

Volume I Supplement 1, 2004

Meeting abstracts

## 48th Annual Meeting of the Society for Research into Hydrocephalus and Spina Bifida

Dublin, Ireland

23–26 June 2004

Published: 23 December 2004

### ORAL PRESENTATIONS

#### S1

##### The enigma of underdrainage in shunting of hydrocephalus

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*Cerebrospinal Fluid Research 2004, 1(Suppl 1):S1*

**Clinical background:** The first reports about mechanical complications after shunting dealt mainly with overdrainage-related problems. But especially since the introduction of hydrostatic valves, complications related to underdrainage gain increasing attention. However, an unequivocal evaluation of underdrainage is hindered by discrepancies in the definition of this entity.

**Materials and Methods:** In a series of 202 patients of different etiologies treated with the hydrostatic Dual-switch-valve (DSV), 22 cases were suspected of suffering from underdrainage. Using a new algorithm to differentiate between different causes of mechanical obstruction on the one hand and “functional” underdrainage, we saw an indication to exchange the DSV to one with a lower opening pressure in 15 cases.

**Results:** Out of the patients with suspected functional underdrainage, only 11 cases did improve clinically and/or radiologically. The failures are probably due to the multiplicity of possible reasons for a functional underdrainage. Besides the wrong choice of a too high pressure level by the surgeon, the intraperitoneal pressure up to now remains a ‘black box’. Furthermore there is a small percentage of cases, especially patients with idiopathic Normal Pressure Hydrocephalus and hydrocephalus following severe brain trauma, in whom the optimal intraventricular pressure-level for improvement after shunting is lower than normal or physiological ICP.

**Conclusions:** The discrepancies in the definition of underdrainage are the main reason for the differences regarding the incidence of this important mechanical complication reported in the shunt-literature. The outcome of our series also stresses the necessity to improve the preoperative diagnostic tools in order to avoid functional underdrainage. Furthermore we want to point out the importance of adjustability of the valve in selected cases.

#### S2

##### The use of image intensification in the management of “programmable” shunt valves

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*Cerebrospinal Fluid Research 2004, 1(Suppl 1):S2*

**Background:** One of the criticisms of the Codman Hakim adjustable shunt valves has been the need to x-ray patients after the valve pressure has been adjusted, to confirm the new pressure setting. Many clinicians complain about the time spent waiting for patients to have their x-ray taken, and of course if the pressure alteration has been inaccurate, a further delay is incurred in re-setting the valve, and waiting for an additional confirmatory x-ray. Indeed, the manufacturers of these valves are looking at ways of confirming the valve pressure setting without the need for x-rays. In August 2003, the authors moved to new purpose-built neurosciences’ accommodation at the James Cook University Hospital in Middlesbrough. With state-of-the-art imaging facilities, including new angiography and image intensification hardware and software, we started to use image intensifiers to assess the shunt pressure setting, alter it appropriately, re-check it and rapidly discharge the patients. The whole process was taking less than 15 minutes. The authors had adopted this process without prior knowledge of any published material. However, despite a publication appearing in the *Journal of Neurosurgery* in 1997 [1] which clearly described the advantages of using fluoroscopy in this context, this seems to have been largely ignored, certainly within the United Kingdom. This presentation will describe the authors’ own experience in using fluoroscopy in adjusting the Hakim programmable valves, emphasising all its advantages, particularly in saving time. Several case illustrations will be presented to demonstrate this. It is hoped this will encourage the wider application of this method to the benefit of both patients and clinicians.

**Conclusions:** Fluoroscopy of “programmable” shunt valves is efficient, accurate and safe, and is to be commended as the best way in dealing with the follow-up and treatment alterations in patients with hydrocephalus fitted with Codman Hakim valves.

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### S3

#### **In-vitro-testing of 1318 hydrocephalus valves. An overview of solved and unsolved problems**

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S3

**Background:** Between 1962 and 1979 121 valves only have been tested. In 1980 Ekstedt published the first major series of 180 specimens. Now we register >1318 valves tested in vitro by 78 authors. Unfortunately cumulative or meta-analyses of the results are not available.

**Materials and Methods:** All papers including technical reports etc. related to valve-tests were evaluated; double publications of the same material were counted once, and papers of companies were excluded.

**Results:** 96% were investigated in 4 countries: 9.0% in USA and England, 14.6% in Sweden and 63.9% in Germany. The number of specimen per group ranged from 1–643, the tested designs from 1–87. Unfortunately in most early, but also current papers the pretest procedures (de-aeration, pre-perfundation) were not described. In 10 papers the temperatures, in 7 the test-fluids are missing, the same is true for many methodological details. Most authors measured the resistance-pressure with a given flow, a few the flow dependent of pressure; 4 groups only practiced both methods. The tests of lifelong implants ranged from 10 seconds up to 365 days; 3 labs reported results up to 3 months, one single group only over 1 year. In spite of a massive impact of deformation forces (external pressure, flexion etc.) most labs made no special tests. Data related to influences of waves, magnetic fields, pumping, sterilization, reflux, protein and particles are scattered.

**Conclusions:** After elimination of doubtful papers the results are relatively homogenous: Related to accuracy and drift the ball-valves are the best followed by diaphragm-designs, while slit- and Orbis-valves showed often problems. With respect to a physiological drainage all simple DP including adjustable valves failed. Advantages of antisiphon- and Orbis-like designs are counterbalanced by safety deficits. The gravitational valves, the available optimum, were investigated by four authors only.

### S4

#### **Treatment of third ventriculostomy failure: re-fenestration or shunt?**

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S4

**Clinical background:** Though endoscopic third ventriculostomy (ETV) has proven to be a valid alternative to shunting for some hydrocephalic patients, the decision to re-fenestrate or shunt after ETV failure is less clear. The aim of this retrospective study was to evaluate the clinical outcome and complications for patients who required re-fenestration or shunting compared to initial ETV cases.

**Materials and Methods:** 189 primary ETVs were evaluated between 1994 and 2002. The failures ( $n = 50$ ), underwent a CINE Phase-Contrast (PC) MRI protocol for evaluation of fenestration

patency. Patients with open fenestrations were shunted, while those with closed were explored for possible re-fenestration. The results of re-operation were compared with the results of the primary ETV. The probability of success in each group was determined statistically with using Kaplan-Meier plot.

**Results:** Of 189 primary ETV patients, 139 (74%) were successful at 2 years. Fifty patients showed clinical failure. On CINE PC MRI protocol, 30 of the failures showed patent CSF flow pattern and underwent shunting. Of the twenty patients with obstructed pattern, 16 were endoscopically re-explored and treated (10 re-fenestration only, 4 re-fenestration + shunt, and 2 shunt only). The remaining 4 were shunted without exploration. As a result a total of 40 of the failures were shunted and 10 were re-fenestrated endoscopically. The success rate for re-fenestration was 50% (5/10) with no complications, and a 62.5% success probability at 2 years, whereas the success rate for shunting was 58% (23/40), with a 39% complication rate and a probability of success of (72%) at 2 years. A total of 144/189 (76.1%) patients remained shunt-free.

**Conclusion:** The majority (3/5) of ETV failures were not due to fenestration closure and required shunting to treat a residual communicating hydrocephalus. Approximately 2/3 of the fenestrations that did appear blocked on CINE MRI studies could be re-fenestrated on re-exploration. Re-fenestration success was not as high as primary ETV success but comparable to shunting. Re-do ETV is justified as a treatment of ETV failure, especially given the low morbidity and possibility of shunt avoidance.

### S5

#### **Shunt revision after major abdominal surgery in patients with Spina Bifida**

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S5

**Clinical background:** Despite the increasing popularity of endoscopic third ventriculostomy (ETV) to treat hydrocephalus in patients with neural tube defects (NTD's) the majority of patients with open NTD's still have ventriculo-peritoneal (VP) shunts in-situ from an early age. Many of these patients progress to need abdominal surgery for bladder problems. No data currently exists as to the risk of shunt dysfunction after abdominal surgery.

**Materials and Methods:** Retrospective study of all patients attending the North West Regional Spina Bifida clinic. Patients with VP shunts who had had abdominal surgery after shunt insertion were identified from our Regional NTD Registry. A case note review was then undertaken to establish the incidence of shunt dysfunction within the group.

**Results:** There were 39 patients who fitted the criteria for the study and whose hospital records were available for review. Of these 9 had shunt dysfunction within 3 months of surgery requiring surgical intervention (23%). A total of 57 abdominal operations had been performed on this patient group whilst a VP shunt was in situ giving a 15.8% risk of shunt malfunction after surgery. Five of the nine patients had a new VP shunt inserted, one had an ETV and 3 had ventriculo-atrial shunts inserted. Five of 15 patients having ileal loops urinary diversions had shunt malfunction compared to just 1 of 24 patients having a bladder augmentation (4.1%) ( $P = 0.018$ ). One patient had a shunt malfunction after a vesicostomy, one after a ureteric re-implantation and one after an ACE procedure. For 6 of the 9

patients having shunt malfunction after surgery this was their second or subsequent abdominal operation compared to 12 of 30 not having shunt problems (ns). The timing of shunt dysfunction was 3 days to 8 weeks after surgery.

**Conclusion:** Shunt malfunction is common after major abdominal surgery in patients with NTD's and VP shunts. Patients and families need to be aware of this. More research is needed looking into the reasons for shunt dysfunction after different interventions

## S6 Phonological processing skills in children with myelomeningocele and shunted hydrocephalus

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S6

**Background:** On-going studies at our hospital, and elsewhere report difficulty with reading comprehension despite adequate word decoding skills in children with myelomeningocele and shunted hydrocephalus (MM/SH). In trying to determine likely origins of comprehension failure, our research team is presently examining the integrity of cognitive and language contributors to the understanding of written text. A potential contributor of interest is phonological processing. Phonological processing (processing of the sound structure of language) is strongly related to mastery of written language (reading and spelling), and has been clearly implicated in reading disabilities. This study reports preliminary data regarding phonological processing skills in a group of children with MM/SH.

**Materials and Methods:** 17 children with MM/SH (age range: 6–16 years) with average intelligence, and monolingual English-speaking backgrounds participated. Exclusionary criteria were: prior history of shunt infection, history of seizure or shunt malfunction within the previous three months, prior diagnoses of attention disorders and/or clinical depression.

Subtests of the Comprehensive Test of Phonological processing were administered to each child individually. Standard scores were obtained within three domains: phonological awareness, phonological memory and rapid naming.

**Results:** One sample *t*-tests revealed comparable performance for the MM/SH group and their age-matched norms for phonological awareness tasks. In contrast, the MM/SH group differed from the population norms in the following ways: poorer phonological memory, and difficulty with rapid naming tasks ( $P < 0.05$ ).

**Conclusions:** Findings begin to explain the reading strengths and weaknesses in children with MM/SH. Adequate awareness of the sound structure of language (phonologic awareness) puts these children at some advantage for being able to read written language (decode) efficiently. Inefficient retrieval of phonological information from long-term or permanent storage, reflected in

poor performance on rapid naming tasks decreases automaticity of word identification. Consequently, this potentially prevents freeing up of cognitive resources for efficient and timely comprehension of written text. Similarly, deficient phonological memory constrains the ability to learn new written and spoken vocabulary. Beyond reading, phonological processing issues reported here have theoretical implications for better understanding of memory and learning differences in this population.

## S7 Neuropsychological assessment of cerebellar malformation in Spina Bifida

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S7

**Background:** It is widely agreed that the typical cognitive profile of children with spina bifida is influenced by medical variables such as hydrocephalus, the height of the lesion and other physical complications [1]. However, very little is known about the specific contribution of the Arnold-Chiari malformation (ACM) in the information processing of these children. The aim of this study is to delineate in the cognitive profile the specific contribution of the ACM by comparing within a group of children with spina bifida among those with and without ACM.

**Materials and Methods:** Fifty-five children between 6 and 14 years of age were recruited from the spina bifida team of the Radboud University Nijmegen, Medical Centre. Of the whole group of children, those with a well documented presence or absence of ACM were included for further analysis (complete group). To eliminate the confounding influence of IQ a selection was made on the criteria of a total IQ of above 70 (non-retarded group). Table 1 presents the patient characteristics of the different subgroups. All children underwent a neuropsychological assessment which consisted of tests on a wide range of cognitive functions, comprising verbal, performal, and general intelligence, visuo-motor processing, selective and sustained attention, simultaneous and sequential memory, word fluency, and speed of information processing. To address the cerebellar cognitive functions, some tasks were included which are expected to measure cerebellar information processing [2,3].

**Results:** Results reveal significant differences in information processing among the children with and those without ACM. In the complete group, children with ACM performed significantly worse on the following cognitive functions: perception, visual-motor integration, verbal functioning, sequential memory, (non)verbal speed, and arithmetics. For the non-retarded group the data reveals a different cognitive profile. In this group, children with ACM showed impairments on tasks which require perception, imprinting and verbal memory, and verbal fluency.

**Table 1 Patient characteristics**

		<i>n</i>	Mean age	Age range	TIQ	VIQ	PIQ
Complete group	ACM-	10	10.5	6.8–14.1	89.6	93.3	87.5
	ACM+	23	10.4	6.5–13.3	72.7	79.8	69.1
Non-retarded group (TIQ>70)	ACM-	9	10.4	7.6–12.5	91.9	95.8	89.2
	ACM+	13	10.2	6.5–13.3	83.7	90.1	79.9

**Discussion:** In the complete group, a cognitive profile of strengths and weaknesses was found that resembles the one associated with hydrocephalus and spina bifida as presented in the literature. However, this typical cognitive profile was not found for the non-retarded group. The non-retarded ACM group showed impairments on cognitive tasks which are hypothesized to be mediated by the cerebellum and can be compared to cognitive deficits related to cerebellar pathology.

This study is part of the multidisciplinary research program 'Prognosis of Spina Bifida' of the Radboud University Nijmegen (The Netherlands).

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#### S8

##### Learning disabilities in a population-based group of children with hydrocephalus

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Cerebrospinal Fluid Research 2004, **1(Suppl 1)**:S8

**Clinical background:** The aim of this study was to assess cognitive functions in a population-based group of children with hydrocephalus. Specific questions to be answered were whether the cognitive outcome differed between children with and those without myelomeningocele (MMC) associated to the hydrocephalus and to see if there was a difference between the children with hydrocephalus present already at birth and those who developed it later during the first year of life, and thirdly to compare children who were born at full term with those born at earlier gestational ages.

**Materials and Methods:** Of all 103 children with hydrocephalus born 1989–1993 in the region, 73 were included in the study. Six children had died, and the 24 lost to follow-up did not differ from the study-group with respect to background variables. Intelligence was assessed with the Wechsler Intelligence Scales or the Griffith Developmental Scales.

**Results:** One third of the children were normally gifted with an IQ over 85, and another 30% had a low average IQ in the range 70-84. Learning disabilities of a more severe degree with an IQ less than 70 was found in 37% of the children. The median IQ for the whole group was 75. The median verbal IQ (VIQ) in those possible to fully assess was 89 and the median performance IQ (PIQ) 76 ( $P < 0.001$ ). An IQ  $< 70$  was found in 42% of the 45 children without MMC, and in 29% of those 28 with MMC. The children without MMC had a median IQ 76 compared to 75 in those with MMC. The IQ-levels in children without MMC varied more than in children with MMC. The latter clustered around the IQ-range 70–85. The 21 (29%) children who were born preterm had a lower IQ (68) than the 52 born at full term (IQ 76), and the 28 (38%) children born with hydrocephalus had a lower IQ (72) than the 45 who developed hydrocephalus later on (IQ 77). Children with cerebral palsy and/or epilepsy ( $n = 22$ ) added to the

hydrocephalus had a lower IQ (66) than those without associated impairments (IQ 78) ( $P < 0.01$ ).

**Conclusions:** Children with hydrocephalus need a thorough neuropsychological assessment before school-age to ensure adequate support and education. Even the one third near normally gifted children with IQ 70–85 needs special attention due to the well-known profile with relatively well preserved verbal functions but greatly impaired perceptual and non-verbal abilities.

#### S9

##### Abnormal visual functions in children with hydrocephalus

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Cerebrospinal Fluid Research 2004, **1(Suppl 1)**:S9

**Clinical background:** Children with surgically treated hydrocephalus manifest a range of ophthalmic disorders. The aim of this study was to assess visual function at school age in a population-based group of children with hydrocephalus.

**Materials and Methods:** All 92 children with surgically treated hydrocephalus born 1989–1993 in the western part of Sweden were invited to participate in the present population-based study. A comprehensive ophthalmologic examination was performed on 75 (82%) of these children and results were compared to those of an aged matched reference group ( $n = 140$ ).

**Results:** Abnormal ophthalmologic findings were found in 83 % of the children. Visual impairment (visual acuity  $< 0.3$ ) was measured in fifteen percent of the children and 34% had mildly reduced visual acuity (0.3–0.8) None in the reference group had a visual acuity of less than 0.5. Refractive errors were found in 47/70 (67%) (ref 9%), predominantly hyperopia. Strabismus was found in 70% (ref 4%) of the children, with almost equal frequency of esotropia and exotropia. Strabismus and visual impairment was more common among the children with hydrocephalus without myelomeningocele (MMC) than in children with MMC. There was no significant difference in ophthalmological outcome between the various aetiological causes of hydrocephalus without MMC. However, children born preterm with hydrocephalus had a tendency for worse ophthalmologic outcome than children born full-term.

**Conclusions:** A majority of children with hydrocephalus had ophthalmological abnormalities. Children with hydrocephalus and MMC were least affected while children born preterm were found to be at a high risk of visual impairment. Based on the high frequency of ophthalmological abnormalities, we suggest that children with hydrocephalus should be assessed by a paediatric ophthalmologist.

**S10****Item analysis of parent behavior ratings of executive function in children with spina bifida/hydrocephalus**

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Recent investigations have identified executive function deficits among children with Spina Bifida and hydrocephalus (SBH; Dennis *et al.*, 1999, Kinsman *et al.*, 1998). Executive functions involve “developing and approach” to performing a task that is not habitually performed (Mahone *et al.*, 2002a). Measurement of executive functions yields separable components including working memory, inhibitory control, and response preparation (Denckla, 1996; Pennington, 1997). Caregiver ratings of children with SBH highlight deficits in metacognition, but not behavioral regulation (Mahone *et al.*, 2002b). Within the metacognition area, parent reports of working memory and initiation problems correlate most significantly with their reports of self-care skills (Ries *et al.*, 2003), suggesting that executive functions may mediate the independent implementation of adaptive skills in those with Spina Bifida. In the present study, parents of 30 children (15 boys, 15 girls, ages 10–18) with SBH completed the Behavior Rating Inventory of Executive Function (BRIEF; Gioia *et al.*, 2000) as part of their child’s routine outpatient visit. The BRIEF Parent Form contains 86 items, on which parents rate their child’s behavior as occurring “never,” “sometimes,” or “often.” The BRIEF is organized into eight scales and two primary indices (Metacognition and Behavioral Regulation). Frequency of item endorsement for the five Metacognition Index scales (Initiate, Working Memory, Plan/Organize, Organization of Materials, and Monitor) was examined in order to identify statements most frequently reported by parents as areas of concern. Items were reported as significant problem areas if rated “often” by at least 40% of the parents in the sample. On the *Initiate* scale, items of greatest concern included “has trouble getting started on homework or chores,” and “lies around the house a lot (‘couch potato’).” On the *Working Memory* scale, items rated most frequently were: “has trouble with chores or tasks that have more than one step,” “needs help from an adult to stay on task,” and “has trouble finishing tasks.” On the *Plan/Organize* scale, problem behaviors included “becomes overwhelmed by large assignments,” and “does not plan ahead for school assignments.” On *Organization of Materials* scale, items endorsed most frequently included “keeps room messy,” “leaves a trail of belongings wherever he/she goes,” and “leaves messes that others have to clean up.” No items were endorsed as “often” at this rate on the *Monitor* scale. Our findings highlight the vulnerability of children with SBH to self-help tasks that depend on motor skills, speed, and the ability to manage multiple steps in chores. In contrast, BRIEF items involving rapid forgetting, boredom, and social intrusiveness were least frequently endorsed as problems by parents of children with SBH.

**S11****Magnetic motor evoked potentials in newborns with spina bifida**

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**Clinical background:** This study is part of the multidisciplinary research program “Prognosis of Spina Bifida” of the Radboud University Nijmegen (The Netherlands). Outcome prediction of spina bifida is difficult and an ongoing discussion about quality of life and selective treatment exists. Since new diagnostic instruments have become available, revision of the Lorber criteria, which were set in 1970, is warranted. Hence, we investigated the applicability of magnetic motor evoked potentials (MEP) in a prognostic model for spina bifida and we aim to determine motor conduction in neonatal spina bifida.

**Materials and Methods:** Magnetic stimulation of cervical and lumbar roots and the cortex was performed in 19 newborns with spina bifida (13 myelomeningocele, 3 myeloschisis, 1 lipomyelomeningocele, 2 spina bifida occulta). Responses were recorded from the tibialis anterior (TA), the quadriceps femoris (QF) and the biceps brachii (BB). As a control, responses were obtained from the TA by electrical peroneal nerve stimulation. Correlations between response characteristics (latency and amplitude) and clinical characteristics (neurosegmental motor level and type of the spinal lesion) were evaluated.

**Results:** Lumbar and cervical stimulation revealed responses in all target muscles in twelve subjects, responses in both the TA and QF in three subjects, responses just in the BB in two subjects and responses in just the TA or QF each in one subject. In contrast, cortical stimulation revealed responses in the BB or the QF each in one single subject only. Statistically significant left-to-right correlations were evident for amplitude, but not for latency. Correlations between neurosegmental motor level and latency and amplitude could not be demonstrated, but a difference in amplitude between different types of lesions appeared to exist.

**Conclusion:** The results have shown that MEP is applicable in newborns with spina bifida. The findings demonstrate that excitable neural tissue is present in or under the spinal lesion, even in very severe types of spina bifida. This is congruent with neuropathological studies. In addition, we were also able to determine motor conduction under the spinal lesion. Cortical stimulation was difficult, however; methodological aspects are likely to account for this. Still, we were able to detect corticospinal motor conduction over the spinal lesion in one infant with a thoracic myelomeningocele. Further considerations about functional implications, neuro-embryological aspects and prognostic value of these results will be discussed.

## S12

### Outcome of 167 fetuses diagnosed in utero as having apparently isolated ventriculomegaly

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S12

**Clinical background:** Ventriculomegaly is an abnormal enlargement of the cerebral ventricles and one of the most frequently diagnosed fetal abnormalities [1]. The condition is classified as isolated when it is seen in the absence of other fetal abnormalities. It is essential that any fetal abnormality is described to parents together with as accurate a prognosis as possible. This allows parents to reach an informed decision as to whether or not they are prepared to continue with a pregnancy. This series aims to clarify the prognosis that should be considered when apparently isolated ventriculomegaly is present on the initial anomaly antenatal ultrasound scan.

**Materials and Methods:** A retrospective cohort review of the clinical case notes of 167 fetuses recorded entered on the database of the Fetal Management Unit at St Mary's Hospital as having ventriculomegaly on the first anomaly ultrasound scan was performed. Findings from ultrasound reports and paediatric case notes were recorded and analysed.

**Results:** 47/167 (28%) cases of apparently isolated ventriculomegaly were later found to have complicating abnormalities. In this series 60 known deaths occurred (including terminations). Of the remaining 107 cases, there were 65 (61%) known live children whose development had been clinically noted. When ventriculomegaly was truly isolated (46 cases), this series showed that approximately 80% of cases had a normal developmental outcome. When apparently isolated ventriculomegaly was reclassified as complicated (19 cases) 42% of cases were judged to have normal development ( $P = 0.002$ ). 13% of cases in this series were found to have an abnormal karyotype. Male fetuses were registered as having isolated ventriculomegaly significantly more often than females ( $P = 0.040$ ).

**Conclusion:** When apparently isolated ventriculomegaly is identified on the initial anomaly antenatal ultrasound scanning, parents should be counselled that the majority of fetuses will progress to a normal developmental outcome. Isolated ventriculomegaly should continue to be classified as resolving, stable or progressive and as mild, moderate or severe but the prognosis assigned to each category is only applicable in the absence of further defects. If isolated ventriculomegaly is found to have complicating abnormalities as in approximately one quarter of this series, a significantly worse outcome is indicated. Male fetuses may have a greater mean atrial width than female fetuses as suggested by previous studies [2,3].

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## S13

### John D Holter and his century valve

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S13

**Background:** On December 22th 2003 John D Holter, one of the fathers of the hydrocephalus valves, died. In 1956 within a few weeks he had invented and produced the Holter-valve for his own son.

**Materials and Methods:** The author reviewed the literature concerning shunt and valve history since the fifties exhaustively. Additional informations base on unpublished personal correspondence with Holter since 1988 and 4 personal meetings. 31 Holter- and 111 Holter-Hausner-valves have been tested in our laboratory.

**Results:** Small trials with valved CSF shunts were made by Nulsen/Spitz in 1949 (3 patients, ball-valve), by Matson/Bush in the early fifties (18 implantations of magnetical ball-valves), by Pudenz/Heyer in 1955 (distal slit valve) and Sikkens/Engelsmann in 1956 (combined ball and slit-valve), but all designs remained prototypes. In 1956 Holters son presented a MMC-associated hydrocephalus, which was treated by Spitz with serial ventricular punctures. The silicone expert Holter was encouraged by Spitz, to design a new valve. The first prototype built in a few days had a diameter of ca. 10 mm and was oversized. The second prototype, produced in a few weeks incl. of catheters, was accepted by Spitz and implanted. For the first time the valve body, lips and catheters were made by silicone, which was introduced in the Neurosurgery as a superior shunt material. In summer 1956 Holter initiated the first commercial shunt production worldwide in a garage in Bridgeport (PA). The good handling, the extreme robustness and the hydraulic properties with a tendency to low flow properties were important preconditions in the successful introduction of shunts. In the seventies Holter developed a crucial slit design and founded a new company (Holter-Hausner). In 1987/88 a problematic charge of a secondary sticking silicone let to dysfunctions, recall and finally to the concourse of the company. It was tragically, that the last work of Holter, who had inaugurated silicone into the Neurosurgery, consisted in the identification of a defective silicone charge.

**Conclusion:** The Holter-valve, produced over 44 years, remains a milestone in the history of hydrocephalus and works still in some 100,000 patients.

## S14

### Pattern of regional white matter CBF in normal pressure hydrocephalus during infusion test

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S14

**Clinical background:** Mean CBF has been demonstrated to be lower in NPH than in normal controls. It is still unclear whether this is cause or effect of the neuronal dysfunction. The present

study aimed at assessing the distribution of baseline and change of regional white matter (WM) CBF in NPH before and during a controlled rise of ICP.

**Materials and Methods:** Ten patients with idiopathic NPH (mean age 69 years) underwent a CSF infusion study via a previously implanted right frontal ventricular catheter connected to a subcutaneous reservoir. CBF was measured by H2150 PET at baseline and then during the steady-state plateau of raised ICP. The PET images were co-registered to 3D structural T1-weighted MR images. In 10 healthy normal volunteers (mean age 45 years) image acquisition and reconstruction were accomplished in the same manner, except that only a baseline CBF determination was performed.

**Results:** The profile of baseline regional WM CBF in NPH patients showed a lowest CBF adjacent to the lateral ventricles with an increasing relationship with distance from the ventricles ( $P < 0.0001$ ), whereas in controls no relationship was apparent ( $P = 0.0748$ ). The percent changes of regional WM CBF in patients during raised ICP showed the deepest decrease close to ventricles with an increasing relationship with distance ( $P = 0.0007$ ).

**Conclusion:** The increasing profile of WM baseline CBF might suggest that a potential mechanism for CBF reduction in NPH is the collapse of the microcirculation induced by a parenchymal interstitial pressure gradient brought about by suffusion of CSF from the ventricles into the parenchyma.

## S15

### Outcome predictors in patients with normal pressure hydrocephalus: Preston NPH study — preliminary results from the first year

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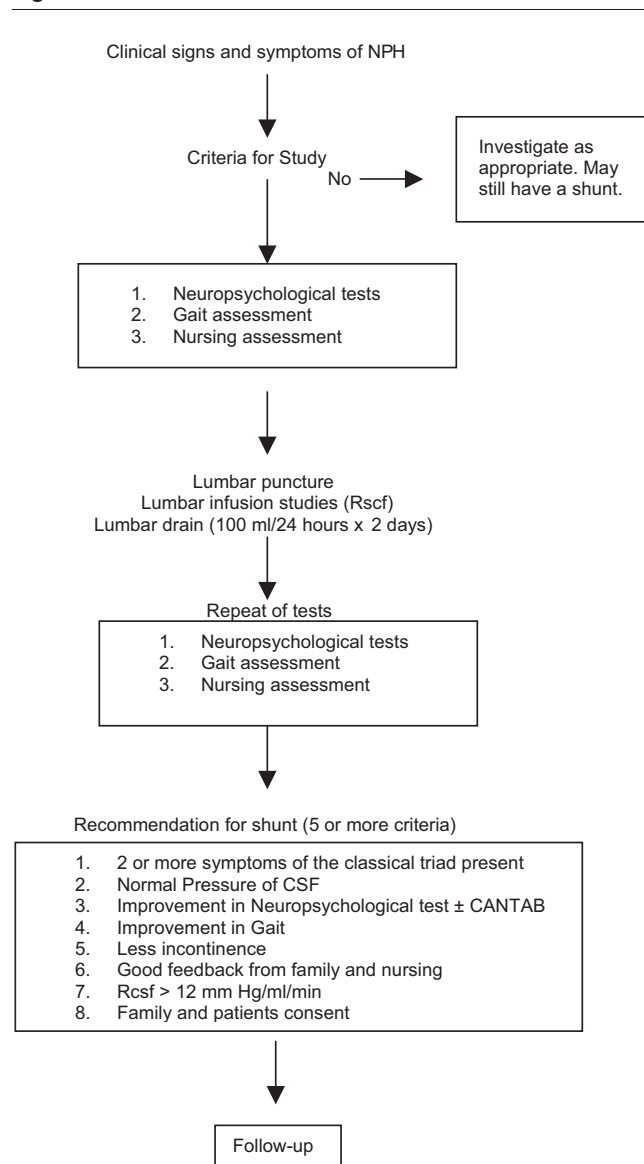
Cerebrospinal Fluid Research 2004, 1(Suppl 1):S15

**Clinical background:** Despite our advances in investigation and our knowledge of the disease over the years, the postoperative results of shunt implantation in patients with Normal Pressure Hydrocephalus (NPH) have not improved significantly. Reliable predictors of the course of the disease need to be identified. In the Preston NPH study we are trying to identify these factors, which are simple, reliable, cost-effective and reproducible in a prospective research.

**Materials and Methods:** Criteria for inclusion were 2 or more clinical symptoms of the classical triad for more than 6 months and a CT/MR scan finding consistent with normal pressure hydrocephalus. Exclusion criteria were defined. Figure 1 gives an evaluation algorithm. Table 1 describes with various tests used. Codman Programmable shunts were used and pressure set at opening pressure. Follow-up of the patients was carried out on all patients irrespective of treatment (Fig. 2).

**Results:** 44 patients were referred for assessment but only 36 met our criteria. 16 were shunted and 15 were not shunted. Average age was 77 years. 73% had Rout more than 12 mmHg/ml/min. Overall, lumbar drain did not significantly alter the performance of patients on the MMSE ( $F(1,28) = 1.7$ , ns) or the verbal fluency test ( $F(1,28) = 0.06$ , ns), However, lumbar drain significantly improved scores on the clock drawing task from 5.2 to 6 ( $F(1,28) = 6.8$ ,  $P < 0.02$ ). Overall, lumbar drain did not significantly alter the performance of patients on the time taken to walk 10 m ( $F(1,28) = 0.03$ , ns), or the time taken to turn 360

**Figure 1**



degrees ( $F(1,28) = 1.6$ , ns). However, lumbar drain significantly decreased the number of steps taken for the 10 m walk from 36 to 28 ( $F(1,28) = 4.8$ ,  $P < 0.05$ ). Similarly, the number of steps taken for the patients to turn 360 degrees also decreased from 8 to 5 ( $F(1,28) = 11.1$ ,  $P < 0.01$ ).

There were no significant differences between patients selected for shunts and those not on any of the neuropsychological tests or gait assessments. Patients selected for shunting showed a significant increase in number of words generated in the verbal fluency FAS task following lumbar drain from 24 to 35, whilst those who were not selected actually showed a small decrease from 32 to 29 ( $F(1,28) = 10.1$ ,  $P < 0.01$ ). Only one patient developed meningitis, two had chronic subdural and one had a shunt revision. Outcome is measured with QOL scores (SF-36, EURO-QOL).

**Conclusion:** Lumbar drain improves test performance on the clock drawing task whilst also improving gait. Verbal fluency (FAS)

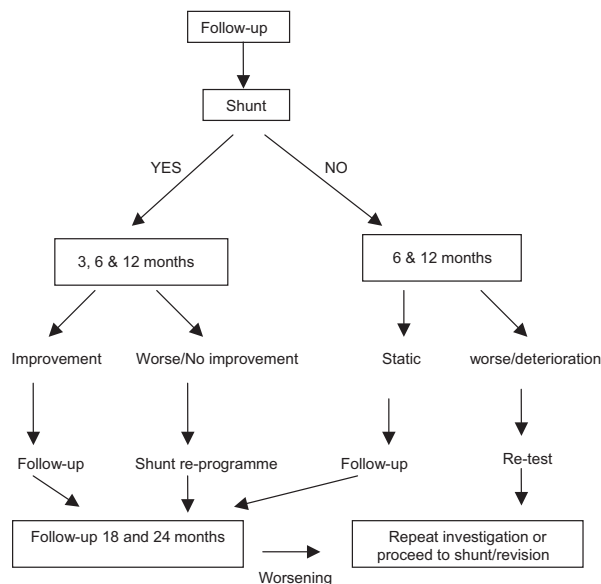
**Table 1**

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Neuropsychological test:	
1. NART – premorbid IQ	
2. BDI – screen for depression	
3. MMSE	
4. Verbal fluency	
5. Clock drawing test	
6. CANTAB:	a. Motor screening
	b. Pattern recognition
	c. Spatial recognition memory
	d. Spatial span
	e. ID/ED attentional set shifting
	f. Reaction time
Gait assessment:	
10 m walking-time/steps	
360° turn-time/teps	
Nursing assessment:	
Interaction	
Family feedback	
Incontinence Pads	
Feeding	

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**Figure 2**



task appeared to selectively improve following lumbar drain in those selected for shunts. There were no overall differences in the neuropsychological or gait performance in the patients selected for shunts and those who were not. Rout > 12 mmHg/ml/min and drainage test predict a positive outcome. Clearly these conclusions must be interpreted with some caution as the sample size is limited and no follow up results are included. These indicate that administering one single test may not be useful in assessing suitability for shunting. However, further assessments need to be undertaken before any firm conclusions can be reached. We plan to recruit and follow up our patients for at least 2 years.

**S16**

**Changes in local cerebral blood flow were associated with functional improvement of patients with idiopathic Normal-pressure hydrocephalus after shunt-treatment – a <sup>15</sup>O-H<sub>2</sub>O- PET-Study**

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S16

**Clinical background:** In idiopathic Normal pressure hydrocephalus (iNPH) symptoms, the “locus of dysfunction” is still not fully understood. The authors investigated local cerebral blood flow in patients before and after shunt treatment questioning whether regional metabolic disturbances might be of relevance to the patients outcome.

**Materials and Methods:** <sup>15</sup>O-H<sub>2</sub>O–PET-CBF studies (Siemens ECAT 951/31, Erlangen, Germany) were performed in 65 patients (76 ± 13 years) with idiopathic normal-pressure hydrocephalus selected for shunt surgery based on clinical and radiological criteria and the presence of B-waves and/or increased CSF-resistance values obtained by a constant lumbar infusion test. PET-CBF studies were done before, at one week and at 7 months after VP-shunt. Clinical outcome was determined at 7 months after shunt placement by grading (scoring) the patients clinical status based on the degree of functional impairment according to the STEIN and LANGFITT scale. Thereby, patients were classified into responders (n = 33) and non-responders (n = 32). Regional specific effects in the <sup>15</sup>O-H<sub>2</sub>O-uptake were assessed using statistical parametric mapping (SPM99, Wellcome Department, London, UK). An uncorrected P < 0.001 (Z > 3.09) on voxel level was selected as a threshold of significance.

**Results:** A high degree of functional impairment obtained by the clinical scale correlated with a reduced <sup>15</sup>O-H<sub>2</sub>O-uptake in an extended area (1239 voxel) in the mesial frontal cortex (Z = 4.41) and the anterior temporal cortex (469 voxel, Z = 4.07). After shunting, <sup>15</sup>O-H<sub>2</sub>O-uptake in the superior frontomesial and frontolateral cortex, both encompassing parts of the supplementary motor areas (Brodmann area 6,8,9), increased in responders (241 voxel, Z = 4.35), while non-responders displayed corresponding decreases in the <sup>15</sup>O-H<sub>2</sub>O-uptake (955 voxel, Z = 4.55). Furthermore, in non-responders a significant symmetric reduction in the sensory motor cortex before surgery was found (right: 140 voxel, Z = 3.83, left: 48 voxel, Z = 3.78).

**Conclusion:** Local cerebral blood flow and its changes after shunting correlated with both clinical impairment before and functional outcome after shunt treatment. Thereby, the relevance of regional metabolic disturbances for symptomatology and functional outcome in idiopathic NPH is underlined. The findings in the frontomesial and the supplementary motor cortex correlate with activation studies in Parkinson’s disease, however, might indicate the significance of supplementary motor areas for initiation and control of movements in idiopathic NPH-patients.

**S17****Neuropsychological profile of patients with normal pressure hydrocephalus and Alzheimer's disease**

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*Cerebrospinal Fluid Research 2004, 1(Suppl 1):S17*

Normal pressure hydrocephalus (NPH) is a potentially treatable neurological disorder if diagnosed accurately and early. If misdiagnosed, or left untreated, the pattern is one of continuing physical and cognitive decline, which becomes increasingly irreversible as more diffuse brain damage is caused. Cognitive profiling is a technique, which can aid early and accurate detection of NPH.

This paper presents the results of two studies showing specific contrasting patterns of neuropsychological dysfunction in subgroups of patients with either early or late stage NPH with patients either in the prodromal stages (mild cognitive impairment) or later stages of Alzheimer's disease. The results demonstrate that there are differential patterns that can be observed in patients with NPH, which can be used effectively within a clinic-context to enhance accurate and early diagnosis and improve long-term prognosis.

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**S18****Changes in pTau in CSF and brain relating to chronic hydrocephalus**

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*Cerebrospinal Fluid Research 2004, 1(Suppl 1):S18*

**Background:** Changes in CSF circulation, as seen in adult chronic hydrocephalus (CH), can result in changes in CSF content, neurodegeneration, a loss of neurological function, and death. The microtubule-associated protein, Tau has been implicated in the pathogenic mechanisms of dementia and neurodegenerative disorders through accumulation in CSF and brain. To date, the relationship between the CSF circulation changes in CH and the levels of tau in CSF and brain has not been studied.

**Materials and Methods:** This study used an experimental model of chronic obstructive hydrocephalus developed in our laboratory to investigate whether changes in CSF circulation could have an effect on the level of Tau protein in CSF and brain. The degree of CH-CSF impairment was determined on the basis of changes in CSF volume, pressure and turnover. CSF levels of Tau were quantified using standard ELISA technique at baseline (pre-CH) and sacrifice (post-CH). To determine the level of Tau protein in brain, immunological and histological methods were used to identify neurons and glial cells, and stereologic cell counting procedure was used to determine the density of Tau+ cells in the brain.

**Results:** Chronic hydrocephalus was surgically induced in 12 adult male canines where the baseline levels of ICP (range 5–16 mmHg) and ratio of ventricle to brain (range 1.14–4.43 × 10<sup>3</sup>) increased 22.2% and 660% respectively. CH also resulted in an average 22.9% decrease in the rate of CSF clearance. In 8 of 12 cases the level of CSF Tau increased an average 52.3%, however in 4 animals a decrease (14.1%) was observed. Overall, the level of Tau in CSF did not significantly correlate with changes in CSF volume, pressure, or turnover. The density of Tau+ cells was assessed in 7 animals (4 CH, 3 CTL) and was significantly higher in the cortex of animals with CH lasting <30 days (25%) and >30 days (18%) when compared to experimental controls (*P* = 0.05). The density of Tau+ cells was also higher in white matter for animals with CH (3-33%).

**Conclusion:** Our preliminary findings suggest that CSF circulation may play a physiologically significant role in the pathophysiology of Tau protein clearance, and in turn may influence brain parenchymal tau levels. These results reinforce the suggestion that Tau may play a role in the dementia of chronic hydrocephalus as has been considered in other dementias. Measures of Tau may be important in developing future diagnostic and/or treatment methods in CH.

**S19****Probable NPH in patients with clinical AD: further support for the AD-NPH syndrome and CSF circulatory failure**

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*Cerebrospinal Fluid Research 2004, 1(Suppl 1):S19*

**Clinical background:** To determine the incidence of elevated CSF pressure (CSFP) in patients with a clinical diagnosis of AD. Several studies have documented the coexistence of AD pathology in NPH patients at a rate greater than chance. There has been no corollary study addressing the incidence of NPH among patients with AD. We report elevated CSFP, consistent with NPH, in a small subset of AD patients (AD-NPH) enrolled in an ongoing clinical trial of chronic low-flow CSF drainage, via a novel VP shunt, in AD.

**Materials and Methods:** Subjects meeting NINDS-ADRDA criteria for probable AD were screened to exclude those with clinical or radiographic signs of NPH before being enrolled in the trial. Opening CSFP was measured during device implantation at a controlled pCO<sub>2</sub> of 40 torr. If mean CSFP were >200 mmH<sub>2</sub>O, the subject was excluded from the study due to probable AD-NPH syndrome.

**Results:** Seven of 210 subjects (3.3%), mean age 66 ± 7 yrs, had CSFP >200 mmH<sub>2</sub>O (mean 249 ± 20). AD subjects CSFP was 143 ± 26 mmH<sub>2</sub>O, *P* = DISCUSSION: Despite strict exclusion criteria, 3.3% of AD subjects were found also to have NPH by intra-operative CSFP measurements. AD patients had a mean CSFP of 143 ± 26 mmH<sub>2</sub>O vs. 249 ± 20 for the AD-NPH group. This is the first set of observations concerning occult NPH in AD subjects, and likely represents an underestimate of the incidence of this "hybrid" condition. We have demonstrated reduced CSF production and turnover in both AD and NPH. Increased resistance to CSF absorption in AD, presumably due to amyloid deposition in the meninges and arachnoid granulations, has now been documented.

**Conclusions:** We suggest that both AD and NPH are physiologically related to CSF circulatory failure. If the initial dominant change is in CSF production, AD results; if decrease in CSF absorption predominates, NPH develops first. The occurrence of either disease may predispose vulnerable patients to developing the other.

## S20

### Cerebrovascular pressure-reactivity in normal pressure hydrocephalus

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S20

**Clinical background:** We investigated the possible relationship between vascular reactivity and the resistance to CSF outflow in a group of shunted and non-shunted NPH patients.

**Materials and Methods:** Sixty eight patients (47 non-shunted and 21 shunted) with NPH have been examined. During the examination ICP was measured in the ventricles (using a needle inserted into a pre-implanted Ommaya reservoir) at baseline and in response to a constant rate infusion (1.5 ml/min) of normal saline. Resistance to CSF outflow (R<sub>csf</sub>) was measured as an increase of ICP divided by the infusion rate. During the test, arterial pressure was monitored continuously using a Finapres finger cuff. Cerebrovascular pressure-reactivity was assessed as a moving correlation coefficient between coherent 'slow waves' of ICP and spontaneous fluctuations of arterial blood pressure (PR<sub>x</sub> index). This variable has been demonstrated previously to correlate with autoregulation of CBF [1]. Positive value of PR<sub>x</sub> reveals impaired cerebrovascular pressure-reactivity, whereas negative values indicate normal reactivity.

**Results:** In non-shunted patients impaired pressure reactivity was associated with lower resistance to CSF outflow: (PR<sub>x</sub> versus R<sub>csf</sub>: R = -0.5; P < 0.0005). This relationship was inverted in shunted patients: PR<sub>x</sub> was positively correlated with R<sub>csf</sub> (R = 0.51; P < 0.03).

**Conclusion:** Cerebrovascular pressure-reactivity is disturbed in patients with normal resistance to CSF outflow, suggesting underlying cerebrovascular disease. After shunting the pressure-reactivity strongly depends on shunt function and may deteriorate when the shunt malfunctions.

#### Reference

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## S21

### A short neuropsychological test battery for measuring functional outcome after shunt placement in patients with normal pressure hydrocephalus

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S21

**Background:** To find a simple neuropsychological test battery that accurately measures functional outcome early after shunting in Normal pressure hydrocephalus (NPH).

**Materials and Methods:** Cognitive and motor function was assessed in 30 NPH patients (65 ± 13 years) at three time

intervals using 10 neuropsychological measures performed at baseline, at one week and at seven months after surgery. Assessment of functional outcome, using the Stein & Langfitt score, occurred at seven months and patients were classified as responders (n = 16) and non-responders (n = 14). To determine most representative measures (test-battery) for the NPH cognitive and motor function, factor analysis was performed on the preoperative neuropsychological results. The pre- and early postoperative results were compared in the two groups and the accuracy of predicting functional outcome by early psychometric test results obtained at one week after shunting was assessed (Logistic regression).

**Results:** Three of the ten psychometric tests analyzed emerged as useful for early assessment of cognitive and motor function in NPH: Visual attention, immediate verbal recall and motor precision. At one week after shunting, changes in these three measures were already different in the two groups; responders had a marked improvement in visual attention, P = 0.004 and motor precision, P = 0.008, when compared to non-responders. In verbal recall responders remained stable whereas non-responders deteriorated, P = 0.007. These early changes correlated with the late functional outcome with an accuracy of 87% (non responders:90%; responders:85%).

**Conclusion:** Three psychometric tests provide early and reliable measures of functional outcome in NPH. In follow-up examination, these tests offer a practical and standardized tool to monitor the patient status, to reset adjustable valves and to compare the clinical results from different centers.

## S22

### Volume transmission of CSF: complications in aging and Alzheimer's disease

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S22

In advanced aging and Alzheimer's disease (AD), there are many degenerative changes in the choroid plexus-CSF system which have adverse effects on CNS nutrient delivery, pharmacokinetics of drug disposition, and the removal of organic anions and proteins from ventricular CSF. The choroid plexus is a key locus for the failure in CSF dynamics, because fluid output from the epithelial cells is compromised following biochemical (oxidations of cellular membrane components and extracellular deposition of Ig complexes) and histological damage. Heat shock protein expression in the choroid plexus is also altered in AD, with HSP 90 showing the greatest elevation of several stress proteins analyzed. The reduced CSF formation, coupled with the ventriculomegaly, results in lower fluid turnover in the normal pressure hydrocephalus (NPH). As CSF turnover decreases, and the transport interfaces become less efficient, there is accumulation of proteins (such as amyloid beta) and deleterious catabolites in the brain interstitium. The compromised volume transmission (or bulk flow) of the CSF through the ventricular system also leads to a diminished supply of micronutrients and growth factors to the brain. In advanced stages of AD, the blood-brain barrier as well as the blood-CSF barrier are more permeable, and so CSF homeostasis can be disrupted. As more attention is focused on investigating the bi-directional transport processes at the CNS barrier systems, and on the chemical

composition and volume of the CSF in AD, and in dementia, it should be possible to get a clearer picture of the effects of extracellular (brain interstitial) fluid dynamics on the progressive deterioration of neuronal function. Our histochemical and immunocytochemical analyses of autopsied human brain and choroidal specimens also support the hypothesis that disruptions in the CNS barriers lead to exacerbation of AD pathology.

**Funding:** Supported by Lifespan (Rhode Island Hospital), the Department of Neurosurgery, and by NIH NS RO1 27601 (CEJ).

## S23

### Hydrocephalus in children-epidemiology and outcome

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*Cerebrospinal Fluid Research 2004, 1(Suppl 1):S23*

**Clinical background:** A population based study on live birth prevalence, aetiology and clinical outcome in children with hydrocephalus.

**Materials and Methods:** All 206 children with hydrocephalus born during the ten-year period 1989–98 in the western part of Sweden. Etiological and clinical information were collected from records.

**Results:** The prevalence of hydrocephalus was 0.8 per 1000 livebirths, for isolated hydrocephalus 0.48 and for hydrocephalus associated with myelomeningocele (MMC) 0.32/1000. The prevalence decreased during the period from 0.54 to 0.43/1000 for simple hydrocephalus and from 0.35 to 0.33/1000 livebirths for MMC.

The aetiology was prenatal in 67/122 (55%) children without MMC, peri-postnatal in 54 (44%) and unknown in one. In children born very preterm the origin was perinatal in 22/24 (92%) almost exclusively caused by cerebral haemorrhage. The cause in most children born at term was prenatal maldevelopments.

A ventriculoperitoneal shunt was inserted in 183/201 (91%) children treated within the region. Ventriculostomy was used as initial intervention in 18 cases and was the final solution to the problem in 14 cases. There was a need for at least one revision in 69%.

Of 195 surviving children 63 had mental retardation, 36 cerebral palsy and 43 epilepsy. No associated impairment was present in 103 children (54%) except for those resulting from the spinal lesion in 55 children with MMC. Information was missing in three children. The prognosis was poor in children born very preterm (gestational age <32 weeks) of whom all 21 children had major neuroimpairments, mental retardation in 14, cerebral palsy in 17 and epilepsy in 13. Another subgroup with relatively poor prognosis was children with isolated hydrocephalus overt at birth where 33/42 (79%) had some associated major neuroimpairment.

**Conclusion:** A decreasing trend of hydrocephalus was observed during the ten-year period. Children born very preterm had a poor outcome. The frequent need for neurosurgical revisions indicated a need for further development of treatment strategies.

## S24

### VP shunt infections – does antisepsis continue to work?

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Shunt complications are serious problems when they occur and can be reduced significantly by taking great care during initial insertion. In 1984, we reported an incidence of 2.4% infection, following the introduction of an antiseptic technique based on Listerian principles. We wanted to review our latest infection rate. This is a 10 year retrospective study, reviewing all medical records of children who had their first VP shunt insertion between 1993 and 2003. A total of 94 children had 150 shunt insertions. Sixty seven out of the 94 children had spina bifida, 13 had progressive hydrocephalus due to intraventricular haemorrhage, 7 had aqueduct Stenosis, 3 had holoprocencephaly, 2 following encephalocoele resection, 1 post meningitis, and 1 with Dandy-Walker syndrome.

There were 3 deaths, two of which were in children with severe spina bifida who had been managed conservatively. These shunts were inserted for palliative reasons in the presence of significant myelomeningocele infections. The third death was due to late arrival of a child with a blocked shunt.

There were 4 children with shunt infections (2.2%) and all were treated successfully. Though normal CRP levels at 6 weeks follow up was reassuring, raised levels did not always correlate with infections. In the 4 children who had shunt infections, it was picked up well before the 6 weeks CRP check. However, no patient with a normal CRP level at 6 weeks was subsequently shown to have shunt infection.

In conclusion, we feel that strict antisepsis is still one of the best ways to prevent shunt infections.

## S25

### VP shunts – what is the commonest complication?

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Whilst a VP shunt is an effective way of draining CSF in hydrocephalus, complications are still a significant problem. We retrospectively analysed charts of 94 children between the years 1993 and 2003 to estimate the common complications. The commonest complication was shunt blockage (30%). This was followed by shunt fractures (4.2%). Infection was 2.2%. When a shunt malfunctions due to blockage, the commonest area of blockage was within the intraventricular component (90%). Most children who presented with shunt blockage needed more than one revision. Overall 44 revisions were carried out in 23 children. Protein levels of CSF did not correlate with frequency of blockage. In an endeavour to establish whether shunt blockage is related to intraventricular catheter position, an analysis is made of the available images. Furthermore, the recent literature in relation to shunt blockage is also reviewed. There were no shunt fractures below the age of three years, and the routine policy of doing an X-ray shunt series should be discouraged in children less than 2 years old with unites shunts.

## S26

### Long term outcome in babies born with open spina bifida and big heads

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S26

**Background:** Hydrocephalus is common in spina bifida. There have been no prospective studies to mean age 35 of babies born with open spina bifida and a birth head circumference  $\geq 90^{\text{th}}$  centile. This study was supported by ASBAH (Association of Spina Bifida and Hydrocephalus).

**Objective:** To investigate long term outcome in terms of survival, CSF shunt history, disability and lifestyle in babies born with open spina bifida and big heads.

**Design:** Prospective cohort study,

**Participants:** Well-documented cohort of 117 consecutive cases of open spina bifida whose backs were closed non-selectively at birth between 1963 and 1971.

**Materials and Methods:** Survivors (mean age 35) and their carers were surveyed by postal questionnaire and telephone interview in 2002.

**Results:** Ascertainment was 100%. Of 54 survivors, 11 were born with a birth head circumference  $\geq 90^{\text{th}}$  centile and 43 with a birth head circumference  $< 90^{\text{th}}$  centile. Survival at age 35 was similar in the two groups: 40% (11/28) compared with 51% (43/89) respectively (NS). All 11 survivors born with big heads had had a CSF shunt inserted compared with 81% (35/43) of the remainder (NS). However 73% (8/11) had needed their shunt revised after the age of 2 compared with 30% (13/43) of the remainder ( $P < 0.05$ ). All 11 survivors born with big heads had visual defects compared with 53% (23/43) of the remainder ( $P < 0.01$ ). Six (55%) were on treatment for epilepsy compared with 4 (9%) of the remainder ( $P < 0.01$ ); four of the eleven had suffered CNS infection. Lifestyles were restricted with only one of the eleven survivors born with a big head living independently in the community compared with 49% (21/43) of the remainder ( $P < 0.05$ ). Only one of the eleven drove a car and none worked in open employment.

**Conclusion:** Although survival at age 35 was similar, long term outcome in babies born with big heads was worse than in the remainder with two of the eleven survivors totally blind, and only one living independently in the community. Birth head circumference  $\geq 90^{\text{th}}$  centile may be a predictor of worse long term outcome in open spina bifida.

## S27

### Assessment of antimicrobial shunt and external drain catheters

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S27

**Background:** In an attempt to reduce the rate of shunt or external drain infection, various "antimicrobial" catheters have been developed. These have given encouraging results on pre-clinical testing, but the test methods are often poorly predictive of clinical performance. Requirements of clinically effective

"antimicrobial" catheters need to be established, and test methods relevant to pathogenesis and infection risk developed in order to avoid waste of research time and investment, and particularly to avoid clinical disappointment. In addition, the principles of effective antimicrobial catheters need to be laid down.

**Materials and Methods:** Three different commercially available "antimicrobial" catheters were assessed using systems developed to determine their likely clinical performance. These assessed spectrum and duration of antimicrobial activity, bacterial adherence, and the tK100 (time taken to kill 100% of adhered bacteria) using chemiluminescence and differential membrane permeability fluorescence. Serial challenge under flow/perfusion was also carried out. Tests were carried out in the presence of a plasma protein conditioning film. In two cases where this was pertinent, mechanical properties were determined and confocal microscopy was done to determine distribution of the antimicrobials in the shunt material. In the third case, the coating was located using pH 4 tetracycline fluorescence.

**Results:** The coated catheter was found to be coated on the outer surface only, and despite the use of huge antimicrobial concentrations it failed to prevent catheter colonisation. The remaining two, one admixed and one impregnated, both showed longlasting antimicrobial activity but only one was capable of achieving tK100. The admixed catheter showed adverse mechanical properties explained by the microscopy results.

**Conclusion:** Design of "antimicrobial" shunt or EVD catheters must take account of the pathogenesis of infection, and they must be subjected to preclinical testing that is highly predictable of clinical efficacy.

## S28

### Intrauterine surgery for myelomeningocele and MOMS

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S28

Ms. Worcester of the Tallahassee Bureau reported in October 2003 that Dr. Joseph Bruner told a world conference in Lisbon that intrauterine myelomeningocele repair (IUMR) results in fewer urinary tract infections, less gastrointestinal reflux, improved leg function and cognitive development and less need for a cerebrospinal fluid shunt. Our experience has been with only 22 cases. The authors of articles from Children's Hospital of Philadelphia (CHOP) and Vanderbilt admit to premature births causing death (5 or 0.03%), infection, development of demoid tumours causing paralysis and maternal morbidity (*N Engl J Med* 2002). And their latest scientific article stated their CSF shunt rate is only 54.8% (*Pediatr Neurosurg* 2003). Our data are from five centres with experience in following patients referred for IUMR to CHOP, Vanderbilt or San Francisco. 20 of 22 mother/patients pairs (91%) are known to have significant complications as follows: 18/22 (82%) have CSF shunts one of whom had cardiac arrest due to high CSF pressure (2 were lost to follow up because their local centre recommended a shunt but the IUMR centre did not), 4 (17%) had the IUMR site dehisce, 4 (17%) developed sepsis — 3 meningitis and 1 sepsis and intracranial bleed due to prematurity, 7 had symptoms of Chiari II (30%) of which 3 (14%) were decompressed and 1 has required both gastrostomy and

tracheotomy with ventilation, 8 patients (36%) were born prematurely and spent prolonged time in the neonatal intensive care nursery, 2 patients had hydromyelia, and one patient each developed mental retardation, tethered cord, broken femur, scoliosis or kyphosis as young infants. Five mothers developed significant complications as follows: one each rupture of the uterus, abruption of the placenta, intrauterine haemorrhage, dehiscence of her abdominal wound and oligohydramnios. These percentages add up to greater than the 91% because some individual pairs had more than one complication.

**Conclusion:** The Management of Myelomeningocele Study (MOMS) being funded by the U S Government in the 3 centres mentioned above is critically important

## S29

### Proteomics study of CSF composition in the developing H-Tx rat.

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*Cerebrospinal Fluid Research 2004, 1(Suppl 1):S29*

Previous work of our group has shown that CSF from affected H-Tx rat fetuses aged E20 and E21 has an inhibitory effect on cortical cell proliferation in culture but that this effect does not occur with normal CSF. The inhibitory effects are removed by heating the CSF suggesting that the active component(s) is a protein(s).

These data led us to the use of a proteomics approach to investigate the protein profile of CSF and compare this between normal and affected CSF from fetuses at late stages of gestation. We compared CSF collected from the lateral ventricles of affected fetuses at E17-E21 to CSF collected from the cisterna magna of normal animals of the same ages. 2D gel results showed significant differences between normal and affected CSF at the different ages. MALDI-TOF Mass spectroscopy was used to identify some of the different proteins and Liquid Chromatography-Mass Spectroscopy was used to confirm the data.

Interesting components, such as a reelin precursor, NGF precursor, alpha-feto protein and apolipoprotein were found to change with age and whether collected from normal or affected animals. Reelin, NGF and alpha-feto protein are all known to have an important role in cortical development. Reelin precursor was present in CSF from normal animals but was absent in H-Tx fetuses aged E21 and P0 (the day of birth). NGF was present in both animal groups but in reduced amounts in the H-Tx rats on Day E21. Alpha-feto protein was present in both and in the same amount. With increasing age the total amount of protein decreases in the CSF of both normal and affected fetuses.

These findings strengthen the hypothesis that CSF has got an important role in normal brain development and in the abnormal development associated with early-onset hydrocephalus.

Proteomics provides an important method for the identification of CSF proteins particularly where the amount of CSF available is small; all other methods require much larger amounts which is a major restriction for the present study. LC-MS is a new technique that identifies large numbers of proteins in very small samples and this will aid the identification, purification and analysis of candidate proteins involved in normal and abnormal development.

## S30

### Linkage analysis for hydrocephalus in the LEW/Jms rat strain

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*Cerebrospinal Fluid Research 2004, 1(Suppl 1):S30*

The Lew/Jms rat is an inbred strain with severe inherited hydrocephalus. The hydrocephalus starts in late gestation and occurs twice as often in males as females. The aim of this study was to locate the genetic loci linked to the hydrocephalus on the rat genome. Methods: Progeny were generated from two different backcrosses with Fischer F344 rats: one bred using male LEW/Jms rats for each pairing and the other using female LEW/Jms rats. Tissue was collected for DNA extraction and the brains were fixed and sliced for measurement of ventricular dilatation. Quantitative trait locus (QTL) mapping is a method whereby genetic loci for a quantitative trait are localized to specific chromosomal regions. A two-stage genome scan was performed on the hydrocephalic progeny and the same number of non-hydrocephalic progeny from both crosses, using a panel of DNA microsatellite markers previously determined to be polymorphic between the LEW/Jms and F344 strains. Linkage of chromosomal regions to hydrocephalus was determined from statistical association between genotype and phenotype ( $\chi^2$  and LOD score). Results: The backcross using male LEW/Jms rats resulted in 918 progeny of which 167 had severe or mild hydrocephalus (18.2%) and there were significantly more affected males than females (109:58,  $P < 0.001$ ). The backcross using female rats resulted in a total of 910 rats of which 182 had severe or mild hydrocephalus (19.9%). Again, there were more males than females with hydrocephalus (102:80) but it was not significant. The mean severity of ventricular dilatation was significantly different for the two crosses ( $0.58 \pm 0.01$ ,  $0.61 \pm 0.01$ ,  $P < 0.05$ ), and both groups had significantly smaller ventricles than the parental LEW/Jms strain ( $0.66 \pm 0.01$ ,  $P < 0.01$  and  $0.05$ ). QTL mapping produced different results for the two crosses. The backcross using two male LEW/Jms rats showed possible linkage on chromosomes 1, 5, 17 and 19. None reached the full significance required for a genome-wide scan and only Chrs 5 and 19 were suggestive for significance. The backcross using two female rats showed possible linkage on Chrs 2, 4, and 17. There was full significance on Chr 2 with a LOD score of 3.91. Combining the data for both crosses also resulted in a locus that was close to full significance on Chr 17, LOD = 2.71. The linkage data for Chrs 1 and 2 showed sex specificity when analysed separately for males and females. Although not fully x-linked, investigations are ongoing to determine if there is partial linkage with the X chromosome. It is concluded that the expression of hydrocephalus in this strain is dependent on different genetic loci for male and female rats.

### S31

#### **Altered expression of sialic acid-bearing glycoconjugates as revealed by lectin binding to choroid plexus in perinatal hydrocephalic rats**

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S31

Glycoconjugates perform key roles in the development and maintenance of the CNS. A chief saccharide element in brain development is sialic acid, usually occurring as N-acetylneuraminic acid. Previous studies by H. Jones et al. demonstrated that glyco-conjugate secretions into CSF, by circumventricular organs like the SCO, may be associated with hydrocephalus development. Therefore, we used 4 lectins (LPA, SNA, MAL-II and WGA), specific for several forms of sialic acid, to probe for alterations in sialic acid-bearing glycoconjugate profiles in the CSF-secreting choroid plexus (CP) of the HTx rat hydrocephalus model. Lectins are proteins that bind to carbohydrate residues in an antibody-like manner. We used 3 cohorts of rats: prenatal (20 days of gestation); neonatal (1 day after birth); and postnatal (4 days). Five choroid epithelial domains/parameters were analyzed: apical cell surface; lateral surface; basal surface; cytoplasm; and all domains considered collectively. Staining intensity was judged visually on a 1+ to 4+ scale, at 400x. Means of sialic acid staining intensity were calculated using 5 animals from each cohort.

**Results:** Staining of controls decreased about 25% per stage, whereas it remained high (4+) in hydrocephalic animals at all stages. At all perinatal stages, sialic acid expression was higher in hydrocephalic animals than in controls. Staining of all cellular domains, normally and in hydrocephalus, was strongest in neonates. With regard to individual domains, the most intense staining of normal and hydrocephalic animals was seen in the apical domain of CP cells. The greatest differential in staining between normal and hydrocephalic rats was in the cytoplasmic domain. We postulate that the enhanced expression of sialic acid-bearing glycoconjugates in CP is related to changes in hydrocephalic CSF parameters.

**Funding:** Supported by Lifespan (Rhode Island Hospital), the Department of Neurosurgery, and by NIH NS RO1 27601 (CEJ).

### S32

#### **The role of cerebrospinal fluid on chick cerebral cortex development**

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S32

**Background:** Cerebrospinal fluid (CSF) is mainly produced by the choroid plexuses within the ventricles of the brain. Hydrocephalus occurs when the normal flow of CSF is obstructed and fluid accumulates. The CSF circulates in a regular manner from the formation of the neural tube and enables it to carry chemical information. From the lateral ventricles CSF passes into the third ventricle and then moves on to the fourth ventricle. CSF leaves the ventricular system and enters the subarachnoid spaces. Ultimately CSF drains out of the subarachnoid space into the sagittal sinus via the arachnoid villi. CSF thus flows through the

ventricular system passing over all regions of germinal activity. In previous studies on a rat model of hydrocephalus, the hydrocephalic Texas (HTx) rat, we showed that CSF has a potential role in the development of the cerebral cortex. In this study chick embryos were used to show the importance of CSF on brain development

**Materials and Methods:** In chick embryos the neural plate and neural tube appear 20 and 28 hours after incubation. The CSF starts to flow immediately after closure of the neural tube and in advance of the formation of the choroid plexuses. This CSF appears to be produced by the brain tissues. The chick embryos were cannulated in situ with a fine capillary tube early in development (days 3 and 5 after incubation) to drain CSF out of the ventricular system. After surgery the embryos were incubated for another 3 days. All the CSF drained and control embryos were collected, fixed in paraformaldehyde and coronal and sagittal 10 µm sections were cut on a microtome and stained with Methyl Green Pyronine and Hematoxyline-Eosin. The thickness of the cerebral cortex, germinal epithelium, intermediate zone and cortical plate and the area of the lateral ventricles were measured in both the control and CSF drained groups.

**Results:** Quantitative measurements have shown that the thickness of the cerebral cortex, germinal epithelium, intermediate zone and the cortical plate and the area of the lateral ventricles in CSF drained embryos were less than those in the control group at the same age. Statistical analysis showed that there is a significant increase in the area of the lateral ventricles and decrease in the thickness of the cerebral cortex, germinal epithelium, intermediate zone and cortical plate when compared to the control group.

**Conclusion:** This study provides confirmatory evidence that CSF is important for normal development of the cerebral cortex.

### S33

#### **Incomplete reversibility of selective hippocampal response after early and delayed shunting in adult kaolin-hydrocephalus – implications for early shunt treatment**

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S33

**Background:** In recent studies of adult kaolin hydrocephalus delayed selective neuronal response was evidenced by findings in the hippocampus. In the present study, it was investigated whether these findings might be reversed by shunting, and whether reversibility might be different when hydrocephalus was shunted at different stages.

**Materials and Methods:** In 20 adult SD-rats kaolin hydrocephalus was induced and immunostaining of neurofilament (NF68), neuronal nitric oxide synthase (NOS), synaptophysin (SYN38) and heat-shock-protein (HSP70) was performed at 2,4,6 and 8 weeks (5 controls). In further 30 hydrocephalic rats, a polyethylene-catheter (PE 10) was placed into the lateral ventricle allowing the CSF to be drained subcutaneously into the neck. Each 15 rats were shunted at 1 week (early) and at 3 weeks (late). Both groups were then investigated at 1,3 and 5 weeks of shunt implantation (5 sham). Immunoreactivity (%) was analysed with the aid of computerized image-analysis;  $P < 0.01$ .

**Results:** In the hydrocephalic rats selective neuronal responses were evidenced by the immunohistochemical changes found in

the CA1 and CA3 sectors: In CA1, NOS staining was positive for all animals at all hydrocephalic weeks, whereas in CA3, HSP70 was positive at 2, 4 and 6 weeks, and at 8 weeks, both sectors were stained. Furthermore, neurofilament staining in CA3 was significantly increased, however, not until 6 weeks. SYN38 staining was increased in both sectors already at 2 weeks; at 4 weeks, greater differences in the immunoreactivity levels have occurred. With an early shunt, NOS was only seen in a few animals. Also, neurofilament staining was reduced in both regions in the one week implantation group. HSP 70 in CA3 was significantly reduced compared to 6 and 8 weeks hydrocephalus whereas it remained increased in CA1. Also for synaptophysin the values for the three and five weeks implantation group were significantly decreased compared to all hydrocephalic weeks. With a late shunt, NOS staining was comparable to the hydrocephalic rats. Also, staining with HSP70 was comparable to 6 and 8 weeks hydrocephalus, while neurofilament staining was identical to that of 4 and 6 weeks hydrocephalus, but showed a good recovery at three and five weeks of implantation. In contrast, synaptophysin reactivity showed maintained increases in both the CA1 and CA3 sectors in all implantation groups.

**Conclusions:** Incomplete reversibility and only partial recovery of selective neuronal response after delayed shunting was evidenced by the findings in the hippocampus. The observed differences between the early and late shunt group might have important clinical implications for early shunting.

### S34

#### Nerve growth factor level in the cerebrospinal fluid in hydrocephalus

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S34

**Background:** There is a significant body of evidence to suggest a physiological role for cerebrospinal fluid (CSF) in both the developing and adult brain. We have previously shown that this fluid has an important role in the developing brain of hydrocephalus Texas (H-Tx) rat. CSF flows through the ventricular system passing over all regions of germinal activity. In congenital hydrocephalus there is a build up of CSF and decrease in the thickness of the cerebral cortex. CSF might be important as a signalling pathway linking the germinal epithelium and the top of the cerebral cortex, which involves coordinating the activity of the germinal epithelium and the migration of cells into the cortex. CSF has the potential to act as a signalling pathway for physiological control since it has been demonstrated to contain molecules such as interleukins, leukoterins, neuropeptides, growth transforming factor-beta (TGF- $\alpha$ ), nerve growth factor (NGF) and brain derived neurotrophic factor (BDNF), which are present at specific times during development and under specific physiological conditions. Thus it is probable that CSF contains growth regulators, which can affect the function of the fetal germinal epithelium.

**Materials and Methods:** In this study CSF from hydrocephalic and normal infants were analysed using SDS-PAGE followed by silver staining. In order to obtain semi-quantitative estimates of the relative amounts of 13 KDa protein, an image analyzer was used to determine the intensities of the band in the respective lanes in silver stained gels. Quantification of the silver stained gels

from repeated experiments ( $n = 10$ ) showed that the amount of 13 kDa protein was clearly increases in the hydrocephalic CSF when compared to the normal CSF. A western blot analysis using anti-NGF antibody as a probe confirmed the presence of NGF. In order to show the relationship of the elevated NGF and hydrocephalus, NGF was injected into the lateral ventricles of chick embryos 3 days after incubation. The embryos were collected 2 days after injection, fixed and 10 micrometer coronal sections were cut ( $n = 10$ ). The sections were analyzed and photographed.

**Results:** The results from SDS-PAGE and immunoblotting showed an increase in the NGF level in the CSF of hydrocephalic when compared to normal group. The results from chick embryo experiments showed a significant increase in the area of the lateral ventricles and a decrease in the thickness of the cerebral cortex in the NGF injected fetuses when compared to the control group.

**Conclusion:** It is concluded that the elevation of NGF concentration in CSF is one of the factors that could induce hydrocephalus.

### S35

#### Neuroradiological criteria of human LICAM syndrome — report of 24 human LICAM mutations including 17 noble mutations and clinical evaluation

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S35

X-linked hydrocephalus (XLH), MASA syndrome and certain forms of X-linked spastic paraplegia (SPG1) and X-linked agenesis of corpus callosum (ACC) are now known to be due to mutations in the gene for the neural cell adhesion molecule LICAM and reclassified as human LI syndrome. The purpose of this study was to perform the nation-wide mutation research of LI gene in Japan and evaluate the clinical futures. We defined the criteria for LI CAM gene mutation analysis in two categories. The first was the patients with hydrocephalus with X-linked inheritance, and the second included the sporadic cases with clinical and neuro-radiological characteristics of XLH or MASA syndrome.

Ninety one samples from 55 families are selected for LI CAM mutation research. We identified 23 types of LICAM gene mutations in 24 families with X-linked hydrocephalus (XLH) and MASA syndrome. Seventeen noble mutations were included in 23 mutations. Of 24 mutations, there were 15 in coding region (class 1-1, class 2-5, class 3-9) and there were 9 mutations in non-coding region. Adducted thumbs, hypoplasia of corpus callosum are seen in all patients. The patients with LI ED mutations showed severe retardation with severe hydrocephalus, patient with LI CD mutations showed moderate retardation without ventricular dilatation. Rippled ventricular wall after shunting, localized hypoplasia of the anterior vermis or total hypoplasia, enlarged quadrigeminal plate and large masa intermedia are characteristic neuroradiological signs in human LI ED (extracellular) mutations. This study further confirms the importance of the LI CD functional regions for axon tract development and the LI ED functional regions for ventricular dilatation in humans.

### S36

#### **Sensory re-innervation of the penis in male patients with spina bifida**

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*Cerebrospinal Fluid Research 2004, 1(Suppl 1):S36*

**Background:** Most of the male spina bifida patients have sensory loss in the glans-penis while having a usable erectile function. Functional sensory re-innervation of the penis would contribute to their quality of life. Transposition of an intact functional sensory nerve to the dorsal nerve of the penis (DNP; S2-S4) might be an option to try to achieve this goal. The first three patients were operated in a prospective pilot study.

**Patients and Methods:** Three spina bifida patients with no sensation of their glans-penis and good sensation in the groin area (ilioinguinal nerve, L1) were selected. Pre- and postoperatively the patients were evaluated by a sexologist to attain information about general and sexual functioning. All three were operated through an incision over the course of the right or left ilioinguinal nerve to the base of the penis. The ilioinguinal nerve was cut distally and the ipsilateral DNP proximally. The two nerve-ends were approximated and joined by microneurography. The first patient (18 years, L4) was operated in December 2001 and in 2002 we operated the two other patients (17 years, L5 and 21 years, L3-L4).

**Results:** In all 3 patients the operated side of the glans and distal shaft has gained an excellent sensory function. The patients are able to discriminate between hot and cold, sharp and soft and have 2-point discrimination at the operated side of the shaft and glans of the penis. The inflicted stimuli however were experienced as if the groin was being touched and were not erogenous in nature in 2 patients, the third has remapped the area. The area innervated by the ilioinguinal nerve has diminished sensation without causing any discomfort, pain or paresthesias to the patient. Results concerning psychologic advancement and development of sexual function are promising. All patients state that they have gained a new part of their body with improved self-esteem.

**Conclusion:** Although the recovery of unilateral sensory function in the glans (and shaft) of the penis is not (yet) erogenous in nature in 2 patients and stimuli are still experienced as stimuli in the groin, the first 3 operations are a technical success with improvement of sexual and psychological functioning of the patients. We believe that ilio-inguinal-to dorsal penile nerve-transposition at an earlier age will contribute to a more effective sensory re-education of the brain.

### S37

#### **Ultrasound augmented urodynamic assessment – implications for areas with limited resources**

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*Cerebrospinal Fluid Research 2004, 1(Suppl 1):S37*

**Background:** Urodynamic assessment forms the basis of urological management in patients with neuropathic bladder. Even with the availability of full video-urodynamic equipment assessment of bladder capacity at differing intra-vesical pressures

can be difficult in the presence of severe vesico-ureteric reflux. This can make decisions about whether bladder augmentation surgery is necessary difficult.

**Materials and Methods:** We have combined real time assessment of bladder volume using portable Sonosite™ ultrasound scanning with video urodynamics to assess true bladder volume and the volume being stored in the upper tracts during urodynamic assessment. The success of this technique allowed the development of a reliable method for urodynamic assessment in countries with limited resources using just a feeding tube to catheterise the patient, a bag of saline, two intravenous giving sets, a measuring device (80 cm plastic rule) and the Sonosite™.

**Results:** The technique of functional bladder assessment will be demonstrated, together with its practical application in both the UK and also in paediatric wards in Khartoum, Sudan

**Conclusion:** Assessment of bladder volume at specific pressures is the basis of urodynamic assessment. This technique allows that assessment to take place in patients where bladder volume can not be predicted from the infused volume. It also allows full bladder assessment in an environment where neither formal urodynamic equipment nor X ray screening equipment is available.

### S38

#### **Use of transdermal oxybutynin in individuals with spina bifida**

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*Cerebrospinal Fluid Research 2004, 1(Suppl 1):S38*

Oxybutynin (OXY) used in combination with clean intermittent catheterisation (CIC), has been the first-line medication for treatment of neurogenic bladder dysfunction over the past two decades. The efficacy of oral OXY in treatment of neurogenic bladder has been demonstrated in several studies. OXY has been shown to increase the maximum bladder capacity, decrease the maximum detrusor pressure with filling, and in combination with CIC, help prevent upper urinary tract deterioration. Until recently, OXY was only available in immediate-release tablets and syrup, both usually requiring dosing two or three times daily, with increased opportunity for missed doses. Intravesical OXY has been used with refractory patients or individuals who could not tolerate the systemic anti-cholinergic side effects, and has been shown to be effective. However, other problems including non-compliance, difficulty with instillation, leakage of medication, etc. have limited its general appeal. With the advent of a long-acting OXY preparation (Ditropan XL), OXY could be given orally just once daily with reduced side-effects for many patients. Even more recently, a transdermal OXY (Oxytrol) delivery system has been tested, FDA-approved and marketed in the United States. A randomised, double-blind, study of transdermal OXY versus immediate-release oral OXY in patients with urge incontinence showed comparable efficacy with lower side effects (Davila 2001). In another study, it was shown that transdermal OXY as a 3.9 mg/day patch (Oxytrol) provides a steady-state level of oxybutynin that is favourable compared to the 10 mg Ditropan XL, with even lower levels of the metabolite, N-desethyloxybutynin, the compound felt to be most responsible for annoying anti-cholinergic side effects (Appell 2003). To date, there is no published study evaluating the use of transdermal OXY in the

treatment of neurogenic bladder dysfunction or in spina bifida. In our Spina Bifida Center, we have begun using the oxybutynin transdermal delivery system (OTDS) in select patients: those with significant side effects and those who had problems with compliance on oral OXY preparations. To date, we have used OTDS in 8 individuals with spina bifida ranging in age from 6 to 41 years (average 19 years). None of the individuals have discontinued the OTDS. All have shown a decrease in side effects compared to oral anti-cholinergics, with similar or improved urinary continence.

Transdermal oxybutynin shows considerable promise in the treatment of neurogenic bladder dysfunction. Further studies of dosing and efficacy are needed, especially in children.

### S39

#### **Kidney control in spina bifida: is ultrasound sufficient or is DMSA scanning needed?**

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S39

**Background:** Prospective pilot study to evaluate the predictive value of ultrasound compared to DMSA-scans for assessment of renal damage in spina bifida patients.

**Materials and methods:** Thirty-five spina bifida patients were evaluated by ultrasound and the outcome of ultrasound was used to predict the outcome of subsequent DMSA-scans of the same patients. Ultrasound parameters were kidney length, dilatation of collecting systems and visible scarring of kidney parenchyma. DMSA parameters were kidney size, shape and split renal function. **Results:** In 21 patients with normal ultrasound, DMSA scan was normal. In 3 patients with abnormal ultrasound (1 scar, 1 abnormal shape of kidney, 1 dilated system), the DMSA scan was normal. In 11 patients with abnormal ultrasound ultrasonography predicted the outcome of the abnormal DMSA scan correctly.

**Conclusion:** Except for a 14% false-positive findings ultrasound is a safe predictor of normal vs abnormal kidneys in pediatric spina bifida patients. This means that kidney control by DMSA scanning can be confined to the small group of patients with severe scoliosis in whom correct visualisation by ultrasound appears to be impossible.

### S40

#### **Review of awareness and management in the event of suspected shunt blockage**

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S40

**Background:** Neurosurgical Services for children in North Wales are provided at some distance by Paediatric Neurosurgeons at the Tertiary Centre in Liverpool, England. In the event of urgent life threatening cases, such as shunt blockage, it is essential that good liaison exists between parents, schools, the local District General Hospital, Community Paediatricians and the Tertiary Centre.

**Aims:** To identify gaps in awareness and knowledge relating to CSF shunt malfunction in children with CSF shunts, amongst their

families, school staff, Community and Hospital Paediatricians, GPs and Health Advisers serving the children. To ensure that any gaps in knowledge and awareness of shunt malfunction are 'plugged' by means of local guidelines. Also, specific guidance should be available at a community, primary care and secondary level to ensure rapid and appropriate referral to the Tertiary Neurosurgical Service.

**Materials and Methods:** 15 children were identified with the ICD10 coding on the NCHS. A postal questionnaire was sent out to involved GPs, SENCOs, Community Paediatricians, school nurses, and senior and junior Paediatricians at the local District General Hospital. The questionnaires were completed personally with the families of children with shunts.

Personal communication was made with: the Tertiary Centre about written protocols for management of shunt blockage, and of written information given to parents; and with ASBAH about local service provided by them, and their available literature.

**Results:** Families seem well informed and confident of their own ability to recognise and act on symptoms of shunt malfunction, but were less confident about various professionals' ability to do so. Professionals (see list in "Aims") responses varied from not being able to recognise symptoms and act on symptoms of shunt malfunction, to being thoroughly competent to do so. Most said they would value written information and local guidance notes.

**Recommendations:** Improve communication and liaison after a CSF shunt insertion or shunt revision, and increase awareness of shunt malfunction and the action required through a communication/liaison pathway. Clarify local community/ward guidance by a proposed pathway in suspected CSF shunt malfunction. Provide clear local guidance on symptoms of shunt malfunction and suggested action for schools, ward Paediatricians, GPs and other medical/nursing professionals.

### S41

#### **Quality of life in spina bifida patients: results of an Italian survey**

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**Background:** The objectives were: 1. to investigate the major topics on the Quality of Life (QOL) of Spina Bifida patients; 2. to evaluate attitudes, the experienced and the behaviours concerning everyday activities, social life participation and familial relationship; 3. to evaluate the information needs; 4. to evaluate the physical and psychological problems related to vesical and intestinal management.

**Materials and Methods:** 1. Qualitative study based on focus groups with parents of patients < 18 years, adult spina bifida patients and care givers (2001); 2. Statistical validation of the questionnaire was based on test-retest analysis (Nov. 2002-Jan. 2003), alpha index of Cronbach and follow up (recall) on 15 patients; 3. The questionnaires were anonymous, self compiled (some help by the parents being allowed) and sent by mail (the whole Italian territory was represented); 4. Statistical analysis of the results was made.

The sample was of 173 patients (51% female and 49% male) with an estimated number of prevalent cases of 4000. The standard error was  $\pm 10\%$  and the confidence index 95%. Some subgroups were studied with test for trend.

**Results:** Open spina bifida were 83% (of which 88% of myelomeningocele); 91% had VP shunt (>40% had had more than 1 procedure). The most important problems affecting the QOL were vesical management (26%), intestinal management (11%) or both (20%), followed by disability due to ambulatory impairment (25%) and sexual problems (15%). Management of urinary incontinence was based on CIC (96% of the sample, started at an early age and self managed in 82%) and drugs (anticholinergics in 53%): 74% wear diapers (no leakage in 19%, once per month in 19%, once per week in 11%, once per day in 17%, more than twice daily in 35%). Stool leakage was absent in 46%, once in a month in 34%, once weekly in 11%, once daily in 4% and more than once in 5%); for bowel management 68% did not use any treatment, 16% enemas, 4% anal plug, 9% drugs). Everyday activities, school attendance, work and hobbies have been investigated: 73% have a computer (versus 9% of Italian population) and 63% access to the internet (versus 18%). The majority of these patients showed a good autonomy about personal hygiene and dressing, less about housework. Decisional autonomy and familial dialogue were poor with excessive protection by the family or care givers.

#### S42

##### **Prevalence of neural tube defects in Ireland 2001–2002, was the folate media campaign effective?**

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*Cerebrospinal Fluid Research 2004, 1(Suppl 1):S42*

**Background:** The aim of this study was to review the prevalence of Neural Tube Defects in the island of Ireland over a two period from 2001–2002. This period followed a high profile campaign on folic acid supplementation by the Departments of Health in both the Republic and Northern Ireland.

**Design setting:** The Irish Paediatric Surveillance unit (I.P.S.U) agreed to include N.T.D's as one of their reporting conditions for the two year period. Paediatrician's reporting a case were asked to complete a questionnaire including obtaining information on mother's folic acid intake. Cases were also identified and verified through other sources including maternity hospital reports, HIPE and the Health Information Unit. The Dublin Eurocat registry had monitored NTD previously in the Eastern Health Board region and also in the Galway region and more recently Cork and Kerry. However there had been no nationwide reporting.

**Results:** Ireland has a population of 5.532million (3.847 republic of Ireland 1.685 northern Ireland). Over the two year period 87 NTD cases were identified, a prevalence rate of 5.379 per 10,000 live births (6.335 in the Republic and 3.768 in Northern Ireland). More detailed information was available on 70, 37% had anencephaly, 57% myelomeningocele. 26 of 40 infants with myelomeningocele survived the first three months of life. Similar to previous studies there were more females born and more born to younger and older mothers. Of the 42 with definite information on folic acid intake, 7 had intake prior to conception for between 2 weeks and 6 months, 14 after conception between 6 weeks and 9 months, taking a dose of 400 mg daily. Of the three families with a history of neural tube defect two mothers had taken pre-conceptual folate, 1 post conceptual. The prevalence will be shown geographically but most clinical cases are within the main centres of population in Dublin, Cork, Galway and Belfast.

**Discussion:** A low uptake of folate supplements was recorded in mothers who subsequently had infants with N.T.D's. 6 mothers including 2 with infants with anencephaly had taken adequate pre and post conceptual folic acid. The fall in prevalence of Neural Tube Defects has been well reported internationally. It has been well documented in the Dublin registry of Eurocat falling from 46.48 per 10,000 live births in 1980 to 15.47 in 1990 and 9.54 in 2001. The large cohort of children detected during the earlier years are now adolescents and young adults and over age for our multidisciplinary clinics, while numbers in the paediatric age group are diminishing. In Belfast Dr. J. McCann and colleagues have set up an excellent clinic for adults with spina bifida. We need to review the specific requirements of this population within the Republic of Ireland and plan appropriate services.

#### S43

##### **Epidemiology of neural tube defects and folic acid** D Shurtleff

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*Cerebrospinal Fluid Research 2004, 1(Suppl 1):S43*

Since the 1930s the birth incidence of Neural Tube defects has been declining worldwide. The birth incidence varies across time and in different geographic areas at the same time.

The birth incidence is much lower than the prevalence detected during the first trimester in both spontaneous and elective terminations. Peaks of birth incidence have been labelled "epidemics". These reports include varying types of cases; some report only "Spina Bifida", whereas others include two or more types of neural tube defects. Several well-designed prospective studies have demonstrated an impressive reduction in the occurrence or recurrence of myelomeningocele and anencephaly following administration of folic acid beginning peri-conceptually. The birth incidence is much lower than the prevalence detected during the first trimester in both spontaneous and elective terminations (Roberts and Lowe, 1975, Creasy and Alberman, 1976; Nishimura, 1970). Chromosome anomalies are detected in up to 15% of early abortuses or by amniocentesis but less than 1% of live born patients with myelomeningocele (Luthy, 1991). The effect of folic acid fortification in North America has been reported in three epidemiological studies to be followed by a 45 to 55% reduction. The data from our clinic includes 440 births from 1981–2003 in Seattle and demonstrates an 80% reduction in the birth incidence of Myelomeningocele beginning in 1981–2000 from 0.4/1000 to 0.08/1000, a five-fold decrease. With the introduction of folic acid fortification there was an increase to 0.16/1000 in 2002, a two-fold increase. In 2003 the birth incidence fell to 0.08 again. Conclusion: Our data demonstrate the effects of intrauterine diagnosis and selective termination prior to fortification of foodstuffs with folic acid. Studies of the effect of folic acid fortification on the birth incidence of Spina Bifida Occulta in communities with a low incidence and active prenatal diagnosis and termination of affected fetuses require longer term studies than published to date.

**S44****Needs assessment of school-going children and adolescents with spina bifida**

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S44

**Background:** The Central Remedial Clinic (CRC) is a national organisation providing a range of specialised services for children and adults with physical disability. One such service provided is a specialist spina bifida service. The aims of the study were: 1. To assess the current level of need among school-going children and adolescents (aged 5–18 years) with spina bifida. 2. To obtain a measure of patient and parental satisfaction with the specialist spina bifida service provided by the CRC. 3. To implement improvements in the service.

**Methods:** The parents of 42 children were invited to participate in the study. All lived in the Eastern Regional Health Authority and attended the specialist spina bifida service in the CRC. All but 1 agreed to participate. Each participated in a semi-structured interview, which included the completion of a questionnaire.

**Results:** Of the 41 children, 22 were attending special schools and 19 were in a mainstream setting. 34.1% were incontinent in relation to bowel function. 56.1% were incontinent in relation to bladder function. The majority required assistance for toileting: 73.2% were dependent in relation to bowel function and 53.7% in relation to bladder function. A significant number were dependent in relation to personal care (61% for washing, 58.5% for dressing). Whilst there was a high satisfaction rating for the service provided by the CRC (92.7% generally happy), 30 families (73.2%) identified the need for additional services, particularly the need for home adaptation and counselling for both the child and parents. Among the improvements suggested by parents were increased information, more therapy and improved communication within the multidisciplinary team.

**Conclusions:** We have highlighted a high level of need within this population. Whilst parents may be happy with the current service provided, there is much room for improvement. The key demand is improved coordination of services, not only among the services provided by the CRC, but among all care-givers providing services on multiple sites in the Dublin area.

**S45****Parental adaptation to having a child with spina bifida: a developmental perspective**

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S45

**Background:** Parents' adjustment to having a child with spina bifida (SB) varies greatly (Wallander et al., 1989, Singh, 2003). A recent meta-analysis of 18 studies (Vermaes, Janssens, & Gerris, submitted) confirmed that although parents of children with SB experience more psychological symptoms than parents of able-bodied children (average effect size Hedges  $d^+ = 0.73$ ; CI 95% = 0.38–0.97) there is within-group heterogeneity ( $Q = 66.21$ ,  $P < 0.001$ ). Three hypotheses were postulated: Parents' psychological adjustment varies as a function of (1) adjustment processes over time; (2) severity of SB: type, lesion level, hydrocephalus, ambulation status, number of shunt revisions, IQ, and school type; and (3) demographic characteristics: child age, child gender, maternal age, paternal age, family ethnicity (Dutch vs. non-Western), SES, marital status, number of children, and the child's birth order.

**Method:** Retrospective interviews were conducted with parents ( $n = 46$  mothers;  $n = 37$  fathers) of 58 children with SB (age  $M = 10.36$ ,  $SD = 2.38$ ; 34 girls). Parents were asked to describe their experiences of the periods: (T1) pregnancy and birth; (T2) baby-toddler period (0–2 years); (T3) preschool period (3–4 years); (T4) middle childhood (5–11 years). After each period they filled out a 13 item questionnaire (4-point Likert scale) of DSM-IV symptoms representing two factors: (1) Internalization-depression and (2) Externalization-irritability. GLM analyses with repeated measures were applied to detect time trends and interaction effects with SB characteristics and demographics.

**Results and Discussion:** As can be seen in Table 1, internalization-depression symptoms decreased steeply after the first years of the child's life and gradually continued to decline into middle childhood. Externalization-irritability symptoms however remained stable over time. The question is whether counseling interventions have interfered with these trends.

Physical parameters of SB did not explain within-group variability of parents' psychological symptoms, but mental parameters (low IQ, attending special education) or threats to the child's mental functioning (shunt revisions) did, especially during the child's preschool and middle childhood years. During the child's middle

**Table 1. Trends in Parents' Psychological Symptoms across the Child's Life Span**

	Group means (SDs)				Time effects (linear)		Time effects (quadratic)	
	Time 1 pregnancy-birth	Time 2 baby-toddler	Time 3 preschool	Time 4 middle childhood	F	p	F	p
<i>Mothers</i>	$n = 55$	$n = 55$	$n = 55$	$n = 55$				
Int-depression	2.18 (0.70)	1.83 (0.68)	1.59 (0.64)	1.55 (0.52)	58.103***	0.000	1.266**	0.003
Ext-irritability	1.85 (0.85)	1.68 (0.69)	1.64 (0.82)	1.70 (0.73)	1.095	0.300	2.427	0.125
<i>Fathers</i>	$n = 33$	$n = 33$	$n = 33$	$n = 33$				
Int-depression	2.10 (0.58)	1.78 (0.50)	1.44 (0.48)	1.48 (0.58)	48.099***	0.000	9.787**	0.004
Ext-irritability	1.59 (0.80)	1.61 (0.77)	1.50 (0.79)	1.52 (0.69)	0.500	0.485	0.003	0.447

\*\*  $P < .01$ , \*\*\*  $P < .001$  (two-tailed).

childhood older parents had higher levels of psychological symptoms than younger parents. Possibly worries about the child's future care and personal midlife concerns play a part. Although the sub-samples were rather small, non-Western parents and parents who had divorced reported significantly more psychological symptoms than other parents in the child's middle childhood years. Stresses around immigration and divorce may provoke increased psychological symptoms in addition to or in interaction with the child's condition.

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#### S46

##### Religious interpretations of suffering by parents of a child with spina bifida

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*Cerebrospinal Fluid Research 2004, 1(Suppl 1):S46*

**Background:** This study is part of the multidisciplinary research program "Prognosis of Spina Bifida" of the Radboud University Nijmegen. In the framework of this program a retrospective study on fifty children with different types of spina bifida and their parents was conducted; the disciplines involved were child neurology, neuropsychology, child & family studies and empirical theology. The empirical theological part of this project investigates the extent to which parents of a child with spina bifida turn to religion when confronted with the diagnosis.

**Materials and Methods:** This presentation will focus on the religious orientation called 'theodicy'. At critical moments, such as the confrontation with spina bifida, people express existential questions, doubts, and ultimate concerns (religious or secular) that people cherish may be challenged. Often the troubling question is: 'Why?', 'Why me or my child?', and "Why does God allow suffering?'. It seems that people cope differently with these questions in which they try to find a meaning of suffering. At these moments, attitudes toward theodicy can be stirred. Two questions will be raised in this presentation: 1. Which attitudes towards theodicy are present among parents of a child with spina bifida? 2. Is there a difference in support of these theodicy attitudes when different levels of church-involvement are taken into account?

**Results:** With regard to the first question five attitudes (on the basis of factor analysis) towards theodicy were found among parents of a child with spina bifida. The average total score at a 5-points-scale (1 = 'total disagreement', 5 = 'total agreement') of the five attitudes indicate that parents on the whole reject the models of retribution (M = 1.6, SD = 0.66), apathy (M = 1.7, SD = 0.73), lament (M = 1.9, SD = 0.87), plan (M = 2.3, SD = 1.14) and doubt the compassion model, though also with an inclination towards rejection (M = 2.6, SD = 1.22). In answer to the second question significant variations of the means are found for the models of retribution ( $\eta^2 = 0.34$ ), compassion ( $\eta^2 = 0.57$ ) and plan ( $\eta^2 =$

0.40) that indicate a far stronger support of the aforementioned models when church involvement increases, leading for instance to positive support of the compassion model of theodicy.

**Conclusion:** Interpretations of the scores on theodicy will be discussed.

#### S47

##### Upper limb function in children with spina bifida

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*Cerebrospinal Fluid Research 2004, 1(Suppl 1):S47*

**Background:** It is axiomatic that children with spina bifida have lower limb dysfunction because of disruption of the nerves supplying the legs. But the cause of any upper limb dysfunction is more difficult to determine. The purpose of this study is to examine upper limb function in a group of spina bifida patients, and to document factors which might have contributed.

**Materials and Methods:** The sample patients were identified from the patients born with spina bifida in the ten year period 1987-96, ensuring that the children would be at least 6 years old. The skin and sensory levels of the lesion were documented as well as the history of hydrocephalus and shunt revision. Upper limb function was determined using measures of coarse (putting pellets in a cup and pegs in a pegboard) and fine (repetitive finger movements, repeated pronation and supination and 20 Claps) movements.

**Results:** There were 24 children for whom a full data set was obtained. In 30% the upper limit of the lesion was thoracic, 60% had a lumbar lesion and 10% a sacral lesion. The incidence of hydrocephalus was 80%, and all but 4 of the shunts required revision in the first year. All the children were found to perform well on the coarse movement tests, with no significant difference from the norm. However with fine movement testing using the tests described above, the children performed significantly poorer than the norm in two of the three tests. One anecdotal finding was that almost 50% of the children are left handed. There appeared to be no correlation with age or level of spina bifida lesion.

**Conclusion:** Children with spina bifida have significant dysfunction in the performance of fine motor tasks than normal children. This finding is present in children aged from 6 to 15 years, suggesting that the problem is present from a very young age.

#### S48

##### Deliveries of babies with neural tube defects in Omdurman, Sudan

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*Cerebrospinal Fluid Research 2004, 1(Suppl 1):S48*

**Background:** Whilst the incidence births of babies with open neural tube defects (NTD's) is falling in the USA and Western Europe, these congenital abnormalities remain a significant cause of morbidity and mortality in Africa. As a first move, prior to looking at the use of folic acid supplementation, we have attempted to define the magnitude of the problem in a Hospital based population in Sudan.

**Study design:** Prospective study of all patients born with open NTD's over a 12 month period in one hospital in Sudan. Index cases were compared with a consecutive group of deliveries of babies born without NTD's (control group = ~2 × index group)

**Setting:** Omdurman Maternity Hospital, Khartoum, Sudan The hospital delivers in excess of 16000 women per year. Ribat University Hospital, Khartoum (delivery rate ~3500 per annum).

**Research tools:** Maternal questionnaire completed after delivery. Formal examination of all infants and follow up questionnaire for surviving infants at one year. Verbal consent to participation was obtained in all cases. Questionnaires were completed by a medical practitioner asking the mother the designated questions (many mothers illiterate).

**Results:** In the year from Feb 2003 to Jan 2004 there were 64 babies born with open NTD's. This gave an incidence of 3.5/1000 deliveries. NTD's were the most common abnormality note at birth, the incidence of all other abnormalities coming to just 2.5/1000 deliveries. 24 babies had anencephaly. 33 were stillborn and there were 20 early neonatal deaths. Young maternal age ( $P = 0.0002$ ) low maternal educational level ( $P = 0.0014$ ), low paternal educational level ( $P < 0.0001$ ) and a previous history of stillbirths ( $P < 0.0001$ ) were all associated NTD births. No index case mothers or control mothers received pre-conceptual folate supplements. Data collected in a different hospital setting and in a community setting confirmed the validity of the Omdurman incidence figure.

**Conclusion:** Delivery of babies with open NTD's remain a significant problem in Sudan. Poor socio-economic status and a previous history of stillbirths are indicators of high risk. The lesions seen were at the severe end of the spectrum of NTD's. Interventive studies looking at the benefit of folic acid supplementation in this population are indicated.

## POSTER PRESENTATIONS

### S49

#### Reasons for shunting and reasons for revision: a survey based on data from the UK Shunt Registry

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S49

Data from the UK Shunt Registry for procedures carried out between May 1999 and April 2002 was examined for the given reason for shunting and the given reasons for subsequent revisions. Sixty-eight per cent of patients receiving shunts had 'secondary' hydrocephalus, with congenital and idiopathic hydrocephalus accounting for 18% and 14% respectively. Patients with Spina Bifida represented 5.1% of shunted patients.

Reasons for Shunting	(%)
Congenital Hydrocephalus	17.8
Cysts	4.1
Tumours	25.0
Infection	5.8
Haemorrhage	25.6
Idiopathic Hydrocephalus	14.6
Other	7.3

The occurrence of underdrainage, overdrainage, disconnection, fracture, infection and migration were broken down by clinical

diagnosis. Underdrainage is by far the most common given reason for revision, and appears not to vary with clinical diagnosis. Infection, disconnection, migration and fracture are associated with young age rather than any particular diagnosis. Overdrainage is particularly high in patients with Chiari malformations

### S50

#### Methylenetetrahydrofolate-dehydrogenase 1958G→A polymorphism is a genetic determinant of NTD risk for Italian mothers

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S50

Neural Tube Defects (NTDs) have a well-established genetic basis, although specific genetic predisposing factors had not been identified until now. Genetic variants of enzymes involved with folate pathway might be expected to have impact on NTD risk. Given its key role in folate metabolism, the methylenetetrahydrofolate dehydrogenase (*MTHFD1*) could represent an attractive candidate in NTD etiology. *MTHFD1* is a trifunctional protein and mediates the interconversion of 5,10-MTHF; 5,10-methenylTHF; and 10-formylTHF. 10-formyl THF and 5,10-methenylTHF are the donor cofactors for *de novo* purine and pyrimidine biosynthesis and, thus, the biosynthesis of DNA. Recently, a polymorphism, G1958A, in the *MTHFD1* gene was suggested as maternal genetic risk factor for NTD in the Irish population. In this study, we examined the impact of the *MTHFD1* G1958A polymorphism on NTD risk in the Italian population by a case-control study and family-based studies. The study population consisted of 95 unrelated Italian NTD children, 42 mothers and 40 fathers who were recruited from the Spina Bifida Center of the Gaslini Hospital, Genoa. A total of 145 healthy individuals were recruited from a blood donors accessible bank and used as control group. The presence of the *MTHFD1* 1958G→A, *MTHFR* (methylenetetrahydrofolate reductase) 1298A→C and *RFC-1* (reduced folate carrier 1) 80A→G polymorphisms was investigated by PCR-RFLP methods. We found no increased risk for *MTHFD1* mutant genotypes of the children and fathers. On the contrary, significant risk estimates resulted for the homozygous 1958AA genotype of the mothers (OR = 3.05;  $P = 0.046$ ). This maternal effect was confirmed by transmission disequilibrium test (TDT) that showed no preferential transmission of 1958A allele to the affected children from informative parents. Since our previous study has shown that the *MTHFR* A1298C and *RFC-1* A80G polymorphisms are genetic determinant of NTD risk for Italian mothers, potential gene-gene interactions were examined. We found a significant interaction between the *MTHFD1* G1958A polymorphism and both *MTHFR* A1298C (4.46-fold increased risk) and *RFC-1* A80G (9.14-fold increased risk) mutant alleles in the mothers. We conclude that a common genetic variant of *MTHFD1* gene, the G1958A, is a maternal genetic risk factor for NTD. These findings highlight the importance of further considering maternal genotype when evaluating NTD susceptibility loci.

## S51

### Update on the Management of Myelomeningocele Study (MOMS): the first 16 months

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S51

The Management of Myelomeningocele Study (MOMS) is a five-year multicenter randomized trial funded by the National Institute of Child Health and Human Development, a part of the National Institutes of Health. This study is designed to compare the safety and efficacy of prenatal and postnatal closure of open neural tube defects. This is felt to be a critical study in the United States where several centers began performing the procedure in 1997 but for which there is very little scientific data to support it as a valid intervention. The protocol specifies that 200 women be enrolled in the trial, with 100 in each group. The Management of Myelomeningocele Study began recruiting patients in mid February of 2003 and enrollment is slower than projected because of several unanticipated issues. The challenges inherent in performing this type of study are significant and are magnified because the study requires that patients randomized to prenatal surgery stay at the MOMS Center performing the procedure until they deliver their child. Many unanticipated problems have been encountered which affect enrollment and these will be discussed as will the solutions which have been found. In addition, baseline data will be presented on the patients screened as well as those enrolled to date.

## S52

### Expectation of life and unexpected death in open spina bifida

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S52

Improvements in the care of patients with spina bifida has led to a tendency to underestimate the high mortality associated with the condition. There are few really long term reviews and those that exist have a high proportion of patients lost to follow up some of whom may in fact be dead. We present a cohort of 117 consecutive cases of open spina bifida who were treated from birth irrespective of severity, between 1963 and 1971. Every case was accounted for in 2002 when the mean age was 35. The causes and circumstances of the 66 deaths were obtained from hospital records, post mortem reports and the Office of National Statistics, supplemented by information from medical and other carers. In the 1960s the early mortality was high and one in three of the children died before the fifth birthday. Thereafter deaths were fewer and of 77 who survived to age 5, 10% died every 10 years. Although some of the deaths were predictable many occurred suddenly and unexpectedly without the patient reaching hospital. These include 2 cot deaths, 3 cases of acute hydrocephalus, 3 epileptic seizures, 3 cases of pulmonary embolism and 2 of acute sepsis in diabetic patients. By being aware of the high prevalence of unpredictable and largely unpreventable deaths, doctors may avoid giving overoptimistic forecasts.

## S53

### Impaired oxygen utilisation in hydrocephalus: a non-invasive study

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S53

Imaging techniques such as ultrasound scanning, MRI scanning and CT scanning, which are currently used in the diagnosis and management of hydrocephalus do not provide information regarding changes observed in cerebral haemodynamics and metabolism in hydrocephalus. Near infrared spectroscopy (NIRS) is a relatively new non-invasive technique, which can fulfil this need. Near infrared spectroscopy can be used to make continuous measurements of oxyhaemoglobin ( $O_2Hb$ ), deoxyhaemoglobin (HHb) and oxidised cytochrome c oxidase ( $Caa_3$ ), which is the terminal enzyme of the mitochondrial respiratory chain. Hence, information regarding changes in haemoglobin oxygen supply and oxygen utilisation in the cell is provided. The summation of  $O_2Hb$  and HHb represents changes in total haemoglobin (tHb) and this provides information regarding perfusion status. The difference between  $O_2Hb$  and HHb is the haemoglobin oxygenation index (HbD) and this reflects net changes in oxygenation. The aim of this study was to determine if the non-invasive technique of NIRS could detect differences in cerebral haemodynamics and oxygen utilisation between hydrocephalic and normal rats from the HTx rat model. Rats were restrained and placed onto an adjustable platform in a supine position. Baseline was established for 5–10 mins following which an increase in intracranial pressure was induced via a 45° head down tilt for 5 mins. After removal of the tilt and return of the rat to the supine position, NIRS monitoring was continued for a further 5–10 mins. A total of 24 normal and 12 hydrocephalic rats were studied. It was found that upon tilting a significant difference in change of HbD concentration was observed between the normal ( $-2.67 \pm 1.49 \mu M/cm$ ) and hydrocephalic ( $7.21 \pm 2.89 \mu M/cm$ ) rats ( $P < 0.005$ ). HbD was greater in the hydrocephalic than in the control group ( $O_2Hb > HHb$ ) and this is suggestive of impaired oxygen utilisation in hydrocephalic rats.

In a preliminary study we investigated the effect of sodium pentobarbitone administration, a known inhibitor of complex I of the respiratory chain. We measured a significant difference in the level of cytochrome c oxidase in hydrocephalic ( $-2.73 \pm 1.07 \mu M/cm$ ,  $n = 4$ ) compared to normal ( $-6.32 \pm 0.51 \mu M/cm$ ,  $n = 5$ ) rats. These preliminary studies are encouraging and suggest that NIRS could be valuable in providing information that is vital for successful management of hydrocephalus.

## S54

### Spinal fusion in children with spina bifida: influence on ambulation level and functional abilities

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S54

**Background and aims:** To determine the effects of spinal fusion on ambulation level and functional abilities in children with spina bifida.

**Materials and Methods:** Ten children (3 males and 7 females) with myelomeningocele were prospectively followed. Their mean age at operation was 9.3 years (standard deviation: 2.4). Spinal curvature was measured according to Cobb. Pelvic obliquity and trunk decompensation were measured as well. The ambulation level was scored according to Hoffer and functional abilities, as well as the amount of caregiver assistance were documented using the 'Pediatric Evaluation of Disability Inventory'. All patients were assessed before surgery, and three times after surgery, with a total follow-up duration of 18 months after surgery.

**Results:** After spinal fusion, magnitude of primary curvature decreased significantly ( $P = 0.002$ ). Pelvic obliquity and trunk decompensation did not change. The ambulation level showed a significant regression ( $P = 0.03$ ). Functional abilities and amount of caregiver assistance concerning self-care and mobility showed a non-significant trend to deteriorate within the first six months after surgery, but recovered afterwards. From pre- to 18 months after surgery, functional skills on self-care showed borderline improvement ( $P = 0.07$ ), whereas mobility did not ( $P = 0.2$ ). Mean scores on caregiver assistance improved significantly on self-care ( $P = 0.03$ ), and borderline on mobility ( $P = 0.06$ ).

**Conclusions:** Within the first six months after spinal fusion, more caregiver assistance is needed in self-care and mobility. It takes about 12 months to recover to pre-surgery level, while small improvement is seen afterwards. After spinal fusion, ambulation often becomes difficult. These findings are important for health care professionals, in order to inform and prepare the patients and their parents properly for a planned spinal fusion.

## S55

### Evolution of neural function in spina bifida occulta and aperta

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S55

**Background:** Spina bifida often results in dysfunction of the central and peripheral nervous system. In spina bifida, the neural tube defect may be covered by skin (SBO) or open (SBA). Fetal surgery in SBA aims to preserve central axonal projections through the meningocele (MMC) and to prevent secondary damage. The present study aimed to determine whether the natural coverage of the neural tube defect in SBO protects central axonal conduction, as could be measured by vesico-urodynamics.

**Objective:** To compare central and peripheral neural innervation between SBO and SBA in a longitudinal fashion.

**Design/Methods:** 17 SBO and 16 SBA children were investigated at ages 1 and 2–4 years. In both groups the defect was at L3 (median value, range resp. L1–S1 (SBO), and Th12–S1 (SBA)). In all children, spinal segments S2–S4 (innervating anal and bladder reflexes) were located caudal to the defect. Central dysfunctional bladder innervation was defined as overactive detrusor or pelvic muscle activity during vesico-urodynamics. Absence of anal reflexes indicated peripheral neural dysfunction. Surgical detethering was electively performed.

**Results:** Only in 1 of 17 SBO children detrusor activity became overactive between year 1 and 2–4. The percentage of children with overactive detrusor activity declined significantly ( $P < 0.01$ ) between years 1 and 2–4, both in SBO (from 47% to 23%) and in

SBA (from 79% to 38%). Similarly the percentage of children with hyperactive pelvic muscle activity declined significantly ( $P < 0.025$ ) in SBO (from 69% to 20%) and in SBA (from 67% to 45%). At neither time point, the percentages were significantly different between SBO and SBA. Concerning LMN dysfunction however, a larger fraction of SBA children had absence of anal reflexes, compared with SBO (86% vs. 31%,  $P < 0.005$ ).

**Conclusions:** 1. Natural covering of the spinal defect in SBO compared with SBA is not associated with improved central innervation of the bladder; 2. Signs of central bladder dysfunction decline in both SBA and SBO children between age 1 and 2–4 years; 3. Peripheral innervation is better preserved in SBO than in SBA, by a mechanism independent of central innervation.

## S56

### Kaolin-induced hydrocephalus in the newborn rat

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S56

**Background:** Hydrocephalus occurs commonly in fetuses and neonates. The most widely used animal model of this condition has been the H-Tx rat. The genetic defect in this rat has not yet been defined. To complement studies in the H-TX rat, we have used the kaolin model in newborn rats. Our goal was to characterize this model with behavioral and biochemical outcome indicators. Furthermore, we hypothesized that nimodipine, which was protective in rats with hydrocephalus that began at 3 weeks age, would also benefit these animals.

**Materials and Methods:** Kaolin (25% suspension, 0.02 ml) was injected into the cisterna magna at 1-day age. Animals were weighed daily. Magnetic resonance imaging was used to define the ventricle size at 7 or 21 days. Developmental behavior analyses included observations of the ability to right after being placed on the back, to orient on a slope (negative geotaxis), to hang from a wire, and to walk on a rotating rod. A separate set of rats was administered pimonidazole (50 mg/kg i.p.) prior to sacrifice to detect hypoxic brain damage. The rats were sacrificed and their brains were removed for biochemical and histological analysis. In the drug treatment experiment, nimodipine was administered at doses previously shown to be effective (4–38 mg/kg/day) beginning after MR imaging at 7 days and continuing for 14 days. Additional comparative tests included the water maze test of memory.

**Results:** Kaolin-injected rats had delayed weight gain and noticeably enlarged heads. They walked with splayed hind limbs and a hunched back. MR imaging at 7 days demonstrated mildly enlarged ventricles and considerable white matter edema. In addition, there were fluid collections outside of the brain particularly dorsal to the cerebellum. At 7 days, geotactic orientation of was delayed in hydrocephalic rats. Biochemical analysis showed reduced ceramide galactosyl transferase, a marker of myelin production, and reduced CNPase, an oligodendrocyte enzyme that seems to play a role in axonal integrity. Myelin basic protein was at not detectable on Western blots in controls or hydrocephalic rats at 7 days. Imaging at 21 days demonstrated severely enlarged ventricles and large extra-cerebral fluid collections. The hydrocephalic rats were impaired in their ability to stay on a rotating rod. Myelin basic protein levels were significantly reduced. GFAP levels were increased.

Pimonidazole adducts were detected in periventricular white matter of hydrocephalic but not control rats. Nimodipine offered no behavioral or biochemical protection when studied in a randomized, blinded experimental manner. The highest doses were fatal.

**Conclusion:** The kaolin model can be used to complement the H-Tx rat model of hydrocephalus. Nimodipine does not appear to be an effective treatment when administered at this early age. This either suggests differences in the pathophysiology of brain damage at different ages or differences in the toxic potential of nimodipine. It also raises questions about the applicability of this type of treatment.

## S57

### The use of electronic devices to cue self-catheterization for adolescents with spina bifida

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S57

Adolescents with histories of myelomeningocele and hydrocephalus (MMH) frequently present with cognitive deficits in areas of executive functioning (EF) thought to be central to the completion of activities of daily living (ADL), particularly ADLs with high initiation and prospective memory requirements such as self-catheterization (SC). This study was designed to determine if auditory cueing provided by an electronic device could be used to help adolescents remember to perform SC without parental prompting. This initial pilot study utilized a single-subject 5-week design with an ABCBC intervention schedule. Data were collected for a 13-year old female subject with MMH (L4), average Verbal IQ, documented executive dysfunction, an adequate continence plan, and periodic incidents of urinary incontinence. Following a week of baseline data collection (condition A), the parent was provided with an electronic cueing device (condition B) that provided the parent with auditory cueing throughout the day (excluding school hours) to assess whether the subject had initiated SC at the scheduled times. During condition C, the subject was provided with a cueing device and was presented with cues to initiate SC 30-minutes prior to parent assessment of catheterization status. The subject required 3 parental reminders to complete SC during the week of baseline data collection, and an average of 1.5 parental reminders per week during conditions B and C. Across conditions, parental reminders to perform SC occurred far more frequently on the weekends (15% of scheduled catheterization events; 6/40) compared to weekdays/schooldays (4% of scheduled catheterization events; 3/75). This pilot data provides preliminary support for future research in electronic cueing to initiate SC, particularly during days of the week when routine environmental cues to perform SC (e.g., academic schedules) are less available to adolescents with MMH.

## S58

### A prospective, randomised, controlled trial to evaluate the efficacy and safety of endoscopic choroid plexus coagulation with third ventriculostomy in the treatment of idiopathic normal pressure hydrocephalus [ISRCTN29863839]

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S58

**Background:** The current treatment of choice for Normal Pressure Hydrocephalus (NPH) is a CSF shunt, however, this carries significant morbidity with reported complication rates following shunt surgery averaging 38%, with a 6% rate of permanent neurological deficit or death [1]. NPH can be viewed as a slowly progressive communicating hydrocephalus. Endoscopic coagulation of the choroid plexus (CPC) has been shown to be an effective treatment of communicating hydrocephalus in children, particularly when it is slowly progressing. It has not yet been evaluated in adults with NPH. Endoscopic third ventriculostomy (ETV) has been shown to be effective in selected cases of NPH. Published results of both endoscopic techniques suggest that complication rates are lower than for CSF shunt surgery. A combination of endoscopic CPC and ETV may provide an attractive alternative to CSF shunting with equivalent rates of responsiveness and lower surgical morbidity. The aim of this study is to evaluate the effectiveness of endoscopic treatment of NPH compared to CSF shunting.

**Study Design:** An equivalence study, with the null hypothesis that there is no significant difference in outcome between treatment with CSF shunting and treatment with endoscopy 3 months after treatment. Consenting patients with a diagnosis of NPH, satisfying the trial inclusion and exclusion criteria, are randomised to either endoscopic surgery or CSF shunt (control) treatment. The primary outcome measure is the Gait Score [2] at 3 months post-operatively. Secondary outcome measures are: operative mortality, frequency of operative complications, Mattis dementia rating score II, NPH Score, Grooved Pegboard Test score, Quality of life (SF36), modified Rankin score, Barthel index. Outcome assessment is blinded.

**Statistical Evaluation:** With a sample size of 32 patients in each group, a two group 5% one sided t-test will have 90% power to detect an effect size of 0.75. Sequential monitoring of major morbidity and mortality rates will be undertaken and the trial terminated if these rates exceed a predetermined threshold.

**Conclusions:** This study aims to evaluate the efficacy and safety of endoscopic CPC with ETV in the treatment of NPH. An interim analysis of results will be presented.

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**S59****Transition: you need to go!!**

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S59

In 1999, the department of Paediatric Rehabilitation, Princess Margaret Hospital for Children did an audit of current transition processes for children with Spinal pathology transferring from paediatric to adult health care. At the time there was poor attendance of transferred patients in 'adult' clinics and 'adult' patients were continuing to utilise paediatric facilities.

Investigation findings were that there was a lack of patient education regarding transfer/adult services and no formal transfer process. In addition, many problems were being experienced by adolescence at the time of transfer, which was impacting on the success of the transfer.

Over the past four years we have developed and formalised transition processes for Spinal Rehabilitation patients graduating from paediatric to adult services using the recommendations from this audit.

Follow up research is planned for early 2004 to determine whether the current transition program for adolescents with Spina Bifida meets their needs and expectations.

**S60****Preconceptual care for women with spina bifida**S Christodoulou, M Kamran, J Thorne, M Lewis, S Vause  
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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S60

**Background:** When women with spina bifida reach reproductive age they may have concerns about the potential complications they may face during pregnancy. Over the last year six women with spina bifida have been seen in our preconceptual clinic.

**Study design:** Retrospective case series  $n = 6$

**Setting:** St Mary's Hospital, Manchester. A tertiary referral centre.

**Aim:** To describe recurrent themes covered during pre-conceptual counselling of women with spina bifida.

**Results:** Common themes emerged during the six consultations. These related to the need for preconceptual folic acid supplementation (6/6), discussion of recurrence risks (6/6), screening for neural tube defects (6/6), management of urinary symptoms and urinary infection (5/6), potential problems with backpain, mobility and the ability to continue to work during pregnancy (6/6), analgesia in labour (6/6), anaesthesia (3/6), mode of delivery (6/6). Management options for the above were discussed. All women reported that they had found the consultation to contain useful information and that the actual risks were not as high as they perceived. They were also reassured by the suggested management plans. Two of the women have become pregnant.

**Conclusion:** For women with spina bifida a preconceptual consultation provides an opportunity to reinforce advice regarding folic acid. The provision of information, acknowledgement of potential problems and the discussion of management options in a preconceptual clinic appears to reduce anxieties about pregnancy.

**S61****Four decades of normal pressure hydrocephalus: are we doing better?**

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S61

**Background:** In the UK it is estimated that about 5% patients with dementia above the age of 60 suffer from Normal pressure hydrocephalus (NPH). This 5% could represent up to 24,000 people who may be suitable for assessment for treatment. Awareness of this condition is constantly rising both among doctors and patients. A recognised difficulty is the confirmation of the diagnosis and selection of those patients who will benefit from treatment. Despite emerging knowledge of over 40 years, the results of patient selection and shunt insertion have not improved significantly.

Since the historic paper by Hakim and Adams in 1965, a great deal of further research has accumulated. Patients are currently classified into those whose NPH has a known cause and an idiopathic group (INPH). Table I highlights the key research findings so far.

**Patient Selection:** No single test is predictive to determine the shunt responders. Over the years several combinations of tests have been used to predict those who will respond to a shunt operation. Surgery is believed to benefit 50–70% of patients where there is a known cause, and 30–50% where the cause is idiopathic if identified correctly. It is equally important to identify

**Table I**

1965	First paper to mention about clinical symptoms and signs of NPH	Adams et al.
1960's	Isotope Scintigraphy	–
1970	Simple Constant –infusion manometric test for measurement of CSF absorption	Katzman and Hassey
1974	Characters of dementia	Albert et al.
1977	CT scan and ICP monitoring in hydrocephalus with dementia	Croccard et al.
1982	CSF fluid tap test	Wikkelso et al.
1982	Conductance to outflow of CSF in normal pressure hydrocephalus	Borgesen et al.
1986	CSF drainage test (120–500 ml for 5 days)	Dilauro
1986	Improvement in neuropsychological tests was observed in patients with a Cout of <0.05 l	Thomsen et al.
1987	Cerebral blood flow in NPH	Mamo et al.
1988	Phosphorus MR spectra in NPH – reversible periventricular acidosis	Arnold et al.
1988	External ventricular drain of 300 ml CSF for 5 days	Haan et al.
1989	Third ventriculostomy in the treatment of NPH (microsurgical)	Magnaes et al.
1993	Resistance to CSF outflow in prediction of outcome after shunting	Delwel et al.
1993	High resolution SPECT in NPH before and after shunting	Waldemar et al.
1996	MR CSF flow studies in NPH	Bradley et al.
1999	CANTAB – Neuropsychological application in NPH	Iddon et al.

**Table 2**

CT	Enlarged ventricles; periventricular hypodensities; flattened cortical sulci; small or absent perihippocampal fissure
MRI	All of the above; especially small or absent perihippocampal fissure
Cerebral blood flow	Reduction in frontal lobe BF; global reduction in cerebral metabolism, periventricular decreased BF, basal ganglia and thalamus reduced BF (Transcranial Doppler, SPECT)
Isotope Cisternography/MRI	Isotope in the ventricles remains static > 72 hours with no distribution over the convexities
Removal of CSF	External lumbar drain, lumbar puncture, external ventricular drain
ICP monitoring	Increase in number, peak and pulse pressure beta waves
CSF markers	Sr Alpha-1 antichymotripsin, Tau proteins, Sulfatides, neurofilament protein & GFAP, Myelin based protein, TNF-alpha, Lipocalin-type PG-D synthase, galanin

patients unlikely to benefit. Shunting, particularly in elderly patients, is associated with a significant incidence of both acute and cumulative longer-term complication. Only a few papers report the extended follow-up of patients and the value of the predicting factors in the long term. A guide to some of the tests and predictive feature identified in the literature is summarised in Table 2.

**Conclusion:** Few studies have examined the long-term prognosis for those with treated and untreated NPH. Indeed, the recent Cochrane review (2002) indicated that shunt insertion was ineffective in treating NPH but this may be due to inappropriate comparison groups and lack of class I evidence. Tests revolving around CSF lumbar puncture, lumbar tap and drainage have been the main stay of assessing likelihood to respond to treatment. But, how reliable is this in predicting outcome? Since the disease is complex and there may not be a gold standard test to predict shunt response, future efforts should be directed towards better identification of the pathogenesis of idiopathic NPH.

Many CSF factors have been identify that can diagnose the disease and predict outcome. MR CSF flow studies can predict shunt responders and PET scans have been used to detect periventricular blood flow improvement post shunt. Non-invasive methods of investigation and prediction of outcome is being increasingly recognised. Treatment has been challenged with ventriculostomy. Thus, it is clear that further work needs to be conducted to ascertain the best way of diagnosing patients likely to benefit from surgery.

**S62**  
**Learning efficiency in children with myelomeningocele and shunted hydrocephalus**

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S62

**Background:** Limited evidence exists regarding the efficiency with which children with MM/SH are able to learn information.

This report describes initial data related to components of learning in children with MM/SH.

**Materials and Methods**

13 children with MM/SH and 8 age-matched non-affected controls (age range: 7–16 years) with average intelligence, and monolingual English-speaking backgrounds, participated. Exclusionary criteria for the MM/SH group were: prior history of shunt infection, history of seizure or shunt malfunction within the previous three months, prior diagnoses of attention disorders and/or clinical depression. Verbal memory tasks (learning word and word-pair lists) and nonverbal tasks (recalling positions of dots) were administered to each child. A Learning Index was computed based on performance across three learning trials of the word-pair and dot location tests. Children were also presented lists of 16 words with 8 exemplars each of two distinct semantic categories (e.g. fruits, animals), and told to make as high a score as possible by learning the words. Value of the words was designated by category membership (e.g. animals = 1; fruits = 10). Performance across three trials was used to determine a Selective Learning score.

**Results:** Children in our study did worse than their age-matched controls on both learning tasks ( $P < 0.05$ ). When asked what strategy was used in the selective learning tasks, 10 of the 13 MM/SH children (76%) said they tried to remember all words. In contrast, all except for one control said they tried to remember the higher point words — the more efficient strategy.

**Conclusions:** Success in school is largely dependent on the ability to selectively recall important facts and ignore less important information. Children with MM/SH in our study were unable to select and remember important information, and did not have a workable strategy. Preliminary findings are consistent with our previous clinical and research findings wherein children with MM/SH focus on many extraneous details, but are unable to remember the main gist of a story/event. Poor acquisition of new material (learning) suggests that children with MM/SH need more trials to learn than their non-affected peers and bears further exploration.

**S63**  
**Determinants of functional independence and quality of life in children with spina bifida**

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Cerebrospinal Fluid Research 2004, 1(Suppl 1):S63

**Objectives:** To investigate determinants of functional independence and study which functional abilities were determinants for 'health related quality of life' in children with myelomeningocele.

**Design:** Cross-sectional study by means of clinical assessment, 'disability' measurement, and questionnaires.

**Setting:** Outpatient spina bifida clinic at a university hospital.

**Participants:** 122 children with myelomeningocele. Mean age 7.9; range 1–18 years.

**Main Outcome Measures:** Functional independence as measured by the 'Pediatric Evaluation of Disability Inventory' (PEDI), and 'Health Related Quality of Life Questionnaire' (HRQL). Uni- and multivariate logistic regression models were used to investigate factors that were determinants for these outcomes. Results were expressed as odds ratios and 95% confidence intervals (CI).

**Results:** Lesion level below L3 (OR: 0.4, CI: 0.1–1.0), mental status of IQ > 80 (OR: 4.2, CI: 1.2–14.9), having no contractures in lower extremities (OR: 3.4, CI: 1.3–8.8), and having normal strength of knee extensor muscles (OR: 4.1, CI: 1.4–11.5), were most strongly associated with independence in self-care. Mental status (OR: 16.1, CI: 2.8–93.9), having no contractures in lower extremities (OR 1.5, CI: 1.4–5.3), and normal strength in knee extensors (OR: 11.0, CI: 1.3–97.0), were the most important determinants for independence in mobility. Concerning functional abilities, being independent with regard to mobility was the most important determinant for HRQL (OR: 5.3, CI: 1.6–17.4).

**Conclusions:** In children with myelomeningocele, good muscle strength, mental ability and being independent in mobility, appeared to be much more important for daily life function and quality of life than other medical indicators of the disorder. This information is of clinical significance in planning a comprehensive and realistic rehabilitation program.

**POSTERS NOT DISCUSSED**

**S64**

**Experiences with arachnoid cysts in children**

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**Background:** Arachnoid cysts are relatively rare. True cysts are congenital. Secondary cysts may result from postinflammatory accumulation of CSF in the subarachnoid space. This examination focussed exclusively on primary cysts. There is a controversy regarding the role and the type of surgery indicated in its treatment. The distribution, clinical features and treatment modalities in different types of arachnoid cysts in our patients are analysed in this study.

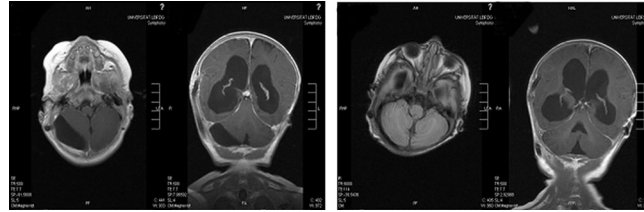
**Material:** Nineteen children were treated ranging from 1 month to 10 years of age. The follow-up-period was 11 years, ranging from 3 months to 19 years. Cyst locations were temporal fossa (n = 7), convexity (n = 4), sellar region (n = 1) and infratentorial (n = 7). Conservative management has been carried out for four children who did not demonstrate any signs of increased ICP or focal neurological impairment. Fifteen patients underwent surgery (Table 1).

**Results:** With exception of three incidental findings, all cases became symptomatic. Due to cyst enlargement with pressure signs or bleeding, most cases in our series showed symptoms such as headache, seizure, hygroma or endocrinologic disturbances.

**Table 1**

	Temporo fossa	Convexity	Sellar region	Infra-tentorial
Neuroendoscopic fenestration		1		
Cystoperitoneal shunting	3	2		3
Open fenestration		1		1
Ventriculoperitoneal shunting	1		1	2
Conservative management	3			1

**Figure 1**



Computer tomography scan of an infratentorial posterior fossa arachnoid cyst with obstructive hydrocephalus. Although successful, open fenestration the rather progressive hydrocephalus required shunting.

Long-time pressure effects from arachnoid cysts lead to secondary pathological changes. The main consequence of infratentorial cysts was an obstructive hydrocephalus. Children with cysts in the posterior fossa were younger than 1 year of age at diagnosis. Six out of seven children with infratentorial cysts developed a progressive hydrocephalus. In contrast, children with supratentorial cysts were significant older (mean 4 years 3 months) at the time of diagnosis. Surgery was urgently indicated because of the development of subdural haematoma or hygroma after minor head trauma for two children with temporal cysts. Shunting device implantation in the cysts was successful for cerebral convexity cysts in two and for temporal cysts in three children. One open and one endoscopic fenestration of convexity cysts required additional shunt insertion caused by clinical symptoms of increased ICP and cyst enlargement, respectively (Fig. 1)

Three cystoperitoneal shuntings and one open fenestration for infratentorial cysts required subsequent ventriculoperitoneal shunt placement in three cases. Epilepsy an seizure disorders without obvious intracranial pressure signs occurred in four children. The incidence of seizure disorders was equivalent to the incidence in isolated hydrocephalus patients. Electroencephalographic findings did not correspond to the site of the cysts in the most cases. Attention-deficit-hyperactivity-disorders were detectable in one child with a prepontine cyst and one child with a cyst in the sellar region. After treatment endocrine dysfunction and neurological deficits did not disappeared completely.

**Conclusion:** Absolute indications for surgery are the presence of progressive hydrocephalus or intracranial hypertension. Neuro-endoscopic fenestration of ventricle-related cysts with or without internal shunting should be tried. In peripheral cysts the insertion of a cystoperitoneal shunt is proved as a save method.

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