increase of plasma in the blood (1929b).

Criticism from the Eye Clinic at Heidelberg.—Serr (1928) argued in the discussion following Schmidt's paper that the osmotic hypotonia of the blood was sufficient to explain the rise of the intra-ocular pressure in glaucoma. A normal eye can compensate the inflow of liquid by an increased outflow of aqueous, but not a glaucomatous eye. Lobeck (1930) from the same clinic, published a detailed criticism with essentially the same arguments. He did not, however, contribute any experiments of his own.

Further Application of the Test.—No further contribution has been made to our knowledge of the mechanism of the test. Later observers (Bloomfield and Kellermann, 1947; Evans, 1942; Heegaard and Larsen, 1931; Kronfeld, 1949; Majorova and Glinika, 1939; Ohm, 1936; Spadavecchia, 1936; Sugar, 1948; Tichomirov, 1940, 1941; Wegner, 1930a, b, c) have investigated mainly the clinical value of the drinking test, by considering the percentage of positive results of the tests in established glaucoma, or by comparing it with other tests. Animal experiments were contributed by Yudkin and Gilman (1933).

There is not complete agreement on the reaction of normal eyes, the usually accepted limit being a rise of 6 mm. Hg. Sugar (1948), however, regards even a rise of 9 mm. Hg, or a ceiling of 32 mm. Hg, as normal.

The test is mostly recommended for chronic simple or wide angle glaucoma (Kronfeld, 1949), but Sugar doubts whether it can not equally be applied in the narrow angle type. He combined it with the lability test of Bloomfield and Kellermann (1947), and then regarded rises of 10 mm. Hg, or a ceiling of 38 mm. Hg, as still normal. Negative tests in established wide-angle glaucoma were attributed by Kronfeld to an anomalous systemic response to the ingestion of water, but unfortunately no details of the systemic anomaly in these cases were reported by him.

The Present Investigations

Terminology.—All patients had primary glaucoma. No eyes with merely suspected glaucoma or with any additional disease were included. The eyes are classified in two ways:

(1) according to the course of the disease into simple or congestive glaucoma. "Simple glaucoma" signifies the absence of any clinical signs of congestion or history of previous congestive attacks; in the presence of either of these the case is classified as "congestive glaucoma".

(2) In most eyes gonioscopy by means of the Goldmann contact lens and the Haag-Streit slit-lamp was performed. These eyes are classified into wide-angle or narrow-angle glaucoma, according to whether the ciliary body was visible or not.

Number of Patients.—There were altogether 42 patients; nineteen patients (34 eyes) in the simple glaucoma group and twenty-three patients (40 eyes) in the congestive glaucoma group.

Gonioscopy was done on 27 eyes of the simple glaucoma group and it was found that eight of them had a narrow and nineteen had a wide angle. When 29 eyes of the congestive glaucoma group were examined with the gonio-lens, eighteen had a narrow, and eleven a wide angle. It is noteworthy that so high a percentage of eyes with a wide angle occur in this group. Four of these eleven eyes had more than half of the angle occluded by peripheral anterior synechiae and all of them had a shallow anterior chamber of less than 2.5 mm. **Methods.**—All patients had no miotics for at least 24 hours and had no breakfast in the morning before the test. They drank the water within 3 minutes on the average, the minimum time being 1 minute, the maximum 5 minutes. It is essential that this last time is not exceeded. A sandwich was given not earlier than half an hour after the ingestion of the water. Patients able to attend several times drank 1,000 cc. at the first visit, 500 cc. in several subsequent tests, then 250 cc. once, and, if all these tests were positive, once 500 cc. normal saline and finally 50 cc. water.

Tonometry.—This was performed by the author in all cases, using the Schiötz X-tonometer with the patient lying flat on his back. The illumination of the room was constant. Readings were taken half an hour before and again immediately before the test, care being taken to start the test neither in a rising nor in a falling spontaneous phase. From this rule 22 exceptions were made; this will be discussed later. A stop watch was started when the patient began to drink and the tonometry was repeated at 10-minute intervals, or more frequently, until the end of the first hour, and then half-hourly.

Urine.—This was collected in the present study before the test, then half-hourly during the next 3 hours; in some cases, however, the patients were available for only 2 hours.

Conductivity Tests.—For these blood was taken from the cubital vein before the test and 4 to 6 further samples between tonometric measurements. It is essential to collect the blood into absolutely dry syringes, needles, and glass tubes. In the first three cases exactly the same amount of heparin was added to each tube, so that after centrifuging, plasma was obtained. As fibrin disturbed the measurement of the conductivity by clotting on the electrodes, all further tests were done with serum only. The glass tubes were corked as soon as the blood was delivered into them, centrifuged, and kept in the refrigerator until the conductivity was tested some 3 hours later. To measure the conductivity the apparatus of Davson, Duke-Elder, and Maurice (1949)* was used.

Results of the Water-Drinking Test

Incidence of Positive Results.—One hundred and sixty-eight water drinking tests with 1,000 cc., 750 cc., 500 cc., and 250 cc. were done on altogether 74 eyes. Control tests with 50 cc. water or 500 cc. normal saline are not included in this number. A rise of the ocular tension of 6 mm. Hg and more, or from a normal tension below 30 mm. Hg to a pressure over 30 mm. Hg, was regarded as a positive result (+). A rise of more than 9 mm. Hg, or from a normal tension below 30 mm. Hg to a pressure over 32 mm. Hg, was regarded as strongly positive result (++) . Details are given in Table I. The approximately equal incidence of positive tests in unoperative eyes with simple glaucoma (77 per cent.) and congestive glaucoma (74 per cent.) is striking. The same holds good when the classification is made into wide angle (positive 70 per cent.) and narrow angle (positive 69 per cent.) glaucoma. The

* I should like to thank these authors for their kind permission to use the apparatus.

high incidence of positive tests in operated eyes was in accordance with the post-operative history of these cases.

Strongly positive tests were obtained in 50 per cent. of the unoperated eyes (in simple glaucoma, eight out of 22; in congestive glaucoma, fourteen out of 23).

TABLE I
Incidence of Positive Tests

Number of eyes		Classification of eyes	Reactions				Number of tests	
			+		++			
			No.	%	No.	%		
74	22	<i>Simple Glaucoma</i> unoperated ...	17	77	8	36	54	168
	12		operated ...	5	41·5	4	33	
	23	<i>Congestive Glaucoma</i> unoperated ...	17	74	14	61	55	
	17		operated ...	7	41	6	35	
56	20	<i>Wide angle</i> unoperated ...	14	70	7	35	55	151
	10		operated ...	2	20	1	10	
	16	<i>Narrow angle</i> unoperated ...	11	69	8	50	51	
	10		operated ...	6	60	2	20	

The incidence of positive tests is approximately the same in unoperated eyes with simple glaucoma as in congestive glaucoma. The width of the chamber angle is unimportant in assessing the result.

Dependence of the Rise of the Ocular Tension on the Amount of Ingested Water.—In the evaluation given above, all tests from 1000 cc. to 250 cc. water were included. For a comparison between 1000 cc. and 500 cc. tests it must be appreciated that in most patients only one test with 1000 cc. was done, but on the average four with 500 cc. were done. The incidence of positive (+) and of strongly positive (++) tests for each group is shown in Table II. No reference is made to the width of the chamber angle as it seemed of minor importance (see Table I). The number of eyes compared in this way is only 42 (fifteen operated and 27 unoperated), as some patients were not willing to attend several times. In the 27 non-operated eyes, positive results were obtained in 21 eyes with 1000 cc. water, and in fifteen eyes with 500 cc. water. In eleven out of the 27 eyes, the increase of tension with a 500 cc. test was slightly greater than with a 1000 cc. test.

The explanation lies in the great variability of the rise of tension

in the same eye after the ingestion of water. For example, in repeated 500 cc. tests the same eye may show a rise of 2, 9, or 12 mm. Hg (patient No. 28 right eye), of 7, 16, or 20 mm. Hg (patient No. 28 left eye), of 7, 11, or 14 mm. Hg (patient No.

TABLE II

Comparative Tests with 1,000 cc. and 500 cc. Water in Identical Eyes

Number of eyes	Classification of eyes	Reactions			
		+		++	
		1,000 cc.	500 cc.	1,000 cc.	500 cc.
<i>Simple Glaucoma</i>					
14	unoperated ...	10	5	3	2
6	operated ...	5	3	4	1
<i>Congestive Glaucoma</i>					
13	unoperated ...	11	10	9	8
9	operated ...	4	3	1	1

The incidence of positive tests is slightly smaller after the ingestion of 500 cc. water than after 1,000 cc. No strongly positive tests were obtained in these eyes with 250 cc. tests. The ingestion of 50 cc. water never resulted in any alteration of the ocular tension.

73). Both eyes tend to react similarly. Thus the rise of 2 mm. Hg in the right eye of the first patient quoted above (No. 28), was coincident with the comparable low rise of 7 mm. Hg in the fellow eye. Anticipating results which will be discussed later it may be mentioned here that this variability is not caused by differences in diuresis, but either by different systemic reactions (quicker or slower restoration of the osmotic pressure of the serum) or by the interference from the spontaneous phases of the ocular tension (the nature of which is as yet little understood but is probably vasomotor) or by both. As has been pointed out, one must also take into account that in most cases only one 1000 cc. test was compared with several 500 cc. tests, among which the test which gave the highest rise of tension was taken for comparison.

Nevertheless, the rise of tension and the incidence of positive tests was clearly greater with 1000 cc. than with 500 cc. The influence on the result of the test of the amount of water drunk is further demonstrated by the fact that in no case did the test with 250 cc. give a rise of tension as high in the same eye as did the test with 1000 cc. No 250 cc. test was strongly positive.

As for the clinical application of the test, which will be discussed at the end of this paper, we may conclude that at least two tests are required before the result can be regarded as negative.

The Curve of the Ocular Tension.—The ocular tension begins to rise in typical positive cases 5 to 10 minutes after the start of the drinking and reaches a peak in 20 to 35 minutes (Figs 1 and 2). Usually it maintains its maximum value not longer than 10 minutes and subsequently begins to fall to the original level or, more frequently, below it. Atypical curves may show a primary fall of the tension (Fig. 3 (a)). It seems improbable that this is

FIG. 1.—R.E. chronic congestive glaucoma. L.E. subacute congestive glaucoma. Neither eye had been operated on. Typical curves.

FIG. 2.—Both eyes chronic congestive glaucoma, not operated on. Typical curves.

In all graphs the tension curve of the right eye is drawn in dots, and that of the left eye in circles. A break in the curves below the arrow signifies the ingestion of water.

a result of massage during the tonometry, as repeated tonometry on other occasions never produced a fall of tension of the same order in these eyes. It presumably occurred, in the present example, during a spontaneous rising phase which also makes a massage effect improbable (Thomassen, 1946). Fig. 3(a) also shows that the tension remained at its maximum longer than indicated above, and fell only after pilocarpine treatment. This was likewise observed in some other patients. The phenomenon is not

associated with any particular structure of the eye, as Fig. 3(b) shows, which is a perfectly typical curve of the same patient obtained on a different day. It is also not due to an abnormal systemic reaction, as is shown by the conductivity curve of the serum in Fig. 3(a), which will be discussed later, together with a further atypical feature—a second (late) rise of tension.

Normal eyes have either no rise of tension at all (Fig. 4), or a rise less than 6 mm. Hg at the same time as glaucomatous eyes have their peak (Fig. 6).

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FIG. 3.—Both eyes chronic congestive glaucoma, not operated on. Atypical tension curves in Fig. 3a (primary fall of tension; the maximum is held for more than 30 minutes). The conductivity curve in Fig. 3a below the tension curves is normal. On another day typical tension curves were obtained (Fig. 3b).

The Mechanism of the Water-Drinking Test

Diuresis.—There is general agreement that a normal individual discharges all the water ingested in a drinking test within four hours, and that most of the urine is produced within the second and third hour (Domarus, 1942). During the two days preceding the test the patient should eat dry food and have a limited quantity of fluid only. Unfortunately this restriction could not be kept by

FIG. 4.—R.E. normal, L.E. acute congestive glaucoma, trephined and cyclo-dialysis. No rise of tension in the normal eye. Fall below the original level after positive test in L.E. The tension of the normal eye falls simultaneously.

the out-patients concerned in this report, and in most cases it was not possible to keep them under observation for four hours. It seems, however, reasonable to regard a diuresis of more than nine-tenths of the ingested water within the first two hours, or of more than the total amount within three hours, as high. On the other hand a diuresis of less than six-tenths within the first two hours, or less than eight-tenths within three hours, is taken as insufficient in the following evaluation.

In the group of simple glaucoma, 29 water tests with control of the urine were done on eighteen patients. Five of the tests showed a delayed (insufficient) diuresis, fifteen a high, and only nine

were between the limits mentioned above.

In the group of congestive glaucoma, 38 water drinking tests with control of the urine were done on 22 patients. In seven of the tests the diuresis was delayed, in twenty it was high, and eleven cases were between these two groups. None of the patients suffered from diseases of kidney or heart.

Details regarding the cases which showed delayed diuresis are of interest, as it might be suggested that the retention of water in the body affects the ocular tension by favouring an oedema, regarded by Magitot (1929a, b) as the essence of glaucoma. From Table III it will be seen that there is no correlation between the rise of the tension and delayed diuresis. It occurred in twelve

tests (19 eyes) but only in five tests was a rise of more than 9 mm. Hg recorded, while in five other tests the rise was less than 6 mm. Hg. Furthermore, in three patients (Nos. 65, 64, and 60) showing a subnormal diuresis, the rise of the ocular tension was greater when a repeated test gave a medium or high diuresis.

In two subjects (Nos. 62 and 45) the reverse happened, and in one patient (No. 25) the rise of tension was the same whether the diuresis was high or delayed.

It will also be seen from these examples that the diuresis may differ from day to day in the same person. Five out of forty patients (Nos. 25, 45, 60, 64, and 85) in this survey had at one time a delayed diuresis and at another test a high diuresis, and two other patients alternated between high and medium diuresis. These observations indicate a great individual variation. One reason for this may be that these subjects were not prepared on the two days preceeding the test with a controlled diet as were the hospitalized patients. Nevertheless the individual variations of diuresis are greater than could be explained in this way, as there was no reason to suppose that the same patient varied his diet to a large extent.

The curve of the specific gravity of the urine, the other criterion of the systemic response to the drinking test, was normal in all but two cases; *i.e.*, it showed a concentrated urine before the test, a dilution up to a specific gravity of 1000 for the main volumes of the urine, and a gradual concentration towards the end of the test.

The diuresis following the ingestion of 500 cc. normal saline was much smaller than after 500 cc. water. This has also been described by Marx (1926c, 1928). In six cases the average within the first two hours was 125 cc. The seventh patient (No. 85) had the exceptionally high amount of 280 cc. urine in two hours, as compared with his very poor diuresis of 190 cc. in two hours after 1000 cc. water. His dilution curve was abnormal. None of the seven patients had a rise of tension with the 500 cc. normal saline test.

Summarizing briefly, in 65 out of 67 tests the dilution curve of the urine was normal, but the diuresis was delayed in twelve tests. The high incidence of insufficient diuresis and the great variability in many patients points to a systemic disturbance associated with glaucoma, though it must be admitted that insufficient controls in healthy subjects have been done. Quick diuresis was not taken as being abnormal, because it was found by other observers (Verney, 1929) in healthy subjects.

It must be emphasized, however, that delayed or high diuresis did not coincide with either a high or a low rise of the ocular

TABLE III

Subnormal Diuresis and Rise of the Ocular Tension

Patient's Number	Type of Glaucoma	Quantity of Water (cc.)	Rise of Tension (mm. Hg Schiötz)		Diuresis (cc.)	
			RE	RE	2 hrs.	3 hrs.
83	Simple unoperated	1,000	+ 9(43/52)	+16(52/68)	190	450
63	Simple unoperated	1,000	+ 6(19/25)	+ 6(19/25)	510	590
		500	0(28)	+ 6(28/34)	90	210
60	RE simple unoperated	1,000	+ 5(54/59)	+11(36/47)	510	810
	LE simple operated	500	+11(63/74)	+14(38/52)	540	640
25	LE simple unoperated	1,000		+ 5(28/33)	1,000	1,130
		1,000		+ 6(32/38)	320	860
77	LE congestive unoperated	1,000		+ 7(27/34)	530	—
5	RE congestive unoperated	1,000	+ 4(18/22)		480	—
101	RE congestive operated	1,000	+10(37/47)	+23(45/68)	490	—
	LE congestive unoperated					
62	Congestive operated	1,000	+ 4(34/38)	+ 2(36/38)	690	—
		500	+ 8(32/40)	+ 6(39/45)	280	—
64	Congestive operated	1,000	+ 2(23/25)	0(32)	240	360
		500	+ 4(21/25)	+ 4(23/27)	520	630
45	Congestive operated	1,000	+ 6(30/36)	+ 9(36/45)	510	560
		500	+ 4(30/34)	+ 3(40/43)	500	610
65	Congestive operated	1,000	+ 7(25/32)	+20(54/74)	300	390
		500	+ 9(23/32)	+27(47/74)	420	500

Eleven patients with subnormal diuresis (in italics).

The numbers in brackets give the ocular tension before the test and at its maximum. There is no correlation between the rise of the ocular tension and the rate of diuresis. For comparison, tests with medium or quick diuresis in the same patients are given in normal print.

tension. Apparently, therefore, the diuresis and the rise of the ocular tension must be considered independent and cannot be brought into causal connection.

The Conductivity of the Serum.—The blood serum in all the cases tested showed an increase of electrical resistance. In 21 cases enough, *i.e.*, from four to six, samples of blood were taken to construct a curve. Two typical examples are given in Figs 5 and 6.

FIG. 5.—Both eyes simple glaucoma, not operated on. The tension of the L.E. was over 80 mm. Hg. Tension curve and conductivity curve, in a general sense, run parallel.

FIG. 6.—R.E. simple glaucoma, trephined. L.E. normal. The tension in the R.E. which is filtering well, does not alter significantly. The normal L.E. shows a rise of tension within normal limits simultaneously with the increase of resistance in the blood serum; the subsequent fall is almost parallel in both curves.

They show that in a general sense the tension and resistance curves run parallel, and that the maximum of the resistance coincides with that of the ocular tension. In other curves (Fig. 7(b)) the former preceded the latter by a few minutes. The resistance curve had a similar shape in all cases, whether the ocular tension rose significantly (Fig. 5), slightly (Figs 6, 8(a), and 8(b)) or not at all (Fig. 7(a)). The maximum occurred at any time between 5 and 38 minutes after the start of the drinking. It appeared that the peak was earlier after the ingestion of 500 cc.

than after 1000 cc. water, and earlier after quick drinking than after slow drinking.

The rise of the resistance was not the same in different subjects, and even in the same subject (Figs 8(a) and (b)) when the test was repeated with the same amount of water. When the effects of a 1000 cc. test and a 500 cc. test in the same patient, were compared it was found that the rise of resistance was larger after the greater volume of water (Figs 7(a) and (b)). The ocular tension did not change at all in the 1000 cc. test, and was within the normal limits (R.E. + 3 mm. Hg, L.E. + 4 mm. Hg) in the 500 cc. tests. Figs 7(a) and (b) and Figs 8(a) and (b) show that the time of the maximum

FIG. 7.—R.E. normal, L.E. chronic congestive glaucoma, not operated on. Figs 7a and 7b both show negative tests. The increase of resistance of the serum is greater after the ingestion of 1,000 cc. water than after 500 cc. The peak of this curve occurs after 37 minutes in the first case and after 5 minutes in the second.

Although some patients showed a greater increase of resistance after 500 cc. water (the maximum increase being 7.7 ohms) than others had after 1000 cc. (the minimum increase being 3.5 ohms), the average rise after 500 cc. water was significantly lower than after 1000 cc. Twelve curves were obtained in the 500 cc. tests with an average rise in resistance of 3.45 ohms. Four 750 cc. tests gave an average of 3.6 ohms, and four 1000 cc. tests an average of 4.8 ohms.

An increase of electrical resistance means that there is a decrease in the number of ions present in a given volume of serum. It is

FIG 8.—Both eyes chronic congestive glaucoma, trephined. The tension curves in Figs 8a and 8b are both normal. The resistance curves are of different heights, though the quantity of ingested water was the same in both cases. The peak occurs after 30 minutes in Fig. 8a and after 39 minutes in Fig. 8b.

unlikely that a fraction of the ions of the normal serum suddenly disappears. The only explanation is that undissociated fluid has been added to the serum in these tests, namely, water absorbed from the intestines. The absorption is a physiological, not a purely physical, process, which will differ in rate and degree in each subject. Subsequent attempts of the body to re-establish osmotic equilibrium by a flow of water from the blood into the tissues will show even greater individual variations. In an eye where the outflow of aqueous is hampered this would lead to a rise of tension simultaneously with, or little later than, the osmotic changes in the blood. The close correlation between the resistance-curve of the serum and the tension curve of the eye confirms this reasoning, and we may conclude that *the osmotic*

changes of the blood cause the rise of the ocular tension in the water-drinking test.

When the initial tonicity of the serum is re-established the outflow of aqueous is augmented by osmotic forces, the aqueous humour now being relatively hypotonic, and indeed in most cases the ocular tension falls soon afterwards, frequently below the original level (Figs 1, 2, 3(b), 4, 7(a) and (b)). There are, however exceptions of two types.

FIG. 9.—Both eyes chronic congestive glaucoma, not operated on. After the primary rise, due to the ingestion of water, a late second rise occurs. Compare Fig. 10.

FIG. 10.—Both eyes chronic congestive glaucoma. R.E. trephined, L.E. not operated on. The resistance curve of the serum shows that the late second rise of the ocular tension is not due to osmotic effects.

(a) The ocular tension remains for more than 10 minutes at the high level attained at the end of the rise. Fig. 3(a) is an example of this; the cause of this irregularity cannot be anatomical, since in another test (Fig. 3(b)) a typical curve was given by the same eyes. The curve of the conductivity of the serum in

Fig. 3(a) shows that this cannot determine the anomalous reaction in this case. The only alternative explanation seems to be that variations of the ocular tension of a vasomotor nature interfered with the osmotic changes of tension. This influence will be discussed later.

(b) The ocular tension rises continuously until it is stopped by miotics (Fig. 9), or, after the primary rise at the usual time (20-35 minutes) it shows a late second rise which continues if untreated (Fig. 10). Fig. 9 shows that the left eye reacted to the drinking test with a relatively small rise within the first 40 minutes, remained at the new level for 10 minutes, and subsequently rose steadily from 25 to 80 mm. Hg. The right eye showed a primary typical rise, and a somewhat atypical fall, and then accompanied the left eye in its rise, until both eyes were given intensive pilocarpine treatment which reduced the tension to a normal level. No subjective symptoms were associated with these changes of tension. This puzzling incident was first attributed to the drinking test itself. Luckily, however, in a second case (Fig. 10) blood samples had been taken before the test and 15 and 30 minutes after drinking. When now, after a primary rise and a subsequent regular fall in the tension of the left (unoperated) eye, a new rise of tension was observed, further blood samples were taken. The conductivity-curve makes it evident that *the second rise is not of osmotic nature, since it happened simultaneously with the re-establishment of the original osmotic pressure of the blood.* Both patients suffered from congestive glaucoma. The patient of Fig. 10 was seen several times later with a spontaneous tension of 70 to 80 mm. Hg in the left eye, although she had taken miotics a few hours previously. Each time intensive pilocarpine treatment normalized her tension. She was returned to her surgeon.

Control Tests with Normal Saline or 50 cc. Water.—It has been shown above that the result of the drinking test depends on the volume of water ingested in, though the variability of physiological regulation may obscure the evidence in individual cases. This is contrary to the findings of Schmidt (1931) who claimed that he obtained exactly the same result with 50 or 20 cc. water as with 1000 cc.

Drinking tests with 50 cc. were done therefore on eight eyes, which had reacted in numerous 500 cc. tests with rises of 8 to 19 mm. Hg. None of these eyes showed the slightest rise of tension.

As a further confirmation of the osmotic basis for the water drinking tests, twelve eyes were tested by the ingestion of 500 cc. normal saline. They too had been selected according to their reactions to 500 cc. water, after which all of them had consistently shown a significant rise of tension. In no case was a rise observed. The small diuresis following this test in six out of seven patients has been described above.

Lack of Evidence for the Action of a Vasomotor Factor.—Thomassen and Leydhecker (1950) have shown that the lability test of Bloomfield and Kellermann (1947) presumably changes the blood volume in the eye and gives positive or negative results according to whether the ocular tension is in a rising or in a falling spontaneous phase. That the same holds good for the venous congestion test, will be shown in another paper.

The influence of spontaneous phases in the tension of the eye on

the result of the test cannot be directly assessed, as the measurement of the phase is made impossible by the changes of tension caused by the test itself. It is, however, possible to determine whether the tension is rising or falling before the beginning of the test and to indicate whether this has any influence on the result.

Fifteen eyes were tested when the tension had fallen 3 to 14 mm. Hg, and seven eyes after the tension had increased 4 to 8 mm. Hg in the preceding 30 minutes. The spontaneous alterations of tension seem to have no decisive influence on the test, but the curves of the drinking test were perhaps modified by them. An example is given in Figs 11(a) to (c), representing curves from the same patient. The 1000 cc. test (Fig. 11(a)) was strongly positive, although it was started after a fall of 5 mm. Hg in the right eye, and of 14 mm. Hg in the left eye, during the 30 minutes preceding the test. The first 500 cc. test (Fig. 11(b)) was started after a fall of tension of both eyes and gave a small rise only, whilst greater rises were obtained when the tension had been constant previously (Fig. 11(c)).

FIG. 11.—Both eyes chronic glaucoma, trephined. See text.

It must be emphasized, however, that this influence of variations of tension on the drinking test is proved to be unimportant by Fig. 11(a), and that there is no evidence that the differences between Figs 11(b) and 11(c) were caused in the way suggested. Similar variations of the rise of tension occurred without any preceding changes of tension in the same eye after the ingestion of the same volume of water.

Irregular curves, as in Fig. 12, cannot be explained by osmotic changes and interference by vascular causes must be postulated.

FIG. 12.—Both eyes simple chronic glaucoma. R.E. not operated on, L.E., iridencleisis. The irregular curve of the R.E. is probably due to vasomotor influences.

negative in a decreasing phase, it was found that this test was as frequently negative as positive in any phase of the drinking test. Since the venous-congestion test works by an alteration of the blood volume of the eye, and since it may be supposed that the spontaneous phases are also caused by vasomotor changes, it can be concluded that *the phases brought about by the drinking test have little if anything to do with vasomotor alterations of the intra-ocular vessels and that hence they are fundamentally different from spontaneous phases.*

Discussion

It was found that the water-drinking test gives approximately the same results in non-operated eyes suffering from chronic simple glaucoma (positive in 77 per cent.) as in congestive glaucoma (positive in 74 per cent.). The width of the chamber angle is also without significance to the results. Repeated tests with the same quantity of water gave different results in the same patient, but variations in the amount of ingested water (50, 250, 500, and 1000 cc.) resulted in rises of ocular tension differing so considerably that there can be no doubt of the importance of this factor.

The resistance of the serum increased simultaneously with, or shortly before, the ocular tension in positive tests, and its increase depended upon the amount of water ingested. The shape and size of the conductivity-curves were about the same whether the ocular tension increased or not. In spite of the frequency of delayed or rapid diuresis no correlation was found between this and the reaction of the ocular tension. Neither was evidence

* Increase of ocular tension of more than 7 mm. Hg after one minute.

obtained that spontaneous, presumably vasomotor, phases are of any importance in determining the rise of tension. They influence the tension-curve only after the maximum is reached.

From these facts it can be concluded that the rise of tension in the drinking test is caused by changes in the osmotic pressure of the blood. Since these changes are the same in both positive and negative tests, normally and negatively reacting glaucomatous eyes must differ from positively reacting eyes either because the inflow of water is not increased when the blood serum becomes relatively hypotonic, or because an increased volume of aqueous can flow out more easily. The former mechanism is improbable according to the results of Kinsey, Grant, and Cogan (1942). Even if the decisive factor determining positive or negative tests is localized in the eye itself, this does not mean, that systemic reactions are unimportant in influencing the result. The degree and rate of the development of hypotonicity in the blood varies considerably in different people, and at different times in the same person. These differences are presumably caused by a varying rate of absorption and of the subsequent exchange of fluids between blood and tissue, which again depends on the amount of liquid taken by the patient on the days before the test, and on his individual regulation of the water exchange. Whether this regulation is hormonal or an autonomous function of the capillary endothelium is a question that must be answered by general physiology.

The mechanism of the water-drinking test as described above, throws new light on de Decker's experiments (1929b). In most cases of retinal detachment subretinal fluid is formed, which will become isotonic with the aqueous humour. When the blood is made relatively hypotonic, the volume of the subretinal fluid will increase, and subsequently the ocular tension rises.

The combination of the water-drinking test with a test altering the hydrostatic blood pressure and/or the amount of blood in the eye, as suggested by Sugar, offers no advantages. Thereby, two fundamentally different provocative tests are mixed, and one can not be sure which factor determines the result. Further research on provocative tests should, on the contrary, attempt to elucidate the mechanism of each test separately with the eventual aim of determining which function of the eye is defective in an individual case. On such a basis it would then be possible to combine tests for the same function or structure. With this knowledge negative tests would also be useful to indicate whether the tested function or structure is normal in a particular case, whereas, with our present knowledge they indicate nothing. It is probable that the

results of such investigations would contribute considerably to our understanding of the causes of primary glaucoma.

Clinical Application

The test gives approximately the same incidence of positive results in all types of primary glaucoma (69-77 per cent. with the 1000 cc. test). It should be applied clinically as follows:

Any treatment with miotics is stopped at least 24 hours before, exceptions being made only in severe cases, who have a rise of tension shortly after miotics are stopped. The tension is taken 30 minutes before and immediately before the test, in order to exclude as far as possible the risk of spontaneous rise of tension being mistaken for a positive result. The patient then drinks 1,000 cc. water in 5 minutes. This should not present any difficulty to the patient. The tension is taken at exactly 15, 25, 35, and 50 minutes after the start of drinking. If this test is negative (rise of less than 6 mm. Hg), a second test with 1,000 cc. is done on another day. If this is again negative, it will not be necessary to repeat this test within 6 months. The tests should be done with 500 cc. water only with patients who find it impossible to drink 1,000 cc. in a few minutes. The incidence of positive results will be smaller with this method.

A final word for the immediate benefit of all glaucomatous patients. The ophthalmologist who is consulted in a case of glaucoma should warn his patient (very sternly) not to drink tea in bed before breakfast as many people do in this country. Two large cups of tea contain approximately 500 cc. liquid. Some of the patients of this paper reacted to this with rises up to 80 mm. Hg Schiötz.

Summary

(1) 168 drinking tests with 250 to 1000 cc. water were done on 74 eyes, 55 of which had not been operated on. A rise of 6 mm. Hg Schiötz and more, or from less than 30 mm. Hg Schiötz to a value above this figure, was regarded as a positive test. A rise of more than 9 mm. Hg Schiötz, or from a tension below 30 mm. Hg Schiötz to more than 32 mm. Hg Schiötz, was taken as a strongly positive test.

It has been shown for the first time that in unoperated eyes the incidence of positive tests is about the same in chronic simple glaucoma (77 per cent.) as in congestive glaucoma (74 per cent.). The width of the chamber angle is unimportant, positive tests occurring in unoperated eyes with a wide angle in 70 per cent., and in unoperated eyes with a narrow angle in 69 per cent.

The incidence of strongly positive tests in the same unoperated eyes was 36 per cent. in simple glaucoma, 61 per cent. in congestive glaucoma, 35 per cent. in wide angle glaucoma, 50 per cent. in narrow angle glaucoma (Table I). The typical

glaucomatous tension curve is monophasic with the peak between 20 and 35 minutes after the patient begins to drink. There is frequently a subsequent fall below the original level.

(2) When the result of tests with 500 cc. and with 1,000 cc. on the same eyes are compared, positive tests are found to be more frequent with 1,000 cc. than with 500 cc.

In unoperated eyes compared in this way, there were positive results with 1,000 cc. in 79 per cent., with 500 cc. in 55 per cent., and strongly positive results with 1,000 cc. in 44 per cent., with 500 cc. in 37 per cent. (Table II).

(3) No strongly positive results were obtained with 250 cc. The rise of tension was in all cases significantly lower than with 500 or 1,000 cc.

(4) Although the rise of tension clearly depends on the amount of water ingested, higher rises occurred in eleven eyes with 500 cc. than with 1,000 cc. [Only one 1,000 cc.-test, but numerous 500 cc.-tests were done on each of these eyes, and the 500 cc.-test which gave the highest rise of tension was taken for comparison.]

(5) There were great variations in repeated tests in the same eyes with the same volume of water. It has been shown that the different reactions of the ocular tension in the same eye is explained at least partially by variations of the physiological reactions following the ingestion of water, *i.e.*, the absorption and subsequent exchange of fluids between blood and tissue.

(6) The conductivity of the blood serum was measured during the drinking tests in 21 patients. It was found that the serum becomes hypotonic after the ingestion of water. The maximum hypotonicity occurred at the same time, or slightly before, the maximum ocular tension. Because of the exact correspondence of the conductivity-curve of the serum and the tension-curve of the eye, and the lack of evidence for any other important factor, it is concluded that *osmotic changes of the blood serum after absorption of water from the intestines cause the subsequent rise of the ocular tension.*

(7) Since the conductivity-curves had a similar shape and height whether the ocular tension showed a rise or not, it is concluded that *the result of the test depends mainly on events in the eye itself.* In positive tests the *outflow of aqueous must be hampered.*

(8) The urine was collected in 67 drinking tests. A diuresis of more than nine-tenths of the ingested water within the first two hours, or of more than the total amount within three hours, was regarded as high. A diuresis of less than six-tenths within the first two hours, or of less than eight-tenths within three hours was regarded as subnormal. According to these criteria the

diuresis was delayed in twelve, medium in twenty and high in 35 tests. Seven out of forty patients showed gross variations in the diuresis on different days. As there is no reason to suppose that the patients changed their diet to a large extent, a high incidence of systemic anomalies must be concluded, if one accepts the standard proposed. There was, however, *no noticeable coincidence of any particular type of diuresis with a high or low rise of the ocular tension*. It must also be remembered that the bulk of the diuresis takes place in the second and third hours, whereas the ocular tension reaches its peak in the first 30 minutes.

In two out of 67 tests the dilution of the urine was abnormal in not forming the typical monophasic curve. No patient suffered from diseases of heart or kidney.

(9) There was *no evidence that vasomotor changes affected the result of the test*. Spontaneous variations of the intra-ocular pressure before the test were unimportant. The venous-congestion-test was just as frequently negative as it was positive in the rising phase of the water-drinking test. This shows that *this rising phase is of a different nature from spontaneous phasic alterations in tension*, the first being due to osmotic differences between serum and aqueous, and second presumably of a vasomotor nature.

(10) Control tests, with 500 cc. normal saline or 50 cc. water, on eyes which had always produced a significant rise of tension in numerous previous tests, resulted in no case in a rise of the ocular tension.

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