the cord is cut across without injury to the membranes, in the same manner as the middle coat of an artery is cut by the ligature. The parts are in perfect apposition. Is it the crushed or scar tissue intervening that prevents possibility of regeneration? It is not so in the peripheral nerves; regeneration begins even though the severed ends be never brought into apposition. The surgeon does no more than place the new nerves into continuity with each other, and even then it is inconceivable that no scar tissue intervene. The new nerves have apparently the power to pierce a thin layer of scar tissue.

Could we hold out hope of regeneration of cord-fibres, with what renewed energy should we strive to find out the *fons et origo* of such lesions as obtain in the terrible diseases known as tabes dorsalis, lateral and disseminated sclerosis, to say nothing of the numbers of old hemiplegias that haunt the out-patient rooms of our hospitals!

I propose in my next lecture to trace the course of the degeneration in the cord, both above and below the lesion.

ERASMUS WILSON LECTURES

ON THE PATHOLOGY OF

GLAUCOMA.

Delivered at the Royal College of Surgeons of England, March, 1889.

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LECTURE I.

MR. PRESIDENT AND GENTLEMEN,—The healthy human eye presents to the educated touch of the surgeon a certain elastic resistance; its flexible walls are kept in a state of moderate tension by the fluids which traverse the chambers. Any eye which presents a decided variation from this characteristic condition, whether in the direction of hardness or of softness, is, as we know by experience, an unhealthy eye. I propose to speak in these lectures of the disorders which are associated with an increased tension of the eyeball, disorders to which we apply the name glaucoma.

With the advance of knowledge the word glaucoma has changed its meaning. In the early days of our art, it was applied without discrimination to the various diseases in which a grey or greenish blue appearance replaces the normal blackness of the pupil. In later times, when a clear distinction had been made between the opacities which lie in the crystalline lens and those which lie behind it, the name was reserved for some of the deeper seated and more destructive disorders, the nature of which remained unknown. Hardness of the eyeball, as a part of such disorders, received at that time only casual notice. In the year 1830, MacKenzie pointed out the frequent overfulness of the chambers in glaucoma, and made the first attempt to relieve that condition by puncturing the tunics. Twenty-five years later, von Graefe, studying the subject with the aid of the ophthalmoscope, convinced himself that this overfulness was no mere complication of the disease, but was the essential cause of the leading symptoms, and was led by this conviction to his beneficent discovery of the curative action of iridectomy. Since that time the name glaucoma, losing its original meaning, has been used to indicate a disease characterised by increased tension of the globe. Certain other characteristics (cupping of the disc, contraction of the visual field) are recognised as consequences of the pressure.

Some writers, however, still deny that what we call glaucoma is necessarily connected with increased pressure. They point to certain exceptional cases in which the contracted field and the excavated disc are found in company with normal tension, and on the strength of these exceptions they maintain that glaucoma is the expression of some unknown agent which usually raises the pressure and excavates the disc at the same time, but which occasionally excavates the disc without raising the pressure. This assumption is, I think, unnecessary. The excess of pressure is sometimes slight; it is often intermittent; it may even be absent for long periods of time; it is very probable, therefore, that these cases of glaucoma with normal tension are cases which have been

examined only during the intermissions of increased tension. Permit me to mention a case in illustration.

Sir William Bowman was consulted by a lady in 1865. He noted (and he has kindly placed the notes at my disposal) increased tension and commencing excavation, diagnosed glaucoma, and spoke of iridectomy. No operation was performed. Twenty years later this lady came under my own care with deeply excavated discs, contracted fields, and impaired vision. I saw her many times; sometimes the tension was quite normal, sometimes it was increased. Vision was still useful, but failing rather rapidly. After consultation with Sir William Bowman, iridectomy was performed on both eyes with good result.¹ Now this lady must have had for years an unmistakable glaucoma, but at times, and probably very frequently, a normal tension. Yet pressure was there at the beginning and it was there at the end. One cannot doubt that it was an essential factor in the process.

Glaucoma, then, may be broadly defined as an *excess of pressure within the eye plus the causes and the consequences of that excess*. To understand the morbid process in its entirety, we must study first the normal intra-ocular pressure and the processes by which it is maintained; secondly, the causes which lead to an excess of pressure; and, thirdly, the consequences of such excess.

Estimation of the Intra-ocular Pressure.—It will be well, in the first place, to consider the means by which the intra-ocular pressure has been measured or estimated.

Fig. 1.

Manometer.—In certain of the lower animals the pressure has been accurately determined by means of the manometer, an instrument which brings the intra-ocular fluid into direct communication with a column of mercury or other fluid. The average normal pressure, the variations due to pulse and respiration, and those produced by ligature of arteries and veins, by section and irritation of nerves, and by the action of certain drugs, have all been ascertained. The manometer has also been applied in a few cases to the living human eye, namely, to eyes doomed to excision, the measurement being made immediately before the operation.

Finger Test.—Under ordinary circumstances it is impossible to measure the pressure in the living human eye, and we have to content ourselves with measuring, as an index to it, the resistance of the tunics. We apply the tips of the two forefingers with light alternate pressure to the upper eyelid while the eye is directed downwards, and we record our observations by means of Bowman's symbols (TN, T+1, T+2, etc.). For daily use no better method than the finger-test has been, or is likely to be, found, and it must be employed constantly by everyone who would deal successfully with diseases of the eye, but it is ob-

¹ *Ophth. Rev.*, 1885, p. 261.

viously inexact. We cannot state with precision the resistance which we feel, and we cannot rely upon the constancy of our sense of touch.

Tonometer.—To obviate this uncertainty, many attempts have been made to substitute for the fingers an instrument of precision—a mechanical tension-measurer or tonometer. I will not attempt to describe the various instruments which have been invented for this purpose; not one of them has hitherto found general acceptance. I will ask your attention rather to the principles which underlie and limit every effort of the kind, my object being not to show how every difficulty may be overcome, but to distinguish the possible from the impossible.

Principles of Tonometry.—This bladder (Fig. 1) will serve to represent the eye. It is filled with water, and is in open communication with the reservoir which stands at a higher level. The pressure in the bladder depends upon the height of the reservoir, and is constant so long as this remains unchanged. Our object is to estimate the internal pressure from the behaviour of the tunics under external pressure. The instrument, therefore, must press upon the eye, and must measure both the force employed and the impression produced. It is easy to measure the force employed; it is less easy to measure the impression produced, for it has more than one dimension; it varies in area and in depth. Are we to measure the area, or the depth, or both?

Area of Impression.—When this flat disc (Fig. 1) is loaded with a certain weight and placed upon the bladder, it flattens the membrane over a certain area; it sinks until it meets with precisely the same pressure from below as from above, then it remains in equilibrium; hence, if I employ a known external pressure, and measure the area of contact, I can calculate the internal pressure; for example, if I load the disc with a weight of 100 grammes, and if I find that the area of contact equals 100 square centimètres, I know that the internal pressure is 1 gramme to 1 square centimètre. If we were to take a second bladder of different size, or of different curvature at the point of contact, or of more extensible membrane, and place it at the same height and in connection with the same reservoir, we should find that the disc, if loaded with the same weight as before, would have the same area of contact as before. We see then that, *assuming that the membrane is perfectly flexible, the area of the impression produced by a known external pressure is a true index to the internal pressure.* It might appear, then, that the problem of ocular tonometry could be solved in this way. More than ten years ago I arrived by experiment at the principle which has just been stated, but concluded that the difficulties of applying it to the eye were insuperable.² Quite recently Professor Fick of Würzburg, following the same theoretical considerations, has invented a tonometer which is correct in principle and very simple in construction.³ A rough and enlarged model (Fig. 2) will explain its action. A flat disc is

Fig. 2.

pressed against the eye through the medium of a spring, and the force exerted by the spring is indicated by the scale behind it. The area of the disc is known: let us say that it is 50 square centimètres. I now press the disc against the bladder until it depresses and flattens exactly its own area of the membrane, neither more nor less, and I see by the scale that the force employed in doing this is, say, 50 grammes; I know that the internal pressure against the flattened area is equal to the external pressure, that is, 50 grammes, or 1 gramme to 1 square centimètre. Now the value of this instrument obviously depends upon one's ability to

depress the membrane precisely to the extent of the disc. A small error in this respect gives a larger error in the estimate of the pressure; thus if the diameter of the depressed membrane be larger or smaller than that of the disc by one-tenth, the area will be at fault by one-fifth, for the areas of circles vary as the squares of their diameters; and the estimate of the internal pressure will be at fault to the same extent. In the actual instrument the diameter of the disc is about 7 millimètres, so that the difficulty of applying it with precision to the eye, covered as the latter is by a more or less compressible conjunctiva, is considerable. Moreover, the readings of the instrument are at the mercy of the operator's wish or prejudice, and it is difficult to apply it with strict impartiality when a little more or a little less pressure will confirm or falsify one's own opinion. The principle of estimating the internal pressure from the area of the impression is unquestionably the right one, and Professor Fick's tonometer is the only one clearly based on this principle. I fear, however, that the difficulty of applying it with precision will be found to cause uncertainty in the results obtained.

Depth of Impression.—The depth is more easily measured than the area; this model (Fig. 3) will serve to show how it may be

Fig. 3.

done. When the three rods are placed vertically upon the bladder without pressure, they adapt themselves to its curvature. When the middle rod is loaded with a certain weight it sinks through a certain distance, as indicated by the scale behind it. This distance varies with the internal pressure, but it varies with other things as well, namely, with the curvature of the surface and with the extensibility of the membrane. Thus if the instrument were placed upon another bladder having the same internal pressure, but a flatter curvature, the impression would be shallower than before; and if the curvature were the same, but the membrane more extensible, it would be deeper than before. Now the sclera of the human eye varies somewhat both as to curvature and extensibility in different individuals, hence *the depth of the impression produced by a known external pressure is not a perfectly true index to the internal pressure.*

And there are other sources of error which cannot be avoided, whichever method we employ. The tunics of the eye are not perfectly flexible; their rigidity varies at different parts and in different individuals. Again, the thickness of the conjunctiva must be taken into account; a swollen conjunctiva pits deeply, irrespective of the yielding of the sclera. And again, it must be remembered that the tonometer itself raises the intra-ocular pressure for the moment, so that even if it could measure the internal pressure accurately we should learn, not the pre-existing pressure, but the pressure as modified by the application of the instrument; the amount of this modification remains unknown, and it varies in different cases according to the ease with which fluid is extruded from the eye.

No tonometer, then, however ingeniously devised, can accurately measure the intra-ocular pressure, or accurately compare one eye with another. Are such instruments of no value? Permit me to exhibit a tonometer which is the outcome of my own study of the subject, and to state what I believe to be its utility. This tonometer⁴ (Fig. 4) exerts a known and invariable pressure on the eye, and indicates the depth of the impression produced. The cross-shaped bar or ram is brought into contact with the eye. The crescent which lies upon it slides backward with a minimum of friction, and communicates its movement to the pointer; the pointer magnifies the movement of the crescent ten times. When the ram is applied to an unyielding surface no impression is pro-

² *Glaucoma, its Causes, etc.* London, Churchill, 1879, p. 48.

³ *Inaugural Dissertation* by R. A. Fick, Würzburg, 1888, and *Transactions of International Ophthalmic Congress, Heidelberg, 1888*, p. 289.

⁴ For details, see *Ophth. Rev.*, 1887, p. 33.

duced, and the pointer stands at 0; when it is applied to a yielding surface it impresses it, the crescent slides back, and the pointer indicates the depth of the pit produced. It only remains to apply this mechanism to the eye with the same force in every case. This is effected by means of a weight and rectangular lever. An important point in the instrument is the mobility of the crescent about its own centre. If the tonometer is applied obliquely instead of perpendicularly to the surface of the eye—and this happens more or less in every instance—the crescent adjusts itself to the surface before it begins to actuate the pointer. Without some such adjustment very accurate measurements cannot possibly be made. The curvature of the crescent is adapted to the average curvature of the eye, and makes no allowance for individual variations; it is impossible to make such allowance without complicating the mechanism. The consequence is that in a sharply-curved eye the tonometer under-estimates the depth of the impression, while in a flatter eye it over-estimates it; but these are errors in the right direction, for, as we have seen, a given pressure pits more deeply in a sharply-curved surface than in a flatter surface, so the one error tends to neutralise the other. If, however, the curve of the eye varies greatly from that of the crescent, a considerable error will arise.

Fig. 4.

If properly handled this instrument does its work well—that is to say, it makes the same pressure in all cases; it measures the depth of the pit with considerable accuracy, and it will not lend itself to the operator's prejudice. Has it any practical utility? For the purpose of comparing the eyes of one person with those of another it is, I think, not much better than the educated finger, for the differences which it may indicate, if they be so slight as to elude the finger, may be due to differences in the curvature or flexibility of the membranes. For comparing the two eyes of the same individual, when they are presumably alike in structure, it is of much greater value; but its chief use is in determining the changes which occur in one and the same eye. Applied to the same spot on successive occasions, it reveals slight changes of the intra-ocular pressure with much greater certainty than the finger, and its indications can be recorded and compared. Thus, I now habitually use it when in doubt as to the efficacy of eserine and cocaine in a case of glaucoma, or as to the need for a second operation. It is not an instrument for rough and ready diagnosis in unskilled hands, for it is more difficult to use than the finger test; but to those who would accurately control the indications afforded by the finger, it may, I think, be recommended.

The manometer, the finger test, and the tonometer in combination, have been useful in determining the pressure which is normally present in the living human eye. If we connect the eye of the dead subject by means of a hollow needle and elastic tube with a column of mercury or other fluid, we can ascertain what pressure is required to induce a degree of tension resembling that of the living eye; we can compare the artificial with the natural tension, either with the finger or more accurately with the tonometer. In like manner we can ascertain what pressures appear

to correspond with our own ideas of T+1, T+2, T+3, or with the various degrees upon the scale of the tonometer.

Amount of the Intra-ocular Pressure.—The foregoing are the means by which the intra-ocular pressure has been estimated. We may next consider the results obtained. Concerning the normal intra-ocular pressure in the eyes of animals, we have a considerable mass of evidence and a very close agreement. The animals chiefly experimented on were rabbits, cats, and dogs, and the precautions taken against error were very minute. In nearly all cases the pressure was between 20 and 30 millimètres of Hg; the average was about 25 millimètres. Slight oscillations were found to accompany pulse and respiration, and a more marked rise was produced by contraction of the external muscles of the eye.⁵

Experiments upon the dead human subject with my own tonometer gave a closely corresponding result. I found that in order to produce a tension resembling that of the living eye, a pressure of about 30 centimètres of water—that is, 25 millimètres of Hg—must be employed, and the same result was obtained on testing with the finger. Other observers employing the tonometer in the same way have placed the normal pressure rather higher than this, in one case even as high as 50 millimètres of mercury; but that this latter figure presents a distinctly glaucomatous tension will be manifest to anyone who will take the trouble to employ the finger test in the mortuary in the manner described. Adolph Weber, trusting the finger rather than the tonometer, estimates the pressure, as I have done, at about 25 millimètres of Hg.⁶

This estimate has lately been confirmed by Wahlfors, who applied the manometer to several human eyes immediately before excision. One of these was a healthy eye, which had to be sacrificed on account of an orbital tumour. The intra-ocular pressure was equal to 26 millimètres of mercury.⁷

Again, in the lower animals, numerous experiments with the double manometer have proved that the pressures in the aqueous and vitreous chambers are equal, or so nearly equal that the difference is not discoverable.⁸ It has been asserted that the vitreous pressure is considerably higher than the aqueous pressure, and some observers have even declared themselves able to detect the difference by placing the fingers on different parts of the globe. This idea, though disproved by accurate observation, is not yet quite abandoned. Experiments of my own upon the freshly excised eyes of animals have shown that the lens is displaced from its normal position by a slight excess of pressure either before or behind it. Thus, an excess in the vitreous chamber equal to 5 millimètres of Hg causes a considerable displacement of the lens and iris, and an excess of 10 millimètres almost abolishes the anterior chamber.⁹ Such differences in the two chambers are quite too small to be detected by the finger, and it is obvious that any comparison of the scleral with the corneal tension by means of the tonometer is fallacious. When such differences do occur in the living eye, they produce, and are manifested by, displacements of the lens and iris forwards or backwards as the case may be.

Concerning the height to which the intra-ocular pressure rises in the human eye under abnormal conditions we have very little evidence. In a case of chronic glaucoma in which the tension had been slightly reduced by an unsuccessful iridectomy, Wahlfors found with the manometer a pressure of 71 millimètres of mercury. Experiments with my own tonometer seem to indicate that the tension which we call +3 corresponds to a pressure considerably higher than this. Much higher pressures have been produced experimentally in the eyes of animals. In one instance a pressure equal to 200 millimètres of mercury was produced by compression of the aorta and simultaneous irritation of the fifth nerve.¹⁰

Secretion and Excretion of the Intra-ocular Fluids.—The maintenance of the normal pressure in the chambers of the eye depends upon the due secretion and the due excretion of the fluids which traverse them. These physiological processes have been most carefully studied during the last fifteen years, and it will be well to review the evidence upon which our knowledge stands at present. It is only by a careful study of these processes that we can hope to unravel the complex pathology of glaucoma.

The intra-ocular fluids flow, like all other secretions, from the blood-stream. Studying their origin from the anatomical point of

⁵ Graefe-Saemisch, *Handbook*, vol. 2, p. 371.

⁶ *Glaucoma, its Causes, etc.*, p. 98.

⁷ *Trans. of Internat. Ophth. Congress*, 1888, p. 268.

⁸ Bellarmino, *Abstract in Ophth. Rev.*, 1887, p. 361.

⁹ *Ophth. Rev.*, 1883, p. 207.

¹⁰ Von Hippel and Gruenhagen. *Von Graefe's Archiv*, vol. xiv, part 2, p. 19. See also *Glaucoma, its Causes, etc.*, p. 103.

view, we find, as possible sources, two vascular membranes, the uveal tract and the retina. We may at once eliminate the retina, for clinical observation shows that complete blockage of the retinal vessels by embolism causes no discoverable change in the fulness of the chambers. The uveal tract (Fig. 5) consists of three distinct parts, namely, the choroid extending forwards as far as the ora serrata, the ciliary portion reaching from the ora serrata to the base of the iris, the iris ending at the margin of the pupil. The functions of these several parts may to some extent be inferred from their structure and relations.

The choroid, by its internal surface, nourishes the external layers of the retina. Its capillaries feed the pigmented epithelium, and the epithelial cells keep the rods and cones in a state of functional activity. The meshes of the capillary plexus become progressively less and less close from the posterior pole to the anterior limit, and this arrangement accords with the varying sensibility of the corresponding zones of the retina. There is no evidence that the choroid nourishes the vitreous body, and it is obviously improbable that a highly organised membrane like the retina, which has many differentiated layers and a separate vascular system of its own, should convey nourishment from the choroid to the vitreous.

The iris has a well-defined optical function, that, namely, of regulating the entrance of light. It is possible that its posterior surface, like the rest of the uveal surface, may have a secretory function as well, and take some part in the formation of the aqueous humour, but this part must be quite a subordinate one, for there are many cases on record in which the iris has been completely absent, either from birth or through injury, and yet there has been no discoverable insufficiency of the aqueous fluid; the tension has been normal.

The ciliary portion of the uveal tract shows a special adaptation for the supply of fluid to the vitreous body, the lens, and the aqueous chamber. Where it is in relation with the vitreous, its secreting surface is extended by a series of grooves and ridges, and where it is in relation with the aqueous chamber it assumes a still more convoluted arrangement well suited for rapid secretion.¹¹

Fig. 5.

The vitreous body has its chief attachments in this region; its limiting membrane adheres firmly to the ora serrata, and in advance of this point is separated from the secreting surface only by a single layer of cylindrical cells; the membranous septa which spring from the limiting membrane in this region are arranged in a manner peculiarly favourable for the entrance of fluid.¹²

Pathological anatomy points to the same conclusion. If we examine eyes which have been excised during the first stage of vitreous infiltration, we find an inflammatory exudation entering the vitreous body from this portion of the uveal tract, the region of its influx being limited posteriorly by the ora serrata. We find also that while a shrinking vitreous readily separates from the retina it always retains its firm connections in the region of the ora serrata. And, again, we find that while very extensive atrophy of the choroid does not necessarily affect the transparency or the volume of the vitreous body, disease in the ciliary region always tends to its destruction.

Experiments upon animals have amply confirmed the inferences previously drawn from these anatomical and pathological facts. Deutschmann found that removal of the ciliary processes together with the iris, which can be done in the rabbit without loss of lens or vitreous, and without causing inflammatory destruction of the eye, is followed by a total arrest of the secretion of the aqueous, and by atrophy of the vitreous body and lens.¹³ Schoeler, Uthoff, and others have found that after subcutaneous injections of fluorescein there is a speedy coloration of the aqueous fluid, and a more gradual coloration of the vitreous body, and that the coloured secretion proceeds from the ciliary processes, and perhaps to a small extent from the posterior surface of the iris also.¹⁴ Lepat has demonstrated the same thing by a somewhat different method; he gave subcutaneous injections of iodide of potassium, enucleated the eyes after various intervals of time, froze them and divided them into zones, and made a quantitative test for iodide in each zone.¹⁵ These and many other experiments agree in showing that the fluids which nourish the vitreous body and lens and fill the aqueous chamber are secreted chiefly, if not entirely, by the ciliary portion of the uveal tract.

In what directions do these fluids travel, and where do they escape from the eye? The aqueous fluid passes from the posterior chamber forwards through the pupil into the anterior chamber. It has been asserted that there is a current passing forwards through the base of the iris, but the evidence is by no means conclusive. It is contrary to physical reasoning to suppose that while the pupil remains open the fluid will traverse the tissues of the iris; moreover, the stream through the pupil is proved by the fact that when the pupillary margin becomes entirely adherent to the lens capsule the fluid collects behind the iris with disastrous consequences.

The aqueous fluid escapes from the eye at the angle of the anterior chamber, by filtering through the ligamentum pectinatum into Schlemm's canal and the veins connected with it. This fact was established by Leber's well-known injection experiments, which showed also that the anterior chamber has no direct communication with the blood vessels, and that the cornea, so long as its posterior epithelium remains entire, is not permeated by the aqueous fluid.

The escape of fluid from the vitreous body has been the subject of much experiment and discussion, and is still not determined with absolute certainty. The question is whether it escapes at the papilla, or through the aqueous chamber, or in both these directions. Schwalbe has described certain lymph passages within the sheath of the optic nerve, which, he says, "find exit in the lymph passages of the skull, and convey not only the lymph formed in the optic nerve, but that also of the retina and vitreous."¹⁶ Stilling has seen a considerable escape of fluid in this region under artificial pressure.¹⁷ The injection experiments of Lepat already referred to appear to show that iodide of potassium injected subcutaneously enters the vitreous from the ciliary body and travels very slowly backwards, and leaves it at the papilla. Still more positive evidence is afforded by some experiments made by Gifford.¹⁸ He injected with special precautions small quantities of water containing indian ink or cinnabar in suspension into the vitreous of rabbits and other animals. The results were definite and constant. On the second day, or later, according as the injection was made farther backward or forward in the vitreous, the ophthalmoscope showed the particles collecting in the excavation of the papilla. On killing the animal a day or two later, the microscope showed the particles passing backwards through the papilla, along the lymph spaces around the

¹³ *Von Graefe's Archiv*, vol. 26, part 3, p. 117; and *Ophth. Rev.*, 1882, p. 149.

¹⁴ See *Ophth. Rev.*, vol. 1, p. 413.

¹⁵ See *Ophth. Rev.*, 1888, p. 84.

¹⁶ *Graefe-Saemisch, Handbook*, vol. 1, p. 50.

¹⁷ *Report of Heidelberg Congress of 1886*, p. 42.

¹⁸ *Archives of Ophthalmology*, 1886, p. 153; and *Ophth. Rev.*, 1886, p. 217.

¹¹ See description by Brailey, *JOURNAL*, September, 1882, p. 577.

¹² See description by Straub, *Von Graefe's Archiv*, vol. 34, part 3, p. 7.

central vessels, and leaving the nerve trunk with the vessels, and passing towards the sphenoidal fissure. They did not enter the sheath of the optic nerve. The current within this sheath has been proved by other experiments to move from the brain towards the eye.

In spite of the evidence put forward by these investigators, it has been difficult to accept the view they advocate, for certain facts seem to point the other way. Schoeler found that artificial occlusion of the supposed posterior outlet caused no discoverable reduction in the amount of fluid escaping from the eye in a given time.¹⁹ More recently, in experiments made by himself and Uhthoff, he failed to find any transit of fluoresceine from the eyeball into the optic nerve or its sheaths. I myself, ten years ago,²⁰ injected solutions of carmine and of aniline purple into the

vitreous of freshly excised pig's eyes, maintained the pressure for five or six hours, then froze the eye, and cut microscopic sections through the posterior pole; there was no colour deeper than the superficial layers of the retina. Again I injected a coloured fluid into the sheath of the optic nerve, after ligaturing the nerve behind the point of injection. The pressure employed was about double the normal intra-ocular pressure, and was maintained at this height during five hours. Microscopic sections showed no trace of fluid having entered the eyeball, although the tissues were deeply stained up to the anterior extremity of the sub-vaginal space.

In favour of the supposition that the vitreous fluid escapes through the aqueous chamber is the fact that it can easily pass in this direction. Leplat has lately proved, with regard to the living eye, that the fluid which rapidly refills the aqueous chamber after it has been emptied by puncture of the cornea is derived in large measure from the vitreous chamber; and this same refilling of the aqueous chamber occurs also in the dead eye, in which the vitreous is the only possible source of the fluid.

In order to test this matter still further, and to obtain, if possible, some information as to the amount of fluid which traverses the chambers in a given time, I undertook last year²¹ another series of injection experiments on the freshly excised eyes of oxen, sheep, and pigs, and, in a few instances, on the human eye after death. The most trustworthy results were obtained with sheep's eyes, for I could have an unlimited supply of these within a few minutes of death. The apparatus employed is shown in Fig. 6, and need not be described in detail. It enables one to make a continuous injection of one or both chambers under a known and constant pressure, and to measure the amount of fluid which passes through the chambers in a given time. The pressure can be varied at will by raising or lowering the reservoirs, and it can be kept absolutely equal in the two reservoirs by opening the tube which connects them; or, when this tube is closed, the reservoirs can be adjusted to give different pressures.

An air bubble in each of the graduated horizontal tubes serves to indicate the movement of the fluid. Its position is noted at regular intervals of time. The cubical content of the tube is known. A pressure of 30 centimètres of water, that is, 25 millimètres of mercury, was adopted as the standard pressure throughout, this being about the normal pressure.

Fig. 6.

The experiments were of several kinds. In one series I injected the anterior chamber only; in another the vitreous chamber only; in a third series, aqueous and vitreous were injected simultaneously under precisely equal pressures; and in a number of other cases I employed different pressures in the two chambers simultaneously, and varied the conditions in many different ways. The details have been described elsewhere; here I need only deal with the results. The following were the averages of ten experiments of each kind; the variations were not great:—

When the anterior chamber only was injected, the escape during the first half hour was 785 cubic millimètres.

When the vitreous only was injected it was 275 cubic millimètres.

When the aqueous and vitreous were injected simultaneously under the same pressure it was 485 cubic millimètres, that is, considerably less than during injection into the aqueous chamber only.

This result, at first sight paradoxical, is explained by the varying position of the iris, and its effect upon the patency of the angle of the anterior chamber—the “filtration angle.” When the anterior chamber only was injected, the iris was displaced a little backwards; when the aqueous and vitreous chambers were injected simultaneously under equal pressures, the iris remained in its normal position, or nearly so; when the vitreous only was injected the iris was displaced a little forwards. In order to observe these displacements accurately, I froze the eyeballs solid while the injection was still going on, and bisected them.

In the fourth series of experiments the vitreous reservoir was raised to a higher level than the aqueous reservoir. For example, keeping the aqueous reservoir at 30 centimètres, as before, the vitreous pressure was raised to 35 centimètres. Under these circumstances the diaphragm between the two chambers, consisting of the lens, zonula, processes, and iris, is displaced forwards until the increased tension of the zonula balances the excess of pressure behind it. Equilibrium being established in the diaphragm, a stream passes through the zonula from the vitreous to the aqueous chamber, and fluid continues to enter the eye through the one needle, and to leave it through the other. The amount which escapes by filtration is then ascertained by subtracting the backward movement of the one bubble from the forward movement of the other. Now, under these circumstances, although the pressure in the aqueous chamber was as high as in the previous experiments, and the vitreous pressure was actually higher, the total escape was reduced to about 50 cubic millimètres in the first half-hour. In the frozen and bisected eye the iris-base was found to

¹⁹ Von Graefe's Archiv., vol. 25, part 4.

²⁰ Glaucoma, its Causes, etc., p. 142.

²¹ Ophth. Rev., July, 1888, p. 193.

be pushed forwards, and in places visibly in contact with the periphery of the cornea. By placing the vitreous reservoir 15 centimètres higher than the aqueous reservoir it was possible to empty the anterior chamber almost completely, and to apply the whole iris close to the cornea; and under these circumstances the escape by filtration from the whole eye appeared in some instances to be entirely arrested.

Similar experiments upon the freshly-excised eyes of oxen, and in one instance on a freshly-excised healthy human eye removed with an orbital tumour, gave closely similar results.

With regard to the escape at the papilla I made some further experiments with the smaller apparatus, shown half-size, in section, in Fig. 6. A circular piece, including choroid, sclera, retina, and optic nerve, is cut from the back of a sheep's eye immediately after death and placed in the box, and the inner tube is tightly pressed down upon it by screwing on the cap of the box. The inner tube is then filled with coloured fluid and connected by a flexible tube with a graduated glass tube and reservoir, as in the other apparatus. Under a pressure of 30 centimètres, as before, there was no perceptible exudation and no coloration on the outer surface after several hours.

These experiments show several points of importance with regard to the freshly-excised eye. They show, firstly, that fluid injected into the vitreous chamber escapes chiefly, if not entirely, through the aqueous chamber; secondly, that a slight excess of pressure in the vitreous chamber displaces the lens and iris forwards, compresses the filtration angle, and impedes the escape of fluid; thirdly, that there is little, if any, escape at the papilla. With regard to the currents in the living eye, they give, of course, no positive information.

(Since this lecture was delivered I have read with much interest that Dr. Leplat, adopting a method nearly the same as that above detailed, has made a further series of experiments upon living animals. His results confirm to a large extent those obtained by myself with the freshly-excised eye. He concludes that the escape at the papilla is about one-fiftieth of the escape at the filtration angle.²²)

If we compare these various observations concerning the movements of the vitreous fluid, it is not difficult, I think, to reconcile the apparent discrepancies.

It appears certain, from the movements of solid particles observed by Gifford, that there is a current passing backwards in the vitreous body, and escaping along the lymph-passages which surround the central vessels of the optic nerve. It appears equally certain that this current moves very slowly, and that the amount escaping in a given time is extremely small as compared with that from the aqueous chamber. Whether the small perivascular spaces in the papilla are rendered impervious by excision of the eye, or whether a small quantity of fluid does actually traverse them during artificial injection of the vitreous chamber, it is difficult to determine. In any case the absence of visible filtration here presents a striking contrast with the free escape which occurs at the filtration angle. It remains uncertain, I think, whether there is a persistent stream from the vitreous to the aqueous chamber. But we have seen that fluid can pass very readily in this direction under a slight excess of pressure in the vitreous chamber; and it seems probable that so long as the partition remains permeable, and the fluid diffusible, any excess of pressure in the vitreous chamber will relieve itself in this way. An intercommunication of this kind between the two chambers appears to be necessary for the maintenance of the lens in its normal position.

Our knowledge of these currents may, then, be briefly summarised as follows: The fluids which nourish the vitreous body and lens, and fill the aqueous chamber, are secreted chiefly by the ciliary portion of the uveal tract. The larger part of the secretion passes directly into the aqueous chamber, forwards through the pupil, and out at the filtration angle. A very much smaller portion passes backwards through the vitreous body, and escapes at the papilla. The hyaloid membrane and zonula which separate the two chambers are readily permeable by the vitreous fluid. The pressure which the fluid exerts against the walls of the chambers is equal to about 25 millimètres of mercury, and is the same, or nearly so, in the two chambers.

To conclude this physiological part of the subject, I may point out that while the circulation of the intra-ocular fluid is necessary to the eye as a living organ, its pressure is necessary to it as an optical instrument—an instrument which is built entirely of soft

materials, but which nevertheless can adjust itself with precision both for direction and for distance. In the larger chamber, where there are no moving parts, the fluid is supplemented by a transparent fibrous tissue, which adds to the safety of the organ. In the smaller chamber there is fluid only, so that the curtain which regulates the admission of light may have perfect freedom of movement. In both chambers the fluid exerts that particular degree of pressure which suffices to maintain the form of the globe, and gives precision to the action of the muscles, external and internal, but does not embarrass the circulation of the blood, the nutrition of the tissues, or the transmission of nerve-currents within the organ.

When the intra-ocular pressure rises above these physiological limitations, we get that complex disturbance which we call glaucoma.

REMARKS ON TROPICAL DIARRHŒA AS SEEN IN THIS COUNTRY.

Read before the Medical Society of London, April 1st, 1889.

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THE subject of these remarks is a peculiar form of diarrhœa which derives its origin from tropical and subtropical countries, notably India, China, Ceylon, and Java, and which is of frequent occurrence in Europe wherever old residents of tropical climates resort. Its symptomatology, etiology, and as much of its pathology as has been ascertained, are described; and the author hopes to show that, though long regarded as a dangerous and even a fatal complaint, it is amenable to treatment if properly and vigorously dealt with.

This "white flux," which has various synonyms, though not always directly related to any well-marked form of climatic or malarial disease, is very insidious in its onset and progress, and very intractable if not early controlled. It is something more than ordinary chronic diarrhœa, though it often supervenes on that disease. In its worst symptoms are often manifested and a dangerous and protracted state of disease established, and it owes its fatality, when continued beyond a certain stage, to irreparable degeneration of the intestinal mucous membrane and glands, and the consequent inability to absorb nourishment. Death is due to anæmia and exhaustion from slow inanition, the channels for the admission of nutrient material being practically interrupted or destroyed.

It has been referred to by observers in India, China, and Java. Many of the examples which came under the author's observation during residence in India were of the variety known as hill diarrhœa, from its proneness to affect dwellers in the hill stations, especially those who had been subjected to the debilitating influences of the plains—atmospheric changes, vicissitudes of temperature, greater altitude, and probably the water being concerned in its causation. This hill diarrhœa and the "white flux" of other parts of India may be regarded as identical, while in some cases it is associated with, or may merge into, certain forms of chronic dysentery.

The author considers that it must be regarded as a climatic disease, though its etiological relations with malaria seem to be remote rather than direct. Though sometimes the sequel of other climatic disease, it may begin spontaneously and often affect, after their return to Europe, people who have not suffered from the diseases of the country they have left, though their health generally must have been affected by climatic influences. There is also a form of intermittent and irregular diarrhœa prone to attack people who return from India with hepatic and splenic derangement, which, though it may be the precursor of white flux is not of so dangerous a character, and from which recovery is often so rapid as to show that it is due rather to functional disorder than to structural degeneration of the intestine. Such forms of bowel-complaint generally do well after the portal system

²² *Annales d'Oculistique*, January-February, 1889.