Cerebrospinal Fluid Shunts in Children

Technical Considerations and Treatment of Certain Complications

KAI ARNELL
Dissertation presented at Uppsala University to be publicly examined in Rosénsalen, Akademiska Barnsjukhuset, Ingång 95, Uppsala, Saturday, December 8, 2007 at 13:15 for the degree of Doctor of Philosophy (Faculty of Medicine). The examination will be conducted in Swedish.

Abstract

Ventriculo-peritoneal shunting is the most commonly used method for the treatment of paediatric hydrocephalus. Despite improved shunts and surgical techniques there are still complications. This retrospective study focuses on diagnoses and treatment of shunt malfunction and infections. Cost/benefit of using a adjustable shunt was assessed. Two adjustable cerebrospinal fluid shunts and their compatible antisiphon devices were compared in-vitro.

In 21 of 46 children the standard shunt was changed to a adjustable one due to over-drainage. Adjustment of the shunt was performed in 73% of the children thereby avoiding surgery in several cases. This was a financial advantage.

Ascites or an abdominal pseudocyst without infection was detected in eight children due to resorption difficulties. A ventriculo-atrial shunt was inserted for a period of time. In three children it could successfully be reverted to a ventriculo-peritoneal.

In six children papilloedema was the only sign of shunt dysfunction. At revision the intracranial pressure ranged from 25 to 52 cm H₂O. Fundoscopic examination in children older than 8 years may detect symptomless shunt malfunction.

During a 13-year period 39 shunt infections were diagnosed. Skin bacteria were found in 80%. Prolonged and anaerobic cultures increased the detection rate by more than one third. The intraventricular infections were treated with intraventricular and systemic antibiotics resulting in quick sterilisation. No relapses were encountered. In five older children with distal catheter infection Propionibacterium acne was found. These were treated with intravenous antibiotics and exchanging of the shunt system.

Strata NSC™ and Codman Hakim™ worked according to the manufacturers except at the lowest setting. The resistance was below and in the lower range of the physiological one respectively. The antisiphon device of Strata shunt had to be placed in line with shunt to function properly.

Keywords: Hydrocephalus, papilloedema, abdominal cyst, cerebrospinal fluid shunt, shunt infection, intraventricular antibiotic instillation, intraventricular antibiotic concentrations, in-vitro testing, antisiphon device

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ISSN 1651-6206
ISBN 978-91-554-7010-4
urn:nbn:se:uu:diva-8295 (http://urn.kb.se/resolve?urn=urn:nbn:se:uu:diva-8295)
Detta lopp innehöll många höga hinder
This thesis is based on the following papers, which will be referred to in the text by their Roman numerals (I-VI).

I Arnell K, Eriksson E, Olsen L
The programmable adult Codman Hakim valve is useful even in very small children with hydrocephalus. A 7-year retrospective study with special focus on cost/benefit analysis.

II Arnell K, Olsen L
Distal catheter obstruction from non-infectious cause in ventriculo-peritoneal shunted children.
*Eur J Pediatr Surg* 2004; 14: 245-249

III Arnell K, Eriksson E, Olsen L
Asymptomatic shunt malfunction detected fortuitously by observation of papilloedema.
*Acta Neurochir* 2003; 145: 1093-1096

IV Arnell K, Enblad P, Wester T, Sjölin J
Treatment of cerebrospinal fluid shunt infections in children with systemic and intraventricular antibiotics in combination with externalisation of the ventricular catheter: efficacy in 34 consecutively treated infections.
*J Neurosurg (3 suppl Pediatrics)* 2007; 107: 213-219

V Arnell K, Cesarini K, Lagerqvist-Widh A, Wester T, Sjölin J
Cerebrospinal fluid shunt infections in children in a 13-year material; experience of the addition of routine anaerobic cultures and comparison of the clinical presentation of *Propionibacterium acne* infection with that caused by other bacteria.
*Submitted*

VI Arnell K, Koskinen L-OD, Malm J, Eklund A
Evaluation of two adjustable CSF shunts – Strata NSC™ and Codman Hakim™ and their compatible antisiphon devices.
*Manuscript*

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<td>CoNS</td>
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Introduction

Definition
The earliest scientific report of hydrocephalus was attributed to Hippocrates (466-377 BC), who described the typical symptoms of headache, vomiting, visual disturbances, and diplopia. He proposed that epileptic seizures caused a liquefaction of the brain. Hydrocephalus is derived from the two Greek words hydor (ὕδωρ = water) and kefalé (κεφαλή = head). From the beginning it referred to an extracerebral accumulation of water. Today paediatric hydrocephalus is defined as an excessive accumulation of cerebrospinal fluid (CSF) in the ventricular system, resulting in a high intracranial pressure (ICP). This causes ventricular dilatation and secondary effects as reduction of brain parenchyma, excessive growth of the head circumference, bulging of the fontanel and widening of sutures. The clinical signs are tiredness, irritation and sunset eyes (Figure 1).

![Newborn baby with pronounced hydrocephalus](image)

Figure 1. Newborn baby with pronounced hydrocephalus (with kind permission from the mother).

CSF formation
CSF is mainly produced in the ependyma of the choroid plexus in the lateral, third and fourth ventricles (Figure 2). The choroid plexus consists of ependymal and subependymal layers connected to each other by
richly vascularised tissue. The surface of the plexus is covered with villi increasing the total area. Experimental data indicate that the formation of CSF is both by secretion and filtration\textsuperscript{60}. The rate of CSF formation in a newborn is about 25 ml per day increasing to about 500 ml per day in an adolescent (0.35-0.40 ml/min)\textsuperscript{60,103}. The total volume of CSF is recycled three times a day\textsuperscript{70}.

![Diagram](image)

\textit{Figure 2. The ventricular system}

**CSF dynamics**

The total volume of CSF is about 50 ml in a newborn and 120 ml in an adult\textsuperscript{1}. CSF passes from the lateral ventricles into the third ventricle, through the cerebral (Sylvian) aqueduct into the fourth ventricle (Figure 2). The CSF continues to the basal cisterns through the lateral foramina of Luschka and the medial foramen of Magendie. From there it enters the subarachnoidal space of the brain and spinal cord. CSF is then absorbed through the arachnoid villi into the venous system. The absorption by the villi is a passive process dependent on the pressure gradient between the CSF and the intracranial sinuses\textsuperscript{29}. The ependyma, the capillaries of the arachnoid, the lymphatics of the meninges, and perivascular tissue may absorb small amounts of CSF\textsuperscript{70}.

ICP varies between individuals, with position and age\textsuperscript{29}. When a patient is lying horizontally, the intraventricular pressure is equal to the lumbar pressure. In the upright position the ventricular pressure is negative and the pressure in the lumbar sac positive. In newborns and infants the pressure is low\textsuperscript{99,103}. In adults it is higher\textsuperscript{53,81}.
Aetiology of hydrocephalus

The aetiology of hydrocephalus in children can be classified as:
1. Overproduction of CSF due to benign intraventricular tumour such as plexus papilloma
2. Obstruction to CSF circulation seen in malformations e.g. aqueductal stenosis, arachnoidal cysts, myelomeningocele (MMC) and atresia of the foramina of Luschka, Magendi and Monroe and tumours. It can also be found after infections (scars) or haemorrhage (blood clot)
3. Insufficient resorption due to haemorrhage or infections.

Treatment of hydrocephalus

Indications for treatment

Medical treatment is rarely considered. It is important with appropriate indications for shunting a hydrocephalic patient. The indication for shunting is a head circumference >2 standard deviations (SD) compared with weight and height, a bulging fontanel, widening of sutures, clinical signs of irritation and tiredness and the ventricular index >0.5\(^86\). In cases with discrete symptoms and a ventricular index <0.5 expectation is recommended, while an operation would result in considerable over-drainage problems.

Options to treat hydrocephalus

Different methods have been used to treat hydrocephalus in children:
1. Reduction of CSF production by irradiation or surgical removal of the choroid plexa
2. Pharmacological reduction of the CSF production (isosorbide, acetazolamide)
3. Surgical removal of the obstruction
4. Surgical shunting of CSF to the venous circulation or peritoneal cavity
5. Third ventriculo-cisternostomy (VCS), an opening between the floor of the third ventricle and cisterna magna
Conservative treatment

Probably the oldest treatment of paediatric hydrocephalus was tight bandaging of the infant’s skull to restrict its size\(^5\). The method was abandoned because of its inefficiency and risk of an increasing ICP. During the eighteenth and nineteenth centuries, diets and dehydration cures were recommended\(^{48,92}\). Other methods used to reduce the CSF production have been irradiation of the choroid plexus and pharmacological therapy with isosorbide or acetazolamide\(^{2,72,96}\). The therapy with acetazolamide may still be used temporarily in mild cases of hydrocephalus and in treatment of pseudotumour cerebri\(^{5,30}\).

Ventricular shunts

**History of ventricular shunts**

In 1744, Le Cat described the first puncture of the ventricular system and external drainage. Almost all reported cases ended fatally\(^{45}\). In 1895, Gärtner proposed shunting as a method to treat hydrocephalus\(^{40}\). In 1907, Payer reported an attempt to drain the ventricles to the sagital sinus using a saphenous vein with the venous flaps as a one-way system\(^{67}\). After that several alternative methods to deviate CSF from the ventricles to for instance the gallbladder, bone marrow and urinary tract were described. Nulsen and Spitz reported in 1949 success in treating one hydrocephalic patient using a two-ball valve unit attached to a polyethylene tube from the ventricle into the superior caval vein\(^5\). Pudenz and Heyer constructed a Teflon valve and implanted it in 1955 into a child as a ventriculo-atrial shunt (V-A). The real break-through came a few months later when Holter constructed a valve in the new silicon material. The valve was implanted by Spitz in March 1956. Serial production started a few months later and until 1990 the valves were made in an almost unchanged fashion\(^5\).

The first valves deviated CSF to the venous system. Serious complications were common\(^{56,84,95}\). Ventriculo-peritoneal (V-P) shunting was started by Ames in 1958 and in the 1970s V-P shunting gained ground first in children and then in adults\(^{73}\).

**Recent shunt development**

Nowadays V-P shunting is the most commonly used method. Since the time of the first shunts more sophisticated shunts have been developed. The CSF shunts can be divided into four different groups according to the mechanism of CSF drainage control.
1. Silicon membrane: the CSF flow through the shunt is regulated by an elastic membrane that changes the area of the outlet orifice e.g. Delta™ shunt.
2. Ball-on-spring: The CSF flow is depending on compression of a spring supporting a ball moving along the cone that constitutes the outlet orifice e.g. Codman Hakim™ and Strata™.
3. Proximal and distal slit shunts: the CSF flow depends on the area of one to several slits in the silicon catheter e.g. Holter™ shunt.
4. Moving diaphragm: the CSF flow is stabilized within a certain fixed ranges of pressure e.g. Orbis Sigma™.

Most shunts are available with a fixed opening pressure. With the introduction of the Sophy™ shunt (SU3), in 1984, by rotating an external magnet, the opening pressure could be adjusted to three different levels. The per-operative decision of the most suitable opening pressure for each individual can still be difficult. Children often require adjustments of the shunt’s opening pressure over time. Newborns, and especially premature babies, are sensitive to even small changes in ICP. It is therefore clinically important to be able to change the opening pressure in small steps to avoid distension and distortion of the nervous tissue. In the late 1980s the adjustable Codman Hakim™ shunt was introduced. It was a further improvement with 18 different opening pressure levels from 3-20 cm H₂O.

Most shunt designs are based on a differential pressure that creates a siphon effect in upright position resulting in over-drainage. The excessive CSF flow during positional changes can be reduced with an antisiphon device (ASD). The ASD is available as a separate device or included in the shunt as in Delta™ and Strata™. The ASD can be flow or pressure regulated.

With these modern CSF shunts, which are technically more complex, it is important to know the basic hydrodynamics of the shunts. It is also important that they work according to the manufacturers and fulfil the standard according to FDA (USA) and EU (Europe). A few independent laboratories have now performed computer based in-vitro tests of shunts based on the new International Standard (ISO 7197:2006).

Ventriculo-cisternostomy
With the development of neuro-endoscopy the VCS can be an alternative in selected cases. The method has been used the last 10-15 years in cases...
with obstructed hydrocephalus as aqueductal stenosis. With the help of ventriculosity a stoma is performed between the bottom of the third ventricle and the cisterna magna. In this method a “physiological” CSF circulation is established with no foreign material or risk for shunt complications. However, complications such as hygroma, infections, CSF leakage and intraventricular haemorrhage have been reported and are not negligible even in experienced hands24. Even this method has a restriction because it can only be used in patients with obstructive hydrocephalus and the success rate is lower for children under the age of one year5,62.

Shunt complications
V-A shunting has a high frequency of serious complications such as pulmonary embolism and bacteraemia55,64,84,85,95. The complications with V-P shunts are less common and less serious, but cannot be avoided completely. Even with optimal surgical technique there are complications such as, short or disconnected catheters, over- or under-drainage, defect shunts, infections and hygromas8,18,69,85.

Symptoms and signs of malfunction
Typical symptoms of shunt malfunction are headache, nausea, vomiting, and a depressed level of consciousness21,50. In younger children a bulging fontanel, splaying of the cranial sutures and an accelerated growth of the skull circumference are found1. A high ICP can also lead to a variety of visual disturbances3,23,41. In some patients the symptoms of shunt malfunction are atypical and therefore difficult to recognize as signs of shunt malfunction58. In older children with a gradually progressive shunt malfunction e.g. short catheters the symptoms are not as pronounced and can even be absent23,41,50.

Signs of shunt malfunction on CT scans include ventricular dilatation, flattening of cerebral sulci, reduced subarachnoidal space and changes of periventricular white matter signal. These signs are not always present. Subependymal gliosis can reduce the compliance of the ventricular wall, and impair or even inhibit the capacity of dilatation of the ventricular system in spite of a high ICP28,35. Splaying of the cranial sutures can sometimes also be detected in older children with gradually progressive shunt malfunction54.
Obstruction

Obstruction is usually the result of short or disconnected catheters due to growth and traction\textsuperscript{18,64,69,85}.

Over-drainage

Older shunts with a fixed opening pressure have a risk for over-drainage with development of slit ventricles or even hygroma. Most children need a progressively higher opening pressure with age\textsuperscript{69,74,102,106}. The symptoms of over-drainage in younger children are retardation of the head circumference growth, hanging fontanel, tiredness and, in longstanding cases, premature synostosis. In older children the symptoms are headache and tiredness after having been upright for a long period. After have been laying down and rested for a while, they are alert again.

Under-drainage

Under-drainage is usually due to proximal or distal obstruction, but can also be caused by a too high opening pressure. In the extremely premature a long peritoneal catheter can cause under-drainage since the flow resistance increases with the length of the catheter\textsuperscript{4}.

Infections

In spite of improved operating technique and antibiotic prophylaxis, infection is still a dreaded complication\textsuperscript{8,16}. It is more frequent in the children under the age of six months, which is a problem since most cases of hydrocephalus are diagnosed during infancy\textsuperscript{19,42,71,98}. Most infections are caused by coagulase-negative staphylococci (CoNS) and anaerobic bacteria derived mainly from the patient’s skin during surgery\textsuperscript{10,16,19,42,98}. Infections usually occur at shunt implantation or revision, but infections can also be haematogenically spread e.g. from infections in the respiratory or urinary tracts.

Younger children with infection usually present with signs of high ICP, high fever and redness over the shunt system. In older children, distal obstruction and sometimes an infected abdominal pseudocyst or abdominal pain is found. An infected pseudocyst has to be separated from a
non-infected pseudocyst depending on CSF resorption difficulties of the peritoneum\textsuperscript{7,22}.
AIMS OF THE STUDY

The general aim of this study was to clinically evaluate the benefit of one adjustable CSF shunt, symptoms and treatment of certain complications and experimentally compare two different adjustable CSF shunts.

The specific objectives were:

• To evaluate benefits and problems using the adult Codman Hakim™ adjustable shunt in children with hydrocephalus (I)
• To calculate the cost/benefit of using non-invasive adjustment of shunt opening pressure (I)
• To determine whether the adult shunt can be used in newborns and even in prematures (I)
• To investigate the cause and treatment options in non-infected abdominal pseudocysts or ascites presenting as distal catheter obstruction (II)
• To characterize and prevent hazardous but asymptomatic shunt malfunction (III)
• To assess the efficacy of a treatment regime for intraventricular shunt infections regarding cure, relapse and mortality rate (IV)
• To analyse the addition of anaerobic and prolonged cultures and infections caused by Propionebacterium acne (V)
• To compare and characterize two adjustable CSF shunts and their compatible ASD regarding opening pressure, resistance, degree of anti-siphon effect and influence of different ASD positions
MATERIALS AND METHODS

The adult Codman Hakim™ (CHA) shunt in children (Paper I)

During October 1992 to December 1999, 122 hydrocephalic children had shunt surgery with 155 CHA shunts at the Department of Paediatric Surgery in Uppsala. All children were from the referral area of our hospital and operated by experienced paediatric surgeons. The very first procedure was an adjustable CHA shunt in 62 children, a non-adjustable shunt in 40 and external ventricular drainage (EVD) in 20. The EVD as first procedure was due to haemorrhage or a need to lower the ICP before definitive shunting. After EVD 14/20 children received an adjustable shunt and the others different non-adjustable shunts. In all, 76 children received an adjustable shunt as their first shunt and the other 46 children had a non-adjustable system. In two extreme prematures a shunt was impossible to implant and therefore a ventricular catheter connected to a peritoneal catheter with fixed resistance was used. A standard frontal approach for the pre-bent ventricular catheter insertion was used. The peritoneal open-end catheter was tunneled sub-cutaneously to the abdomen.

Myelomeningocele (MMC) and intra-cerebral/ventricular haemorrhage were the dominating aetiologies of hydrocephalus among the children. Children, who were older than 15 years or had a brain tumour, were excluded as most of them were operated at the Department of Neurosurgery.

Age at implantation of the CHA shunt

The patient’s age of implantation with the CHA shunt varied from pre-term to 15 years (median 4 months). In the group less than 1 month of age six children had a corrected age of 37 weeks and five less than 37
weeks. Two children were operated at 31 and 32 weeks of gestation respectively. The children older than six months had a non-adjustable shunt, which was changed to CHA.

The medical records of all children were evaluated regarding age at shunting, complications, adjustments, financial benefit and long-term results according to a standardized protocol.

Distal obstruction due to non-infected abdominal cyst (Paper II)

Between 1974 and 2001, shunt malfunction with distal catheter obstruction due to a peritoneal CSF resorption difficulty was detected in 8 shunt-dependent, hydrocephalic children.

The medical records were evaluated regarding aetiology of hydrocephalus, type of shunt, age, infectious screening, therapy and follow-up.

“Asymptomatic” shunt malfunction (Paper III)

Between 1982 and 2000, six hydrocephalic children had a shunt malfunction detected merely by the presence of papilloedema. The children, aged 8-14.5 years, were not mentally retarded and were asymptomatic or had discrete symptoms of shunt malfunction. All children were regularly followed by routine check-ups. Four of five had previously normal neuro-ophthalmic examination and one had a known visual impairment. The medical records were evaluated regarding the cause of hydrocephalus, type of shunt, pre- and per-operative findings and outcome.

Treatment of intraventricular CSF shunt infections (Paper IV)

To identify cases with intraventricular shunt infection the medical records of all children with hydrocephalus operated by a paediatric surgeon at the
Departments of Paediatric Surgery or Neurosurgery, University Hospital, in Uppsala, during January 1992 – December 2004 were reviewed. The aetiology of hydrocephalus, age at onset of infection, clinical presentation, causative agent, laboratory data, treatment, sterilisation of cultures, relapse and mortality were recorded.

In children with suspected infection externalisation of the shunt system was performed proximal to the valve and the distal catheter tip was sent for cultures. When the suspicion was mild the distal catheter was initially externalised at the thoracic level. If an intraventricular CSF shunt infection was then verified, the distal catheter and the shunt were removed and externalisation proximal to the valve was performed. CSF was collected from the externalised catheter for prolonged cultures and analysis of glucose and leukocytes.

Intraventricular CSF shunt infection was defined as 1) growth of bacteria from the catheter tip or CSF and 2) the presence of either a glucose ratio (CSF/blood) of <0.45, a CSF glucose concentration of <2.5 mmol/L or a CSF leukocyte count of >250 x 10⁶/L. In some cases the CSF glucose concentration was not available. If the leukocyte count in these cases did not meet the criteria for intraventricular shunt infection, the infection was classified as suspected. Cure was defined as sterilisation of CSF and resolution of clinical symptoms.

Standard treatment of proven intraventricular shunt infections included daily intraventricular antibiotic instillations combined with intravenous or per oral antibiotics. CSF antibiotic concentration analysis was collected just before the next instillation. The concentration interval between 7 and 17 mg/L for both vancomycin and gentamicin was chosen to be well above the minimal inhibitory concentrations (MICs) of sensitive bacteria. The intraventricular antibiotic instillations were continued for 5-10 days depending on culture results, CSF laboratory parameters and clinical symptoms. The same burr hole was used at the replacement, but the ventricular catheter was exchanged and new location of the shunt and distal catheter was used. Systemic antibiotic treatment was given to the day after shunt replacement. Ten children were due to different reasons given intravenous antibiotics only before the intraventricular treatment was started.

In four children, where the treatment started with intravenous antibiotics alone, CSF was collected for antibiotic concentration. The CSF samples were collected at 2 h after the intravenous injection of meropenem, cefotaxime and cloxacillin and at 1 h after the end of the 2-h infusion of vancomycin.
Intraventricular and distal catheter infections (Paper V)

The medical records of all hydrocephalic children having an shunt operation during January 1992 to December 2004 were reviewed, focusing on all types of CSF shunt infections, causative agent, culture proceedings, laboratory data, clinical presentation and treatment.

For the diagnosis of intraventricular shunt infection, the criteria used in Paper IV were used. A distal catheter infection was defined as bacterial growth from the distal catheter CSF in combination with either a positive culture from the tip or a repeated positive CSF culture in the presence of normal CSF glucose and leukocyte concentration (<5 × 10^6/L). Shunt infections with CSF leukocyte counts in the interval of 5 - 250 × 10^6/L and normal or unavailable glucose values were classified as suspected intraventricular, whereas cases with normal CSF leukocyte count and unavailable glucose values were considered unclassifiable.

In four of the children with distal catheter infection, CSF was collected for antibiotic concentration analysis at 2 h after the intravenous injection of the antibiotics meropenem, cefotaxime and trimethoprim concentrations.

Evaluation of two CSF shunts and their antisiphon devices (Paper VI)

Six Strata NSCTM (Non-siphon control) and Codman HakimTM CSF shunts were tested with or without the corresponding ASD, Delta Chamber™ and Siphonguard™. Both CSF shunts are adjustable and have a ball on spring mechanism, but their ASD have different mechanisms (Fig 3 a-d).
All shunts were tested with their original proximal and distal catheters. Before the tests all shunts were soaked in deaerated water for at least 24 hours and simultaneously perfused with 0.33 mL/min. The shunts and antisiphons were kept in water bath between the different tests.

Test rig
The set-up for shunt testing has previously been described\textsuperscript{33,57} and is carefully described in Paper VI. Briefly it is a computer controlled fully automated device, which regulates the pressure and collects the data. It is regulated by air pressurizing a 5-dm\textsuperscript{3}-sealed water-filled bottle (Fig. 4). From the pressure drop over a glass constriction with known resistance the flow of water was calculated. The CSF shunt was mounted on a horizontal plate and to simulate the subcutaneous tissue pressure submerged into water\textsuperscript{44}. Outflow from the shunt was led into an overflow container with constant water level (i.e., zero pressure level) or to a level of 30 cm H\textsubscript{2}O (22.1 mm Hg) below zero level, when testing with a distal hydrostatic pressure (i.e., siphoning test). Abdominal pressure was simulated with outflow from the shunt at a level 8.7 cm (6.4 mm Hg) above the zero pressure level\textsuperscript{27}. The experimental set-up was built into an incubator at 37\textdegree C.

\textit{Figure 3.} a. Strata NSC\textsuperscript{TM} with five different settings b. Codman Hakim\textsuperscript{TM} with 18 different settings c. Delta Chamber\textsuperscript{TM}, pressure regulated, has two silicon diaphragms seated above and under the outlet reducing the effect of negative hydrostatic pressure d. Siphonguard\textsuperscript{TM}, flow-controlled, with two pathways where the second way is always open and has a ten times higher resistance than the first. The first way will close when the flow is too high (Figure from Paper VI). The pictures were kindly supplied from Medtronic and Johnson& Johnson.
Test protocol

The software was developed in Lab view (National Instruments, Austin TX, USA) as described in Paper VI. It regulated the pressure proximal to the shunt, i.e. the simulated ICP, according to a triangular waveform with duration of 60 min. The pressure was regulated between zero and the lowest multiple of 500 Pa (3.8 mm Hg) resulting in a maximum flow exceeding 1.2 mL/min. The wave had to be repeated without interference for acceptance in calculation.

The calculations are described in Figure 5. The static resistance were determined as the slope of a linear regression between 0.6 and 1.2 mL/min from cycles without interference. The dynamic resistance was calculated between 0.05-0.2 mL/min²⁷. The opening pressure was estimated at the crossing between the regression line and the abscissa. The static resistance was used in all calculations except in calculation with abdominal pressure and at siphoning test of Strata NSC™, because the flow was not high enough, hence the dynamic resistance was used.
The CSF shunts and ASD

Every shunt was tested at its highest, lowest and middle opening pressure level without ASD. The opening pressure and resistance were determined at all positions both with and without hydrostatic component (i.e. the simulated abdominal pressure).

One Strata NSC™ shunt at performance level 1.5 (middle opening pressure) was investigated with six different Delta Chambers™. One Codman Hakim™ shunt set to 10 cm H₂O was investigated with six different Siphongards™. The ASD was placed in line with, 10 cm above or 20 cm below the ventricular catheter tip simulating positions commonly used in patients (Fig. 6).
Figure 6. The ASD positioned in line with, 10 cm over or 20 cm below the ventricular catheter tip (Figure from Paper VI).

The opening pressure and resistance were determined at all positions without and with siphoning test.

Statistics

Values are expressed as mean ± SD. Paired t-test was used to test for differences within groups. P < 0.05 was considered statistically significant and Bonferroni correction was used for multiple tests.
RESULTS

The CHA shunt in children (Paper I)

Reason for changing to a CHA shunt
In 46 out of 122 children the first shunt system was non-adjustable. In 21 of these children the shunt was changed to a CHA shunt because of over-drainage. In the other 25 children the reason for changing the shunt was obstruction, under-drainage, infection, or an old or malfunctioning shunt (Table 1). In the children with obstruction, the non-adjustable shunt was changed to a CHA shunt during the procedure to be able to adjust the pressure later.

Table 1. Reason for changing to an adjustable shunt (Table from Paper I)

<table>
<thead>
<tr>
<th>Reason</th>
<th>N:o of children</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over-drainage</td>
<td>21</td>
<td>46</td>
</tr>
<tr>
<td>After suspected or proven infection</td>
<td>9</td>
<td>20</td>
</tr>
<tr>
<td>Proximal obstruction</td>
<td>9</td>
<td>20</td>
</tr>
<tr>
<td>Under-drainage or distal obstruction</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Old shunt</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Defect shunt</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>46</td>
<td>100</td>
</tr>
</tbody>
</table>

Complications with the CHA shunt
Sixty-six (54%) children did not require shunt revision and 56 children had one to five revisions. There was no operative mortality. In total 97 complications requiring surgical intervention (0.8/child) occurred in 122 children (Table 2).
Table 2. 

<table>
<thead>
<tr>
<th>Complications</th>
<th>No of complications</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proximal obstruction</td>
<td>35</td>
<td>36</td>
</tr>
<tr>
<td>Distal obstruction</td>
<td>29</td>
<td>30</td>
</tr>
<tr>
<td>Suspected or proven infection</td>
<td>21</td>
<td>22</td>
</tr>
<tr>
<td>Defect shunt</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Subcutaneous CSF leakage</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Pressure necrosis</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Hygroma</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>97</td>
<td>100</td>
</tr>
</tbody>
</table>

The proximal obstructions were mainly due to a too short ventricular catheter. Of the 29 distal catheter obstructions, 16 were due to short catheters and 13 were disconnections. Shunt infection was suspected in 21 children, of which 15 were confirmed. In 8 cases the shunt was deficient. Subcutaneous leakage of CSF was due to a too wide hole in the dura mater. Pressure necrosis of the skin over the shunt was seen in two disabled children at five months and three years after shunt implantation. The shunts were located just behind the ear on their favourite sleeping side.

Adjustments of the CHA shunt opening pressure

Adjustments were performed in 89 out of 122 (73%) children and in one third of them more than three times. In most children adjustments were performed to treat or avoid over-drainage.

Resetting of shunt opening pressure was defined as a change > 2 cm H₂O. Accidental resetting at MRI occurred in 16 of 42 investigations (38%). Non MRI-related resetting of the opening pressure was found in five children.
Economy

The cost-benefit analysis was based on the 76 children, who got the CHA shunt as their first shunt, including those with a previous ventricular drainage. Shunt opening pressure was adjusted later in 57 children of whom 12 children had severe symptoms of over-drainage. Without the possibility of adjustment, they would have their shunt exchanged to avoid the risk of hygroma or premature synostosis, or both. There were also 12 children with insufficient increase of head circumference in whom the opening pressure was adjusted by 6-12 cm H₂O within a year postoperatively.

The calculations were based on the costs of implanting a shunt at our hospital for the year 2003. The total cost for one child undergoing surgery (1019 €), anaesthesia (609 €), a new non-adjustable shunt (761 €) and 4 days hospital admission (924 €) was 3696 €, and for the 24 children thus 152,592 € in all. The cost for an adjustable shunt was 1522 €. The cost for all 76 adjustable shunts used as first shunts was 57826€. An outpatient visit, including a lateral skull radiograph taken after adjustment costs 380 €. A total of 192 visits and adjustments were performed at a cost of 73043 €. The difference in cost of the re-operations compared with the difference of the shunt-price and cost for the outpatient visit is therefore 21713 €.

Follow up

All children were followed up for 1-86 months (median 56 months). Three died from non shunt-related reasons. Two children with successfully drained arachnoidal cysts have been shunt independent for 45 and 72 months.
Distal obstruction due to non-infectious abdominal cyst (Paper II)

The pseudocysts or ascites were presented with distal shunt malfunction in all children. Three of them also had abdominal symptoms such as distension or pain. The pseudocysts and the ascites were confirmed with an abdominal ultrasound in 7 out of 8 children.

All children were initially treated on the suspicion of a CoNS infection with externalisation, intravenous and intra-ventricular antibiotics, until repeated cultures remained negative. Prolonged aerobic and anaerobic cultures of CSF and culture of the distal catheter tip in all children failed to detect bacterial growth. Fungal culture of CSF was negative in 3/3 and viral detection was negative in 2/2 children.

At laparotomy, the peritoneum and the intestinal serosa were hyperaemic and oedematous in all children. Two also had bowel adhesions (Figure 7a-b). The lumen of the catheter sheath was pale and without signs of inflammation (Figure 7c-d). The peritoneal reaction did not include a fibrin coating usually found in bacterial peritonitis.

Since no infection was proved, V-P shunting was tried 1-3 times without success before a V-A shunt was inserted without any problems. Four of the eight children underwent a distal revision after 6-24 years due to short atrial catheter with distal obstruction. At the revision, the distal catheter was successfully replaced into the abdominal cavity in three of the children. The fourth child developed an infectious abdominal pseudocyst. After treatment of the infection this child got a new V-A shunt due to persistent peritoneal reactions.

At follow-up (5-58 months) of the three children with replaced abdominal catheter there were no abdominal cysts or ascites. The other five children with a V-A shunt had no shunt related problems at follow-up (6 months-23 years).
Fig 7. *Bowel adhesions with hyperaemic peritoneum, b. Hyperaemic and oedematous intestinal serosa, c. The hyperaemic outside of the catheter canal, d. The pale inside of the catheter canal (Figures from Paper II)*

Shunt malfunction without symptoms (Paper III)

At previous shunt revisions these patients had typical symptoms of high ICP but no papilloedema. Papilloedema was detected in three children at a routine check-up and in one child at an ophthalmological examination as a screening of shunt malfunction because of slight headache. In the other two children the papilloedema was detected at a normal visual check-up. The patients are described in Table 3. At direct questioning, three children still denied symptoms, but two admitted a sensation of pressure behind the eyes, one of them visual difficulties (had a previous known visual impairment) and one slight headache. In five children a CT scan was done and three showed a discrete ventricular enlargement and the other two were unchanged.
Table 3. Clinical data on patients with shunt malfunction without symptoms (Table from Paper III)

<table>
<thead>
<tr>
<th>Aetiology of hydrocephalus</th>
<th>Age at previous revision</th>
<th>Age in years at diagnosis of papilloedema</th>
<th>Protrusion in dioptres</th>
<th>Papillary haemorrhage</th>
<th>ICP at revision in cm H$_2$O</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemorrhage</td>
<td>6 months</td>
<td>8</td>
<td>+3</td>
<td>No</td>
<td>&lt;25</td>
</tr>
<tr>
<td>Aqueductal stenosis</td>
<td>-</td>
<td>10</td>
<td>+2</td>
<td>No</td>
<td>40</td>
</tr>
<tr>
<td>Aqueductal stenosis</td>
<td>-</td>
<td>12</td>
<td>+3</td>
<td>No</td>
<td>45</td>
</tr>
<tr>
<td>Haemorrhage</td>
<td>-</td>
<td>13</td>
<td>+3</td>
<td>Slight</td>
<td>25</td>
</tr>
<tr>
<td>MMC</td>
<td>3.5 years</td>
<td>13.5</td>
<td>+4-5</td>
<td>Slight</td>
<td>&gt;40</td>
</tr>
<tr>
<td>Dandy Walker cyst</td>
<td>1 year</td>
<td>14.5</td>
<td>+3</td>
<td>Signs of atrophy</td>
<td>52</td>
</tr>
</tbody>
</table>

After the shunt revision, the papilloedema disappeared in five children without any visual reduction. In the child with signs of atrophy of the optic nerve at the first examination, the vision reduction did not improve.

Treatment of intraventricular CSF shunt infections (Paper IV)

During the study period, 237 children had 474 shunt operations. There were 30 verified and 4 suspected shunt infections in 30 children. In all infections bacterial growth from both the catheter tip and CSF was found. Causative bacteria in relation to age at infection as well as symptoms and laboratory parameters are presented in Tables 4 and 5, respectively.
Table 4. *Causative bacteria in 30 patients stratified by age (some patients had more than one infection)* (Table from Paper IV)

<table>
<thead>
<tr>
<th>Age</th>
<th>Coagulase-negative staphylococci</th>
<th>S. aureus</th>
<th>Propionibacteria</th>
<th>Entero-cocci</th>
<th>E. coli</th>
<th>Other gram-negative rods</th>
<th>β-haemolytic streptococci</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 12 months</td>
<td>11</td>
<td>5</td>
<td>-</td>
<td>1</td>
<td>1</td>
<td>3</td>
<td>-</td>
</tr>
<tr>
<td>1-2 years</td>
<td>3</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>3-6 years</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>7-15 years</td>
<td>4</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>19</td>
<td>7</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>1</td>
</tr>
</tbody>
</table>
Table 5. Signs of shunt infection and laboratory parameters at admission (Table from Paper IV)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temperature, °C, median (range), (n=34)</td>
<td>38.8 (37.0-40.9)</td>
</tr>
<tr>
<td>Redness over shunt system</td>
<td>17/34</td>
</tr>
<tr>
<td>C-reactive protein, mg/L, median (range), (n=34)</td>
<td>123 (8-365)</td>
</tr>
<tr>
<td>WBC in blood, x10⁹/L, median (range), (n=33)</td>
<td>13.6 (5.9-41.6)</td>
</tr>
<tr>
<td>WBC in CSF, x10⁶/L, median (range), (n=34)</td>
<td>94 (0-5560)</td>
</tr>
<tr>
<td>Glucose ratio, median (range), (n=8)</td>
<td>0.16 (0.09-0.45)</td>
</tr>
<tr>
<td>Glucose concentration, mmol/L, median (range), (n=25)</td>
<td>0.5 (0.25-2.4)</td>
</tr>
</tbody>
</table>

Specific treatment and cure rate in different infections

Intraventricular shunt infections caused by coagulase-negative staphylococci (CoNS) and *S. aureus* were treated with daily intraventricular instillation of vancomycin (1-10 mg per day) and a few days of intravenous vancomycin or cloxacillin, followed in some cases by oral flucloxacillin. In one child the CoNS infection was treated with externalisation at the thoracic level and intravenous vancomycin during 37 days with still positive culture before externalisation of the ventricular catheter and initiation of intraventricular instillations. After two instillations the culture was negative. In another child with a *S. aureus* infection treatment was initially started with intravenous cloxacillin and externalisation of the ventricular catheter. After 14 days with persisting positive cultures, intraventricular and intravenous therapy with vancomycin was started.

Intraventricular infections caused by *E. coli*, enterococci, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Haemophilus influenzae* and β-haemolytic streptococci responded promptly to the combination of the ventricular instillation and intravenous administration of appropriate antibiotics.
Duration of treatment

Intraventricular instillations were continued for a median of 8 days (range 3-17 days). Median duration of intravenous treatment in all patients was 10 days (range 4-45 days). Median duration of intravenous treatment when combined with intraventricular instillations was 7.5 days (range 4-16 days). No further antibiotics were given after shunt replacement, with exception of two children who were treated with oral antibiotics for 4 or 10 days. No adverse effects related to the intraventricular antibiotic treatment were reported.

Cure rate

The effect of intravenous antibiotic treatment alone, with or without externalisation of the shunt system, and CSF antibiotic concentrations found are summarised in Table 6.
Table 6. *Antibiotic concentration after intravenous antibiotics and results of CSF cultures (Table from Paper IV)*

<table>
<thead>
<tr>
<th>Bacterial agents</th>
<th>Antibiotics</th>
<th>Dosage mg/kg/day</th>
<th>Treatment days</th>
<th>Externalisation</th>
<th>Culture result</th>
<th>Antibiotic concentration mg/L</th>
<th>Albumin concentration mg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Klebsiella pneumoniae</em></td>
<td>meropenem</td>
<td>120</td>
<td>14</td>
<td>At the thoracic level</td>
<td>pos</td>
<td>0.7</td>
<td>657</td>
</tr>
<tr>
<td><em>Haemophilus influenzae</em></td>
<td>cefotaxime</td>
<td>300</td>
<td>6</td>
<td>Proximal to shunt</td>
<td>pos</td>
<td>&lt;2</td>
<td>206</td>
</tr>
<tr>
<td><em>S. aureus</em></td>
<td>cloxacillin</td>
<td>100</td>
<td>14</td>
<td>Proximal to shunt</td>
<td>pos</td>
<td>&lt;10</td>
<td>638</td>
</tr>
<tr>
<td>CoNS</td>
<td>vancomycin</td>
<td>60</td>
<td>37</td>
<td>At the thoracic level</td>
<td>pos</td>
<td>1.2</td>
<td>33</td>
</tr>
</tbody>
</table>
After initiation of intraventricular antibiotic treatment and externalisation of the ventricular catheter, all infections were cured. At the start of intraventricular antibiotic treatment, all cultures were positive, and no culture turned positive after once having been negative. Clinical symptoms resolved before or in parallel with sterilisation of the CSF.

Relapse and mortality
During a follow-up period of 6 months, there were no relapses and no mortality. Three children had four recurrent infections caused by other bacteria. There were no relapses with the same bacterial strain.

Intraventricular and distal catheter infections (Paper V)

During the study period 474 shunt operations were performed in 237 children (Fig 7). There were 39 shunt infections in 35 children.

![Figure 7. Shunt operations performed 1992-2004 (Figure from Paper V)](image)

In 30 cases the shunt infection was classified as intraventricular, 5 as distal catheter infection and 4 as suspected intraventricular. Anaerobic cultures
resulted in detection of \( P. \) acne in 6 children and prolongation of cultures for \( \geq 4 \) days in growth of CoNS in 5 cases and \( P. \) acne in one case. The six children with \( \text{Propionibacterium acne} \) infection were older than those infected by other bacteria and the type of infection was significantly different with an intraventricular infection in one case and a distal catheter infection in 5 cases (\( p<0.001 \)).

Infection by skin bacteria as CoNS, \( S. \) aureus and \( P. \) acne were predominantly the result of operative procedures. In children in whom the shunt infection was secondary to bacteraemia a wider range of bacteria was seen such as \( \beta \)-haemolytic streptococci group G, enterococci, and gram-negative rods. The infections with \( P. \) acne infection were different compared with that of other bacteria and occurred after distal revision or shunt puncture.

The time from presumed contamination to manifest infection varied between 1-28 weeks within 38 of the 39 infections. The longest interval was seen in a child with CoNS infection and a laparotomy performed 52 weeks earlier. In infections caused by propionibacteria, the median time from presumed contamination to manifest infection was 9 weeks compared with 3 weeks for other bacteria.

Children less than 12 months of age, with intraventricular shunt infections caused by CoNS, were severely affected with systemic symptoms. Eight out of the eleven children demonstrated obvious local symptoms. In the 8 children more than 12 months of age, the body temperature was lower and none of them showed local symptoms. All children with infections caused by \( S. \) aureus had systemic symptoms and all but one had local symptoms. Infections caused by gram-negative rods or \( \beta \)-haemolytic streptococci were all associated by systemic symptoms. All children with \( P. \) acne infection showed signs of distal catheter obstruction and four had an abdominal pseudocyst. Body temperature was significantly lower than in children with infections caused by other bacteria (\( p<0.001 \)). With the exception of two children, the child with intraventricular infection and another with a ventriculoatrial shunt there were no systemic or local signs in children infected by propionibacteria.

Treatment of the children with distal catheter infection

The five children with distal catheter infection and growth with \( P. \) acne, had their distal catheters externalised at the thoracic level and were according to the protocol only treated with antibiotics systemically. This treatment involved meropenem (\( n=2 \)), cefotaxime (\( n=1 \)), trimethoprim/sulfamethoxazole (\( n=1 \)) intravenously or rifampicin and fusidic acid orally (\( n=1 \)). Regardless susceptible bacteria and treatment for several days, antibiotic concentrations were low, sterilisation rate poor and no cure was achieved (Table 7).
Table 7. Treatment with intravenous antibiotics in valve/catheter infection with P. acne and antibiotic CSF concentrations (Table from PaperV)

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Dosage mg/kg/day</th>
<th>Treatment days</th>
<th>Culture</th>
<th>Antibiotic conc. mg/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>meropenem</td>
<td>100</td>
<td>10</td>
<td>pos</td>
<td>0.5</td>
</tr>
<tr>
<td>meropenem</td>
<td>100</td>
<td>14</td>
<td>pos</td>
<td>0.6</td>
</tr>
<tr>
<td>cefotaxime</td>
<td>75</td>
<td>7</td>
<td>pos</td>
<td>&lt;2</td>
</tr>
<tr>
<td>trimethoprim-sulfamethoxazole</td>
<td>6/30</td>
<td>5</td>
<td>pos</td>
<td>0.57*</td>
</tr>
<tr>
<td>rifampicin+fusidic acid</td>
<td>14/23</td>
<td>8</td>
<td>pos</td>
<td>NA**</td>
</tr>
</tbody>
</table>

*trimethoprim; **NA not analysed

Despite the continuous growth of bacteria in the CSF, the whole shunt system was replaced after 5-14 days antibiotic therapy in 4 children. In the fifth child, having two shunts, only the distal part and the valve of the infected shunt were replaced after 8 days of treatment. Per operative treatment with cloxacillin (n=3), vancomycin (n=1) and meropenem (n=1) were given intravenously together with one dose of intraventricular vancomycin (n=4). With the exception of one child who also received oral antibiotics the first postoperative day, no further antibiotic treatment was given. Cultures from the central CSF (n=5) and ventricular catheter tip (n=4) at operation were all negative, whereas cultures from inside the shunt were all positive. Body temperature normalised in the child with fever and no relapses occurred within a 2-year follow-up period.

Evaluation of two CSF shunts and their antisiphon devices (Paper VI)

CSF shunt systems

The pressure flow curves for Strata NSC™ and Codman Hakim™ CSF shunts were generally smooth and continuous, although the Codman Hakim™ closed discontinuously in steps (Fig. 5). The opening pressure was significantly dependent on the performance level settings and at the highest and middle setting the opening pressure was nearly the same (Fig. 8). At the lowest setting the Strata NSC+™ was close to zero but Codman Hakim™ was double compared to the specification.
The resistance in the Strata NSC™ was lower than in the Codman Hakim™ where resistance was in the lower part of the physiological resistance interval³⁴ (Fig. 10). In Codman Hakim™ the resistance was not significantly dependent on the performance levels. We found significant difference in resistance for the Strata NSC™ between setting 1.5 and 2.5, but they were small and without practical importance (mean difference <0.36mm Hg/ml/min).

Figure 8. Opening pressure in Strata NSC™ performance level 0.5, 1.5 and 2.5 and Codman Hakim™ setting levels 3, 10, 20 cm H₂O (Figure from Paper VI).

Figure 9. The resistance in Strata NSC™ and Codman Hakim™. The shaded area is the interval of the physiological resistance³⁴ (Figure from Paper VI).
The simulated abdominal pressure resulted in a significant increase of the opening pressure for both Strata NSC™ and Codman Hakim™. In all tested Strata NSC™ shunts at the lowest setting with abdominal pressure a minor (0.06-0.3, mean 0.18 mL/min) backflow was found.

There were individual variations regarding opening pressure and resistance in both CSF shunt models. The variations in opening pressure at the three settings ranged between 0.4-4 mm Hg in both tested shunt types (Fig. 8). In resistance the variations at the different settings for both CSF shunt models were very small (Fig. 9).

Placement of ASD (Fig. 7)

In simulated lying position the Delta Chamber™, but not the Siphonguard™, influenced the opening pressure (Table 8). The ASD placed above the Strata NSC™ increased the opening pressure and the inverse if lowered.

Table 8. Static opening pressure and resistance for Strata NSC™ and Codman Hakim™ with the antisiphon device at different positions. All data are for simulated lying position (Fig. 5) (Table from Paper VI)

<table>
<thead>
<tr>
<th>Position</th>
<th>Strata NSC™ Opening pressure</th>
<th>Strata NSC™ Resistance</th>
<th>Codman Hakim™ Opening pressure</th>
<th>Codman Hakim™ Resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>cm</td>
<td>mm Hg</td>
<td>mm Hg/mL/min</td>
<td>mm Hg</td>
<td>mm Hg/mL/min</td>
</tr>
<tr>
<td>±0</td>
<td>10.3±0.6</td>
<td>3.3±0.2</td>
<td>8.9±0.2</td>
<td>5.7±0.1</td>
</tr>
<tr>
<td>+10</td>
<td>18.8±0.3</td>
<td>3.3±0.2</td>
<td>9.1±0.1</td>
<td>5.9±0.5</td>
</tr>
<tr>
<td>-20</td>
<td>6.2±0.2</td>
<td>3.9±0.2</td>
<td>8.9±0.7</td>
<td>5.8±0.2</td>
</tr>
</tbody>
</table>

At siphoning test of the Strata NSC™ with Delta Chamber™ the flow did not close. In Codman Hakim™ the resistance the second way were approximately ten times that of the first way at siphoning test in all positions. The primary pathway closed at a medium flow rate of 4 mL/min.
Complication frequency

V-P shunting is the most commonly used method treating paediatric hydrocephalus. With the adjustable shunts the results have improved, but even with meticulous surgical technique there are complications\textsuperscript{8,64,69,85}. In our material of 122 children followed for on average 50 months there were 0.8 complications that required surgery occurred per child (Paper I). In literature 0.2–0.5 complications/child have been reported, but usually the follow-up was shorter\textsuperscript{15,51,78}. Growing individuals tend to outgrow their catheters and therefore the incidence of complications increases with the longer follow-up. I recommend that investigations on treatment of hydrocephalus in children include length of follow-up and number of complications per child. This would make it possible to compare different studies.

Symptoms and signs of shunt malfunction

Many children with shunt malfunction present with typical symptoms as headache, nausea, vomiting and/or lethargy\textsuperscript{21,50}. Palpation of the shunt can sometimes be helpful, but is not always reliable. Shunt malfunction can lead to life-threatening complications\textsuperscript{3,63,64,85}. Hence, all changes in the shunted child’s behaviour, well-being, eyesight and temper should be critically evaluated with respect to shunt malfunction.

Older children with slowly progressing or intermittent shunt malfunction may have discrete clinical signs of increased ICP. Therefore malfunction can be difficult to detect, as illustrated by our children with papilloedema in Paper III. Papilloedema as the only sign can be masked by the children’s capacity to accommodate. Attention to ophthalmological signs of an increased ICP is important\textsuperscript{23,41,50}. Eyesight disturbances due to a high ICP can reflect damage to either the anterior visual pathway, or to the posterior visual pathway with different degrees of ‘cortical blindness’\textsuperscript{3,41,50}. The shunt malfunction in our reported children (Paper III) was slowly progressive. This allows the child to adapt to the high ICP, which can result in a loss of vision\textsuperscript{25,46}.

A high ICP can also induce a dilatation of the ventricular system and reduction of the subarachnoidal space at CT scan. CT scan is recognised not to be a completely reliable indicator of shunt function, as we found in Paper III,
which has also been reported by others.\textsuperscript{21,50,54,63} Stiffness in the ventricular wall, as a result of subependymal gliosis has been proposed to explain the difficulty in dilating the ventricular system.\textsuperscript{28,35} The splaying of cranial sutures seen on skull X-ray in two of our children (Paper III), despite their age of 8 and 12 years, indicates that the shunt malfunction may have been longstanding and partly been compensated for by the increase in head circumference.

**Proximal and distal obstruction**

In our material (Paper I) we used only a frontal approach for the ventricular catheter. With this method it is not possible to avoid relative shortening and retraction of the catheter, when the children grow. Earlier we used a parietal burr hole with which the catheter could function for a longer period of time. However, proximal obstructions then were more frequent due to narrow lateral ventricle and interposition of the choroid plexus over the catheter slits.\textsuperscript{56} Proximal disconnection is nowadays not as common as when we started with the frontal approach. We nowadays have a better knotting technique and place the shunt nearer the burr hole to minimise the traction. To reduce the risk of proximal obstruction and disconnection, I recommend a frontal approach with the longest possible catheter and a short distance from the burr hole to the shunt.

Distal obstruction due to outgrowth of the peritoneal portion of the distal catheter is a well-known problem reported in the literature.\textsuperscript{56} This was rare in full-term babies and older children in our series probably because full-length catheters were used already at the primary operation. In our material in Paper I there were disconnections of the distal catheter in 13 of our 29 children with distal obstructions (10\%). This could be because the edge of the ligation site of the CHA shunt was not prominent enough. As the children grow there is more traction on the distal catheter than in an adult patient. This may explain the higher frequency of disconnections in our material of only children compared with that of 4\% in a study of children and adults.\textsuperscript{12} In another paediatric material there was also a high frequency of disconnections reported.\textsuperscript{78} This problem can now be avoided by using a unitised shunt.

An abdominal cyst or ascites can also give a distal obstruction as described in Paper II, IV and V. The cyst can be infectious (Paper IV and V) or non-infectious (Paper II). Infection, especially from CoNS, is known to induce intra-abdominal pseudocyst formation causing distal obstruction.\textsuperscript{39,49,78,82} In the infectious cysts the omentum wraps around the distal catheter tip to form a cyst isolating the infected CSF from the abdominal cavity.\textsuperscript{22} The non-infectious pseudocysts have no epithelium and the walls consist of intestinal serosa or peritoneum. The pseudocyst or ascites are due to an unknown peritoneal CSF reaction as in our eight reported children in
Paper II, who had a V-A shunt inserted after several V-P trials. To distinguish between the infected and non-infectious pseudocysts, it is important to be aware that CoNS grows slowly and requires prolonged culture to be detected, and that \textit{P. acne} needs anaerobic cultures\cite{16,79,82,94}.

**Adjustment of the CHA shunt (Paper I)**

The shunt pressure adjustments are especially important in children to obtain the optimal opening pressure for each patient\cite{13,51,69,74,102,106}. As the ventricular volume stabilises within a year most of the adjustments are made within the first 6 months after shunt insertion\cite{20,69}.

In our material we adjusted the pressure in 73\% of the children compared with 31\% to 64\% in other reports\cite{12,51,69,78,102,106}. The higher number of adjustments in our material is probably because it comprised only children, some of which were prematurely born needing adjustments in small, repeated steps. In a similar study all children (100\%) required adjustment of the shunt opening pressure\cite{74}.

In most cases the failure to adjust the shunt depends on difficulties getting the programmer head in the right position e.g. premature removal of the programmer head or problems holding the head in a fixed position when the child is moving their head. In our material, four shunts could not be adjusted despite several attempts. In one child the shunt was replaced but in the other three the lower opening pressure was preferred to a new operation and the associated risk of complications. In the replaced shunt a fibrin clot was detected. Few shunts with inability to adjust are also reported in the literature and a fibrin clot was also found to be the reason in others\cite{51,75,106}.

The shunt is sensitive to a magnetic field of $\geq 1.5$ Tesla. There is a risk of accidental changing of the shunt opening pressure at MRI\cite{38,66}. In our study we had an accidental changing rate of 38\% compared with 27\% in a similar study\cite{105}. At an experimental study of brain MRI with the CHA shunt positioned in the retro-auricular region an accidental changing of the opening pressure was found in 80.6\% of the investigations and with the shunt on the anterior chest in 63.9\%\cite{61}.

Accidental non-MRI dependent changing has been reported\cite{61,106}. This may be caused by strong magnetic fields, such as those from household magnets, loudspeaker magnets and head sets, when located close to the shunt. One experimental study has showed that the shunt opening pressure could be changed by filliping the shunt\cite{61}. Accidental reseting without MRI in our material was 4\%, similar to another study\cite{106}.
Economy with the CHA shunt (Paper I)

With non-invasive adjustment of the shunt opening pressure, revisions with exchange of the shunt due to over-or under-drainage were reduced as well as the risk of post-operative infections or other complications.105. Only six shunts in our material had to be exchanged due to adjustment failure, not holding the pressure or spontaneous adjustment. Every avoided operation or complication reduced health care costs and patients’ suffering. The possibility of treating subdural hygroma due to over-drainage with adjustments of the opening pressure in an outpatient clinic instead of a surgical drainage was also a financial benefit12,75,105. The risk of developing premature cranio-synostosis due to over-drainage is minimized with the adjustable shunts and additional surgery is then avoided. In our material no child had premature cranio-synostosis similar to another report51. When analysing the costs for shunt replacements, treating hygroma and the parent’s loss of income, we found a clear financial benefit, even if the adjustable shunt is more expensive and needed radiological assessment after pressure adjustment. With the new programming unit with ultrasound there will be a further financial saving because less X-ray control will be needed. It is only when the child is crying loudly or the shunt is blocked that the ultrasound in the programmer head cannot identify the adjustment steps.

Paediatric aspects of CHA shunt (Paper I)

The adult shunt has many advantages in children including prematures. We were able to successfully implant the CHA shunt in children with a corrected age of 32 gestational weeks or weighing 1800 g. In children the CHA shunt is easy to identify and to test, which is important when the younger children do not always co-operate. The size of the pre-chamber makes it easy to identify and to puncture. We found the introducer easy to handle and bend so that the shunt can be placed in the desired position although others have reported problems51. The introducer tip is sharp and care must be taken during its use in infants since the tip can penetrate the skin. In the unitised shunt, the introducer still has to be improved to be able to tunnel without damaging the catheter when using a frontal approach. When the children grow, the adult shunt is not as difficult to identify and test as the smaller infant model, which can be overgrown by bone.

In our material only two children had pressure sores over the shunt. In another study also of only children skin problems with pressure sores over the shunt were reported56. In younger and disabled children we believe that it is important to be aware of the problem and place the shunt so that it is not exposed to pressure.
Infections (Paper IV and V)

Infection of CSF shunts is one of the most common infections in neurosurgery with an incidence in recent studies of 8 to 12%\(^{8,32,71}\). Skin bacteria, such as CoNS and *Staphylococcus aureus* cause most of the CSF shunt infections\(^{15,71,93}\). Gram-negative bacteria are found in approximately 20%\(^{88}\). Treatment of shunt infections varies among paediatric neurosurgeons\(^{17,32,52,101}\). For the diagnosis of intraventricular shunt infection, the criteria used in the Paper IV and V was slightly modified from those used in a recent study by Wang *et al*\(^{98}\).

By the addition of anaerobic cultures (Paper V) at every sampling occasion and prolongation of the cultures for at least one week, the number of positive cultures increased from 28 to 39 in our study. This represent an increase in the detection rate by more than one third which emphasizes the importance of these measures in the diagnosis of cerebrospinal shunt infection. A similar regimen has previously been proposed in Paper II and by others\(^{16,76,79,94}\), but the relative increase in diagnostic value has to our knowledge not previously been evaluated. Some authorities have advocated that the cultures should be continued up to 14 days before reported as negative\(^{36,76}\).

By adding anaerobic cultures there is an increased risk of finding *P. acne* contamination from the skin. The risk of contamination at percutaneous puncture of the Rickham reservoir or the antechamber has been demonstrated\(^{80,100}\), but the risk was minimized in our material by collecting peroperative cultures at the externalisation. The fact that the cultures were positive from both the catheter tip and the CSF indicates that it is not just an asymptomatic shunt contamination as discussed by Steinbok *et al*\(^{89}\). In addition, the signs of shunt dysfunction, infection and absence of other causative bacteria indicates the clinical relevance of the *P. acne* infections found in paper V. The six patients in Paper V with a shunt infection caused by *P. acne* represent an infection rate of 1.3%, which is of the same magnitude as that reported by Everett *et al* of 1.7%\(^{36}\).

Higher age, previous puncture of the prechamber or revisions seem to have predisposed to shunt infections with *P. acne*. Previous shunt surgery is considered to be the most common port of entry for these bacteria\(^{16,97}\), whereas puncture of the shunt has seldom been reported. Propionibacteria have been reported to cause late-onset cerebrospinal fluid shunt infection\(^{97}\) and, therefore, a longer incubation time was to be expected. In children with *P.acne* infection time from presumed contamination to infection was longer than for the other infections and fulfilled the criteria of late-onset infection\(^{97}\).

The clinical picture at infection with *P.acne* was associated with milder symptoms, lower CSF leukocyte count and higher glucose ratio than with other bacteria. Propionibacteria have previously been shown to cause intraventricular infection\(^{16,36,87,97}\) and there are also some cases described with
blocked shunts and glomerulonephritis. In our study, one patient demonstrated the full clinical picture of an intraventricular infection with pleocytosis and low glucose ratio. In this case the symptoms were not clearly distinguishable from those of the other bacteria. The majority cases only demonstrated signs of distal catheter infection with catheter obstruction and in four of them pseudocyst formation that is most compatible with the well-documented low virulence of propionibacteria.

In Paper V it was notable that the majority of infections after first insertion occurred in children with non-healed wounds or when another surgery was performed. This may explain why the risk of infection was the same at first insertion and revision and probably these situations should if possible be avoided. In paper V, as in others, CoNS was the most common causative agent and the risk of shunt infection was higher below one year of age. Of special interest is the finding that CoNS infections were considerably more aggressive in these children than in older children.

Treatment of intraventricular infections

In Paper IV the institutional protocol for treating intraventricular infections with intraventricular antibiotics from the start in combination with systemic treatment and shunt removal, was evaluated. The strength of this study was, that only three surgeons were responsible for the treatment and it was a high degree of adherence to the protocol. The 10 children not treated according to the protocol were those, who started with intravenous antibiotics alone. Because all of these children demonstrated growth in the CSF culture, when treatment was started according to the protocol, they were all included together with those given standard treatment from the start.

A treatment regimen like ours, with intraventricular instillations was proposed already several years ago, but in recent studies the decision has often been left to the surgeon’s preference. The preangulated ventricle catheter was left in place in most of our patients until shunt replacement. This was based on the belief that it might be hazardous to change the ventricular catheter if there were slit ventricles. We also wanted to avoid the straight EVD catheter to press against the ventricle wall. Despite having the ventricular catheter left in place, cultures became negative after a median of 3 days (range 1-6 days). When the cultures were not obtained daily the true time for sterilisation is probably shorter. Our sterilisation data compared well with others, or were even possibly better than, those in the study by Kestle et al. and were in the equivalent of those reported by Pfausler et al. In our study all patients cleared their infection during treatment. This result is even better than, the result from a recent study by Turgot et al. in which 2 out of 31 children were not cured during
treatment despite removal of all shunt components in combination with intraventricular and systemic antibiotics. In a study by Brown et al., the effect of antibiotics administered systemically and intraventricularly with the shunt left in situ was reported. Intraventricular antibiotics were instilled via a separate access device. As in our study the cure definition required absence of relapse within 6 months. With this definition, a cure rate of only 84% was found, which was less than the lower 95% CI limit of our results. Because the ventricular catheter was left in place in both our and the study of Brown et al. the adherence of bacteria to the shunt or distal catheter may account for the difference. Another reason might be that CSF trough concentrations of vancomycin and gentamicin in the study by Brown et al. were held to <10 mg/L and < 2mg/L, respectively, and the majority of our patients had concentrations above 10 mg/L for both antibiotics. It is also important to flush carefully so the instillated antibiotics will reach the ventricular system and not be left in the drainage catheter. Unfortunately, there was no information about the doses of intraventricular antibiotics used in the study by Turgot et al. As in many other studies antibiotics administered intraventricularly, no side effects were observed.

The 10 children initially treated with intravenous antibiotics alone, with or without externalisation of the system at the start of the treatment, demonstrate the limitations of our strategy. They had persistent growth of bacteria at a medium of 8 days. However, it must be emphasised that to some extent these children represent a negatively selected group. The children would not have been referred to our hospital, if they had responded to the treatment. Despite antibiotics in high doses recommended for treatment of bacterial meningitis, low CSF concentrations were found in our study (Table 8). Although the method for cloxacillin concentration was not sensitive enough to test low CSF concentrations, the minimal concentration to kill causative bacteria in the presence of a foreign body was not enough. The low antibiotic concentrations may have been an important factor for the poor sterilisation. The low-grade inflammatory response, as demonstrated by the comparatively low CSF albumin concentration, may not allow antibiotics to pass into CSF to the same extent as in acute bacterial meningitis caused by more virulent bacteria.

The duration of intraventricular treatment less than 10 days on most children is considerably shorter than the durations of antibiotic therapy reported from the studies of 17 to 37 days Turgot et al. and Kestle et al., and in the lower range of those reported in the studies by Whitehead et al. and Brown et al. Despite a relatively short duration of antibiotic therapy, no relapses occurred in our study.

The choice of intravenous cloxacillin and vancomycin as systemic treatment in our protocol was based on previous personal experience. Treatment with Rifampicin has been proposed by others and its ability to penetrate into the ventricular system with low-grade inflammation makes it a theo-
retically better choice. However, the poor penetration and low CSF concentrations of cloxacillin and vancomycin suggest that in some patients the need of systemic treatment is not necessary. On the other hand, it must be emphasized that our data concerning non-staphylococcal infections are limited.

Treatment of distal catheter infection

Recommended treatment of propionibacterial shunt infection has been removal of the shunt components in combination with administration of systemic antibiotics\textsuperscript{16,91,97}. In the cases with distal catheter infections (Paper V) with P. acne the shunt components was removed in the presence of positive cultures, which indicates that antibiotic treatment prior to surgery is most probably not necessary. Antibiotic treatment perioperatively seems to be sufficient because there was no further antibiotic treatment in four of the five children and just one day in the fifth and yet there were no relapses within the 2-year follow-up period. Thus, our data support the suggestion by Thompson \textit{et al}\textsuperscript{91} that cerebrospinal shunt infection caused by \textit{P. acne} can be treated with short-term per operative antibiotics and replacement of the shunt components, at least in distal catheter infections.

All children with distal catheter infection demonstrated growth in the shunt at the removal. The shunt seems to be able to harbour the bacteria inside for a long time and from there a low-grade infection at the distal end of the catheter may be sustained with the gradual development of pseudocyst formation and shunt block. Furthermore, our data, with persisting growth despite high intravenous doses of antibiotics indicate that the propionibacteria will not be eliminated if the child is prescribed antibiotics for some reason or another, even if the bacteria are susceptible to the antibiotics given. Given this fact distal catheter/valve infection seems to be a more appropriate name. Although not shown in paper V, this infection, if undiagnosed, may represent a possible explanation for relapses in distal catheter obstruction in patients in whom the shunt components have not been replaced. In all children in the present study, cultures from the central CSF and ventricular catheter tip at operation were negative. This may suggest that removal of the distal catheter and the valve only may be sufficient in cases with distal catheter/valve infection but this need further investigation.

Evaluation of CSF shunt characteristics (Paper VI)

The hydrodynamic characteristics of two adjustable CSF shunts were investigated and both types worked according to specification except at the lowest setting with abdominal pressure in the Strata NSC\textsuperscript{™}. In both shunts the opening pressure at the middle and highest setting was nearly the same, but at the lowest setting in Strata NSC\textsuperscript{™} the opening pres-
sure was near zero. In nearly all cases of paediatric hydrocephalus such a low pressure will not be used; however at normal-pressure hydrocephalus in adults it can be an alternative. The variation in resistance in both shunts was very small. The Strata NSC resistance was lower than the physiological one, when Codman Hakim was in the lower part of the normal variation. This was a difference between their characteristics. The clinical importance of this should be evaluated. In the future a more physiological alternative may perhaps be a shunt with a possibility of changing the hydrodynamic resistance in contrast to the actual situation.

The hydrostatic effect cannot be managed by increasing the opening pressure of an adjustable shunt but an ASD can reduce the effect of siphoning, which we showed in the study. According to the manufacturers, the Delta Chamber has to be placed in line with the ventricular catheter tip to work properly. The results of this study confirm the importance of these instructions, showing that the hydrodynamic characteristics, specifically in the upright position, change significantly with the placement of the ASD. At a placement in a previous shunted patient this is particularly important to remember since it is common to place the ASD away from the original shunt, thereby avoiding the scalp and its increased infection risk. In Siphonguard the different positions did not interfere with the function. At a later insertion the ASD could be placed on the neck or thorax. Neither the opening pressure nor the resistance was changed in the Codman Hakim shunt with the Siphonguard, hence it could be added at the first insertion even in small children.

The Codman Hakim closed in steps (Fig. 6) and the Strata NSC at the lowest setting with abdominal pressure indicated a backflow, which exceeded the maximum allowed by the international standard (ISO standard 7197, 2006) was probably due to the smooth reduction of the pressure. This would probably not be seen in vivo since the normal physiological pulsations where these variations would “shake” the shunt mechanism, causing a smoother closing of the Codman Hakim and a closing of the Strata NSC when the differential pressure is equal to the estimated opening pressure. However, even if a Strata NSC probably will reflux in a patient, the opening pressure is unnecessarily low. We also, suggest, that the Strata NSC should be calibrated in production so that the opening pressure at level 0.5 is set to the same level as the standard Strata with the build in ASD.

When the ASD can be implanted at the first CSF shunt implantation even in children the built-in ASD can be used and the separate one is only needed for shunted patients without ASD.
The results in this thesis have shown that

- the non-invasive adjustment in small steps made it possible to set the opening pressure to an optimal level based on the requirement of the individual child
- the non-invasive adjustment at the outpatients clinic resulted in fewer hospital stays for re-operations and subsequent risks of complications
- in spite of its higher costs, the adult Codman Hakim™ shunt reduced health care costs by avoiding re-operations, shunt replacements and surgical complications due to over or under drainage
- the adult Codman Hakim™ shunt can be used even in small (1.800g) children
- in shunted children with abdominal pseudocysts or ascites the distal catheter has to be externalised to perform prolonged aerobic and anaerobic cultures of CSF and the distal catheter tip to exclude an infectious cause
- when the subsequent replacement of the distal catheter into the peritoneal cavity is unsuccessful in a patient with non-infected abdominal pseudocyst or ascites due to a peritoneal resorbing difficulty a ventriculo-atrial shunting has to be performed. However, if later shunt malfunction occurs, without signs of infection, replacement of the distal catheter into the peritoneal cavity can be performed without a new peritoneal reaction.
- fundoscopic examination in children (>8 years) may detect symptomless shunt malfunction and prevent visual impairment or blindness
- treatment of CSF shunt infections with a relative high dose of intraventricular antibiotics in combination with systemic was safe and gave a quick sterilisation with low relapse and mortality rate despite short therapy.
- the addition of anaerobic cultures and prolonged observation time resulted in an increase by one third in the number of infections. Infection with P. acne resulted in mild clinical symptoms that may be overlooked if adequate anaerobe cultures are not obtained.
- both the tested CSF shunts worked properly with good reproducibility. The resistance in Strata NSC™ was below the normal value, whereas Codman Hakim™ was in the lower range. The ASD of Strata NSC™ had to be placed in line with the tip of the ventricular catheter for optimal function, but not that of Codman Hakim™

Hos 21 av 46 barn med en icke ställbar shunt byttes denna till en ställbar pga. överdränage. Ändring av motståndet hos den ställbara shunten utfördes hos 73 % av barnen. Hos flera barn undveks därigenom en ny operation med ett byte av shunten. Detta gav en påtaglig ekonomisk vinst och minskat prykligt lidande.

En ökad ansamling av hjärnvätska (likvorcysta) kan förekomma i bukhålan vid en infektion. Hos 8 barn upptäcktes en ökad mängd hjärnvätska i buken som ej berodde på infektion utan på svårigheter hos bukhinnan att suga upp likvor. Dessa barn fick i stället en shunt till hjärtat. Tre av dem fick senare shuntstopp och då kunde hjärnvätskan ånyo ledas till bukhålan.

Svullnad av synnervens inträde i ögat (staspapill) var det enda tecknet på shuntstopp hos sex barn. Vid åtgärd av shuntstoppet uppmättes ett klart förhöjt tryck i ventrikelsystemet som varierade mellan 25 och 52 cm H₂O. En undersökning av ögonbottnarna hos barn som är äldre än 8 år kan upptäcka shuntstopp utan symptom genom påvisandet av en svullen av synnerv.


De undersökta ställbara shuntarna Strata NSC™ och Codman Hakim™ fungerade enligt information från tillverkarna utom vid lägsta inställningen, där öppningstrycket var nära noll respektive nästan det dubbla. Resistansen (flödesmotståndet) i shuntarnStrata NSC™ var under det fysiologiska området
medan Codman Hakim™ låg i nedre delen av området. Strata NSC™s antisifon behövde placeras i nivå med shunten för att fungera optimalt, medan Codman Hakims™ ej påverkades av placeringen.
Acknowledgement

I would like to express my gratitude to my co-authors and everybody involved in this project and in particular to

All hydrocephalic children and their patient parents, who have taught me so much.

Tomas Wester, my tutor and co-author for discussions and support.

Per Enblad, co-tutor and author, giving me positive support

Jan Sjölin, co-tutor and author for sharing my interest in shunt infections and for having so many interesting discussions and giving active encouragement.

Jan Malm and Anders Eklund, co-authors at Neurocentrum in Umeå, for having positive attitudes and patience when introducing me to the importance of opening pressure, resistance and flow in shunts.

Margit Lundmark, for teaching and giving me technical assistance

Colleagues, staff at the operation theatre and all friends at the Department of Paediatric Surgery.

All paediatric neurologists for their interest and giving me active support.

All colleagues at the Department of Neurosurgery for welcoming me to be a part of your department.

Jan Enskog for your kindness and skilful curing of my spine: the basic prerequisite for this thesis

My daughters, Pysse and Marie, their families and my grandchildren, Martin and Samuel, for always making me happy and encouraging me to go on.
This work was supported by grants from Her Royal Highness the Crown Princess Louise’s Foundation for Scientific Research and by the Swedish Research Council (Grant 2005-3047).

Financial disclosure: Medtronic PS Medical Inc. contributed the Strata NSC™ shunts and the Delta Chambers™ and Codman Johnson & Johnson Co the Codman Hakim™ shunts and the Siphonguards™. The companies did not claim any service in return. The authors do not have any financial interest in the companies.
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