THE VENOUS PRESSURE OF THE EYE AND ITS RELATION TO THE INTRA-OCULAR PRESSURE.

BY W. STEWART DUKE-ELDER (Plimmer Research Fellow).

(From the Department of Physiology and Biochemistry, University College, London.)

In the estimation of the venous pressure of the eye, five different methods have hitherto been employed with results so much at variance that the whole question of the physiology of the aqueous is still a matter of dispute. By some observers it is held that a pressure difference exists between the chambers of the eye and the exit veins such as to allow a drainage of fluid by a hydrostatic flow, by others that absorption occurs by osmotic forces alone; some have concluded that the pressure gradient from capillary to aqueous is sufficient to allow the formation of the latter by a process of simple transudation, while others insist that it is not sufficient, and that consequently the mechanism of formation is a secretory one, involving an active expenditure of energy by the cells of the ciliary body.

These experimental procedures may be briefly reviewed:

1. The compression method of v. Recklinghausen was employed by Seidel (29) and Hiroishi (14), who, applying a pressure chamber over the episcleral veins as they are seen under the conjunctiva, found the pressure at the point of their obliteration to be very much lower (10-18 mm. Hg in dogs and rabbits) than the intra-ocular pressure. The measurement here made, however, is that of the pressure in the veins outside the eye virtually in the orbit, and to assume that it represents the intra-ocular venous pressure is quite unjustified.

2. A very large number of experimenters, most recently Seidel (28) and Hiroishi (14), have drawn conclusions as to the method of exit of the intra-ocular fluids, and the relative pressures in the eye and in the veins, from experiments involving the injection of dyes. A dye having been introduced into the anterior chamber, the appearance of colouring matter in the episcleral veins is taken as necessarily indicating a fall in pressure between these two points. The introduction of a needle, however, into the eye, and the injection thereinto of any material profoundly changes the pressure equilibrium, and completely alters the circulation. The conditions thus obtaining can in no way be called normal, and therefore physiological conclusions based on intra-ocular injections are patently open to criticism.

3. Weiss (35), experimenting on rabbits, inserted a cannula into a vortex vein, thus measuring the pressure directly. He obtained very varying results. The venous pressure ranged from 33 to 63 mm. Hg and was invariably higher than the intra-ocular, the ratio varying from 12:10 to 19:10. Lullies (19), using the same technique in dogs, came to the same conclusion, his results varying from 21 to 39 mm. Hg. The blockage of a vortex

vein, however, involves the production of hyperæmia with which the collateral venous channels are unable to cope, and this invalidates any pressure readings thus obtained. The inadequacy of the anastomoses can readily be seen in the case of the albino rabbit: if a ligature be passed round one of these veins subconjunctively, a zone of hyperæmia appears, which is seen most clearly in the iris, limited to the quadrant drained by the vein in question; later a considerable rise of intra-ocular pressure occurs (10-20 mm. Hg). In the dog the same reaction occurs although it is much less pronounced, a rise in pressure of 7-10 mm. resulting. The variation in rise of pressure is due to a difference in the richness in anastomoses in these animals; in the dog there is a direct communication between the anterior (ciliary) system of veins and the posterior (vortex), in the rabbit there is not; on obliterating one efferent channel in the dog, therefore, more anastomotic avenues are available than in the rabbit, and the rise of pressure is less marked. Lullies' results are consequently more nearly correct than those of Weiss, and of the former's the lowest come nearest to the truth.

4. With a view to determining the relative pressure relation between the aqueous and the venous channels, Wedgefarth (34) introduced a fine needle into an episcleral vein in the dog, pushed it down through the sclera into the anterior chamber, and then withdrew it and ligated the vein; since no blood flowed into the eye, he concluded that the pressure in the latter was greater than the venous pressure. A fistula was here made, however, at a moment when the normal pressure equilibrium was completely disturbed; it was made through raw tissue, and immediately afterwards the blood flow was stopped, thus providing every opportunity for the formation of clots; while the methods adopted subsequently to demonstrate the patency of the channel were merely such as would wash away any newly formed clot which might have been deposited at the time of fistulisation.

5. Bailliart (2) and Magitot (22) have made an extensive study of the ocular circulation by making use of a compression tonometer, which registers the force applied by the excursion of a standardised spring. On compressing the globe of the eye with the footpiece of this instrument, the veins at the optic disc are simultaneously observed through the ophthalmoscope. In a certain proportion of eyes there is a spontaneous pulse in these veins just at their exit at the optic nerve head (58 p.c., Bailliart); the increment of pressure on the globe necessary to abolish this pulse shows how much higher the maximum venous pressure is than the intra-ocular pressure. Of the others which show no spontaneous pulse, 12 p.c. show the pulse if the globe is compressed; the pressure thus required to produce the pulse shows again how much higher the venous pressure is than the intra-ocular. In the remaining 30 p.c. no pulse can be elicited on pressure; in these the venous pressure is consistently below the intra-ocular. These deductions are, however, open to criticism, since, as will be pointed out later, several complicating factors other than mere pressure differences enter into the mechanics of the formation of the venous pulse of the eye.

The pressure in the intra-scleral veins. The consideration of the above results leads to the conclusion that the essential feature of any technique to determine the pressures of the venous exits must be the maintenance of a normal intra-ocular pressure as well as the avoidance of any venous hyperæmia. As best fulfilling these conditions, the technique employed by Carrier and Rehberg(7) in the estimation of capillary pressure was adopted and modified to suit the conditions of the case.

Dogs were employed in the investigation, since these are the most convenient laboratory animal with tolerably large veins, and in them, as we have seen, the anastomoses of the venous channels are very efficient. Injection experiments in these animals show that the venous blood from the uveal tract is drained by two systems: (a) from the anterior part of the chorioid, the ciliary body, and iris by a complicated, inter-anastomosing ring plexus in the substance of the sclera (taking the place of the Canal of Schlemm), which empties into a second ringplexus-the Circle of Hovius-running round behind the corneo-scleral junction, near the surface of the sclera, but still in its substance, being covered by a thin layer of scleral tissue through which it is clearly visible; (b) from the main body and posterior part of the chorioid by four or five vortex veins which leave the eye equatorially and are carried away via the recti muscles. The Circle of Hovius is drained by two veins, or groups of veins, anteriorly, running forwards to join the orbital veins, and posteriorly by intra-scleral vessels, running backwards to anastomose with the vortices, lying, like the Circle of Hovius itself, in the outer layers of the sclera, and visible through its substance.

A piece of glass tubing 4 mm. in diameter was drawn to a very fine sharp point at the end, the process being repeated several times to obtain a very short and fine tip. A side arm near the point was connected by a rubber tube to a levelling bulb filled with physiological citrate solution. As the levelling bulb is raised and lowered the citrate column in the tube follows suit, and a pressure is therefore exerted at the capillary tip equal to the height of this column. When the tip is immersed in blood, there is a theoretical error in the pressure measurements obtained depending on the difference between the surface tension of the citrate solution and blood, but its magnitude is so small that it may be neglected. When the tip is inserted into the lumen of a vein, blood will flow into the tube if the venous pressure is higher than the pressure of the citrate column; if the venous pressure is lower, citrate will flow into the vein. By raising and lowering the levelling bulb and observing the capillary point through a dissecting microscope, a very exact pressure measurement can be obtained. The intra-scleral veins of the Circle of Hovius and the posterior anastomosing veins just described are ideal for the method, since under the microscope they appear large enough for the capillary point to be introduced into them without hesitation and for it to be held in their lumen for some time. Meanwhile, the investing scleral tissue, by keeping the vessel patent, ensures the ready entrance of the point into the lumen, and at the same time allows perfect freedom for the continuance of the circulation (observable under the microscope), thus preventing any hyperæmia or damming up of the

stream. The lateral pressure is thus measured while retaining a free and undisturbed flow in the veins, and at the same time leaving the intraocular conditions wholly unaffected. The degree of accuracy attained is seen in that the mean variation of six readings taken in each experiment was ± 0.25 c.c. citrate (0.18 mm. Hg).

Anæsthesia was induced by chloroform-ether, and maintained by intravenous chloralose. The scleral veins were reached by slitting up the lids back to the orbital margin in the mid-line, and keeping them retroverted by stitches. The conjunctiva was then incised behind the limbus, and dissected back until the veins were exposed. The dissecting microscope was then focussed on the exposed sclera, direct illumination being obtained from a strong light concentrated by a lens system.

Precautions were taken to record the intra-ocular pressure with as little disturbance as possible. In the first experiment it was taken directly by a compensated manometer filled with saline which was inserted into the eye, using an air bubble inserted into a horizontal capillary tube as an index of equilibrium, and no measurements were taken until 15 minutes after the pressure changes following the introduction of the needle had disappeared. In the second experiment the tension of the two eyes was taken by a tonometer and was found to be equal: this instrument does not give absolute measurements with accuracy, since the recorded pressures vary with the radius of curvature of the globe, and with the resistance of the coats of the eye to the deforming force of the tonometer, but it is accurate for comparative measurements in the same individual at different times, or between the two (approximately equal) eyes of the same individual at the same time. Since the pressures in the two eyes may thus be considered identical, the pressure was taken in the second eye by the saline-filled manometer, and the reading transposed to the first eye. In the third experiment the tension was taken with a tonometer, and the venous pressure then observed; the manometer was then inserted, and after equilibrium had been established at the original intra-ocular pressure, the venous pressure was again taken, and a similar reading again obtained.

The pressures recorded in three dogs were these (each the average of six readings):

No. of dog	I.O.P.	V.P.	Difference: V.P.—I.O.P.
1	22 mm. Hg	23.5 mm. Hg	1.5 mm. Hg
2	(300 mm. citrate) 26 mm. Hg	(320 mm. citrate) 28 mm. Hg	2 mm. Hg
3	(350 mm. citrate) 25 mm. Hg (340 mm. citrate)	(380 mm. citrate) 26 mm. Hg (350 mm. citrate)	l mm. Hg

The venous pressure in the intra-scleral veins, therefore, is slightly above the intra-ocular pressure under normal conditions, the pressure difference averaging 1.5 mm. Hg.

The pressure in the extra-scleral veins. The technique of Seidel(29) was adopted, a glass cylinder being used as a pressure-chamber whose base was formed of a membrane of softened cellophane, and which was in communication with a manometer and levelling bulb containing warmed saline. The intra-ocular pressure was taken as in the previous experiments both by tonometer and manometer. The pressure was estimated in the subconjunctival veins near the corneo-scleral junction, that point being taken as standard of measurement when the first signs of interference with the blood flow became apparent: this precaution is necessary in order to eliminate the factor of hyperæmia, since, if the pressure be maintained, the vein originally emptied of blood refills and begins to pulsate, and a vessel which originally required 15 mm. Hg to obliterate it, now requires a pressure of 20 mm. Hg. Over a series of 12 experiments on dogs results comparable to those of Seidel were obtained, although they were slightly higher: the pressure in the veins soon after their exit from the eye varies from 5 to 8 mm. Hg below the intra-ocular pressure, the average figure being 7.2. It may be repeated that the interpretation put upon these results by this observer is not admitted, viz. that they represent the intra-ocular venous pressure; the rapid drop in magnitude after leaving the eye is only to be expected, the pressure level falling to that obtaining generally in the veins of the orbit and head.

The pressure in the intra-ocular veins. The retinal circulation is, except for very minor anastomoses, anatomically separated from the chorioidal, but, since the venous pressures throughout the eye will be shown to vary with and be dependent upon the intra-ocular pressure, it would seem probable that the exit pressures throughout the eye are to all intents and purposes equal. Although, for anatomical reasons, the pressures in the capillaries of the two circulations are unequal, there is a large amount of evidence which goes to show that the entrance and exit pressures are similar, and that the same pressure gradient exists in both systems, although it is unequally proportioned. In the iris of many animals there are vessels of such a size as to be observed readily through a binocular loupe. On applying graduated amounts of pressure to the globe of the eye by means of a dynamometer, these eventually pulsate and finally are obliterated as the diastolic and then the systolic pressures are reached: these changes take place in the iris *pari passu* with similar changes in the retina. This was first noted by Leplat(13) in the dog, and Bonnefon(5) in the rabbit, while Magitot and Bailliart(23) noted the same relation in the cat. Bleidung(4), by compressing the eye by a pressure chamber through which ophthalmoscopic examination was possible, concluded that in man the circulatory conditions in both retinal and chorioidal systems varied together; and, taking advantage of a case of a vascularised persistent pupillary membrane, Vossius(32) noted the parallelism in the behaviour of the vessels therein with those of the retina.

The intra-ocular venous pressure was therefore studied in the retinal vein, inasmuch as it is easily observable by means of the ophthalmoscope, and is less readily influenced by a delicate vaso-motor mechanism which reacts to any intra-ocular manipulation by an immediate response than are the veins of the iris and ciliary body. The relation between the intraocular pressure and the venous pressure was determined by the establishment of a fistula between a vein on the optic disc and the cavity of the eye. The outer canthus was slit up, and a very fine needle with a knife point inserted through the sclera behind the ciliary body and lens into the vitreous. Guided by observation through the ophthalmoscope, the point of the needle was approximated to the termination of a retinal vein upon the optic disc, and then the handle was carefully supported for 15 minutes until any pressure reaction due to the introduction of the instrument had subsided. That any such reaction is small, provided the needle is sharp enough and small enough, was demonstrated by repeated controls carried out with a manometer inserted into the eye. Still under direct vision through the ophthalmoscope, the slightest movement given to the needle now suffices to pierce the wall of the vein with the knife point. It is easy to differentiate an artery from a vein, and even if a mistake is made, the result is at once apparent: on piercing an artery the fundus at once fills with blood; in the case of a vein a small jet of blood flows out more slowly, and forms, initially, a cone in the vitreous in the track of the needle. This would seem to happen invariably in dogs, in cats, and in rabbits since it was tried in a large number of animals, 25 in all, with an identical result. Since the blood flows out of the vein, the venous pressure is higher than the intra-ocular, and any deviation from normal caused by the slight movement of the needle will act in the direction of raising the ocular pressure, and so confirm rather than vitiate the result.

That the difference between the two is not large is seen in the occurrence of a spontaneous venous pulse at the disc in many individuals and animals. Normally there is a pressure pulse in the eye of an amplitude of a little over 2 mm. Hg, corresponding with the systole of the retinal artery, and showing a sudden ascent, a sustained plateau, and a slow descent. Alternating with this the veins at the disc may show an inverse pulsation, being compressed at the summit of the arterial systole, and in many cases, where this is absent normally, the application of a small amount of pressure (2-3 mm. Hg) to the globe is sufficient to induce it. In other cases increased pressure on the globe fails to induce a pulse at all; in these, however, the same pressure relation holds good, as is seen by measurement of the intra-scleral venous pressure, and by the establishment of a fistula in a retinal vein. Bailliart's conclusions. which were reached on very insecure grounds, cannot therefore be accepted, for the occurrence of a venous pulse at the disc depends on factors more complicated than pressure differences alone; thus it tends to be abolished by the neutralising effect in the optic nerve of the pulsation of the retinal artery, alongside which vessel the vein runs in close association for some distance, or by any condition which tends to obstruct the unimpeded flow of blood, as, for example, venous engorgement (Helfreich (12)), or by marked rotation of the eyes to the side (Graves(10)), a movement which will kink the vein. Moreover, the external pressure which must be applied to the eye to induce a nonspontaneous pulse is no accurate measure of the normal difference between the venous and the intra-ocular pressures, for, since the one varies with the other, the latter cannot be approximated to the former without altering it also, thus leaving the initial pressure difference between them guite unknown.

The variation of venous pressure with intra-ocular pressure. It has been established in a general way that the intra-ocular pressure varies very closely with the venous pressure. On tying the vortex veins as they issue from the eye very large intra-ocular pressures, up to 80 and 90 mm. Hg, are registered. Ligature of a single vein produces the same effect to a lesser degree, as we have seen in discussing the experimental technique of Weiss and Lullies; ligature of all the veins produces in a short time a shallow anterior chamber, a dilated pupil, a hyperæmic iris, and engorged and swollen vessels throughout the eye—later the cornea becomes opaque, the tension remains stony hard, and further ophthalmoscopic examination becomes impossible. These effects find ample confirmation in the observations of several workers, the majority of whom were investigating the effect of the venous circulation on glaucoma— Adamük(1), Ulrich(31), Leber(17), Bartels(3), Weber(33), v. Schul-

W.S. DUKE-ELDER.

tén (26), Koster (16) and Magitot (21). The somewhat equivocal results that have been obtained on ligation of the jugular veins are readily explained when the extremely free anastomoses are taken into consideration; thus Adamük(1), Graser(9), v. Schultén(26) and Parsons(25) produced only a slight increase of intra-ocular pressure thereby. When, however, the channels are all simultaneously impeded the result is more marked, as on passing a ligature round the neck (Bonnefon(6)), or by compressing the thorax (Mazzei(24)), while L. Hill(13), by compressing the vena cava, demonstrated that a rise of pressure here was followed by a proportionate rise in the intra-ocular pressure. A large amount of clinical evidence, moreover, is available on the production of glaucoma by the obstruction of the efferent veins by traumatic, thrombotic, or inflammatory processes: Seefelder(27), Magitot(20), Christel(8), Heerfort(11), Stähli(30), Ischreyt(15), and others.

A similar relation obtains on raising the intra-ocular pressure. A mercury manometer with a levelling bulb was connected with the eye of a cat, and the behaviour of the veins of the retina watched as the pressure was raised. As the intra-ocular pressure rises the veins show no compression until a pressure of 65–70 mm. Hg is reached, when they begin to be slightly reduced in size; at higher pressures—70–80—when the flow through the arteries is beginning to become intermittent owing to the diastolic pressure being overcome, they become definitely constricted, but they are not obliterated until a pressure of 115 mm. Hg is reached—a pressure which stopped the flow in the arteries, and very nearly approximated the carotid level of 120 mm. Hg. At this point ophthalmoscopic examination reveals that the veins, which in the lower stages of pressure increment had been engorged, have now been reduced to mere streaks, the contained blood taking up a granular appearance as circulation ceases.

In order to determine the relative values during the variation of pressure, the venous pressure was measured in the intra-scleral veins by the capillary manometer already described, while the intra-ocular pressure was raised by a mercury manometer inserted into the eye. On raising the intra-ocular pressure, the pressure in the veins just before their exit from the sclera was observed to fall slightly below that obtaining in the eye: thus with an intra-ocular pressure of 40 mm. Hg the venous pressure at this point was found to be 39 mm. Hg. At the same time ophthalmoscopic examination showed the intra-ocular veins to be engorged. A needle was then introduced into the posterior part of the eye as in the previous series of experiments, and the same result obtained as formerly on the establishment of a fistula—a hæmorrhage into the eye—demonstrating that the intra-ocular venous pressure was still higher than the chamber pressure. A further reading of the intra-scleral venous pressure was then made, and the results confirmed the previous finding, that the pressure at this point was slightly less than the artificial pressure maintained in the eye.

This would seem to have an important bearing on the physiology of the intra-ocular pressure and the mechanism called into action to maintain it at a normal level. The results obtained suggest that the venous pressure in the eye is always slightly higher than the chamber pressure, and that, while there is a pressure decrement in the veins through the scleral coat, normally the pressure at the exit is still in excess of that in the eye. This organ thus falls into line with the rest of the body wherein the venous pressure is slightly higher than the tissue pressure. Owing to the delicate nature of the venous walls which could withstand no degree of pressure from outside without collapsing, it is an essential postulate for the maintenance of a continued circulation that the arterial pressure should be higher than the capillary, the capillary higher than the venous, and the venous higher than the chamber pressure. When the intra-ocular pressure is raised the circulatory system is compressed. That part with the lowest lateral pressure will give way first, that is, the veins at their point of exit will tend to be obliterated. As soon as this occurs the blood flow will be checked, the vis a tergo from the arteries will pile up pressure, the constriction will be forced open, and the circulation will proceed at a higher pressure level. This process will repeat itself in a cumulative manner until the available force from the arteries is exhausted, that is, until the pressure of the ophthalmic artery has been reached, at which point the entire circulation will cease, and the vessels will be obliterated. In the meantime, the pressure at the venous exits inside the eye has approximated to the chamber pressure, the pressure decrement in the vessels through the sclera, with their lumen kept always patent by the investing scleral tissue, still obtains, and the pressure in the intra-scleral veins near the outside of the ocular coat now falls below the intra-ocular pressure. The Canal of Schlemm, situated favourably as it is in the middle of the thickness of the sclera, *i.e.* in the middle of this pressure decrement, will now acquire a pressure less than the chamber pressure, a hydrostatic flow will be set up, draining off aqueous, lowering the intra-ocular pressure, and acting as a safety-valve tending to restore the normal pressure conditions of the eye.

PH. LXI.

28

CONCLUSIONS.

1. Methods are described for the measurement of the venous pressure of the eve for which is claimed a closer approximation to the normal conditions than is obtained by methods employed hitherto.

2. Normally the venous pressure in the eye and in the vessels passing through the coats of the eye is slightly higher (1-2 mm. Hg) than the intra-ocular pressure; immediately on leaving the eye there is a rapid fall.

3. The venous pressure varies directly and very intimately with the intra-ocular pressure.

4. On a rise of intra-ocular pressure, the venous pressure within the sclera, and therefore the pressure in the Canal of Schlemm, falls below the intra-ocular pressure.

5. Under normal conditions the aqueous is absorbed into the capillary-venous stream by osmotic forces alone; under conditions of raised pressure a hydrostatic outflow may occur.

REFERENCES.

- Herrences.
 Adamük, E. Ann. d'Ocul. 154, pp. 257, 648. 1917; 155. p. 453. 1918; 156. p. 656. 1919; 160. p. 593. 1923; "La Circulation Rétinienne." Paris, 1923.
 Bartels, M. Zeit f. Augen. 14, pp. 103, 258, 458. 1005.
 Bleidung, C. Arch. f. Augen. 94. p. 198. 1924.
 Bonnefon. Ann. d'Ocul. 158, p. 762. 1921.
 Bonnefon. Ibid. 159, p. 840. 1922.
 Carrier, E. B. and Rehberg, P. B. Skandinav. Arch. f. Physiol. 44. p. 20. 1923.
 Graves, B. Brit. Journ. Ophthal. 65, p. 271. 1922.
 Graves, B. Brit. Journ. Ophthal. 65, p. 437. 1922.
 Heifreich, F. Ibid. 28. Pt. 3. p. 1. 1882.
 Graves, B. Brit. Journ. Ophthal. 18, p. 121. 1924.
 Heifreich, F. Ibid. 28. Pt. 3. p. 1. 1882.
 Hill, L. Proc. Roy. Soc. B, 85. p. 439. 1912; Proc. Roy. Soc. Med. 6. Pt. 3. p. 31. 1913.
 Hill, L. Proc. Roy. Soc. B, 85. p. 439. 1912; Proc. Roy. Soc. Med. 6. Pt. 3. p. 31. 1913.
 Hill, L. Proc. Roy. Soc. B, 85. p. 439. 1912; Proc. Roy. Soc. Med. 6. Pt. 3. p. 31. 1913.
 Hill, L. Proc. Roy. Soc. B, 85. p. 439. 1912; Proc. Roy. Soc. Med. 6. Pt. 3. p. 31. 1913.
 Hill, L. Proc. Roy. Soc. B, 85. p. 439. 1912; Proc. Roy. Soc. Med. 6. Pt. 3. p. 31. 1913.
 Hill, L. Proc. Roy. Soc. B, 85. p. 439. 1912; Proc. Roy. Soc. Med. 6. Pt. 3. p. 31. 1913.
 Hill, L. Proc. Roy. Soc. B, 85. p. 439. 1912; Proc. Roy. Soc. Med. 6. Pt. 3. p. 31. 1913.
 Hill, L. Proc. Roy. Soc. B, 85. p. 439. 1912; Proc. Roy. Soc. Med. 6. Pt. 3. p. 31. 1913.
 Hill, L. Proc. Roy. Soc. B, 85. p. 439. 1912; Proc. Roy. Soc. Med. 6. Pt. 3. p. 31. 1913.
 Hill, L. Proc. Roy. Soc. B, 85. p. 439. 1912; Proc. Roy. Soc. Med. 6. Pt. 3. p. 31. 1913.
 Hill, L. Proc. Roy. Soc. B, 85. p. 439. 1912; Proc. Roy. Soc. Med. 6. Pt. 3. p. 31. 1913.
 Hill, J. Arch. f. Ophthal. 41. p. 757. 824. 1925.
 Magitot, A. Ann. d'Ocul. 154. p. 667. 1917.
 Magitot, A. Annet. Ocular Circulation." London, 1903.
 V. Schu