Ophthalmic pulse studies

I. Influence of intraocular pressure

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The relationship of the ophthalmic pulse amplitude to the intraocular pressure has been described in rabbits and dogs. The effect of a suction cup on the intraocular pressure has been investigated in rabbit eyes and human eyes. Sample pulse tracings have been obtained using a suction cup on rabbits and man. Two estimates were made of the volume changes associated with the ophthalmic pulse wave: (1) by using the pressure variation and ocular compliance, (2) by direct measurement with a mercury strain gauge. An analogue model, dependent only on mechanical properties of the eye and ocular blood vessels, has been described which gives an approximate reproduction of the pulse amplitude versus intraocular pressure curve. In any study correlating pulse amplitude with a disease process, the intraocular pressure at the time of measurement must be considered. Comparisons of the ophthalmic pulse in two eyes can actually be done only at the same intraocular pressure. Increased pulse amplitude in glaucoma can be explained by the response of the pulse amplitude to the intraocular pressure.

The pulsatile character of the intraocular pressure was recognized in cannulated eyes by Weber in 1850 and as oscillations of the lever arm of the indentation tonometer by Schiötz in 1905. The pulse is also revealed by oscillations of the contact lines in applanation tonometry. Langham and Casey recorded the ophthalmic pulse using a fluid-filled suction cup system, and others have used electronic tonometers and dynamometers. The ophthalmic pulse has been used as a substitute for ophthalmodynamometry in estimating carotid circulation. Britton and associates used the ophthalmic pulse and carotid compression maneuvers to trace the path of collateral circulation in thrombosis of the internal carotid. Davanger has found an enlarged ophthalmic pulse at higher intraocular pressure.

Peripheral pulses are being studied in peripheral vascular disease. The pulse amplitude, the first derivative of the pulse upslope, the pulse timing, the ratio of flow to pulse, and pharmacologic effects on all of these are being evaluated in clinical vascular disease.

Each of the clinical methods for estimating the ophthalmic pulse elevate the intraocular pressure; therefore, any analysis of the ophthalmic pulse must include the effect of intraocular pressure.

Methods

Cannulation experiments. The ophthalmic pulse was recorded from the eyes of healthy New Zealand rabbits weighing 2 to 3 kilograms each. Urethane anesthesia was used, approxi-
Valve to pressure supply syringe

Fig. 1. Manometric system.

Fig. 2. Definition of the amplitude of the pulse in intraocular pressure.

mately 6 Cm. per rabbit. The anterior chambers were cannulated with 23 gauge cannulas. These were connected to a Sanborn 267B transducer by approximately 20 cm. of PE 50. (Fig. 1). The transducers were led to 1100 B carrier preamplifiers in a Sanborn 350 direct writing eight channel recorder. A simultaneous EKG or femoral arterial pressure was monitored. The cannulas and transducers were filled with normal saline. The frequency response of the manometric system was checked by the use of a pressure step function produced by a balloon puncture. The frequency response was on the order of 100 c.p.s. with about a 5 per cent overshoot to the step function.

The ophthalmic pulse was recorded at normal intraocular pressure, using zero suppression in the 1100 B carrier preamplifier. Stepwise 5 mm. Hg elevations of the intraocular pressure were performed until the intraocular pressure exceeded the systolic pressure in the femoral artery. At each pressure level, the supply valve was closed, and the pulse was recorded.

Similar stepwise reductions in the intraocular pressure were made until the intraocular pressure was about 15 mm. Hg. The process of elevation to above systolic pressure and reduction to normal levels was repeated from three to five times. When the intraocular pressure was increasing or decreasing, the following procedure was used for averaging the pulse amplitude. A line was drawn connecting the peaks of the pulses and a line connecting the bases of the pulses. The vertical height between these two lines was used to estimate the pulse height (Fig. 2).

The same procedure was used in six eyes of three collie dogs under pentobarbital anesthesia.

Mercury gauge experiments. In three rabbits the same cannulation experiment described above was performed, with the addition of a fine latex tube filled with mercury around the equator of the cannulated eye. This tube was held in place by four stay sutures. As the eye enlarges during a pulse, the latex tube stretches, the cross sectional area of the mercury decreases, and the length of the mercury column increases. The resistance of the column of mercury increases with good linearity for small changes in length. This mercury-filled latex tube, called a mercury strain gauge, was connected to an impedance matching Wheatstone bridge and then to a Sanborn 1100 B carrier preamplifier in the 350 recorder. Small rapid volume increments of saline were injected into the anterior chamber to provide a resistance versus volume calibration of the mercury gauge and a direct estimation of the pulsatile volume changes of the eye.

Suction cup experiments. Healthy New Zealand rabbits, similar to those described above, were placed under urethane anesthesia, and the vitreous was cannulated approximately 6 mm. behind the limbus. The same pressure recording equipment was used as previously. The rabbit
eyes were set at varying initial intraocular pressures. A suction cup with a 10, 12, or 14 mm. diameter was applied. The supply pressure valve was closed; then the suction in the cup was increased stepwise, and the intraocular pressure recorded at each level of suction.

Sample records of the ophthalmic pulse were made with a suction cup at different intraocular pressures, and simultaneous pulses were obtained from the vitreous cavity.

Human eyes were enucleated at necropsy. Intraocular pressure was measured at each level of suction for initial intraocular pressures of 17 and 38 mm. Hg by techniques similar to those used on the rabbits. The bell-shaped suction cup described by Langham was used.

Also, records of the ophthalmic pulse were made in patients at different levels of suction.

Results

Cannulation experiments. Successful plots of the ophthalmic pulse amplitude versus the intraocular pressure were obtained in 31 rabbit eyes.

Normal intraocular pressure in these rabbits under urethane anesthesia varied between 17 and 22 mm. Hg. The ophthalmic pulse amplitude at this intraocular pressure was about 0.2 mm. Hg. The pulse contour was blurred and irregular. A respiratory wave was often superimposed at a frequency of about 0.5 per second and an amplitude of about 1.5 mm. Hg.

Curve 1. As the intraocular pressure was increased, the pulse amplitude increased until it reached a plateau of about 1.5 mm. Hg at an intraocular pressure of about one half the diastolic pressure in the femoral artery. In most rabbit eyes, the pulse amplitude remained at this level as the pressure was increased until the intraocular pressure equaled the diastolic pressure in the femoral artery. When the intraocular pressure was increased further, the pulse amplitude decreased to zero at the point where the intraocular pressure reached the systolic pressure in the femoral artery. If the intraocular pressure was increased further, the pulse remained at zero. This plateau curve was followed by 22 of 31 rabbit eyes on the first stepwise elevation and will be called Curve 1, as shown in Fig. 3. The height of this plateau was 1.5 mm. Hg (σ = 0.6).

Curve 2. When the intraocular pressure was reduced, the pulse amplitude curve did not follow the same plateau as the

![Fig. 3. Pulse in intraocular pressure versus intraocular pressure. Curve 1 is usually obtained as the intraocular pressure is raised for the first time: Curve 2 is obtained with increasing or decreasing intraocular pressure on all subsequent determinations and occasionally on the first determination.](http://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/932993/)
ascending curve, Curve 1. Instead, the pressure continued to rise as the intraocular pressure fell below diastolic pressure and formed a bell-shaped curve shown in Fig. 3, called Curve 2. The peak of this curve was 2.3 mm. Hg ($\sigma = 1.2$). As the intraocular pressure was raised again, the pulse amplitude followed the same curve. Subsequent pulse amplitude versus intraocular pressure curves followed Curve 2 in all eyes. There was, however, some variation in the first ascending pulse amplitude versus pressure curve. In 4 of the 31 eyes a bell-shaped curve, like Curve 2, was obtained in the first stepwise elevation of pressure.

Curve 3. In 5 of the 31 eyes, the pulse contour followed Curve 1 until the intraocular pressure was close to diastolic value, where the pulse amplitude rose to the amplitude of Curve 2. Curve 2 was followed from then on. This pattern is shown as Curve 3 in Fig. 4.

Representative ophthalmic pulse wave forms at different intraocular pressures are shown in Fig. 5. EKG lead III is shown simultaneously for timing. A spontaneous premature beat that did not result in ventricular contraction appears in Fig. 6. The resultant fall in intraocular pressure is shown. This premature beat relates a QRS complex on the EKG to the corresponding peak in ophthalmic pulse.

The timing of the ophthalmic pulse is difficult because the waves have slightly different patterns at different pressure elevations. However, there do not appear to be any gross differences in the arrival of the pulse wave at different intraocular pressures (Fig. 5). The first derivative ($dP/dt$) appeared related only to the pulse amplitude. We found no significant effects from oculocardiac or oculorespiratory reflexes.

In the dog, the pulse amplitude rose with intraocular pressure and ascending and descending curves were in better agreement than in rabbit eyes. The pulse contours were similar to those in rabbit eyes; however, the plateau of Curve 1 was slightly more rounded.

Mercury gauge experiments. The volume pulse wave form obtained with a mercury resistance gauge in a rabbit eye is shown in Fig. 7. The simultaneous pressure contour from the anterior chamber and the right femoral artery is shown. The pressure contour from the anterior...
Fig. 5. Wave form and phase of intraocular pulse at different intraocular pressures.

Fig. 6. Effect of a spontaneous premature beat (Δ) on intraocular pressure pulse wave form, permitting correlation of a QRS complex to an individual pulse.

Fig. 7. Wave form of ophthalmic pulse obtained with a mercury strain gauge, compared to simultaneous pressure wave obtained in the vitreous of the same rabbit eye. Approximate volume calibration of pulse from the mercury gauge = 0.5 mm$^3$.\(^3\)
chamber is definitely more rounded than usual and probably represents a change in the compliance of the eye from the slight tension of the latex tube around the eye. On calibration of the mercury resistance gauge, the volume pulse averaged 0.5 mm.² between intraocular pressures of 35 to 50 mm. Hg. This compares with 0.6 mm.² obtained over the same pressure ranges with the use of figures for the compliance of the rabbit eye obtained in our laboratory by standard methods. These findings are consistent with the pressure pulse in the eye being caused entirely by a change in volume equivalent to the pressure change.

**Suction cup.** The intraocular pressure versus suction curves for eyes with different initial intraocular pressures are illustrated in Fig. 8. The intraocular pressure versus suction calibration was roughly similar with different size cups. A record of the ophthalmic pulse obtained with a suction cup is visualized in Fig. 9. Generally, the pulse amplitude with a suction cup was slightly lower than the vitreous pulse obtained simultaneously with a needle, and the wave form was always somewhat more rounded. The use of a thin latex membrane over the suction cup further reduced the pulse amplitude, and the use of the membrane was abandoned. The shape of the pulse amplitude versus intraocular pressure curve when the suction cup was used was very similar to that in cannulated eyes. However, there was even more variation; analyses were not done on this data.

The pressures reached in human eyes with various levels of suction at two levels of initial intraocular pressure are graphed in Fig. 10, while Fig. 11 shows an ophthalmic pulse recorded from a patient with the Langham suction cup.

**Discussion**

A fixed change in ocular blood volume produces a larger change in intraocular pressure as the intraocular pressure increases. When the intraocular pressure exceeds diastolic arterial pressure, blood can flow into the eye only during part of the pulse cycle. These facts may explain the initial increase in pulse amplitude and

![Fig. 8. 14 mm. suction cup on rabbit eye. Effect of suction on intraocular pressure from three different levels of initial intraocular pressure.](http://iovs.arvojournals.org/pdfaccess.ashx?url=data/journals/iovs/932993/ on 05/29/2017)
later decrease, but do not permit an exact prediction of the shape of the amplitude versus intraocular pressure curve. The plateau of the pulse amplitude versus intraocular pressure curve disappears on subsequent determinations; therefore, some change must occur in the blood vessels during these experiments. It is possible that the elevated intraocular pressure reduces the blood flow through the eye sufficiently to initiate changes in the properties of the vessel wall.

To understand the mechanics of the effect of intraocular pressure on the ophthalmic pulse amplitude, we turned to a preliminary analogue computer model of the eye developed by William W. Whetham in collaboration with us. This model is shown in Fig. 12. The model is based on a simplified concept of the eye which is depicted in Fig. 13. In this model, pressures are in millimeters of mercury, flows are in cubic millimeters per minute, and time is in minutes except where noted.

Our preliminary model does not include neural, osmotic, or chemical effects.

Table I

<table>
<thead>
<tr>
<th>Term</th>
<th>Symbol</th>
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<tbody>
<tr>
<td>Intraocular pressure</td>
<td>( P )</td>
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<tr>
<td>Blood pressure in the blood reservoir</td>
<td>( P_b )</td>
</tr>
<tr>
<td>Transmural pressure</td>
<td>( P_m = P_a - P )</td>
</tr>
<tr>
<td>Venous pressure outside the globe</td>
<td>( P_v )</td>
</tr>
<tr>
<td>Ocular volume</td>
<td>( V_a )</td>
</tr>
<tr>
<td>Ocular blood volume</td>
<td>( V_b )</td>
</tr>
<tr>
<td>Aqueous inflow</td>
<td>( q_i = 2 \text{ mm}^3 \text{ per minute (constant)} )</td>
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**Fig. 9.** 14 mm. suction cup on rabbit eye. Ophthalmic pulse record.

**Fig. 10.** Suction cup on enucleated human eye. Effect of suction on intraocular pressure from two levels of initial intraocular pressure.
Aqueous inflow is assumed constant (see Table I for symbols). It was planned to use both the linear and square root pressure-flow relationships for aqueous and blood. In preliminary work with the model, simulations of the effects of constant rate infusion, carotid ligation, venous ligation, and pressure decay curves were obtained, and the model predicted the responses of the intraocular pressure, blood volume, blood inflow, blood outflow, aqueous outflow, and total ocular volume better with the square root relationship:

$$q_o = C_2 (P - P_{ev})^{1/2}$$

with $C_2$ constant. This pressure-flow relation is the one predicted by theoretical hydrodynamics for flow from a reservoir through a small orifice. Although Becker and Constant found a linear pressure-flow relationship in enucleated eyes, experiments in enucleated rabbit and cat eyes by Armaly and in the eyes of dead cats by Clausen and Harris suggest that the facility of outflow decreases with increasing intraocular pressure when the depth of the anterior chamber is carefully controlled. Aqueous outflow facility is normally defined:

$$C = \frac{q_o}{P - P_{ev}}$$

If

$$q_o = C_2 (P - P_{ev})^{1/2}$$

with $C_2$ constant, then $C$ is not constant; instead

$$C = \frac{C_2}{(P - P_{ev})^{1/2}}$$

In enucleated eyes $P_{ev}$ equals zero and the $C$ is inversely proportional to the square root of intraocular pressure. This is a fair approximation for certain physiological conditions.
approximation of Armaly's experimental results.

The pressure flow relationships for ocular blood flow are not known. Organs with autoregulation, like the kidney, have a pressure-flow relationship which approximates the square root. Others, like the rabbit ear, show a linear pressure-flow relationship. The changes from Curve 1 to Curve 2 resemble the changes in peripheral circulation in the reactive hyperemia test and suggest that considerable tone is normally present in the ocular vessels. In our first working model, blood inflow was assumed to be:

$$q_A = G_A (P_A - P_B)^{1/2}$$

with $G_A$ constant and equal to 26 mm.$^3$ (mm. Hg)$^{-1}$. Blood outflow was:

$$q_B = G_B (P_B - P_{ev})^{1/2}$$

where $G_B$ is a function of transmural pressure, $P_M$, and was adjusted to give an inflow and outflow of 200 mm.$^3$ per minute at normal steady state ($P = 19, P_M = 11, P_A = 90, P_B = 30, P_{ev} = 10$ mm. Hg), and a linear decrease in blood outflow to zero as intraocular pressure is raised and $P_M$ approaches zero. Bill's experiments in living rabbits and Moses' model suggest this response. A low level of blood flow was assumed to facilitate the integration of $q_A - q_B$ to obtain blood volume. With a more stable analogue computer, blood flow levels up to 2,000 mm.$^3$ per minute will be used and will improve the computer response to simulated step...
changes in venous pressure. $G_2$ is a constant adjusted to give 2 mm.$^3$ per minute aqueous outflow when $P = 19$ mm. Hg and $P_{ev} = 10$ mm. Hg. The initial pressure-volume relationship used was Friedenwald's$^{18}$, $K = 0.046$ mm.$^3$ (for natural logarithms). The pressure-volume relationship in the blood reservoir is an approximation of that found in veins,$^{14}$ with $\lambda$ about 0.08 mm.$^3$. Later models will explore other pressure-volume and pressure-flow relations for blood and aqueous, and a different simulation of aqueous secretion may be used (see Table II).

Fig. 15. Simulation of a 33 mm.$^3$ per minute infusion beginning at the step in $dV/dt$, showing changes in parameters predicted by analogue model.
### Table II. Mathematical relations

<table>
<thead>
<tr>
<th>Mathematical relation</th>
<th>Symbol</th>
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<tbody>
<tr>
<td>Aqueous outflow</td>
<td>$q_s = G_s (P - P_{ov})^{\frac{1}{2}}$</td>
</tr>
<tr>
<td>Blood inflow</td>
<td>$q_A = G_A (P_A - P_B)^{\frac{1}{2}}$,</td>
</tr>
<tr>
<td>Blood outflow</td>
<td>$q_n = G_n (P_n - P_{ov})^{\frac{1}{2}}$,</td>
</tr>
<tr>
<td>Intraocular pressure versus volume</td>
<td>$\ln \frac{P}{P_0} = K (V - V_0)$</td>
</tr>
<tr>
<td>Blood volume versus transmural pressure</td>
<td>$\ln \frac{P_m}{P_{m0}} = \lambda (V_n - V_m)$</td>
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The model was applied to the intraocular pulse problem by simulating a 33 c.mm. per minute constant rate infusion which produced a slow increase in pressure. A slow pulse was applied in the arterial supply pressure. The ophthalmic pulse pressure wave was recorded with an AC system, and the pulse amplitude was plotted against the intraocular pressure. This resulted in a curve which is shown in Fig. 14.

The model gives fair predictions of the pulse amplitude versus intraocular pressure curve. The pulse amplitude at normal intraocular pressure is of the right magnitude, the peak pulses are also approximately of the right magnitude, and the fall of the intraocular pressure begins close to diastolic pressure. The actual analogue computer trace is shown in Fig. 15 and shows the simulated arterial pressure $P_A$, the transmural pressure $P_m$, the intraocular pressure response $P$, an inverted pulse amplitude, the rate of change in ocular volume, ocular blood volume, the blood inflow, and the blood outflow.

Changes will have to be made in our preliminary model to reproduce the plateau type curve, Curve 1, or to obtain a better reproduction of the more usual, Curve 2. Even our preliminary model gives a fair prediction of the final pulse amplitude versus intraocular pressure curve. It is also consistent with the data of Bettman and colleagues on blood volume changes and Bill's work on relative intraocular pressures of the eye with different intraocular pressures.

### REFERENCES