A manometric study of the rate of fall of the intraocular pressure in the living and dead eyes of human subjects

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The relationship between the rate of flow of the aqueous humor and the intraocular pressure in living and dead human eyes has been studied by two manometric techniques. The first comprised a record of the pressure decay curve and a separate determination of the pressure-volume relationship for the same eye. The pressure-flow relationship was then calculated from the rate of pressure change and the corresponding volume decrement. The second experimental approach has been to determine the relationship between the intraocular pressure and the rate of flow of aqueous humor in conditions of steady state. Studies have been made on 7 eyes before and immediately after enucleation, on 7 cadaver eyes in situ, and on 10 enucleated eyes. In dead eyes, the rate of outflow was found to be directly proportional to the intraocular pressure. In living eyes, analysis of the pressure decay curve indicated that the relationship between pressure and flow was approximately linear over the observed pressure ranges but that at pressures approaching the normal steady state, the relationship was consistent with the suppression of aqueous humor formation by small increases in pressure. The results of steady-state perfusion studies on living eyes were in agreement with this conclusion.

Our knowledge of the rate of formation and the resistance to outflow of the aqueous humor in human subjects is based almost exclusively on the results of tonographic analysis. This method measures the rate of fall of pressure during the ocular hypertension caused by the weight of a tonometer resting on the eye. Under these conditions the resultant volume of aqueous humor lost from the eye is assumed to be the sum of the change in the volumes of corneal indentation and scleral distention.

In order to place the analysis of pressure decay curves on a sound theoretical basis and also to assess the accuracy of the accepted methods for the analysis of tonograms and pressure decay curves determined by indirect techniques such as the pressure cup technique, it is desirable if not mandatory to determine the pressure-flow relationship in the living eye by a direct manometric technique. This has been the main object of this investigation in which the hydrodynamic relationship between the rate of flow of the aqueous humor and the intraocular pressure in living and dead human eyes has been studied by two manometric methods.

The first technique comprised a manometric record of the pressure decay curve and the determination of the pressure-volume relationship for the same eye. The pressure-flow relationship was then calculated from the rate of pressure change and the corresponding volume decrement.
The second experimental approach has been to determine the relationship between the intraocular pressure and the rate of flow of aqueous humor in conditions of steady state. For this purpose the equilibrium pressure has been determined for a series of influsions of saline at constant rates into the anterior chamber. Under these experimental conditions the pressure-flow relationship is independent of "ocular rigidity." The results of the two techniques in individual eyes were found to agree, whereas significant differences were found when the conventional pressure-volume relationships of Friedenwald were used.

Studies have been made on 7 eyes before and immediately after enucleation, on 7 cadaver eyes in situ, and on 10 enucleated eyes.

Methods

Pressure decay curves from 7 human eyes were obtained prior to enucleation or orbital exenteration, and each eye was also studied in vitro immediately following its removal. Four of these eyes were removed because of choroidal melanomas, while 3 were obtained during the course of an orbital exenteration. The anterior segment of each eye was normal and none of the eyes had glaucoma. In addition, 10 eye-bank eyes were studied at times varying from 24 to 90 hours after death, and 7 cadaver eyes in situ were examined 3 to 12 hours after death. In no case, except one to be discussed subsequently, was there any reason to suspect that any of the cadaver or eye-bank eyes was abnormal.

For all eyes the procedure for manometric studies described in an earlier paper was utilized. A 21 or 23 gauge needle attached to a short piece of polyethylene tubing was inserted into the anterior chamber at the temporal limbus. This cannula was in turn attached to a four-way plastic block with self-contained taps as described by Langham. A 21 gauge needle was used for influsions of saline into the eye, and a 24 gauge needle was used for influsions of known volumes of saline. For living eyes in /3-propiolactone or ethylene oxide. Following reassembly the system was filled with boiled physiologic saline and carefully examined for leaks and trapped air bubbles.

The recording system was balanced and calibrated to give a deflection of 2 mm. per millimeter of mercury for the pressure decay curves. It should be emphasized that there have been no untoward reactions resulting from these studies in vivo under either local or general anesthesia. Measurement of the pressure-volume relationship on 6 of the living eyes has been described in detail in a previous paper. Calculation of the pressure-flow relationship from a pressure decay curve was made by dividing the curve into a number of small segments of 15 or 20 second time intervals. Over this short interval the rate of fall of pressure was approximately linear. The initial and final pressures of each linear segment were used to derive the volume change, and the average rate of flow was then calculated, knowing the time interval.

This rate of infusion greatly exceeds the rate of outflow of aqueous humor but a correction for this loss was made in the manner described previously. The technique described by Langham was utilized to determine steady-state intraocular pressures for known rates of infusion of saline. For this purpose the taps in the plastic block were turned to connect the eye to the pressure transducer and the continuous infusion apparatus. The saline reservoir was used to set the intraocular pressure either slightly above or below the anticipated steady-state value. At least three influsions were made on each dead eye. The procedure for influsion studies on living eyes was similar; the steady-state pressure was determined initially, then two influsions at different rates were made, and finally the steady-state pressure was measured again.

The eye-bank eyes had been refrigerated and were allowed to warm to room temperature before the study began. Each eye was supported in saline-moistened cotton with the cornea uppermost. If the eye had been previously cannulated, a needle of slightly larger diameter than that initially used was passed through the original puncture site so that leaks were avoided. The studies on cadaver eyes were all carried out in the morgue of the Johns Hopkins Hospital, making use of portable electronic equipment.

Pressure measurements and recordings were made by means of Sunborn 267-B pressure transducers, Sanborn 350-1100B or 150-1100AS carrier preamplifiers, and Sanborn 200 or 150 direct writing recorders. The infusion device was that described by Langham, calibrated to deliver small volumes of saline at a constant rate. Prior to an experiment the entire apparatus was disassembled, cleaned and sterilized as required for living eyes in either /3-propiolactone or ethylene oxide. Following reassembly the system was filled with boiled physiologic saline and carefully examined for leaks and trapped air bubbles.

The recording system was balanced and calibrated to give a deflection of 2 mm. per millimeter of mercury for the pressure decay curves. It should be emphasized that there have been no untoward reactions resulting from these studies in vivo under either local or general anesthesia. Measurement of the pressure-volume relationship on 6 of the living eyes has been described in detail in a previous paper. Calculation of the pressure-flow relationship from a pressure decay curve was made by dividing the curve into a number of small segments of 15 or 20 second time intervals. Over this short interval the rate of fall of pressure was approximately linear. The initial and final pressures of each linear segment were used to derive the volume change, and the average rate of flow was then calculated, knowing the time interval.
To plot the relationship between flow and pressure, the average pressure increment of each small segment was plotted against the average flow rate.

**Results**

**Manometric studies on enucleated eyes.**

A series of 10 enucleated human eyes was studied at room temperature 24 to 96 hours after death. The relationship between the pressure and the volume of fluid infused into each individual eye was determined by both the rapid and the continuous infusion techniques, and the results are recorded in Table I. The values of the coefficients of ocular rigidity determined by the two techniques were similar and the values for the different pressures agreed with those reported in a similar study on freshly enucleated human eyes.3

The rate of decay of pressure in the same eyes was studied over the pressure range of approximately 50 to 10 mm Hg. In 9 out of 10 eyes the pressure fell smoothly and approached a limiting value of approximately 10 mm Hg within 10 minutes. In the tenth eye, the pressure fell more slowly and reached a limiting pressure of 10 mm Hg in 30 to 40 minutes. The rate of fall of pressure was not constant over the entire pressure range but did approximate a constant value for pressures from 30 to 15 mm Hg. This is illustrated in the result included in Fig. 1. In this eye the pressure decay curve followed the double exponential equation \( P = 41e^{-0.227t} + 14e^{-1.72t} \) over the pressure range of 55 to 15 mm Hg.

The pressure-flow relationship of each eye was calculated by use of the pressure volume data recorded on the same eye, and a typical result is included in Fig. 1. In all of the 10 enucleated eyes the rate of outflow of aqueous humor appeared to be directly proportional to the pressure and this was confirmed by calculation of the linear regression coefficient. The average regression coefficient was 0.972 ± 0.01 (10) (arithmetic mean ± standard error of the

### Table I. The coefficients of ocular rigidity of 10 enucleated eyes measured at varying initial pressures by the rapid technique and by the continuous infusion technique (200 \( \mu l \) min.\(^{-1}\))

<table>
<thead>
<tr>
<th>Initial pressure (mm. Hg)</th>
<th>Rapid</th>
<th>Steady infusion (200 ( \mu l ) min.(^{-1}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>0.0144 ± 0.0008</td>
<td>0.0150 ± 0.0010</td>
</tr>
<tr>
<td>20</td>
<td>0.0157 ± 0.0007</td>
<td>0.0135 ± 0.0007</td>
</tr>
<tr>
<td>25</td>
<td>0.0126 ± 0.0006</td>
<td>0.0135 ± 0.0007</td>
</tr>
<tr>
<td>30</td>
<td>0.0136 ± 0.0007</td>
<td>0.0127 ± 0.0008</td>
</tr>
<tr>
<td>35</td>
<td>0.0115 ± 0.0004</td>
<td>0.0121 ± 0.0005</td>
</tr>
<tr>
<td>40</td>
<td>0.0108 ± 0.0010</td>
<td>0.0115 ± 0.0005</td>
</tr>
<tr>
<td>45</td>
<td>0.0107 ± 0.0004</td>
<td>0.0109 ± 0.0005</td>
</tr>
<tr>
<td>50</td>
<td>0.0103 ± 0.0004</td>
<td>0.0102 ± 0.0005</td>
</tr>
<tr>
<td>55</td>
<td>0.0098 ± 0.0004</td>
<td>0.0099 ± 0.0005</td>
</tr>
</tbody>
</table>

Fig. 1. Manometric studies on enucleated eyes. A, A typical pressure decay curve. B, The same curve plotted on semilogarithmic paper; the two straight lines indicate the two exponential components. C, The pressure-flow relationship of the same eye. D, The pressure-flow relationship on 9 individual eyes summarized.
mean) which is highly significant of a linear relationship between flow and pressure decrements. The corresponding linear equation for each eye is shown in Table II. The average outflow facility for all eyes excluding the first was 0.55 ± 0.06 (9) μl min⁻¹ mm. Hg⁻¹ at room temperature. The first value was excluded in this analysis as the facility was extraordinarily low compared with the remainder. The average value of the constant was -0.42 ± 1.1 (9) μl min⁻¹ which is not significantly different from zero. The results, therefore, are consistent with the concept that in enucleated eyes the rate of flow is directly proportional to pressure over the pressure range of 15 to approximately 55 mm. Hg. Below 15 mm. Hg the outflow facility was found to decrease and the pressure reached a limiting value of 5 to 10 mm. Hg, similar to the critical closure pressure observed in manometric studies on rabbits⁸ and cats.⁹

By way of comparison the pressure decay curves were analyzed by Friedenwald's coefficient of ocular rigidity of 0.0215. The average correlation coefficient was 0.816 ± 0.08 (10) and the average facility was 0.17 ± 0.08 (9) μl min⁻¹ mm. Hg⁻¹, a value well below that calculated from the observed pressure-volume relationship of individual eyes.

### Table II. The pressure-flow relationship in enucleated eyes

<table>
<thead>
<tr>
<th>Observed range</th>
<th>r</th>
<th>r²</th>
<th>F = CP + K</th>
<th>Hours after death</th>
</tr>
</thead>
<tbody>
<tr>
<td>17-60</td>
<td>0.984</td>
<td>0.953</td>
<td>0.08P + 0.21</td>
<td>36</td>
</tr>
<tr>
<td>15-57</td>
<td>1.000</td>
<td>0.969</td>
<td>0.71P + 0.07</td>
<td>70</td>
</tr>
<tr>
<td>17-55</td>
<td>0.969</td>
<td>0.990</td>
<td>0.50P - 0.3</td>
<td>70</td>
</tr>
<tr>
<td>16-55</td>
<td>0.992</td>
<td>0.898</td>
<td>0.50P - 0.9</td>
<td>26</td>
</tr>
<tr>
<td>15-55</td>
<td>0.965</td>
<td>0.941</td>
<td>0.77P + 4.3</td>
<td>25</td>
</tr>
<tr>
<td>17-48</td>
<td>0.978</td>
<td>0.460</td>
<td>0.71P - 0.6</td>
<td>24</td>
</tr>
<tr>
<td>12-27</td>
<td>0.880</td>
<td>0.851</td>
<td>0.31P - 0.4</td>
<td>24</td>
</tr>
<tr>
<td>19-52</td>
<td>0.991</td>
<td>0.957</td>
<td>0.43P - 4.0</td>
<td>24</td>
</tr>
<tr>
<td>15-50</td>
<td>0.965</td>
<td>0.806</td>
<td>0.77P + 4.0</td>
<td>98</td>
</tr>
<tr>
<td>10-76</td>
<td>0.993</td>
<td>0.987</td>
<td>0.25P + 0.2</td>
<td>48</td>
</tr>
</tbody>
</table>

The equation $F = CP + K$ is the linear correlation coefficient calculated from the pressure-volume relationship measured on each eye and the pressure decay curve (Column 1), $r$ is the linear regression coefficient when Friedenwald's coefficient of ocular rigidity is used in the analysis of the same pressure decay curve.

The pressure-flow relationship of dead eyes in situ. The results of steady-state perfusion studies on the eyes of 7 cadavers 3 to 12 hours after death are shown in Fig. 2. Three or four infusions were made on each eye and the results on individual eyes approximated closely to a linear pressure-flow relationship passing either through or close to the origin.

The pressure-flow relationships of the same eyes were then calculated from an analysis of a manometric pressure decay curve and the results were compared with those derived from the steady-state perfusions. In 5 of the 7 subjects the pressure-flow relationship determined by the two procedures agreed well and two typical examples are shown in Fig. 3. In the two remaining eyes the agreement was poor over the initial 60 to 90 seconds, but good for the remaining 180 to 240 seconds of the decay curve. This discrepancy could have been due to a lack of pressure equilibration throughout the eye when the pressure was decreasing at the maximal rate. In the 5 eyes in which there was good agreement between the results of the two techniques, the average linear regression coefficient relating flow and pressure was 0.959.

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Fig. 2. The steady-state relationship between pressure and flow in dead eyes in situ. The figure summarizes the results on the eyes of 7 cadavers examined within 3 to 12 hours of death. The line of lowest slope was recorded from a subject 71 years old with a long clinical history of chronic simple glaucoma, whereas the line of greatest slope was recorded from a girl of 7 years.
Fig. 3. The comparison of the pressure-flow relationship in dead eyes in situ determined by two manometric techniques; the figure shows the results on eyes of two subjects. The results of the steady-state perfusion studies are indicated by the filled-in circles, and the pressure-flow relationship derived from the pressure decay curve and the pressure-volume relationship of individual eyes is indicated by the open circles. The open squares indicate the results of the analysis using Friedenwald's coefficient of ocular rigidity (0.0215).

Fig. 4. A typical record of the pressure decay curve recorded manometrically from the anterior chamber of a normal eye. The steady-state intraocular pressure of this eye was 16 mm. Hg ± 0.01 and the average facility 0.27 ± 0.06 μl min⁻¹ mm. Hg⁻¹.

One patient in this group was of particular interest. He was a 71-year-old Negro male who had been followed in the Wilmer Out-Patient Department for 10 years with a diagnosis of chronic simple glaucoma. When first seen, his intraocular pressure measured 40 mm. Hg in the right eye and 27 mm. Hg in the left eye. Abnormal intraocular pressures were noted on two other occasions prior to the introduction of miotic therapy. His optic discs were normal and his visual fields showed an early arcuate scotoma. He was treated for 10 years until the day of his death with a 2 per cent solution of pilocarpine given topically 3 times daily, and on this medication his tension ranged between 15 and 23 mm. Hg while the facility of outflow varied from 0.10 to 0.19 in the two eyes. Within 5 hours of his death from an acute myocardial infarction, his eyes were studied in situ in the manner previously described. Steady-state perfusions indicated that the outflow facilities in the two eyes were 0.16 and 0.17 μl min⁻¹ mm. Hg; these values are lower than any other within this group. Analysis of the pressure decay curve in one eye again showed a linear relationship between pressure and flow, and the facility was found to be 0.17.
Manometric studies on living human eyes. The steady-state intraocular pressure was recorded manometrically in 7 subjects. The values ranged from 13 to 20 mm. Hg with a mean value of 17.3 ± 0.94 (7) mm. Hg. The mean pressure of the same group of eyes measured by applanation tonometry prior to the operation was 14.6 ± 1.1 mm. Hg and 15.2 ± 2.3 mm. Hg in the experimental and control eyes, respectively. The mean manometric pressure is less than the value of 19 mm. Hg reported by Estrada in a group of patients having varied clinical conditions. It is also below the mean pressures of 20.6 ± 0.57 mm. Hg recorded in rabbits and 20.1 ± 0.37 mm. Hg recorded in cats. On the other hand, it agrees well with the mean pressures of 15.4 ± 2.5 mm. Hg (A.M. ± S.D.) and 16.1 ± 2.8 mm. Hg accepted for human subjects recorded by applanation and Schiötz tonometry.

A typical manometric pressure decay curve on a normal eye is seen in Fig. 4. The pressure fell smoothly toward the steady-state value, which was attained within 10 to 20 minutes. When the pressure increment (pressure minus the steady-state pressure) was plotted on semilogarithmic paper, it was found that the rate of fall of pressure was not constant but decreased with decreasing intraocular pressure over the observed pressure range. A more detailed analysis of these curves was not attempted as it had not been possible to record the complete approach of the decay curve to the steady state.

The pressure-volume relationship of each eye was determined and the results were used to calculate the pressure-flow relationship from the pressure decay curve. Results on two eyes which were typical of the whole group are shown in Fig. 5. In these eyes flow was found to vary directly with pressure over the range of pressures observed. Similar results were found in all eyes, and in view of the apparent linear relationship between flow and pressure increments, correlation coefficients and regression equations were calculated. These results are summarized in Table III. The mean linear correlation coefficient was 0.952 ± 0.022. On the assumption that the outflow facility is given by the slope of this regression equation, its average value in the group of 7 eyes was 0.31 ± 0.05 (7) µl min⁻¹ mm. Hg⁻¹. By way of comparison, the pressure decay curves were

![Fig. 5. The pressure decay curves in two living eyes recorded manometrically and the corresponding pressure-flow relationships calculated from using the pressure-volume relationship of the individual eyes. The straight lines represent the linear regression equations.](https://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/932890/)
analyzed by use of the Friedenwald coefficient of ocular rigidity of 0.0215, and the
results are included in Table III. The linear correlation coefficient was again
found to be highly significant and the linear equations for each eye were cal-
culated. It will be seen that in all eyes the outflow facility was significantly below
that calculated using the pressure-volume relationship of that eye. The mean value of
the intercept in the linear equation relating flow and pressure was 0.36 ± 0.22 and
0.84 ± 0.32 μl min⁻¹, when calculated using individual PV curves and Friedenwald's
coefficient, respectively. The rate of flow of aqueous humor in these eyes was cal-
culated from the flow equation, using P as the outflow pressure, i.e., the steady-state
intraocular pressure minus the episcleral venous pressure which was assumed to be
10 mm Hg. The average rate of flow was 2.26 ± 0.40 (7) μl min⁻¹; compared with
an average value of 0.85 ± 0.12 (7) μl
min⁻¹ when the Friedenwald coefficient
was employed.

Table III. The pressure-flow relationship in living human eyes calculated from the
pressure decay curve

<table>
<thead>
<tr>
<th>Pressure range</th>
<th>Po</th>
<th>Correlation coefficient</th>
<th>F = C Δ P + K</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-22</td>
<td>15</td>
<td>0.965</td>
<td>0.36 + 0.31</td>
</tr>
<tr>
<td>35-17</td>
<td>13</td>
<td>0.973</td>
<td>0.48 + 0.75</td>
</tr>
<tr>
<td>45-26</td>
<td>18</td>
<td>0.954</td>
<td>0.31 + 1.17</td>
</tr>
<tr>
<td>50-29</td>
<td>17</td>
<td>0.971</td>
<td>0.24 + 2.54</td>
</tr>
<tr>
<td>61-27</td>
<td>19</td>
<td>0.922</td>
<td>0.14 + 0.66</td>
</tr>
<tr>
<td>43-28</td>
<td>19</td>
<td>0.970</td>
<td>0.50 + 1.5</td>
</tr>
<tr>
<td>50-31</td>
<td>20</td>
<td>0.941</td>
<td>0.34 + 1.07</td>
</tr>
</tbody>
</table>

The first column indicates the limits of pressure of the observed decay curve. Column 2 shows the steady-state pressure. Column 3 gives the linear correlation coefficients calculated either from the individual PV measurements (top) or from Friedenwald's coefficient of ocular rigidity of 0.0215 (bottom). Column 4 gives the regression equa-
tion relating flow (F), the outflow facility (C), and the pressure increment (ΔP), and K is the constant.
In two living eyes perfusion studies were undertaken to determine the influence of varied rates of infusion on the steady-state intraocular pressure. The influence of a constant infusion of saline into the anterior chamber on the intraocular pressure is shown in Fig. 6. In this condition the intraocular pressure increased steadily to approach a new steady state within 10 minutes. When the intraocular pressure was raised above this level, the intraocular pressure fell smoothly toward the same steady-state pressure. A more rapid determination of the steady-state pressure was obtained in all subsequent perfusions by first bringing the intraocular pressure just below and then just above the anticipated value as described in a previous paper.⁸

One of the two results is shown in Fig. 7 and indicates that the pressure-flow relationship was not linear. Pressure decay curves were recorded in the same eyes and a pressure-flow curve was calculated for each eye using the individual pressure-volume relationship. The pressure-flow relationship calculated by the two techniques agreed satisfactorily (Fig. 7). In comparison, the slope of the pressure-flow relationship calculated on the basis of Friedenwald's coefficient of ocular rigidity was significantly lower than that of the steady-state perfusion results.

The eyes from these subjects were re-studied by use of manometric techniques immediately after enucleation. Again pressure decay curves were recorded manometrically, pressure-volume relationships determined, and the pressure-flow relationships calculated. The results are tabulated in Table IV. The results were similar to those found in the series of enucleated eyes considered earlier, but in this series the average outflow facility was 0.22 ± 0.036 (6) μl min⁻¹ mm. Hg⁻¹ which is significantly less than those eyes left for 1 to 4 days. The value is, however, similar to the

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Fig. 7. The comparison of the pressure-flow relationship in a normal living eye calculated from steady-state perfusions (filled-in circles) and from an analysis of the pressure decay curve and individual measurements of the PV relationship (open circles). The open squares show the results of the analysis of the pressure decay curve using Friedenwald's coefficient of ocular rigidity (0.0215).

Fig. 8. The pressure-flow relationship in an eye immediately after enucleation. The left-hand figure shows the pressure decay curve and the right-hand figure the results of steady-state perfusions (●—●) and analysis of pressure decay curve by the individual PV relationship (O—O) and by Friedenwald's coefficient (□—□).
Table IV. The equation relating pressure and flow in 6 eyes immediately after enucleation

<table>
<thead>
<tr>
<th>Pressure range (mm Hg)</th>
<th>Correlation coefficient</th>
<th>F = CP + K</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-17 [4]</td>
<td>0.953</td>
<td>P = 0.35</td>
</tr>
<tr>
<td>58-17 [3]</td>
<td>0.997</td>
<td>P = 0.18</td>
</tr>
<tr>
<td>37-14 [2]</td>
<td>0.948</td>
<td>P = 0.25</td>
</tr>
<tr>
<td>60-25 [5]</td>
<td>0.985</td>
<td>P = 0.09</td>
</tr>
<tr>
<td>48-17 [1]</td>
<td>0.980</td>
<td>P = 0.20</td>
</tr>
<tr>
<td>43-10 [6]</td>
<td>0.996</td>
<td>P = 0.27</td>
</tr>
</tbody>
</table>

The equation was calculated from the pressure decay curve (Column 1) and from measurements of the pressure-volume relationship in individual eyes. The figures in brackets refer to the corresponding living eye as recorded in Table III (i.e., the top row in Table III is eye 1).

average value found in eyes in situ examined within 3 to 12 hours of death. The mean intercept in the linear pressure-flow equation was \(-0.48 \pm 0.51\) (6) \(\mu l\) min\(^{-1}\). In 2 of these eyes steady-state perfusion studies were made and the results were again found to agree closely with those derived from an analysis of the pressure decay curve (Fig. 8).

Discussion

The results of experiments on dead eyes showed that there was a simple hydrodynamic relationship between the pressure in the eye and the rate of outflow of aqueous humor for pressures ranging from 15 to 50 mm Hg. This relationship was linear, and consequently the outflow facility must have been constant. At pressures below 15 mm Hg the outflow resistance began to increase and a complete collapse of the drainage vessels occurred at pressures of 5 to 10 mm Hg. A similar value for the closure pressure of the drainage vessels has been found in both rabbit and cat eyes and probably reflects the tension exerted by the sclera on the intrascleral veins. If the comparison of the perfusion studies made on eyes at varying times after death suggests that there was no rapid postmortem change in the outflow mechanism, for the mean value of the outflow facility in the group of eyes studied immediately after enucleation was not significantly different from that of the group of eyes studied 3 to 12 hours after death. On the other hand, the outflow facility of the group of enucleated eyes studied 24 to 96 hours after death was significantly higher than in the two previous groups. Consequently, postmortem changes in the outflow mechanism must be taken into account in eyes kept at 4° C. for this period of time.

The perfusion studies on the dead eyes enabled the steady-state pressure-flow relationship to be derived independently of a knowledge of the elastic properties of the eye. They formed a basis, therefore, to determine the accuracy of pressure-flow relationship derived from the pressure-volume relationship and the pressure decay curve. The pressure-volume relationships of these eyes were in close agreement with those found in a previous study on freshly enucleated eyes\(^{6, 7}\) and also with those of other investigators\(^{6, 7, 12}\) who have observed the relationship to differ significantly in qualitative and quantitative aspects from the Friedenwald relationship. Therefore, the observation that the pressure-flow relationship on individual eyes derived by the two different techniques agreed, strongly suggests that the analysis of the pressure decay curves using individually determined pressure-volume relationships is valid and accurate. In contrast, the pressure-flow relationship derived using Friedenwald's coefficient gave a curve of significantly lower slope in all enucleated eyes. It is certainly true that the pressure-flow relationship based on an individual pressure-volume relationship would be expected to give better agreement with the steady-state perfusion results than when an average pressure-volume coefficient was used, but good agreement was also found between the results of the two techniques when the average pressure-volume relationship determined on a separate group of enucleated eyes was employed.

The living eye. Two of the eyes used in this study were believed to be completely normal and had 20/20 vision. Each of the remaining eyes had a small melanoma in
the posterior section, but the finding that pressures in pairs of eyes of individual subjects agreed well and that the outflow facilities measured tonographically were between 0.25 and 0.55 suggests that the ocular dynamics of these eyes were also within the physiologic range. It was of interest, therefore, to find that the mean steady-state intraocular pressure of these eyes was 17.3 ± 0.94 (7) mm. Hg, which is very similar to the mean pressure generally accepted for normal eyes on the basis of applanation tonometry and on the latest calibration tables for a standard Schiötz tonometer.

All but one of these patients was anesthetized with Fluothane and the possibility arose that the steady-state pressure might have been modified by this drug. In this respect, Magara and Collins have reported that Fluothane anesthesia in 20 normal subjects caused the mean intraocular pressure to fall from 16.36 ± 2.58 (A.M. ± S.D.) to 12.64 ± 3.51 mm. Hg measured by Schiötz tonometry. The anesthesia was given over short periods of time, but the authors considered that the results would not be expected to differ if anesthesia had been continued. This conclusion must be seriously questioned, however, for during the period from consciousness to general anesthesia the intraocular pressure will not be in a condition of steady state but will fall with the relaxation of the extraocular muscles and also with a possible decrease in general blood pressure; under these conditions it is necessary to allow sufficient time for the volume of aqueous humor to increase to offset the volume increase of the eye. This equilibration takes from 10 to 15 minutes, and therefore the results of Magara and Collins need not be in disagreement with the steady-state pressures recorded in this study if their measurements were taken with the eye not in equilibrium. Unfortunately, the authors did not record in their paper the actual times at which their readings were taken.

The relationship between pressure and flow in the living eye derived by the two techniques indicates that it approximates direct proportionality over a range of pressures 10 to 25 mm. Hg above normal. Thus it is probable that the rate of formation of the aqueous humor and the outflow facility were approximately constant over this range of pressures. There is, however, reason to believe that the rate of formation was not constant as the pressure approached the normal equilibrium value, because extrapolation of the linear regression gave a positive intercept on the flow axis. This suggests that small increases in pressure caused a suppression of the rate of formation of the aqueous humor equivalent to the value of the intercept on the flow ordinate. The regression equations were con-

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**Fig. 9.** The pressure-volume relationship of living eyes. The half-filled circles represent the means derived from 6 eyes by Prijot; the filled-in circles represent the means derived from 8 eyes by Ytteborg; the open circles and bars represent the arithmetic mean ± standard error of the mean of 7 eyes studied in this paper. The open squares represent the Friedenwald relationship using a coefficient of ocular rigidity of 0.0215.
sistent with a maximal suppression of 0.34 μl min." out of a total mean formation rate of 2.26 μl min." Steady-state perfusion studies were too few to yield constructive information on this aspect, but it was of interest that, in both living eyes studied, the pressure-flow relationship was curvilinear and consistent with a significant suppression of aqueous humor formation by an increase in the intraocular pressure.

The general agreement of pressure-flow relationships determined by the steady-state perfusion technique with those calculated from the pressure decay curve in both living and dead eyes raises the important question of the validity of the pressure-volume relationship in general use for the analysis of tonographic decay curves. The pressure-volume relationship of the living eye has now been studied in at least 23 eyes by three groups of investigators3, 10, 17, 18 and the results are shown graphically in Fig. 9. In this figure the results have been expressed in terms of the volume required to increase the intraocular pressure from an initial value of 10 mm. Hg, and it will be seen that the results of the three groups of investigators are in good agreement. These results are significantly above the pressure-volume relationship based on a coefficient of ocular rigidity of 0.0215. The present observations on living eyes indicate that serious consideration should now be given to the general adoption of this new pressure-volume relationship for the analysis of tonograms and all pressure decay curves.

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REFERENCES