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THE MECHANISM OF DRAINAGE OF THE CEREBROSPINAL FLUID

BY

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THE cerebrospinal fluid (CSF) is secreted continuously into the ventricles, and this requires a mechanism for outflow into the vascular system; it is generally accepted that the major escape route is through the arachnoid villi, which are essentially evaginations of the subarachnoid space into the lumen of the large dural sinuses. Other sites of drainage have been suggested, e.g. from the spinal subarachnoid space into the large spinal veins associated with emerging nerve routes (Elman, 1923; Brierley and Field, 1948; Pollay and Welch, 1962) but these are, at most, subsidiary pathways.

So far as the mechanism by which CSF is absorbed into the venous blood, Weed suggested (Mortensen and Weed, 1934; Weed, 1935) that there were two physical factors favouring passage from subarachnoid space to vessel lumen, namely the higher hydrostatic pressure in the cerebrospinal fluid, and the difference of colloid osmotic pressure between the virtually protein-free CSF and the plasma (fig. 1). Whilst there is little doubt that the hydrostatic difference of pressure is an important factor, the significance of the colloid osmotic pressure of the plasma has been called into question on both theoretical and anatomical grounds (Davson, 1956; Welch and Friedman, 1960). Thus Davson argued that for the colloid osmotic pressure to be effective, the membranes separating the CSF from the blood in the dural sinus, i.e. the endothelium of the sinus and the immediately subjacent layer of arachnoid tissue,

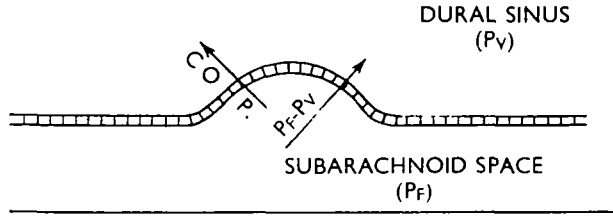

FIG. 1.—Illustrating Weed's concept of the pressures governing absorption of CSF. The effective pressure is the sum of ($P_F - P_V$) and the colloid osmotic pressure, C.O.P. P_F = CSF pressure; P_V = dural sinus pressure. (Davson, 1956. "Physiology of the Ocular and Cerebrospinal Fluids.")

would have to exert a constraint on the passage of the protein molecule, in particular serum albumin, and this would necessarily lead to an accumulation of protein in the CSF that would finally reduce the difference of colloid osmotic pressure to a negligible value. Thus there is a normal influx of plasma proteins into the CSF, partly in the original secretion and partly as a result of diffusion from the adjacent nervous tissue (*see*, for example, Frick and Scheid-Seydel, 1960; Hill *et al.*, 1958, 1959; Tveten, 1965) and, since there is no lymphatic system in the tissue, the only means of clearing this protein must be through the normal drainage channels; it seems most unlikely, therefore, that these channels would offer appreciable restraint to the passage of the protein molecules. The histological and physiological studies of Welch and Friedman (1960) have also cast doubt on Weed's hypothesis; these authors described microscopically visible discrete openings from the subarachnoid space into the lumen of the dural sinus; and, when they separated two chambers by portions of dura containing arachnoid villi, they found that particulate matter of diameter as large as 7μ (erythrocytes) was able to pass from the arachnoid side into the other chamber. There seemed to be a valvular action, so that there was only flow when a critical opening pressure of some 10 cm. H_2O was exerted on the arachnoid side.

Recently, however, Shabo and Maxwell (1968*a*) have questioned Welch and Friedman's interpretation of their anatomical and physiological studies, on the basis of an electron-microscopical study. According to them, the membranes separating CSF and blood are intact, and they have argued that the absorption of protein from the CSF is by phagocytosis. It seemed therefore that the matter required reinvestigation, and in the present paper experiments are described supporting the earlier contention that the colloid osmotic pressure is not a significant factor in the reabsorption of cerebrospinal fluid. The measurements to be described consisted, essentially, of the resistance to flow of fluid injected into the lateral ventricles of the rabbit.

Experimental

Experiments were on rabbits (2·5–4 kg.) under pentobarbitone (Nembutal) anæsthesia; cannulæ were inserted into the lateral ventricles as described by Pollay and Davson (1963).

An artificial CSF was perfused into the lateral ventricles either at constant speed or at constant pressure, and the steady-state pressure and flow-rate were recorded over a range of pressures. The experimental set-ups are shown schematically in the combined illustration of fig. 2. For constant flow-rate, injection was carried out by a variable-speed motor driving two syringes connecting separately to cannulæ in the left and right ventricles; connexions were made to a manometer as close to the point of entry into the ventricles as practicable and pressures in the separate ventricles could be recorded by turning the Tap, T, appropriately.

Independent experiments, in which the pressure in the ventricle itself was measured, showed that corrections for resistance to flow along the terminal few centimetres of the system were negligible.

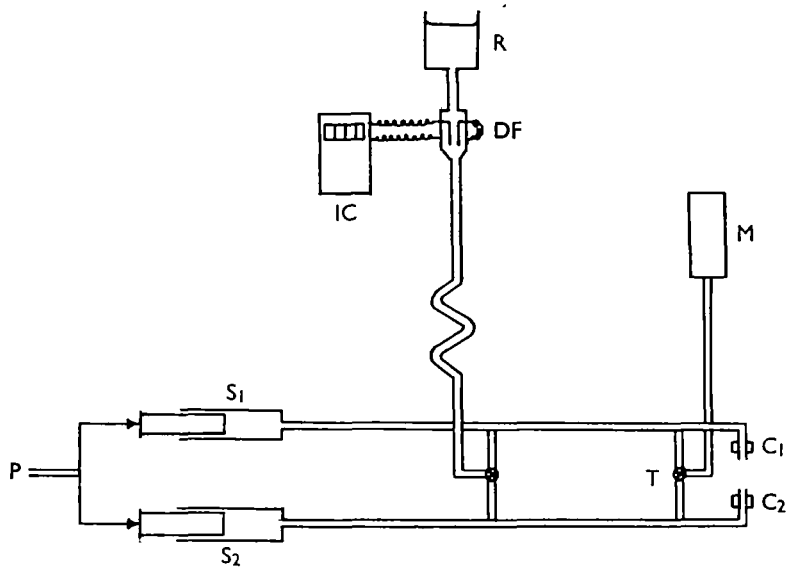

FIG. 2.—Combined diagram illustrating the techniques for constant-flow and constant-pressure experiments. For constant-flow, the syringes S_1 and S_2, driven by the pump, P, infuse fluid through the cannulæ C_1 and C_2; pressure is measured by the manometer, M. For constant-pressure, the syringes are cut out of the circuit and the reservoir, R, with its drop recorder-flowmeter, DF, is brought in. Pressure is measured as before with the manometer M. IC=Impulse counter.

For constant pressure infusion, a reservoir of variable height contained the artificial CSF. The fluid passed through a drop-recorder and thence to a T-junction connecting with the two ventricular cannulæ. The pressure in the tubing close to the ventricular cannulæ was recorded, as before, by the manometer, M.

When it was wished to perfuse directly into the subarachnoid space, rather than into the ventricle, a cannula described earlier by Bito, Bradbury and Davson (1966) was employed; essentially it consisted in a metal tube ending in the aperture of a base-plate that was clamped over a small slit in the dura to form a watertight seal.

THEORETICAL

If the flow through the system follows Poiseuille's Law, we may write, for any given steady-state pressure, P_1, and flow-rate, Q_1:

$$Q_1=\frac{P_1-P_v}{R} \qquad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(1)$$

where R is the resistance to flow and P_v is the pressure in the dural sinus into which the fluid drains. For a new pressure, P_2, and its corresponding flow-rate, Q_2, we have:

$$Q_2=\frac{P_2-P_v'}{R} \qquad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(2)$$

where P_v is the new value of the dural sinus-pressure. If this pressure remains unchanged with varying rates of flow, then we have from (1) and (2)

$$\frac{P_2-P_1}{Q_2-Q_1}=R \qquad \text{or } \triangle P/\triangle Q=R$$

Thus the slope of $\triangle$ P versus $\triangle$ Q should be a measure of the resistance to flow, provided the dural sinus-pressure remains reasonably constant with varying rate of flow.

This assumption is not strictly true, but the fact that the dural sinuses are enclosed within the tough dura suggests that they are unlikely to be seriously affected by changes in intracranial pressure; experimentally, moreover, the demonstration by Wright (1938) that—even when the CSF pressure was raised to the diastolic arterial pressure—there was no sign of collapse of the dural sinuses, supports the notion that their walls are held open by attachment to the dura, so that there is free communication with the large veins of the neck. Furthermore, Weed (1935) found that raising the CSF pressure of dogs from 250 to 500 mm. saline by continuous infusion caused negligible changes in the sagittal sinus pressure.

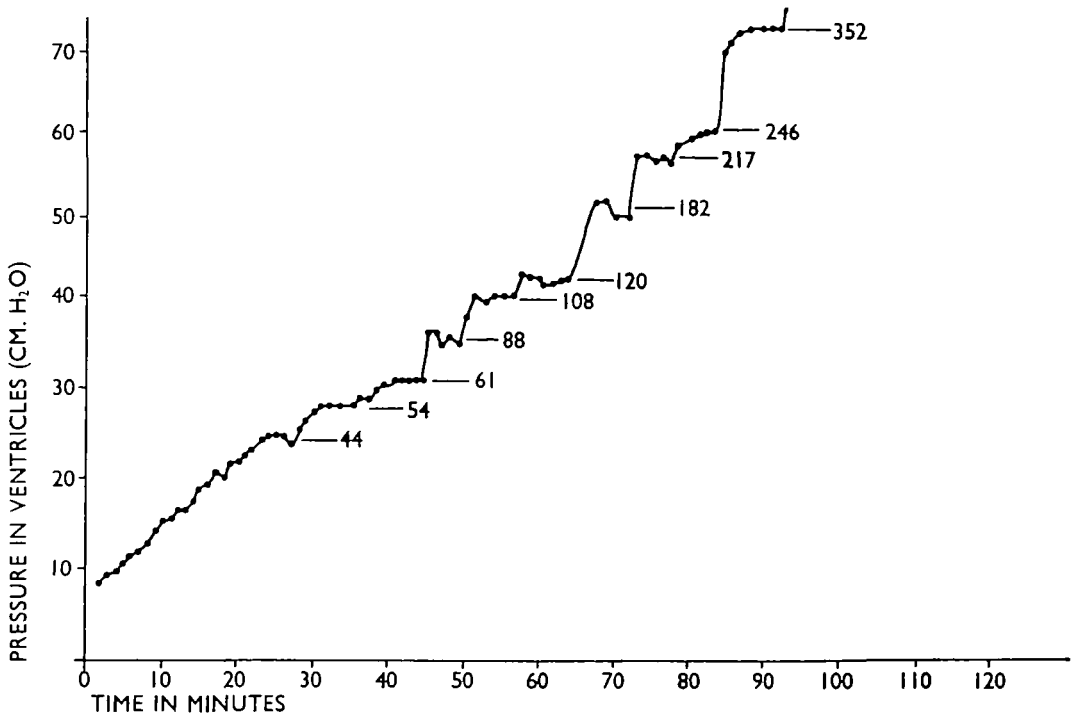

FIG. 3.—Constant-flow technique showing increase in pressure when the flow-rate is increased in steps. Plateau readings of pressure are indicated by the bars and the numbers indicate the flow-rates, in µl./min. Ordinate: Intraventricular pressure in cm. H_2O. Abscissa: Time in minutes from beginning of injection (at 44 µl./min.).

RESULTS

Constant flow-rate technique.—Fig. 3 illustrates the changes in intraventricular pressure when artificial CSF was injected into the ventricles at rates that were increased step-wise from 44 to 352 μl./min.; the pressure rises with each increase in flow-rate to reach a reasonably steady plateau. Fig. 4 (circles) shows the curve

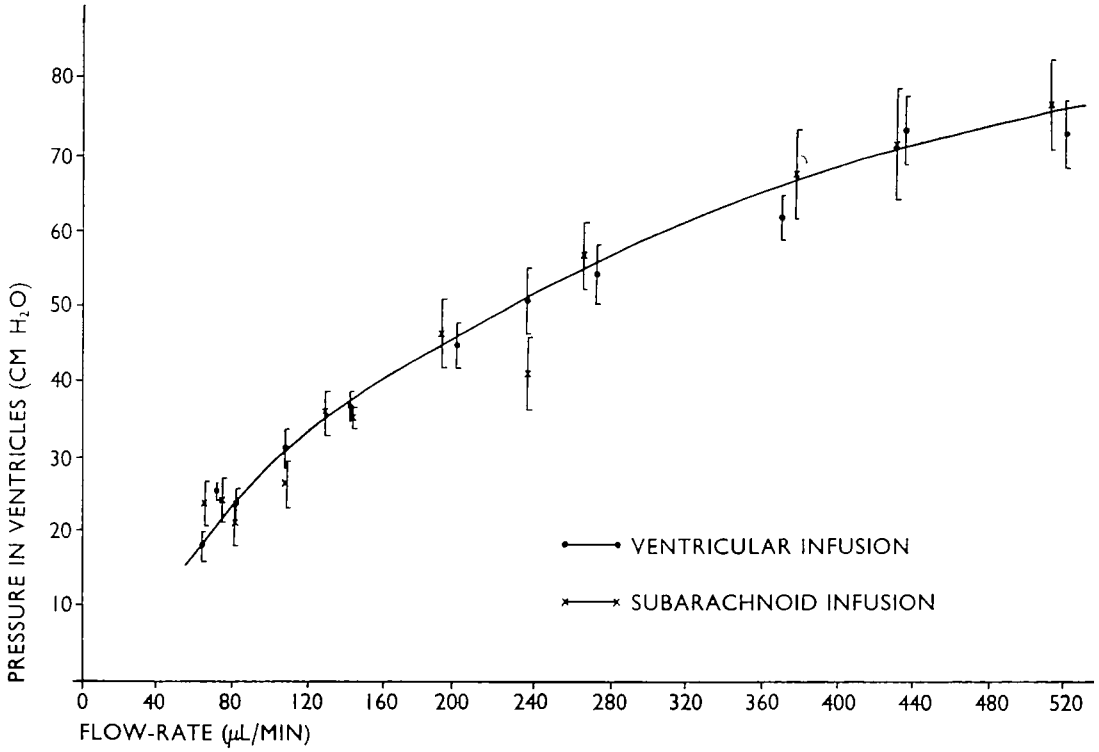

FIG. 4.—Pressure-flow curve derived from constant-flow type of experiments. Filled circles indicate mean of 9 experiments based on intraventricular infusion. Crosses indicate mean of 7 experiments based on subarachnoid infusion. Brackets indicate ± S.E. Ordinate: Intraventricular pressure in cm. H_2O. Abscissa: Flow-rate in μl./min.

obtained by plotting the average plateau-pressures, obtained from 9 separate animals, against the corresponding flow-rates. The relationship is not simply linear and suggests that, as the rate of flow increases, the resistance $\triangle P/\triangle Q$, falls. Thus the estimated resistance to flow over the flow rates 20–120 and 120–280 μl./min. are 0·27 and 0·14 cm. H_2O/μl./min.

It could be argued that the limiting resistance to flow from ventricles to blood was in the aqueduct of Sylvius rather than the arachnoid villi; in this case the fall in resistance at high flow-rates could easily be accounted for by a dilatation of the aqueduct at the higher infusion-rates. In a separate series of experiments the infusion-cannula was inserted into the subarachnoid space, and the experiments repeated. The points

in fig. 4 marked with crosses are the results obtained with these subarachnoid infusions and it will be seen that they do not deviate significantly (except perhaps at a flow-rate of about 200 μl./min.) from the results with ventricular infusion.

It is safe to conclude, then, that the measurements are, indeed, good approximations to the resistance to flow from subarachnoid space to blood.

Constant pressure technique.—Perfusion experiments on the eye (Bárány, 1962) indicated that a more satisfactory estimate of resistance would be obtained by establishing a fixed fluid-pressure through a reservoir and measuring the rate of flow into the ventricles when a steady-state had been achieved. In the cerebrospinal system it was indeed found that a steady-state was achieved more rapidly and was less variable when this technique was employed, so that in subsequent studies this was the technique of choice. Fig. 5 shows the changes in flow-rate, measured with a drop-recorder, when the pressure in the ventricles was increased stepwise, and fig. 6 shows the corresponding pressure-flow curve (for ease of comparison with fig. 4

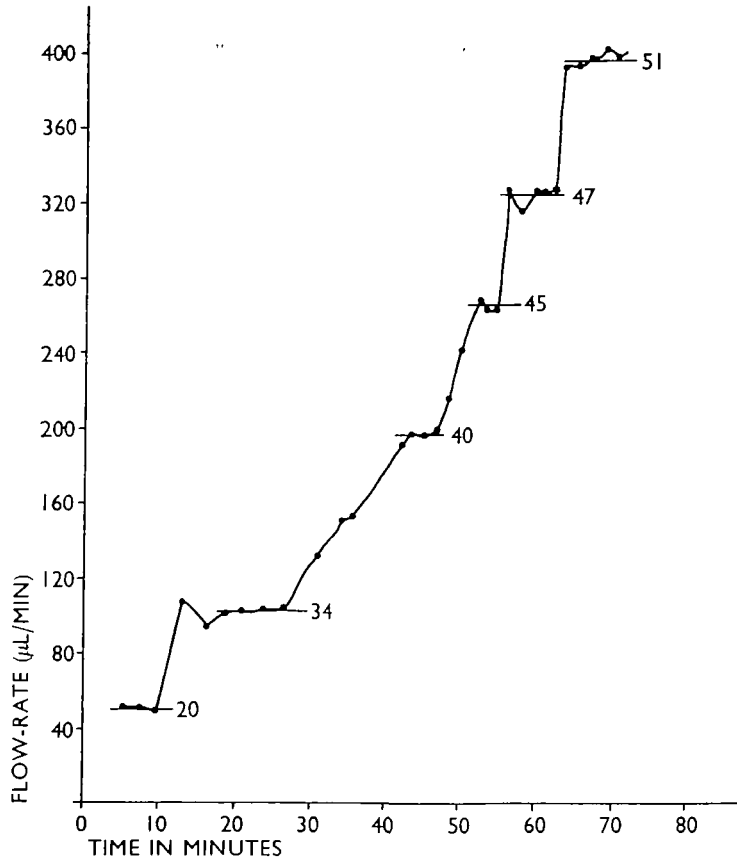

FIG. 5.—Constant-pressure technique. Showing increases in flow-rate when the pressure in the ventricle is increased step by step. The numbers indicate the intraventricular pressures established by raising the reservoir to successively increasing heights. Ordinate: Flow-rate in μl./min. Abscissa: Time after establishing the first pressure (20 cm. H_2O).

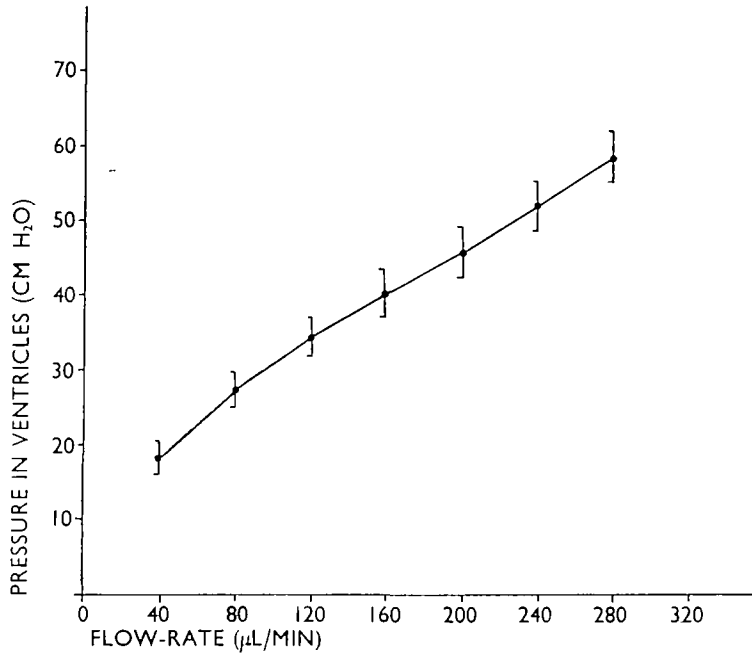

FIG. 6.—Pressure-flow curves derived from 10 constant-pressure type of experiments. Ordinate: Intraventricular pressure in cm. H_2O. Abscissa: Flow-rate in μl./min.

the independent variable, which is now the pressure, has been plotted as ordinate instead of abscissa). The curve is much more closely linear than those obtained by the constant flow techniques but the two overlap quite closely at the higher flow-rates. The estimated resistance at the two flow-rates, 20–120 and 120–280 are now 0·19 and 0·147 respectively, so that it would seem that the high resistance to fluid at low pressures is a feature of the constant flow technique and may well be an artifact since it is by no means easy to obtain a steady-state pressure at the slower rates of infusion.

If Weed's hypothesis is correct, increasing the colloid osmotic pressure of the artificial CSF infused into the ventricles should reduce the rate of flow at a given pressure. Fig. 7 shows the effect of switching from an infusion of artificial CSF to an infusion of the animal's own plasma when the pressure in the ventricles was established at 32 cm. H_2O. Since the colloid osmotic pressure of the plasma proteins is of the order of 40 cm. H_2O, the change should produce a virtual cessation of flow. In fact there was only a gradual fall in rate and this was not reversed by switching back to the artificial CSF. The result suggests that the plasma was blocking the escape routes mechanically, due, perhaps, to the presence of minute clots in the plasma. It is unlikely that the colloid osmotic pressure of the plasma proteins was exerting a significant effect since, with a flow-rate of some 100 μl./min. and a total volume in the cerebrospinal fluid of about 2,000 μl., there should have been 99 per cent replacement of the fluid in about 7 min. yet during this period there was no

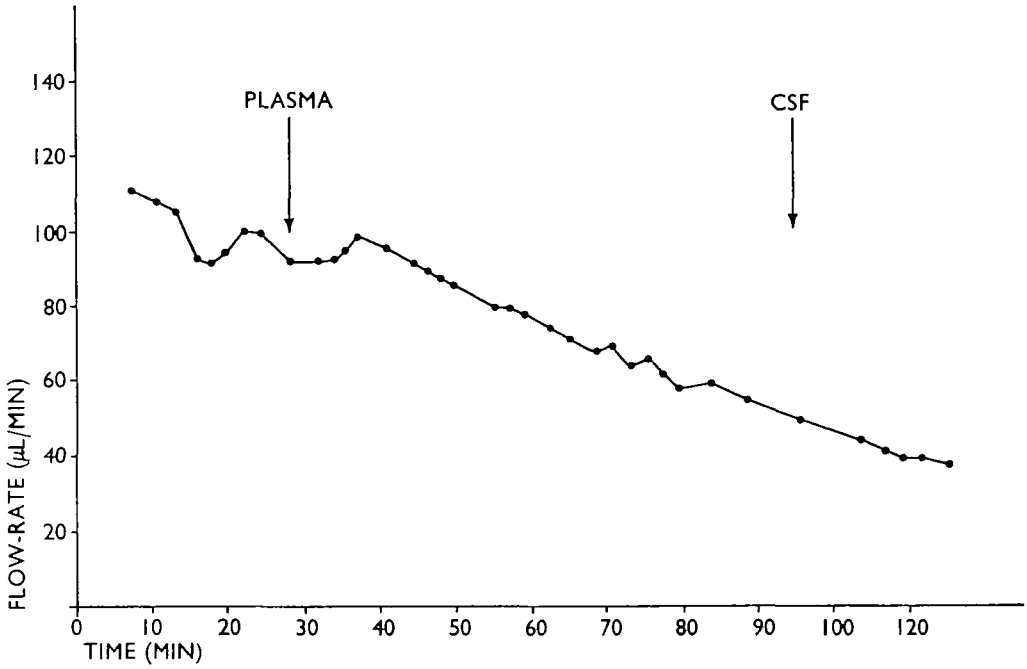

FIG. 7.—Constant-pressure type of experiment. An intraventricular pressure of 32 cm. H_2O was established, and the flow-rate recorded as a function of time. At the first arrow the infusion fluid was changed to the animal's own plasma, and at the second arrow the fluid was changed back to artificial CSF. Ordinate: Flow-rate in μl./min. Abscissa: Time in min. from establishing the steady intraventricular pressure.

significant change in flow-rate. A number of other experiments with either plasma or serum gave variable results; usually there was a steady decrease in flow-rate but, on returning to artificial CSF, the original flow-rate was not restored. The greater viscosity of plasma or serum must have been a factor in reducing flow-rate, but the irreversibility of the changes indicates that the blocking factor was the more important. Filtering the plasma through a membrane of average pore-diameter 0·45 μ made no difference. A more crucial test was made by comparing flow-rates on switching from artificial CSF to a solution containing a dextran; in this way solutions of varying colloid osmotic pressure but about the same high viscosity could be compared and the danger of small clots was avoided. The results were quite definite (fig. 8). Thus a solution containing 10 g./100 ml. of a dextran of molecular weight 500,000 caused a fall in flow-rate of 78 per cent whilst the estimated colloid osmotic pressure of the solution was only 3·7 cm. H_2O. Another solution, containing 13·6 g./100 ml. of a dextran of molecular weight 60,000–90,000, with an estimated colloid osmotic pressure of 33 cm. H_2O, caused a fall in flow-rate of 72 per cent. The viscosities of the solutions, estimated roughly by the time of flow through a length of capillary tubing, were equal and some ten to fifteen times that of the artificial CSF so that it would seem that the viscosity of the dextran solution was the determining

factor in reducing rate of flow. As fig. 8 shows, the effects of the dextran, unlike those of plasma, were reversible, so that the irreversible effects of plasma and serum were probably due to the presence of particulate matter in these fluids.

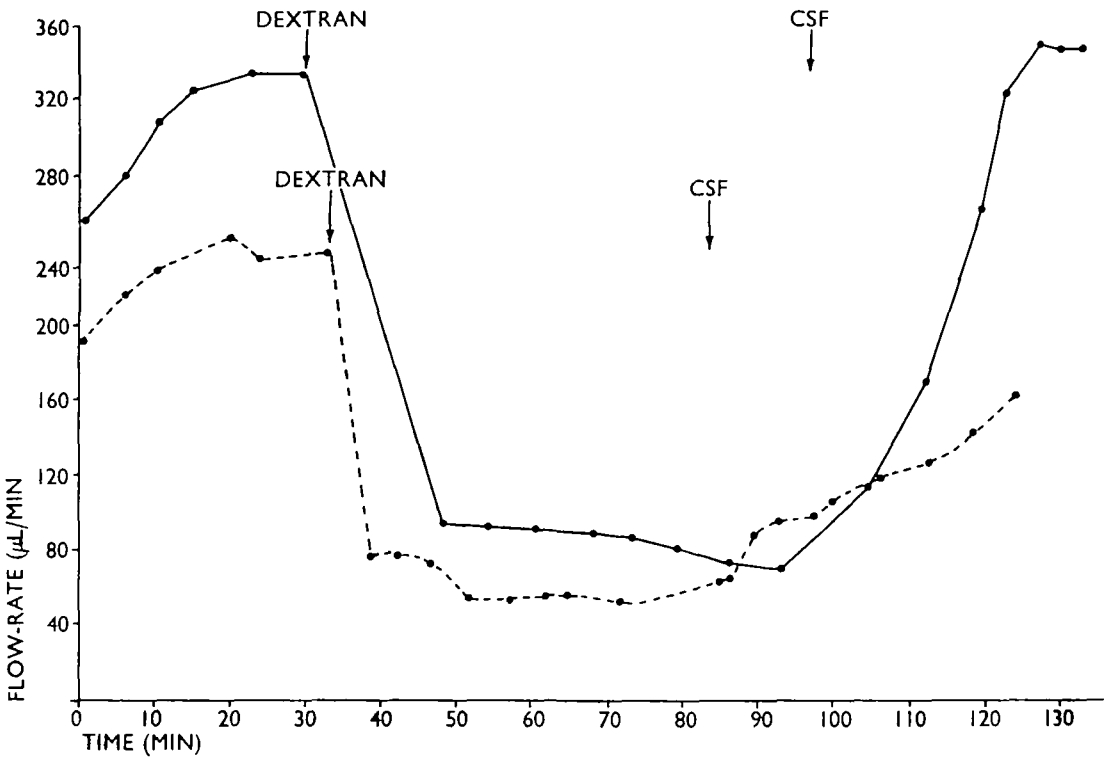

FIG 8.—Constant-pressure type of experiment showing effects of switching from artificial CSF to dextran—CSF (first arrows) and back to artificial CSF (second arrows) at a constant intraventricular pressure of 37 cm. H_2O. Full line: Low molecular weight-high colloid osmotic pressure dextran. Broken line: High molecular weight-low colloid osmotic pressure dextran. Ordinate: Flow-rate in μl./min. Abscissa: Time in min. from establishing the steady intraventricular pressure.

Effects of particulate matter.—Intracisternal injections of kaolin cause hydrocephalus in dogs (Dixon and Heller, 1932; Schurr, McLaurin and Ingraham, 1953; Bering and Sato, 1963) presumably by blocking the pathways through the arachnoid villi; in the following experiments various particulate suspensions were added to the infusion fluid, and they caused a large, and usually irreversible, decrease in flow-rate; fig. 9 shows the effects of kaolin, whole blood and colloidal graphite; there is a pronounced steepening of the pressure-flow curves by comparison with the control.

In these experiments 0·1 to 0·2 ml. of the suspension was injected into each ventricle before beginning the infusion. The kaolin and colloidal graphite (Aquadag) suspensions contained approximately 25 per cent of solid matter.

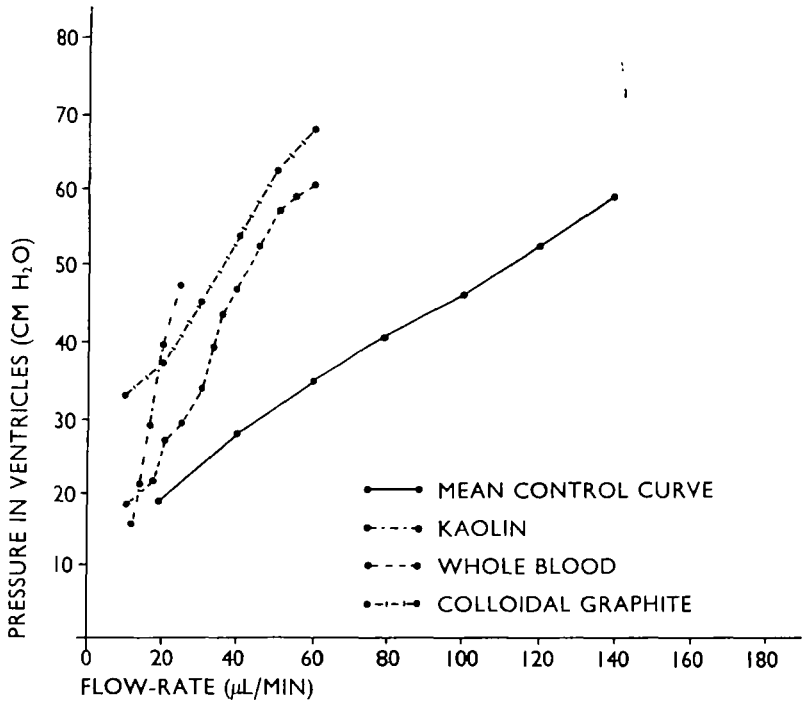

FIG. 9.—Constant-pressure type of experiments showing effects of particulate matter on flow-rate as a function of intraventricular pressure. The curve in full lines is the one taken from fig. 6. Ordinate: Flow-rate in μl./min. Abscissa: Time in min. from establishing the steady intraventricular pressure.

DISCUSSION

The resistance to flow measured in this work is probably a valid experimental parameter, indicating the resistance to flow through the arachnoid villi since the pressure-flow values obtained by direct infusion into the cortical subarachnoid space fall within the same range as those obtained by ventricular infusion. This suggests that the flow along the aqueduct of Sylvius is relatively unimpeded, and it also indicates that puncture of the dura that necessarily follows the passing of the metal cannula into the lateral ventricles does not disturb seriously the flow mechanisms in the experimental animals. Presumably the tissue makes an adequate seal round the cannula. As indicated, earlier, it would have been more satisfactory to have measured the dural sinus pressure, instead of assuming that it remained constant over the range of fluid-pressures studied; technically this would have been difficult and, in fact, the approximate linearity of the pressure-flow relationship when the constant-pressure technique was employed suggests that the sinus-pressure did not increase appreciably as that of the perfusing fluid rose. This accords with the experience of Weed (1935) in the dog and is to be expected from the anatomy of the dural sinuses—their value as the ultimate drainage receptacle consisting in their insulation from changes in intracranial pressure by virtue of being buried in the inelastic dura; this

is in contrast with the intracranial veins whose pressure is directly related to the intracranial pressure (Noell and Schneider, 1948).

The main purpose of this study was to determine whether the drainage of the cerebrospinal fluid could be described in terms of flow through pores that were large compared with the diameters of the main proteins of the plasma. The finding that the dextrans reduced the rate of flow by virtue of their viscosity rather than their colloid osmotic pressure indicates unequivocally that molecules of the order of 60,000–90,000 weight are unable to exert a significant colloid osmotic pressure across the tissue separating CSF from blood. This accords well with the studies of Welch and Friedman mentioned earlier. The finding that substituting the infusion fluid by the animal's own plasma or serum causes a diminished rate of flow (fig. 7) could be explained by the higher viscosity, but the failure to re-establish the normal flow-rate by switching back to artificial CSF indicates a blockage of the channels, perhaps because of the presence of minute fibrin aggregates, but the fact that the same effects are obtained after filtering through a 0·5 μ pore membrane would suggest that the smallest pores in the rabbit's arachnoid villi are considerably smaller than 7 μ, the limiting size of particles able to escape across the arachnoid villi in Welch and Friedman's preparation of the monkey's dura. The absence of an effect of the colloid osmotic pressure of the infusing fluid is in disaccord with the experiments of Weed (1935), who carried out similar experiments to those described here, infusing with a normal Locke fluid and with a fluid containing gelatin to give a colloid osmotic pressure of 9·8 cm. saline; he found that the result obtained with the gelatin solution fell on the same straight line as the controls when the rate of flow was plotted against the "effective filtration pressure," given by the hydrostatic pressure plus the difference of colloid-osmotic pressure. Since the colloid osmotic pressure of the gelatin solution (9·8 cm. H_2O) was small compared with the total pressures involved, namely 300 to 600 mm. saline, it seems unlikely that any effects of the altered colloid osmotic pressure would, in fact, have been experimentally observable.

The claim of Shabo and Maxwell (1968*b*) that proteins are only removed from the CSF by phagocytosis, and are unable to cross the membrane covering the arachnoid villus, is based on electron-microscopical observations. The present experiments in which the infusion fluid was the animal's own plasma make this claim unlikely; thus the plasma was infused under a pressure of some 32 cm. H_2O, i.e. less than the colloid osmotic pressure of the plasma proteins; during the time required for 99 per cent replacement of the fluid in the system by the infused plasma there was no appreciable change in rate of flow, so that the colloid osmotic pressure of the plasma was not being exerted. It seems most unlikely that, during the perfusion, the plasma proteins were being removed by phagocytosis at such a rate as to leave the plasma virtually free of proteins during the infusion.

If phagocytosis were the normal method of removing the small amounts of proteins that enter the CSF during secretion, it would be surprising to find the rate

of appearance in the blood of labelled proteins injected into the CSF to be linearly related to the rate of secretion of CSF, yet this is actually found (Sweet *et al.*, 1950).

Studies on ventriculo-cisternal perfusion, during which the pressure in the subarachnoid space was varied, carried out in several laboratories, have provided figures from which estimates of resistance to drainage may be made; under these conditions a large part of the flow escaped through a cannula in the cisterna magna and the "overspill" into the blood, by way of the arachnoid villi, was estimated by the clearance of inulin, which was assumed to escape only by this route and not across the ependymal linings. These estimates have been summarized by Cutler *et al.* (1968), and range from 390 cm.min.ml.$^{-1}$ in the cat through 132 in the goat to 13 cm.min.ml.$^{-1}$ in man. The figure obtained in this work for the rabbit, using the constant-pressure technique, was 0·147–0·19 cm.min.μl.$^{-1}$ or 147–190 cm.min.ml.$^{-1}$, and is thus considerably less than that of the cat and comparable with that of the goat. In general, we should expect the resistance, measured in these ways, to be an inverse function of the volume of cerebrospinal fluid, since, so far as is known, the cerebrospinal fluid-pressures in different species do not vary widely, whilst the absolute rates of secretion increase with increasing volume of the fluid (*see*, for example, Davson, 1967, p. 131). Thus man, with the largest volume of CSF, secretes some 350 μl./min., whilst the rabbit secretes only some 10–12 μl./min., so that, other things being equal, we should expect the resistance in the rabbit to be some thirty times that of man; if we accept Cutler *et al.* figure of 13 cm.min.ml.$^{-1}$ for man, the resistance for the rabbit will be 390 cm.min.ml.$^{-1}$, i.e. about twice that actually found. It could well be that the CSF pressure in the rabbit is lower than that in man, or rather the pressure-drop between CSF and dural sinus; in this event a lower resistance would be required to allow the appropriate rate of flow.

Summary

The mechanism of drainage of the cerebrospinal fluid has been reinvestigated in the light of the claim that the membranes covering the arachnoid villi are impermeable to protein.

Methods of measuring the resistance of the drainage channels to an imposed flow are described.

This resistance to flow is not affected by the colloid osmotic pressure of an artificial CSF infused into the ventriculo-subarachnoid system, so that it is concluded that the drainage channels allow an unrestricted passage of proteins through their pores.

Large increases in resistance may be provoked by introducing whole blood, kaolin or colloidal graphite into the ventricles.

REFERENCES

BÁRÁNY, E. H. (1962) The mode of action of pilocarpine on outflow resistance in the eye of a primate (*Cercopithecus ethiops*). *Invest. Ophthal.*, **1**, 712–727.

BERING, E. A., Jr., and SATO, O. (1963) Hydrocephalus: changes in formation and absorption of cerebrospinal fluid within the cerebral ventricles *J. Neurosurg.*, **20**, 1050–1063.

BITO, L. Z , BRADBURY, M. W. B., and DAVSON, H. (1966) Factors affecting the distribution of iodide and bromide in the central nervous system. *J. Physiol., Lond.*, **185**, 323–354.

BRIERLEY, J. B., and FIELD, E. J. (1948) The connexions of the spinal sub-arachnoid space with the lymphatic system. *J. Anat.*, **82**, 153–166.

CUTLER, R. W. P., PAGE, L., GALICICH, J., and WATTERS, G. V. (1968) Formation and absorption of cerebrospinal fluid in man. *Brain*, **91**, 707–720.

DAVSON, H. (1956) "Physiology of the Ocular and Cerebrospinal Fluids." London· Churchill.

—— (1967) "Physiology of the Cerebrospinal Fluid." London: Churchill.

DIXON, W. E., and HELLER, H. (1932) Experimentelle Hypertonie durch Erhöhung des intrakraniellen Druckes. *Arch. exp. Path. Pharmak.*, **166**, 265–275.

ELMAN, R. (1923) Spinal arachnoid granulations with especial reference to the cerebrospinal fluid. *Johns Hopkins Hosp. Bull.*, **34**, 99–104.

FRICK, E , and SCHEID-SEYDEL, L. (1960) Untersuchungen mit J^{131}-markiertem β-Globulin zur Frage der Abstammung der Liquoreiweisskörper. *Klin. Wschr.*, **38**, 1240–1243.

HILL, N. C., GOLDSTEIN, N. P., MCKENZIE, B. F., MCGUCKIN, W. F., and SVIEN, H. J. (1959) Cerebrospinal-fluid proteins, glycoproteins, and lipoproteins in obstructive lesions of the central nervous system. *Brain*, **82**, 581–593.

——, MCKENZIE, B. F., MCGUCKIN, W F., GOLDSTEIN, N. P., and SVIEN, H. J. (1958) Proteins, glycoproteins and lipoproteins in the serum and cerebrospinal fluid of healthy subjects. *Proc. Staff Meet. Mayo Clin.*, **33**, 686–698.

MORTENSEN, O. A., and WEED, L. H. (1934) Absorption of isotonic fluids from the subarachnoid space. *Am. J. Physiol.*, **108**, 458–468.

NOELL, W., and SCHNEIDER, M. (1948) Zur Hämodynamik der Gehirndurchblutung bei Liquordrucksteigerung. *Arch. Psychiat. Nevenkrankheilkunde*, **118–180**, 713–730.

POLLAY, M., and DAVSON, H. (1963) The passage of certain substances out of the cerebrospinal fluid. *Brain*, **86**, 137–150.

——, and WELCH, K. (1962) The function and structure of canine arachnoid villi. *J. surg. Res.*, **2**, 307–311.

SCHURR, P. H., MCLAURIN, R. L., and INGRAHAM, F. D. (1953) Experimental studies on the circulation of the cerebrospinal fluid and methods of producing communicating hydrocephalus in the dog. *J. Neurosurg* , **10**, 515–525.

SHABO, A. L., and MAXWELL, D. S. (1968*a*) The morphology of the arachnoid villi: a light and electron microscopic study in the monkey. *J. Neurosurg* , **29**, 451–463.

——, —— (1968*b*) Electron microscopic observations on the fate of particulate matter in the cerebrospinal fluid. *J. Neurosurg* , **29**, 464–474.

SWEET, W. H., SELVERSTONE, B., SOLOWAY, S., and STETTEN, D., Jr. (1950) Studies of formation, flow and absorption of cerebrospinal fluid. II. Studies with heavy water in the normal man. *Surg. Forum*, pp. 376–381.

TVETEN, L. (1965) Cerebrospinal-fluid proteins in obstructive lesions of the central nervous system. *Acta neurol. scand.*, **41**, 80–91.

WEED, L. H. (1935) Forces concerned in the absorption of the cerebrospinal fluid. *Am. J. Physiol.*, **114**, 40–45.

WELCH, K., and FRIEDMAN, V. (1960) The cerebrospinal fluid valves. *Brain*, **83**, 454–469.

WRIGHT, R. D. (1938) Experimental observations on increased intracranial pressure. *Aust. N.Z. J. Surg.*, **7**, 215–235.

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