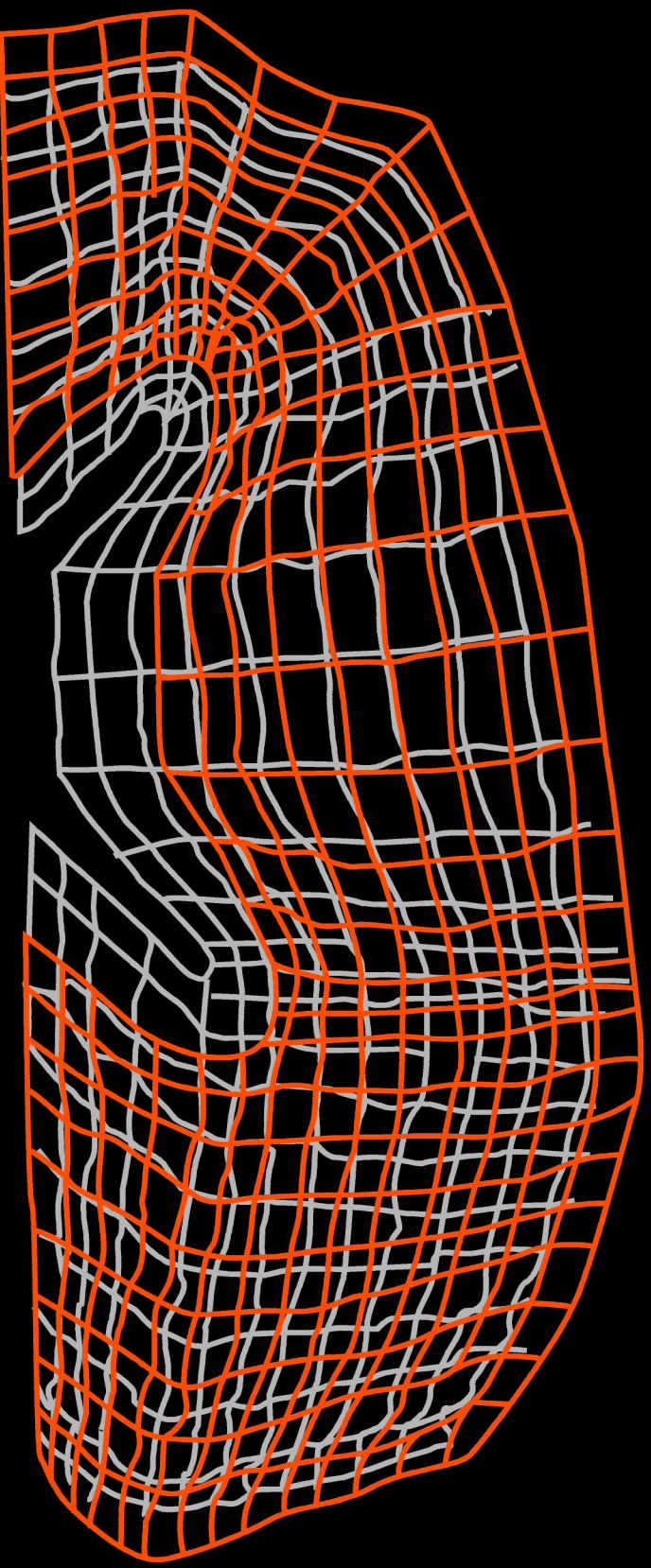

HYDROCEPHALUS IN CHILDREN

Epidemiology and outcome

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2007

Göteborg University

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“Faber est suae quisque fortunate”

Sallustius 86-34 BC

Abstract

Aims: To analyse trends in the live-birth prevalence of infantile hydrocephalus and hydrocephalus associated with myelomeningocele (MMC) during the period 1989-2002 and to study the outcome in terms of learning disability, cerebral palsy, epilepsy and visual deficits. Another objective was to explore motor function and disability profiles in various aetiological and gestational-age subgroups and to see whether treatment complications and neuroradiological findings correlate with outcome.
Material and methods: A population-based study of all 262 live-born children with infantile hydrocephalus and hydrocephalus associated with MMC born in 1989-2002 in western Sweden. Aetiological and clinical information was collected from medical records, neuroimaging and ophthalmological examinations. A subgroup of 114 children were clinically examined and interviewed.
Results: The live-birth prevalence of hydrocephalus was 0.77 per 1,000 live births, 0.48 for infantile hydrocephalus and 0.29 for hydrocephalus associated with MMC. The prevalence of infantile hydrocephalus decreased from 0.55 in 1989 to 0.48 per 1,000 in 2002, while that of MMC decreased from 0.35 to 0.16 per 1,000 during the same period. The prevalence in children born extremely preterm increased dramatically, with a gestational-age-specific prevalence of 13 per 1,000 in 1989 compared with 45 per 1,000 live births in 2002. During the same period, the perinatal mortality in these children decreased from 40 to 15 per 1,000 live births. A ventriculoperitoneal shunt was the first surgical intervention in 230 children (88%), while an endoscopic ventriculostomy was performed in 31 (12%). At least one surgical revision was required in 64% of the children. Of children with infantile hydrocephalus, 63% had at least one associated impairment, compared with 33% in the MMC group, apart from the consequences of the spinal lesion. Visual and other ophthalmological impairments were identified in the majority of the children. Very preterm birth was associated with a high risk of visual impairment. No child with normal neuroimaging had any associated neurological or visual impairment, compared with eleven of twelve with impairments in children with generalised parenchymal lesions.
Conclusions: A decrease in the prevalence of infantile hydrocephalus was noted during the period 1989-1998, but it did not continue in 1999-2002. The stagnation was mainly explained by the increased survival of children born extremely preterm with post-haemorrhagic hydrocephalus. The aetiology of the hydrocephalus and gestational age at birth were important for outcome. The majority of the children had some associated neuroimpairment, such as learning disability, cerebral palsy or epilepsy, and more than three-quarters had ophthalmological abnormalities. Neuroimaging was found to be useful for aetiological, treatment and outcome considerations.

Key words: Prevalence, epidemiology, hydrocephalus, MMC, treatment, outcome

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II Eva-Karin Persson, Gudrun Hagberg, Paul Uvebrant
Disabilities in children with hydrocephalus-a population based series of children aged four to twelve years.
Neuropediatrics 2006; accepted for publication

III Eva-Karin Persson, Susann Andersson, Lars-Martin Wiklund, Paul Uvebrant
Hydrocephalus in children born in 1999-2002. Epidemiology, outcome and ophthalmological findings.
Childs Nerv Syst 2006; accepted for publication

IV Susann Andersson, Eva-Karin Persson, Eva Aring, Barbro Lindquist, Gordon N Dutton, Ann Hellström
Vision in children with hydrocephalus
Dev Med Child Neurol 2006; 48:836-841

Abbreviations

CSF	cerebrospinal fluid
CT	computed tomography
ETV	endoscopic third ventriculostomy
ICF	International Classification of Functioning, Disability and Health
ICP	intracranial pressure
IH	infantile hydrocephalus.
IQ	intelligence quotient
ICIDH	International Classification of Impairment Disability and Handicap
MMC	myelomeningocele
MRI	magnetic resonance imaging
SD	standard deviation
VA-shunt	ventriculoatrial shunt
VA	visual acuity
VP-shunt	ventriculoperitoneal shunt
WHO	World Health Organization
WISC-III	Wechsler Intelligence Scale for Children-III
WPPSI-R	Wechsler Preschool and Primary Scale of Intelligence-Revised

Introduction

Hydrocephalus was described by Hippocrates (466-377BC) and by early and medieval physicians, who believed that the disease was caused by the extracerebral accumulation of water. There is no evidence of surgical procedures during that period. In the tenth century, the evacuation of intracranial fluid in hydrocephalic children was described (Aschoff et al. 1999). In the late nineteenth century, the knowledge of surgery and pathophysiology made interventions possible. During the first decades of the twentieth century, various kinds of shunt system were tested (Aronyk 1993), with high failure and complication rates. In 1922, Dandy described an open ventriculostomy procedure performed via a lateral subtemporal approach, but the mortality rate was high (Dandy 1945). In 1923, Mixter described the endoscopic perforation of the floor of the third ventricle, endoscopic third ventriculostomy (ETV), but it was not a success because of technical problems and complications (Mixter 1923) and for many decades ETV was not used. During the last decade, ventriculostomy has once again been used more frequently as an alternative to shunt treatment. Around 1960, the use of shunts became more common, as materials and techniques had improved. The use of modern shunts resulted in a reduction in mortality from 50% to about 10% (Hadenius et al. 1962).

Before the shunt era, many of the children did not receive any surgical treatment and were taken care of at home or in institutions. The natural history of untreated hydrocephalus was poor. In a study from 1962 by Hadenius and Hagberg (Hadenius et al. 1962), 180 children with untreated hydrocephalus were examined during their first year of life and were then followed for between three and 20 years. At the follow-up, fewer than half of them were alive and half that group was found to have mental retardation. It needs to be remembered that hydrocephalus is still an untreatable condition in most of the developing countries.

Photo from a hospital in Kenya 2001. Informed consent was obtained from the mother.

The incidence of hydrocephalus varies in epidemiological studies from different parts of the world. In Saudi Arabia, a prospective study from 1996-1997 reported a birth prevalence of 1.6 per 1,000 live births (Murshid et al. 2000). Children with neural tube defects were excluded and all the children were diagnosed within the first 28 days of life. In spite of this, the incidence was much higher than in the developed countries during the same period. In a study from Utah in 1940-1979 (Blackburn and Fineman 1994), the incidence of congenital hydrocephalus was 0.7 per 1,000 live births, which is more in accordance with the results in Swedish studies.

There has been an interest in epidemiological studies of childhood hydrocephalus in Sweden for many decades. Hagberg et al. published a study in 1963 (Hagberg et al. 1963) in which the incidence of hydrocephalus with an onset before the end of the first year of life was found to be 0.85 per 1,000 live births, excluding those with myelomeningocele (MMC). Since then, follow-up studies have been conducted in the western part of Sweden by Fernell and co-workers (Fernell et al. 1986, Fernell et al. 1994). During the first few decades, interest focused on children with infantile hydrocephalus, but, since 1989, children with hydrocephalus associated with MMC have also been included (Persson et al. 2005).
There was a significant increase in prevalence from 1979 to 1986 and this was thought to be due to the enhanced survival of children born very preterm (Fernell et al. 1994) with a high risk of developing hydrocephalus with intraventricular haemorrhage as the cause. The increase did not continue in the following years, probably due to the improved perinatal care of these high-risk infants.
In children with hydrocephalus associated with MMC, the prevalence has decreased during the last few decades, mainly due to the increased use of early prenatal ultrasonography, leading to the termination of MMC pregnancies (Bygdeman and Ahlenius 2005). The improved maternal nutrition and addition of folic acid before and early in pregnancy have probably contributed to the decrease, but the enrichment of flour is still not in use in Sweden and this has therefore not played an important role in the decreasing prevalence (Honein et al. 2006).

The outcome in terms of learning disabilities, cerebral palsy, epilepsy and visual impairments varies in the subgroups and different gestational age groups of children with hydrocephalus. Children born preterm with a risk of cerebral haemorrhage are more vulnerable and have neuroimpairments in the majority of cases (Fernell et al. 1994), while another subgroup with an increased risk of a poor outcome comprises children with hydrocephalus present already at birth (Fernell et al. 1987).

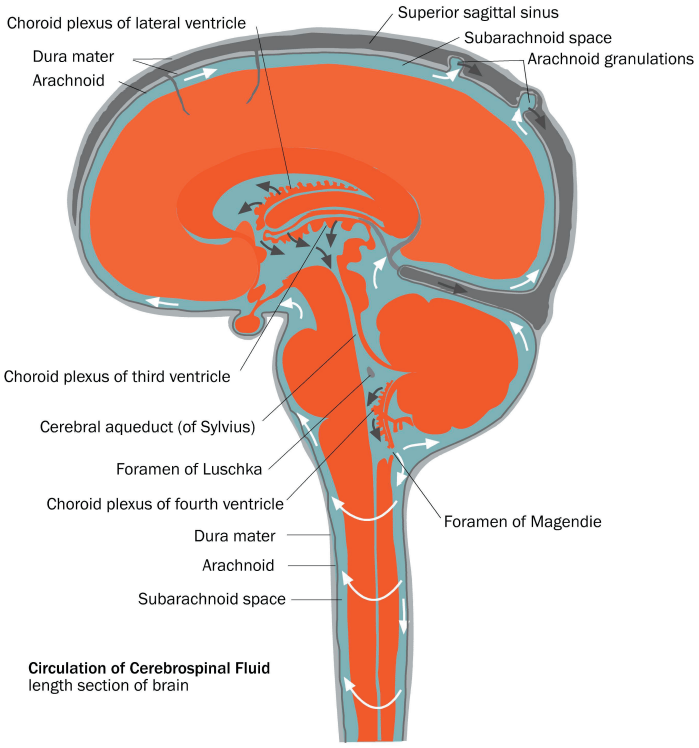
Background

Hydrocephalus is a clinical entity in which a disturbance in the circulation of the cerebrospinal fluid (CSF) causes the accumulation of intraventricular CSF, resulting in progressive ventricular dilation (Mori et al. 1995). It is characterised by increased intracranial pressure, increased CSF volume and the dilation of the CSF spaces. The diagnosis is based on the analysis of the size of the ventricles. The ventricles can also be enlarged due to atrophy of the brain and this condition has to be distinguished from hydrocephalus.
In infants with open sutures between the skull bones, the diagnosis can be made clinically by measuring an increase in head circumference. In older children with closed sutures, there is a compression of the peripheral CSF spaces, which can be seen using neuroimaging (Evans 1942).

In the majority of cases, the physiological mechanism underlying hydrocephalus is an obstruction of the CSF circulation, reduced re-absorption and, in a few cases, the overproduction of CSF. Hydrocephalus can be classified into communicating and obstructive forms; the difference is whether or not there is a free flow of CSF from the ventricles through the aqueduct and foramina to the spinal compartment (Dandy 1920). Dandy stated that almost every kind of hydrocephalus could be called obstructive, as it is the CSF absorption that is obstructed in communicating hydrocephalus. Several mechanisms lead to the obstruction of the CSF flow; they include primary malformations, haemorrhages and post-infectious scarring.

CSF is produced by the choroid plexus of the lateral, third and fourth ventricles. The production is approximately 10 ml per hour, corresponding to 200-250 ml a day in a small child, and it increases to about 20 ml an hour or 400-500 ml a day in adolescents (Yasuda and Tomita 2002). The total CSF volume depends on the age of the person and is about five ml in a newborn child and reaches the “adult” volume of 80-150 ml at the age of about five years. The CSF flows through the third ventricle and the cerebral aqueduct to the fourth ventricle and through the foramen of Magendie and the lateral foramina of Luschka into the subarachnoid space. The narrowest passage in the ventricular system is the cerebral aqueduct or the aqueduct of Sylvius. The CSF flows around the tentorium and is thought to be re-absorbed into the venous system through arachnoid villi into the sagittal sinus. Some of it flows down towards the lumbar subarachnoid space and has recently been shown by Edsbagge and co-workers (Edsbagge et al.2004) to be re-absorbed from the spinal canal as well. The CSF is important as it protects the brain and the spinal cord, regulates the intracranial pressure (ICP) within physiological limits and regulates the extracellular environment in the brain (Emerich et al. 2005).

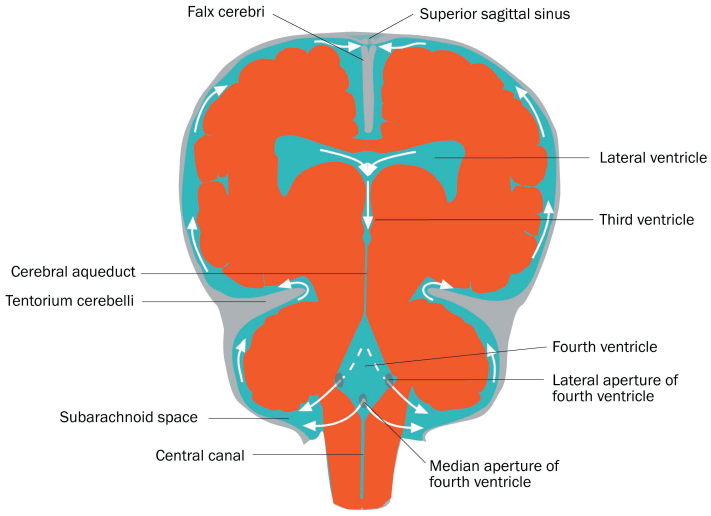
Hydrocephalus is a complex disorder with a significant impact on the brain not only macroscopically. It has an effect on physiology, biochemistry and on the ultrastructure of the brain. The macroscopic changes lead to the distortion of structures, such as the compression of white and grey matter. The cerebral blood vessels may be af-



fected and this may result in the reduction of the cerebral blood perfusion. These changes are important for the severity of the consequences of hydrocephalus.

The mechanism behind the ventricular enlargement has been a matter of discussion. A possible transmantle pressure gradient with higher pressure inside the ventricles than over the convexity has been postulated. Stephensen (Stephensen et al. 2002) and co-workers, however, found no such pressure gradient. They were able to explain the measured pressure difference as the hydrostatic pressure difference. In a study by Greitz and Greitz (Greitz et al. 1997), the ventricular dilation in communicating hydrocephalus was explained by disturbances in hemodynamics by processes causing reduced compliance of the arteries, such as arteritis and spasm, reduced compliance of the subarachnoid space, as in meningitis and arachnoiditis, and reduced compliance of the intracranial space. Obstructive hydrocephalus was explained by processes restricting the intraventricular CSF flow leading to an increased amount of CSF not being absorbed and resulting in enlarged ventricles.

The ventricular expansion displaces the surface of the brain and compresses the cortical veins, leading to venous congestion and a subsequent increase in ICP. The expansion of the ventricles also affects the surrounding brain structures and the increase in ICP may cause cerebral oedema affecting the white matter and eventually also the grey matter.



Circulation of Cerebrospinal Fluid
cross section of brain

Factors such as age at onset, the duration of disease and aetiology are also essential. The stage of maturation at the time of hydrocephalus is of importance, as the brain is still developing. Many maturational processes are affected in a negative way; they include the myelination process during which protective sheaths are formed around axons (Flechsig 1901). This is vital for the function of the brain and is negatively affected by the increase in ICP in hydrocephalus.
The white matter, especially in the periventricular region, is affected by compression and this is more obvious in young children than in older persons. There is also a thinning of the corpus callosum and of the cerebral cortex. The reduction in the corpus callosum and the internal capsule is of specific importance for cognition (Fletcher et al. 1992).

Brain development
There is a classification system for congenital hydrocephalus in the "Perspective Classification of Congenital Hydrocephalus" (Oi et al. 1994), where each of the clinico-embryological stages reflects the process of the neuronal maturation in the hydrocephalic child from stage I-V.
I: Week 8-21. The main process is neuronal proliferation.
II: Week 22-31. Cell differentiation and migration are the main processes during this period.
III: Week 32-40. Axonal maturation is the main process. This is a period during which hydrocephalus may develop.
IV: Week 0-4 postnatally. Dendritic maturation is the main process.

V: Week 5-50 of postnatal age. Myelination is the main process.
Stages IV-V are the main periods for the development of infantile hydrocephalus.

Definitions and classification

Definitions

Hydrocephalus was defined as ventricular expansion due to elevated intraventricular pressure with an increased amount of intraventricular cerebrospinal fluid, manifested during the first year of life.

Prenatal referred to the period before the onset of labour, *perinatal* from the onset of labour resulting in delivery to the 28th day of life and *postnatal* to the period from day 29 up to the age of one year. A *prenatal origin* was considered in the presence of prenatal malformations or maldevelopments of the CNS explaining the hydrocephalus, a *perinatal origin* was considered in the presence of perinatal intraventricular haemorrhage or infection and a *postnatal origin* was considered in the case of obvious postnatal events.

Children born at *term* were those born after 36 completed weeks of gestation, *moderately preterm birth* comprised those born between 32 and 36 weeks of gestation, *very preterm* were those born between 28 and 32 weeks and *extremely preterm* those born before 28 completed weeks of gestation.

Hydrocephalus overt at birth was defined as congenital hydrocephalus with a head circumference larger than +2SD above the mean both for gestational age and for birth length (Fernell et al. 1987).

Cerebral palsy was defined according to the criteria proposed by Mutch et al. (Mutch et al 1992), while *epilepsy* was defined as two or more unprovoked epileptic seizures.

Mental retardation was defined as an IQ measured or estimated to be less than 70 according to ICD 10.

Infantile hydrocephalus: hydrocephalus not associated with MMC or with malignant tumours and developing during the first year of life (Fernell et al. 1986). Different malformations such as Dandy-Walker, X-linked hydrocephalus, arachnoidal cysts and aqueductal stenosis belong to this group, as do post-infectious and post-haemorrhagic hydrocephalus.

Post-haemorrhagic hydrocephalus: arachnoiditis is caused by the blood and haemorrhagic debris in the ventricles that most often obliterates the posterior fossa or the aqueduct of Sylvius.

Post-infectious hydrocephalus: obstructions in various parts of the CSF pathways that may result in increased intracranial pressure and hydrocephalus. The various infectious agents and treatment of the infection are important for outcome.

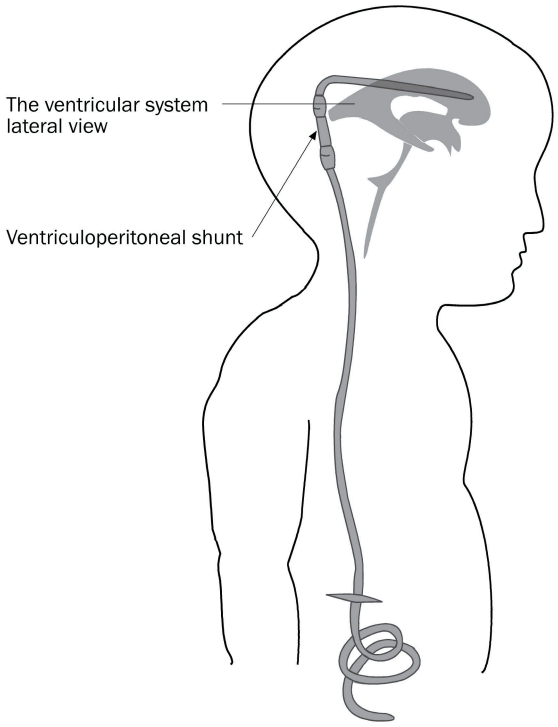
Hydrocephalus associated with MMC: several factors are important for the pathogenesis of hydrocephalus. The Arnold-Chiari type II malformation with an abnormal disposition of the brain stem, a deformity of the posterior fossa, where the cerebellar tonsils prolapse through the foramen magnum and the fourth ventricle is displaced. Other factors are aqueductal stenosis as a consequence of the Arnold-Chiari II malformation and the distal tethering of the spinal cord in the MMC, displacing posterior fossa structures downwards (Boltzhauser et al. 2002).

The surgical closure of the MMC is related to the development of hydrocephalus in

various ways. One-third of the children already have hydrocephalus at birth (Persson et al. 2005) and there have been studies on the intrauterine repair of MMC. The children developed hydrocephalus in 59% of the cases compared with 91% of children with a post-partum closure of the MMC (Bruner et al. 1999).
Hydrocephalus associated with malignant tumours in the posterior fossa: not included in the studies.

Treatment
The treatments of hydrocephalus in the early twentieth century with shunts of different kinds, plexus coagulation and ventriculostomies of various kinds were not successful (Shapiro et al. 1972, Torkildsen 1939, Ziemnovicz 1950). The mortality rate was high and the developmental outcome poor. The results of treatment from the first half of the twentieth century were evaluated by Hagberg (Hagberg 1962) and Laurence and Coates (Laurence and Coates 1962). The mortality rate varied from 45% to 53% in the different studies. During the fifties, the treatment gradually improved, more and better shunts were introduced and there was a therapeutic breakthrough. The mortality rate decreased successively to about five to 15%.
Most patients today are treated with a ventriculo-peritoneal shunt. Ventriculo-atrial shunts have not become very popular because of the higher risk of complications (Horwitz and Rizzoli 1982). During the last fifty years, valves of various kinds have been developed, differential pressure valves, followed by adjustable flow-regulated valves, gravitational and antisiphon valves and devices. Most shunt systems consist of a proximal catheter, a reservoir, a valve to regulate pressure and flow and a distal catheter ending most commonly in the peritoneal cavity where the CSF is absorbed.

The insertion of a CSF shunt is a common procedure at neurosurgical centres. The equipment that is used is a proximal catheter, which usually has several openings. The catheter is placed in the ventricle that is going to be drained. Shunts often fail because the catheter is occluded by some tissue. Reservoirs are used for measuring pressures, for pumping and to check if the shunt is working and to obtain fluid samples percutaneously. In very preterm children with ventricular dilation associated with intraventricular haemorrhage, the temporary use of a subcutaneous reservoir or repeated lumbar punctures have delayed the implantation of a ventriculo-peritoneal shunt to prevent the risk of infection, mechanical obstruction (de Vries et al. 2002) and awaiting the spontaneous resolution of the hydrocephalus, which is common in this situation (Volpe 1981). This can prevent parenchymal injury and have an important effect on the neurodevelopmental outcome.
Ventriculostomy has been more commonly used during the last 10-15 years. The principle is to perform a stoma in the bottom of the third ventricle and from there lead the CSF to the subarachnoid spaces where it can be re-absorbed. There are advantages to this procedure, as it is not very invasive and foreign materials are not left in the ventricles, which minimises the risk of infection. The ventriculostomy remains open in many patients, but occlusions may occur (Dalrymple and Kelly 1992).



Re-ventriculostomy can be performed and it has the same success rate as the first operation (Cinalli et al. 1999). Age limits and indications for ventriculostomy have been the subject of discussion and many people (Navarro et al. 2006, Scarrow et al. 2000) claim that it should be used only for aqueductal stenosis in children more than one year of age. Others (Buxton et al. 1998) argue that it is the aetiology and not the age that is important for outcome.

In recent years, ETV has been used more frequently all over the world. In Uganda, for example, it is used together with plexus cauterisation to eliminate the risk of shunt complications which are difficult to handle in the developing countries (Warf 2005). Improvements in technology and neuroradiology have made ETV safer, with reduced morbidity and mortality rates (Drake 1993, Jones et al. 1994).

Complications

The failure rate for all implanted shunts has been reported to be about 40% by one year and 50% after two years (Kestle et al. 2000). There are some predictive factors for repeated shunt failure – the age of the patient at the initial operation and the time interval since the prior surgical revision (Tuli et al. 2000). The risk of shunt infection is 8-10% during the first months in large trials (Enger et al. 2003). It is highest

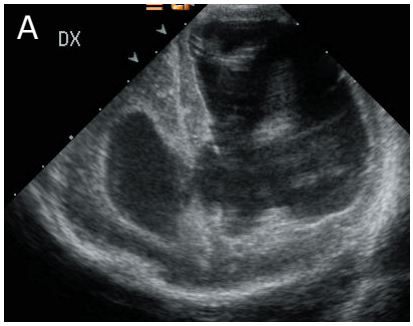
during the first two months after surgery and 90% of these infections occur during the first six months (Baird et al. 1999). Infectious complications are responsible for increased morbidity and mortality and lengthy hospitalisation periods.
The non-infectious shunt complications include obstructions, over-drainage, mechanical failures, ventricular loculations and abdominal complications. Obstruction can occur at any time after shunt surgery. The most common forms of late shunt failures are fractures of the catheter, over-drainage and abdominal complications such as pseudocysts or perforations.
An isolated fourth ventricle is a serious complication after the surgical treatment of post-haemorrhagic hydrocephalus in children born preterm. It is caused by the excessive drainage of CSF via a shunt system changing the CSF pathways, which results in the isolation of the fourth ventricle. One course of treatment for this could be the endoscopic placement of a stent in the aqueduct, as suggested by Cinalli et al. (Cinalli et al 2006**).**

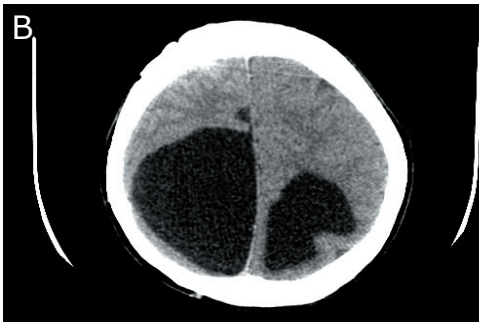
Neuroradiology
Neuroradiological examinations are important when it comes to clarifying the aetiology, planning the surgical intervention and following the changes in ventricular size.
The ventricles become enlarged as a result of accumulated CSF. In acute hydrocephalus, the ventricles may not have expanded because of the rapid progress, whereas, in more slowly progressing hydrocephalus, the ventricles can get very large. There are different neuroradiological examinations that can be used, depending on the purpose, the age of the child and whether or not the anterior fontanel is closed.

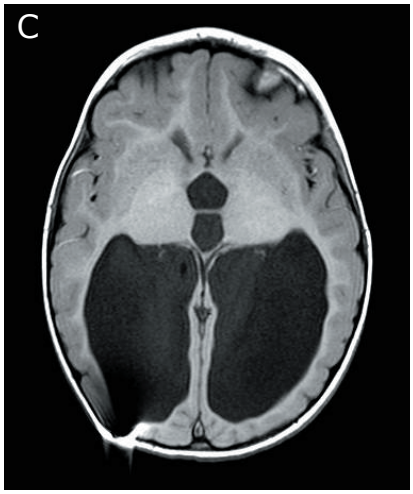
Ultrasonography
This is the screening procedure in small children when the anterior fontanel is still open. It can also be useful for follow-up after treatment to check the ventricular size. It is difficult to obtain an impression of the third and fourth ventricles using this method and, to clarify aetiology, other neuroimaging modalities are often needed.

Computed tomography (CT)
CT is excellent for analysing the sizes of the ventricles and, when the ventricles are enlarged, to distinguish hydrocephalus from atrophy. In children older than two to three years of age with a closed anterior fontanel, hydrocephalus is usually associated with the compression of the subarachnoid spaces, which can be visualised using CT. However, in communicating hydrocephalus, the subarachnoid spaces may appear normal. After shunting, a CT scan is often sufficient as a follow-up investigation.

Magnetic resonance imaging (MRI)
This imaging modality is the preferred method, as it does not expose the child to radiation and it is sensitive in the detection of parenchymal lesions and in revealing the aetiology of the hydrocephalus. To some extent, it can also visualise the CSF flow to investigate the patency of the aqueduct or after ETV.







A. Ultrasonography of the brain of a child born preterm with a periventricular haemorrhagic infarction.

B. Computed Tomography (CT) of hydrocephalus with ventricular dilation.

C. Magnetic resonance image of hydrocephalus caused by aqueductal stenosis.

Outcome

Cognition

In a study from 1962 of children with untreated hydrocephalus, the survival to adult life was around 20% and only 38% of them had IQ scores in the average range (Laurence and Coates 1962). The intellectual performance is affected even if the hydrocephalus is treated and the overall IQ is in the low-average range or below (Heinsbergen et al. 2002, Lindquist et al. 2005, Lumenta and Scotarczak 1995) As a group, children with MMC have higher IQ scores than other subgroups with hydrocephalus (Hoppe-Hirsch et al. 1998, Kao et al. 2001). The verbal intelligence is often better preserved than the non-verbal (Dennis et al. 1981, Lumenta and Scotarczak 1995, Riva et al. 1994), but an advanced vocabulary does not always correspond to an understanding of the meaning of words or the context and these children often have problems with pragmatics and discourse (Brookshire et al. 1995, Dennis et al. 1994, Taylor et al. 1960).

Many children with hydrocephalus have problems with visual perception, visuo-construction, visuo-orientation and recognition of faces (Houliston et al. 1999).

It is also common for them to have problems with executive functions such as planning, organisation and using strategies (Fletcher et al. 1996).

Attention

Early-onset hydrocephalus is frequently associated with behavioural problems (Dennis et al. 1981, Fernell et al. 1987, Lindquist et al. 2006, Lumenta and Scotarczak 1995). Behavioural problems have been reported in as many as 40% of children with hydrocephalus (Connell and Mc Conell 1981, Fernell et al. 1991, Lindquist et al. 2006) and autism spectrum disorders are common (Fernell et al 1991, Lindquist et al. 2006). The children do not always perceive these problems themselves.

Few studies have focused on attention processes in children with hydrocephalus, but, in a study from 1996, Fletcher (Fletcher et al. 1996) showed that children with hydrocephalus had deficits in selective and focused attention. Children with MMC have been found to be more easily distracted and inattentive than controls (Tew et al. 1980, Vachha and Adams 2005).

Motor function

Motor impairments are common. In a study by Hoppe-Hirsch (Hoppe-Hirsch et al. 1998), 60% of children with surgically treated hydrocephalus had some motor deficit at follow-up. This was well in accordance with a study by Heinsbergen, in which 61% of the children with surgically treated hydrocephalus had a musculoskeletal dysfunction (Heinsbergen et al. 2002). The aetiology and gestational age at birth have an important effect on the severity of the motor disability. Many children born preterm with hydrocephalus after a perinatal cerebral haemorrhage develop cerebral palsy. Fernell (Fernell et al 1987) found cerebral palsy in 47% of 61 children with hydrocephalus born preterm, compared with 26% of those born at term (Fernell et al. 1988a). There was a significant correlation between the motor dysfunction and the origin of the hydrocephalus.

In children with MMC, the motor function is dependent on the spinal lesion and about half these children learn to walk, with or without aid (Bowman et al 2001).

Epilepsy

Children with hydrocephalus often have a convulsive disorder. Fernell (Fernell et al.1988a, Fernell et al. 1988b) reported epilepsy in 22% of children with hydrocephalus born at term and 33% of children born preterm. A higher rate was found by Kokkonen (Kokkonen et al. 1994), who reported that 54% of those with hydrocephalus that had been shunted during childhood had been treated for epilepsy before 25 years of age.

The aetiology of the hydrocephalus and the presence of neuroradiological abnormalities in the brain parenchyma have an important impact on the risk of developing epilepsy. In some studies, the presence of a shunt appears to increase the risk of developing seizures. Most of the seizures are of the partial type and involvement of the side contralateral to the shunt placement has been suggested by some to indicate shunt-related cortical injury (Bourgeois et al. 1999, Klepper et al. 1998). This has been contradicted by Saukkonen, who found no correlation between the side of the shunt insertion and the epileptogenic activity on the EEG (Saukkonen et al. 1990).

Vision

In children with hydrocephalus, the dilation of the ventricles and the increase in ICP can cause damage to the occulomotor pathways, the optic nerves and the optic radiation, which can explain why many children have visual impairments. The posterior visual pathways are close to the lateral ventricles and may be damaged by the dilation of the ventricles. Optic atrophy can result from the traction or compression of the optic nerve (Moore 1990). Other visual impairments, such as reduced visual acuity, visual field defects and strabismus, have been described in several studies (Biglan 1990,Lorber 1967, Mankinen-Heikkinen and Mustonen 1987,), as well as visual perceptual problems (Houliston et al. 1999). In a population of surgically treated children with hydrocephalus, Aring (Aring et al. forthcoming) found strabismus in 69% and nystagmus in 44%; these are high rates compared with other studies (Biglan 1990, Mankinen-Heikkinen and Mustonen 1987,). In an earlier study by Fernell (Fernell et al 1988), the rate of strabismus was 32%, while 22% had optic atrophy.

Other associated problems

Some children, about 15%, develop precocious puberty, which needs to be treated in some cases, and recurring periods of headache, nausea and somnolence are not uncommon.

Special problems in children with MMC

Children with MMC have a complex situation. As a consequence of the spinal lesion, they have a variety of problems apart from the hydrocephalus (Verhoef et al. 2005). They have a neurogenic bladder and bowel dysfunction and need specialist care and follow-up throughout their lives (Mattson and Gladh 2005). Their motor

impairment is often prominent and many deteriorate as they grow up. About half the children manage to walk by themselves, some with aid (Bowman et al 2001). Their upper limb function is also frequently affected and the cause of this has been discussed by Norrlin et al., for example (Norrlin et al. 2003). They often develop scoliosis and there is a risk of progressive neurological symptoms due to the tethered cord syndrome.

Aims

General: to investigate the live-birth prevalence, aetiology, treatment and clinical outcome in children with hydrocephalus treated surgically during their first year of life and born in 1989-2002 in western Sweden.

Specific:

1. To analyse trends in the live-birth prevalence of hydrocephalus during the 14-year period 1989-2002. To see whether the decreasing trend of infantile hydrocephalus in children born preterm continued and whether the prevalence of hydrocephalus associated with MMC diminished

2. To study outcome in terms of learning disabilities, cerebral palsy and epilepsy in different aetiological subgroups and gestational age groups of children with hydrocephalus

3. To explore motor function and impact on participation in various aetiological and gestational age subgroups in a 10-year cohort of children with hydrocephalus

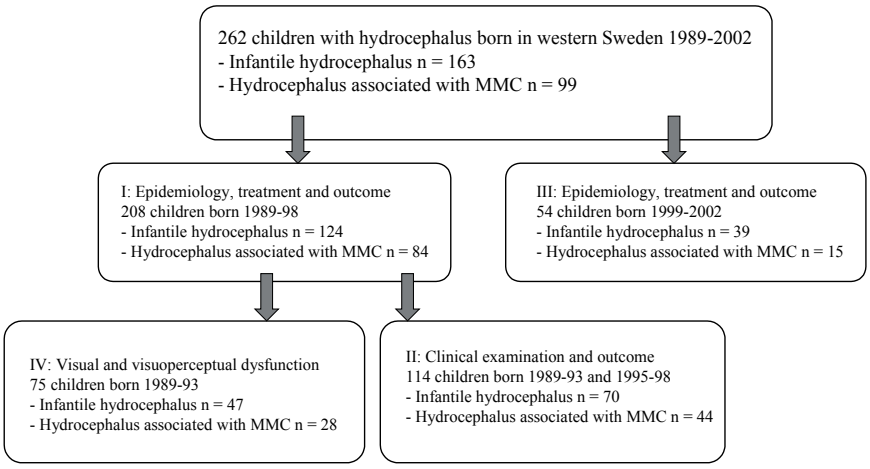
4. To analyse whether modern neonatal care and neurosurgical technique have reduced mortality, morbidity and complications

5. To see whether neuroradiological findings correlate with outcome

6. To study the ophthalmological consequences of hydrocephalus and their relationship to aetiology and brain lesion patterns

Subjects and methods

The study area was the western part of Sweden, the counties of Västra Götaland, Värmland and Halland, an area with 2.03 million inhabitants comprising 23% of the total population of Sweden, 8.9 million people. The study population comprised the 335,394 live births in the area during the 14-year period 1989-2002.
The identification of children with hydrocephalus was based on the assumption that all children with these conditions had been referred to a paediatric clinic and registered with a diagnosis of hydrocephalus according to the Swedish version of the International Classification of Diseases 1987 (ICD9) and 1997 (ICD10). All the registers at the paediatric departments and at the single neurosurgical unit in the region were scrutinised and all the children fulfilling the criteria for hydrocephalus with a need for surgical treatment and who were born in the study area were included in the study.
Hydrocephalus was defined as the presence of a condition with ventricular expansion due to elevated intraventricular pressure and an increased amount of intraventricular cerebrospinal fluid manifested during the first year of life. Two groups were identified; simple or infantile hydrocephalus not associated with MMC or intracranial malignant tumours and hydrocephalus associated with MMC.



Paper I
The study group consisted of 208 infants born alive during the period 1989-1998 and fulfilling the criteria for infantile hydrocephalus (n=124) or hydrocephalus associated with MMC (n=84). In the infantile group, boys dominated: 77 boys vs. 47 girls. In the MMC group, there were 44 boys and 40 girls.
The mean age of the children at the latest follow-up was eight years (range 2-13 years).
Eleven of the 208 children had died during their first years of life, six with infantile hydrocephalus and five with MMC.

Paper II
The study group comprised 114 children from a population-based series of 176 children born during the periods 1989-1992 and 1995-1998 in the western health care region of Sweden. Ten children had died before the study, five with infantile hydrocephalus and five in the MMC group, while another 52 of the remaining 166 (31%) children had either moved out of the region (n=20) or were unwilling to participate (n=32). These 62 children did not differ in terms of gender or aetiology but were more often born very preterm, 21 per cent vs. six per cent. There were 63 boys and 51 girls and their mean age at the time of the clinical examination was eight years (range 4-12 years).

Paper III
The study group consisted of 54 infants born alive during the period 1999-2002 and fulfilling the criteria for infantile hydrocephalus (n=39) or hydrocephalus associated with MMC (n=15). Among the children with infantile hydrocephalus, there were 25 boys and 14 girls, while there were nine boys and six girls among the children with MMC. The children were followed prospectively from birth up to 2.5-6.5 years of age (median 4 years and 3 months). Ophthalmological abnormalities were investigated at the ages of one year and ten months to six years and five months (median 4 years and 4 months). Six of the 54 children had died during their first years of life.

Paper IV
From a population-based series of 103 children born in western Sweden during the period 1989-1993 and fulfilling the criteria for infantile hydrocephalus or hydrocephalus associated with MMC, 75 children were included in the ophthalmological follow-up. Six children had died shortly after surgery, five underwent treatment in another region, 15 children declined participation and two had moved out of the region. There were 47 children with infantile hydrocephalus and 28 with MMC, 41 boys and 34 girls, and the median age of the 75 children was nine years and four months (range 7 years 4 months-12 years 10 months). There was a control group of 140 children without disability, 76 boys and 64 girls aged four years to 15 years (mean 9 years 10 months).

Methods

Information about birth characteristics, as well as the aetiology of hydrocephalus, treatment, complications and additional major impairments, was obtained from records from rehabilitation centres and paediatric and neurosurgical departments in *Papers I-IV.*

Information about cognition was gathered from clinical records and from neuropsychological tests in the form of the Wechsler Intelligence Scale for Children-III (Wechsler 1991), developed for ages six to 16 years, and the Wechsler Preschool and Primary Scale of Intelligence-Revised (Wechsler 1992), for children aged three to seven years. The Griffiths Developmental Scales (Alin-Åkerman and Nordberg 1980) were used for children aged below three years.

Information about the age at start of walking (Lundberg 1979), speech and accompanying neuroimpairments in *Paper II* was gathered from interviews with the parents and clinical records.
In *Paper II,* all examinations, including Movement ABC, and the interviews with the 114 children and their parents were made by the author (E-K P). Head circumference, weight and height were recorded. In children with MMC, height was measured as arm span**.**
The standardised Movement Assessment Battery test for children (Movement ABC) (Henderson and Sugden 1992) was used to test measure fine- and gross-motor function, including static and dynamic balance, in the 114 children in *Paper II*. The test part consists of 32 items divided into four groups adapted to different age groups. A score was given for each of the parts of the test, resulting in a total motor score. Scores below the 5th centile indicate definite motor problems and scores between the 5th and 15th centile indicate borderline motor functions. Of the 70 children with infantile hydrocephalus, 68 were assessed with the complete test, whereas the 44 children in the MMC group only took part in tests of fine-motor function.

The impact of hydrocephalus on activities in daily life and participation was assessed with the handicap code from the WHO's International Classification of Impairments, Disabilities and Handicaps (ICIDH) (World Health Organization 1980) in *Paper II*. It includes six dimensions; orientation, physical independence, mobility, occupation (i.e. school for children), social integration and economy (not included in this study). The dimensions are rated from 0 to 8. A total score was calculated as the sum of the scores for the five dimensions divided by five.
In *Papers III-IV,* the various ophthalmological tests were performed by an ophthalmologist (SA) and an orthoptist. The best corrected visual acuity (VA) was tested with the KM-books chart (Hedin and Olsson 1984), Kay's charts (Kay 1983) at a distance of three metres and, in the youngest children, the Cardiff chart (Adoh et al. 1992) at a distance of one metre. Refraction was measured in cycloplegia, visual fields were tested with the Goldmann perimetry and stereopsis was tested with the

TNO test (Marsh et al. 1980). To detect strabismus, cover and uncover tests were performed for near and distance fixation. The anterior segments were examined with a slit lamp and nystagmus was noted. Indirect ophthalmoscopy and colour fundus photography were performed after pupil dilation. Visuo-perceptual problems were identified by structured history relating to five functions, namely recognition, orientation, perception and movement through depth, perception of movement and simultaneous perception (Houliston et al. 1999).

In *Paper II,* the records from the most recent neuroradiological examination from 95 of the 114 children were re-evaluated together with a neuroradiologist; they were based on MRI in 20, CT scan in 73 and ultrasound in two children. Postoperative follow-up information was missing in 19 cases. The mean duration between the last surgical intervention and the most recent radiological examination was 2.5 years.
In *Paper III,* all 54 children had a neuroradiological examination before the first surgical intervention and after the latest revision evaluated by a neuroradiologist (L-M W). The findings were categorised into five groups as 0: no parenchymal lesion, I: small/moderate periventricular leukomalacia, II: extensive white-matter loss, III: focal white-matter loss with grey-matter lesions and IV: generalised severe white- and grey-matter pathology.

Statistical methods
The frequency of hydrocephalus is expressed as prevalence per 1,000 live-born children. For descriptive purposes, means, SD, range and median were determined. The following statistical tests were used: Fisher`s exact test and $\chi^2$ tests were used for fourfold tables. For comparisons between two groups, the Mann-Whitney U-test was used for ordered and continuous variables and Spearman`s rank correlation was used for correlation analysis. The "trend in proportions" by Armitage (Armitage) was used for trend analysis. The level of significance was set at $p < 0.05$.

Results

Epidemiology

The epidemiological part of the study comprised all 262 live-born children with surgically treated infantile hydrocephalus or hydrocephalus associated with MMC born in 1989-2002 in western Sweden. The prevalence of hydrocephalus was 0.77 per 1,000 live births, 0.48 in children with infantile hydrocephalus and 0.29 for children with MMC. The prevalence of infantile hydrocephalus decreased from 0.55 in 1989 to 0.48 per 1,000 in 2002 and in children with MMC from 0.35 in 1989 to 0.16 per 1,000 in 2002. The decreasing trend in children with infantile hydrocephalus did not continue during the period 1999-2002, mainly because of the increased survival of extremely preterm children with a high risk of developing hydrocephalus after cerebral haemorrhage. During the same period, the prevalence of hydrocephalus associated with MMC remained stable.

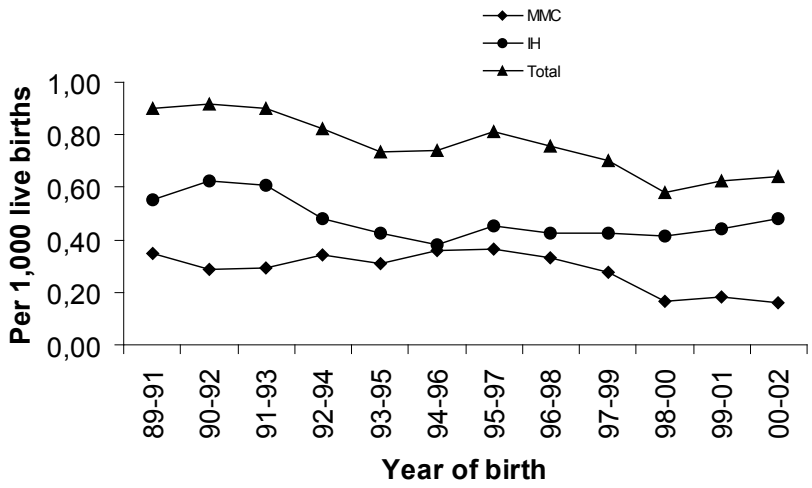


Fig 1. The prevalence of hydrocephalus per 1,000 live births in western Sweden in children with infantile hydrocephalus (IH) and hydrocephalus associated with myelomeningocele (MMC) (birth years 1989-2002; three-year moving average).

In children with infantile hydrocephalus born at term or moderately preterm, the prevalence decreased during the 14-year period, but, in those born very preterm, the prevalence instead increased from 0.12 to 0.18 per 1,000 and this occurred during the period 1998-2002, as shown in Fig 2.

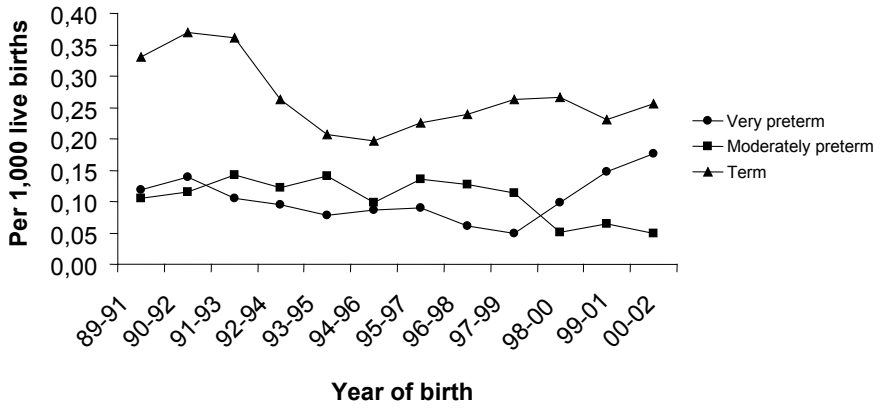


Fig 2. The prevalence of infantile hydrocephalus per 1,000 live births in different gestational age groups (three-year moving average).

The changes in prevalence from 1989 to 2002 were most evident in children born extremely preterm where there was an increase in the gestational age-specific prevalence from 13 to 45 per 1,000 live births. During the same period, the perinatal mortality in children born extremely preterm decreased from 40 to 15 per 1,000 live births.

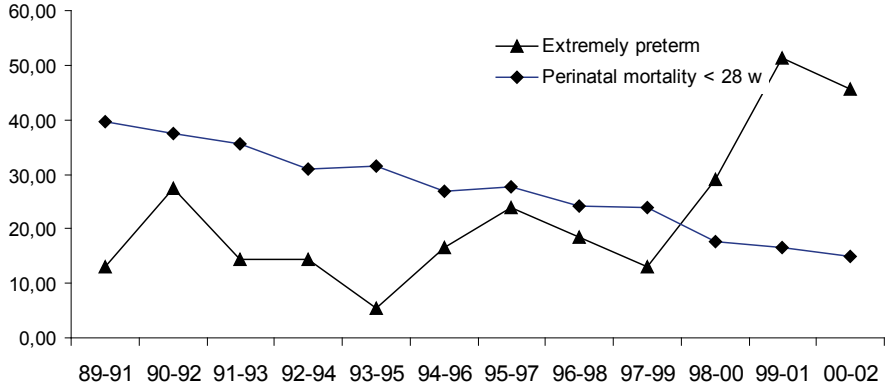


Fig 3. The gestational age-specific incidence in children with hydrocephalus born extremely preterm (< 28 weeks of gestation) in western Sweden, in relation to perinatal mortality (birth years 1989-2002; three-year moving average).

When the results were combined with those from the period 1967-1994, from the same region, it was obvious that there was an increasing trend in infantile hydrocephalus up to the period 1987-1990, followed by a decreasing trend. The shift in the trend mainly followed that of the very preterm group, where a significant increase in the crude prevalence was seen between the periods 1967-1970 and 1983-1986 ($p < 0.0001$). It was followed by a significant decrease between the periods 1983-1986 and 1995-1998, when the crude prevalence was reduced in children born very preterm from 0.16 to 0.07 per 1,000 live births, ($p < 0.05$). During the last four-year period, the prevalence in children born very preterm has again increased to 0.18 per 1,000 live births.

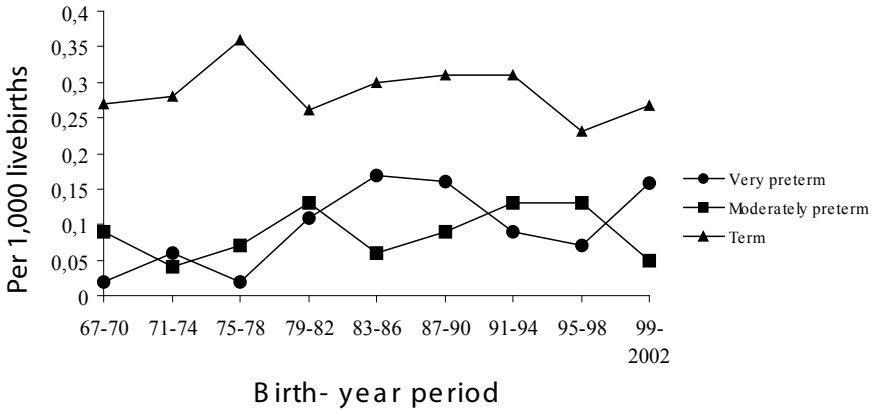


Fig 4. The prevalence of surgically treated infantile hydrocephalus in western Sweden (birth years 1967-2002).

Aetiology

Of all the children with infantile hydrocephalus born in 1989-2002, 92 of 163 (56%) were born at term, 34 (21%) moderately preterm and 37 (23%) very or extremely preterm. Of the children with MMC, the majority, 82 of 99 (83%), were born at term.

The pathogenetic period was prenatal in 189 of 262 (72%) of the children, perinatal in 65 (25%) and postnatal in eight children (3%). The prenatal origin was mainly various malformations such as aqueductal stenosis, arachnoidal cysts and MMC. In children born very or extremely preterm (n = 37), all but two had a perinatal origin in the form of a cerebral haemorrhage.

	Very preterm n=37 (%)	Moderately preterm n=51 (%)	Term n=174 (%)	Total n=262 (%)
Prenatal	2 (5)	37 (73)	150 (86)	189 (72)
Perinatal	35 (95)	12 (24)	18 (10)	65 (25)
Postnatal	0 (0)	2 (4)	6 (3)	8 (3)

Table 1. Aetiology of hydrocephalus in 262 children by gestational age groups (birth years 1989-2002).

Treatment

The first surgical procedure had been performed during the first month of life in 133 of 261 (51%) children, between one and six months in 107 (41%) and after the age of six months in 21 infants (8%). Information was missing in one case. A ventriculoperitoneal shunt was the first surgical intervention in 230 children (88%) and ETV was performed in 31 (12%). There was a need for at least one revision in 168 of 261 children (64%). In children initially treated with ETV, eleven of 31 (35%) did not require any revision. Information was missing in one case.

The most common cause of revision was mechanical, followed by infection. In children born in 1999-2002, an infection during the first six months after surgery occurred in ten per cent.

Outcome

Additional neuroimpairments in the form of learning disabilities, cerebral palsy and epilepsy, by gestational age in children with infantile hydrocephalus and hydrocephalus associated with MMC born in 1989-2002, are shown in Table 2.

	IH				MMC	IH + MMC
	Extremely-very preterm	Moderately preterm	Term	Total IH		Total
	n=37 (%)	n=33 (%)	n=92 (%)	n=162* (%)	n=99 (%)	n=261* (%)
Learning disabilities	25 (68)	20 (61)	29 (32)	74 (46)	16 (16)	90 (34)
Cerebral palsy	29 (78)	10 (30)	14 (15)	53 (33)	3 (3)	56 (21)
Epilepsy	19 (51)	12 (36)	20 (22)	51 (31)	9 (9)	60 (23)
Deaths	1 (3)	1 (3)	8 (9)	10 (6)	7 (7)	17 (7)
No impairment	2 (5)	11 (33)	47 (51)	60 (37)	66 (67)	126 (48)

* one child missing

Table 2. Outcome in 262 children with infantile hydrocephalus (IH) and hydrocephalus associated with myelomeningocele (MMC) by gestational age groups. Information was missing in one child born moderately preterm.

Of the children with infantile hydrocephalus, 63% had at least one associated impairment compared with 33% in the MMC group. All three major impairments, learning disability, cerebral palsy and epilepsy, were significantly more frequent in children with infantile hydrocephalus than in children with MMC. The rate of impairments in children with infantile hydrocephalus increased with decreasing gestational age at birth.

In *Paper I,* it was noted that the rate of revisions had an impact on outcome and those children that had more than two revisions had significantly more associated neuroimpairments, but this was not confirmed in *Paper III*, perhaps due to the small number of children in that study.

Seventeen of the 262 children (6%) born in 1989-2002 died during their first years of life, ten with infantile hydrocephalus and seven with MMC.

Cognition

Learning disability was found in 90 of 261 (34%) of the children with hydrocephalus born in 1989-2002, 46% in children with infantile hydrocephalus and 16 per cent in children with MMC. In children born preterm, learning disability was found in 45 of 70 children (64%), most commonly in children born very and extremely preterm where two-thirds had this impairment. Half the children examined clinically in *Paper II*, with a prenatal origin and with hydrocephalus overt at birth, had learning disabilities compared with 16 per cent of those who developed hydrocephalus later.

Speech development, investigated in *Paper II*, was significantly less delayed in children with MMC than in children with infantile hydrocephalus, in eight of 44 (18%) compared with 34 of 70 (49%).

Motor function

Motor problems were common in both groups of children with hydrocephalus. In children with infantile hydrocephalus in *Paper II*, 19 of 70 (27%) had cerebral palsy compared with none in the MMC group. Fine- and gross-motor function was investigated in *Paper II* in 114 children born in 1989-1993 and 1995-1998. The aetiology was infantile hydrocephalus in 70 and MMC in 44 children. In children with infantile hydrocephalus, the start of walking was delayed and the median age for independent walking was 16 months, while in the MMC group 23 of 44 were able to walk, 13 of them autonomously.

The results according to Movement ABC revealed that three-quarters of the children with infantile hydrocephalus performed below the 5th centile and therefore had definite motor problems and, when children with cerebral palsy were excluded, 61% still had definite motor problems. Children with MMC had specific problems due to their spinal lesion and were only able to perform the fine-motor tests. Fine-motor problems were evaluated in children with both infantile hydrocephalus and MMC and the results are shown in Fig 5. In both groups, nearly three-quarters of the children had definite motor problems.

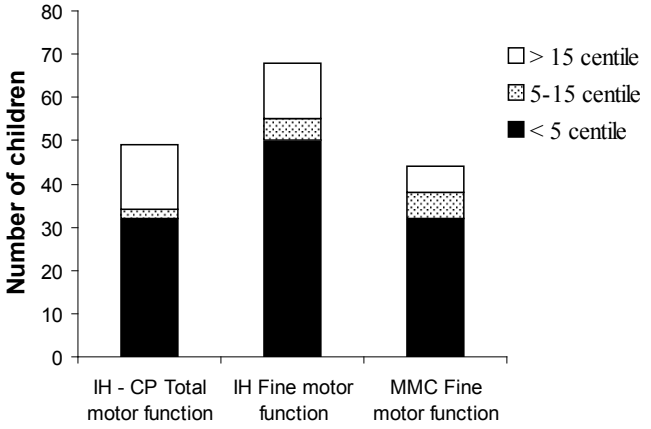


Fig 5. Total and fine-motor function in 68 children with infantile hydrocephalus (IH) according to the Movement ABC and fine-motor function in 44 children with hydrocephalus associated with myelomeningocele (MMC). Nineteen children with cerebral palsy were excluded. Information was missing in two children with infantile hydrocephalus.

Epilepsy

In children born with infantile hydrocephalus in 1989-2002, epilepsy was found in 51 of 162 (31%) compared with nine of 99 (9%) children with MMC. Half the children born very or extremely preterm had epilepsy. In *Paper II,* among children with a prenatal origin of hydrocephalus and hydrocephalus overt at birth, 13 of 39 (33%) had epilepsy compared with six of 50 (12%) of those with a prenatal origin but without hydrocephalus already at birth.

Ophthalmological outcome

In *Paper IV,* ophthalmological abnormalities were found in 62 of 75 children (83%). There were 47 children with infantile hydrocephalus and 28 with MMC and a comparison group of 140 healthy children. The distribution of ophthalmological findings in all the children examined is shown in Table 3

Visual impairment (binocular visual acuity <0.3) was found in eleven of 73 (15%) of the children with infantile hydrocephalus and in none with MMC. Refractive errors were present in 47 of 70 (67%) children, while strabismus was present in 51 of 74 (69%).

Cognitive visual dysfunction was found in 38 of 64 (59%) of the children. Visuoperceptual problems were more common in children with associated neuroimpairments, such as cerebral palsy and epilepsy. In this group, all the children had these problems, as did 17 (82%) of those with a full-scale IQ of < 70. Children with MMC were least affected by ophthalmological impairments.

		Hydrocephalus without MMC	Hydrocephalus with MMC	Comparison group
		n=47	n=28	n=140
Visual acuity				
	Binoc.3m Md	0.65	0.9	1.0
	(range)	(fix-1.25)	(0.4-1.25)	(0.5-1.25)
Refraction		n (%)	n (%)	n (%)
	Hyperopia	24/43 (53)	9/27 (33)	12/140 (9)
	Myopia	5/43 (12)	2/27 (7)	7/140 (5)
	Astigmatism	21/43 (49)	14/27 (52)	31/140 (22)
Strabismus				
	Esotropia	14/46 (30)	12/28 (43)	4/140 (3)
	Exotropia	17/46 (37)	4/28 (14)	1/140 (1)
	Dyskinetic	3/46 (7)	1/28 (4)	0
Visuo-perceptual problems		25/36 (69)	13/28 (46)	4/140 (3)

Table 3. Visual acuity, refraction, strabismus and visuo-perceptual problems in children with hydrocephalus (n=75), with or without myelomeningocele (MMC), and a comparison group (n=140).

Ophthalmological outcome was also investigated in 40 of 48 children born in 1999-2002 in *Paper III*. Ophthalmological abnormalities were revealed in 32 (80%) of the children. Contrary to the findings in the cohort born in 1989-1993, there was no significant difference in visual outcome between children with infantile hydrocephalus and those with MMC. Low visual acuity was significantly more common among children with optic atrophy, learning disability, cerebral palsy and epilepsy ($p<0.001$, $p=0.01$, $p<0.05$ and $p=0.05$) respectively. The majority of the children examined, 21 of 34 (62%), had refractive errors and strabismus was found in half the children. Of the eight children with optic atrophy, all had at least one associated impairment.

When the two studies were taken together, a visual impairment (VA < 0.3) was found in 21%, refractive errors in 65% and strabismus in 64% of the children examined.

Participation

The impact on participation and activities in daily life was assessed with the ICIDH. Children with infantile hydrocephalus had a more severe handicap than children with MMC in the dimensions of orientation and social integration, with the opposite situation for the dimensions of mobility and physical independence. The resulting total handicap score was of the same magnitude in both groups.

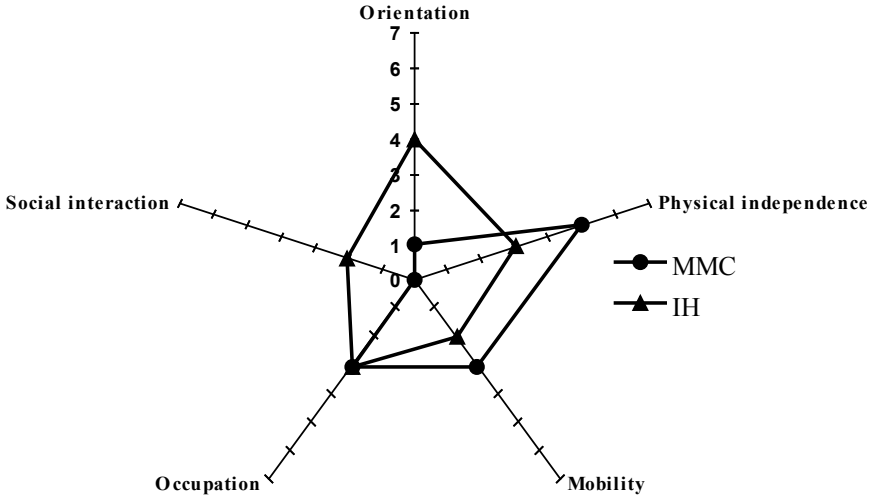


Fig 6. Distribution of median handicap scores according to the International Classification of Impairments, Disabilities and Handicap in 70 children with infantile hydrocephalus (IH) and 44 children in the group with myelomeningocele (MMC).

Neuroradiology

In *Paper II,* almost half the 95 children examined still had enlarged ventricles at follow-up, about 40% had ventricles of normal size and 14 children had collapsed ventricles. Information was missing in 19 cases. In children with either enlarged or slit ventricles at follow-up, additional neuroimpairments were more common. Learning disabilities were significantly more frequent in children with either enlarged or slit ventricles ($p<0.05$).

	Enlarged n = 45 (%)	Normal n = 36 (%)	Slit n = 14 (%)
Learning disabilities	21 (47)	7 (19)	5 (36)
Cerebral palsy	9 (20)	4 (11)	3 (21)
Epilepsy	12 (27)	8 (22)	4 (29)
No impairment	21 (47)	23 (64)	7 (50)

Table 4. Ventricular width at follow-up in 95 children with hydrocephalus in relation to associated neuroimpairments.

There was no significant correlation between visual acuity and enlarged or collapsed ventricles at follow-up.

In *Paper III*, 30 of the 54 children had been examined with MRI and 24 with CT. The correlation between neuroimaging findings and neurological impairments is shown in Table 5.

	Normal n=6	I n=5	II n=13	III n=18	IV n=12	Total n=54
Lerning disabilities	0	3	5	8	7	23
Cerebral palsy	0	1	3	6	7	17
Epilepsy	0	0	2	9	5	16
Deaths	0	1	0	1	4	6
No impairment	6	0	8	5	1	20

Table 5. Outcome in 54 children with hydrocephalus in relation to neuroradiological findings Normal: no parenchymal lesion, I: small/moderate periventricular leukomalacia, II: extensive white-matter loss, III: focal white-matter loss with grey-matter lesion, IV: generalised severe white- and grey-matter pathology.

No child with normal imaging had any associated neurological impairment, compared with eleven of twelve with some impairment in children with generalised lesions and no child with normal imaging was visually impaired.

Discussion

Epidemiology in children with hydrocephalus has been the subject of debate in Sweden for five decades (Fernell et al 1986, Hagberg et al. 1963). In most parts of the world, especially in the undeveloped countries, it is difficult to perform epidemiological research, but much higher birth prevalences than those in Sweden, for example, have been reported (Murshid 2000). In the latest four-year cohort from 1999-2002 in western Sweden, we found a live-birth prevalence of 0.48 per 1,000 for children with infantile hydrocephalus and 0.18 for children with MMC.

The gestational age-specific prevalence of hydrocephalus during the same period increased particularly in children born extremely preterm, with a concomitant decrease in perinatal mortality of the same magnitude. As a result, although children born extremely preterm nowadays have a better chance of survival, they run the risk of a perinatal intracerebral haemorrhage, in some cases leading to hydrocephalus and often to other neurological impairments (Futagi et al. 2005, Resch et al. 1996).

The prevalence of hydrocephalus in children born at term decreased at the beginning of the nineties but has since remained fairly stable. The reason for the decrease may have been the more sophisticated management of the critically ill, newborn, full-term infant, as well as improved methods for the prenatal detection of hydrocephalus in the same way as for MMC.

For children with MMC, the prevalence decreased to half during the 14-year period 1989-2002 and a decreasing trend has also been seen in other countries. The cause of this decrease varies between countries; in some (Honein et al. 2001, Wynn 1998) the folic acid enrichment of flour and the use of extra folic acid in young fertile women have been of importance, but enrichment has not yet been introduced in Sweden due to a discussion about the potential adverse effects of folic acid. In Sweden, the decrease in the number of live-born children with MMC was mainly caused by the

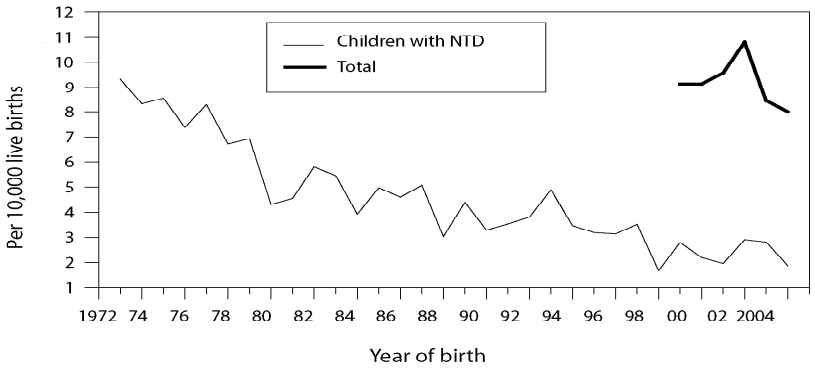


Fig 7. Newborn children with neural tube defects (NTD) (anencephaly, encephalocele, MMC) in 1973-2004. For the period 1999-2004, the total number of NTD pregnancies (live-born children and terminated pregnancies) is presented.

increased use and quality of ultrasonography early in pregnancy, detecting neural tube defects and leading to early termination (Bygdeman and Ahlenius 2005). In the last few years, there have only been 20 to 25 newborn children with MMC a year in Sweden, while the rate of MMC pregnancies is still in the same range as in the 1970s (The National Board of Health and Welfare 2004**).**

For decades, the most common treatment for hydrocephalus has been a ventriculo-peritoneal shunt. In the present study, it was the initial treatment in 88% of the cases. The shunts are continuously becoming more advanced and specialised (Drake and Kestle 1998)**,** but complications are still common. Mechanical problems such as obstruction and disconnection are the most common, followed by infections (Lumenta and Scotarczak 1995). Infections most frequently occur during the first six months postoperatively (Enger et al. 2003). In our latest prospective four-year study, infections within the first postoperative month occurred in five per cent of cases and in other studies infections after up to 19% of the procedures have been reported (Casey et al.1997). Many factors are important – the age of the child, with an increased risk of infections up to approximately six months of age (Casey et al. 1997), aetiology and, in several studies, the experience of the surgeon (Cochrane and Kestle 2003).
There was a need for revision in almost two-thirds of the cases, due to infections, mechanical and other problems. This was in accordance with Heinsbergen, who reported that two-thirds required at least one revision (Heinsbergen et al. 2002).

ETV was performed as the primary treatment in twelve per cent of the children, more frequently in the last four-year period than at the beginning of the 14-year period, 22% vs. 9%. ETV was also used at an early stage during the first year of life and in different aetiologies. It was successful in eleven of 31 cases (35%). Some authors have reported a low success rate in children below two years of age (Jones et al. 1990), but others have argued that it is the aetiology and not the age that is most important in determining whether or not ETV will work (Beems and Grothenius 2002). It has been reported to be successful in between 50% and 90% of populations comprising both children and adults (Beems and Grothenius 2002, Choi et al. 1999, Tisell et al. 2000). The best results have been reported in patients with an aqueductal stenosis.
It is to be hoped that the use of ETV will also be more common in western Sweden, as the morbidity and mortality is low and the risk of complications in the form of infection is low (Beems and Grothenius 2002, Choi et al. 1999).

We found that the rate of revisions correlated significantly with outcome in terms of neuroimpairments in the study from 1989-1998, but this was not confirmed in the later study from 1999-2002. The findings in the third of these studies were more in accordance with the findings of Lumenta and Riva (Lumenta and Scotarczak 1995, Riva et al. 1994), who did not find any such association.

Outcome in the form of accompanying neuroimpairments, such as learning disability, cerebral palsy, epilepsy and visual impairment, was more frequent in children with infantile hydrocephalus than in children with MMC (Casey et al. 1997, Meyer-Heim et al. 2003**)**. Children with MMC have a wide variety of urological and motor problems due to their spinal lesion, but they are better off when it comes to associated impairments (Mattson and Gladh 2005). This was confirmed by Heinsbergen et al. (Heinsbergen et al. 2002) and Mori et al. (Mori et al. 1995), who found that a congenital origin and hydrocephalus associated with MMC had a better developmental outcome than hydrocephalus with an acquired cause. This was apparent in the clinically examined children born in 1989-1998, where associated impairments were more common in those with infantile hydrocephalus than in the children with MMC. Only one-third of the latter group had any major neuroimpairment compared with almost two-thirds of those with infantile hydrocephalus.
Other studies have confirmed the risk of a poor outcome in children with a peri- or postnatal cause vs. a prenatal origin of the hydrocephalus (Casey et al. 1997, Hoppe-Hirsch et al. 1998, Mirzai et al. 1998, Resch et al. 1996). In particular, children born very or extremely preterm with post-haemorrhagic hydrocephalus run a high risk of associated neuroimpairments. Almost all the children of this kind (95%) in this study had some associated neuroimpairment, compared with half the children born at term. This correlation was also found by Heinsbergen (Heinsbergen et al. 2002).

Cognitive impairments of varying severity were common in children with hydrocephalus. Hoppe-Hirsch found learning disability in 40% of the children, while 28% had an IQ of between 70 and 90 in a follow-up study 10 years after shunting (Hoppe-Hirsch et al. 1998), rates close to those found in this study. Casey (Casey et al. 1997) reported that hydrocephalus after intraventricular haemorrhages or infections resulted in cognitive problems and that these children were twice as likely to require special schooling as those with congenital hydrocephalus. This was also in accordance with our study, where two-thirds of the children born very or extremely preterm and with post-haemorrhagic hydrocephalus had learning disabilities compared with one-third of the children born at term. Another group with cognitive problems was made up of children with hydrocephalus overt at birth, where half the children had learning disabilities. Fernell (Fernell et al. 1987) stated that this group had a poor prognosis and two-thirds of the children surviving to two years of age had neurological sequelae.

Motor problems were common in children with infantile hydrocephalus, as well as in children with MMC. In surgically treated children, Hoppe-Hirsch (Hoppe-Hirsch et al. 1998) reported motor deficits in more than half the children. Fernell found that 28% of the children born at term had cerebral palsy, while the corresponding figure for those born preterm was 47% (Fernell et al 1988a, Fernell et al. 1988b).
In the present study, one-third of the children with infantile hydrocephalus had cerebral palsy, but the figure for children with MMC was only three per cent.
Children with MMC had lower limb impairments due to the spinal lesion, but, in

a majority of cases, they also had motor problems in the upper limbs. These upper limb problems can have a considerable impact on the ability of children with MMC to manage their daily lives (Norrlin et al. 2003, Turner 1986). Turner found that the majority of the children with MMC had upper limb problems and there was no definite correlation to the level of the lesion (Turner 1986).
Motor problems other than cerebral palsy were also common in children with infantile hydrocephalus. The extent of the problems became clear when 114 of the children with hydrocephalus born in 1989-1998 were examined using the Movement ABC test battery. This is a well-known, evaluated and widely used test battery. There were some problems using the test as some children did not quite understand the instructions and some did not manage to keep to the time limits in order to finish some parts of the test. In spite of this, it was remarkable that the majority of the children had severe motor problems, even when those with cerebral palsy were excluded, and also that three-quarters of the children with MMC had significant upper limb involvement.
These motor problems in children with hydrocephalus most probably have a considerable impact on their daily lives.

Epilepsy is often associated with hydrocephalus (Kokkonen et al 1994, Saukkonen et al. 1990). The underlying mechanisms have been the subject of controversy. It has been suggested that the brain lesion underlying the hydrocephalus, the presence and location of the shunt and the rate of revisions are all related to epilepsy (Bourgeois et al. 1999, Klepper et al. 1998). In this study, epilepsy was found in one-third of the children with infantile hydrocephalus compared with ten per cent of the children with MMC, suggesting that the underlying brain lesion rather than shunt treatment or revisions is the major cause of the epilepsy. Epilepsy was more common in children born very or extremely preterm, which was in accordance with earlier studies by Fernell (Fernell et al. 1988a, Fernell et al. 1988b). In our study, epilepsy was found in nearly half the children with severe generalised parenchymal lesions compared with none of the children with normal neuroimaging findings (Klepper et al. 1998).

Hydrocephalus may cause multiple ophthalmological and visual disorders and visual function deficits were identified in the majority of the children investigated in this study (Andersson et al. 2006). Those with MMC had a better visual outcome than children with infantile hydrocephalus. The visual outcome was not easy to compare with other investigations because of differences in the age of the children, aetiology of hydrocephalus and examination methods (Aring et al. forthcoming, Heinsbergen et al. 2002). Strabismus was found in more than two-thirds compared with about half the children in other studies (Biglan 1990, Mankinen-Heikkinen and Mustonen 1987, Rabinowicz 1974).
Reduced visual acuity to less than 0.3 was found in 15% of the children born in 1989-1993 compared with 33% of those born in 1999-2002. This difference could partly be explained by the gestational age variation between the two periods, reflecting different aetiologies. In the last period, 25% of the children were born very pre-

term, compared with eight per cent during the first period, and children born very preterm run a higher risk of visual impairments than those born at term (Gaston 1985, Rabinowicz 1974,).

In children born in 1999-2002, there was a tendency, even if it was not significant, towards a correlation between the severity of the visual impairment and neuroimaging findings and also with decreasing gestational age. The lack of significance was possibly due to the limited number of children in this part of the study.
Visuo-perceptual problems were found in more than half the children, resembling the findings reported by Houliston (Houliston et al. 1999**),** and even higher rates were found in children with associated impairments such as cerebral palsy and epilepsy.

To explore the consequences of hydrocephalus for the child and the family and to see how activities in daily life and participation were affected, the intention in this study was to use the new International Classification of Functioning, Disability and Health (ICF) (World Health Organization, 2001). However, as the ICF had not yet been adapted to children and to make comparisons possible with other paediatric disability groups assessed in the same way, we chose the handicap code from the WHO's International Classification of Impairments, Disabilities and Handicaps (ICIDH) (World Health Organization 1980). The ICIDH revealed a differing profile between children with MMC and those with infantile hydrocephalus, but the total handicap was of the same magnitude in both groups. Children with infantile hydrocephalus had more problems and thereby a higher handicap score for social independence and orientation, but they had fewer problems when it came to motor activities. The opposite was the case for children with MMC, whose problems were related to the dimensions of mobility and physical independence, problems caused by the spinal lesion rather than the hydrocephalus. As was the case for impairment load, children born at term had a better outcome than those born preterm in terms of handicap. When compared with other childhood disability groups, it was found that children with hydrocephalus had handicap scores somewhere in between those with epilepsy, who had a milder handicap, and those with CP and mental retardation, who had a more severe handicap (Beckung and Uvebrant 1997, Beckung and Hagberg 2000). In children with infantile hydrocephalus, the aetiology and thereby the extent and nature of the brain lesion is very heterogeneous and this may explain the variation in handicap profiles. Some children had only minor problems, but the majority had a variety of often severe disabilities. The profile in children with MMC was more homogeneous.

Neuroimaging was found to be useful for aetiological, treatment and outcome considerations and more than half the children born in 1999-2002 had had an MRI and the remainder had had a CT scan. Especially at the beginning of the study period starting in 1989, it was not always possible to get an MRI before the first surgical intervention. It is to be hoped that the use of preoperative MRI will increase, so that the best treatment method, ETV, fenestration of cysts, resection of obstructive pro-

cesses or shunt insertion, can be chosen and aetiological and prognostic information can be obtained.

Of children born in 1989-2002, more than half were born at term with a prenatal origin of the hydrocephalus, in many cases with subtle parenchymal lesions, whereas many of the children born preterm had severe parenchymal lesions as a result of a perinatal cerebral haemorrhage. Another prognostic factor when it came to additional neuroimpairments was the status of the ventricles at follow-up. Impairments were more common in children with either enlarged or collapsed ventricles; this was most obvious for learning disabilities. Hoppe-Hirsch also found (Hoppe-Hirsch et al. 1998) that the size of the ventricles was important for outcome, but only if there was a persisting major dilation, whereas Saukkonen (Saukkonen et al. 1990) reported that collapsed ventricles could aggravate epilepsy.
Kim (Kim et al. 2000) stated that, in children treated with ETV, neuroimaging together with cognitive testing was a way to evaluate the effect of treatment.
In the children born during the latest four-year period, there was a significant correlation between the extent and nature of the parenchymal lesions found at neuroimaging and cerebral palsy and epilepsy, but there was no correlation between neuroimaging and visual acuity, except that no child with normal neuroimaging findings had a visual impairment.

Conclusions

- A decreasing live-birth prevalence of hydrocephalus was noted in 1989-1998. This trend continued until 1999-2002, but no further decrease was noted during that period. This was mainly explained by the increased survival of children born extremely preterm with post-haemorrhagic hydrocephalus. During the study period, a decreasing trend for hydrocephalus associated with MMC was noted.
- The aetiology and gestational age at birth were important for outcome. Neurological impairments were present in more than half of the children. Children with infantile hydrocephalus born very or extremely preterm had the poorest outcome.
- The majority of the children with infantile hydrocephalus and hydrocephalus associated with MMC who were clinically examined in various gestational age groups, had definite motor problems even when those with cerebral palsy were excluded. The effect on participation was of the same magnitude for children with infantile hydrocephalus and for those with MMC, but they had difficulties in different dimensions.
- Improved neonatal care has increased the survival of children born extremely preterm but it has not yet reduced the incidence of post-haemorrhagic hydrocephalus in these children. The most common neurosurgical treatment during the 14-year period was ventriculo-peritoneal shunt. The shunt systems are being continuously improved, but revisions are still required in more than half the children and the use of ETV and the development of other alternatives to shunt treatment are urgently needed.
- Neuroimaging was found to be useful for aetiological, treatment and prognostic considerations. Children with generalised parenchymal lesions had a poor outcome, with neurological impairments in the majority of cases.
- Ophthalmological abnormalities were found to be very frequent and were observed in more than three-quarters of the children.

It can be concluded that it is important continuously to develop more sophisticated methods for the prevention of hydrocephalus and the management of children with hydrocephalus, especially for those born very and extremely preterm who run a high risk of a poor outcome.

Sammanfattning på svenska

Introduktion: Epidemiologiska och kliniska uppföljningsstudier av barn med hydrocefalus har bedrivits i Sverige i drygt 40 år. Det har varit av intresse av att studera förändringar i förekomst i olika orsaksgrupper samt hos barn med olika graviditetslängd.
Frågeställningar: Att analysera trender i förekomsten av spädbarnshydrocefalus och hydrocefalus associerat med ryggmärgsbråck under perioden 1989 till 2002. Uppföljning av barnen för att se i vilken utsträckning de utvecklar funktionshinder i form av mental retardation, cerebral pares, epilepsi och synproblem. Att undersöka motorisk funktion och bedöma handikapprofil i olika orsaksgrupper samt hos barn med olika graviditetslängd samt för att se om behandling, komplikationer och neuroradiologiska fynd korrelerar med de funktionshinder barnen har vid uppföljningen.
Metodik*:* En populationsbaserad studie av alla 262 barn med spädbarnshydrocefalus och hydrocefalus associerat med ryggmärgsbråck födda under perioden 1989-2002 i västra Sverige. Information om orsaken till hydrocefalus och kliniska uppgifter om barnet har hämtats från medicinska journaler, från röntgenarkiv samt från oftalmologiska undersökningar. Etthundrafjorton barn genomgick en neurologisk och motorisk undersökning och intervjuades tillsammans med sina föräldrar.
Resultat: Förekomsten av hydrocefalus var 0.77 per 1,000 födda barn, 0.48 för infantil hydrocefalus och 0.29 för barn med ryggmärgsbråck. Förekomsten av spädbarnshydrocefalus minskade från 0.55 år 1989 till 0.48 år 2002 och för barn med ryggmärgsbråck från 0.35 till 0.16. Förändringen i förekomst under åren 1989-2002 var tydligast i gruppen av barn med spädbarnshydrocefalus och extremt för tidigt födda barn där den graviditetslängds specifika förekomsten ökade från 13 till 45 per 1,000 födda, medan dödligheten i samband med förlossningen och nyföddhetsperioden i samma graviditetslängdsgrupp under samma period minskade från 40 till 15 per 1,000 födda. En slang från hjärnans hålrum till bukhålan (ventriculo-peritoneal shunt) var det första kirurgiska ingreppet för 230 barn (88%), endoskopisk ventriculostomi (ett hål från hjärnans hålrum till dess utsida) gjordes i 31 fall (12%). Minst en revision krävdes hos 64% av barnen. Bland barnen med spädbarnshydrocefalus hade 63% minst ett associerat funktionshinder såsom mental retardation, cerebral pares eller epilepsi, jämfört med 33% av de med ryggmärgsbråck. Associerade funktionshinder var signifikant vanligare hos de med spädbarnshydrocefalus än hos de med ryggmärgsbråck. Andelen barn med funktionshinder ökade vid kortare graviditetslängd. Oftalmologiska problem och synpåverkan förekom hos en majoritet av de undersökta barnen. Barnen med ryggmärgsbråck hade synproblem i mindre utsträckning än de med spädbarnshydrocefalus. Synskada förekom hos 15% av barnen födda 1989-1993 jämfört med hos 33% av barnen födda 1999-2002. En förklaring till denna skillnad var att 25% av barnen i den senare gruppen var mycket eller extremt för tidigt födda jämfört med enbart åtta procent i den första gruppen. Risken för synskada är mycket högre hos mycket för tidigt födda barn. Inget barn med normal neuroradiologisk bild hade några associerade neurologiska eller synrelaterade funktionshinder jämfört med elva av tolv av barnen med generaliserade hjärnvävnadsskador.

Slutsatser: Förekomsten av hydrocefalus minskade under perioden 1989-1999 men detta fortsatte ej under perioden 1999-2002. Orsaken var till stor del en ökad överlevnad av extremt för tidigt födda barn med hydrocefalus efter hjärnblödning och en minskande förekomst av hydrocefalus associerat med ryggmärgsbråck. Den vanligaste behandlingen var ventrikulo-peritoneal shunt och över hälften av barnen genomgick minst en revision. Orsaken till hydrocefalus och graviditetslängd vid födelsen var av betydelse för förekomsten av associerade funktionshinder. En majoritet av barnen hade något funktionshinder såsom mental retardation, cerebral pares eller epilepsi och över tre fjärdedelar hade oftalmologiska avvikelser. Neuroradiologiska undersökningar var betydelsefulla för etiologiska och behandlingsmässiga överväganden.

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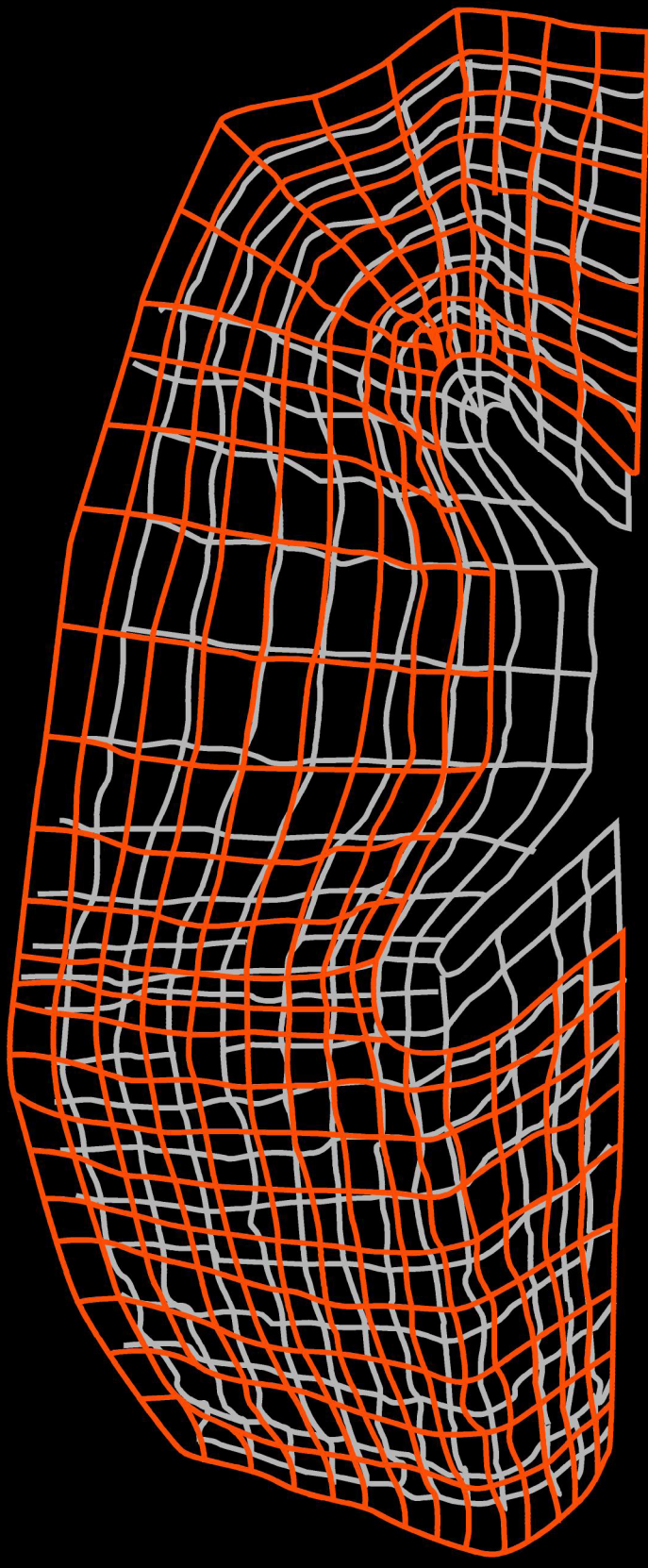

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