MODIFICATION OF OUTFLOW FACILITY*

By variations in aqueous formation and ocular tension

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Experimental and clinical studies have demonstrated that the lowering of ocular tension by acetazoleamide (Diamox, Lederle) results from an impairment of aqueous formation which, with high dosage, attains about 50 percent.[4-7, 9, 14, 15, 20, 21] Our tonographic investigations in both normal and glaucomatous patients, before and after administration of Diamox, have confirmed this conclusion. The present study shows variations in outflow facility which apparently have not been previously noted.

I. Investigation of glaucomatous patients

A. Methods

Each tonographic test was of four minutes' extent. From calculations made from the tables of Friedenwald[1] the results were expressed in resistance to aqueous flow (R) and its inverse, the facility of outflow (C).

(Both R and C are given in discussing the results of tonography since European authors favor the former expression and American authors the latter. In an individual case, $R = 1/C$, but the arithmetical averages of R are not exactly the inverse of the arithmetical averages of C.

In this investigation the eyes studied included 38 with open-angle glaucoma and 15 with secondary glaucoma. Angle-closure glaucoma was rigorously excluded since such cases often exhibit rapid spontaneous variations in ocular tension and facility of outflow. Tonographic tests were made before and after administration of Diamox. A tablet of Diamox (250 mg.) was given at six, four and two hours before tonography. After an interval of one or more days each case was similarly retested and the average of the two tests was used for the record.

B. Results

The data of patients with open-angle glaucoma are individually listed in Table 1. The reduction of aqueous production (F) by Diamox was confirmed. In the high dosage used, the formation of aqueous was reduced by an average of 46.9 percent. The table reveals a slightly decreased resistance to flow (−4.68 percent) and a definitely increased facility of outflow (+13.29 percent).

The data of patients with secondary glaucoma are similarly listed in Table 2. Aqueous production was reduced 50.72 percent; the resistance to flow diminished (−9.21 percent), and the facility of outflow increased (+27.26 percent).

In Table 3 the cases of open-angle glaucoma in which the pretreatment tension was high (26 to 52 mm. Hg) are compared to those in which the pretreatment tension was relatively low (18 to 26 mm. Hg). In Group I, Diamox reduced production of aqueous 49.54 percent; resistance to flow decreased 14.21 percent; facility of outflow increased 23.20 percent. These changes are statistically significant. In the latter group the production of aqueous was reduced 44.38 percent, but the changes in resistance to and facility of outflow were negligible. The same deductions hold whether the calculations are according to the 1954 or the 1955 tables of Friedenwald (table 4).

In Table 5 a like comparison is made with cases of secondary glaucoma. In Group 1 the original tensions were 44 to 63 mm. Hg. In this group Diamox reduced the production of aqueous 43.63 percent; the resistance

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TABLE 1

EFFECT OF DIAMOX (250 MG., ×3) ON INTRAOCULAR PRESSURE (Po), PRESSURE OF FLOW (Pa), RESISTANCE TO FLOW (R), FACILITY OF OUTFLOW (C) AND AQUEOUS PRODUCTION (F) IN 38 CASES OF OPEN-ANGLE GLAUCOMA. THE INDICIAL NUMBERS INDICATE VALUES BEFORE ADMINISTRATION OF DIAMOX (N_1) AND DURING ITS ACTION (N_2). THE FORMULA, $\Delta\%\ Pa = \frac{Po_1 - Po_2}{Po_1 - 10} \times 100$, ASSUMED 10 MM. HG AS THE VALUE OF THE EPISCLERAL VENOUS PRESSURE (Pv)

Eye	Po_1	Po_2	% ΔPa	R_1	R_2	% ΔR_1	C_1	C_2	% ΔC	% ΔF
1	51.88	30.04	−51.68	10.33	8.57	−17.03	0.096	0.117	+21.87	−41.89
2	41.60	16.26	−80.18	10.24	6.53	−36.23	0.098	0.153	+56.12	−69.15
3	41.11	28.41	−40.82	13.10	7.98	−39.08	0.076	0.125	+64.47	− 2.95
4	36.21	18.42	−67.27	8.43	6.07	−28.00	0.119	0.165	+38.65	−55.62
5	35.65	25.43	−39.84	13.74	8.40	−38.86	0.073	0.119	+63.01	− 1.60
6	31.76	15.91	−72.84	9.75	6.18	−36.61	0.103	0.162	+57.28	−57.39
7	30.08	16.42	−68.04	4.80	6.65	+38.54	0.208	0.150	−27.88	−77.03
8	29.88	18.05	−59.51	9.19	10.71	−16.54	0.109	0.093	+14.67	−65.27
9	29.49	16.66	−65.82	7.15	7.89	+13.50	0.140	0.127	− 9.28	−69.10
10	28.66	14.31	−76.90	6.59	4.30	−34.74	0.152	0.233	+53.28	−64.66
11	28.56	16.29	−66.11	16.50	13.62	−17.45	0.061	0.076	+24.59	−58.92
12	28.10	15.62	−68.95	14.17	13.20	− 6.84	0.070	0.073	+ 4.28	−66.92
13	28.03	20.01	−44.48	5.07	4.81	− 5.13	0.197	0.208	+ 5.58	−41.41
14	27.83	15.33	−70.10	9.84	6.20	−36.99	0.102	0.161	+57.84	−52.49
15	27.68	20.96	−38.01	5.51	5.43	− 1.43	0.181	0.184	+ 1.65	−37.39
16	26.92	17.67	−54.67	5.69	6.97	+22.50	0.176	0.143	−18.75	−62.83
17	26.60	22.69	−23.55	3.83	3.36	−12.27	0.261	0.298	+14.17	−19.86
18	26.35	16.60	−59.63	8.40	7.26	−13.57	0.119	0.138	+15.96	−53.09
19	26.26	18.80	−45.87	3.90	3.75	− 3.84	0.256	0.267	+ 3.51	−43.75
20	25.43	20.15	−34.22	5.34	5.36	+ 0.37	0.187	0.187	0	−34.37
21	24.76	16.34	−57.04	4.37	4.16	− 4.80	0.229	0.240	+ 4.80	−54.89
22	24.60	13.82	−73.83	5.79	7.22	+24.69	0.173	0.139	−19.65	−78.96
23	24.16	13.48	−75.42	5.10	7.63	+49.60	0.196	0.131	−33.16	−81.22
24	23.60	16.60	−51.47	10.83	10.91	+ 0.74	0.092	0.092	0	−52.00
25	23.52	14.64	−65.83	9.43	7.83	−16.97	0.106	0.128	+20.75	−59.03
26	23.55	17.67	−43.39	7.56	5.14	−32.01	0.132	0.195	+47.72	−16.76
27	23.30	19.23	−30.60	4.44	4.31	− 2.93	0.225	0.232	+ 3.11	−28.66
28	23.12	18.42	−35.82	7.38	6.25	−15.31	0.136	0.160	+17.64	−24.72
29	22.36	16.60	−46.11	3.55	3.40	− 3.94	0.282	0.294	+ 4.25	−43.96
30	22.25	14.96	−59.51	3.70	6.64	+79.45	0.270	0.151	−44.07	−77.34
31	22.21	20.01	−18.02	6.34	9.06	+42.90	0.158	0.110	−30.37	−42.71
32	22.20	18.05	−34.02	7.15	5.75	−19.58	0.140	0.174	+24.28	−18.13
33	22.17	17.30	−40.01	6.67	4.82	−27.73	0.150	0.207	+38.00	−17.03
34	21.29	14.34	−61.55	14.22	8.31	−41.56	0.070	0.120	+71.42	−34.18
35	20.96	18.42	−23.17	7.29	8.92	+22.36	0.137	0.112	−18.24	−37.33
36	20.42	17.30	−29.94	5.95	5.11	−14.12	0.168	0.196	+16.66	−18.28
37	19.30	16.60	−29.03	6.56	7.66	+16.76	0.152	0.131	−13.81	−39.01
38	18.90	11.85	−79.21	4.55	6.11	+34.28	0.220	0.164	−25.45	−84.61
Mean:	27.11	17.57	*−52.18*	7.70	6.91	*− 4.68* (±4.4)	0.153	0.162	*+13.29* (±4.74)	*−46.96* (±3.45)

TABLE 2

EFFECT OF DIAMOX (250 MG., ×3) ON INTRAOCULAR PRESSURE (Po), PRESSURE OF FLOW (Pa) RESISTANCE TO FLOW (R), FACILITY OF OUTFLOW (C) AND AQUEOUS PRODUCTION (F) IN 15 CASES OF SECONDARY GLAUCOMA

Eye	Diagnosis	Po_1	Po_2	% ΔPa	R_1	R_2	% ΔR_1	C_1	C_2	% ΔC	% ΔF
1	Glaucoma capsulare	62.38	39.00	−44.63	19.54	14.95	−23.49	0.051	0.067	+ 31.37	−27.61
2	Thrombosis central vein	59.37	48.17	−22.68	13.53	19.03	+40.65	0.074	0.052	− 29.73	−45.20
3	Glaucoma posttraumatic	53.35	20.01	−76.91	11.77	6.04	−48.68	0.085	0.166	+ 95.29	−27.90
4	Glaucoma after lens extraction	52.22	24.90	−64.70	10.16	12.47	+22.73	0.098	0.080	− 18.37	−71.32
5	Thrombosis central vein	49.94	28.17	−69.53	19.00	8.40	−55.78	0.053	0.119	+124.53	−31.42
6	Glaucoma capsulare	48.17	22.11	−52.55	23.00	15.44	−32.87	0.043	0.065	+ 51.16	−29.52
7	Glaucoma postinfammatory	45.76	32.43	−37.27	7.98	5.36	−32.83	0.125	0.187	+ 49.60	−90.84
8	Glaucoma posttraumatic	44.69	30.94	−39.63	8.85	7.14	−19.32	0.113	0.140	+ 23.89	−25.25
9	Glaucoma postinflammatory	37.78	22.65	−54.46	13.32	8.27	−37.31	0.075	0.121	+ 61.33	−26.92
10	Glaucoma postinflammatory	32.20	15.97	−73.10	12.40	13.40	+ 8.06	0.081	0.075	− 7.40	−75.55
11	Glaucoma after lens extraction	31.80	18.05	−63.07	8.74	14.21	+62.58	0.114	0.070	− 38.59	−77.51
12	Glaucoma after lens extraction	28.49	19.84	−46.78	7.05	6.19	−12.19	0.142	0.162	+ 14.08	−39.69
13	Glaucoma postinflammatory	26.21	14.76	−70.63	10.06	8.20	−18.48	0.099	0.122	+ 23.23	−63.97
14	Glaucoma after lens extraction	23.85	13.50	−74.73	15.19	13.50	−11.12	0.066	0.074	+ 12.12	−71.43
15	Glaucoma after lens extraction	22.69	16.60	−47.99	7.14	8.56	+19.89	0.140	0.117	− 16.43	−56.74
Average:		41.26	24.47	*−55.91*	12.51	10.74	*− 9.21* (±8.66)	0.091	0.108	*+ 27.26* (±10.88)	*−50.72* (±5.48)

TABLE 3

EFFECT OF DIAMOX ON PRESSURE OF FLOW (Pa), RESISTANCE TO FLOW (R) FACILITY OF OUTFLOW (C) AND AQUEOUS PRODUCTION (F) IN 38 CASES OF OPEN-ANGLE GLAUCOMA, DIVIDED INTO TWO GROUPS ACCORDING TO THE INITIAL INTRAOCULAR PRESSURE (Po_1)

	Number of Cases	Po_1 Mean (mm. Hg)	% ΔPa	% ΔR	% ΔC	% ΔF
Group 1 from 26 to 52 mm. Hg	19	31.70	*−57.76*	*−14.21* (±4.76)	*+23.20* (±6.46)	*−49.54*
Group 2 from 18 to 26 mm. Hg	19	22.53	*−46.74*	*+4.85* (±6.76)	*+3.36* (±6.59)	*−44.38*

TABLE 4

COMPARISON OF THE EFFECT OF DIAMOX ON PRESSURE OF FLOW (Pa), RESISTANCE TO FLOW (R) AND AQUEOUS PRODUCTION (F) IN GROUP 1 OF TABLE 3 CALCULATED ACCORDING TO THE TONOGRAPHIC TABLES OF 1954 AND OF 1955 RESPECTIVELY

	Po_1	Po_2	% ΔPa	% ΔR	% ΔF
Table 1954	31.70	19.15	*−57.62*	*−14.21*	*−49.54*
Table 1955	30.70	19.04	*−55.63*	*−12.45*	*−45.70*

to flow decreased 18.69 percent and the facility of outflow increased 40.97 percent. In Group 2 the tensions were 22 to 38 mm. Hg. Diamox reduced aqueous production 58.83 percent but the changes in resistance to and facility of outflow were negligible.

In Table 6 the cases in Tables 3 and 5 are combined. In combined Group 1 the original tensions were 27 to 63 mm. Hg. Diamox reduced aqueous production 46.21 percent; the resistance to flow decreased 13.28 percent and the facility of outflow increased 29.01 percent. In combined Group 2 the original tensions were 18 to 27 mm. Hg. Diamox reduced aqueous production 46.72 percent, but the changes in resistance to and facility of outflow were inappreciable.

C. COMMENT

Tables 3 and 6 demonstrate that the reductions of aqueous production and ocular tension effected by Diamox are accompanied by a lessened resistance to flow and an increased facility of outflow, when the initial tension is high (group 1); but this does not occur when the initial tension is low (group 2). This difference would be missed unless the cases of high and low ocular tension were considered separately (tables 1 and 2). These tables show variations in facility of

TABLE 5

EFFECT OF DIAMOX ON PRESSURE OF FLOW (Pa), RESISTANCE TO FLOW (R), FACILITY OF OUTFLOW (C) AND AQUEOUS PRODUCTION (F) IN 15 CASES OF SECONDARY GLAUCOMA, DIVIDED INTO TWO GROUPS ACCORDING TO THE INITIAL INTRAOCULAR PRESSURE (Po_1)

	Number of Cases	Po_1 Mean (mm. Hg)	% ΔPa	% ΔR	% ΔC	% ΔF
Group 1 from 44 to 63 mm. Hg	8	51.98	−50.98	−18.69 (±12.01)	+40.97 (±19.60)	−43.63
Group 2 from 22 to 38 mm. Hg	7	29.00	−61.53	+ 1.63 (±12.30)	+11.60 (±12.18)	−58.83

TABLE 6

EFFECT OF DIAMOX ON PRESSURE OF FLOW (Pa), RESISTANCE TO FLOW (R), FACILITY OF OUTFLOW (C) AND AQUEOUS PRODUCTION (F) IN THE TOTAL CASES OF OPEN-ANGLE AND SECONDARY GLAUCOMA, DIVIDED INTO TWO GROUPS ACCORDING TO THE INITIAL INTRAOCULAR PRESSURE (Po_1)

	Number of Cases	Po_1 Mean (mm. Hg)	% ΔPa	% ΔR	% ΔC	% ΔF
Group 1 from 27 to 63 mm. Hg	27	38.60	−57.64	−13.28 (±5.47)	+29.01 (±7.64)	−46.21
Group 2 from 18 to 27 mm. Hg	26	23.35	−48.66	+2.90 (±5.34)	+3.76 (±5.07)	−46.72

outflow (C), but not in resistance to flow (R). The increased facility of outflow in Group 1 produced no change in the depth of the anterior chamber detectable by slit-lamp observation.

The lessened resistance to flow noted in Group 1 cannot be due to errors in the 1954 tonographic tables since the findings are confirmed with the 1955 figures[12] (table 4). That the reduction in aqueous formation induced by Diamox is of the same magnitude in both Groups 1 and 2 is further evidence of the validity of the calculations.

The variations in the facility of outflow can be explained by assuming that an impairment of excretion is effected by high intraocular pressure which is relieved as the intraocular pressure falls. The conditions of flow are not identical before and after the canal of Schlemm. The flow of aqueous after the canal is through more or less anastomosing conduits having a general radial direction. But before the canal the narrow trabecular spaces anastomose irregularly and offer a considerable resistance to the flow of aqueous which is likely to be enhanced by the squashing due to high intraocular pressure. Perfusion experiments were designed to test this hypothesis.

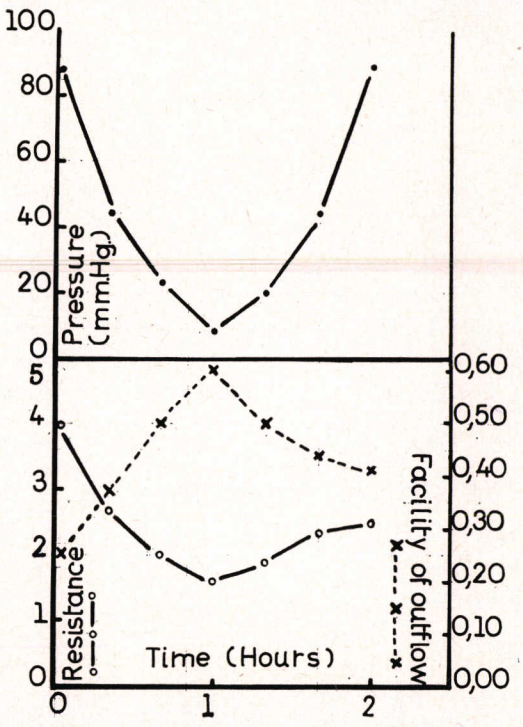
II. EXPERIMENTS ON THE ENUCLEATED EYES OF ANIMALS

A. METHODS

Freshly enucleated pigs' eyes were used for perfusion tests. The perfusion liquid had the following composition: NaCl, 0.7 percent (nine parts); buffered to pH 7.0 with M/15 K H_2PO_4 (four parts) and M/15 Na H_2PO_4 (six parts). The solution was introduced into the anterior chamber by a needle perforating the cornea and a manometer checked the induced intraocular pressure.

B. RESULTS

The facility of outflow diminished as the pressure of the perfusion liquid rose; and vice versa (graph 1). These effects did not



Graph 1 (Weekers, et al.). Variation of facility of outflow and of resistance as a function of the pressure of the perfusion liquid in the enucleated pig eye.

result from changes in the depth of the anterior chamber which, to biomicroscopic observation, were minimal and inconstant.

C. Comment

These experiments in enucleated pigs' eyes demonstrated that the facility of outflow is influenced by the pressure of the perfusion liquid. Marked ocular hypertension diminished the facility of outflow, that is, increased the resistance. Previous perfussion experiments on the eyes of cattle and horses produced the same result (graph 2).[26]

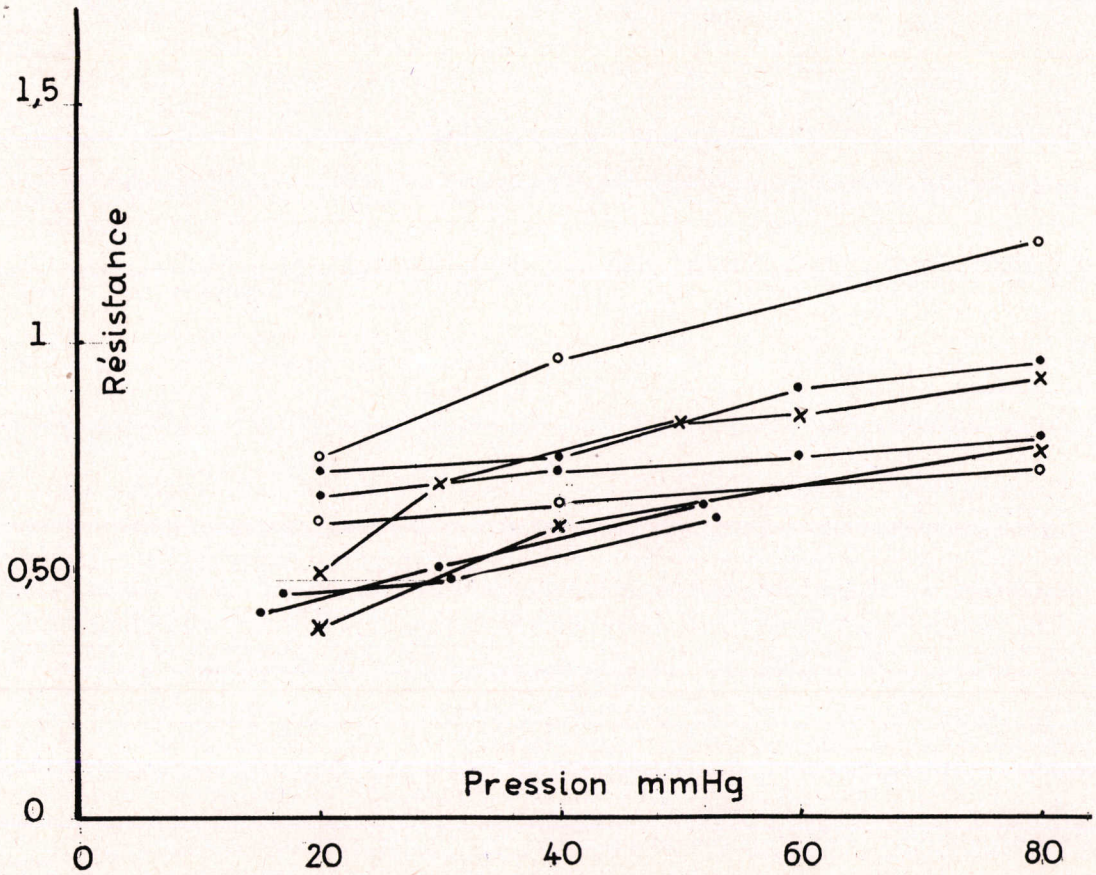
III. Experiments on normal human subjects

A. Methods

Tonographic tests were made on 24 normal eyes in patients ranging from 36 to 76 years of age, before and after administration of Diamox, 250 mg., six times during the preceding 24 hours. Those in which the ocular tension fell below 12 mm. Hg under the influence of Diamox were discarded, as the assumption made in the usual calculations of an episcleral venous pressure of 10 mm. Hg should have been controlled in a measure. This left 18 cases suitable for study.

B. Results

The effects of Diamox on aqueous production, resistance to flow, and facility of outflow (table 7) confirm again that the reduction in ocular tension induced by Diamox results primarily from suppression of



Graph 2 (Weekers, et al.). Variation of resistance to flow with the pressure of the perfusion fluid.
x —— x Eyes of horse. Perfusion with Ringer's solution.
o —— o Eyes of cattle. Perfusion with Ringer's solution.
• —— • Eyes of cattle. Perfusion with aqueous humor.

TABLE 7

EFFECT OF DIAMOX ON INTRAOCULAR PRESSURE (Po), PRESSURE OF FLOW (Pa), RESISTANCE TO FLOW (R) FACILITY OF OUTFLOW (C) AND AQUEOUS PRODUCTION (F) IN 18 NORMAL EYES

Eye	Po_1	Po_2	Δ% Pa	R_1	R_2	Δ% R	C_1	C_2	Δ% C	Δ% F
1	17.30	14.00	−45	2.90	2.90	0	0.344	0.344	0	−45
2	14.00	12.36	−41	5.11	5.21	+ 2	0.196	0.192	− 2	−42
3	18.00	13.50	−56	3.90	3.94	+ 1	0.256	0.254	− 1	−57
4	19.50	13.45	−64	4.16	4.00	− 4	0.240	0.250	+ 4	−62
5	15.91	15.00	−15	4.12	3.56	− 14	0.243	0.281	+16	− 2
6	19.60	18.00	−17	5.12	6.72	+ 31	0.195	0.149	−24	−36
7	18.80	18.00	−10	4.69	4.78	+ 2	0.213	0.209	− 2	−11
8	17.30	13.00	−59	4.38	5.70	+ 30	0.228	0.175	−23	−68
9	20.42	18.80	−16	5.03	5.85	+ 16	0.199	0.171	−14	−27
10	17.30	15.91	−19	6.02	4.51	− 25	0.166	0.222	+34	+9
11	15.91	12.36	−60	5.51	6.45	+ 17	0.181	0.155	−14	−66
12	22.17	19.61	−21	3.53	4.90	+ 38	0.283	0.204	−28	−43
13	21.30	16.61	−42	3.31	3.73	+ 12	0.302	0.268	−11	−48
14	18.80	12.36	−73	3.86	3.99	+ 3	0.259	0.251	− 3	−74
15	22.17	16.61	−46	2.95	4.44	+ 50	0.338	0.225	−34	−64
16	14.64	12.36	−49	6.20	7.26	+ 17	0.161	0.138	−14	−56
17	20.42	12.91	−72	2.30	5.17	+124	0.434	0.193	−56	−87
18	16.61	12.36	−64	4.74	5.21	+ 11	0.211	0.192	− 9	−68
Mean:	18.28	14.84	−43	4.32	4.90	*+17.21* (±7.5)	0.247	0.215	*−10* (±4.64)	*−47* (±6.1)

aqueous formation. This amounts to 47 percent, a figure identical to that obtained in glaucomatous subjects. In the normal individual the decreased tension is accompanied by an increased resistance to flow (+17.21 percent) and a reduced facility of outflow (−10.0 percent). The findings with the tonometric tables of 1955 are essentially similar (table 8).

C. COMMENT

The reduced facility of outflow that accompanies induced ocular hypotension results apparently from a modification of the outflow channels. Observations suggest that the phenomenon of homeostasis affects the physiologic regulation of ocular tension:[11]

1. The ligation of the common carotid in the rabbit effects primarily a lessening of aqueous production and a lowering of ocular tension. But the tension returns to normal before the local arterial pressure can be restored. From this observation Bárány[2] concluded that the fall in tension became compensated by an increased resistance to flow and confirmed this view by finding that, six days after the intervention, the resistance to flow as measured by perfusion of the enucleated eyes was higher in the eye on the operated side than in its fellow.[3]

2. Tonographic studies by Kornblueth and Linnér[19] in rabbit eyes demonstrated that the reduced tension due to aqueous suppression was partially compensated by increased resistance to aqueous flow.

3. Friedenwald and Linnér[12] showed by appearance time of fluorescein in the pupillary area that para-amino-hippuric acid

TABLE 8

COMPARISON OF THE EFFECT OF DIAMOX ON PRESSURE OF FLOW (Pa), RESISTANCE TO FLOW (R) AND AQUEOUS PRODUCTION (F) IN 18 NORMAL EYES CALCULATED ACCORDING TO THE TONOGRAPHIC TABLES OF 1954 AND OF 1955 RESPECTIVELY

	Po_1	Po_2	Δ% Pa	Δ% R	Δ% F
Table 1954	18.28	14.84	−43	+17.2	−47
Table 1955	18.40	14.76	−44	+21.4	−50

lessened the secretion of aqueous without, however, appreciably lowering ocular tension. This was explained by an accompanying increased resistance to aqueous flow.

4. Becker and Constant[8] in tonographic studies on rabbits demonstrated that the ocular hypotension resulting from impairment of aqueous production by Diamox was partially masked by increased resistance to aqueous flow. Confirming evidence was secured by the measurements of bicarbonate and ascorbic acid in the anterior and posterior chambers.

5. In the normal human the drop in ocular tension that follows a single dose of Diamox does not last as long as the period of lessened aqueous production. The more rapid restoration of normal ocular tension is partially due to a compensatory increase of resistance (Becker[6]).

6. In tonographic studies of normal eyes deRoetth[10] showed that an increased osmotic pressure of the blood effected a reduced production of aqueous and an increased resistance to flow. Conversely, a decrease in the osmotic pressure of the blood caused an increased production of aqueous and a lessened resistance to flow. These changes in resistance were not noted in glaucomatous eyes.

All these observations indicate that the ocular hypertension caused by decreased production of aqueous provokes a compensatory increase of resistance to flow. This occurs with Diamox, ligature of the common carotid, and injection of substances which lessen aqueous secretion. Our observations on normal eyes are analogous (tables 7 and 8).

IV. Clinical considerations

This study confirms the suppression of aqueous flow by Diamox and reveals the interaction between the level of intraocular pressure and resistance to flow. The clinical importance of these points justifies further comment:

1. *The suppression of aqueous production by Diamox.* Under the influence of Diamox the production of aqueous falls from 2.15 to 1.04 cu. mm. per minute in normal subjects; from 2.46 to 1.27 cu. mm. per minute in open-angle glaucoma; and from 2.64 to 1.49 cu. mm. per minute in secondary glaucoma—a reduction of approximately one half. Diamox, even in strong doses, never suppresses entirely the formation of aqueous. The persistance of a current, reduced to 1.0 to 1.5 cu. mm. per minute, accounts for the following clinical observations:

a. The aqueous veins are usually visible even when the hypotensive action of Diamox is most marked.

b. Continuous prolonged treatment with Diamox does not threaten the transparency of the crystalline lens. Experience with retrociliary diathermy has shown that a flow of 1.0 cu. mm. per minute is adequate for lenticular metabolism, though a complete suppression of aqueous formation rapidly provokes opacification.

c. Diamox alone does not normalize ocular tension unless the resistance to flow is very moderate. The flow necessary to maintain normal ocular tension can be calculated from the formula, $Po = (F \times R) + P v$. This requires data of the intraocular pressure, the resistance to flow, and the episcleral venous pressure.

2. *The interaction between intraocular pressure and resistance to flow.* The interaction between intraocular pressure and resistance to flow is manifested quite differently in ocular hypertension and in ocular hypotension. An elevated resistance increases the intraocular pressure and this in turn increases the resistance (tables 3, 4, 5, 6). On the other hand, ocular hypotension consecutive to a reduction of flow unleashes the reaction of homeostasis and causes a compensatory increase of resistance (tables 7 and 8).

The interaction between intraocular pressure and resistance to flow explains the following observations:

a. In an open-angle glaucoma in which

the tension is only moderately elevated epinephrine (two percent) lowers the ocular pressure by a reduction of the formation of aqueous without an accompanying change of resistance. This conclusion is supported by fluorometric and tonographic studies. But if the elevation of tension is marked the instillation of epinephrine causes also a diminution of resistance, as revealed by the tonographic measurements made before and after.[22, 26] This is explained by the assumption of trabecular compression by high intraocular pressure followed by decompression when the ocular tension falls.

b. Retrociliary diathermy effects a reduction of ocular tension by a reduction of aqueous formation.[25] With a modification of technique[24] this intervention can cause an almost complete suppression of aqueous secretion causing a marked fall of tension even in eyes affected by absolute glaucoma. In some of these cases tonography revealed an increased facility of outflow, analogous to that noted after administration of Diamox (tables 3, 4, 5, 6) and after the instillation of two-percent epinephrine.

c. Goldmann[13] showed that compression of the globe accelerated the exit of aqueous and from this observation devised a method of measuring resistance to flow. But if the pressure on the globe is excessively strong, the flow of aqueous is suppressed. Kleinert[18] labelled this phenomenon, "maximum compensation." It appears to be an extreme case of the increased resistance provoked by very high intraocular pressure.

The effect of homeostasis in causing an increased resistance to flow when the ocular tension falls below the physiologic level because of reduced aqueous formation is not evident in glaucoma[10] (tables 3, 4, 5, 6). This may be interpreted as due to the following considerations: (a) Glaucomatous lesions of the excretory channels prevent homeostasis; (b) elevated resistance follows only hypotension, while in glaucoma the ocular tension is still higher than normal after Diamox (tables 3, 4, 5, 6) or after intravenous injection of hypertonic solutions;[10] (c) the diminution of resistance effected by trabecular decompression may mask the phenomenon of homeostasis.

The interplay of intraocular pressure resistance and flow complicates the interpretation of tonographic findings. The simplest situation occurs when the ocular tension is between 18 and 30 mm. Hg, since a tension of 30 mm. Hg is insufficient to cause any trabecular compression.

Summary

Tonographic studies of the effect of Diamox on the ocular tension of normal subjects and those with open-angle and secondary glaucoma reveal that intraocular pressure is determined by the interaction of diverse factors including the phenomenon of homeostasis. This interplay must be considered for a valid interpretation of tonographic findings. This research confirms that of previous authors in showing that Diamox in high dosage causes a reduction in aqueous formation of about 50 percent.

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