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CSF hydrodynamic studies in man

2 Normal hydrodynamic variables related to CSF pressure and flow[1]

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SUMMARY With the patient in the supine position, the subarachnoidal space was infused with artificial CSF at several constant pressure levels. The resulting flow of liquid was recorded. By draining CSF at a low pressure the CSF production rate was determined. Normal values are given and discussed for (1) the resting pressure, (2) the conductance of the CSF outflow pathways, (3) the formation rate of CSF, (4) the pressure difference across the CSF outflow pathways, and (5) the sagittal sinus pressure. None of the variables showed any age dependence, nor was there any sex difference.

The method of constant pressure CSF infusion has already been described and the general findings discussed (Ekstedt 1977). Normal reference values of the different hydrodynamic variables are required. The variables discussed in this paper are only those relevant to the flow of CSF, while those related to the volume/pressure relationship will be reported separately. Preliminary results have been reported by Ekstedt (1975) and Ekstedt and Fridén (1976).

Methods

The methods were described in detail by Ekstedt (1977). Briefly, with the patient in a sitting position two needles were inserted in a single lumbar intervertebral space and connected by tubes, filled with artificial CSF, to pressure transducers. The patient was then brought to the supine position and remained so during the rest of the investigation. The *resting CSF pressure* (p_{clr}) was recorded during, at least, one hour. Thereafter a bottle with artificial CSF was connected to one of the needles and its pressure raised above the resting CSF pressure. When flow had stabilised, the CSF pressure and corresponding inflow of artificial CSF were measured. About eight to 10 different pressure/flow values were taken, up to a pressure of about 6 kPa. There was a rectilinear relation between flow and pressure. The regression line of flow on pressure was calculated. This is the *conductance of the CSF outflow pathways* (G_{op}) (Fig. 1). After stopping infusion the pressure was monitored during the next 20 to 30 minutes. The pressure then usually attained the same value as the resting pressure at the beginning of the investigation.

The pressure in the infusion bottle was then decreased to 0.25 kPa. When the rate of drainage had stabilised, after the initial high rate, the drainage was extended for another 20 to 30 minute period, used for measurement of the *CSF formation rate* (q_f). In most cases the CSF was then reinfused until the initial resting pressure was attained.

The *pressure difference across the CSF outflow pathways* (P_{dop}) and the *pressure in the sagittal sinus* (p_{ss}) were calculated with the use of the following formulae

$p_{dop}=q_f/G_{op}$

$p_{ss}=p_{clr}-p_{dop}$

All pressures were always referred to the sagittal midpoint of the skull with the patient in a strict supine position.

It should be strongly stressed that the supine position of the patient is one of the most important aspects of the whole method. It has proved very difficult to maintain the position of the patient constant during the several hours of experiment if he or she is in the lateral recumbent position. In the supine position this offers no problem.

UNITS OF MEASUREMENTS

SI units have been used throughout.

Pressure:

1 kilopascal (1 kPa)=7.5 mmHg=102 mmH_2O.

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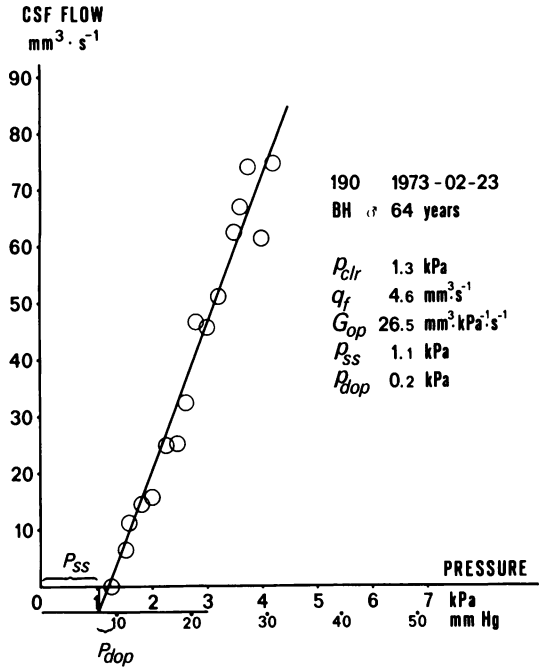


Fig. 1 *Example of the relation between pressure and flow obtained in a patient aged 64 years, considered to be "normal". Abscissa: the CSF pressure obtained when the flow at each level has stabilised after the initially higher flow rate. Ordinate: the corresponding inflow of artificial CSF from the bottle to the patient's subarachnoid space. There is obviously a rectilinear relation between pressure and flow which is also true in the majority of all other recordings made. The regression line of flow on pressure, the conductance of the CSF outflow pathways (G_{op}), has been calculated according to the formula given in the text. The horizontal line below the abscissa represents the CSF formation rate of 4.6 mm³ s⁻¹ obtained in this patient. The intersection of this line with the regression line thus represents the pressure that should have existed if there were no production of CSF and thus no outflow through the arachnoidal villi—that is, the pressure of the CSF recipient, mainly the sagittal sinus. Below this pressure no elimination of CSF can occur. For further information, see Ekstedt (1977).*

The hydrodynamic conductance of the CSF outflow pathways has the dimension $mm^3\ kPa^{-1}s^{-1}$.
$1\ mm^3\ kPa^{-1}s^{-1}=6 \cdot 10^{-3}$ ml $(cmH_2O)^{-1} \cdot min^{-1}$
$=8 \cdot 10^{-3}$ ml. $(mmHg)^{-1} \cdot min^{-1}$.
The regression line has been calculated according to the formula

$$G_{op}=\frac{\Sigma[(p_{cl}-p_{clr}) \cdot q]}{\Sigma (p_{cl}-p_{clr})^2}$$

where p_{cl} and q are the individual data pairs of pressure and flow obtained when the initially higher inflow of CSF has levelled off to a stable value after each change of infusion pressure. This method forces the regression line through the resting pressure value which is considered to have more precision than any one of the experimental points obtained during infusion.

To facilitate comparisons for those not accustomed to SI units of measurement, conversion scales are given in Fig. 2 where the normal values obtained are also indicated.

SUBJECTS

The hydrodynamic investigations have only been performed on suspicion of altered hydrodynamics in patients. The project was approved by the hospital ethical committee, and the informed consent of the patient was obtained in each case. To date 947 investigations have been performed on 820 patients during a period of six years. The last 850 investigations were carried out in strict accordance with the methods described.

This paper reports only the findings in normal investigations. Deciding which patients should be considered "normal" is not easy. Among the 820 patients it has been possible to select 58 (31 women and 27 men) whose medical history, medical and neurological investigation, and follow-up for at least two years, made it highly probable that they had no organic neurological or circulatory disorder. When using these 58 patients as reference an additional 350 patients in the sample could be considered to have entirely normal CSF hydrodynamics; these, however, are not included in the present paper. A further 42 patients had only a resting pressure recording, but were also to be considered "normal" according to the above principles and incorporated in the sample, making a total of 45 women and 55 men. The age distribution of the "normal" patients is shown in Fig. 3.

The answer to the question of what is normal and abnormal in intracranial hydrodynamics must be based on an investigation of a group considered *beforehand* to be normal. It seems likely, however, that the results of such an investigation will not be very different from those obtained here, but some changes are inevitable. Meanwhile we have to rely on the present provisionally normal subjects.

Results

The distribution of measurement values for resting pressure (p_{clr}) in the supine position is shown in Fig. 4. All values were obtained at the end of a recording period with a duration of 60 minutes or more. During the last 15 minutes or more there had been no upward or downward trend in the recordings. The mean resting pressure was 1.38 kPa (SD=0.19, 5–

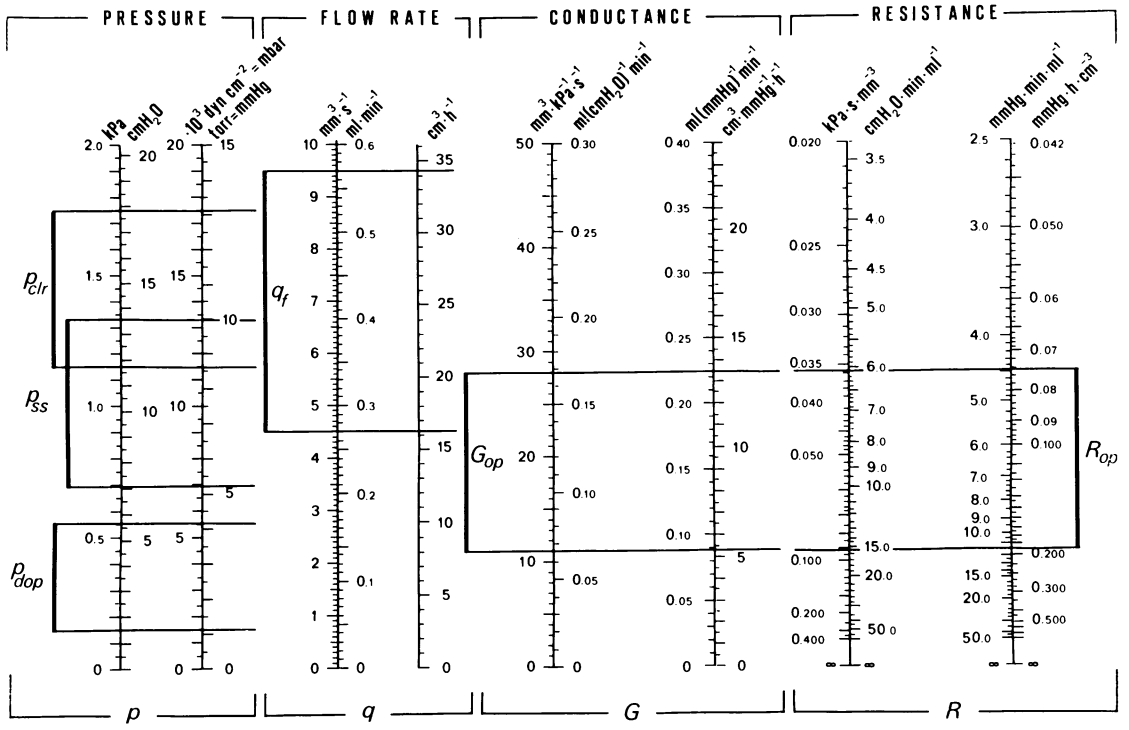


Fig 2 *Scales for conversion of other units of measurements to SI units and reverse. The 5–95% normal limits for the variables are indicated. The relation between conductance (G) and resistance (R) is: $G = 1/R$.*

95% within 1.15–1.75 kPa, n=100). There was no correlation (R=−0.1) between the patient's age and the resting pressure. In all 58 recordings the relation between pressure and inflow of artificial CSF during the infusion was rectilinear.

CONDUCTANCE OF THE CSF OUTFLOW PATHWAYS

The distribution of values for conductance (G_{op}) is shown in Fig. 5. The mean value was 17.98 $mm^3 \cdot kPa^{-1} \cdot s^{-1}$ (SD=4.06, 5–95% of the values fell within 12.0–26.0 $mm^3\ kPa^{-1}s^{-1}$, n=58). There was no correlation between age and conductance (R=−0.3).

CSF FORMATION RATE

Formation rate (q_f) at the pressure 0.25 kPa was found to be 6.67 $mm^3 \cdot s^{-1}$ (SD=0.1, 5–95% fell within 4.5–9.4 $mm^3 \cdot s^{-1}$, n=58) (Fig. 6). There was no correlation between age and CSF formation rate (R=−0.3).

PRESSURE DIFFERENCE ACROSS THE CSF OUTFLOW PATHWAYS

The mean calculated pressure difference (in normal

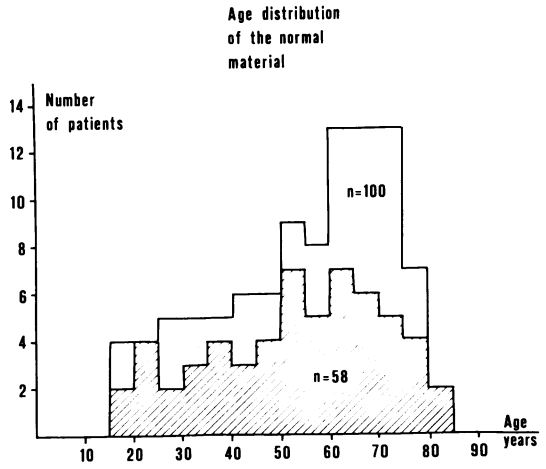
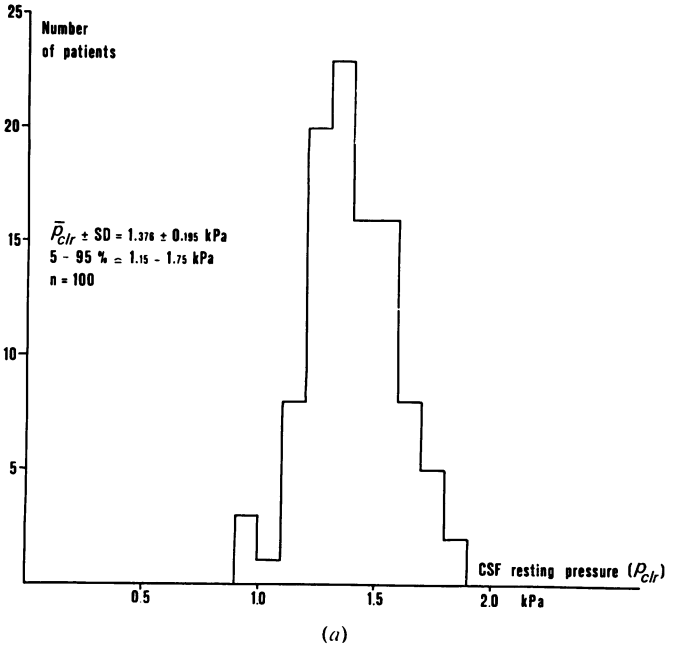
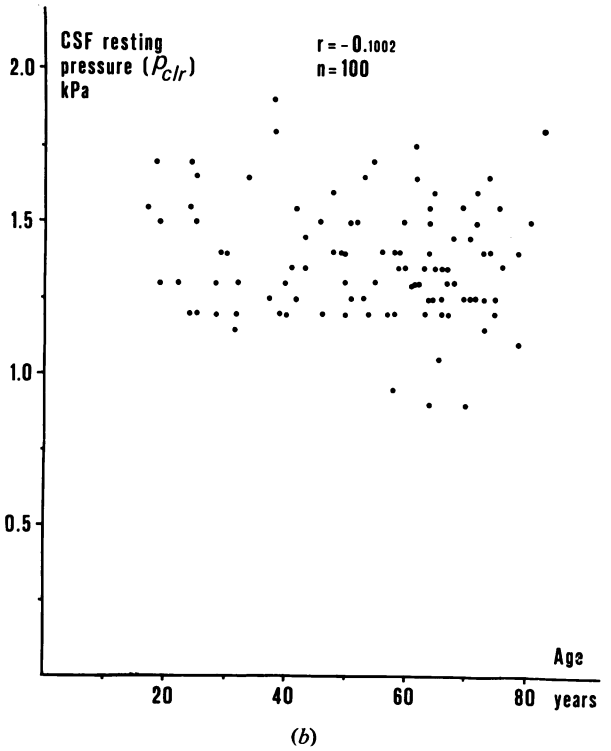


Fig. 3 *Age distribution of subjects. The shaded area represents the 58 patients in which the complete hydrodynamic investigation was performed, the unshaded area the further 42 patients in whom only a CSF resting pressure recording was performed.*



(*a*)



(*b*)

Fig. 4 *CSF resting pressure distribution* (*a*) *and age dependence* (*b*).

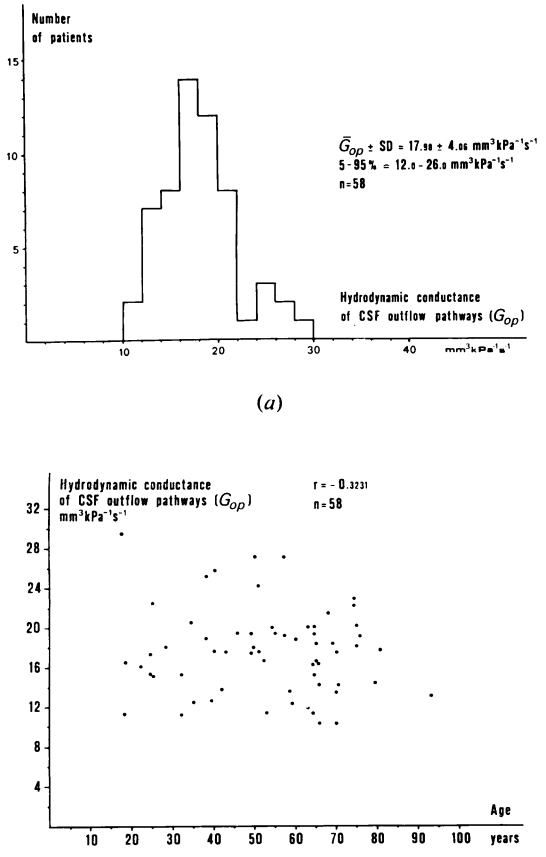


Fig. 5 *Distribution of values for the hydrodynamic conductance of CSF outflow pathways (a) and age dependence (b).*

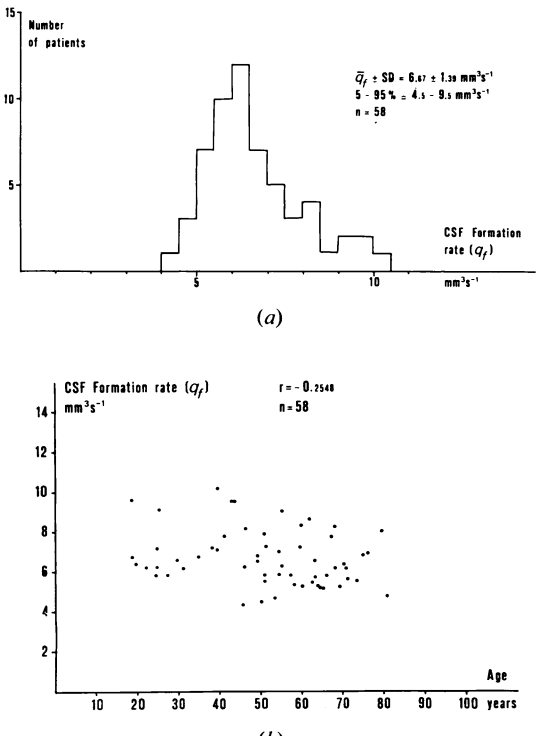


Fig. 6 *Distribution of values for CSF formation rate (a) and age dependence (b).*

people the pressure across the arachnoidal villi ($P_{dop}=\frac{q_f}{G_{op}}$) was found to be 0.37 kPa (Fig. 7) (SD=0.10, 5–95% fell within 0.25–0.55 kPa, n=58). There was no correlation between age and the pressure difference (R=0.03).

SAGITTAL SINUS PRESSURE

Finally, the mean calculated value for the sagittal sinus pressure ($p_{ss}=p_{clr}-p_{dop}$) (Fig. 7) was 1.00 kPa (SD=0.20, 5–95% fell within 0.70–1.35 kPa, n=58). There was no correlation with age (R=0.1).

There was no difference between females and males for any of the variables which are summarised in the Table and indicated on the scales in Fig. 2.

Discussion

RESTING PRESSURE OF CSF

Normal values for the CSF resting pressure in the supine position have not been reported in the literature. The pressure level, of course, depends on which reference point is chosen. In the present investigation the cranial sagittal midpoint was used, which corresponds to the external osseous auditory meatus, the jugular bulb, and approximately to the centre of the right atrium. This reference point proved to give about the same pressure values as when recording was made with the patient in the lateral recumbent position and the level of the spine was chosen as a reference (Ekstedt, 1977). Therefore there should not generally be any gross differences between the pressure levels obtained in the two positions.

Tourtellotte (1966) performed open manometry in 105 healthy volunteers in the lateral recumbent position and found an average CSF pressure of 1.47 kPa with SD 0.32. Gilland (1969) made isometric CSF pressure recordings with a pressure transducer in 15 healthy volunteers in the lateral recumbent

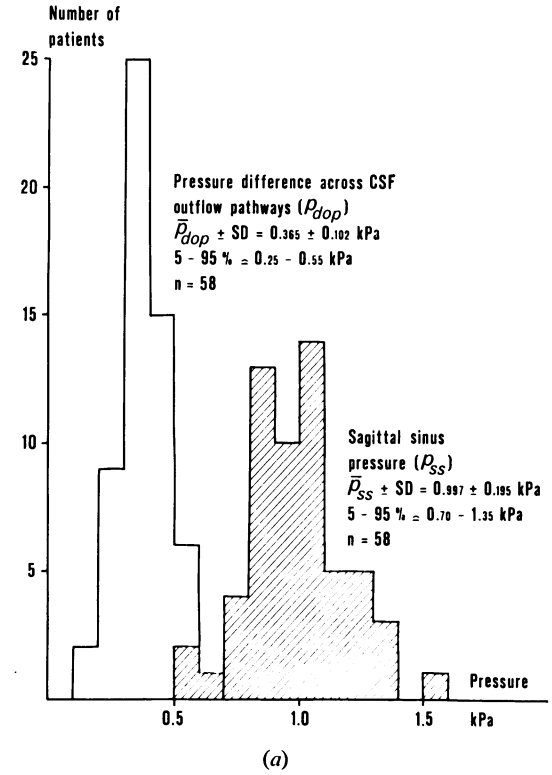


Fig. 7 *Distribution of values for the pressure differences across CSF outflow pathways (a, unshaded area) and the values for sagittal sinus pressure (a, shaded area); b shows the age dependence of the two variables.*

Table *Normal values for CSF hydrodynamic variables (58 patients (for p_{clr} 100) 15–83 years)*

	M	*SD*	90% *within*
Lumbar resting pressure (p_{clr})	1.38 kPa	0.19	1.15– 1.75
Conductance of CSF outflow pathways (G_{op})	17.98 $mm^3\ kPa^{-1}s^{-1}$	4.06	12.0 –26.0
CSF formation rate (qf)	6.67 $mm^3\ s^{-1}$	1.39	4.5 – 9.5
Pressure difference across outflow pathways (p_{aop})	0.37 kPa	0.10	0.25– 0.55
Sagittal sinus pressure (p_{ss})	1.00 kPa	0.20	0.70– 1.35

Supine horizontal position. Reference level: cranial sagittal centre; constant pressure infusion method with artificial CSF.
No sex differences in variables nor any age dependence.

position. He found an average value of 1.41 kPa with SD 0.30 kPa and a range of 0.99 to 1.96 kPa. These authors made a joint study in 31 healthy volunteers in the lateral recumbent position (Gilland *et al.* 1974). In half the experiments a very thin needle (26 gauge) was used, and an average CSF pressure of 1.54 kPa (SD 0.35) was obtained. In the other half of the experiments a thicker needle was used (22 gauge), and the average pressure value then obtained was 1.42 kPa (SD 0.36 kPa) (not statistically different from the last value). The measurement values were taken after 10 minutes of continuous recording. The mean values are close to the mean value obtained in the present investigation and statistically not significantly different from them. However, the dispersion of values is less in the present investigation. Gilland *et al.* (1974) reported 95% tolerance limits of 0.4–2.45 kPa when using the fine needle, and 0.5–2.55 kPa when using the gross needle. The values are obviously based on the standard deviations because the observed range of pressure values were 0.8–2.3 kPa. In the present investigation the distribution of values was non-Gaussian, and, therefore, it was preferred to define the tolerance limits to the limits within which 5–95% of the actual observations fell (as is also done with the other variables).

CONDUCTANCE OF THE CSF OUTFLOW PATHWAYS

With regard to the hydrodynamic conductance of the CSF outflow pathways, no information from normal man can be obtained from the literature. With the ventriculolumbar perfusion technique, Cutler *et al.* (1968) found values of about 13 $mm^3\ kPa^{-1}s^{-1}$ in eight children with subacute sclerosing panencephalitis and four children with pontine gliomas (but all with normal resting CSF pressures).

In the paper presenting the constant rate CSF infusion method of Katzman and Hussey (1970), no calculations of conductance were made by the authors. It is, however, possible to make some gross estimations using their published data. From their Fig. 3 one can calculate the following values for conductance in recordings which they considered normal: 14, 16, 21, 22, 23, 23, 30, 32, 35, 45, 55, 115 · $mm^3\ kPa^{-1}s^{-1}$. In their test they consider an increase of the pressure from 1.2 to 3.0 kPa during an infusion at a constant rate of 12.7 $mm^3\ s^{-1}$ as the upper normal limit. These values represent a conductance of 7 $mm^3\ kPa^{-1}s^{-1}$.

Martins (1973) used the constant rate infusion technique and calculated the resistance to drainage (which is the inverse of conductance). He does not give any individual values, but by measurement on his Fig. 3 on the recordings that he had considered normal from the hydrodynamic point of view, one finds values of conductance of 8, 10, 12, 16, 17, 20, 24 $mm^3\ kPa^{-1}s^{-1}$.

Janny *et al.* (1975) used constant rate infusion by the intraventricular route. They studied 12 patients with Alzheimer's disease as a reference group and found the measurement values of resistance to lie between 5 and 15 mmHg · ml^{-1} min, which recalculated to conductance corresponds to 8–25 $mm^3\ kPa^{-1}s^{-1}$. Thus the results obtained by others with ventriculolumbar perfusions or constant rate lumbar CSF infusions are in agreement with the conductance values obtained in this investigation.

In normal subjects the conductance of the subarachnoid space is probably very high in relation to that of the arachnoidal villi, which means that the villi almost entirely determine the value of the conductance. In pathological cases, however, it may be assumed that there may be adhesions and other types of blocking of the subarachnoid space, and these may be responsible for a decrease of the conductance.

Some authors (Martins, 1973; Janny *et al.*, 1975) have used the resistance of the outflow pathways which is simply the inverse of the conductance. To the author, conductance has seemed somewhat more appropriate for the following reasons: the arachnoidal villi are coupled in parallel, and within each villus there are open channels, also coupled in parallel with each other. A change of the properties of the villi will, then, reflect itself directly on conductance while the relation to resistance will be inverse. Furthermore, in a hydrodynamic system involving a capacitance, a flow is caused by a pressure difference and, therefore, a diagram of the flow/pressure relation should preferably be drawn with pressure on the abscissa and flow on the ordinate, the angle coefficient of the regression line then representing the conductance. In the study of the hydrodynamics of the eye, the conductance (facility of outflow) has become standard, which is a further argument in its

favour. However, conversion between resistance and conductance is easily made by a simple inversion.

With regard to the calculation of conductance, all investigations done (947) have been subject to calculation according to the different formulae and methods described by Ekstedt (1977, p. 110). Both in normal and in pathological cases there is very rarely a difference in the value between the methods of more than one or two digits, and often the difference is only in the decimal position. The choice of calculation method for regression thus does not seem to be crucial. When only one experimental point of corresponding pressure (p_{cl}) and flow (q) is available, obtained by constant pressure or constant flow method, equation $G_{op}=\frac{q}{p_{cl}-p_{clr}}$ gives reasonable precision in the estimate of the conductance.

FORMATION RATE OF CSF

With regard to CSF formation rate Cutler *et al.* (1968) in ventriculolumbar perfusion experiments found values between 3.3 mm^3s^{-1} and 10 mm^3s^{-1} in 12 children between the ages of 5 and 13 years with pontine gliomas or subacute sclerosing panencephalitis treated by local infusion of immunosuppressive drugs. The mean rate was estimated to be 5.8 mm^3s^{-1}. Masserman (1934) estimated CSF formation rate by removal of 20–30 ml CSF and measuring the time for restoration of the pressure. In 83 patients he found a mean value of 5.3 mm^3s^{-1}.

With a modified Massermann method, removal of 10 ml CSF and measurement of the time for pressure to return, Katzman and Hussey (1970) found CSF formation rates between 3.8 mm^3s^{-1} and 6.4 mm^3s^{-1} in 11 patients. The average value was 5.4 mm^3s^{-1}. Sjöqvist (1937) made open ventricular drainage in neurosurgical patients and found values of CSF formation rate of about 6 mm^3s^{-1}.

An important question is whether or not the CSF pressure influences the rate of formation. Is the rate higher at 0.25 kPa pressure, used in this investigation, than at the normal resting pressure? Rubin *et al.* (1966) found no influence between the pressure levels 0–2 kPa, neither did Cutler *et al.* (1968) in the range of -1 to $+2$ kPa, both using perfusion techniques in humans. Heisey *et al.* (1962) made the same observation in perfusion experiments in goats, Bering and Sato (1963) in dogs, Hochwald and Wallenstein (1967) in cats, Heisey and Michael (1971) in the freshwater turtle, and Anderson and Heisey (1972) in chickens. In contrast to these investigations, Calhoun *et al.* (1967) and Frier *et al.* (1972) in calves, Hochwald and Sahar (1971) in cats and rabbits, and Sahar (1972) in an isolated choroid plexus preparation found decrease of the formation rate with increasing pressure. Thus, the question of a pressure dependence of CSF production rate must still be considered as unanswered. In the range 0.25 kPa–2.0 kPa the influence is probably not important. There is also another open question; are the arachnoidal villi really tight when the CSF pressure is lowered below the sagittal sinus pressure? Can there be any back flow of plasma into the subarachnoid space under the present investigative premises? No information is available on this matter. However, if this is the case, the effect would be equal to an increase of the CSF formation rate which seems unlikely in the light of the above reasoning.

PRESSURE DIFFERENCE ACROSS THE CSF OUTFLOW PATHWAYS

The pressure difference across the CSF outflow pathways, ($p_{dop}=q_f/G_{op}$), has been calculated according to principles that seem to be well supported by the isolated sinus wall experiments of Welch and Friedman (1960) and the animal CSF infusion experiments of Davson *et al.* (1970). The rectilinearity of the pressure/flow relation, found in all experiments reported in the present investigation as well as in the majority of all other experiments in pathological cases made by the author, is also a strong indication that the arachnoidal villi have open channels and that these channels, when once opened by pressure, do not further distend at increasing pressure. No numerical values from man can be found in the literature.

SAGITTAL SINUS PRESSURE

The calculated sagittal sinus pressure ($p_{ss}=p_{clr}-p_{dop}$) agrees well with the values found by Shulman *et al.* (1964) in normal dogs (24 animals). Their mean value was 0.9 kPa$\pm$ 0.3 kPa in an experimental situation when the mean CSF pressure was 1.5$\pm$0.3 kPa. The sagittal sinus pressure in patients with brain tumours was directly measured by Martins *et al.* (1974), and seems to lie in the same range as those determined in the present investigation. It is not yet finally settled whether or not there are any elastic forces in the arachnoidal villi which would give an opening pressure which must first be overcome before any flow can start through the villi. If so, as concluded by Welch and Friedman (1960) from their isolated sinus wall experiments, the real sagittal sinus pressure should be somewhat lower than the calculated value. The question needs further study.

It should also be stressed that the calculations of p_{dop} and p_{ss} are based on the assumption that the arachnoidal villi have a considerably lower conductance than the subarachnoid space. This is probably true in normal subjects, but does not exclude the possibility that it is otherwise in some pathological cases. Subarachnoid adhesions may

exist in postinfectious or posthaemorrhagic conditions and, if so, the calculated values of p_{dop} and pss are probably different from the real ones. This question also needs further study.

The absence of correlation between age and any of the variables is astonishing. One would at least expect some age-dependent connective tissue changes in the arachnoidal villi causing a decreased conductance at higher ages, but it does not appear to be so. It is, of course, important to know whether this non-dependence on age is true for the whole period down to the neonatal period, and thus whether these normal values can be used. This is another question that requires further elucidation. Finally, it should be stressed that the variables will be the same irrespective of the method used for obtaining the data—the constant pressure or the constant flow method.

References

Anderson, D. K., and Heisey, S. R. (1972). Clearance of molecules from cerebrospinal fluid in chickens. *American Journal of Physiology*, **222,** 645–648.

Bering, E. A., and Sato, O. (1963). Hydrocephalus: changes in formation and absorption of cerebrospinal fluid within the cerebral ventricles. *Journal of Neurosurgery*, **20,** 1050–1063.

Calhoun, M. C., Hurt, H. D., Eaton, H. D., Rousseau, J. E., and Hall, R. C. (1967). *Rates of Formation and Absorption of Cerebrospinal Fluid in Holstein Male Calves*. Bulletin 401. Storrs Agricultural Experiment Station: The University of Connecticut, Storrs.

Cutler, R. W. P., Galicich, J., and Watters, V. (1968). Formation and absorption of cerebrospinal fluid in man. *Brain*, **91,** 707–720.

Davson, H., Hollingsworth, G., and Segal, M. B. (1970). The mechanism of drainage of the cerebrospinal fluid. *Brain*, **93,** 665–678.

Ekstedt, J. (1975). CSF hydrodynamics studied by means of constant pressure infusion technique. In *Intracranial Pressure II*, pp. 35–41. Edited by N. Lundberg, U. Pontén, and M. Brock. Springer: Berlin.

Ekstedt, J. (1977). CSF hydrodynamic studies in man. 1. Method of constant pressure CSF infusion. *Journal of Neurology, Neurosurgery, and Psychiatry*, **40,** 105–119.

Ekstedt, J., and Fridén, H. (1976). CSF hydrodynamic especially in the adult hydrocephalus syndrome. In *Intracranial Pressure III*, pp. 177–185. Edited by J. W. F. Beks, M. Brock, and D. C. Bosh. Springer: Berlin.

Frier, H. I., Gallina, A. M., Rousseau, J. E., Jr., and Eaton, H. D. (1972). Rates of formation and absorption of cerebrospinal fluid in the very young calf. *Journal of Dairy Sciences*, **55,** 339–344.

Gilland, O. (1969). Normal cerebrospinal-fluid pressure. *New England Journal of Medicine*, **280,** 904–905.

Gilland, O., Tourtellotte, W. W., O'Tauma, L., and Henderson, W. G. (1974). Normal cerebrospinal fluid pressure. *Journal of Neurosurgery*, **40,** 587–593.

Heisey, S. R., and Michael, D. K. (1971). Cerebrospinal fluid formation and bulk absorption in the freshwater turtle. *Experimental Neurology*, **31,** 258–262.

Heisey, S. R., Held, D., and Pappenheimer, J. R. (1962). Bulk flow and diffusion in the cerebrospinal fluid system of the goat. *American Journal of Physiology*, **203,** 775–781.

Hochwald, G. M., and Sahar, A. (1971). Effect of spinal fluid pressure on cerebrospinal fluid formation. *Experimental Neurology*, **32,** 30–40.

Hochwald, G. M., and Wallenstein, M. (1967). Exchange of albumin between blood, cerebrospinal fluid, and brain in the cat. *American Journal of Physiology*, **212,** 1199–1204.

Janny, P., Flori, B., Georget, M., and Veyre, A. (1975). La résistance à l'ecculement du liquide céphalo-rachidien dans l'hydrocéphalie à pression normale. *Revue Neurologique*, **131,** 211–217.

Katzman, R., and Hussey, F. (1970). A simple constant-infusion manometric test for measurement of CSF absorption. 1. Rationale and method. *Neurology (Minneapolis)*, **20,** 534–544.

Martins, A. N. (1973). Resistance to drainage of cerebrospinal fluid. Clinical measurement and significance. *Journal of Neurology, Neurosurgery, and Psychiatry*, **36,** 313–318.

Martins, A. N., Kobine, A. I., and Larsen, D. F. (1974). Pressure in the sagittal sinus during intracranial hypertension in man. *Journal of Neurosurgery*, **40,** 603–608.

Masserman, J. H. (1934). Cerebrospinal hydrodynamics. Clinical experimental studies. *Archives of Neurology and Psychiatry (Chicago)*, **32,** 523–553.

Rubin, R. C., Henderson, E. S., Ommaya, A. K., Walker, M. D., and Rall, D. P. (1966). The production of cerebrospinal fluid in man and its modification by acetazolamide. *Journal of Neurosurgery*, **25,** 430–436.

Sahar, A. (1972). The effect of pressure on the production of cerebrospinal fluid by the choroid plexus. *Journal of the Neurological Sciences*, **16,** 49–58.

Shulman, K., Yarnell, P., and Ransohoff, J. (1964). Dural sinus pressure in normal and hydrocephalic dogs. *Archives of Neurology, (Chicago)*, **10,** 575–580.

Sjöqvist, O. (1937). Beobachtungen über die Liquorsekretion beim Menschen. *Zentralblatt für Neurochirurgie*, **2,** 8–18.

Tourtellotte, W. W. (1966). A selected review of reactions of the cerebrospinal fluid to disease. In *Neurological Diagnostic Techniques*, pp. 25–26. Edited by W. S. Fields, Charles C. Thomas: Springfield, Illinois.

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