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CSF hydrodynamic studies in man[1]

1. Method of constant pressure CSF infusion

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SUMMARY The constant pressure method for the study of the hydrodynamics of CSF is presented. By infusing artificial CSF at constant pressures and recording the resultant flow, it is possible to obtain information about the hydrodynamic conductance of the CSF outflow pathways. By lowering the infusion pressure below the pressure of the sagittal sinus all CSF produced can be collected and the CSF formation rate may thus be calculated. There is a rectilinear relationship between CSF pressure and the flow necessary to maintain the pressure. It is thus concluded that the arachnoidal villi, when once opened, are not further distended by pressure. This method makes possible indirect calculation of the pressure of the sagittal sinus and the pressure difference between the subarachnoid space and the sagittal sinus.

Since the introduction of lumbar puncture by Quincke in 1878 measurement of the lumbar CSF pressure has become a routine procedure in clinical work. Numerous attempts have been made to acquire more information about the hydrodynamics of the CSF than only that related to pressure. Ayala (1923, 1925) drew conclusions concerning the pressure/volume relationship in the craniospinal space by studying the pressure decrease after withdrawal of a certain volume of CSF. Masserman (1934) withdrew CSF and studied the time for return of the CSF pressure to its initial value. He thereby estimated the rate of production of CSF. By reinjection of the CSF, information about elimination was also obtained. Schaltenbrand and Wördehoff (1947) further elaborated this method to the status of a clinical diagnostic procedure. Sokolowski (1974) has also used a single bolus injection of fluid for studying the CSF hydrodynamics.

Constant flow rate, subarachnoid infusions were first performed in human subjects by Foldes and Arrowood (1948). They pointed out that, when increasing the flow rate, the CSF pressure rose but soon reached a plateau which was higher as the flow rate was higher. The relationship between pressure and rate of infusion was, however, not linear. Rubin *et al.* (1966), Cutler *et al.* (1968), and Lorenzo *et al.* (1970) were the first to use the method of ventriculoventricular or ventriculolumbar perfusion in human studies. By adding various trace substances to the perfusion solution, CSF formation and elimination could be measured at different pressure levels. The necessity for ventricular puncture restricts the use of the method to special human cases and to animal experiments.

Katzman and Hussey (1970) developed a clinical test based on constant rate fluid infusion. Their test started with removal of 10 ml of CSF. The pressure return to the initial value was studied by open manometry in order to determine the rate of formation of CSF. Saline was then infused at a constant rate of 12.7 mm^3/s (0.76 ml/min) during 40 to 60 minutes. Sometimes a higher infusion rate of 32 mm^3/s (1.9 ml/min) was also used. The plateau values of the pressure at the different infusion rates were the parameters used to describe the CSF absorption. Clinical experience with the method was described by Hussey and Schanzer (1970).

Nelson and Goodman (1971) modified the constant rate infusion method by using the rate of rise of CSF pressure as the measured parameter. They also used artificial CSF instead of saline for infusion and electromanometric recording of the CSF pressure. Martins (1973) used the constant rate

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infusion method but treated the results in another way by calculating the resistance to drainage of CSF. Trotter *et al.* (1974) also used a modified Katzmann and Hussey method. They read the CSF pressure after 20 minutes infusion at a rate of 12.7 mm^3/s (0.76 ml/min) and five minutes after a change of the rate to 32 mm^3/s (1.91 ml/min). Di Rocco *et al.* (1976) have also used the constant rate infusion test in human studies. A recent extensive review of the physiology of the CSF, including numerous references, is that of Welch (1975).

In the present paper, another technique for the study of the hydrodynamics of the CSF is described, the constant pressure infusion method. The infusion pressure is kept at a constant level and the resulting CSF flow recorded. Constant pressure infusion has been used for investigating the hydrodynamics of the animal eye (Becker and Constant, 1956; Armaly, 1959; Bárány, 1962, 1964) and of CSF in animal experiments (Davson *et al.*, 1970), but not previously for human investigations. Constant pressure infusion permits a detailed analysis of the CSF hydrodynamics, mainly because much more experimental data of pressure/flow can be obtained during a given time period than with the constant rate infusion method. The present study has been preliminarily reported by Ekstedt (1973, 1975) and Ekstedt and Fridén (1976). In a modified version the method has also been used by Portnoy and Croissant (1976).

Methods

INVESTIGATION CHAIR/BED

The chair used was modified from an investigation chair common in Swedish hospitals. Originally, it was supplied with a back support made of springs and steel bands. This was replaced by a bottom of double canvas reinforced by straps on critical sites. An opening of 150×150 cm was made centred about the fourth lumbar spinal process.

By means of a sterile tape sheet (Steridrape No. 1092, 3M Company, Minnesota, USA) fastened to the skin, a sterile field for puncture was obtained. After the lumbar puncture the chair was folded back to a horizontal position. The chair is shown in Fig. 1.

LUMBAR PUNCTURE

For pressure recording a 0.9×90 mm lumbar needle was used (conductance 35 $mm^3 \cdot kPa^{-1} \cdot s^{-1}$). For infusion a 1.2×100 mm needle was used (conductance 85 $mm^3 \cdot kPa^{-1} \cdot s^{-1}$).

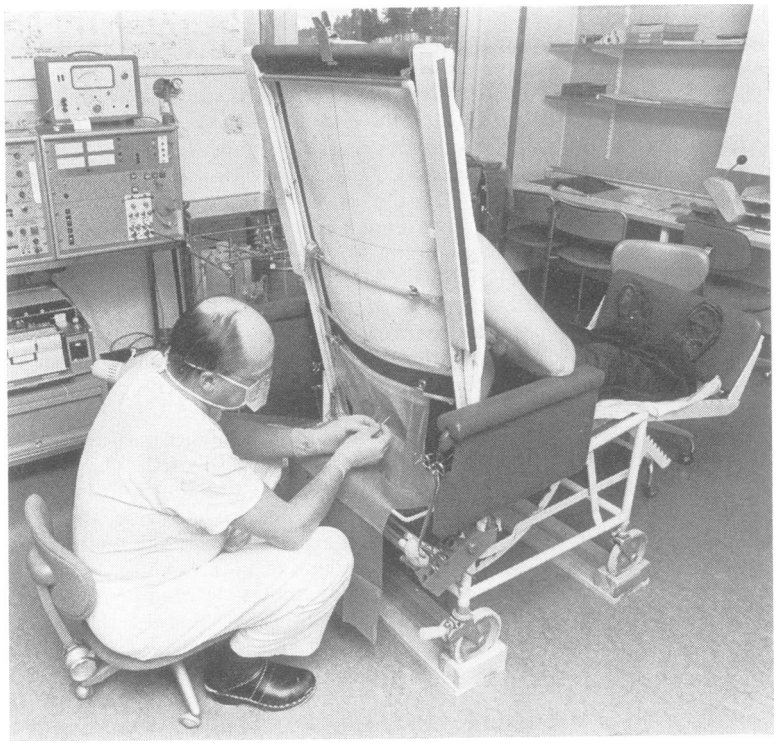

Fig. 1 *Experimental chair/bed. The lumbar needles are inserted via the opening in the back support with the patient in the sitting position. The chair is then folded back and the rest of the investigation made with the patient supine.*

The needles were connected to the experimental equipment with non-elastic PVC tubes filled with artificial CSF. The tubes and stopcocks were disposable, replaced for each experiment.

PRESSURE RECORDING

Two pressure transducers (Hewlett-Packard 1280 C, Waltham, Mass., USA) were used. They were connected to carrier frequency amplifiers (Hewlett-Packard 8805 B). All connections between tubes were made by means of plastic three-position stopcocks (Viggo, Helsingborg, Sweden). Calibration was made by connecting the transducer with either of two sterile water columns, one with its water level at the height of the zero reference level of the patient, the other 306 mm above that level, thus corresponding to a pressure of 3 kPa. The accuracy of pressure measurement was better than 0.03 kPa. Careful flushing of tubes, stopcocks, and transducers was performed before each experiment to avoid air bubbles. The compliance of the pressure recording system, measured at the tip of the lumbar needle, proved to be less than mm^3/kPa. The pressure signals during recording were usually low pass filtered with a time constant of 0.05–0.01 s.

CSF INFUSION

During the first 50 experiments a 0.9 % saline solution was used. Nearly all patients experienced some kind of discomfort during the infusion. Sometimes there were very prominent signs of distress, which necessitated termination of the investigation. In a few cases the patient became very excited, requiring intravenous sedation. In most cases the side-effects took the form of pain, paraesthesia or paralgesia (especially in the legs and buttocks), urgency for vomiting or defaecation, and symptoms from the autonomous nerve system, such as piloerection or sweating. The side-effects with saline were similar to those that have already been reported by Weed and Weyeforth (1919) and by Nelson and Goodman (1971). It was obvious that an infusion solution that could produce such dramatic symptoms should not be considered suitable for these types of experiments, and that it was potentially dangerous. The side-effects also made it very difficult for the patient to keep a stable position for any length of time. Therefore, a solution closely resembling the one devised by Elliot and Jasper (1949) (the B solution) was made. The first 200 bottles contained glucose but in later bottles the glucose has been omitted without notable effect.

The solution was prepared in two bottles (90 ml and 10 ml) which were mixed immediately before the experiment.[3] The solution was made by the hospital pharmacist and contained Na^+ 145.7 mmol/l; K^+ 4.0 mmol/l; Ca^{++} 1.4 mmol/l; Mg^{++} 0.4 mmol/l; Cl^- 130.4 mmol/l; HCO_3^- 21.7 mmol/l; HPO_4^- 0.6 mmol/l; pH = 7.40.

The differences in side-effects when using the artificial CSF instead of saline were considerable. There was no reaction of the type described above. In three cases (of 783) there was a meningitic reaction with fever for a few days. All patients recovered completely. In these three cases the rest of the contents of the bottles were sent for bacteriological examination; however, there was no bacterial growth. There might have been chemical or viral contamination.

The artificial CSF was at room temperature in both bottle and tubes. However, about 50 mm of the needle was within the body and thus heated the solution. In *in vitro* experiments when a 50 mm segment of the needle was heated to 37.0°C it was found that when flow was below 25 $mm^3\ s^{-1}$ the artificial CSF had a temperature of more than 34°C when leaving the tip of the needle. At 100 $mm^3\ s^{-1}$ the temperature was 29°C. It has not been considered essential to preheat the artificial CSF.

INFUSION APPARATUS

The experimental set-up is shown in Fig. 2. The bottle with artificial CSF hung about 200 mm below the reference level (the cranial mid-point). The infusion pressure was created with a membrane air pump (aquarium pump Rena super 300, Annecy, France) which pumped air into the bottle. An adjustable air leak maximised the air pressure. The voltage to the air pump was automatically adjusted by a servo device.

The air entering the pump was filtered by a sterile filter (Aga Sterile Filter 323 900 002, Stockholm, Sweden). The air leaving the air leak was again led into the pump, so that there was very little intake of new air into the pump. Furthermore, the output from the pump was twice filtered by means of Munktel air filters MS 20 (Stora Kopparberg, Grycksbo, Sweden). The air was then free of any particles and sterile.

LIQUID FLOW RECORDING

The infusion bottle was suspended by a thin nylon wire in a strain gauge transducer. The tubes leading air into the top of the bottle and taking fluid from the bottom of it were pliable, exerted no elastic forces on the bottle and acted on it only by their weight.

The bottle had a volume of 120 ml. Before and after

[3] *Solution I* (90 ml): NaCl: 7.98 g; KCl: 0.33 g; $CaCl_2 \cdot 2\ H_2O$: 0.22 g; $MgCl_2 \cdot 6\ H_2O$: 0.08 g; HCl 1 mol/l to pH 2.8; pyrogen free distilled water to 1.0 l. Autoclaved at 120°C for 20 minutes. *Solution II* (10 ml): $NaHCO_3$: 18.2 g; $Na_2HPO_4 \cdot 2\ H_2O$: 0.98 g; pyrogen free distilled water to 1.0 l. Autoclaved at 110°C for 35 minutes.

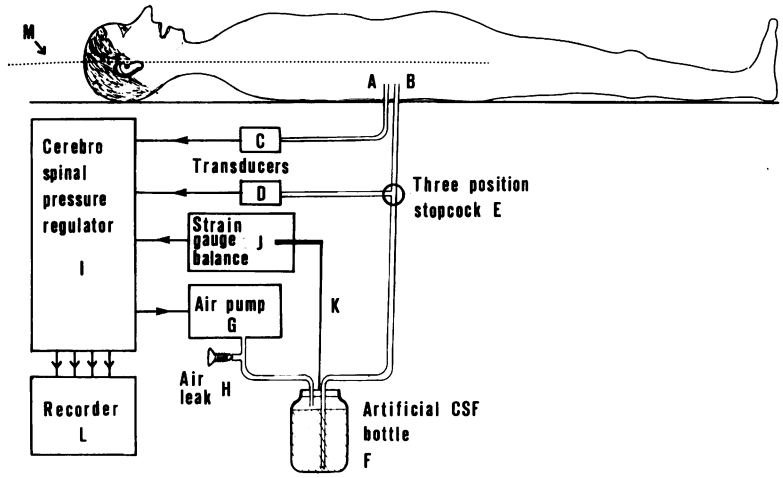

Fig. 2 *Experimental set-up. The patient is lying supine with two lumbar needles (A and B) in the subarachnoid space. A is connected to transducer C with a tube filled with artificial CSF. Similarly the needle B is connected to transducer D. By means of stopcock E, connection can be made to bottle F, containing artificial CSF. The bottle can be pressurised by air from the air pump G. Air is leaking through the adjustable valve H in order to maximise the pressure and to permit a smoother regulation. The power to the air pump is delivered by the cerebrospinal pressure regulator I, governed by either C or D. Flow is calculated by weighing the bottle in the strain gauge balance J, in which the bottle is hung up with a 0.30 mm fishing line K. A multi-pen recorder L records the result graphically. The sagittal midpoint of the cranium is chosen as the reference level (M).*

each experiment the balance was calibrated by applying a 5 g weight to the bottle.

On the ink recorder (Rika Denki KA 4 Tokyo, Japan) 1 g represented a deflection of 25 mm on the 250 mm wide paper. The accuracy of measured weight was better than 0.03 g.

REFERENCE LEVEL FOR PRESSURE

In 10 patients the intraspinal pressure was first recorded in the lateral recumbent position with the reference line along the spine. The patient was then turned to the supine position and the pressure again measured in relation to the external auditory meatus. The procedure was repeated a few times. It was then found that a reference level at the cranial midpoint between inion and glabella best corresponded to the reference level of the spine in the lateral recumbent position. This point was therefore chosen as reference point for all measurements. On the exterior, it corresponds to a level through the mandibular joint and to the anterior part of the osseous channel of the external auditory meatus. It also corresponds to the level of the foramina of Monro chosen by Janny (1974) as his reference point. In seven patients radiographs were taken of the skull and thorax with the patient in a supine position. The chosen point of reference then proved to correspond reasonably well with the centre of the right atrium. If another point of reference is chosen, the pressure will change with the weight of the water column that separates the reference points.

UNITS OF MEASUREMENTS

SI units have been used throughout. Pressure: 1 kilopascal (1 kPa) = 7.5 mmHg = 102 mmH_2O. The hydrodynamic conductance of the CSF outflow pathways has the dimension $mm^3\ kPa^{-1}\ s^{-1}$.

$1\ mm^3\ kPa^{-1}\ s^{-1} = 6 \cdot 10^{-3}\ ml\ (cmH_2O)^{-1} \cdot min^{-1} = 8 \cdot 10^{-3}\ ml.\ (mmHg)^{-1} \cdot min^{-1}$.

EXPERIMENTAL PROCEDURES

With the patient in the sitting position the needles were inserted in the L3–L4 or L4–L5 intervertebral space after local anaesthesia of the skin and the intraspinal ligament with 1% lidocaine (Xylocaine, Astra Södertälje, Sweden). Care was taken to insert the needles with minimal trauma. Multiple punctures of the dura mater were avoided. Two millilitres of CSF were withdrawn with a syringe for protein determination and cell count and immediately replaced by the same amount of artificial CSF. This also served as a check of correct needle position

in the subarachnoid space. The amount lost during the needle insertion was also replaced. The patient was then folded back to the supine position and the pressure transducers were adjusted to the reference level. The different steps of the procedures are shown in Fig. 3.

The resting pressure was recorded continuously. Usually 60 minutes of recording was aimed at, but sometimes a shorter time could be allowed if the curve was steady. The resting pressure was not measured until there had been a period of at least 15 minutes without any upward or downward trend.

In order to detect whether there was any leakage around the lumbar needles 20 experiments were performed in the following way: the resting pressure was recorded during 30 minutes and, if constant during the last 15 minutes, the chair/bed was folded to the sitting position and kept so for 15 minutes. Thereafter, the chair was again folded back to the supine position and recording of the resting pressure continued for a further 30 minutes. During sitting, the hydrostatic pressure on the needle insertion area was increased by the weight of the column of the spinal liquid and the flow through a leak should have increased. The resting pressure when the patient was then folded back to the supine position should have been lower if there was a CSF leak around the needles.

The infusion was then started. The first infusion pressure was chosen to be about 0.5 kPa above the resting pressure. The pressure was kept at this level until the rate of flow had levelled off after the initial high rate and the CSF pressure was constant. Then the pressure level was increased by a further 0.5 kPa and the same procedure was repeated. The pressure was kept at a certain level for at least five minutes. In most cases a final pressure of 6 kPa was aimed at, but sometimes, when there was a very good drainage, the content (120 ml) of the bottle with artificial CSF was not sufficient to attain this level. Eight to 15 corresponding values of pressure flow were obtained in each case. A part of a recording is shown in Fig. 4.

The next step was the 'post-infusion'. The connection to the bottle was shut off and the pressure was allowed to return spontaneously by elimination of CSF through the physiological pathways. This was continued until a steady plateau value was recorded, which, in most cases, closely corresponded to the initial resting value. If this level was different from the initial resting value, there was a strong suspicion that the resting pressure had been wrongly recorded and the investigation was therefore often repeated some days later. In some 20 experiments the infusion was also continued after the maximum pressure was reached. Infusion pressure was lowered in steps of 1 kPa. This was done in order to detect any hysteresis in the pressure/flow relationship.

In 10 experiments the pressure was, for a period of one hour, switched between two high values every five to 10 minutes, to detect possible changes in flow with time.

The next step in the investigation was then to perform the drainage. The pressure in the infusion bottle circuit was lowered to 0.25 kPa. This caused an outflow of CSF from the subarachnoid space into the bottle. Initially, the rate of outflow was high, but within 10 to 15 minutes the rate levelled off when the intraspinal pressure approached the pressure in the infusion circuit. The drainage period was planned to last one hour but sometimes had to be shortened because the investigation had persisted for more than three hours and the patient might be hungry and unwilling to cooperate. In some cases the drainage was postponed to a separate investigation a few days or some weeks later. This part of the

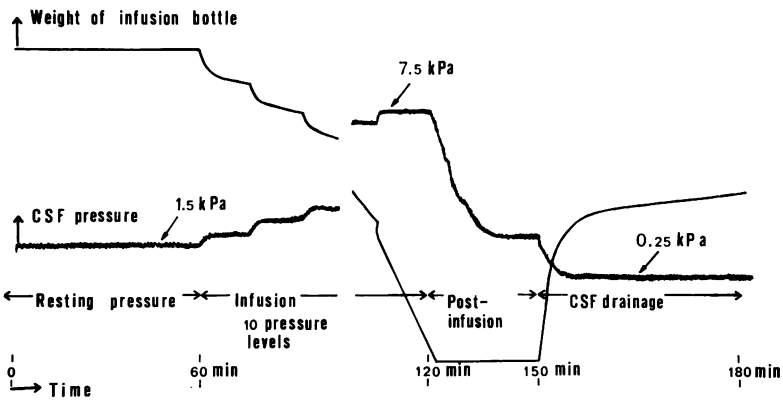

Fig. 3 *Schematic layout of the investigation. During 30–60 minutes the resting pressure is recorded. The CSF pressure is then increased in steps of 0.5 kPa up to a maximum of 7.5 kPa. The resulting decrease in the bottle weight is shown in the upper trace. After obtaining the highest pressure the bottle is shut off and the pressure return followed during the postinfusion period. During the period of CSF drainage the CSF pressure is lowered below that of the venous pressure in the sagittal sinus. When the pressure has stabilised the outflow is equal to the CSF production rate.*

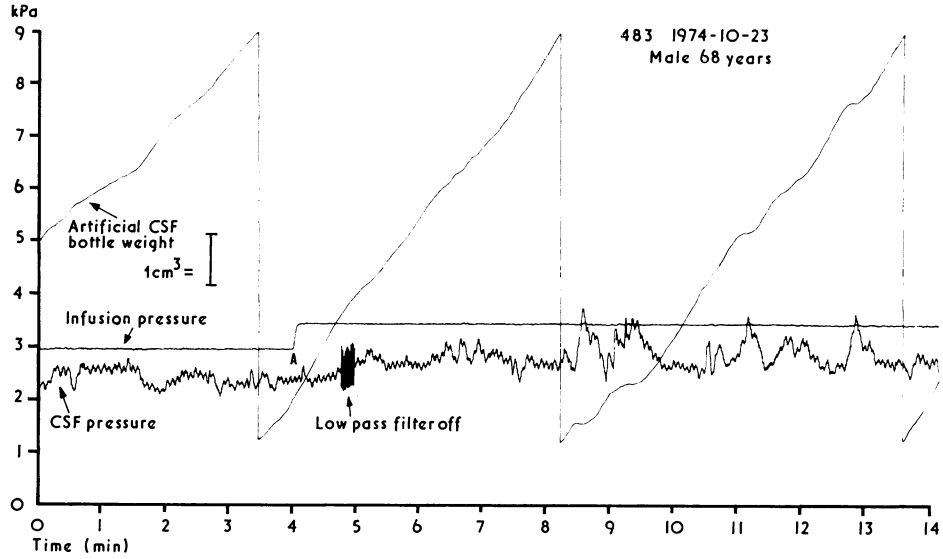

Fig. 4 *Part of an actual recording during infusion. At A the infusion pressure is changed by 0.5 kPa, which causes an increase of flow measurable from the bottle weight curve. A different plateau value for the infusion pressure and CSF pressure is caused by the resistance in the lumbar needle through which infusion is made. This is the reason why a separate needle for CSF pressure recording is convenient.*

investigation was done in order to determine the rate of formation of the CSF. A part of a recording is shown in Fig. 5.

If the intracranial resting pressure was considerably increased from the beginning of the experiment or if the investigation had given a suspicion of an intracranial, space-occupying lesion, then no drainage was performed because of the risk of tentorial herniation.

In order to minimise post-lumbar puncture headache, the drained CSF was in most investigations reinfused until a pressure was attained which exceeded the resting pressure by 0.5 kPa. Reinfusion was not made in those cases where the clinical result of a pressure lowering was to be investigated.

Once every 10 minutes, or at the end of each pressure level, during the infusion period, the blood pressure and pulse rate were measured with a semiautomatic sphygmanometer cuff recorder (Metronik A 900 Köln, W-Germany).

CALCULATIONS

All experimental data were measured from the multichannel ink recorder. The CSF pressure was subject to variations with time. The arterial pulse synchronous and respiration synchronous variations were low pass filtered with a time constant of 0.05 s. There were still slower variations of the pressure, with a frequency of one or more waves per minute. When selecting a part of the recording for measurement, the mean pressure had to be constant during several minutes. During this time the slope of the weight curve had to be as constant as possible and approximated by a straight line. At the time of experiment a check was always made that there was a well measurable part of the curve before proceeding to a new pressure level.

All calculations were made on a small calculator, Compucorp 445-44[4] (Computer Design Corporation, Los Angeles, Calif., USA). The output from the calculator is shown in Fig. 6.

Three different methods were employed for the calculation of the curves. In *method 1* the value of the resting pressure is given a very strong weighting. It is thus considered that the curve should pass through the point of the resting pressure and the regression line was calculated according to Snedecor and Cochran (1971, p. 166).

$$G_{op} = \frac{\Sigma[(p_{cl} - p_{clr}) \cdot q]}{\Sigma(p_{cl} - p_{clr})^2}, \qquad \text{Formula 1}$$

(G_{op} = the hydrodynamic conductance of CSF outflow pathways, p_{cl} = the actual CSF pressure, p_{clr} = the resting CSF pressure, q = the actual flow of artificial CSF).

When there is an experimental error both in the X and Y measurement values the following formula

[4]The programme was written by Ulf Ekstedt.

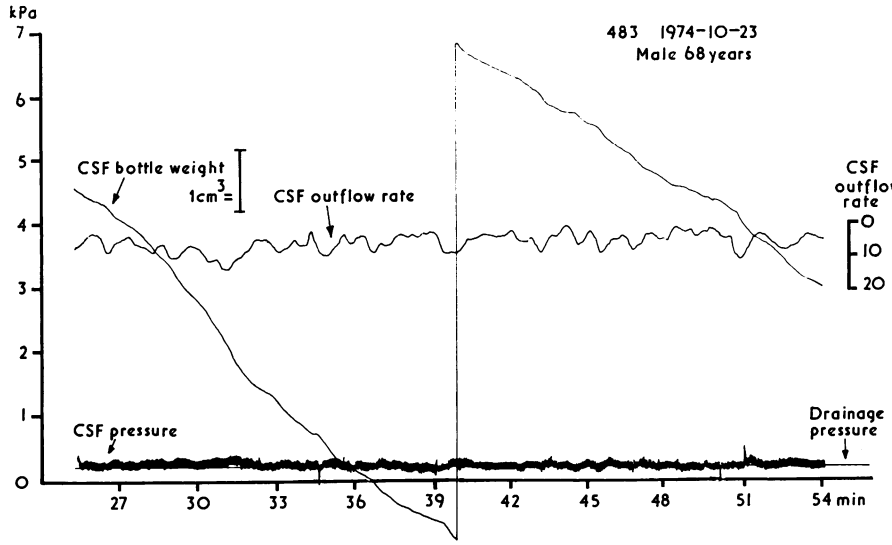

Fig. 5 *Part of an actual recording during drainage. The drainage pressure is 0.25 kPa. The CSF pressure has stabilised at a slightly higher value because of the pressure drop caused by the CSF flow in the needle resistance. The CSF formation rate is calculated from the increase of the bottle weight. For monitoring purposes during the investigation the instantaneous formation rate is calculated and displayed on the recording.*

may be theoretically more suitable. It has been calculated for the last 300 investigations but proved to give values for G_{op} that differed very little from those obtained by formula 1.

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

If using the constant rate infusion method the following formula will probably be more accurate.

$$G_{op} = \frac{\Sigma q^2}{\Sigma[(p_{cl} - p_{clr}) \cdot q]} \qquad \text{Formula 3}$$

In *method 2* the point for the resting pressure is omitted entirely from the calculation. All the other experimental points were used for a conventional regression analysis by the method of least squares. A value of the resting pressure was then calculated from this regression line and the calculated value was compared with the actually recorded value.

In *method 3* each experimental point is taken in relation to the resting pressure. The slope of the line joining the experimental point and the resting pressure point was calculated. The mean value of all these values was then calculated.

SUBJECTS

To date 783 investigations have been performed in 705 patients aged between 3 days and 92 years during a period of six years. About 500 investigations have been performed strictly according to the procedures described here. All investigations were made for diagnostic purposes because of a suspicion of altered CSF hydrodynamics and none on volunteers. The project was approved by the ethics committee of Uppsala University. The findings in pathological cases will be reported separately. In the material 58 patients (aged 17–83 years) have been selected as probably not having any intracranial or circulatory disease, judged by medical history, clinical neurological investigation, and further medical development. These patients constitute the normal material. The CSF hydrodynamic parameters in these patients will be reported separately by Ekstedt. In the present paper this group of patients is also used as a reference group for normality. Of course, this post-experimental method of deciding which patient shall be considered as normal or not is open to criticism. However, in the absence of an investigation on healthy volunteers, which is, for obvious reasons, difficult to do, the present 58 patients must serve as a provisional normal sample.

Results

In the present paper the results will be presented from the qualitative point of view only. The general character of the resting CSF pressure recording was the same for the supine position as for the lateral

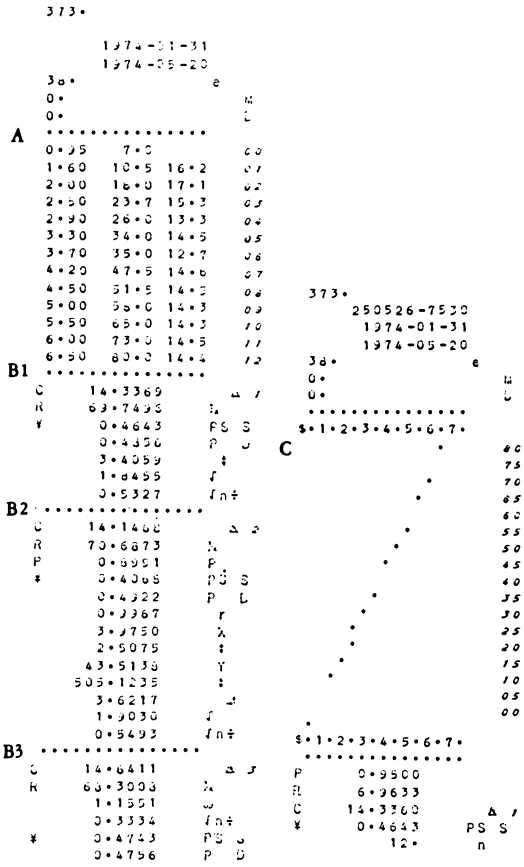

Fig. 6 *Output from the calculator. First the original data are listed (A). Then the regression line of the experimental points is calculated by three different methods (B1, B2, B3, see text). The experimental points are then automatically plotted with pressure in kPa as the abscissa and flow rate in* $mm^3 s^{-1}$ *as the ordinate (C).*

recumbent. It was found to be very important not to turn the head, as this invariably increased the pressure.

In three investigations, where the intraventricular pressure was recorded during the whole experimental procedure, the arterial pulse synchronous variations were about 10% higher intraventricularly, but in all other respects the pressure was always equal. This held true both for the spontaneous variations in pressure and the variations induced during the infusion. There is thus no reason to believe that a CSF hydrodynamic investigation should give different results when performed *via* the ventricles than when performed by the lumbar route.

In 20 experiments, when raising the patient to a sitting position for 15 minutes and thereafter resuming the supine position, there was only one case which showed decrease of the pressure by 0.4 kPa. In all other cases the post-sitting value within a few minutes approached the pre-sitting by ±0.1 kPa (Fig. 7). Hydrostatically increasing the pressure on a dural rift should induce a leakage. It can then be assumed that a leakage around the needle, as described by Lundberg and West (1965), did not occur frequently in the present experiments.

During the infusion period the patient usually experienced only slight unpleasantness. Sometimes he became sleepy and fell asleep at pressure levels above 5 kPa and then woke up again when the pressure decreased. Pulse and blood pressure were usually unaffected.

All spontaneous variations in the CSF pressure were exaggerated at increasing mean pressure. In spite of this it was nearly always possible to obtain well measurable sections of the pressure and weight curves even at the highest pressure levels.

In Fig. 8a is shown a pressure flow diagram from an investigation which was, from the technical point of view, very successful. There is no doubt that the relation between pressure and flow is linear. The conductance, calculated by the three methods described in the Method section, were all numerically close to each other. It has been postulated that if the three methods give values that differ by less than 15%, the pressure/flow relation can be considered rectilinear.

In the majority of the several hundred recordings there seems to be a rectilinear relation between pressure and flow. This holds true for patients considered to be normal from the point of view of CSF hydrodynamics (Fig. 9) as well as for patients with abnormal CSF hydrodynamics (Fig. 10). In a few cases, however, an obviously nonlinear relationship between pressure and flow was obtained which could not be explained by technical errors (Fig. 11). In many early experiments there was a tendency for lower pressure values to give unexpectedly high flow values, and this was dependent upon the fact that there was not enough time left for the flow curve to level off. When this fact was noticed, this source of error was eliminated.

In 20 experiments the infusion pressure was increased in steps of 0.5 kPa up to a pressure of 6.5 kPa and thereafter again decreased in steps of 1.0 kPa. The flow values obtained with increasing pressure did not differ significantly from those obtained with decreasing pressure.

In five experiments the pressure was alternatively held at 4.5 or 5.5 kPa in periods of five minutes for 60 to 90 minutes in order to detect possible changes in the outflow pathways with time—for example, a distention of the arachnoid villi. There was no systematic change in the outflow conductance detectable in these experiments (Fig. 12).

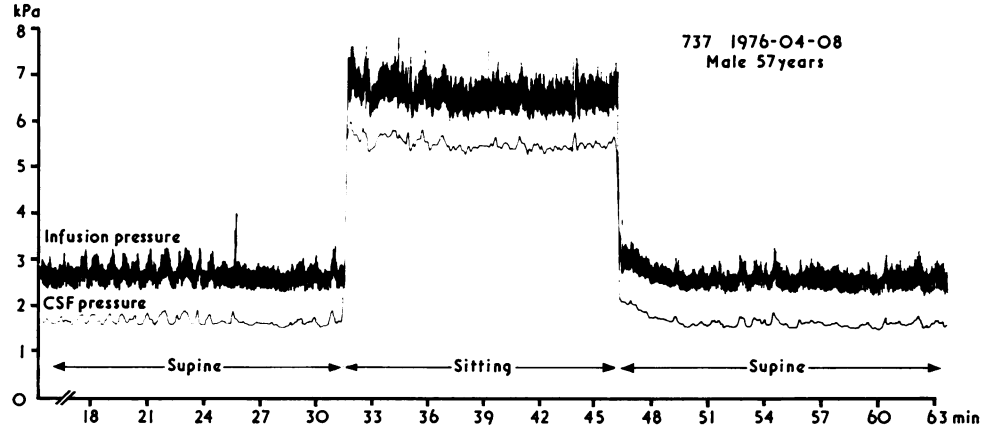

Fig. 7 *CSF pressure recorded during supine–sitting–supine position. The curve with the large arterial pulse synchronous pressure variations is unfiltered, the other curve is low pass filtered with −3db frequency 0.05 Hz. The baselines of the curves are separated by 1 kPa in order not to interfere with each other. The scale of the ordinate refers to the filtered curve. After resuming the supine position there is no pressure decrease to indicate a CSF leakage during sitting.*

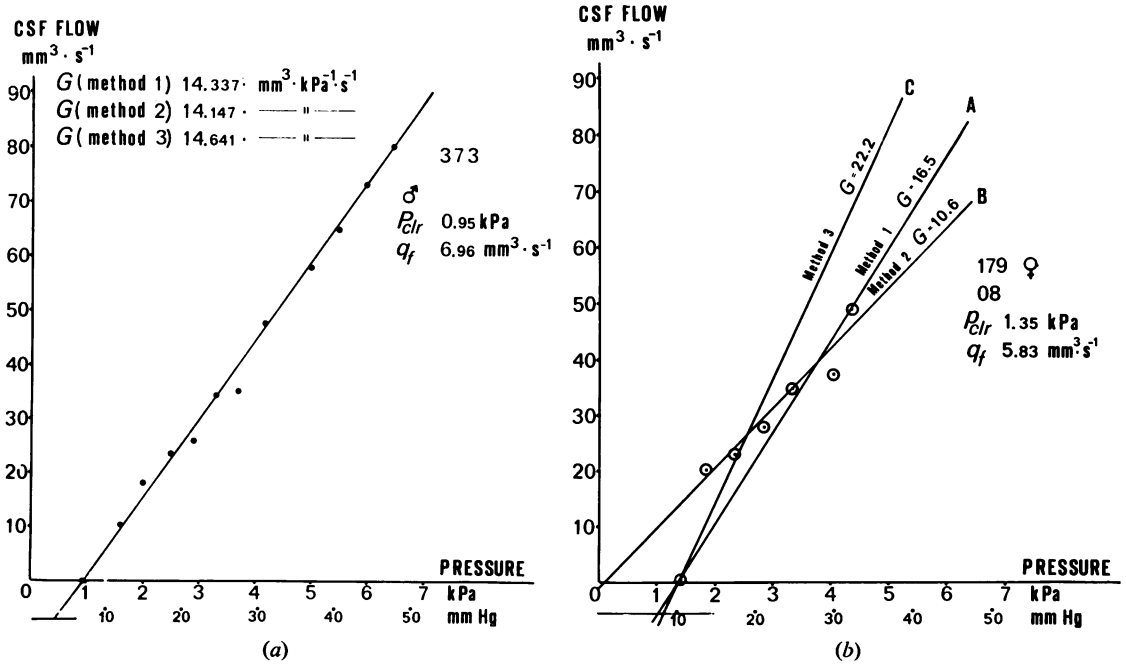

Fig. 8 *Relation between pressure and flow in two patients. The CSF pressure is the abscissa. The inflow through the lumbar needle of artificial CSF when the pressure has stabilised is the ordinate. The symbols are defined in Fig. 9 (a) is from a technically very successful experiment (the same as shown in Fig. 6). There seems to be no doubt that the experimental points can be approximated with a straight line. The three different methods for calculation of the regression coefficients all give practically the same value. (b) is, from a technical point of view, a less satisfying experiment. The three calculation methods all give bad fits for the regression lines and the regression coefficients are all different.*

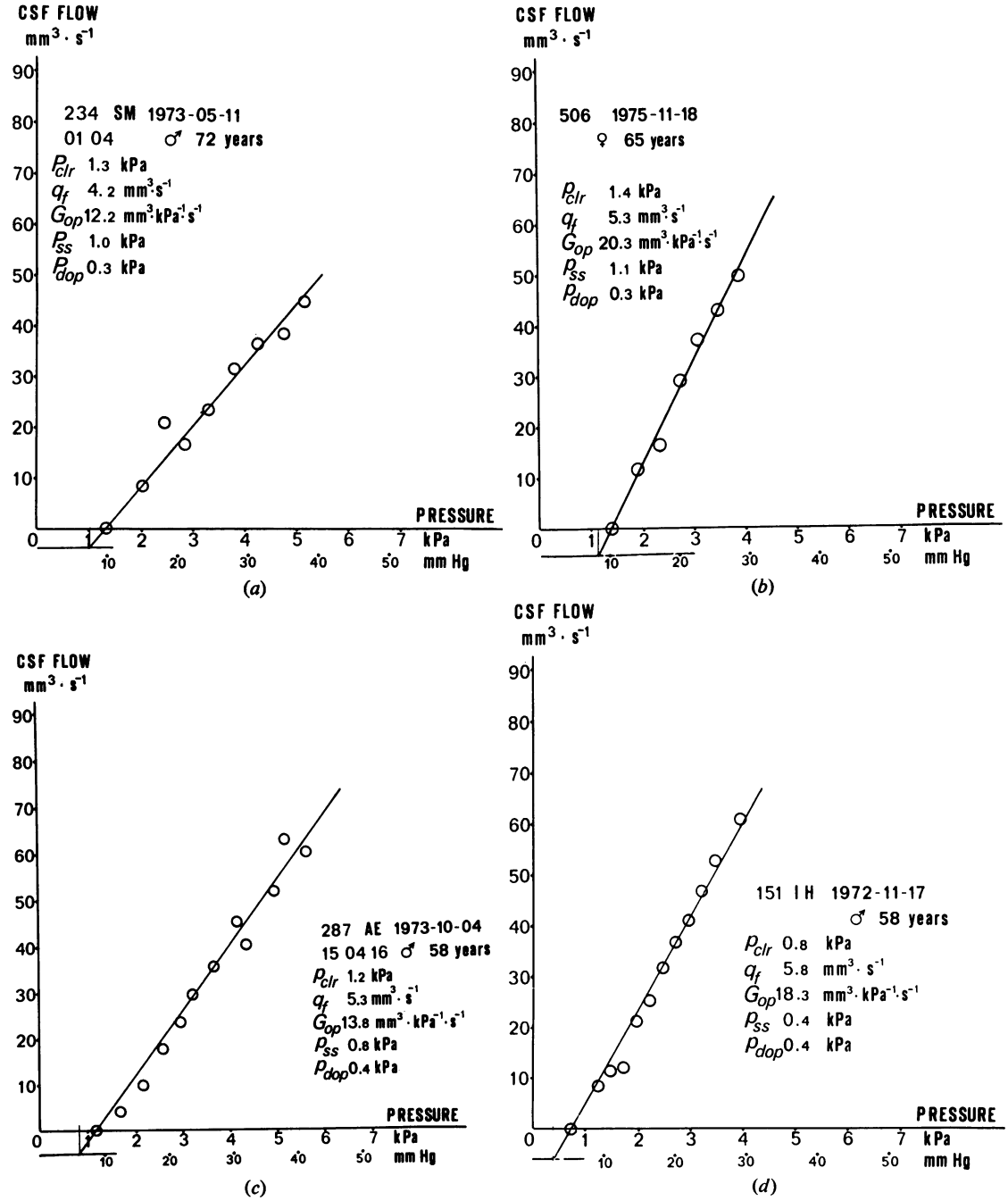

Fig. 9 *Pressure/flow diagrams from patients, normal as regard CSF hydrodynamics. CSF pressure on abcissa. CSF inflow through the needle on ordinate. The numbers denote: investigation number, date of investigation, sex, and age of patient, p_{clr}: resting CSF lumbar pressure, q_f: CSF formation rate, G_{op}: conductance of CSF outflow pathways, p_{ss}: sagittal sinus pressure, p_{dop}: pressure difference across CSF outflow pathways. In this and all other graphs the line is the regression line of pressure on flow calculated according to method 1 (see text, formula 1). There is a rectilinear relation between pressure and flow. The horizontal line under the abscissa denotes the CSF formation rate. It represents the ordinate value for zero outflow of CSF through the arachnoid villi. The regression line is linearly extrapolated to the zero outflow line. The intersection point represents the CSF pressure that should have existed if there were no internal production of CSF—that is, the sagittal sinus pressure (see formula 4).*

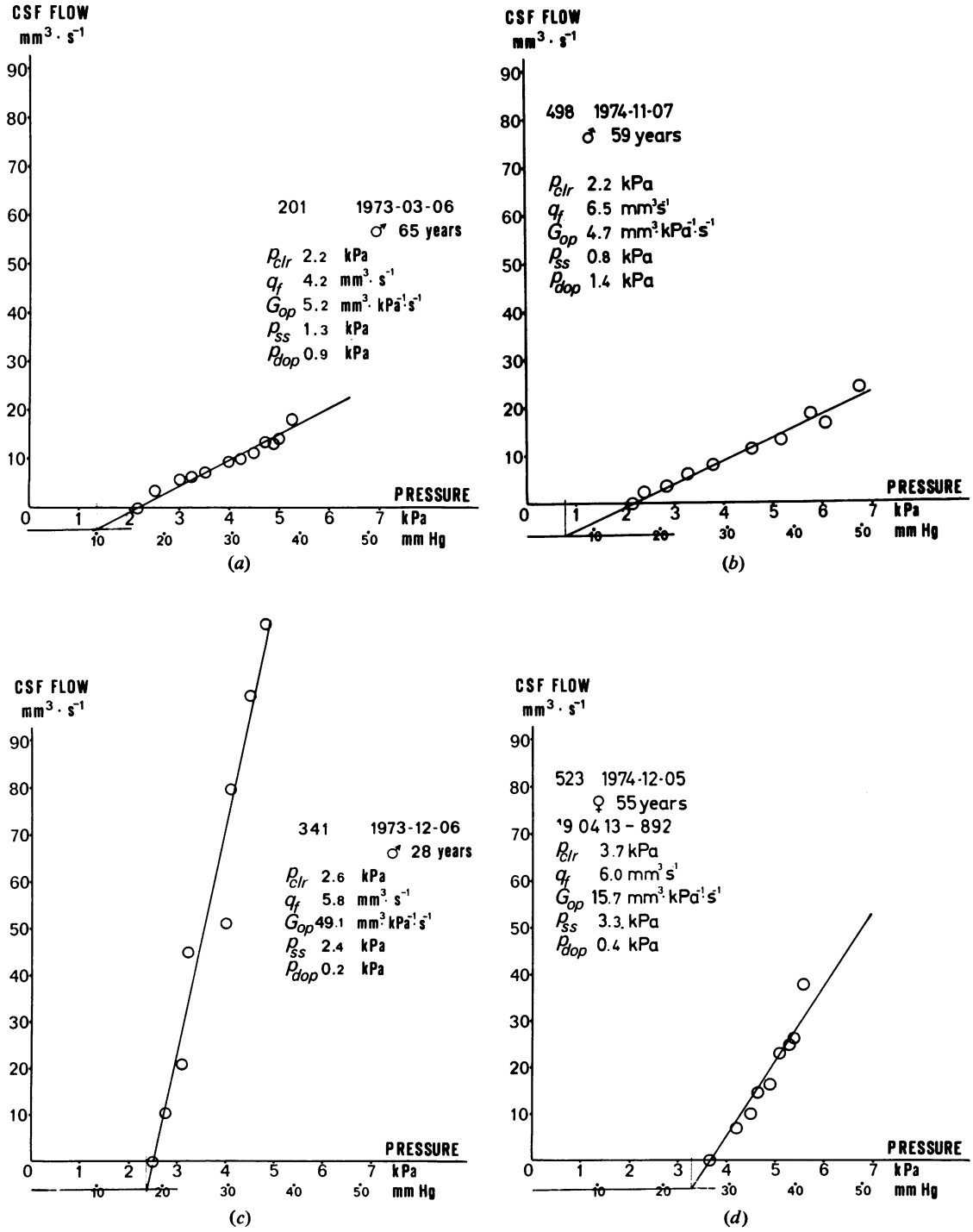

Fig. 10 *Pressure/flow diagrams for patients with increased CSF pressure due to decreased conductance (a, b) or increased sagittal sinus pressure (c, d). Symbols as in Fig. 7. There is a rectilinear relation between pressure and flow.*

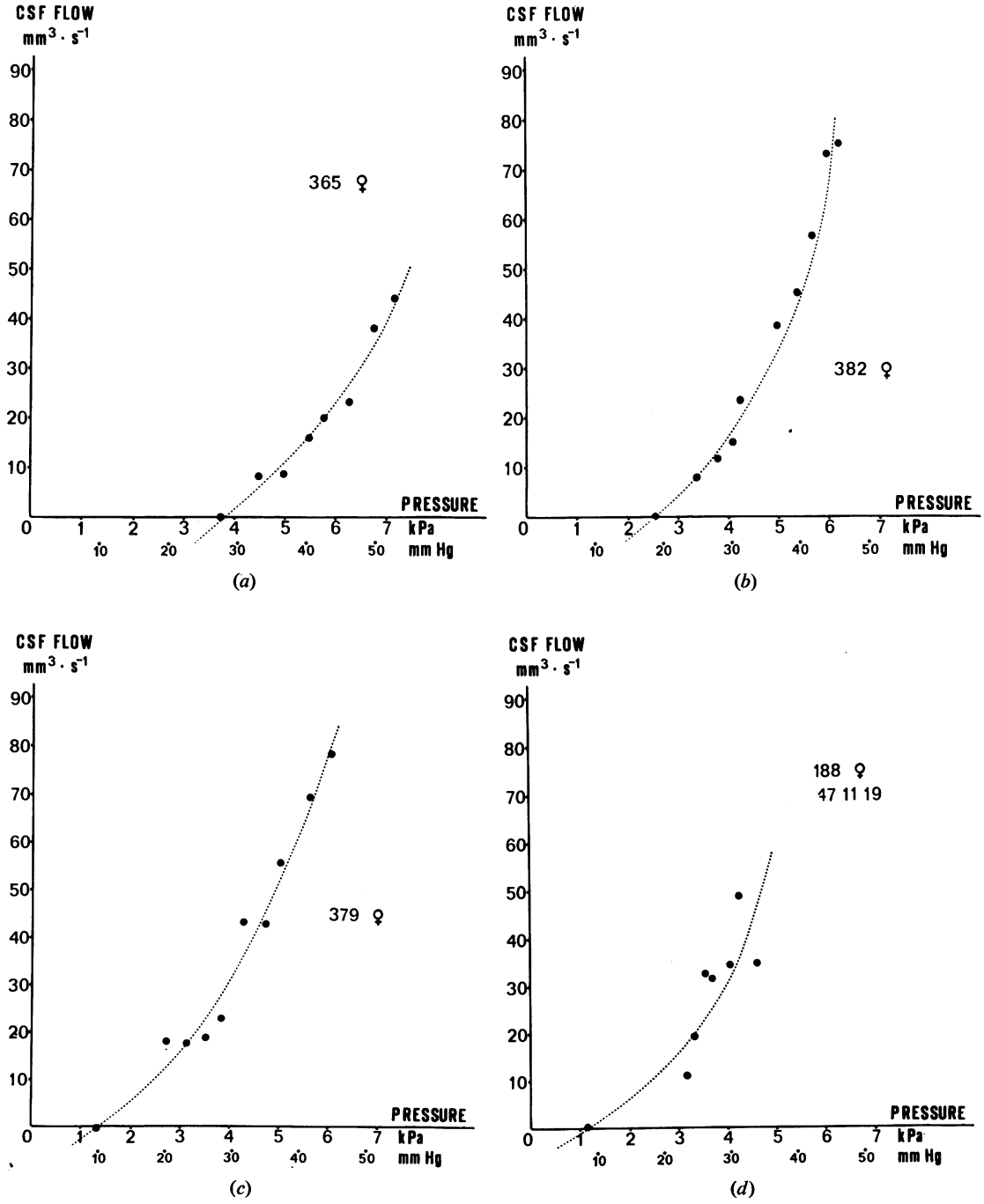

Fig. 11 *Pressure/flow diagrams that were exceptions to the usual rule of rectilinear relationship between pressure and flow. The recordings (a) and (b) from patients with sinus thrombosis. Patient (c) had sequelae after a traumatic intracranial haemorrhage with secondary porencephaly. Patient (d) had had a pneumoencephalogram three days earlier. At a later investigation her pressure/flow curve was again straight.*

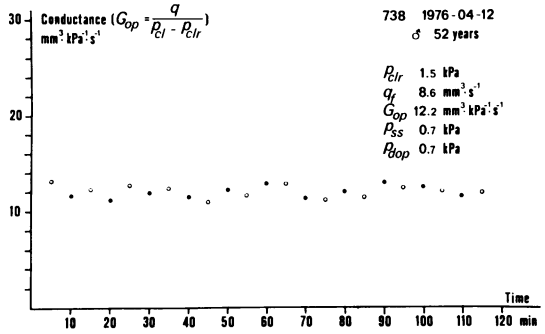

Fig. 12 *Extended CSF infusion. Every five minutes the CSF pressure changed between 4.5 kPa and 5.5 kPa. Time on abscissa. On the ordinate the conductance was calculated according to the formula in the Figure. There was no systematic change in the conductance during the 115 minute period. In the post-infusion period the pressure returned to the pre-infusion value.*

In the usual type of experiment the pressure was allowed to return spontaneously in the post-infusion period. The plateau value then obtained was usually very close to or identical with the resting pressure obtained before the infusion. This held true also in the experiments where the pressure had been kept at a high level for an extended time. During the drainage period there were usually no subjective sensations felt. Only a few patients developed headache during the procedure. On rising after the investigation, however, most patients who were left with a subnormal CSF pressure felt a throbbing headache of the type that is usual after lumbar puncture.

In Fig. 13 is shown the result of a several-hour long drainage where the CSF formation rate was determined for each 15 minute period. The variation in rate between the different periods is only slight.

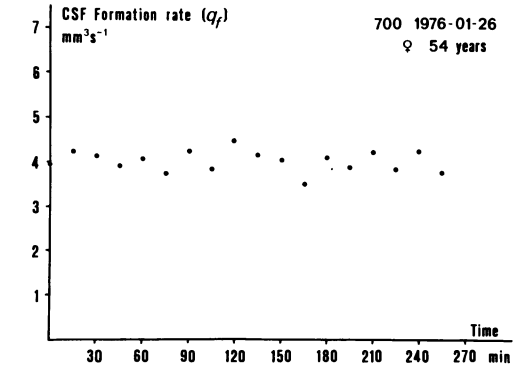

Fig. 13 *Extended CSF drainage. When the rate of outflow through the needle had stabilised the CSF formation rate was calculated for each 15 minute period and the calculated formation rate plotted.* $q_f \pm SD = 4.0 \pm 0.2$.

Discussion

Welch and Friedman (1960) made *in vitro* perfusions of small discs of the sagittal sinus in young monkeys. They found that the flow through the arachnoid villi started at a critical opening pressure. The general shape of the pressure/flow curve was that of an upward bend very similar to the curves from the present investigation shown in Fig. 11. The authors concluded that the drainage of CSF was through open channels from the subarachnoid space into the dural sinuses. Colloid osmotic pressure had no influence on the flow. The upward bend of the pressure/flow curve was interpreted as caused by an elasticity of the arachnoid villi. Further, in the rabbit experiments of Davson *et al.* (1970), made with a constant pressure technique, there seems to be an upward bend of the pressure/flow curve. However, the deviation from the straight line is so slight that it may lie within the experimental error.

In the present investigation a rectilinear relationship was found. This held also for the youngest patients, the very youngest being 3 days old, and can therefore not be explained as a decreased elasticity of the arachnoid villi due to age. Portnoy and Croissant (1976) have also confirmed a rectilinear relation between pressure and flow in human experiments with a slightly different technique.

The finding of equal flow values at a certain pressure level when going from lower to higher pressures as when going from higher to lower pressures makes it reasonable to assume that the arachnoid villi do not get further distended at increasing pressure, at least not at pressures below 6 kPa.

Martins *et al.* (1974) made direct measurements of the sagittal sinus pressure in man *via* median burr holes while they increased the CSF pressure by means of intraventricular infusion. In most of their experiments the sagittal sinus pressure was unaffected when increasing CSF pressure by up to 6 kPa. Altered sagittal sinus pressure can thus not explain the rectilinearity of the ratio.

There still remains the possibility of a distension of the villi and thus increased conductance at increasing pressure if that is compensated by a compression of the lateral lacunae of the sinus and thus causes a decrease of the number of villi that could pass CSF to the sinus. This viewpoint is purely hypothetical and has no support in the literature. It is highly unlikely that two mechanisms should balance each other so well as to nearly always give a rectilinear relationship between pressure and flow.

The regression-line of flow on pressure is the hydrodynamic conductance of the CSF outflow pathways. The conductance of the intracranial pathways, especially in the aqueduct and in the basal cisterns

and the subarachnoid space over the hemispheres, is probably very high in relation to the conductance in the arachnoid villi. The conductance of the outflow pathways may thus certainly be considered as the conductance of the arachnoid villi only. However, in pathological cases there may be blocking of CSF circulation in the subarachnoidal space—for example, because of adhesions.

Leakage around the needles is probably only exceptionally an outflow pathway for the CSF in the experimental situation (Fig. 7).

The flow through the arachnoid villi will, according to Davson *et al.* (1970), be determined by the pressure difference between the subarachnoid space and the venous sinus. The following relation will then probably be correct when the system is in dynamic equilibrium.

$$p_c = p_{ss} + \frac{q}{G_{op}} \qquad \text{Formula 4}$$

where

p_c = the cerebrospinal fluid pressure,

p_{ss} = the sagittal sinus pressure,

q = the rate of flow of CSF through the villi, normally the formation rate of CSF (q_f),

G_{op} = the conductance of the arachnoid villi.

There may also be an opening pressure of the arachnoid villi—that is, the pressure necessary to open up the valves before any fluid can pass at all. This pressure was found by Welch and Friedman (1960) to be 0.1–0.5 kPa (10–50 mmH_2O) in their monkey preparation. However, this opening pressure disappeared when the detergent polysorbate 80 was added to the perfusate. This finding makes it probable that the opening pressure was caused by stickiness of the valvular structure. Once the valve has opened there ought not to be any force acting against flow which should have been the case if there was an opening pressure caused by a 'spring loaded valve'. Valvular stickiness cannot influence the following calculation of the sagittal sinus pressure.

From Formula 4 it can be inferred that, if there were no CSF flow through the arachnoid villi, the CSF pressure should be equal to the sagittal sinus pressure. In all the pressure/flow diagrams presented in Figs 7–9 a horizontal line is drawn under the X-axis. The position of this line corresponds to the formation rate of CSF for the particular patient. This line then represents the real zero-flow through the arachnoid villi. If the pressure/flow curve is extrapolated down to this level, a pressure value is obtained which should have existed in the subarachnoid space if there had been no flow of CSF through the arachnoid villi. The calculation holds true only under the assumption that a rectilinear extrapolation of the pressure/flow curve can really be made. If the curve should deviate in either direction, another value for the sagittal sinus pressure should be obtained. Whether or not the assumption of a rectilinear extrapolation is true can only be proved when the sagittal sinus pressure is measured directly during a CSF hydrodynamic experiment. Discussion of the different CSF hydrodynamic parameters will be postponed to a later paper.

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