In various sites throughout the body, fluids of different chemical composition are produced and these include saliva, gastric juice, pancreatic juice, bile, urine, aqueous humour, cerebro-spinal fluid, tissue fluid and lymph. The common origin or mother liquor of all these fluids is the blood, although the mechanism of formation of these diverse biological products is not similar. Of these various fluids, tissue fluid and lymph would appear to be closely akin to blood plasma and a well-marked inter-relationship has been drawn between the three fluid systems to which they belong—namely, the connective tissue or cellular interspaces, the lymphatic system and the vascular system.

The Vascular System.—This system contains blood corpuscles and plasma. It is a closed system of tubes leading from the heart by arteries, arterioles, and capillaries to the tissue spaces throughout the body, thence by the veins back to the heart.

The Lymphatic System.—This system contains protein-rich fluid called lymph. The lymphatic system is derived from veins and the lymphatic vessels invade the body as do the blood vessels. These lymph vessels have the same relationship to the tissue spaces as have the blood capillaries. There is thus no continuity between the tissue spaces and the lymph channels.

The Tissue Spaces.—These are intermediate in position between the vascular system and the lymphatic system. This system is by virtue of its structure, function, and contents quite independent of the two preceding systems. The tissue spaces contain fluid and this fluid must be distinguished from lymph. It is important to distinguish between the contents of these fluid systems, for much confusion exists because of the loose way in which people refer to them.

1. **Lymph** : this is fluid inside the lymphatic system.
2. **Tissue fluid** : this is fluid in the areas outside the blood and lymph capillaries in cellular or connective tissue interspaces.

* Lecture delivered at the Royal London Ophthalmic Hospital on November 11, 1938.
3. **Plasma**: this is the unclotted fluid of the blood in the vascular system.

These fluids differ from one another, for example chemically such as in their protein and NaCl content. The protein is greatest in the plasma and least in the tissue fluid.

The nature of the interchange that occurs between these systems is a complex one including the passage of gases, water, inorganic salts, organic crystalloids, and in certain tissues colloids. The factors that play a part in bringing about the interchange can best be demonstrated by Fig. 1.

This figure shows diagrammatically the structure of a normally functioning vascular and lymph capillary. A vascular capillary has the following characteristics:—

1. It has an afferent and an efferent vessel. The former is usually an arteriole and the latter a vein but this is not always the case. For example, in the liver, the afferent vessel is a vein not an artery.

2. Its walls are composed of a single layer of endothelial cells.

3. All interchanges of fluid, salts, dissolved gases, take place...
exclusively through the capillary wall and not through the walls of arteries or of veins.

4. It has a reciprocal permeability:—*i.e.*, it allows the passage of fluids, salts, and gases across its walls with equal freedom in both directions.

5. Its membrane or wall is semi-permeable; *i.e.*, whereas water, salts, and gases are allowed free passage over the membrane to the tissues, the plasma proteins are not. The plasma proteins are retained inside the capillary and on this account they exert a most important property—namely, that of absorbing water from the tissue side of the membrane to the plasma.

There are several factors which govern the passage of fluid in and out of the capillary, to the tissue spaces and to the lymphatic system.

*The Interchange over the Capillary Membrane.*—Let us assume that the intra-capillary or hydrostatic pressure at the mid-point of the capillary is 25 mm. Hg. On the arterial side of this point, the hydrostatic pressure will be a rising one indicated by 25 +; on the venous side a falling one indicated by 25 −. These are assumptions that agree with actual measurements made by Landis (1930) on the capillaries of man and animals. Again let us assume that the various colloidal constituents of the plasma, which are unable to pass over the capillary membrane exert an absorptive or osmotic pressure of 25 mm. Hg—an assumption that also agrees with actual measurements that have been made. The intracapillary or hydrostatic pressure drives fluid and dissolved substances out of the vessel into the tissues while the osmotic pressure of the plasma proteins draws fluid back again into the capillary. There is a third factor, the tissue fluid pressure. Little is known about it, but it has been demonstrated that the tissue pressure counters in a small degree the filtration pressure and is in the region of 9 mm. Hg—see Landerer (1884). In the diagram, I have indicated by arrows the flow in and out of the capillary. When as happens normally these forces balance one another, there is no accumulation of fluid in the tissue spaces and there is a constant and continual interchange of fluid occurring.

*The Flow of Fluid into the Lymphatic Vessels.*—It is probable, though by no means certain, that two forces are at work in guiding fluid into the lymphatic system. These are the osmotic pressure of the lymph, and the hydrostatic pressure of the fluid in the connective tissue spaces. Once the fluid has entered the lymphatic system and becomes lymph, its passage onwards to the large lymph channels and to the thoracic duct is hastened by massage and active muscular movement. There is no doubt that the lymphatic route is the one way that protein is removed from the subcutaneous tissues. The wall of the lymph capillary is much
more permeable to protein than the blood capillary, and Drinker believes that "protein-containing fluid leaving the blood stream moves into the lymphatic almost as easily as through the tissue spaces." (Drinker and Field, 1933). The function of the lymphatics is therefore to remove material from the tissue spaces which is not absorbed by the blood capillaries.

Very briefly then, the relative values of the blood capillary and the lymphatic capillary regarding fluid interchange are as follows:
1. The blood capillary determines the water content of the tissues.
2. The lymphatic capillary removes protein and has little to do with the water content.

The factors, therefore, which normally play a part in the distribution of fluid throughout the body are:—
1. The hydrostatic pressure in the capillaries.
2. The colloid osmotic pressure of the plasma.
3. The pressure of fluid in the tissues.

Do these physical forces govern the formation of the specialised fluids in the body such as the cerebro-spinal fluid, aqueous humour, gastric juice, or bile? In other words, when the mechanism for the interchange of tissue fluid breaks down and water-logging or dehydration of the tissues take place, are these specialised fluids similarly affected? The behaviour of these various specialised fluids throughout the body, after disturbances in the fluid equilibrium, might give an indication as to their nature; whether they are dialysates, secretions, exudates or transudates. It is generally accepted that the tissue fluid and lymph are formed by the process of dialysis, the simple laws of which have just been described.

I am now going to consider conditions where the normal fluid interchange between the capillary and the tissue spaces is upset, and later we shall determine whether the equilibrium in these specialised fluid systems is in any way disturbed. A disturbance in the tissue fluid equilibrium occurs in the following conditions.
1. When the colloid osmotic pressure of the plasma falls.
2. When the osmotic pressure of the blood is suddenly raised.

In the first condition, water-logging occurs, and in the second, dehydration.

A fall in the colloid osmotic pressure of the plasma.—If the osmotic pressure of the plasma proteins falls from a normal of 25 mm. Hg to 10 mm. Hg, a condition represented in the second diagram, is created.

Owing to the fall in the suction power, as it were, of the plasma proteins, there is a relative increase in the filtration pressure. As the colloid osmotic pressure is now no longer able to counterbalance the hydrostatic pressure in the capillaries on theoretical
grounds, stagnation of fluid in the tissue spaces should result—and clinically in fact this does occur.

The causal relationship between nephrotic or generalised oedema and depleted plasma proteins was first drawn attention to by Epstein (1914, 1917, 1917a, 1922), who was investigating the mechanism of oedema in nephrosis. Nephrosis is a disease which is characterised by certain well-marked features—Bennett, Dodds and Robertson (1931).

Clinically.—There is generalised oedema with no cardiovascular changes (thus no retinal changes, no elevated blood-pressure, and no cardiac hypertrophy are present).

Biochemically.
1. Heavy albuminuria.
2. Absence of haematuria.
3. Doubly refractile lipoids in the urine.
4. Oliguria.
5. Reduced B.M.R.
6. The blood chemistry is normal except the plasma proteins are greatly diminished and the cholesterol is raised.

In explaining this syndrome, Epstein has stated that as a result of the massive albuminuria the plasma proteins became depleted (i.e., the plasma proteins were simply lost through the kidneys). A stage was finally reached when the plasma proteins were so depleted that their osmotic pressure was no longer able to counterbalance the hydrostatic pressure in the capillaries which forced the fluid from the blood stream into the tissues. Thus more fluid was pushed out into the tissues than was attracted back again, and oedema resulted. The conception of Epstein was later confirmed by actual osmotic pressure measurements in a case of generalised oedema when it was found there was a pressure of
50 mm. of water in favour of filtration from blood to tissues—Krogh (1925). Leiter (1928) gave the first direct proof that oedema occurred in intact animals if the plasma proteins were experimentally reduced:—

Healthy dogs were bled twice daily of 400 to 500 c.c. of blood. The blood was centrifuged and the corpuscles suspended in Ringer's solution re-injected. By this means the plasma proteins were gradually reduced without anaemia. On the fifth day oedema appeared accompanied by ascites, hydrothorax, and pulmonary oedema. By this time the plasma proteins had fallen from a normal of 7 gm. per cent. to 3 gm. per cent. and their osmotic pressure from 28 mm. to 15 mm. Hg.

I have seen the onset of oedema in cases of ascites after the peritoneal fluid had been removed by tapping. This was due to a rapid loss of proteins from the blood into the abdomen causing a fall in the level of the plasma proteins. In a large series of cases of nephritis and nephrosis with oedema, I have found the plasma proteins to be consistently reduced and their osmotic pressure to be below 15 mm. Hg.

In general terms, then, it may be said that whereas there are several other factors that influence the interchanges of fluid throughout the body, the plasma proteins play a very important part and stagnation of fluid in the tissues or nephrotic oedema appears when the colloid osmotic pressure of the plasma falls to 15 mm. Hg.

We now come to the second method of upsetting the fluid equilibrium of the body.

Raising the total osmotic pressure of the blood.—The following observations were made after the total osmotic pressure of blood had been raised by the intravenous injection of hypertonic solutions of 30 per cent. NaCl and 50 per cent. glucose—Robertson (1938). The amount given in each case was 5 c.c. per kg. at the rate of 2 c.c. per min. The following diagram shows the changes which occur in the haemoglobin after the injection of these solutions.

The line 00₁ in Fig. 3 represents the end of the injection and the space to the left of this line the time in minutes of the injection. The point on the line 00₁, joined by dotted lines represents the theoretical dilution of haemoglobin one would expect from an injection of 5 c.c. per kg. assuming the blood volume is 70 c.c. per kg. of body weight. You will note the theoretical dilution is 92 per cent. It will be seen that the dilution of haemoglobin was greatly in excess of 92 per cent., or the dilution caused simply by the addition of the volume of injected fluid. There must, therefore, have been a withdrawal of fluid from the fluid reserves throughout the body as a result of the hypertonic nature of the
injection. Immediately the injection was completed the haemoglobin began at once to concentrate, indicating the vascular system was getting rid of the fluid that had been attracted to it. In about 30 to 45 minutes the haemoglobin was practically normal again. The main facts brought out by these experiments are:

1. Hypertonic solutions such as 30 per cent. NaCl and 50 per cent. glucose attract a large volume of fluid from the tissue spaces producing a blood volume about twice normal.

2. The fluid is attracted from the tissues only during the period of injection.

3. The greatest blood volume is obtained the moment the injection is stopped, therefore the tissues are most dehydrated at that moment.

4. Immediately the injection is completed, the vascular system discharges fluid back to the tissues again and in $\frac{1}{2}$ to $\frac{3}{4}$ hour the blood volume is normal and the water content of the tissues is normal.

5. Lastly, these changes occur quite independently of the kidneys for similar findings are found after bilateral nephrectomy.
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Briefly, these investigations on the fluid equilibrium in the body may be summarised:

1. When the plasma proteins of the blood become depleted through any cause such as—
   (a) Excessive loss.
   (b) Destruction.
   (c) Impaired production,
and their colloidal osmotic pressure falls from a normal of 25 mm. Hg to 15 mm. Hg or less, there is an increased production of tissue fluid or fluids produced by dialysis and this is made manifest by the presence of nephrotic oedema, hydrothorax, and ascites.

2. When the total osmotic pressure of the blood is suddenly raised by the intravenous injection of a hypertonic solution, while the injection is taking place, fluid is drawn into the vascular system very rapidly in an attempt to dilute the strong solution. So rapidly is this fluid transferred and equilibrium established that when the injection stops, the transfer of fluid from the tissues stops. At once fluid pours back from the vascular system to the tissues and in \( \frac{1}{2} \) to \( \frac{3}{4} \) hour the blood volume is normal and so is the fluid content of the tissues. In terms of tissue fluid therefore, we can say that after the injection of hypertonic solutions:
   (a) The tissue fluid volume is at a minimum the moment the injection stops.
   (b) The tissue fluid volume is back to normal in \( \frac{1}{2} \) to \( \frac{3}{4} \) hour.

The behaviour of dialysates to changes in the fluid equilibrium is thus simply and easily defined.

What changes occur in the production of the aqueous humour when there is a disturbance in the formation of dialysates such as occurs in the pathological and experimental conditions that have just been described? First with regard to depletion of the plasma proteins.

Fall in the colloid osmotic pressure of the plasma.—It has been shown that the plasma proteins become very depleted in nephrosis and certain forms of nephritis, and that when this occurs generalised or nephrotic oedema results. I have made observations (Robertson, 1938) on the intra-ocular pressure in a series of thirty cases of nephritis or nephrosis with gross generalised oedema and I have found that the intra-ocular pressure measured with the Schiötz tonometer was within normal limits. It can be argued that the tonometer is not an instrument giving absolute and accurate measurements of the intra-ocular pressure, being influenced as it is by other conditions in the eye such as the elasticity, thickness, and circumference of the cornea. If the tonometric readings are taken by the same observer, however, on the same patient, with the same instrument, then the observations are of great relative value. A series of tonometric measurements
on individual cases throughout the period of oedema to recovery would therefore give valuable information. Lipoid nephrosis is a disease that may give such an opportunity and I have been able to carry out serial observations on a few cases of this rare disease.

Fig. 4 shows diagrammatically the findings in a typical case of lipoid nephrosis from the stage of oedema to that of complete recovery. When first observed the patient had gross generalised oedema, ascites, and hydrothorax. Her urine contained 1 gm. of protein per cent. Under treatment the oedema gradually subsided and this chart demonstrates the changes noted during her illness.

1. The Osmotic Pressure of the Plasma Proteins.—When first observed the plasma proteins were so depleted that their osmotic pressure was only 7.5 mm. Hg as compared with a normal of 30 mm. Hg. On theoretical grounds, therefore, oedema was inevitable and it was in fact present in a marked degree. Gradually regeneration of the plasma proteins occurred and you will
see there was an increase in the colloidal osmotic pressure reaching a normal level about 9 to 12 months later.

Oedema.—The variations in the degree of water retention in the tissues is demonstrated very well by the weight chart. This patient's normal weight was 136 pounds. When first observed her weight was 169 pounds and as the oedema subsided her weight fell steadily to 112 pounds. There was thus 57 pounds of oedema fluid retained in the tissue spaces. At this point (112 pounds) she was free from oedema and we note that the osmotic pressure of the plasma proteins had risen above 15 mm. Hg. There is, therefore, a certain level of the colloid osmotic pressure of the plasma known as the oedema-level which lies just above 15 mm. Hg. Above this level—no oedema; below this level—oedema. The gain in weight after this point signified she was putting on flesh as clinical improvement took place and the plasma proteins continued to regenerate.

The Intra-ocular Pressure.—The intra-ocular pressure when first measured was 22 mm. Hg. It was within normal limits, and throughout the progress of this case no significant change was noted in the intra-ocular pressure which lay between 19 and 22 mm. Hg.

The conclusions we draw from these observations are that the eye does not share in the water-logging common to other tissues of the body. The equilibrium level of the intra-ocular pressure is not maintained by the hydrostatic pressure in the capillaries minus the difference in osmotic pressure between the aqueous humour and blood.

Let us now consider the eye when the second method of upsetting the fluid equilibrium is employed.

Raising suddenly the Total Osmotic Pressure of Blood.—Fig. 5 shows diagrammatically the changes which occurred in the intraocular pressure after the intravenous injection of 30 per cent. NaCl. The intraocular pressure was measured directly by the insertion of a cannula into the anterior chamber. During the blocked interval A the injection was given. After the injection was completed, there was a gradual fall in the intra-ocular pressure reaching its zero in about 60 minutes and remaining at this level for at least the next hour. The fall in the intra-ocular pressure was quite independent of the blood pressure. In terms of the volume of aqueous humour in the eye the curve of the intra-ocular pressure shows that as soon as the injection of NaCl was finished, the volume of aqueous began to diminish for the next hour, thereafter for the following hour at least the volume remained at a low level. How long it would remain subnormal I did not attempt to determine, but experience with 30 per cent. NaCl therapy in glaucoma shows the intra-ocular pressure may be kept
down for 24 to 48 hours. Put in another way, the injection of 30 per cent. NaCl stopped or greatly diminished the formation of the aqueous. How does the fluid exchange in the eye compare with that of the tissues? They differ markedly. If the intra-ocular fluid behaved like ordinary tissue fluid, then—

1. The greatest fall in the intra-ocular pressure should occur the moment the injection stopped, for you will remember the haemoglobin was at its dilutest and thus the transfer of fluid at its maximum.

2. At the end of the injection there should be a rapid climb back to normal in about 46 minutes. I have marked it "x" for you will remember at that time the haemoglobin was normal and the fluid content of the tissues was back to normal.

Fig. 6 shows diagrammatically the changes which occurred in the intra-ocular pressure after the intravenous injection of 50 per cent. glucose. During the blocked interval A the injection was given. It will be noted that no significant fall took place in the intra-ocular pressure. In other words the formation of aqueous
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Humour appeared to be little disturbed by the injection of 50 per cent. glucose. Once again the fluid exchange in the eye and the tissues differs; 50 per cent. glucose attracted a large volume of fluid from the tissues as evidenced by a great dilution of the haemoglobin, but none of that fluid came directly from the eye.

It is apparent that the eye does not behave as a simple fluid depot as do the connective tissue spaces, and the aqueous humour does not appear to be formed by the same process as the tissue fluid on the following grounds.

1. When the osmotic pressure of the plasma proteins in the blood falls below 15 mm. Hg and it can no longer counterbalance the hydrostatic pressure in the capillaries:
   (a) Nephrotic oedema results—i.e., there is an excessive formation of tissue fluid.
   (b) There is no increased production of aqueous humour.
2. Fifty per cent. glucose in doses of 5 c.c./kg., by reason of its hypertonicity withdraws a large volume of fluid from the tissues diluting the haemoglobin accordingly, but no fluid would appear to be withdrawn from the aqueous humour.
3. Thirty per cent. NaCl, which is 3½ times stronger than 50

![Graph showing B.P. and Hb. changes after injection of 50 per cent. glucose.](http://bjo.bmj.com/)

**Fig. 6.**
per cent. glucose dehydrates the tissue markedly. It also inhibits the formation of the aqueous humour; but the mechanism of dehydration of the tissues and that governing the inhibition of aqueous humour are not alike. Thus:

(a) Dehydration of the tissues is greatest as the injection is being finished, and it has disappeared in \( \frac{1}{4} \) hour.

(b) The inhibition of the formation of aqueous humour may continue for 24 hours. Further, in the 60 minutes period after the injection, the fluid content of the eye is decreasing at a time when the ordinary fluid depots of the body are increasing their fluid content. At the end of an hour when the fluid content of the tissues is normal, the eye is most severely dehydrated.

If the eye does not behave like any ordinary fluid depot, and the formation of aqueous humour does not depend on the simple laws that govern the formation of simple dialysates like tissue fluid and lymph, what does it resemble?

It occurred to me to compare the changes in the intra-ocular pressure after these hypertonic injections with what happened to

![Graph](image-url)  
**Fig. 7.** Gastric secretion after histamine stimulation.
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a generally accepted secretion. The gastric secretion was chosen as one easily studied.

Diagram 7 shows the curves of the secretion of free HCl and the volume of gastric juice produced in cats after the subcutaneous injections of histamine 1 mg. hourly. In addition, there is plotted the gastric secretion expressed as a factor—the product of total acid and volume over 100. This curve is a mean of six normal controls. In the subsequent figures the gastric secretion factor alone will be plotted to avoid confusion with other observations such as blood-pressure, intra-ocular pressure, and haemoglobin which were taken simultaneously. We note that a rapid rise in the concentration of free HCl occurred reaching a maximum of 160 c.c. N/10 NaOH and being maintained at that level indefinitely. The volume of gastric juice is being secreted at a uniformly constant rate of 6 to 10 c.c. an hour. The gastric secretion factor shows a gradual rise.

Effect of 30 per cent. NaCl intravenously.

**By permission of Jl. of Physiol., Vol XClIII, p. 432, 1938.**
markedly diluted at the end of the injection, but thereafter immediately concentrating and returning to normal in about $\frac{1}{4}$ hour. The intra-ocular pressure showed a definite gradual fall quite independent of the blood pressure. The lowest intra-ocular pressure was reached about 90 minutes after the injection and it remained low for at least the next hour. The volume and acidity of the gastric juice were both lowered (in some experiments complete inhibition for 3 to 4 hours occurred) and this is demonstrated by a gradual fall in the gastric secretion factor. If we consider that the stomach is receiving a continuous stimulation with histamine, the most powerful gastric stimulant known, then it is apparent that the inhibiting action of hypertonic NaCl must be great.

Effect of 50 per cent. glucose—5 c.c./kg. at 2 c.c./min.—As in previous experiments it will be seen from Fig. 9 that the haemoglobin became diluted at the end of the injection, then rapidly returned to normal. However, there was usually no effect on either the intra-ocular pressure or on the gastric secretion.

In comparing the gastric secretion with the intra-ocular pressure it is important to decide exactly how much information the intra-ocular pressure gives about the formation of the aqueous humour.

*By permission of Jl. of Physiol., Vol. XCIIII, p. 434, 1938.
Assuming the blood pressure is constant, the intra-ocular pressure is a mean of the volume of aqueous produced and that eliminated. Therefore, a fall in the intra-ocular pressure may be due to:

1. Diminished production.
2. Increased elimination.
3. A combination of these two.

During the injection of 30 per cent. NaCl it is probable that any fall which occurs in the intra-ocular pressure is due to an increased elimination of the aqueous humour, for Weed (1922) found the cerebro-spinal fluid was absorbed by two routes in addition to the normal mechanism through the arachnoid villi under similar experimental conditions. Immediately after completion of the injection, osmotic equilibrium is established throughout the body, so any fall in the intra-ocular pressure which takes place after this must be due to a failure in the production of the aqueous by some more complex mechanism than one of dialysis.

In comparing the stomach and the eye, it would appear perhaps less open to criticism to compare the volume of gastric juice produced with the intra-ocular pressure, and the curve of the secretion of free hydrochloric acid with that of the specific secretion in the eye. Fortunately for the purposes of our comparison now, it does not matter for the curve of volume of gastric secretion intimately follows that of the curve of free hydrochloric acid. We see then that the behaviour of the gastric secretion after 30 per cent. NaCl and 50 per cent. glucose bears some sort of relationship to the behaviour of the intra-ocular pressure under similar experimental conditions. Thirty per cent. NaCl inhibited gastric secretion and during that period of inhibition of the gastric secretion, the intra-ocular pressure gradually fell. Again 50 per cent. glucose had no effect at all on the gastric secretion nor had it any on the intra-ocular pressure.

From the above experiments it would appear therefore that the formation of the aqueous humour in many respects does not resemble that of the so-called interstitial fluid like lymph, pleural or peritoneal fluids. In many respects the control of the equilibrium level of the intra-ocular pressure which is related to the formation of the aqueous humour, resembles the control of the gastric secretion.

So far a study has been made of the means by which the equilibrium level of the intra-ocular pressure can or cannot be altered after artificial variations have been made in the osmotic pressure of the blood, and there would appear to be evidence that the behaviour of the eye cannot be explained adequately by the simple laws which govern dialysis.

In conclusion I would like to discuss certain aspects of the eye which have a bearing on its fluid equilibrium and these are—
1. The question whether the aqueous humour circulates.

2. Where the aqueous humour is formed.

3. Where the aqueous humour is absorbed.

*The Circulation of the Aqueous Humour.*—In the same way as there has been controversy regarding the mechanism of the formation of the aqueous humour, so it has been stated by various observers that there was no circulation whatsoever, and that there was a circulation. The views of these different schools of thought are important for their respective beliefs influenced them in their theories on how the aqueous humour was formed. The supporters of the non-circulation or stagnant aqueous theory maintained that the only movement present was an interchange of water and ions across the capillary membrane all around the eye. The nature of this simple interchange of fluid has already been described in Fig. 1 showing a normally functioning capillary. All the movement that occurs is a to and fro one. The supporters of the circulation theory believed that there was a definite through and through circulation from the posterior chamber to the angle of the anterior chamber. The supporters of the stagnant aqueous maintained it was formed by a process of dialysis or ultra-filtration, whereas the supporters of the circulating aqueous maintained it was formed by a process of secretion or transudation.

The evidence now would appear to be more strongly in favour of the view that the aqueous humour does circulate, but curiously enough the acceptance of this view by certain workers did not prevent them at the same time still supporting the theory that the aqueous was produced by dialysis and thus theoretically stagnant. The evidence that a circulation exists is supported by observations of Priestley Smith (1927) some time ago, and more recently by Friedenwald and Pierce (1931). To give one or two examples:

1. There is the condition of iris bombé, where an iridectomy restores a channel from the posterior to the anterior chamber with relief of the secondary glaucoma.

2. Cells which were cast off from a melanoma of the iris have been shown by microscopic studies to be lodged in the tissues around the angle of the anterior chamber throughout its circumference.

3. A case has been described of a child with very small lenses. In one eye on one occasion the lens slipped over the pupil and formed with the iris a complete barrier between the anterior and posterior chamber. The iris slowly bulged forward around the edge of the lens and the anterior chamber became evacuated. As soon as the iris approached the cornea the intra-ocular tension began to rise.

It has been calculated by Friedenwald and Pierce that the rate
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of flow of the aqueous humour is in the region of 1 c.mm. per minute.

The site of formation of the aqueous humour.—To be consistent the upholders of the dialysate theory must, as I believe they do, maintain that the aqueous humour is produced with equal freedom by diffusion through the capillaries of all the intra-ocular vessels of the ciliary processes, iris, and retina. Because of the through and through circulation, however, it would seem that the formation of fluid must take place in the posterior chamber; and of the structures in the posterior chamber evidence points to the ciliary processes as being the probable site of the production of the fluid. There is first of all their histological structure; the lack of fluid which results from their removal or cutting off of their blood supply, and the absence of changes in the intra-ocular pressure after removal or absence of the iris or arrest in the blood supply of the retina.

The site of removal of the aqueous humour.—To be consistent upholders of the dialysate theory should maintain that the aqueous humour is absorbed through the same capillaries as it is produced for one of the characteristics of the capillary membrane is its reciprocal permeability. There is evidence, however, that no absorption of aqueous humour can take place from the posterior chamber—i.e., the type of membrane only allows a flow of fluid in one direction. The aqueous humour can only escape through the walls of the anterior chamber, and there seems ample evidence to show that the greatest, if not the only exit, is through the canal of Schlemm.

How does the fluid get into the canal of Schlemm? That is a question which is not easy to answer. Very little indeed is known with certainty about the nature, structure, function and contents of this most important canal.

Contents.—It is now generally accepted that under normal conditions it contains aqueous humour, but in venous stasis it may contain blood due to backflow from veins.

Connections.—It has no direct communication with the anterior chamber and is separated from it by a layer of endothelium. It communicates freely with the anterior ciliary veins into which the aqueous eventually empties.

Structure.—It has not the structure of a vein, but closely resembles a lymphatic channel. It is certainly not a vascular capillary as has been several times referred. A vessel which (a) allows fluid traffic in one direction only; (b) does not normally contain red cells; and (c) begins as a cul-de-sac so to speak and enters the venous system, cannot be a vascular capillary.

The fluid, therefore, cannot enter the canal by osmosis, for not being a capillary there is no plasma there to absorb it. It is
not known with certainty whether the pressure in the canal of Schlemm is greater, equal to, or less than that of the intra-ocular pressure. It may be that the canal pressure is not static and that at times it may fall below the intra-ocular pressure to allow the aqueous to enter it by simple filtration; thence by propulsion to be sent on to the veins. Various methods have been described to explain the mechanism of the exit of the aqueous humour, but none has given complete satisfaction.

The conclusions from a further study of the fluid equilibrium of the body and of the eye are similar to the views expressed by me previously—Robertson (1937) (1938).

1. The formation of the aqueous humour is not governed by the same simple laws that govern the lymph, pleural and peritoneal fluids and other dialysates. Dialysis is therefore not a satisfactory explanation of the production of the aqueous humour.

2. When the osmotic equilibrium in the body is disturbed in various ways the fluid formed in the stomach and the eye are disturbed rather similarly. This suggests that a secretory process in the eye may play some part in controlling the intra-ocular pressure.

3. Ample evidence is available that the aqueous humour circulates from the posterior to the anterior chamber.

4. Evidence seems to point to the site of formation of the aqueous humour being in the ciliary process.

5. The aqueous humour leaves the eye at the angle of the anterior chamber into Schlemm's canal by some process which is not osmosis, and no fluid can leave the eye normally by the posterior chamber.

REFERENCES

Bennett, Dodds and Robertson (1931).—Quart. Jl. Med., Vol. XXIV, p. 239.


Krogh (1925).—Anatomy and Physiology of the Capillaries (New Haven), p. 265.

Landier (1884).—Die Gewebsspannung in ihrem Einfluss auf die Ortlliche Blut— und Lymphbewegung. Vogel, Leipzig.


