Further studies on the influence of the intraocular pressure on aqueous humor dynamics in cynomolgus monkeys

Anders Bill

$^{131}$I-albumin was used to determine the rate of bulk outflow from the anterior chamber in one eye and $^{125}$I-albumin was used in the other. In 10 eyes at a spontaneous intraocular pressure of $8.0 \pm 0.7$ mm Hg, uveoscleral flow was $0.63 \pm 0.08 \mu$L per minute and flow by fast, vascular routes was $0.53 \pm 0.07 \mu$L per minute. When the intraocular pressure was lowered to 2 or 4 mm Hg by letting aqueous flow into a reservoir, drainage of anterior chamber fluid into the blood by way of fast routes stopped almost completely. At 2 mm Hg, the bulk flow into the uveoscleral routes was reduced by an average of 63 per cent, but at 4 mm Hg uveoscleral flow was normal in 4 of 5 eyes. Adjusting the intraocular pressure from the spontaneous level to 35 mm Hg by inflow from a reservoir gave an average outflow into the general circulation that was $12.0 \pm 2.3 \mu$L per minute higher than in the control eyes. Uveoscleral flow was not raised significantly. Pseudofacility was $0.055 \pm 0.013 \mu$L per minute per millimeter Hg. In dead eyes uveoscleral flow appeared to be pressure sensitive in a wider pressure range than in living eyes. It is concluded that in cynomolgus monkeys aqueous humor passes out through the conventional vascular routes into the episcleral veins and passes out through uveoscleral routes that drain its high molecular components into the suprachoroid and the episcleral tissues. However, pinocytosis, in the uveal blood vessels, plays little role for bulk drainage of aqueous humor. In living cynomolgus eyes, within the range 8 to 35 mm Hg, the intraocular pressure (IOP) is determined by the recipient venous pressure ($P_v$), the net rate of aqueous humor formation ($F_n$), the rate of aqueous outflow by uveoscleral routes ($F_u$), and the gross facility of outflow ($C_g$) according to $IOP = P_v + (F_n - F_u)/(C_g - 0.06)$.

Since the discovery of the aqueous veins by Ascher, there has been little doubt that in primates the aqueous humor is drained predominantly through anterior vascular routes, that is from the anterior chamber into the canal of Schlemm and from there through delicate vessels anastomosing with the intrascleral veins. Recent studies in monkeys have shown, however, that from a physiological point of view there are two types of bulk drainage of anterior chamber aqueous humor. There are fast drainage routes by which high molecular substances in the aqueous humor are rapidly carried into the general circulation and slow routes by which high molecular substances are carried into the episcleral tissues by way of the anterior uvea, the suprachoroid, and the sclera. The drainage by fast routes is, no doubt, dominated by the flow through Ascher's vascular routes, but pinocytosis into the uveal capillaries might also...
contribute. Fine with the use of electron-microscopy studies has, in fact, reported that both in the iris and the ciliary body there is aqueous humor transport into the capillaries by pinocytosis. The magnitude of this flow was not known.

Previous studies have shown that the flow through the fast routes and through the slow ones are regulated in very different ways. A moderate increase in intraocular pressure that raised fast route drainage five times had no significant influence on the flow through the slow uveoscleral routes. Further, pilocarpine, which tends to reduce the resistance of the fast outflow routes, almost completely stops uveoscleral flow while atropine in eyes treated with pilocarpine tends to increase uveoscleral flow and reduce vascular flow.

The purpose of the present investigation was (1) to try to evaluate the contribution of pinocytosis into the uveal blood vessels to aqueous humor drainage, and (2) to study the influence of great variations in intraocular pressure on the drainage of anterior chamber fluid by uveoscleral routes in living and dead eyes. The results also give some new data for the influence of the intraocular pressure on the rate of formation of aqueous humor.

Methods

Experiments in living animals. Cynomolgus monkeys (Macaca irus) of both sexes and weighing 2.1 to 3.2 kilograms each were employed. The animals were anesthetized by intravenous pentobarbital sodium (30 mg. per kilogram body weight), and heparin 1,500 I.U. per kilogram body weight was given to prevent clotting. A femoral vein was connected to a motor-driven syringe containing a solution of 131I-albumin or 125I-albumin; the tubing to the vein contained the same solution.

A femoral artery was cannulated and connected to a pressure transducer for measurements of the mean arterial blood pressure. Arterial blood samples could be collected from the tubing. Both eyes were cannulated with three cannulas (Fig. 1). These were introduced into the anterior chamber by a needle gun as described by Sears. In the right eye one needle connected the anterior chamber to a pressure transducer and a reservoir mounted on a weight sensing transducer. The tubing and the reservoir had been filled with a solution containing no labeled material. The other two needles connected the anterior chamber to precision syringes coupled in push-pull in such a way that the contents of the syringes, a solution of 131I-labeled albumin, could be washed to and fro through the anterior chamber without changes in anterior chamber volume or pressure. The left eye was similarly connected to syringes containing 131I-labeled albumin, a pressure transducer, and a reservoir that was continuously weighed. In experiments with an inflow from the reservoir into the left anterior chamber, the reservoir and the tubing connecting it to the eye were filled with the same solution as the syringes. The tubings to the eyes were drawn through extensions of water baths near the eyes. The temperature of the fluid entering the eyes was about 35° C. The basal solution used has been described by Bárány. A multipoint recorder was used for recording.

The procedure followed was to connect the eyes to the reservoirs which had been adjusted to a height above the eye that gave an intraocular pressure of 11 mm. Hg during the rest of the cannulations. The tubings to the reservoirs were then clamped, and after 10 minutes the intraocular pressure on both sides had stabilized at the spontaneous level. The mixing of the contents of the syringes and the anterior chambers was then started and at the same time the intraocular pressure on the left (131I) side was adjusted to 2 or 4 or 35 mm. Hg with the reservoir. In the former two cases there was an outflow into the weighed reservoir and in the latter case there was an inflow of labeled fluid from the reservoir. After 1 hour with mixing every 5 minutes the
tubing connecting the reservoir to the left (131I) eye was clamped and the radioactive anterior chamber fluid on both sides was replaced by inactive solution. Blood samples were taken 30 and 60 minutes after the mixing of the aqueous humor with the labeled solution, and samples of the fluid in the syringes were taken after the first mixing and 30 and 60 minutes later. After the eyes had been thoroughly washed with inactive solution, the intravenous infusion into the femoral vein of 125I-albumin or 131I-albumin was started at an infusion rate of 10 μL per minute. The concentration of labeled protein in the fluid infused was about the same as that in the fluid used in the eye. If the intraocular pressure on the 131I-albumin side had been adjusted to a low level previously, then 125I-albumin would have been infused; if it had been adjusted to a high level, then 125I-albumin would have been infused intravenously. Blood samples were collected at the start of the infusion and 30 minutes later when the infusion was stopped. The animal was killed and the eyes and the pericircular tissues were dissected and analyzed for 125I and 131I after drying. All samples were small and of similar size which permitted counting of 125I without correction for adsorption in the samples.

Some 5 hour experiments with labeled albumin in the anterior chambers were performed with the intraocular pressure of one side set at 1.5 mm Hg and the one on the other side at 3.0 mm Hg. Calculations. In the case of intravenous infusion of 131I-albumin during the 30 minutes of infusion, the radioactivity per gram blood brought about by 131I-albumin increased while that of 125I-albumin tended to fall. The percentage fall in activity of 125I-albumin was determined, and it was assumed that if there had been no intravenous infusion of 131I-albumin there would have been the same percentage fall in 131I activity of the blood. The difference between the observed final 131I-albumin concentration in the blood and that which would have been found if there had been no intravenous infusion represented the increase in blood activity produced by the infusion. The total amount of albumin infused in counts per minute was divided by the figure for the activity increase in counts per minute per gram blood to obtain a value for the blood equivalent albumin space (BEAS). In the case of intravenous 125I-albumin infusion the BEAS was calculated analogously. In cynomolgus monkeys over the period 30 to 120 minutes during a constant rate infusion, BEAS changes from 7.0 to 7.4 per cent of the body weight. This corresponds to an increase of 6 per cent of its value in 90 minutes. The change is due to penetration of protein into the tissue fluids. It was assumed in the experiments reported here that the labeled albumin which had entered the general circulation from the anterior chambers during the 60 minute period of active solution in the anterior chambers had become distributed in 102 per cent (100 + 6 • 30/90) of the BEAS calculated. The rate of rapid flow (Fa) in microliters per minute of anterior chamber fluid into the blood from the left eye was calculated as

\[ F_a = \frac{1.02 \cdot \text{BEAS} \cdot 131\text{I}_{\text{BEAS}}}{131\text{I}_{\text{BEAS}} \cdot 60} \]

where 131I is the activity of the blood in counts per minute per gram due to 131I-albumin at the end of the first 60 minute period. 131I_{BEAS} is the mean value for the activity in counts per minute per microliter of the fluid collected from the syringes connected to the left eye. The flow of anterior chamber fluid into the blood on the right side was calculated analogously.

In the calculations of the rate of outflow into the uveoscleral routes it was taken into account that some labeled protein in the eyes and orbits were due to the blood contents of the tissues and extravascular labeled protein that had leaked out of the blood vessels. Evidently the 131I-albumin recovered in the right (125I) eye and orbit in counts per minute, 131I_{BEOS}, was due to such factors. It was assumed that the same amount of 131I-albumin was present in the left eye and orbit for the same reason. The total radioactivity in counts per minute due to 131I-albumin in the left eye was 131I_{BEAS}. Uveoscleral flow (Fu) in microliters per minute in the left eye could then be calculated according to

\[ F_u = \frac{131\text{I}_{\text{BEAS}} - 131\text{I}_{\text{BEOS}}}{131\text{I}_{\text{BEAS}} \cdot 60} \]

Uveoscleral flow in the right eye was calculated analogously. In the 5 hour experiments with the intraocular pressure set at low pressures on both sides the BEAS was assumed to be 8 per cent of the body weight.

Definitions. In eyes at a normal intraocular pressure, that is with no inflow or outflow from the reservoirs, the rate of aqueous humor production was defined as the rate of outflow of protein-labeled fluid from the anterior chamber by way of vascular and uveoscleral routes. In eyes with an extra inflow from the reservoir the rate of aqueous production was calculated as the total outflow of labeled anterior chamber fluid from the eye minus the steady state inflow from the reservoir. In eyes with outflow into the reservoir the rate of aqueous production was the sum of this outflow and the flow of labeled fluid into blood and uveoscleral routes. Diffusion contributes one component to calculated uveoscleral flow, which will be discussed later.

Experiments in dead animals. The rate of accumulation of radioactive albumin in the intraocular and episcleral tissues was determined at
different intraocular pressures by a procedure similar to that used in the living animals. Heads from dead cynomolgus monkeys were used. They were obtained from a vaccine producer. All experiments were performed at room temperature and within 48 hours after killing. In experiments in which the heads were used later than 6 hours after the killing, they were stored at 2° C. until used.

Fluid containing 131I-albumin was continuously washed through the anterior chambers of the eyes at a rate of 50 μL per minute, and the intraocular pressure was regulated so as to give an inflow of labeled fluid into the two eyes of 0 and 4 μL per minute in one group, 2 and 5 μL per minute in another, and 4 and 10 μL per minute in a third group. After 60 minutes with radioactive fluid in the anterior chambers, this fluid was replaced by inactive fluid, and the eyes were removed and dissected.

In the statistical treatment of the data any differences between the two sides were calculated from paired data. The two eyes of each animal constituted a pair. All limits in the text are plus-minus standard error of mean.

Results

Experiments in living animals. The animals were in good condition. In the 1 hour experiments the average mean arterial blood pressure at the start was 87.5 ± 3.2 mm. Hg. At the end it was 85.0 ± 3.7 mm. Hg. The average BEAS was 7.30 ± 0.24 per cent of the body weight.

Experiments at low intraocular pressures. Tables I and II summarize the results of the 1 hour experiments. Both at 2 and 4 mm. Hg the flow of labeled protein into the general circulation from the eye was almost completely stopped. At 2 mm. Hg the flow of labeled fluid into the tissues around the anterior chamber was on an average 0.15 ± 0.03 μL per minute. When compared to the flow on the control side (which had its spontaneous pressure), the average reduction was 62.7 ± 11.5 per cent. The reduction was significant, P < 0.01. In all experiments the rate of formation of aqueous humor was higher on the side with low intraocular pressure than on the control side.

Table III summarizes the results of the 5 hour experiments. In most eyes maintained at a pressure of 1.5 mm. Hg only...
small amounts of labeled material were recovered in the ocular tissues, and the flow into the general circulation of labeled anterior chamber fluid was very low. In the eyes maintained at an intraocular pressure of 3.0 mm. Hg relatively large amounts of labeled anterior chamber fluid were recovered in the tissues in 3 of 6 experiments. Also in these eyes the flow into the general circulation was very small in 5 of 6 eyes.

Experiments with high intraocular pressure. Table IV presents the results of these experiments. In the eyes with 35 mm. Hg intraocular pressure the rate of outflow into the general circulation was on an average 12.0 ± 2.3 μL per minute higher than in the control eyes. The mean rate of flow into the tissues was 0.10 μL per minute higher in the eyes with a high pressure than in the other ones. This difference was not significant. In all experiments the net rate of aqueous humor production was much lower in the eye at high pressure than in the control. The mean value for the difference divided by the average pressure rise on the high pressure side was 0.509 ± 0.095 μL per minute per millimeter Hg. This figure represents the suppression of the rate of aqueous humor formation that was produced by a rise of 1 mm. Hg in intraocular pressure. The gross facility of outflow was calculated from the rate of inflow from the reservoir into the anterior chamber and the pressure rise that caused this inflow. The mean value was 0.509 ± 0.095 μL per minute per millimeter Hg.

The control eyes. The mean intraocular pressure in the 16 control eyes at the start was 8.0 ± 0.7 mm. Hg. There was no significant change in mean pressure with time. The rate of uveoscleral drainage of aqueous humor was 0.63 ± 0.08 μL per minute; the rate of flow into the general circulation was 0.53 ± 0.07 μL per minute. The mean rate of aqueous humor production in the control eyes was 1.16 ± 0.09 μL per minute. To permit a comparison with data obtained in dead animals, the amount of labeled protein recovered in the ciliary body, the choroid-retina preparation, and the sclera was calculated. It corresponded to 25.1 ± 3.3 μL anterior chamber fluid.

Experiments in dead animals. Since in the experiments with bulk outflow from the anterior chamber there was no blood flow in the extraocular tissues that could

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**Table III.** The apparent drainage of aqueous humor by vascular routes and by uveoscleral routes in eyes maintained at low intraocular pressures

<table>
<thead>
<tr>
<th>Drainage by vascular routes (μL/minute)</th>
<th>Drainage by uveoscleral routes (μL/minute)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOP 1.5 mm. Hg</td>
<td>IOP 3.0 mm. Hg</td>
</tr>
<tr>
<td>0.02</td>
<td>0.16</td>
</tr>
<tr>
<td>0.04</td>
<td>0.04</td>
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<tr>
<td>0.02</td>
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<td>0.01</td>
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<td>0.03</td>
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<td>0.03</td>
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</tbody>
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**Table IV.** Net formation of aqueous humor and the drainage of anterior chamber fluid in eyes at normal and 35 mm. Hg intraocular pressures

<table>
<thead>
<tr>
<th>Drainage by vascular routes (μL/minute)</th>
<th>Drainage by uveoscleral routes (μL/minute)</th>
<th>Net formation of aqueous humor (μL/minute)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IOP 35 mm. Hg</td>
<td>Control</td>
<td>IOP 35 mm. Hg</td>
</tr>
<tr>
<td>22.18</td>
<td>0.16</td>
<td>1.55</td>
</tr>
<tr>
<td>14.24</td>
<td>0.18</td>
<td>0.36</td>
</tr>
<tr>
<td>11.56</td>
<td>0.30</td>
<td>0.96</td>
</tr>
<tr>
<td>10.90</td>
<td>0.43</td>
<td>0.60</td>
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<tr>
<td>10.30</td>
<td>0.63</td>
<td>0.45</td>
</tr>
<tr>
<td>5.35</td>
<td>0.57</td>
<td>0.46</td>
</tr>
</tbody>
</table>
help to wash radioactive fluid out of the extraocular blood vessels and since storage probably had increased the permeability of these blood vessels, it did not seem justifiable to calculate values for uveoscleral flow in the same way as in the in vivo experiments. It seemed possible to draw some conclusions, however, from the amounts of labeled protein which were recovered in the ciliary body, the choroid, and the sclera and which, therefore, most probably had not leaked out of the vascular routes. In 10 eyes with no inflow from the reservoir, 4.2 \( \mu \)L had entered the tissues mentioned. On the side with an inflow from the reservoir of about 4 \( \mu \)L per minute an average of 58.5 \( \mu \)L was recovered in the ciliary body, the sclera, and the choroid preparation. The mean difference between the amount recovered in these tissues on the two sides, 54.4 \( \pm \) 8.4 \( \mu \)L, was significant, \( P < 0.01 \). In 10 experiments with inflow rates of 2 and 5 \( \mu \)L per minute in the two eyes, the average recovery figures after 1 hour were 34.6 and 64.8 \( \mu \)L, respectively. The mean difference between the eyes, 30.3 \( \pm \) 7.5 \( \mu \)L, was statistically significant, \( P < 0.01 \). In 7 experiments with inflow rates of 4 and 10 \( \mu \)L per minute the average recovery figures were 109.2 and 142.4 \( \mu \)L, respectively. The average intraocular pressure required to give inflow rates of 4 \( \mu \)L. and 10 \( \mu \)L per minute were 14.1 mm. Hg and 32.6 mm. Hg, respectively.

In the experiments without inflow into one eye a measure could be obtained for the effect of diffusion on protein drainage from the anterior chamber. In the 10 eyes the average recovery in the ocular and extraocular tissues was 12.8 \( \pm \) 1.1 \( \mu \)L. Of this apparent volume an average of 1.1 \( \pm \) 0.2 \( \mu \)L was recovered in the ciliary body, 2.4 \( \pm \) 0.4 \( \mu \)L in the sclera, and 0.7 \( \pm \) 0.3 \( \mu \)L in the choroid preparation.

**Discussion**

**Diffusion and flow.** The dead eyes without an inflow and thus without a bulk outflow from the anterior chamber, diffusion into the ocular and extraocular tissues gave an apparent uveoscleral flow of 12.8 \( \mu \)L per 60 minutes = 0.21 \( \mu \)L per minute.

In living eyes too, diffusion contributes to the accumulation of radioactive protein in the tissues around the anterior chamber. However, for reasons discussed previously, a diffusion usually seems to be of minor importance for the elimination of protein from the anterior chamber. This opinion is supported by the fact that in the living monkeys with normal eye pressure, during 60 minutes on an average 25.1 \( \mu \)L labeled fluid had entered the ciliary body, the choroid, and the sclera which parts in dead eyes with no inflow from the reservoir appeared to contain only 4.11 \( \mu \)L after the same period of time. Further, in a previous study with pilocarpine-induced tone in the ciliary muscle, the average recovery in the tissues in 2 hour experiments was 8.4 \( \pm \) 1.2 \( \mu \)L and uveoscleral flow was calculated to be 0.07 \( \pm \) 0.01 \( \mu \)L per minute. The present findings in dead eyes suggest that even with no tone in the ciliary muscle very little labeled protein diffuses into it. Strictly, it cannot be excluded that in the dead eyes at low pressure the spaces between the muscle bundles may be more narrow than at normal pressures. Diffusion of labeled albumin into the muscle in the present experiments in dead eyes may therefore have been less than it would have been at a normal pressure. Still it seems very probable that the figure for uveoscleral flow in pilocarpine treated eyes represents near to a maximum figure for the overestimation in uveoscleral flow determinations that may be caused by diffusion in 2 hour experiments. In 1 hour experiments the error may be larger but is of course less than twice that in the 2 hour experiments mentioned which is less than 0.14 \( \mu \)L per minute. The error cannot be corrected in the individual eye but if effects on uveoscleral flow are judged from pairs of eyes (control and treated), it seems reasonable to assume that any differ-
ences are due mainly to differences in flow.

**Mode of bulk drainage of aqueous humor.** The present experiments confirm that the rate of rapid flow of aqueous humor into the general circulation is very much influenced by the intraocular pressure. Uveoscleral flow in living animals is very little influenced by changes in pressure between 4 and 35 mm Hg but is clearly reduced at 2 mm Hg. In dead animals uveoscleral flow appears to be pressure sensitive from low levels up to at least a pressure somewhere between 14 and 32 mm Hg. The reason for the difference between dead and living animals is not clear.

In the 1 hour experiments with living animals at an intraocular pressure of 4 mm Hg when there was still a normal movement of labeled material into the anterior uvea, there appeared to be very little, 0.00 to 0.02 \( \mu \text{L} \) per minute, movement of labeled fluid into the general circulation. This indicates that very little labeled material entered the blood vessels of the uvea by pinocytosis and diffusion.

In the 5 hour experiments, too, the rate of flow of labeled material into the general circulation was very low in the eyes maintained at an intraocular pressure of 1.5 mm Hg. In the eyes at 3.0 mm Hg the flow rate was very low in 5 of 6 eyes; in the sixth the venous pressure may have been very low making it possible for some aqueous humor to pass through the vascular routes. In all these experiments small amounts of the labeled protein passing through the uveoscleral routes may have arrived in the blood via the lymph vessels.

Pinocytosis is generally thought to be a pressure insensitive process. Then, since in most of the 60 minutes and 5 hour experiments, at 4 and 3.0 mm Hg, respectively, considerable amounts of labeled albumin were present in the uveal tissues and little arrived in the blood, it seemed justifiable to conclude that if there was any drainage of aqueous humor by pinocytosis into the uveal blood vessels it would account for only a few per cent of the total drainage at normal intraocular pressures.

**Intraocular pressure and net formation of aqueous humor.** In a previous study\(^1\) it was shown that in deeply anesthetized animals with a mean arterial blood pressure of 70 mm Hg the rate of aqueous formation is reduced by a rise in intraocular pressure. The average figure for the suppression was 0.123 \( \mu \text{L} \) per minute per millimeter Hg. It was suggested that in normal animals the suppression tendency might be smaller. In rhesus monkeys Brubaker and Kupfer,\(^2\) also using a method which was supposed to give an overestimate of the normal suppression tendency, reported a value of 0.19 \( \mu \text{L} \) per minute per millimeter Hg. In the present experiments the average difference in net formation between the eyes at high pressure and the controls corresponded to a suppression of 0.055 ± 0.013 \( \mu \text{L} \) per minute per millimeter Hg. The animals were in a better condition than in the previous experiments; the mean arterial blood pressure was about 85 mm Hg. Experiments in animals with a procedure similar to that used in the present study but with less precision in the determinations of aqueous humor production have shown that in two similar groups of 10 animals each the average aqueous humor production at 10.8 mm Hg was 1.31 \( \mu \text{L} \) per minute and at 22.0 mm Hg it was 0.68 \( \mu \text{L} \) per minute.\(^4\)

In the same study in two other groups with 10 animals in each and at the same two pressures, the corresponding flow figures were 1.17 and −0.17 \( \mu \text{L} \) per minute. These values give tentative values for suppression of aqueous humor formation of 0.056 \( \mu \text{L} \) per minute per millimeter Hg and 0.120 \( \mu \text{L} \) per minute per millimeter Hg, respectively (average value 0.088 \( \mu \text{L} \) per minute). Taken together, the studies in cynomolgus monkeys suggest that in experiments when the animals are in good condition the suppression of the rate of aqueous production is of the order of 0.05 to 0.10 \( \mu \text{L} \) per minute per millimeter Hg, and that at low blood pressures it may be higher.

The physiological basis for the suppression of net rate of aqueous humor forma-
tion by a rise in intraocular pressure is not clear in details. It has been reported previously that an increase in intraocular pressure reduces the rate of blood flow through the uvea and reduces also the effective hydrostatic filtration pressure in the uveal capillaries. This latter effect may give a reabsorption of fluid from the anterior and posterior chambers or a reduced contribution to aqueous humor formation by ultrafiltration.

The fact that at an intraocular pressure of 2 mm. Hg the rate of aqueous humor production was very much increased gives no information about the normal regulation of the secretion of aqueous humor. Both backflow of plasma from the vascular outflow routes and leakage of interstitial tissue fluid from the uvea may have contributed to give the high rate of flow. Also the figures for aqueous production at an intraocular pressure of 4 mm. Hg may have been influenced by such mechanisms.

**Gross facility, pseudofacility, and vascular route facility.** The figure for the suppression of net formation of aqueous humor by a rise in intraocular pressure, 0.055 μL per minute per millimeter Hg, has the dimensions of facility, and in conventional facility measurements the suppression appears as a pseudofacility component included in the gross facility determined. In the present experiments pseudofacility accounted for 10.8 ± 1.7 per cent of the total gross facility. The previous determinations both in cynomolgus monkeys and in rhesus monkeys gave values of about 30 per cent. As mentioned above the previous results were obtained in animals suspected to have an exaggerated pseudofacility because of low blood pressure or with methods that may have given overestimates of the pseudofacility.

In the present experiments in living animals the flow through the uveoscleral routes was not significantly influenced by the intraocular pressure in the pressure range 4 to 35 mm. Hg. These routes therefore did not contribute significantly to the gross facility determined. Thus, about 90 per cent of the gross facility was due to vascular route facility.

**The intraocular pressure.** The present results indicate that in cynomolgus monkey, under steady state conditions, the intraocular pressure (IOP) is a function of the net rate of aqueous humor formation (Fₙ), the rate of uveoscleral drainage (Fᵤ), the recipient venous pressure (Pᵥ), and the vascular route facility of outflow, which is approximately 0.06 μL per minute per millimeter Hg less than the gross facility (Cᵥ).

\[
IOP = Pᵥ + \frac{(Fₙ - Fᵤ)}{(Cᵥ - 0.06)}.
\]

Both in rabbits and cats uveoscleral flow is a negligible fraction of the total flow. Whether there is uveoscleral drainage of aqueous humor in the human eye is not known at present. The magnitude of the pseudofacility in human eyes also has not been determined but on indirect evidence it has been suggested by Goldmann to be about 0.05 μL per minute per millimeter Hg.

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