Chapter 3  Cerebrospinal fluid dynamics and hydrocephalus shunts

Introduction

To understand the mechanism of shunt functioning and shunt dysfunctioning, it is necessary to know the normal CSF dynamics and CSF composition and also to know the varying physical properties of the different shunt systems. In addition, an overview of the current knowledge of interactions between shunts and CSF and the causes of shunt dysfunctions might be valuable. Therefore, this chapter will give background information on CSF hydrodynamics and shunt physiology.

3.1 Cerebrospinal fluid dynamics

3.1.1 CSF flow and production

Under normal physiological circumstances, CSF is largely produced in the choroid plexus (50-80%)\(^76\). In addition, there is extrachoroidal production of which the actual extent and location is unknown. The assumption that the spinal subarachnoid space was responsible for the extrachoroidal CSF production was rejected by Marmarou in 1973\(^84\) and Sahar in 1972\(^108\). The ventricular wall has been reported to produce as much as 30% of the extrachoroidal CSF\(^76\). Choroidal CSF is secreted into the ventricles and exits the fourth ventricle through the midline foramen of Magendie and the lateral foramina of Luschka into the cisterna magna and juxta brain stem cisterns. Some of the CSF flows dorsally by the intracranial subarachnoid spaces and cisterns toward the convexities of the brain\(^3\). Here it is absorbed through the arachnoid granulations into the venous system. The rest of the CSF descends around the spinal cord and is absorbed into the extensive venous network surrounding the spinal cord\(^76\).

The CSF is secreted continuously at a normal rate of around 0.34 ml/min. In 1966, Rubin\(^107\) found a rate of 0.37 ml/min; In 1968 Cutler\(^32\) reported a rate of 0.35 ml/min. He found a reduced production of 0.30 ml/min in hydrocephalus patients. On the other hand, in patients with a plexus papilloma, rates of 1.05 to 1.43 have been reported\(^84,90\). The current hypothesis for the mechanism of CSF secretion is based on the assumption that the osmotic gradient which attracts the bulk water of secreted CSF, is caused by active Na\(^+\) transport toward the ventricle by the Na\(^+\)/K\(^+\)-ATPase of the choroid epithelial cell\(^60\). Similarly, a Na\(^+\)K\(^+\)/2Cl\(^-\), cotransporter is directed to the ventricle. Na\(^+\) in the cell is pro-
vided by an Na+/H+ exchange system. H+ and HCO₃⁻ are obtained by the action of carbonic anhydrase on H₂O and CO₂. HCO₃⁻ is exchanged for Cl⁻. There are several factors influencing CSF formation rate. A high CSF osmolarity is known to increase the CSF formation rate. On the other hand, a high plasma osmolarity decreases the CSF formation rate. The pH is also mentioned as having an influence on CSF production. A metabolic or respiratory alkalosis reduces CSF production, whereas a metabolic or respiratory acidosis hardly influences the formation rate. Another factor is the cerebral perfusion pressure, being the difference between arterial blood pressure and intracranial pressure. Animal experiments showed that raising intracranial pressure did not reduce CSF formation rate as long as the cerebral perfusion pressure was maintained above a certain level. Lowering arterial blood pressure reduced CSF production. Raising CSF pressure lowered the CSF formation rate. Studies in hydrocephalus patients showed that CSF production decreased with 0.003 ml/min per mm CSF pressure elevation. Several drugs have been reported to influence CSF formation rate. Acetazolamide and ouabain inhibit CSF production by inhibition of carbonic anhydrase and the Na+/K+-ATPase, respectively. Also, dexamethason (by inhibiting the Na⁺/K⁺-ATPase) and the diuretics furosemide and chlorthiazide (by inhibiting the Na⁺K⁺/2Cl⁻ cotransporter) reduce CSF formation. Spironolacton and cholera toxin stimulate CSF production. Of the hormones, the atriopeptins (Atrial Natriuretic Factor, ANF) diminish CSF production. Hypothermia is known to reduce CSF formation as much as 11% per degree centigrade between 31° and 41°C.

3.1.2 CSF absorption
The most important sites of CSF absorption are the arachnoid granulations on the cerebral convexities as well as the villi in the spinal subarachnoid space. Other possible sites have been reported by McComb in 1983. In a review he described several reports of lymphatic drainage of CSF and also some reports on CSF absorption by the choroid plexus. Earlier, alternative absorption sites where reported by DiChiro et al in 1972 and by Bradbury in 1980. DiChiro described CSF drainage through the olfactory nerve pathway; Bradbury and Cole showed drainage to cervical lymph nodes through the optic nerve sheath. The resistance to absorption is low, so that a normal individual can absorb CSF at a rate three to four times the normal rate of CSF formation. The colloid-osmotic pressure existing between the virtually protein-free CSF and plasma may be an important factor affecting absorption. Another factor is the CSF hydrostatic pressure. The rate of absorption increases linearly with CSF pressure. The exact mechanism of absorption is unknown. Possible mechanisms could be that lining cells of the arachnoid granulations contain vesicles that move material across the cell by pinocytosis or existing intracellular channels and possibly passages or tubules that may move material through the cell.

3.1.3 CSF composition
As described above, CSF is not just a protein-free plasma filtrate. CSF has a lower potassium and calcium concentration than plasma, whereas sodium and chloride concentrations are higher (see table 3.1). The blood-brain barrier has a selective permeability to
proteins and amino-acids. The majority of proteins consist of three proteins: albumin, β-globulins and γ-globulins (see table 3.1). CSF contains only a few cells. These cells are either of local origin or they originate from the blood. Erythrocytes are only found in case of trauma or a pathological hemorrhage. They are cleared rapidly by phagocytosis, beginning already within 2-6 hours after a bleeding. Leukocytes in CSF consist of small lymphocytes, large lymphocytes and monocytes/histiocytes (see table 3.1). Ependymal cells may be present in children under ten years of age. Choroid epithelial cells are seen occasionally. Polymorphonuclear cells are found in acute infection, eosinophils in allergic/anaphylactic reactions. In case of neoplasm of the nervous system, neoplastic cells can be found.

Several neurotransmitters can be found in the CSF. Other substances present in CSF are peptides, hormones and vitamins\textsuperscript{76}.

### Table 3.1 CSF composition

<table>
<thead>
<tr>
<th></th>
<th>CSF</th>
<th>plasma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Electrolytes (mM)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>potassium</td>
<td>2.86</td>
<td>4.63</td>
</tr>
<tr>
<td>sodium</td>
<td>147</td>
<td>150</td>
</tr>
<tr>
<td>calcium</td>
<td>1.14</td>
<td>2.35</td>
</tr>
<tr>
<td>chloride</td>
<td>113</td>
<td>99</td>
</tr>
<tr>
<td>Protein (mg% for CSF, g% for plasma)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>total protein</td>
<td>20-50</td>
<td>5-7</td>
</tr>
<tr>
<td>albumin</td>
<td>0.45-0.75</td>
<td>0.43-0.55</td>
</tr>
<tr>
<td>β-globulin</td>
<td>0.08-0.16</td>
<td>0.09-0.19</td>
</tr>
<tr>
<td>γ-globulin</td>
<td>0.06-0.14</td>
<td>0.15-0.22</td>
</tr>
<tr>
<td>Cells (in %)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>lymphocytes</td>
<td>70-90</td>
<td>20-45</td>
</tr>
<tr>
<td>monocytes</td>
<td>10-16</td>
<td>2-10</td>
</tr>
<tr>
<td>granulocytes</td>
<td>&lt;1</td>
<td>40-75</td>
</tr>
</tbody>
</table>

#### 3.1.4 Pressure in CSF and other compartments

As human beings consist for more than 75% of water, the body may be considered as one giant fluid column with a height equal to the body length, if only there was one big fluid compartment. However, the body is divided in several compartments which are not hydrodynamically connected to each other. The pressure in one compartment is calculated by adding or subtracting a hydrostatic pressure difference to/from a certain point within the compartment of which a reference pressure is known. In 1976 Magnaes described changes in CSF pressure related to body position\textsuperscript{80,81}, including neurosurgical patients as well as controls. Rapid tilting initiated waves in blood pressure and CSF filling pressure\textsuperscript{80}. Controls as well as hydrocephalic patients showed transient waves in CSF pressure. Only patients with elevated intracranial pressure showed stationary waves in CSF pressure; they also presented clinical symptoms. Magnaes suggested that the CSF
pressure waves were related to changes in cerebral blood volume, probably reflecting the postural blood pressure wave and autoregulation. He also looked at the level of the zero CSF pressure point, which is the point at which the fluid pressure is equal to atmospheric pressure, and the hydrostatic indifferent point (HIP)\textsuperscript{81}. The HIP is the point at which the fluid pressure in a sitting position equals the pressure in a lateral position\textsuperscript{43}. In a sitting position, the pressure in the caudal part of the neuraxis increases, varying from 320 to 630 mm H\textsubscript{2}O with a mean of 490 mm H\textsubscript{2}O. Thus, the mean level of zero CSF pressure in a sitting position will be 49 cm above the level of lumbal puncture. This corresponds to a zero CSF pressure point at the level of the first cervical disc, or the base of the neck. In hydrocephalic patients the HIP, and thereby the zero CSF pressure point, was shifted caudally after shunting. The pressure decrease was larger in a sitting position than in a lateral position. Clinically, this means that the zero pressure point may be a useful variable in control of CSF shunt function.

The pressure in the right atrium is slightly positive compared to atmospheric pressure\textsuperscript{43}. The pressure in the peritoneal cavity depends on the place where it is measured, the abdominal contents, the abdominal wall musculature tone, et cetera\textsuperscript{43}. Overall, peritoneal pressure can be considered basically equal to atmospheric pressure. Intrapleural pressure is consistently subatmospheric due to the characteristics of the chest wall.

3.2 Pressure, resistance, flow and viscosity in a shunt system

A shunt system is intended for transport of liquid from a high-pressure compartment to a low-pressure compartment. The shunt system is built up from a series of tubes interconnected by a valve. The valve is a mechanical resistance device which regulates flow. To describe valve functioning, four basic principles of fluid dynamics are important: pressure, flow, resistance and viscosity\textsuperscript{43}.

3.2.1 Pressure
Pressure (p) can be defined as the force (F) per unit area (A). This definition is expressed in the following equation:

\[ P = \frac{F}{A} \]  

The s.i. units of these variables are: P in N/m\textsuperscript{2}, F in N, A in m\textsuperscript{2}.

A fluid column with a height h (m) having a density of mass \( \rho \) (kg/m\textsuperscript{3}) generates a hydrostatic pressure P of:

\[ P = h.\rho.g \]  

where g (m/s\textsuperscript{2}) is the gravity acceleration.
3.2.2 Flow
The amount or volume V (m$^3$) of fluid that passes a cross sectional area A (m$^2$) of the transport system per second is defined as flow, $\varphi$ (m$^3$/s).

3.2.3 Resistance
Flow depends on the difference in pressures ($\Delta P=P_2-P_1$) of the two compartments and the resistance $R$. The resistance (N/m$^2$.s) can be calculated according to the next equation:

$$R = \frac{P_1-P_2}{\varphi}$$

(3)

The pressure difference generates a force on the particles of the fluid, thereby causing an initial acceleration. This results in velocity of the particles. Moving particles undergo a reversely directed force that is caused by friction between the particles among themselves and also between the particles and the inner wall of the tube or other parts of the transport system. Particles near the wall show velocities close to zero, whereas particles at the axis have maximum velocities. The way the velocity is distributed along the cross-section of a tube is referred to as the profile of the velocity. A profile may express a laminar or turbulent flow pattern. At a turbulent flow, $R$ depends on flow velocity, whereas at laminar flow, $R$ does not depend on flow. Excluding transient moments of high pressure due to, for example, coughing, CSF shunt systems will expose laminar flow. It is possible to calculate $R$ with Poiseulle’s law:

$$\varphi = \frac{\pi r^4 \Delta P}{8. L \eta}$$

(4)

where $L$ (m) is the length of a tube with inner radius $r$ (m) and $\eta$ (in N.s/m) the viscosity of the fluid. Substituting 3 into 4 yields:

$$R = \frac{8. L \eta}{\pi r^4}$$

(5)

The flow $\varphi$ strongly depends on the dimensions of the shunt system expressed in radius (fourth law relation), pressure difference ($\Delta P$), length ($L$) and viscosity ($\eta$). Viscosity depends on many factors among which is the temperature (see 3.2.4).

3.2.4 Viscosity
Viscosity is the resistance of a fluid against shear forces. Water has the lowest viscosity in our system. Adding protein to water increases viscosity. Blood e.g., has a rather high viscosity. Viscosity is influenced by temperature. If the temperature increases, the viscosity decreases.
In shunt physiology, viscosity is relevant in two respects: firstly the temperature dependence of viscosity, secondly the influence of viscosity on resistance and flow. In Poiseuille’s law (equation 4), resistance is a linear function of viscosity: if viscosity doubles, resistance will double.

3.2.5 Siphoning
In physiological conditions, cerebrospinal fluid circulation is hardly influenced by body posture, because there is only a slight difference in hydrostatic pressure between the sites of CSF production and absorption into the sagittal sinus and the other absorption sites. The positive pressure difference, which is usually about 2-3 mm Hg, facilitates CSF absorption.

However, in patients treated with ventriculoperitoneal shunts, CSF is drained from the ventricles to the abdominal space. The hydrostatic pressure difference between these sites can be as high as 60-80 cm H₂O, depending on body position. This difference may accelerate drainage of fluid from the site of higher pressure to that of lower pressure. In a supine position the intracranial pressure in patients with CSF shunts is comparable to that in healthy persons. The normal intracranial pressure in an upright position is -65 mm H₂O, indicating that a zero intracranial pressure level exists at 65 mm below the brain vertex. However, as mentioned above, this normal upright intracranial pressure cannot be maintained by differential pressure shunts because of the extra hydrostatic pressure due to the difference in height between the endings of the ventricular and the peritoneal catheters.

Problems of overdrainage may occur. E.g., in an infant with a fluid-filled shunt system of 30 cm in length, there will be a 30 cm difference in height between the proximal and distal end of the shunt system in the upright position, which corresponds to a pressure difference of 300 mm H₂O. This may entirely abolish the effect of low and medium pressure valves.

To maintain a normal upright intracranial pressure, an anti-siphon device (ASD) can be used. Another name for this device is a zero pressure device. When upright, it acts as a closing valve by means of a mobile membrane that moves in response to a difference in pressure across it. CSF flow is allowed to occur as long as there is a positive intracranial pressure above the level of the anti-siphon device. If the intracranial pressure above the level of the ASD drops to zero, the membrane will be pushed against the orifice, thereby increasing the resistance to flow, preventing further siphoning.

Gruber et al. in 1984 as well as Tokoro in 1994 found that an ASD was effective in preventing overdrainage in adults and children. Tokoro showed that an ASD was less effective in children than in adults. Gruber reported that the use of an ASD in connection with the regular shunt system reduced the number of complaints and shunt dysfunctions over a period of more than 6 years.

3.2.6 Measuring flow in shunt systems
During the past decades, much effort has been spent on measuring fluid flow in shunt systems. Percutaneous thermistors, thermosensitive liquid crystals (chameleon print)
and clearance of isotopes have been used to measure flow. All these methods had the disadvantage that they could only be used for a short period. In 1983, Hara presented a model for measuring flow in shunts which was based on air bubbles induced by electrolysis within the shunt system which could be observed by an ultrasonic Doppler technique. This system enabled measurements for longer time periods. Hara described 24-hour flow patterns in two patients. The flow varied between 0.05 and 0.78 ml/min. In 1987 Kadowaki used the same method and found a flow varying from 0.01 ml/min to 1.93 ml/min. Both authors reported circadian rhythms in the flow patterns with peaks in the morning and at night during REM sleep phases. This nocturnal increase in intracranial pressure could be related to intracranial vasodilation. Also, shunt flow was influenced by changes in body position as well as increases in intracranial pressure acting due to increases in intrathoracic pressure or abdominal pressure.

3.3 Shunt materials

Shunts tend to be in contact with the brain and CSF for prolonged periods of time. In addition, a well-functioning shunt system is important to the patient’s well-being. The bottom line for the material constituting shunts is biocompatibility. Several factors pertaining to biocompatibility are: cytotoxicity, sensitization, irritation, intracutaneous reactivity, genotoxicity and hemocompatibility. Only in the long run, acute or chronic toxicity and carcinogenicity are important. Materials should be chemically highly inert to be used for shunts safely.

Only a few materials are currently used in shunt systems. The most frequently used material is silicone rubber. It is used in catheters, valves and access chambers and antisiphon devices. Some of the very favorable properties of silicone rubbers are their thermal stability, their resistance to oxidation and ozone, their chemical inertia to many chemicals, their low surface energy and their high gas permeability. Stainless steel, synthetic ruby, titanium and plastics are other components of shunt systems. These materials are mainly used in valves or needle stops.

In 1987, Echizenya et al. conducted a study on 25 shunts that had been implanted for 6 days to 10 years. Four shunts showed surface deposits of calcium phosphate, probably caused by mechanical stress. In addition, surface wrinkles, microscopic holes and tiny particles which appeared to be aluminium crystals could be found. Echizenya et al. suggested these changes to be caused by degradation of the silicone rubber. The physical properties indicated a progressive change with a considerable deterioration after implantations of more than 5 years. In 1991, Schoener et al. studied explanted catheters and valves by electron microscopy. In 19 out of 36 systems they observed a foreign-body reaction. Dysfunction occurred in 22 out of 36 valves. In a 1994 study by Brydon et al. on 43 explanted shunt valves, a dysfunction rate of 77% was found. Valves with metal components had a high tendency to accumulate debris. On the contrary, only a few polymer valves showed accumulation of debris. Also, only the polymer valves functioned
well after infection, whereas five out of six valves containing metal components performed badly. In a recent review on shunt complications dealing with tissue reactions, Del Bigio reported that cellular debris or blood can cause dysfunction of valve components. Moreover, chronic inflammation could contribute to degradation of shunt components, whereas glial tissue or choroid plexus were found to infiltrate ventricular catheters driven by mechanical pressure.

These studies show the need for further investigations on improvement of biocompatibility and biodurability of shunt systems. In conservative treatment of shunt infection, success might depend on the material and construction of the valve.

3.4 Valve mechanics and valve types

3.4.1 Valve mechanics

Basically, a valve is a device which opens and permits flow when a certain pressure level is exceeded. Below that pressure the valve is closed.

The opening pressure refers to the pressure level at which the valve opens, whereas the closing pressure is defined as the pressure level when the valve closes during decrease of pressure. The mechanical behavior of the material, with emphasis on silicone rubbers of which parts of the valve can be composed, is the reason for differences between opening and closing pressures. Silicone material is easy to deform, has a non-perfect elasticity and may have adhesive properties.

The static characteristics of a valve can be presented in a flow-pressure (φ-P) curve. Figure 3.1 shows some examples. Fig. 3.1a represents an ideal valve: opening pressure equals closing pressure. Below the opening pressure the valve acts as an infinite high resistance that completely blocks the flow, whereas at the opening pressure any forward directed (positive) flow is allowed passage. Fig. 3.1b is typical for a valve performing badly. The sharp transition at the opening pressure is replaced by a gradual changing course which also allows negative directed flows which implies leakage.

The shape of the silicone material tends to adapt slowly to altered flow conditions. As a result there is a bad reproducability of the flow-pressure relationship when comparing the curves resulting from a low to a high flow and reverse. This effect of non-reproducability is called “hysteresis”. The dynamic behavior of the elastomere material can be visualized in pressure-time (P-t) plots at a step function flow input. Before the step function the flow is zero. A flow-controlled circuit forces a predefined flow to settle regardless of the pressure. At the onset of the flow step function, the pressure starts at zero level and will gradually increase until the valve opens. The gradual course is due to the compliance of the tubing material and other parts of the valve feeding circuit. Fig. 3.2 shows some examples of different material behavior. Fig. 3.2a represents a well-functioning valve with no adhesive behavior and a time-independent curve. The pressure increases towards the opening pressure and reaches without too much delay the asymptotic level which belongs to the flow value. Fig. 3.2b shows an increase to a high pressure level which is
caused by adhesiveness of the valve to its orifice. At maximum pressure, the valve opens quickly, then the pressure rapidly declines to the equilibrium (operating pressure). The effect of the temporary elevated pressure level is referred to as 'overshoot'. Fig. 3.2c.

**Figure 3.1** Flow-pressure curves of: an ideal valve (a), and a bad-performing valve (b).

**Figure 3.2** Pressure-time plots at a step function flow input. A well-functioning, time-independent valve is represented in a. b shows the plot of an adhesive valve with overshoot, while in c the slowly adapting valve with a different pattern of overshoot is represented. d shows the pressure time plot of a leaking valve.
shows a very slowly increasing pressure to the equilibrium level. This can be explained by a leaking valve and the slowly (reversely) adapting shape of the valve mechanism.

3.4.2 Valve types most commonly used in our clinical study

Ball and spring valve
The mechanical principle of this type of valve is a metallic spring exerting force on a ball which is located at a conical orifice that can be occluded by the ball. The ball used to be made of metal, but currently it is made of industrial corundum (sapphire or ruby). The hydrodynamic characteristics of this valve depend on tension and deformability of the spring on one hand and of the cone shape and diameter on the other hand. Because silicone rubber is not used in this valve, there are no problems like hysteresis and ‘drift’. This valve does incorporate an ‘on/off’ principle, leading to a high flow immediately after the opening of the valve which might bring an increased risk of overdrainage. The spring ball valve we tested was the Hakim valve (see chapter 4).

Diaphragm valves
The principle of this type is based on a mobile and flexible silicone membrane which moves in response to pressure differences, leading to a circular flow pattern. The hydrodynamics of this valve depend on elasticity, tension and thickness of the membrane as well as on shape and size of the orifice in the valve. There is a risk that at excessive pressure differences the membrane may collapse. Another problem is the non-linear increase in resistance of the membrane with enlargement of its surface which may lead to overdrainage. Because the valve is made of silicone, basic problems as hysteresis and drift may arise. We tested three diaphragm valves of this type: PS medical, Pudenz and Accu-flo (see chapter 4).

Complex valves
The complex valve we tested in the laboratory was the Orbis sigma valve (see chapter 4). This valve consist of an extremely delicate mechanism. A tight conical cylinder is inserted into a ring which is attached to a pressure-sensitive silicone membrane. The inner diameter of the ring is slightly larger than the outer diameter of the conical cylinder. The distance between cylinder and ring varies with the pressure, leaving more or less space for the passage of CSF. The system is vulnerable and sensitive to increased proximal pressure. The membrane is easily damaged, and the ring or cylinder may dislocate. The flow valve has the smallest outlet of all valves (<0.01mm).

The whole concept is based on the rate of CSF production, which is about 20-25 ml per hour in adults in a normal situation. The small outlet of the Orbis sigma flow-valve only allows a maximum flow of 25 ml per hour and protects adequately against overdrainage. In 1987, Kadowaki et al. reported that during nightly REM phases CSF production may amount to 60 ml per hour. This may invoke problems of underdrainage when
this valve is used. Also, the small outlet of the Orbis Sigma valve is prone to obstruction. Schoener et al. (1992) conducted electron microscopic studies on explanted orbis Sigma valves and observed disturbances in the shape of the valve as well as evidence of local immune reactions around the cylinder. Aschoff also expressed his doubts on the functioning of the Orbis Sigma valve with regard to the small outlet of the valve, as well as the rigid flow limitation.

**Slit valves**

These valves consist of a ‘slit’ in a silicone layer. The principle is based on memory properties of silicone: after deformation the material will resume its original shape, which may take a variable time in the range of seconds to days. There are two types of slit valves: proximal and distal slit valves.

The proximal valves consist of either a side slit at the lower catheter-end, or they may have one or multiple slits at the upper end. Proximal slit valves we tested were the Holter valve and Phoenix valve. Distal slit valves consist of a closed silicone catheter with slits of varying length and number at the distal end. We tested the Raimondi valve as the only distal slit valve.

This type of shunt has little resistance to flow because there are no flow-restraining elements in the system. An increase in resistance of the whole system can be obtained by reducing the inner diameter of the connecting catheters.

### 3.5 Protein concentration and shunt functioning

In 1969, Rayport and Reiss and in 1970 Hakim et al. reported that an increase in protein concentration resulted in an equal or higher flow capacity with Hakim valves and decreased flow capacities in other valve types. In 1968, Steinke also concluded that an increased protein concentration impaired valve functioning and therefore decreased flow which was confirmed by Schubert et al. in 1979.

However, in most of the early experiments testing CSF valves, the influence of changes in temperature was not tested. Tests were conducted at room temperature (21°C), in stead of body temperature (37°C). This lower temperature alone resulted in a considerable increase in viscosity, a restriction of flow and eventual occlusion of the catheter as well as the valve. This was reported by Van der Veen in 1972 and stated again by Brydon et al. in 1995.

In 1973, Jährig and Steiner included temperature in their study of the correlation between total CSF protein and viscosity and they reported that at a stable temperature there was a direct correlation between CSF composition and viscosity. In their studies, they related CSF viscosity to that of distilled water at the same temperature. Using this method, they found that the relative viscosity increased linearly with elevations of CSF protein up to a concentration of 60 g/l. In 1972, Van der Veen concluded that for protein concentrations less than 8.5 g/l, increases in viscosity could not be responsible for shunt mal-
functioning. He also tested at a constant temperature. He did mention, however, the possibility of the presence of fibrinogen in high-protein CSF with the risk of clotting and shunt obstruction. In 1990, Aschoff et al.\textsuperscript{10} tested valves at an albumin concentration of 5 g/l and compared these results with a control group tested without addition of protein. No difference was found. In 1992, Pudenz et al.\textsuperscript{102} were not able to detect any differences in hydrostatic properties of valves perfused with an artificial CSF containing 4 g protein/l either. Valve dysfunction occurred, however, with protein solutions of 15 g/l. According to Pudenz et al. these dysfunctions were caused by obstruction through fibrin particles and cryoglobulin aggregates. It must be remarked, that normal CSF does not contain fibrin particles.

Brydon et al. (1995\textsuperscript{24}; 1996\textsuperscript{26}) investigated the relation between CSF protein concentration and absolute viscosity at 37\textdegree C in 126 CSF samples with varying protein concentrations (50\% < 0.5 g protein/l, 80\% < 2.0 g/l, 11\% > 3 g/l). It turned out that the protein concentration hardly influenced CSF viscosity\textsuperscript{24}. When flow of the most viscous CSF (9.5 gramms protein/liter) was compared with flow of the least viscous CSF (<0.45 g protein/liter), it was observed that the flow of CSF with the highest protein concentration was only reduced by 7\% compared to that of CSF with the lowest protein concentration. Also, they rejected the theoretical possibility of high protein concentration leading to valve sticking. In a subsequent report\textsuperscript{25}, Brydon et al. described the effect of protein concentration on the functioning of shunt valves. A high surface tension tends to disturb the opening of a valve in the way a layer of water hinders the lifting of a flat object from a table. The addition of protein to water (or CSF) will decrease the surface tension and facilitate the opening of the valve. Surface tension also depends on the angle of contact between the surface of a solid substance and a liquid, which per se depends on the degree of hydrophilic and hydrophobic interactions. In the study in which the surface tension in CSF with varying protein concentrations was measured, it appeared that the surface tension decreased with rising protein concentrations. Above the concentration of 1 g/l, increasing protein had no effect on surface tension. In practice, the opening pressure of valves will be reduced by this decrease in surface tension.

Thus, at body temperature, a high protein concentration of up to 9 g/l only slightly increases CSF viscosity and in this way does not impair shunt functioning. On the other hand, a high protein concentration reduces surface tension and lowers the opening and closing pressures. This is supported by clinical results: back in 1965 Eckstein\textsuperscript{46} reported successful shunt functioning in the presence of a protein concentration as high as 40 g/l. It must be remarked however, that under certain pathological conditions, high total protein levels may be associated with the appearance of fibrinogen in the CSF\textsuperscript{5,126}. This fibrinogen can polymerize and form fibrin clots which obstruct the shunt\textsuperscript{102,126}. In that circumstance, high protein levels can cause shunt dysfunction.
3.6 Blood and shunt functioning

Several authors\textsuperscript{110,129} have pointed to the adverse effect of high numbers of erythrocytes on shunt functioning in vivo. In 1984, Walters et al\textsuperscript{129} reported that an erythrocyte count of more than 1000/\textmu{l} would increase the risks of shunt dysfunction. In 1993, Sainte Rose et al\textsuperscript{110} stated that placing a ventricular catheter in a ventricle full of blood was ‘doomed to failure’. The negative effects of an increased erythrocyte count on shunt functioning in vivo is probably not to be attributed to an increase in viscosity. In 1973, Jährig and Steiner\textsuperscript{67} reported that erythrocyte or leucocyte counts of up to 50,000/\textmu{l} only influenced viscosity in the third decimal. The only report on in vitro testing\textsuperscript{26} of shunt systems with CSF containing varying erythrocyte counts was by Brydon et al. in 1996. He perfused valves with blood suspensions containing 10,000 to 50,000 erythrocytes/\textmu{l}. Perfusion of Hakim and PS medical valves with CSF containing 10,000 erythrocytes/\textmu{l} did not show any impairments in valve functioning. At higher concentrations, opening as well as closing pressure increased, as did the difference between opening and closing pressure. Also, in some cases, the valve’s closing time increased from 5 to 15 minutes. This was explained by erythrocyte sedimentation which might have affected the closing of the valve. Obstruction may also occur because of adhesions mediated by platelets.